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ORIGINAL ARTICLE

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Professional communication of doctors in wartime: A trauma-informed approach

Natalia V. Stuchynska[1], Nina P. Lytvynenko[1], Natalia M. Savelyuk[2], Pavlo V. Mykytenko[1], Yaroslava Ye. Kalba[2], Olha S. Miroshnichenko[1], Svitlana A. Shabatska[1]

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ABSTRACT

Aim: To identify discourse markers of a trauma-informed communicative model in professional medical dialogue.

Materials and Methods: The empirical basis consisted of a collection of «doctor–patient» dialogues recorded between 2022 and 2025. Two samples of doctor speech were formed: in dialogues with patients being internally displaced persons (IDPs) (n=36) and with patients residing in rural regions (n=48). Content analysis was performed using the Textanz software. The study employed a set of general scientific and linguistic methods, including bibliosemantic analysis, content analysis, psychosomatic and comparative analyses, as well as discourse analysis of communicative strategies and descriptive statistics.

Results: A total of 7770 statistically significant lexical units were recorded. In interactions with internally displaced persons, doctors demonstrated a higher frequency of the pronoun «you» (49.11% vs. 44.42%) and a lower proportion of the pronoun «we» (5.20%). The category «Communication and its components» dominated among verbs (33.63% vs. 30.48%). In interactions with patients from rural regions, a higher frequency of the pronoun «we» and a more even distribution of verb categories were observed, indicating a partnership model of communication; in working with IDPs, a patient-centered approach with an emphasis on individualization predominates, whereas in interactions with patients from rural regions, a shared decision-making model prevails.

Conclusions: Medical communication under martial law generates a spectrum of trauma-sensitive professional discourses. The identified discourse markers can be integrated into medical university curricula and clinical communication protocols.

KEY WORDS: professional communication, martial law, doctors

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INTRODUCTION

Since February 24, 2022, Ukraine's healthcare system has been operating under an unprecedented burden. The number of patients with acute stress reactions, post-traumatic stress disorder, and chronic psychotraumatization has risen sharply. According to the World Health Organization, more than 14.6 million Ukrainians required humanitarian assistance as of the end of 2024, and nearly 5 million people became internally displaced [1, 2]. The "doctor–patient" dialogue under these conditions becomes a psychologically burdened interaction that can either facilitate recovery or cause additional harm through re-traumatization [3, 4].

The concept of trauma-informed care (TIC) was systematized by the US Substance Abuse and Mental Health Services Administration (SAMHSA). The approach is based on six principles: safety; trust and transparency; mutual support; collaboration and partnership; empowerment, voice, and choice; and cultural, historical, and gender sensitivity [5]. The linguistic and discursive dimension of TIC remains understudied, particularly in zones of armed conflict [6, 7].

J. Pennebaker [8] found that trauma survivors exhibit characteristic changes in pronoun usage and frequency of emotional words. Y. Tausczik and J. Pennebaker [9] demonstrated that computerized text analysis can reliably identify psychological states from linguistic patterns. A. Asanova and O. Khaustova [10] identified typical challenging situations in "doctor–patient" interactions, and O. Chaban and O. Khaustova [11] described the medical and psychological consequences of wartime distress.

Our previous studies focused on the psycholinguistic features of doctors' professional communication [12, 13] and the gender characteristics of medical communication [14]. The present study shifts the focus to traumatic aspects.

AIM

The aim of the study is to identify discourse markers of a trauma-informed communicative model in professional medical dialogue.

MATERIALS AND METHODS

The empirical basis consisted of a collection of «doctor – patient» dialogues gathered between 2022 and 2025 during official consultations in compliance with ethical, bioethical, and legal standards, and with the voluntary informed consent of all participants [12–14]. The dialogues were typologized according to the category of the patient's traumatic experience. Two samples of doctor speech were formed:

- Sample 1 – dialogues with IDP patients (n=36; individuals from Donetsk, Luhansk, Zaporizhzhia, and Kherson oblasts);
- Sample 2 – dialogues with civilian patients (n=48; residents of Kyiv, Ternopil, and Vinnytsia oblasts; data from [12]).

The transcribed texts were subjected to content analysis using the Textanz software. Words with a frequency of 3 or more were included in the analysis. For each sample, the frequency of parts of speech, dominant categories, and discourse markers was calculated according to the adapted SAMHSA model [5].

FRAMEWORK

The research was performed within the framework of a research topic «Professionally oriented language practices in the education of students of medical education» (2023–2026; № state registration 0123U105310).

RESULTS

A total of 7770 statistically significant lexical units were recorded: 2733 in Sample 1 (IDPs) and 5037 in Sample 2 (civilians). The qualitative and quantitative results for the first sample are summarized in Table 1.

The most frequent – comprising more than one-third of all recorded statistically significant words among the main parts of speech in professional medical doctor–patient communication – are pronouns (total count: 961, accounting for 35.16%). Within this part of speech, the category "You" clearly dominates (almost half – 49.11%). This result is expected given the doctor's professional role position in the context of the trauma-informed approach, which reflects the principle of cooperation and participation.

The category "I" occurs approximately three times less frequently (142 lexemes – 14.78%), demonstrating the doctor's patient-centered focus. At the same time, the low proportion of the "We" category (50 – 5.20%) may be an indicator of insufficient application of the "peer-to-peer" principle. It is advisable to recommend that doctors use the lexemes "we" and "our" more frequently to reinforce the effect of team-based interaction.

The second most frequent part of speech was the noun (741 – 27.11%), with the dominant category "Diseases and Their Symptoms" (181 – 24.43%). Among lexemes: "problems, complaints" (78), "pain" (23), "stress, tension" (16). The absence of jargon is positive, reflecting adherence to the principles of transparency and the peer-to-peer model. Addressing patients by name was recorded in only 24 of 36 dialogues (66.67%). The "health" category proved to be one of the least frequent (11 – 1.48%).

The third was the verb (559 – 20.45%), with the dominant category "Communication and its components" (211 – 33.63%). Doctors invite patients to "speak, recount" (66 lexemes), confirm what they heard with "I understand, understood" (41), and use "let's" for encouragement. The proportion of verbs in "Diseases and Their Symptoms" (104 – 18.60%) exceeds "Treatment and Its Options" (79 – 14.13%), indicating the need to shift the emphasis toward positive prognoses.

The fourth was the adverb (405 – 14.82%), with the dominant category "Temporality" (133 – 32.84%): "now" (44), "after, then" (39), "today" (10). The category "Uncertainty, imprecision" accounts for 16.54%, which may both reflect adaptation to the patients' situation and become a factor of "stagnation" in the traumatic situation.

The adjective was less represented (55 – 2.01%), with a predominance of "neutral" forms (37 – 67.27%). Adjectives with positive connotations total only 7 (12.73%). The numeral was the least frequent (12 – 0.45%). This fact can be explained in various ways. First, in conditions of uncertainty, reality is difficult to quantify. Second, the majority of the recorded dialogues in the "doctor–patient" system reflect an initial consultation, when it is still difficult to operate with specific figures.

In Table 2, we present examples of those categories and lexemes that appear in doctors' speech during their interactions with IDP patients, but currently in small numbers. This reflects the potential – the nearest "zones of development" for medical personnel in terms of further aligning the content of professional medical communication with the principles of the trauma-informed approach.

Thus, Ukrainian doctors generally take into account the core principles of the trauma-informed approach in their professional communication with IDPs, including transparency of content and the peer-to-peer model. The areas of potential growth are associated with increasing the proportion of communal pronouns "we", personalized nouns, verbs with positive prognostic value, adverbs of certainty, and adjectives with positive connotations.

Table 1. Dominant categories and lexemes of the main parts of speech. (Sample 1 – IDPs; total number of statistically significant words – 2733)

Part of Speech	Doctors' Sample		
	Total count / %	Primary Category (abs. / rel. count)	Primary Lexemes
Pronoun	961 / 35.16%	«You» (473 / 49.11%)	«You», «To you»
Noun	741 (27.11%)	«Diseases and Their Symptoms» (181 / 24.43%)	«problems», «complaints», «diseases»
Verb	559 (20.45%)	«Communication and its components» (188 / 33.63%)	«speak, recount», «understand»
Adverb	405 (14.82%)	«Temporality» (133 / 32.84%)	«now», «after», «then»
Adjective	55 (2.01%)	«Neutral» (37 / 67.27%)	«possible», «general»
Numeral	12 (0.45%)	–	«time», «three», «first», «several»

Source: compiled by the authors of this study

Table 2. «Zones of potential development» of professional communication in the system. «doctor – IDP patient» in the context of the trauma-informed approach

Part of Speech	Categories	Lexemes
Pronoun	«We»	«we», «our»
Noun	«Examination, Treatment, and Outcomes»	«effect», «result»
	«Communication and its components»	«question»
	«Health»	«health»
Verb	«Communication and its components»	«thank you»
	«Treatment and its options»	«to help»
Adverb	«Certainty, precision»	«indeed»
	«Familiarity and generalization»	«usually»
Adjective	«Positive»	«healthy», «good»

Source: compiled by the authors of this study

Table 3. Dominant categories and lexemes of the main parts of speech in doctors'. Speech (Sample 2 – civilians; total number of statistically significant words – 5037)

Part of Speech	Total count / %	Primary Category (abs. / rel. count)	Primary Lexemes
Pronoun	1,621 / 32.18%	«You» (720 / 44.42%)	«You», «Your»
Noun	1,272 / 25.25%	Diseases and Their Symptoms (253 / 19.89%)	«problems», «pain», «diseases»
Verb	1,099 / 21.82%	Communication and its components (335 / 30.48%)	«speak», «think», «understand»
Adverb	834 / 16.56%	Temporality (249 / 29.86%)	«after», «then», «now», «often»
Adjective	174 / 3.45%	Neutral (99 / 56.90%)	«that», «possible», «general»
Numeral	37 / 0.73%	–	«time», «several», «one», «first»

Source: compiled by the authors based on [12]

We now focus on the analysis of the characteristics of doctors' speech in communication with patients residing in relatively safe regions. Such analysis will allow us to compare the identified features of the trauma-informed approach with discursive practices in a less pronounced traumatic context.

Doctors' speech in dialogues with civilian patients (Sample 2): data obtained from our previous study [12]. Results are presented in Table 3.

In Sample 2, pronouns also rank first (32.18%), but the proportion of «You» is lower (44.42% vs. 49.11%), indicating a more balanced model. The noun category «Diseases and Their Symptoms» has a lower proportion (19.89% vs. 24.43%), while «Examination, Treatment, and Outcomes» ranks second (213 – 16.75%), reflecting a greater emphasis on diagnostics. Among verbs, the «Communication» category has a lower proportion (30.48% vs. 33.63%). Adjectives are more broadly represented (3.45% vs. 2.01%) with a lower proportion of «neutral» forms (56.90% vs. 67.27%), indicating greater emotional diversity.

The analysis of doctors' speech in Sample 2 (patients from rear regions) reveals a communicative model close to Sample 1 but more balanced. The lower proportion of the «You» form (44.42% vs. 49.11%) indicates that doctors concentrate the discourse on the patient's person less intensively, distributing attention between

procedures and clinical aspects. This is evidently related to the fact that such patients do not have as acute a sense of trauma, which reduces the need to verbally «hold» them at the center of attention.

The shift from the category «Diseases and Their Symptoms» (19.89% vs. 24.43%) to «Examination, Treatment, and Outcomes» (16.75%) points to a greater emphasis on the diagnostic-therapeutic domain, whereas in Sample 1 the higher concentration of pain-related lexemes reflects a longer presence in the patient's emotionally loaded field. The lower proportion of communication verbs (30.48% vs. 33.63%) demonstrates that metacommunicative efforts (providing feedback, checking comprehension accuracy) are less pronounced in a safer communicative environment.

The most telling difference lies in adjectives: a higher overall proportion (3.45% vs. 2.01%) combined with a lower percentage of neutral forms (56.90% vs. 67.27%) indicates greater emotional differentiation of the vocabulary. In the frontline context, doctors probably resort to emotional restraint as a defense mechanism, whereas in rear regions they have more communicative space for evaluation and emotional responsiveness.

DISCUSSION

The present study continues our previous work [12–14] with a shift in analytical focus from gender to the type of traumatic experience of the patient. The results demonstrate that medical communication under martial law generates a spectrum of trauma-sensitive communicative models determined by the nature of the traumatic impact.

In interactions with IDP patients, doctors demonstrate an enhanced "You"-orientation (49.11%), a higher frequency of communicative verbs (33.63%), and encouraging constructions. From the perspective of the trauma-informed approach, this pattern corresponds to the phenomenon of testimony described by J. Herman [15] as a fundamental mechanism of recovery after political violence. B. Van der Kolk [16] also emphasized the importance of verbalizing traumatic experience. Our data provide empirical linguistic confirmation of this phenomenon in the context of a wartime medical consultation.

In interactions with civilian patients, doctors display a more balanced discourse: a higher proportion of adjectives (3.45% vs. 2.01%), a lower proportion of neutral forms among them (56.90% vs. 67.27%), and greater emphasis on diagnostics and treatment. This is consistent with a lesser need for narrative stimulation and a more partnership-oriented model of communication.

The identified discourse markers (empathy markers, open-ended questions, avoidance of directive pressure) can serve as indicators for evaluating the trauma sensitivity of clinical communication [5, 6].

Doctors intuitively adjust their communicative strategies depending on the patient category, yet this adaptation is not systematic. Considerable variability indicates the need to develop trauma-informed communication skills already at the stage of professional training. Thus, the methodology of applying the trauma-informed approach must extend beyond current clinical practice into the space of medical education. Medical university students must acquire the competence to recognize linguistic markers of trauma in patients' speech and to respond with appropriate communicative strategies [7, 19, 20].

The effectiveness of such training directly depends on incorporating contemporary approaches to the digitalization of medicine [22–24], the potential of elective disciplines [23], and distance learning formats [25, 26]. In practice, this involves integrating trauma-informed communication modules into professional language courses, introducing selective educational components oriented toward the digitalization of medical communication and the use of artificial intelligence, as well as simulation-based training using authentic dialogues and specialized workshops [19–21].

CONCLUSIONS

Based on a comparative discourse analysis of doctors' speech in dialogues with patients who are internally displaced persons and patients from rear regions, the following was established:

1. Medical communication under martial law is characterized by the adaptation of the doctor's professional discourse depending on the type of traumatic experience of the patient.
2. In interactions with internally displaced persons, doctors demonstrate patient-centered discourse with an enhanced «You»-orientation (49.11% vs. 44.42%), a higher frequency of communicative verbs (33.63% vs. 30.48%), and encouragement constructions.
3. In communication with patients from rear regions, a higher frequency of the pronoun «we» and a more even distribution of verb categories with greater emphasis on diagnostics is observed, indicating a partnership model of communication.
4. Doctors demonstrate adaptive trauma-informed communicative behavior, but its unsystematic nature confirms the need for targeted professional training.
5. The identified discourse markers and communicative strategies should be integrated into medical university curricula, trauma-informed communication training programs, and clinical protocols to reduce the risk of re-traumatization.

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CONFLICT OF INTEREST
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ORIGINAL ARTICLE

CONTENTS

Venous thromboembolism in urothelial bladder cancer - scope of the problem and patients' perspectives: VTE-UBC

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ABSTRACT

Aim: This study investigates the scope of VTE in people with UBC in the UK and explores their understanding of VTE from their experience of having cancer and anti-cancer treatments, alongside the perspectives of healthcare professionals (HCPs).

Materials and Methods: A sequential mixed-methods study was applied: Phase I - quantitative, exploring the incidence and risk factors for VTE in UBC, by cohort of UK Hospital Episodes Statistics (HES) data and a retrospective case-control analysis using data from two UK NHS trusts. Phase II - semi-structured interviews among patients with UBC and HCPs, utilising thematic analysis.

Results: VTE incidence in people with UBC was around 6.0 per 1000 patients, determined from UK national datasets. Cystectomy and stage IV disease significantly (OR 2.88, 95% CI 1.63-5.07, P<0.001; and OR 4.41, 95% CI 1.85-10.50, P=0.002 respectively), whilst chemotherapy showed borderline statistical significance for risk of VTE (OR 2.56, 95% CI 1.03-6.32, P=0.041). Three major themes emerged from the interviews: 'all about the cancer' (thrombosis risk was not a priority for patients with UBC), 'a labyrinthine process' (information about VTE was bewildering and compartmentalised) and 'improving the poor deal' (suggestions offered to improve communication around VTE were identified).

Conclusions: VTE is an important clinical problem in patients with UBC. The analysis of this study confirms that the treatment type and metastatic disease are the main risks factors associated with increased VTE risk, HCPs can build on the findings of this study to progress individualised care through multidisciplinary, and patient-centered VTE prevention plans during inpatient encounters.

KEY WORDS: VTE, bladder cancer, cancer-associated thrombosis

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INTRODUCTION

Urothelial bladder cancer (UBC) is one of several cancer types where people are at high risk for venous thromboembolism (VTE). According to Sandhu et al. (2010), the risk of VTE among UBC patients is highest within the first six months of diagnosis [1]. Treatment for UBC may include surgery (most commonly cystectomy or transurethral resection of bladder tumour (TURBT)), chemotherapy, or a combination, each of which carry their own associated risk of VTE. In people with UBC who undergo cystectomy, rates of VTE are estimated to be between 3% and 19.1% [2, 3]. The cumulative incidence of VTE continues to rise long after cystectomy, but the highest VTE incidence rates occur 20 days after surgery [4]. Medical comorbidities may also increase the risk of VTE in UBC patients.

In England and Wales, urologists and medical oncologists are expected to follow the National Institute for Health and Care Excellence (NICE) guidelines when embarking on formulation of a treatment regimen. International studies mentioned that cystectomy and systemic chemotherapy are associated with raised VTE risk, analysis of UK data quantifying these risks in patients with UBC were limited. The systemic review in this study summarised evidences on association between VTE risks and UBC, but this could not provide UK data on incidence according to receiving systemic chemotherapy or metastatic stage of UBC. Thus, the current study was planned to find this gap using UK national and local NHS datasets.

As such, treating UBC patients might vary in relation to other countries. In the UK, there limited specific data

assessing VTE incidence according to the type of treatment and the stage of the UBC. Although published international studies and our own recent systematic review evidence found increased VTE risk after cystectomy and receiving systemic chemotherapy, robust primary UK data mainly examining receiving chemotherapy and metastatic disease in UBC have been insufficient. Therefore, the present study analyses UK national data and NHS local data to specify this evidence gap using UK national and local NHS datasets [5].

By providing information about signs, symptoms, risk factors, and thromboprophylaxis measures to people with UBC, HCPs strive to reduce overall risk and associated morbidity of VTE. A lack of understanding may mean that patients do not present early enough, which may lead to further complications [6]. Therefore, it is essential to listen to people with UBC, explore their experience of cancer and seek their understanding of VTE.

AIM

The VTE-UBC study objectives were thus as follows; (1) establish the incidence, risk factors and associations of VTE in bladder cancer patients using UK data; and (2) explore patients' understanding of VTE, including their understanding of risk, the content of information received and gaps in communication, alongside HCPs' perspectives on VTE and UBC.

This study is based on the doctoral thesis of Dr. Omar Riyadh Abdullah, titled "Venous thromboembolism in bladder cancer patients: a scope of problem and patients' perspectives", submitted to the University of Warwick, United Kingdom, in 2021 [7].

MATERIALS AND METHODS

The VTE-UBC study, consists of two Phases, making up a 'mixed methods' study. All quantitative data used in this study were obtained from UK primary records. Phase I embraces a quantitative paradigm and Phase II, qualitative.

PHASE I

STUDY DESIGN AND DATA SOURCES

The purpose of the quantitative phase was to investigate VTE incidence and risk factors in patients with UBC in the UK. Two distinct sets of data were collected.

A quantitative retrospective cohort analysis was carried out to assess VTE incidence in UBC patient groups. Data from the UK's 'Hospital Episode Statistics' (HES) were obtained for all people with UBC, who had undergone systemic chemotherapy treatment and/or radical cystectomy between April 2013 and April 2018 to identify those re-attending with VTE within 12 months in NHS trusts throughout England.

Following this, a retrospective case-control (1:2) method was applied to the local data (large teaching hospitals where authors OA and/or AY had worked) to assess difference in the rates of VTE with exposure to a defined risk factor. These data were collected from two independent NHS trusts; NHS University Hospitals Coventry and Warwickshire (UHCW) and Queen Elizabeth Hospital Birmingham (QEHB), from the previous 10 and 7 years respectively. Patients were included if they were adults (18 years old and over) with histologically or clinically confirmed diagnosis of bladder cancer with or without VTE. They were excluded if they had a history of VTE prior to UBC diagnosis.

Risk factors assessed were as follows; VTE incidence rate in UBC patients treated with or without systemic chemotherapy within 12 months of starting to receive chemotherapy, VTE incidence in UBC patients treated with or without cystectomy within 12 months post-surgery, and any association between VTE events. Data was analysed using SPSS.

DATA ANALYSIS

For HES data, an estimation of the incidence rate and trend of VTE in patients with UBC was conducted over 5 years, between 2013 and 2018.

For local data, the VTE incidences of patients with UBC were estimated from the cohort data received from informatics offices at QEHB and UHCW. After this, case control study design was used to calculate the odds ratio to determine whether exposure to a specific confounder is a risk factor of VTE:

- Gender (Male, Female)
- Urothelial carcinoma (Yes, No)
- Grade (1,2,3)
- Has had chemotherapy (Yes, No)
- Has had surgery, cystectomy (Yes, No)
- Stage (non-muscle invasive, muscle invasive, metastatic)
- Has had chemotherapy plus cystectomy (Yes, No)
- Presence of comorbidities (Yes, No)

Multivariate linear and logistic regression were used to assess the independent associations between baseline VTE complications and possiblerisk factors. Comorbidities comprising hypertension, diabetes mellitus, heart failure, ischemic heart disease, chronic obstructive pulmonary disease, pneumonia and second type of cancer, were identified as confounders during the logistic regression analysis.

PHASE II

STUDY DESIGN

Phase II of VTE-UBC research a qualitative research methodology was used. Individual semi-structured interviews with people with UBC and HCPs. Several key questions were asked, using a guide (Appendix 1).

The NHS Trusts - UHCW and QEHB - were chosen as research sites for conducting phase II. Patients and HCPs were recruited by direct contact with the Research and Development offices (R&D) at QEHB and UHCW.

Purposive sampling was used to recruit participants in July 2019 at UHCW and in October 2019 at QEHB and was completed on 1 March 2020 at both hospitals. People with UBC at high VTE risk were chosen to be recruited for the study.

Eligible patients were recruited via a clinical nurse specialist (CNS), or via approach during their visit to the outpatient clinic. HCPs who had clinical responsibility or delivered care to people with UBC were recruited via email invitation. This included surgeons, medical oncologists and nurses.

DATA ANALYSIS

Audio-recordings were nonymized and transcribed by an expert at Warwick Medical School. Thematic analysis was then undertaken, in which the researcher compared within and between data from the interviews to gain insights into participants' views and understandings of the risk of thrombosis.

ETHICAL APPROVAL

This article has ethical approval University of Warwick. Every process followed the international research ethics protocols and had sufficiently strong measures to ensure confidentiality and privacy of data of the participants.

RESULTS

PHASE I

From HES data in England, there were 1076 patients with UBC and new VTE recorded in between 2013 and 2018. In total 87% of these UBC patients were above 60 years old, and 75% were male.

Within this data set, the annual VTE incidence in UBC patients was found to be 6 in every 1000 patients (0.6%), while the VTE incidences in patients who had undergone cystectomy and chemotherapy were 14 per 1000 (1.4%) and 29 per 1000 (2.9%), respectively.

Across the two local NHS trusts, 2892 patients with UBC were recorded in total between 2007 – 2018 in UHCW and 2011 – 2018 in QEHB. Across both trusts, the annual VTE incidence in patients with UBC was around 6.1 per 1000 (0.61%). This increased to 56 per 1000 (5.6%) in people with UBC treated with radical cystectomy, and 76 per 1000 (7.6%) in those treated with chemotherapy. In patients who received both chemotherapy and radical cystectomy, the incidence was 88 per 1000 (8.8%). As in the HES data, most patients were aged 60 years or older at the time of diagnosis and the majority (73.7%) were male.

Across both NHS trusts, 176 patients with UBC and VTE were recognised and matched with 352 control subjects to perform unadjusted and adjusted logistic regression analysis. Treatment type, disease stage and the presence of a second cancer (a second cancer is a new cancer that's unrelated to previous bladder cancer) have significant association with VTE in people with UBC. This regression model demonstrated that there was a significant association of treatment and stage with VTE (P<0.001) (Table 1).

In the combined trust analysis, the odds ratio of VTE for patients with UBC who had a cystectomy or chemotherapy were significantly higher in patients who had a trans urethral resection of bladder tumour (TURBT), with statistically significant differences. Patients who had cystectomy (OR = 2.64, 95% CI 1.49-4.68; P=0.001). Chemotherapy was associated with a borderline increase in VTE risk (OR = 2.40, 95% CI 0.96-5.99; P = 0.061). For patients who had both chemotherapy and cystectomy the odds ratio was about 7 times greater than for those patients who had TURBT, the difference being statistically significant: OR = 7.45, 95% CI 1.86-10.62; P=0.001).

A further logistic regression model explored the association of VTE with all comorbidities (except second type of cancer), treatments and stage (Figure 2). Five types of comorbidities were examined against their association with VTE. It was found that only 'second type of cancer' had a significant risk of VTE (OR = 0.23, 95% CI 0.10-0.53; P=0.001). Other co-morbidities, as well as chemotherapy, had no significant risk of VTE with (OR = 2.40, CI 0.96-5.99; P = 0.061) (Table 2).

PHASE II

PARTICIPANT CHARACTERISTICS

PATIENT GROUP

Patients with muscle-invasive UBC who had undergone a cystectomy and/or received systemic chemotherapy (n=18) consented to participate in this qualitative study.

Table 1. Association of VTE in patients with UBC with treatment, stage, co-morbidities, gender, histology, and grade of UBC at QEHB

			Unadjusted		* Adjusted	
Variables	**QEHB (2011-2018)**		**OR (95%CI)**	**P value**	**OR (95%CI)**	**P valuev**
	Cases (n=55)	**Controls (n=110)**				
Treatment						
TURBT	16 (29%)	79 (71.8%)				
Cyst.	20 (36.3%)	23 (20.9%)	4.29 (1.92-9.60)	0.012	4.61 (1.12-19.00)	0.034
Chemo.	4 (7.2%)	6 (5.4%)	9.87 (1.66-58.58)	≤0.001	4.81 (0.39-59.20)	0.220
Chemo & Cyst.	15 (27.2%)	6 (5.4%)	12.34(4.15-36.66)	≤0.001	11.89(1.91-73.84)	0.008
Stage						
NMIBC	18 (32.7%)	81 (73.6%)				
MIBC	22 (40.0%)	29 (26.3%)	3.66 (1.71-7.84)	0.001	0.70 (0.15-3.13)	0.643
Metastatic	15 (27.2%)	2 (1.8%)	33.75(7.08-160.82)	≤0.001	8.54 (1.32-55.22)	0.024
Co-morbidities	30 (54.5%)	40 (36.6%)	0.51(0.26-0.98)	0.046	0.76 (0.34-1.67)	0.496
Gender						
Male	42 (76.3%)	82 (74.5%)	0.90 (0.42-1.93)	0.799		
Female	13 (23.6%)	28 (25.4%)				
Histology						
Urothelial	52 (94.5%)	94 (85.4%)	0.33 (0.09-1.21)	0.097		
Non-urothelial	3 (5.4%)	17 (14.5%)				
Grade						
1	2 (3.6%)	6 (5.4%)				
2	2 (3.6%)	7 (6.3%)	1.36 (0.64-2.90)	0.422		
3	51 (92.7%)	97 (88.1%)				

Notes: OR – odds ratio, Cyst.– Cystectomy, Chemo.– Chemotherapy, Uro.-Urothelial TURBT – Trans Urethral Resection of Bladder Tumour, MIBC – Muscle InvasiveBladder Cancer, MI – Muscle Invasive, NMIBC – Non-Muscle Invasive Bladder Cancer, MI – Muscle Invasive

*Adjusted odds ratios were calculated from a multivariable logistic regression modelthat included treatments received (cystectomy, chemotherapy, cystectomy with chemotherapy), stage at diagnosis (expressed in non-muscle-invasive, muscle- invasive, and metastatic), comorbidities (have comorbidities vs no comorbidities).

Source: Compiled by the authors of this study

HEALTHCARE PROFESSIONALS' GROUP

Thirteen HCPs were recruited for interviews; four clinical nurse specialists, five urologists and four clinical oncologists.

Codes, categories, subthemes and major themes were elicited from the data (Figs 1 and 2). Three major themes, namely 'All about the cancer', 'A labyrinthine in process', and 'Improving the poor deal' describe the communication around VTE and patients' understanding of VTE.

THEME 1: ALL ABOUT CANCER

Receiving a cancer diagnosis is scary and may cause great shock accompanied by psychological distress. Patients have to manage these emotions alongside receiving large quantities of new information about their cancer. Therefore, receiving information on potential sequelae such as VTE, can be difficult to assimilate and retain.

Urothelial bladder cancer patients were generally overwhelmed with their cancer diagnosis, and this was their primary focus.

"I was more concerned about the bladder cancer than I was the blood clotsso it was just part of the process as far as I could see… yes, there were too many other emotions going on to focus on one particular aspect of it… it was more the cancer risk than thrombosis risk!" P014

Bladder cancer patients were preoccupied with their cancer and thus did not pay as much attention to information about blood clots during their appointments. This was also noted by HCPs:

"They are primarily focused on cancer, and they want to you know get to the treatment and put it behind

Table 2. Association of VTE in patients with UBC with treatment, stage, co-morbidities without 2nd cancer and 2nd cancer at QEHB and UHCW

Variables	OR (95%CI)	P-value
Treatment		
TURBT		
Cystectomy	2.64 (1.49-4.68)	0.001
Chemo.	2.40 (0.96-5.99)	0.061
Chemo. & Cystectomy	7.45 (3.14-17.71)	≤0.001
Stage		
NMIBC		
MIBC	0.70 (0.38-1.30)	0.266
Metastatic	4.45 (1.86-10.62)	0.001
Co-morbidities (no Ca)	0.98 (0.65-1.48)	0.944
Second cancer	0.23 (0.10-0.53)	0.001

Source: Compiled by the authors of this study

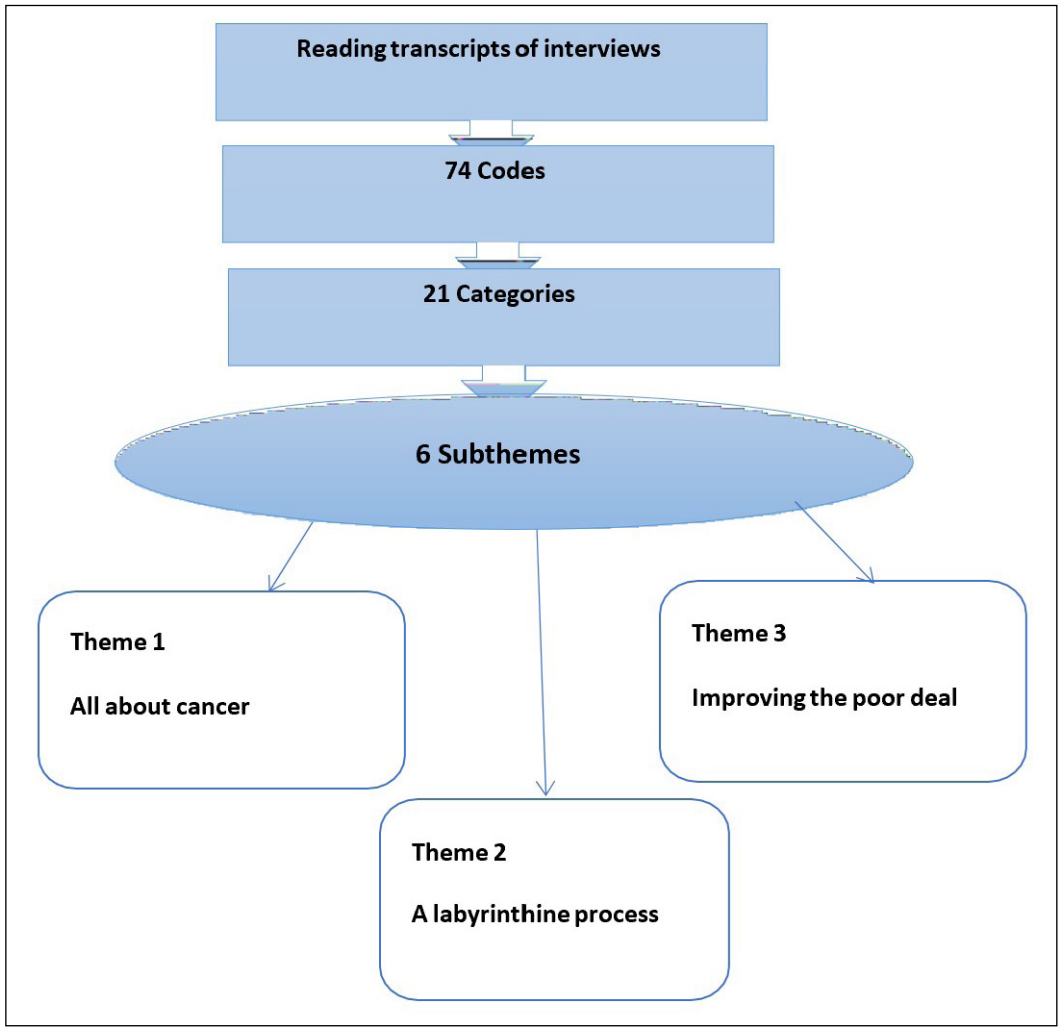


Fig. 1. Process to establish main themes
Source: Own materials

them as best as they can so most peoplewould listen to that and take the advice… occasionally some people are alarmed but most people are too focused on cancer." HC012

Patients with UBC experienced a high burden of information at all stages of the cancer care continuum. They therefore struggled to focus on VTE and had difficulties recalling any information provided on VTE.

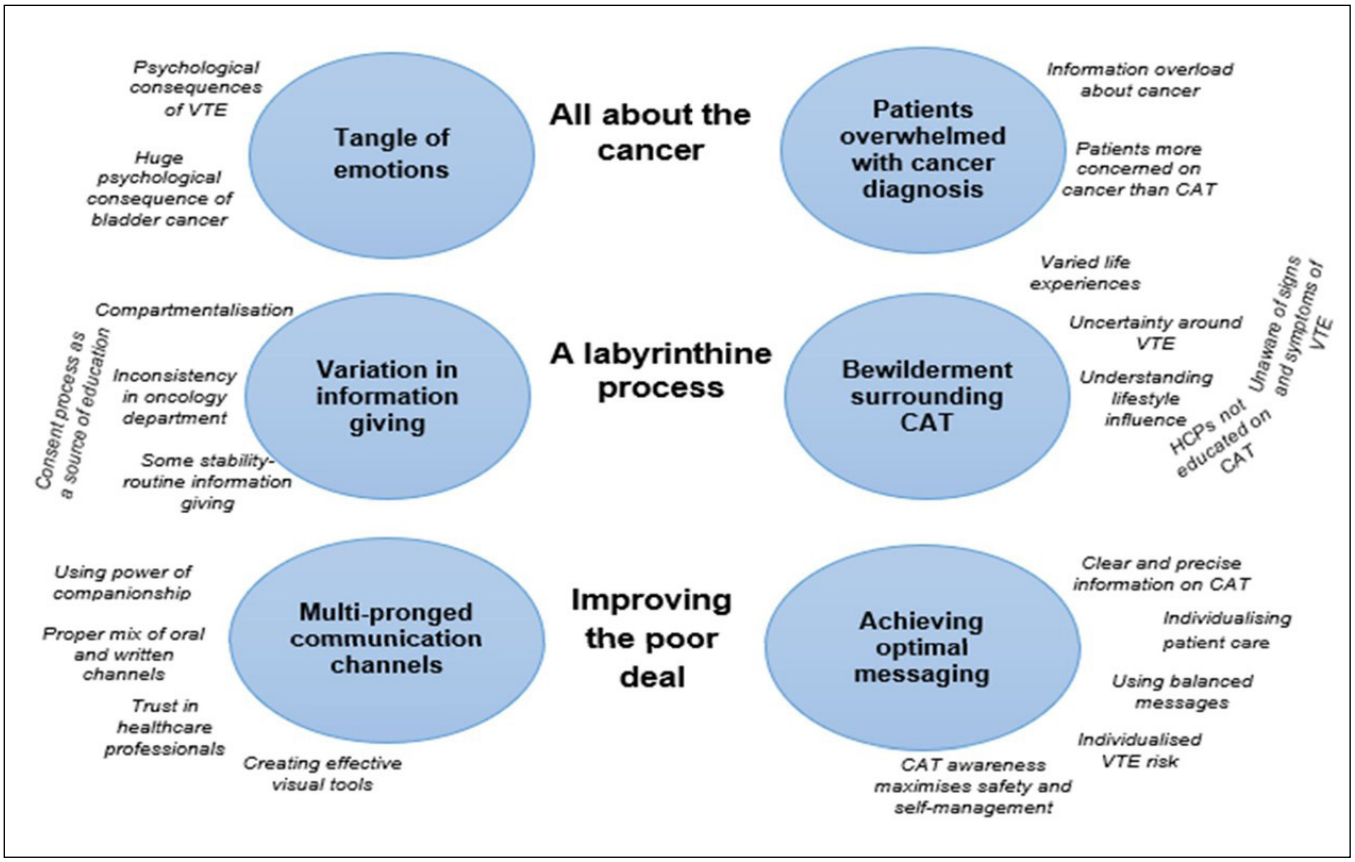


Fig. 2. Categories, main themes and subthemes
Source: Own materials

"No, it was like an information overload on bladder cancer that's why (my mind)…Err… no going back to it as I say we had an information overload…we had that much information leaflets… verbal…" P007

Interviews with patients revealed that they were overwhelmed, with their cancer diagnosis, tangled up in emotions around cancer and lacked information around VTE.

THEME 2: A LABYRINTHINE PROCESS

Patients generally had poor or limited information on VTE and its relationship with UBC, and the communication process around VTE between HCPs and UBC patients varied. Patients often needed to be treated in more than one department, such as the urology department and an oncology department. HCPs in each department have their own approach regarding communication about VTE.

In the urology department, nurses and urologists took a while to inform each UBC patient about the risk factors and complications of the cystectomy, including VTE. They explained the risk of clots as part of the routine information they provided in their pre-surgical counselling to patients who had a cystectomy and generally explained how VTE can be prevented. The HCPs in this study talked about anticlotting injections and stockings, and some also routinely offered lifestyle advice:

Yes, specifically when they're having surgery…a bladder removal operation and tell them about the measures that we take to prevent thromboembolism such as Heparin prophylaxis and compression stockings." HC007

"If they maintain activity then the risk can be reduced but beyond that I don't give them any formal information it's just a short discussion… it's a short conversation about it." HC0010

Patient selection of whom to discuss VTE with or with whom not to do so did not depend on patient characteristics (weight, mobility, smoking, family history, etc.), but mainly on the type of treatment and related risk of VTE:

"We don't choose whether they're male or female or anything like that it's just that if they have that surgery then yes, we'll go through it with them." HC004

Overall, HCPs were keen to discuss awareness of VTE including blood clots, risk factors for developing blood clots, thromboprophylaxis measures and understood the importance of the communication process to minimise the risk of VTE.

THEME 3: IMPROVING THE POOR DEAL

Informing UBC patients about blood clots aims to improve outcomes and empower decision making and prevention. In general, HCPs also assumed that effective communication around blood clots may encourage self-care and awareness:

"Yes, potentially yes…. I think it's something that they can actually do, something for themselves." HC001

Both methods on providing this information, and ways in which the patient wished to receive this information, were varied. One patient mentioned that he needed the facts without adding any emotion, as he believed the facts represent the reality:

"I think just the message… add fear to it I mean if you lay out the facts… the facts will speak for themselves there's no need to put a fear factor into it I just need to know the information!" P014

The vast majority of patients preferred a combination of verbal and written communication. Patients extract more information from reading because the leaflets remind them about the information they may have missed during verbal communication:

"I think it would be best to have it written down… cos I think people take itin more when they're reading it rather than listening…I think if they've got something to read keep picking up and reading about it I think that's… rather than… I think that's better than just being told… cos you can be told,and you can walk out and there it's gone!" P016

Most HCPs suggested using visual tools such as pictures and figures to explain what VTE is and what the associated risk factors. HCPs expected the viewer to grasp and understand clearly what VTE is and its related risk by using pictures and figures:

"So, the ideal is using pictures…'" HC005

"Right I feel the best thing would be pictures and your figures so pictures and figures together will make a huge difference. You tell them what thromboembolism is and why you get thromboembolism and the ways that we can reduce the risks of thromboembolism." HC006

Companions are central to the psychological and physical support of cancer patients, albeit some patients do not have companions. Cancer patients required mental support as much as they needed medical support.

"Yeah I… you know I bring a relative with me cos there's a lot you'll be shown you know what I mean if you are not computing what's been said at least you've got a relative there that might… you know have picked up on that." P006

DISCUSSION

This study, to our knowledge, is the first mixed-methods study which explores the incidence rate and risk factors for VTE in patients with UBC using UK data, in conjunction with identifying gaps in patient education that hinder the patients' role in VTE prevention.

Our findings revealed that VTE for people with cancer is a significant clinical problem often overlooked and neglected due to the overwhelming attention given to anti-cancer treatments and 'surviving' cancer. Knowing that VTE is the second most common cause of death in ambulant cancer patients [8] affords a standpoint for change, using the perspectives of both patients and healthcare professionals. Understanding the scope and being able to communicate this risk to patients is essential in making this change.

In this study, the statistical analysis of national and local UK data on VTE in UBC patients showed that the overall VTE incidence in the UK was lower than has been found in the previous UK literature [9]. Incidence was found to be highly connected to cancer profile and treatment type. Logistic regression analysis showed cystectomy, cystectomy with systemic chemotherapy, metastatic stage and a second type of cancer are associated with a significantly increased risk for VTE. Moreover, this study demonstrated that patients who had both cystectomy and chemotherapy appeared to carry the highest risk for VTE; greater than those who underwent cystectomy only. A systematic review and meta-analysis of chemotherapy risk of VTE in UBC showed similar results, that is systemic chemotherapy raises the risk for VTE beyond the already increased risk imposed by surgery and cancer [9]. Further studies should look to investigate the strength of this association further in order to inform guidelines appropriately.

Phase II of the study confirmed that the HCPs and patients understandably focus mostly on their cancer rather than sequelae such as VTE.

Some patients in this study experienced psychological distress including fear, anxiety, stress, and depression, which is consistent with other studies [10]. These strong emotions can make the comprehension of complex information difficult and may affect patients' perceptions of VTE [11]. The overwhelmed mental state in cancer patients may affect patients' ability to take in all aspects of medical information, including VTE preventive measures [12].

In this study, effectiveness was demonstrated to be through the use of clear factual language, through verbal and written means, and supported by the use of diagrams and pictures. The supportive upshots of having a companion during clinical consultations also improved patients' awareness of VTE [13].

The overall outcome of this study has shown there is an opportunity here for all clinicians to put into practice simple steps during patient encounters, to identify

and communicate VTE risk and mitigation strategies to patients. All patients with UBC should be assessed for their risk for VTE as part of a standard procedure and then individualised information can then be offered. This should be achieved in conjunction with effective communication skills and strategies, with awareness of the challenges patients face when receiving information in the context of a diagnosis of UBC. This move will help to improve communication around VTE, which should provide better understanding of VTE, encourage patients' adherence to thromboprophylaxis and decrease VTE events within this group.

CONCLUSIONS

VTE-UBC is, to our knowledge, the first mixed-methods study exploring VTE in people with UBC in the UK. This study highlights the clinical importance of VTE in UBC patients, and the challenge of communicating this risk effectively to patients. By presenting the scope of the problem using UK national and local NHS data, and by integrating patient and healthcare professionals' perspectives, this study should be used to inform clinicians and clinical guidance in both what information regarding VTE should be communicated to people with UBC and how it can be communicated effectively. Further studies should look to strategies implementation methods and assess their effectiveness. After describing the problem, this study provides some points for improving VTE prevention in UBC care:

- Routine thrombosis risk assessment should be integrated into standard UBC care, especially in advanced stage and when need combined treatment.
- Multimodal communication combining verbal discussion, written information and visual tools can improve patients' understanding about VTE risks.
- Standardised patient education on VTE signs, risks and prevention should be communicated in clear language through out the treatment pathway.
- It is important to involve family members or companions during counsultations for better understanding and retain important information.
- More studies required to evaluate the implementation and effectiveness of these startegies to reduce VTE incidence within patients with UBC.

In this way, VTE prevention in UBC can become not only more evidence-based, but also more patient-centred.

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CONFLICT OF INTEREST
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CREATIVE COMMONS 4.0

Appendix 1. Interview topic guide

Bladder cancer patients

Preamble / Introduction – thank you and purpose of the interview. What a venous thromboembolism is – deep vein thrombosis (DVT) and pulmonary embolism (PE)

1. Briefly introduction from the patient on themselves and their cancer pathway so far
2. Knowledge about clots associated with the cancer.

a. If yes, Probe – e.g., causes of clot formation in your condition?

3. Knowledge on the possibility of getting a clot.
4. Knowledge on how to identify if you have a clot.

(Probe: Do you know what the signs and symptoms are of having a clot?)

5. Knowledge about surgery and relation to clots as well as knowledge about medication and having the medication to prevent clots?

(Probe – if yes, who, what, when, how, how long?)

6. Knowledge about chemotherapy and relation to clots? If yes, tell me if told about clots – who, what, when
7. Discussing anti-clotting treatment at any other time apart from surgery? (probe: injections or tablets)

If no. go to Q10.

If yes, the experience of receiving the blood thinners what, when, how long

8. If not mentioned above, knowledge patient has about the benefits and challenges or risks of anti-clotting treatment?

(Probe – heard about bleeding risk?)

9. This research is hoping to improve how the risk of clots is communicated to cancer patients. Going back to the information you received from XYZ about clots, tell me a little bit about your experience of receiving this information.

(Probe: How did it make you feel? Is there anything that could be improved/changed to make the experience better?)

10. Discussion on the best way to inform patients about their risk of developing clots? Why?

(Probe: What is the best method of presenting risk information to patients? Using numbers, percentages, words, figure, combinations or all (present the tools), individual risk or average, fear messages or positive messages?).

Healthcare professionals

1. Briefly introduction from participants on themselves and their speciality
2. What is the knowledge about venous thromboembolism (DVT and PE) given to the patients?
3. Type of information given to the cancer patients about venous thromboembolism risk in cancer which will be answered by the following questions:

a. Do you tell your cancer patients about the signs and symptoms of thromboembolism?

b. Do you tell your cancer patients about different preventative approaches that could affect getting thromboembolism?

c. Do you tell your cancer patients about the risk of chemotherapy for thromboembolism?

d. Do you tell the patients about the risk of surgery for the thromboembolism?

4. Do you inform your cancer patients about the benefits and challenges or risks of anti- clotting treatment?

(Probe: Do you inform your cancer patients about the bleeding risk?)

5. This research is hoping to improve how the risk of thromboembolism is communicated to cancer patients. Could you tell me a little bit regarding your experience of informing cancer patients about this information?

(Probe: How did it make them feel? Is there anything that could be improved/changed to make the experience better?)

6. Discussion on the best way to inform patients about their risk of developing thromboembolism, Why?

(Probe: What is the best method of presenting risk information to patients? Using numbers, percentages, words, figure, combinations or all (present the tools), individual risk or average, fear messages or positive message.

ORIGINAL ARTICLE

CONTENTS

Factors affecting the progression of glaucomatous optic neuropathy after antiglaucoma surgery in patients with primary open-angle glaucoma

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ABSTRACT

Aim: To identify and analyze the key clinical, structural, and functional factors influencing the progression of glaucomatous optic neuropathy after antiglaucoma surgical intervention in patients with POAG, as well as to determine their prognostic value for optimizing postoperative patient management.

Materials and Methods: A retrospective observational cohort study included 56 patients (56 operated eyes) with primary open-angle glaucoma who underwent unilateral antiglaucoma surgery and were followed dynamically in the postoperative period. Based on follow-up results, patients were divided into two groups: with postoperative disease progression (n = 20) and without progression (n = 36).

Results: Postoperative disease progression was not associated with age, sex, axial length, or phacomorphic syndrome. Besides, disease progression was significantly associated with elevated plasma LOX1 concentration (≥ 80.1 pg/mL), reduced neuroretinal rim area (≤ 0.7 mm^2), and elevated preoperative IOP (≥ 25 mmHg). In multivariate logistic regression analysis, reduced neuroretinal rim area ≤ 0.7 mm^2 (OR = 12.9; 95% CI: 3.4–49.1; $p < 0.05$) and preoperative IOP ≥ 25 mmHg (OR = 7.6; 95% CI: 1.9–29.4; $p < 0.05$) remained independent predictors of postoperative disease progression, while plasma LOX1 showed moderate discriminative performance (AUC = 0.664).

Conclusions: Postoperative progression of glaucomatous optic neuropathy in patients with primary open-angle glaucoma is determined by a combination of structural, biomechanical, and systemic vascular-related factors. Preoperative IOP, neuroretinal rim morphology, and plasma LOX1 levels have prognostic significance and should be considered for postoperative risk stratification and individualized follow-up.

KEY WORDS: glaucoma, surgery, inflammation, optometry, diagnostics, trabecula

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INTRODUCTION

Glaucoma remains one of the leading causes of irreversible blindness worldwide. According to global epidemiological projections, the number of patients with glaucoma may reach 112 million by 2040 [1], highlighting the urgent need for early diagnosis and effective control of disease progression. Primary open-angle glaucoma (POAG) is the most common type of glaucoma and is characterised by a chronic, slowly progressive, and often asymptomatic course, which frequently leads patients to seek medical attention at advanced stages when visual loss becomes irreversible [1, 2].

Despite the variety of pathogenetic mechanisms involved, elevated intraocular pressure (IOP) remains the only reliably established modifiable risk factor for the progression of glaucomatous optic neuropathy. International randomised clinical trials have confirmed that reducing IOP slows both visual field deterioration and structural changes of the optic nerve head in patients with glaucoma across different stages [2]. Nevertheless, postoperative IOP stability is equally important, as it has been shown that IOP fluctuations, even when the mean pressure remains within normal limits, can accelerate glaucoma progression. The postoperative period in POAG patients is considered particularly critical because, even after achieving target IOP, some patients continue to demonstrate structural or functional deterioration. It is known that after surgical intervention, structural changes of the optic nerve head and retina may continue to evolve despite satisfactory IOP levels, which may be partially explained by vascular, biomechanical, and neurodegenerative influences [2, 3].

Special attention in the pathogenesis of glaucoma progression is given to systemic biological mechanisms, including oxidative stress, endothelial dysfunction, inflammatory responses, and reduced neurotrophic sup-

port, all of which can affect both the resistance of ocular tissues to increased IOP and their ability to recover after surgery [4, 5]. In this context, the investigation of plasma biomarkers such as lysyl oxidase-1 (LOX1)—a molecule involved in oxidative tissue damage and apoptosis—has gained particular importance [5]. Elevated LOX1 levels may be associated with increased susceptibility of the optic nerve to damage, making this biomarker a promising candidate for assessing the risk of glaucoma progression, including in the postoperative period.

Given the complexity of POAG pathogenesis and the variety of factors influencing postoperative outcomes, identifying clinical and biochemical predictors of progression is essential for optimising postoperative management [1, 2, 6]. The identification of these predictors not only helps detect high-risk patients but also contributes to developing personalised monitoring and treatment strategies tailored to the individual risk profile. Therefore, our study aimed to provide a comprehensive assessment of clinical, morphological, and biochemical factors potentially influencing the progression of glaucomatous optic neuropathy after antiglaucoma surgery in patients with POAG.

AIM

The aim of the study was to identify and analyze the key clinical, structural, and functional factors influencing the progression of glaucomatous optic neuropathy after antiglaucoma surgical intervention in patients with POAG, as well as to determine their prognostic value for optimizing postoperative patient management.

MATERIALS AND METHODS

A retrospective observational cohort study was conducted to evaluate factors associated with the progression of glaucomatous optic neuropathy after antiglaucoma surgery in patients with POAG. All patients were subjected to dynamic postoperative follow-up, during which clinical, structural, and functional parameters were assessed in the postoperative period in order to determine the presence or absence of glaucoma progression. The study design included comparison of preoperative baseline data with follow-up observations obtained after surgical intervention. The surgical procedure performed was a minimally invasive tunnel trabeculopuncture. The mean duration of postoperative follow-up was 43 months. The main study group included 56 patients (56 operated eyes) with primary open-angle glaucoma who underwent antiglaucoma surgical intervention. Only patients with unilateral surgery were included in the analysis; therefore, one operated eye per patient was evaluated, and the unit of analysis was the individual patient.

The study group consisted of 26 men (46.4%) and 30 women (53.6%), with a median (Me) age of 63.0 years (interquartile range [IQR]: 56.0–71.0). According to the results of dynamic postoperative follow-up, disease progression was detected in 20 patients (35.7%), while 36 patients (64.3%) demonstrated no signs of progression. Based on these findings, patients were divided into two groups for further analysis: a group without postoperative glaucoma progression and a group with postoperative glaucoma progression.

All patients enrolled in the study underwent comprehensive ophthalmic examinations and treatment at the clinical facilities of the Department of Ophthalmology and Optometry of Postgraduate Education, Institute of Postgraduate Education, Bogomolets National Medical University.

All patients underwent a comprehensive ophthalmic evaluation, which, in addition to standard examinations, included the assessment of horizontal cup-to-disc ratio; vertical cup-to-disc ratio; presence of β-zone peripapillary atrophy; presence of neuroretinal rim notching in the inferior sector; and focal loss of the retinal nerve fibre layer (RNFL).

Quantitative measurements were obtained for the ganglion cell complex in the peripapillary and paramacular regions. The temporal peripapillary RNFL thickness was assessed, and the volume of the neuroretinal rim was measured, alongside its correlation with the qualitative characteristics of the corresponding optic nerve head regions.

Fig. 1 presents fundus photography and optical coherence tomography (OCT) images of the optic nerve head (ONH) of patient H., 65 years old, diagnosed with stage III POAG in the right eye and stage II POAG in the left eye.

Measurement of the LOX1 biomarker level in plasma was performed using a solid-phase enzyme-linked immunosorbent assay (ELISA). Blood plasma samples were collected in sterile Eppendorf tubes in the clinical diagnostic laboratory as residual material obtained after routine blood testing. Plasma was prepared according to standard protocols via centrifugation, then frozen at −20°C and transported to the research laboratory under controlled cold-chain conditions. LOX1 concentrations were measured using the Human LOX-1 ELISA Kit (Invitrogen, Thermo Scientific, USA; Catalogue No. EHOLR1; Lot 371031324; sensitivity 2 pg/mL), following the manufacturer's instructions.

Statistical analysis was performed using the EZR software package (version 1.55; R statistical environment). The distribution of continuous variables was assessed

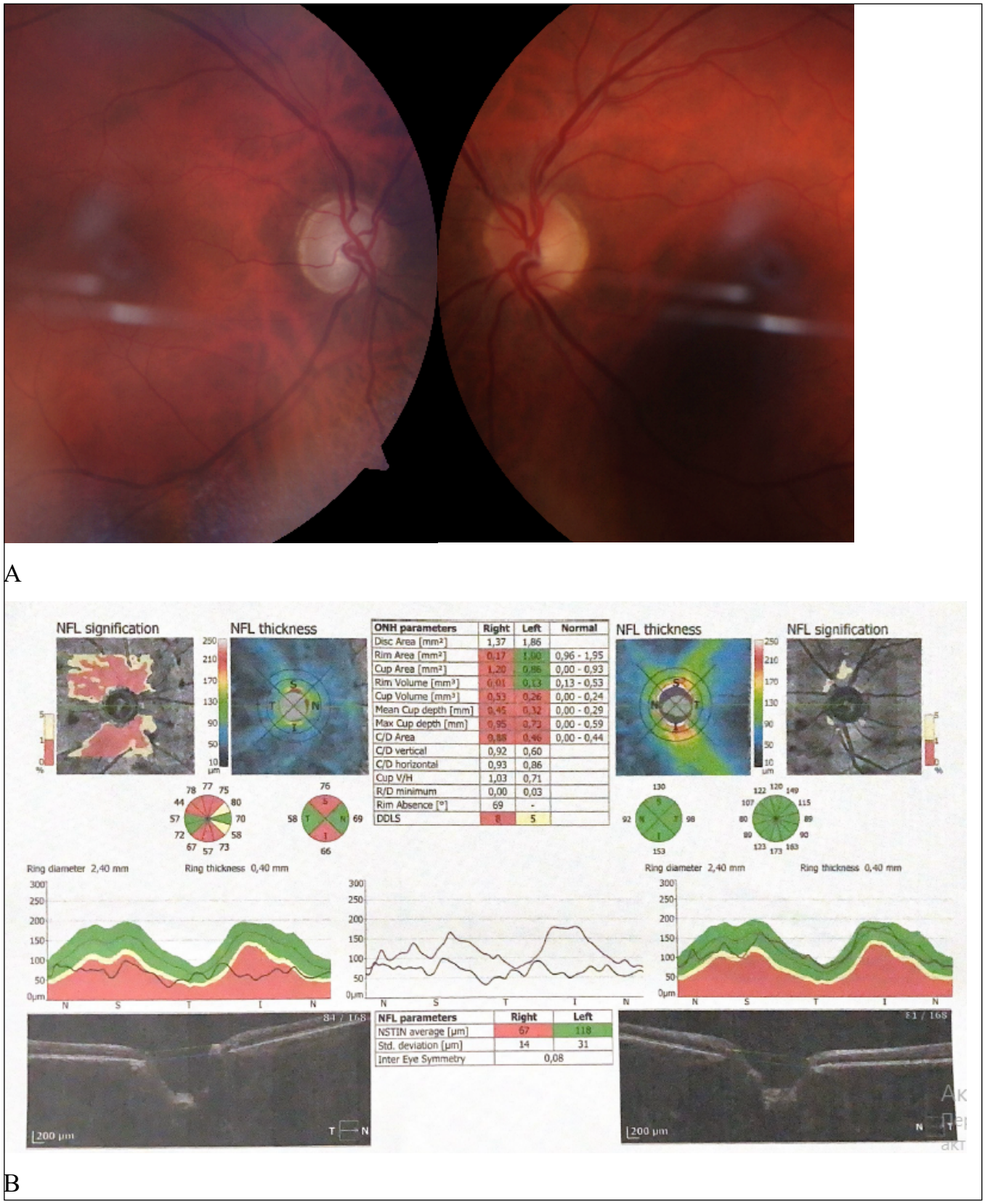


Fig. 1. Patient H., 65 years old, POAG stage III (right eye), stage II (left eye): A – fundus photo of the ONH; B – OCT results
Picture taken by the authors

using the Shapiro–Wilk test. As most continuous variables did not follow a normal distribution, quantitative data were presented as Me (IQR) and analysed using non-parametric statistical methods. Comparisons between two independent groups were performed using the Mann–Whitney U test. Categorical variables were

Table 1. Characteristics of patients with and without postoperative disease progression

Variable	Disease progression (n =20)	Without disease progression (n =36)	p
Age, years	64.5 (56.0-72.0)	63.0 (57.0-71.0)	0.751
Women (N = 30)	10 (50.0 %)	20 (55.6 %)	0,783
Men (N = 26)	10 (50.0 %)	16 (44.4 %)	
Phacomorphic syndrome (N = 23)	11 (55.0 %)	14 (38.9 %)	0,275
Without phacomorphic syndrome (N = 33)	9 (45.0 %)	22 (61.1 %)	
Anterior-posterior axis, mm	24.54 (23.18–24.98)	23.56 (22.83–24.91)	0.235
Neuroretinal area, mm^2	0.75 (0.70–0.80)	0.50 (0.445–0.50)	< 0.001
IOP, mm Hg	28.5 (25.5–31.0)	19.0 (18.0–23.0)	0.001
LOX1, pg/mL	49.65 (33.42–170.79)	41.40 (29.68–56.70)	0.045

Source: compiled by the authors of this study

expressed as absolute values and percentages and compared using Fisher's exact test.

Postoperative glaucoma progression (presence or absence of progression) was treated as a binary dependent variable for regression modelling. Univariate analysis was initially performed to assess the association between individual clinical, anatomical, and biochemical variables and postoperative progression of glaucomatous optic neuropathy. Variables demonstrating a potential association with postoperative progression in univariate analysis were subsequently included in a logistic regression model. Multivariate logistic regression analysis was applied to identify independent predictors of postoperative glaucomatous optic neuropathy progression. The results of logistic regression analysis were expressed as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). Receiver operating characteristic (ROC) analysis was performed for variables identified as significant predictors in logistic regression analysis to evaluate their discriminative ability. The area under the ROC curve (AUC), sensitivity, and specificity were calculated, and optimal cut-off values were determined based on ROC curve analysis. A p-value < 0.05 was considered statistically significant.

ETHICS

The study was conducted in accordance with the main provisions of the Council of Europe Convention on Human Rights and Biomedicine, the Declaration of Helsinki of the World Medical Association (1964, with subsequent amendments including the 2000 version), as well as current regulatory acts of Ukraine: "Fundamentals of Ukrainian Legislation on Health Care" (1993), "On the Protection of Personal Data" (2010), and "On Higher Education" (2017). All patients were fully informed about the nature of the study and provided written informed consent for diagnostic examination and treatment.

FRAMEWORK

The work was carried out at the Department of Ophthalmology and Optometry of Postgraduate Education of the Institute of Postgraduate Education of Bogomolets National Medical University and is a fragment of the scientific research project «Theoretical and practical aspects of improving clinical and experimental methods of diagnosis, treatment and prevention of diseases and injuries of the organ of vision and their complications» (state registration number 0123U104207; term: 2023-2026).

RESULTS

All ophthalmological parameters presented in the following tables were assessed in the operated eyes only. As only patients who underwent unilateral antiglaucoma surgery were included in the study, one operated eye per patient was analysed. Based on dynamic postoperative follow-up, patients were divided into two groups: those with postoperative glaucomatous optic neuropathy progression (n = 20) and those without disease progression (n = 36) (Table 1).

The median age of the entire study population was 63.0 years (IQR: 56.0–71.0). There was no statistically significant difference in age between patients with postoperative disease progression and those without progression (median 64.5 years [IQR: 56.0–72.0] vs 63.0 years [IQR: 57.0–71.0]; p = 0.751).

Sex distribution did not differ significantly between groups. Among women (n = 30), postoperative progression was observed in 10 patients (50.0%), while 20 patients (55.6%) showed no progression. Among men (n = 26), progression occurred in 10 cases (50.0%), and 16 patients (44.4%) had no progression (p = 0.783).

Phacomorphic syndrome was not significantly associated with postoperative disease progression.

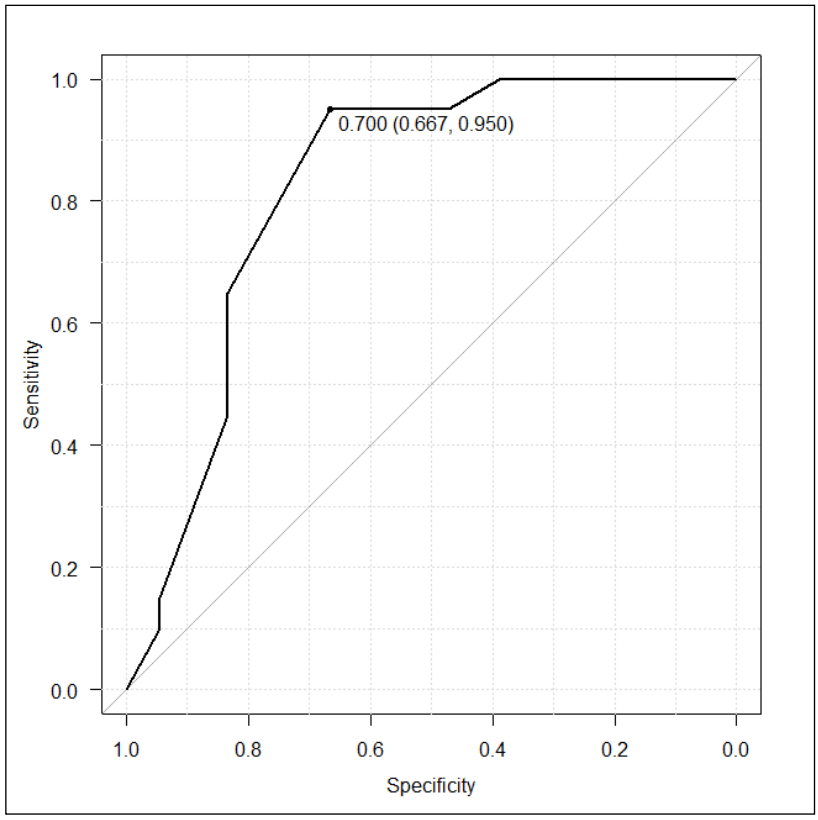


Fig. 2. ROC curve of the logistic model predicting the frequency of POAG progression after surgical antiglaucoma intervention depending on the size of the neuroretinal strip area before surgery. AUC = 0.824
Picture taken by the authors

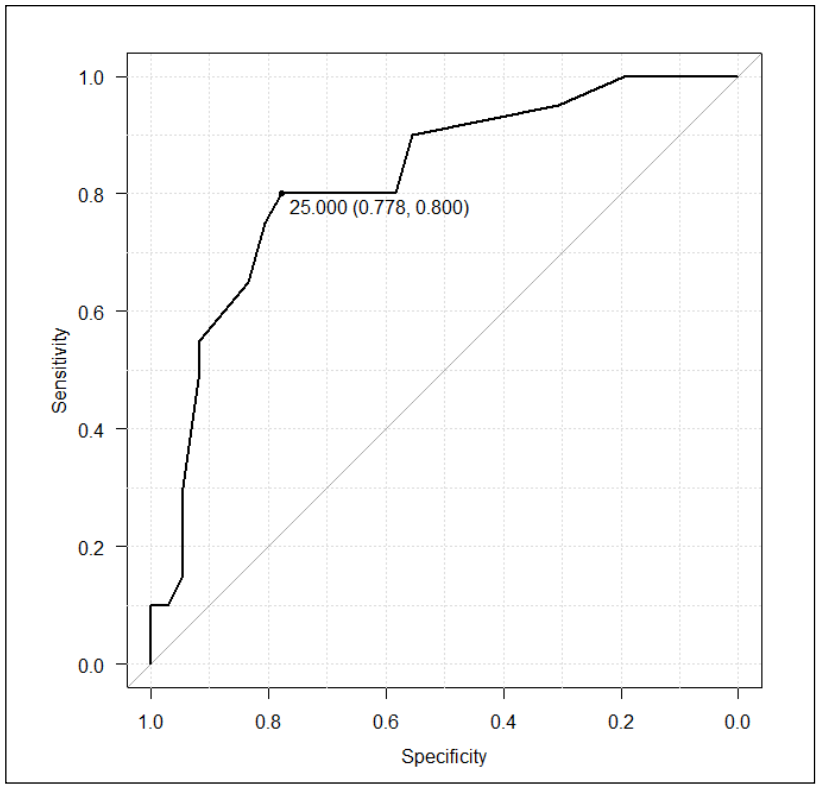


Fig. 3. ROC curve of the logistic model predicting the frequency of POAG progression after surgical antiglaucoma intervention depending on the value of IOP before surgery. AUC = 0.822
Picture taken by the authors

Progression was detected in 11 of 23 patients (55.0%) with phacomorphic syndrome and in 9 of 33 patients (45.0%) without phacomorphic syndrome (p = 0.275).

Preoperative intraocular pressure differed significantly between the two groups. Patients with postoperative disease progression had a substantially higher IOP compared with those without progression (median 28.5 mmHg [IQR: 25.5–31.0] vs 19.0 mmHg [IQR: 18.0–23.0], Mann–Whitney U test, p < 0.001).

Neuroretinal rim area was significantly lower in patients with postoperative disease progression than in patients without progression. The median

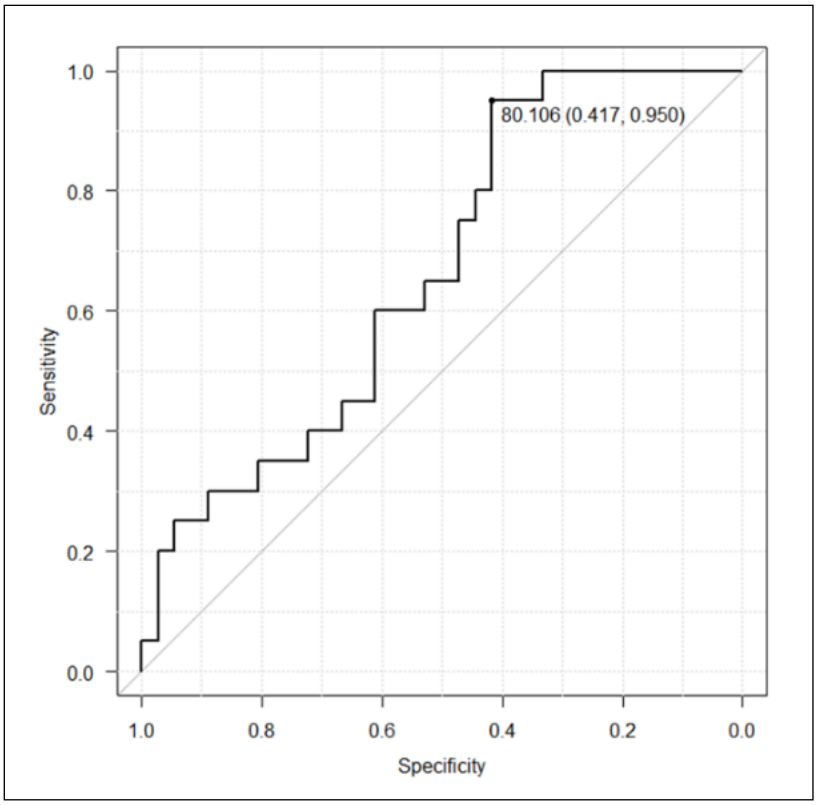


Fig. 4. ROC curve of the logistic model predicting the frequency of POAG progression after antiglaucoma surgery depending on the value of LOX1 in the blood plasma of glaucoma patients before surgery. AUC = 0.664
Picture taken by the authors

Table 2. The certain binary risk factors in the groups of patients with and without postoperative disease progression

Variable	Disease progression (n =20)	Without disease progression (n =36)	p
Neuroretinal area ≤ 0,7 mm² (N = 23)	18 (90.0 %)	6 (16.7 %)	<0.001
Neuroretinal area > 0,7 mm² (N = 33)	2 (10.0 %)	30 (83.3 %)	
IOP < 25 mmHg (N = 20)	2 (10.0 %)	18 (50.0 %)	0.003
IOP ≥ 25 mmHg (N = 36)	18 (90.0 %)	18 (50.0 %)	
LOX1 ≥ 80.1 pg/mL (N = 19)	17 (85.0 %)	2 (5.6 %)	<0.001
LOX1 < 80.1 pg/mL (N = 37)	3 (15.0 %)	34 (94.4 %)	

Source: compiled by the authors of this study

Table 3. Multivariate analysis of factors associated with postoperative glaucomatous optic neuropathy progression

Variable	OR	95% CI	p
Neuroretinal rim area ≤ 0.7 mm²	12.9	3.4 – 49.1	< 0.05
Preoperative intraocular pressure ≥ 25 mmHg	7.6	1.9 – 29.4	< 0.05
LOX1 ≥ 80.1 pg/mL	2.2	0.8 – 6.1	0.12

Source: compiled by the authors of this study

neuroretinal rim area in the progression group was 0.50 mm² (IQR: 0.445–0.50), compared with 0.75 mm² (IQR: 0.70–0.80) in the non-progression group ($p < 0.001$).

Plasma LOX1 concentrations showed a statistically significant difference between groups. Patients without postoperative disease progression had lower median LOX1 levels compared with patients with progression (median 41.40 pg/mL [IQR: 29.68–56.70] vs 49.65 pg/mL [IQR: 33.42–170.79]; $p = 0.045$) (Table 1).

The ROC analysis was performed for variables that demonstrated a statistically significant association with postoperative glaucomatous optic neuropathy progression in order to assess their individual discriminative ability. It should be emphasised that ROC analysis represents a single-factor assessment and does not account for interactions between variables within the multivariate model.

ROC analysis demonstrated a high discriminative ability of the preoperative neuroretinal rim area for

predicting postoperative disease progression. A cut-off value of < 0.7 mm^2 was associated with a high risk of progression, yielding an AUC of 0.824 (95% CI: 0.716–0.932). Sensitivity and specificity at this threshold were 95.0% and 66.7%, respectively (Fig. 2).

Preoperative IOP also showed high discriminative performance in ROC analysis. An IOP threshold of ≥ 25 mmHg was associated with postoperative progression, with an AUC of 0.822 (95% CI: 0.706–0.937). At this cut-off value, sensitivity was 80.0%, and specificity was 77.8% (Fig. 3).

Plasma LOX1 concentration demonstrated moderate discriminative ability for postoperative progression. A preoperative LOX1 cut-off value of ≥ 80.1 pg/mL was associated with postoperative progression, with an AUC of 0.664 (95% CI: 0.520–0.808). Sensitivity and specificity at this threshold were 95.0% and 41.7%, respectively (Fig. 4).

Based on the results of ROC analysis, optimal cut-off values were determined for continuous variables demonstrating significant discriminative ability. These cut-off points were subsequently used to categorise patients and to perform a comparison of categorical (binary) risk factors between patients with and without postoperative disease progression (Table 2).

According to the data in Table 2, all the studied binary variables demonstrated a statistically significant association with postoperative glaucomatous optic neuropathy progression. In the next step, the neuroretinal area, IOP, and LOX1, adjusted for other previously described parameters, were evaluated using multivariate logistic regression analysis.

As shown in Table 3, multivariate logistic regression analysis identified reduced neuroretinal rim area (< 0.7 mm^2) and elevated preoperative IOP (> 25 mmHg) as independent predictors of postoperative disease progression. A neuroretinal rim area < 0.7 mm^2 was associated with a markedly increased risk of progression (OR = 12.9, 95% CI: 3.4–49.1; $p < 0.001$), while preoperative IOP > 25 mmHg also remained an independent predictor (OR = 7.6, 95% CI: 1.9–29.4; $p < 0.001$).

Plasma LOX1 concentration, although significantly associated with disease progression in univariate analysis, did not retain independent predictive significance in the multivariate logistic regression model after adjustment for structural and pressure-related factors (OR = 2.2, 95% CI: 0.8–6.1; $p = 0.12$) (Table 3).

DISCUSSION

The findings of this study indicate that, following antiglaucoma surgery in patients with primary open-angle glaucoma, the progression of glaucomatous optic neuropathy is determined not only by the achieved postoperative IOP level but also by a combination of preoperative morphofunctional characteristics and, likely, vascular factors. This aligns with the modern understanding of glaucoma as a multifactorial disease in which structural and functional deterioration may persist even after successful surgical reduction of IOP. Several studies have demonstrated that after trabeculectomy, some patients experience a slowing of visual field loss, whereas others continue to show progression despite satisfactory IOP control [7–9].

Our analysis confirms that high preoperative IOP is an important predictor of future glaucomatous optic neuropathy progression, even after successful surgical treatment. This observation is consistent with published findings showing that eyes with higher preoperative IOP peaks exhibit worse preservation of macular ganglion cell complex (GCC) parameters in subsequent years. Specifically, eyes with lower preoperative peak IOP demonstrate better preservation of the thickness of the macular nerve fiber layer (mNFL), macular ganglion cell layer (mGCL), and inner plexiform layer (mIPL) compared to eyes with higher peak IOP, even when their postoperative IOP levels are similar [8, 10].

Another significant factor is the status of the neuroretinal rim. A thinner neuroretinal rim and a larger cup-to-disc ratio can be considered morphological indicators of increased vulnerability of the optic nerve head to subsequent damage. Although partial reversal of cupping and changes in optic nerve head topography have been observed in some patients after trabeculectomy, these morphometric improvements do not always correspond to long-term structural stability [8]. Therefore, the baseline configuration of the optic nerve head — including neuroretinal rim condition — should be considered a prognostically significant parameter during postoperative follow-up.

The results of previous studies indicate that achieving target IOP alone may not fully prevent disease progression. One plausible explanation is the influence of vascular mechanisms [9]. For example, a more rapid decrease in peripapillary vessel density following trabeculectomy has been associated with visual field deterioration, suggesting an independent contribution of microcirculatory impairment. Epidemiological and clinical data also indicate the role of systemic vascular dysregulation — including hypotension, blood pressure variability, and impaired autoregulation — in maintaining the risk of progression after surgery [10].

Although direct clinical evidence regarding the role of LOX1 in the progression of glaucoma after antiglaucoma surgery is still limited, known mechanisms of its biological activity support its potential as an important factor in the pathogenesis of glaucomatous optic neuropathy. LOX1 is a transmembrane receptor whose expression increases

in response to oxidative stress, dyslipidaemia, endothelial dysfunction, and tissue ischaemia — all of which are processes associated with vascular forms of glaucoma [5].

Retinal ganglion cells (RGCs) are especially sensitive to microcirculatory disturbance and oxidative stress. Activation of LOX1 triggers the generation of reactive oxygen species (ROS), reduced nitric oxide (NO) bioavailability, and initiation of apoptosis through caspase-dependent pathways [5, 10].

In glaucoma, characterised by reduced perfusion pressure and impaired autoregulation, LOX1 activation may exacerbate the metabolic vulnerability of RGCs, thereby increasing the risk of progression even when postoperative IOP remains within the target range [4].

Thus, even after achieving satisfactory postoperative IOP control, elevated systemic LOX1 levels may contribute to ongoing microvascular ischaemia and RGC loss, clinically manifesting as continued progression [5, 7].

The limitations of this study include the relatively small sample size and its retrospective design. Furthermore, because glaucoma is inherently multifactorial, the dominant influence of preoperative IOP, optic nerve head morphology, and vascular factors must be interpreted with caution [4, 9].

Nevertheless, LOX1 appears to be a promising pathogenic biomarker contributing to progression risk, although it should not be considered a sole determinant. Patients with elevated LOX1 levels should be regarded as high-risk and require closer ophthalmic follow-up and more intensive postoperative monitoring [5–7].

Overall, the combination of elevated preoperative IOP, morphological parameters, and systemic biochemical markers may enable more accurate risk stratification and support the development of personalised postoperative management strategies for patients with primary open-angle glaucoma.

CONCLUSIONS

1. Postoperative progression of glaucomatous optic neuropathy in patients with POAG is a multifactorial process that may occur despite successful surgical reduction of intraocular pressure. This underscores the importance of identifying patients at increased risk during postoperative follow-up.
2. Elevated preoperative IOP ($\geq$ 25 mmHg) was identified as an independent predictor of postoperative disease progression. Patients with higher preoperative IOP demonstrated a significantly increased risk of structural and functional deterioration after surgery.
3. Reduced neuroretinal rim area ($\leq$ 0.7 mm^2) was found to be an independent predictor of postoperative glaucomatous optic neuropathy progression. This parameter reflects advanced baseline optic nerve damage and is associated with a markedly unfavorable postoperative course.
4. Plasma LOX1 concentration showed a significant association with disease progression in univariate analysis; however, it did not retain independent predictive value after adjustment for structural and pressure-related factors. These findings suggest that LOX1 may serve as an adjunctive biomarker, although its clinical relevance requires further confirmation in larger prospective studies.

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ORIGINAL ARTICLE

CONTENTS

L-selectin as a systemic biomarker of retinal damage in type 2 diabetes

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ABSTRACT

Aim: To evaluate the clinical significance of serum L-selectin (sCD62L) levels as a biomarker of retinal damage in patients with type 2 diabetes mellitus (T2DM) by correlating its concentration with the stages of diabetic retinopathy (DR) and clinical and morphological parameters of the retinal state.

Materials and Methods: A total of 124 patients (124 eyes) were examined: 95 patients with T2DM (ranging from mild non-proliferative to proliferative DR) and 29 age- and sex-matched controls. Diagnostic techniques included BCVA assessment, SD-OCT (Topcon 3D OCT-1000), and serum ELISA for L-selectin determination.

Results: A significant 2.5-fold increase in serum L-selectin levels was identified in the T2DM cohort compared to controls ([mean ± standard error] 31.2 ± 8.6 ng/mL vs. 12.5 ± 3.5 ng/mL; $p < 0.001$). A progressive upward trend in marker concentration was observed relative to pathology severity: from (median [interquartile range]) 24.7 (20.4–29.0) ng/mL in mild non-proliferative DR ($p < 0.001$ vs. control group [12.5 (10.1–14.9)] ng/mL) to 39.5 (35.1–43.9) ng/mL in the proliferative stage ($p < 0.001$ vs. control group). Positive correlations were found between L-selectin levels and HbA1c ($rs = 0.816$, $p < 0.001$), as well as central retinal thickness ($rs = 0.467$, $p = 0.002$).

Conclusions: CD62L is a significant biomarker of systemic inflammation and vascular dysfunction in T2DM, reflecting the severity of diabetic retinopathy and the risk of blood-retinal barrier disruption.

KEY WORDS: ophthalmology, optometry, diabetic retinopathy, inflammatory biomarker

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INTRODUCTION

Diabetes mellitus (DM) has reached pandemic proportions, emerging as one of the most significant global health challenges of the 21st century. Current projections suggest that the number of individuals living with diabetes will increase to 700 million by 2045 [1]. Among its various microvascular complications, diabetic retinopathy (DR) remains a leading cause of preventable blindness in the working-age population, affecting approximately 22.27% of patients worldwide [1, 2]. Despite advances in laser therapy and anti-VEGF treatments, the social and economic burden of DR continues to grow, necessitating a deeper understanding of its early developmental stages [2].

The pathogenesis of DR is traditionally viewed through the lens of microvascular damage; however, contemporary research increasingly emphasizes the role of chronic low-grade systemic inflammation and neurodegeneration [2, 3]. Chronic hyperglycaemia triggers a cascade of metabolic disturbances, including oxidative stress and activation of the polyol pathway, which collectively stimulate the release of pro-inflammatory cytokines and adhesion molecules [4–6]. These biochemical shifts often manifest as subtle neuroretinal alterations even before the clinical appearance of microaneurysms or haemorrhages [2, 4]. Consequently, there is an urgent clinical demand for sensitive and specific systemic biomarkers capable of identifying patients at high risk of rapid disease progression before irreversible structural damage occurs [5, 6].

Leukostasis — the abnormal adherence of leukocytes to the retinal capillary endothelium — is a critical early event in the breakdown of the blood-retinal barrier (BRB) [4, 5]. This process is mediated by a specialized family of cell adhesion molecules known as selectins. Among them, L-selectin (CD62L), which is constitutively expressed on the surface of most circulating leukocytes, plays a pivotal role in the initial "rolling" phase of leukocyte recruitment [3, 4, 7]. Upon cellular activation, the extracellular domain of L-selectin is proteolytically cleaved from the cell surface in a process termed "shedding", leading to increased levels of its soluble form (sCD62L) in the systemic circulation [3, 7].

Despite its theoretical importance, the diagnostic and prognostic value of soluble L-selectin in type 2 diabetes mellitus (T2DM) remains a subject of ongoing debate. While some studies have suggested depletion of L-selectin due to chronic receptor exhaustion in advanced stages of metabolic disease, others, most notably Karadayi et al. [8], have reported a significant elevation of the marker correlating with the severity of retinal ischemia [8–10]. These discrepancies in the literature underscore the necessity for a systematic evaluation of sCD62L dynamics across the full clinical spectrum of DR — from mild non-proliferative changes to advanced proliferative disease [9, 10].

Furthermore, while the correlation between systemic inflammation and DR is well documented, few studies have integrated biochemical markers with precise structural parameters obtained via spectral-domain optical coherence tomography (SD-OCT) [10]. Establishing a clear link between sCD62L concentrations and clinico-morphological indicators, such as central retinal thickness, could provide a more comprehensive framework for personalized screening and risk stratification in patients with T2DM [7, 10].

AIM

To evaluate the clinical significance of L-selectin as a biomarker of retinal damage in patients with type 2 diabetes mellitus (T2DM) by comparing its levels across different stages of diabetic retinopathy (DR) and correlating them with clinical and morphological parameters.

MATERIALS AND METHODS

The research was designed and conducted as a prospective cohort study using a case-control framework. The study analysed clinical and laboratory data from a total of 124 eyes belonging to 124 subjects. The primary study cohort consisted of 95 patients with confirmed type 2 diabetes mellitus complicated by various stages of diabetic retinopathy (DR). For comparison, a control group was formed, consisting of 29 subjects with no history of carbohydrate metabolism disorders or systemic inflammatory diseases, matched to the main group by age and gender.

The demographic profile of the participants was recorded at the time of inclusion. The mean age in the main cohort (T2DM patients) was 66.8 ± 0.75 years, while the mean age in the control group was 64.2 ± 1.20 years. Within the main cohort, the gender distribution comprised 65 women (68.4%) and 30 men (31.6%). In the control group, there were 16 women (55.2%) and 13 men (44.8%).

The metabolic status of the participants was assessed using standard laboratory tests. In the main cohort, the mean fasting blood glucose level was 8.51 ± 0.82 mmol/L, and the mean glycated haemoglobin (HbA1c) level was 7.36 ± 0.15%.

According to the clinical severity of retinal pathology, patients with T2DM were stratified into three subgroups: Group 1 (n = 29) included patients with mild non-proliferative diabetic retinopathy (NPDR); Group 2 (n = 35) consisted of patients with moderate and severe NPDR; and Group 3 (n = 31) comprised patients with proliferative diabetic retinopathy (PDR).

Ophthalmological screening was performed in a specialised clinical setting and included a comprehensive range of standard and advanced techniques. Initial assessments included visometry (best-corrected visual acuity [BCVA]), autorefractometry, non-contact tonometry, and computerised static perimetry. Anterior segment biomicroscopy and gonioscopy were performed to exclude comorbidities. Detailed fundus ophthalmoscopy was conducted under pharmacological mydriasis (using 1% tropicamide) with a Volk SuperField aspheric lens (USA) and a Goldmann three-mirror contact lens. These examinations strictly followed the international Early Treatment Diabetic Retinopathy Study (ETDRS) protocol to ensure diagnostic consistency.

For the objective assessment of clinico-morphological retinal changes, spectral-domain optical coherence tomography (SD-OCT) was utilised. Scans were performed using a 3D OCT-1000 device (Topcon, Japan), with a focus on measuring central retinal thickness (CRT). All retinal complications and stages of diabetic retinopathy were classified in accordance with the International Clinical Diabetic Retinopathy Disease Severity Scale developed by the American Academy of Ophthalmology (AAO, 2002) [1].

The biochemical analysis involved measuring the concentration of soluble L-selectin (sCD62L) in blood serum. Samples were processed using an enzyme-linked immunosorbent assay (ELISA) with Human sL-selectin INSTANT kits (Invitrogen, USA), according to the manufacturer's instructions.

Statistical analysis was performed using IBM SPSS Statistics v. 27.0. The normality of continuous variable distributions was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean (M) ± standard error of the mean (SEM) for normally distributed data, and as median (Me) with interquartile range (Q1–Q3) for non-normally distributed variables; categorical variables are expressed as counts and percentages. Two-group comparisons were per-

Table 1. Clinical and laboratory parameters of the studied groups (M ± SEM)

Parameter	Control group (n=29)	Main group (n=95)	p
BCVA, decimal units	0.95±0.05	0.60±0.03	< 0.01
CRT (SD-OCT), μm	265±8.4	318±11.2	< 0.05
L-selectin, ng/mL	12.5±3.5	31.2±8.6	< 0.001

Source: compiled by the authors of this study

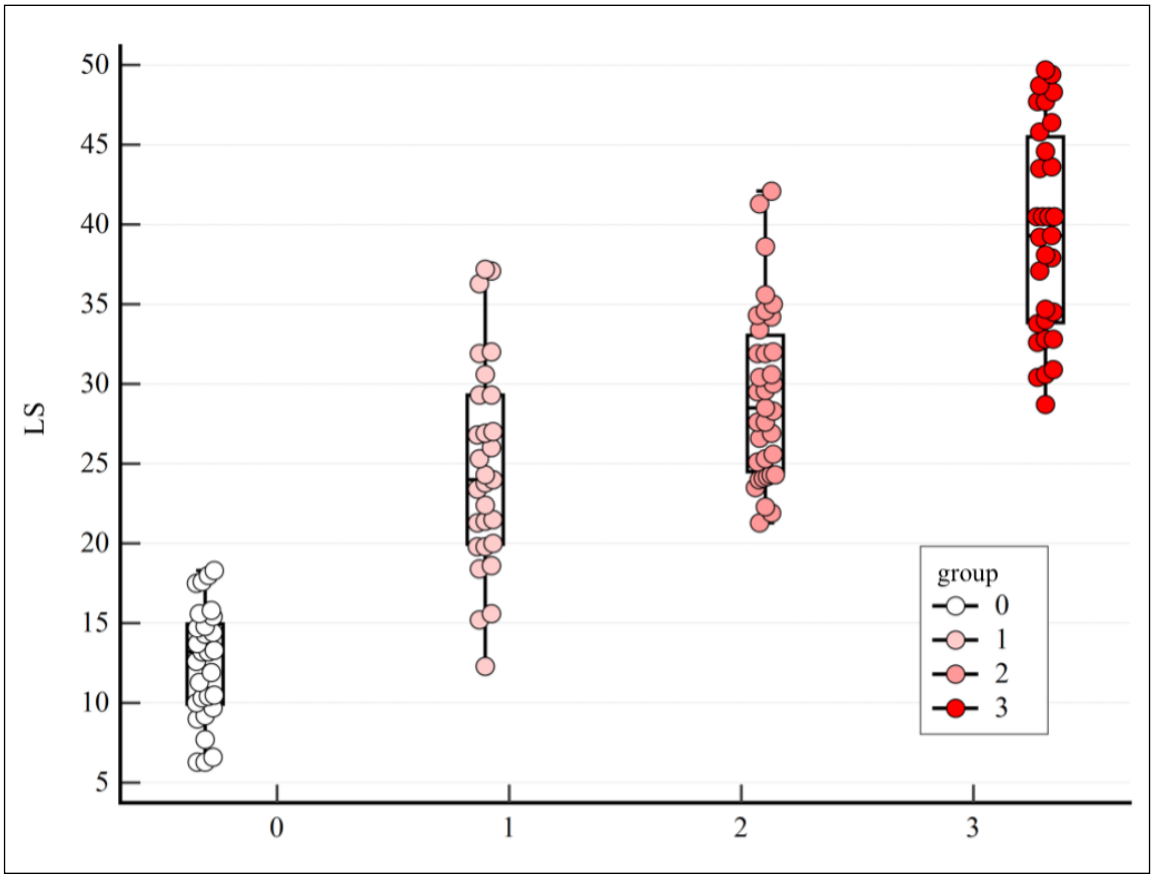


Fig. 1. The L-selectin levels (ng/ml) across the studied groups (box-and-whisker plot with dot plot). Group 0: controls; group 1: mild NPDR; group 2: moderate/severe NPDR; group 3: PDR. Pairwise comparisons: $p_{0-1} < 0.001$; $p_{0-2} < 0.001$; $p_{0-3} < 0.001$; $p_{1-2} = 0.006$; $p_{1-3} < 0.001$; $p_{2-3} = 0.004$
Picture taken by the authors

formed using Student's t-test or the Mann–Whitney U test, as appropriate. Comparisons among four groups were made using one-way ANOVA with Scheffé post hoc testing or the Kruskal–Wallis test with post hoc Mann–Whitney U tests for pairwise comparisons. Correlations were assessed using Spearman's coefficient (rs). A two-sided p-value < 0.05 was considered statistically significant (with Bonferroni correction applied).

ETHICS

The researchers followed all protocols and procedures required by the Biomedical Research Ethics Committee and conformed to the Ukrainian legislation on health care, the Declaration of Helsinki (2000), and European Society Directive 86/609 on human participation in biomedical research, ensuring adherence to all standards for the adequate protection and well-being of participants. Written informed consent was obtained from all participants (or their legal representatives) prior to inclusion in the study, following a full explanation of the study's nature, aims, and potential risks. The study protocol and the informed consent form were reviewed and officially approved by the local Ethics Committee.

FRAMEWORK

The work was carried out at the Department of Postgraduate Ophthalmology and Optometry of the Institute of Postgraduate Education of the Bogomolets

Table 2. The correlations of L-selectin level with certain clinical and clinico-morphological parameters (total cohort, n=124)

Parameters	Correlation coefficient (rs)	Significance (p)
HbA1c, %	0.816	< 0.001
Fasting glucose	0.526	< 0.001
CRT	0.467	0.002
BCVA	–0.412	0.004

Source: compiled by the authors of this study

National Medical University and is a fragment of the department-initiated research project «Theoretical and practical aspects of improving clinical and experimental methods of diagnosis, treatment and prevention of diseases and injuries of the organ of vision and their complications» (state registration number 0123U104207; term: 2023-2026).

RESULTS

Analysis of demographic indicators confirmed the comparability of the main and control groups. No statistically significant difference was found in mean age (66.8 ± 0.75 years vs. 64.2 ±1.20 years; p =0.089). Gender distribution was homogeneous: the study cohort included 65 women (68.4%) and 30 men (31.6%), while the control group included 16 women (55.2%) and 13 men (44.8%) (p = 0.265).

Significant functional and structural alterations were observed in the T2DM cohort compared to healthy controls (Table 1).

Serum concentrations of L-selectin exhibited a distinct, stepwise upward trend that directly correlated with the clinical severity of DR (Fig. 1).

Thus, in early manifestations (mild NPDR), serum L-selectin levels showed a 2.0-fold increase (Me = 24.7; Q1–Q3: 20.4–29.0 ng/mL) compared with the control group (Me = 12.5; Q1–Q3: 10.1–14.9 ng/mL; p < 0.001). As the pathology progressed to moderate and severe NPDR, the concentration increased 2.3-fold (Me = 28.5; Q1–Q3: 24.9–32.1 ng/mL; p < 0.001 vs. control group). The proliferative stage (PDR) was characterised by peak values — 3.2 times higher than in the control group (Me = 39.5; Q1–Q3: 35.1–43.9 ng/mL; p < 0.001 vs. control group).

The correlation analysis revealed a strong positive association between sCD62L and HbA1c levels (rs = 0.816, p < 0.001). Additionally, moderate positive correlations were found with fasting glucose (rs = 0.526, p < 0.001) and CRT (rs = 0.467, p = 0.002), while a moderate negative correlation was identified with BCVA (rs = –0.412, p = 0.004), indicating that higher biomarker levels are associated with functional visual decline (Table 2).

DISCUSSION

Our study identified a significant 2.5-fold increase in serum sCD62L levels in the total T2DM cohort (n = 95) compared with healthy controls, confirming the systemic nature of inflammatory responses in diabetic microangiopathy [1, 2]. These results demonstrate a strong correspondence with the foundational data of Karadayi et al. [8], supporting the universal nature of leukocyte activation mechanisms in retinal damage, regardless of regional characteristics of the clinical sample [8]. Such stability of the indicator underscores the role of L-selectin as a reliable marker of systemic inflammation in diabetes mellitus [1, 8].

The pathogenetic significance of elevated sCD62L is explained by the mechanism of intensive "shedding" — the proteolytic cleavage of the molecule from the surface of activated immune cells. According to studies by A. Ivetić (2018) [3], this process, mediated by metalloproteinases such as ADAM17, is a critical step in the initiation of leukocyte–endothelial interaction, particularly the "rolling" phase. High concentrations of the soluble form reflect hyperactivation of neutrophils and lymphocytes, facilitating their subsequent diapedesis through the blood-retinal barrier into retinal tissues [4, 5, 7].

The strong positive correlation established in this work between L-selectin levels and HbA1c identifies prolonged hyperglycaemia as a primary trigger for shedding of adhesion molecules [6, 7]. This inflammatory cascade disrupts the integrity of endothelial tight junctions, leading to plasma exudation and formation of macular oedema [5, 10]. The direct correlation with CRT according to SD-OCT data provides morphological evidence that sCD62L acts as a key mediator of structural macular changes during diabetes progression [10].

In contrast to earlier theories regarding potential receptor exhaustion, our results demonstrate a stepwise increase in sCD62L corresponding to the severity of DR, which aligns with contemporary data by Siddiqui et al. (2023) [7]. This confirms the marker's potential as a prognostic factor for the transition of the disease into advanced, vision-threatening stages [9, 10]. While the study design does not allow definitive establishment of causal links, the obtained data

open prospects for the development of targeted therapies aimed at inhibiting adhesion molecules to prevent irreversible complications of T2DM [5, 7].

LIMITATIONS OF THE STUDY

Despite the significant findings, several limitations should be acknowledged. First, the cross-sectional design of the study allows identification of associations but precludes definitive establishment of causal relationships between sCD62L levels and DR progression. Second, the sample size, while sufficient for statistical analysis, was limited to a single clinical centre; larger multicentre longitudinal studies are required to validate these biomarkers across diverse populations. Third, the current analysis focused on a single adhesion molecule; future research incorporating a broader panel of inflammatory and angiogenic markers could provide a more comprehensive understanding of molecular interactions in the diabetic retina. Finally, the study did not evaluate dynamic changes in L-selectin levels following therapeutic interventions, such as anti-VEGF therapy or laser photocoagulation, which remains a promising direction for further investigation.

CONCLUSIONS

1. Serum L-selectin levels increase stepwise with DR severity, reflecting intensified systemic leukocyte-endothelial activation.
2. Positive correlations with glycemic markers identify chronic hyperglycemia as a primary driver of systemic L-selectin shedding.
3. Elevated sCD62L levels correlate with increased CRT, supporting its role in blood-retinal barrier disruption.
4. Serum L-selectin serves as a potential supplementary biomarker for identifying patients at risk for advanced microvascular complications.

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ORIGINAL ARTICLE

CONTENTS

Genetic, clinical, and laboratory profile of pediatric patients with familial mediterranean fever at Duhok City

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ABSTRACT

Aim: To describe the clinical picture, laboratory findings, and MEFV mutation profile of FMF children in Duhok, Iraq, and to examine the influence of consanguinity on genotype-phenotype relationships.

Materials and Methods: Cross-sectional study (Jan 2017-Jan 2025) of 92 children ≤16 years meeting Tel-Hashomer criteria and with molecularly confirmed MEFV mutations. Data on demographics, family history, consanguinity, symptoms, attack characteristics, acute-phase reactants, genotype, colchicine response, and complications were collected retrospectively and prospectively. Analyses used SPSS v27 (chi-square, t-test, logistic regression; $P<0.05$.

Results: Mean age 8 y; 65% male; parental consanguinity 79%; positive family history 63%. Fever (100%) and abdominal pain 85% were universal; arthritis 46.7% and growth retardation 61% were notably high. Mean attack labs: WBC 12.9×10^9/L, ESR 50 mm/h, CRP 63 mg/L. MEFV alleles: E148Q 38%, M694V (22%), V726A (15%), M680I (12%). Exon-10 homo/compound heterozygotes (M694V/M680I) were linked to earlier onset, more frequent/longer attacks and higher ESR/CRP (OR≈3, $p<0.001$); simple E148Q carriers had milder disease. Colchicine was effective in 94.6% of patients; no amyloidosis was observed. Consanguinity independently predicted the presence of two pathogenic exon-10 alleles $p=0.02$.

Conclusions: Duhok's pediatric FMF cohort shows classic fever/serositis but higher arthritis, growth failure, and an unusual predominance of the low-penetrance E148Q mutation, likely driven by extreme consanguinity. Exon-10 mutations confer a severe phenotype, while colchicine remains highly effective. Targeted genetic counseling and early mutation-guided management are warranted in this high-consanguinity population.

KEY WORDS: pediatric FMF, MEFV mutations, E148Q, M694V, consanguinity, colchicine response

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INTRODUCTION

A genetic autoinflammatory disease, familial Mediterranean fever (FMF) is most common in populations that originated in the Mediterranean region, including Turks, Armenians, Arabs, and Jews [1-3]. It is caused by mutations in the MEFV gene, which is found on chromosome 16p13.3, and has an autosomal recessive inheritance pattern [4]. This gene encodes the regulatory protein pyrin, which is necessary for controlling innate immunological responses [2]. Mutations primarily impair this regulatory mechanism and cause unchecked inflammatory activity through the overproduction of interleukin-1 beta (IL-1β), which manifests clinically as recurrent fever, serositis (e.g., peritonitis, pleuritis, and pericarditis), arthritis, and erysipelas-like skin eruptions. If AA amyloidosis is not identified and treated promptly, patients may suffer from the potentially lethal consequences of the condition [5-6]. In FMF children, the presentation can be very variable-not just between kids, but also by the particular MEFV mutation carried. The most common MEFV variants-M694V, M680I, V726A, and E148Q-are linked with a variety of clinical presentations that differ by ethnicity [7] of special mention is that M694V is frequently found to be linked with a higher risk of AA amyloidosis, more severe and more frequent flares, and earlier occurrence of the disease in life [8-9]. Awareness of the child's mutation pattern in clinical practice facilitates more personalized monitoring and therapy and predicts the course of the condition. Iraqi Kurdistan Region, and here Duhok province, is increasingly burdened by familial Mediterranean fever (FMF) within families, thus it's a new public health problem. One of the key reasons why children are more likely to inherit autosomal recessive diseases such as FMF is increasing consanguineous (closely related) marriage here. In nearby provinces like Sulaymaniyah, tests have already detected a high percentage of Kurdish children with FMF, most of whom had two pathogenic MEFV mutations-same (homozygous) or different (compound heterozygous) [10]. This suggests that there is urgent need of regionally focused and community-based research- both to map the most frequently occurring mutations, as well as the effect of these mutations on

health of children specifically in local settings. Although MEFV mutations have been observed in Kurdish patients in non-Kurdistan countries, we do not yet have any clear, firm information on the most common MEFV mutations among children of Duhok, their frequency and their most common outcomes. This gap should be addressed to ensure that the affected families receive proper treatment, are diagnosed early enough, and their care is better. One has no need to be a rocket scientist to realize that the genetic makeup of FMF among children in Duhok-it is giving children the best opportunity. Determining the most common MEFV mutations in these individuals may help the medics diagnose the disease earlier and more accurately, allowing it to treat the disease early and most importantly prevent the children of the disease against long-lasting effects that could be deadly such as amyloidosis-a sneak thief disease that destroys the kidneys among other organs over a period [11]. The first-line treatment of most children with FMF remains colchicine, and it is not hard to see why: by taking it daily, it could reduce the crippling flare-ups and prevent the deposition of amyloid to occur at all [12-13]. Children are not all identical, although some mutations have been linked to more difficult or severe disease, and under these circumstances, colchicine may be an inadequate treatment by itself. In these children, newer options of IL-1 inhibitors may become a game-changer. This is why it is significant to make customized treatment depending on genetic information. A one-size-fits-all approach will not work when even the disease is different in each kid. Through the correlation of particular mutations with clinical appearance, we can proceed to a proper kind of individualized care: the right treatment, of the right child, at the right time. To fill these gaps in our knowledge and to offer to children FMF in Duhok even better, a significant requirement is the systematic case study which has been verified by genetic tests. Determining the exact genetic mutations and clinical manifestation that occurs in this population, the researchers will be able to design the diagnostic tests and treatment regimens that will be specific to the local conditions. That is, understanding the appearance and functioning of FMF in the children of Duhok will help the doctors to stop relying on the rules that fit all and head to the realm of customized and personalized medicine, which will offer every child the most effective help possible.

AIM

The purpose of this study is to develop a descriptive image of Familial Mediterranean Fever (FMF) in kids in Duhok, the Iraqi Kurdistan. The researcher is interested in knowing exactly how the disease is manifested in this community, what the most widespread MEFV gene mutations is, how that type of mutation in Marriage between relatives affects the mechanism of the inheritance and how it is manifested in children. In the end, the research findings will positively impact the clinical practice. Which would assist doctors in diagnosing FMF at a young age earlier, make individual treatment choices subject to a particular child mutation, and enhance our question-and-answer skills with regard to preventing severe complications such as amyloidosis. The current study considers a guide for improving the long-term outcomes of the children with FMF in the areas.

MATERIALS AND METHODS

STUDY DESIGN

A descriptive Cross sectional design were used, with a point in time snapshot of FMF for children.

STUDY SETTING AND DURATION

The current study was conducted in the Department of Pediatrics at Heevi Pediatrics Teaching Hospital.. Data were collected from pediatric patients who met the study criteria through clinics and medical facilities in Duhok Governorate. To ensure a comprehensive medical overview, follow-up was conducted from January 2017 to January 2025, providing an eight-year dataset that offered a more accurate basis for characterizing familial Mediterranean fever and analyzing temporal trends.

STUDY POPULATION

INCLUSION CRITERIA

Bestowing to the Tel-Hashomer diagnostic framework, age children 2 and 16 years, diagnosed with FMF clinically and genetically. Tel-Hashomer Criteria Overview [14].

MAJOR CLINICAL CRITERIA

- Generalized peritonitis
- Unilateral pleuritis or pericarditis
- Ankle, knee, or hip monoarticular arthritis
- Just a fever

MINOR CLINICAL CRITERIA

- Frequent episodes of fever
- An erythematous rash that resembles erysipelas, especially on the lower limbs
- A first-degree relative's verified FMF diagnosis

DIAGNOSTIC CLASSIFICATION

– Definitive FMF: one major criterion in conjunction with two minor criteria. or Two major criteria
– Probable FMF: One major with one minor criterion.
– Possible FMF: One major criterion or two minor ones
Only patients who were admitted to hospital wards during the study period or who were actively monitored at outpatient clinics were included.

EXCLUSION CRITERIA

– Patients with unconfirmed FMF diagnoses or insufficient clinical records.
– Cases of periodic fever illness with secondary or alternative causes.

SAMPLE SELECTION

Largest cohort that meets inclusion criteria for diagnosis as verified by molecular (gene-based) testing.

DATA COLLECTION METHODS

Both prospective and retrospective data were collected:
– Examining past medical records is the retrospective component.
– Direct clinical evaluation and structured interviews with patients and/or guardians comprise the prospective component.

COLLECTED VARIABLES INCLUDE

– Age, sex, ethnic origin, and family history of FMF are examples of demographic traits.
– Clinical parameters include age at disease onset, frequency and duration of episodes, and symptomatology (fever, chest and abdominal pain, joint involvement, and dermatologic manifestations).
– Genetic analysis: Genetic analysis revealed specific MEFV mutations, such as M694V, V726A, and others.
– Regarding treatment data: Attention was paid to the use of colchicine, as well as the effectiveness of the treatment, in addition to levels of adherence.
– Complications include Long-term medical conditions or complications related to the disease.

DATA COLLECTION TOOLS

– A meticulously designed and structured questionnaire for future documentation.
– A complete and comprehensive review of the hospital's electronic and paper records regarding data retrieval.

ETHICAL CONSIDERATIONS

The regional ethics committee and the Duhok Directorate of Health were used to get ethical approval. Informed consent of all the minors involved was obtained through their legal guardians. Every process followed the international research ethics protocols and had sufficiently strong measures to ensure confidentiality and privacy of data of the participants.

DATA ANALYSIS STRATEGY

– Analyzed all the data using SPSS (version 27).
– Used descriptive statistics to summarize the main demographic and clinical information.
– Applied statistical analyses (chi-square, t-tests, and logistic regression) to investigate possible correlations between genetic mutations and the degree of the disease or disease complications.
– Finally, we conducted a narrowed-down analysis to determine the impact of certain MEFV gene variants on the clinical symptoms of the patients.

ANTICIPATED LIMITATIONS

– Potential for recall bias in retrospective data.
– Limited access to comprehensive genetic screening, which may restrict full mutation profiling.
– The small sample size may be a constraint to the external validity and the generalization of results.

RESULTS

The age of study sample ranged between 2-16 years, with mean age about 8 years, SD=3.57, and regarding to the sex, researcher found nearly two-thirds 65.2% were males while the female account 34% of the sample (Table 1).

Parental consanguinity was reported in a rather impressive majority 79.3-1 of participants, and this fact is remarkable in light of the genetic etiology of Familial Mediterranean Fever (FMF). Similarly, 63% of them had a positive family history, which supports the hereditary nature of the disorder. In the religious membership, the dominant majority 91.3% was Muslim, with Ezediyan 6.5% and Christian 2.2% communities represented in the minority. The urban-rural ratio of incidence displayed a marginally higher prevalence rate of FMF in urban areas 66.3 compared to rural areas 33.7.

Table 2 shows, all reported cases 100% had a clinical manifestation of fever, which supports the importance of this criterion as a key diagnostic finding in Familial Mediterranean Fever. The second most common symptom was the abdominal pain, which was experienced

Table 1. Demographic characteristic of FMF patient

Variable		Frequency	Percent
Age		2-16 years Mean 8.02 years Std. deviation 3.57	
Gender	Male	60	65.2
	Female	32	34.8
Consanguinity	Yes	73	79.3
	No	19	20.7
Family history	Positive	58	63.0
	Negative	34	37.0
Religions	Muslims	84	91.3
	Christian	2	2.2
	Ezediyans	6	6.5
Residence	Urban	61	66.3
	Rural	31	33.7

Source: Compiled by the authors of this study

Table 2. Clinical characteristics of FMF patient

Variable		Frequency	Percent
Fever	Yes	92	100.0
Abdominal pain	Yes	78	84.8
	No	14	15.2
Arthritis	Yes	43	46.7
	No	49	53.3
Appetite state	Normal	38	41.3
	Decreased	54	58.7
Stunted growth	Yes	56	60.9
	No	36	39.1
Chest pain	Yes	3	3.3
	No	89	96.7
Skin lesion	No	92	100.0
Myalgia	Yes	29	31.5
	No	63	68.5
Headache	Yes	9	9.8
	No	83	90.2

Source: Compiled by the authors of this study

by 84.8% of the group of patients. The presence of arthritis was reported as a joint involvement in close to half of the subjects 46.7% which suggests a frequent extra-abdominal manifestation. Appetite change in the sample under investigation was observed in most of them; 58.7% of the total respondents reported appetite decrease and 41.3% reported normal eating. The other important problem was stunted growth, which was found in over 60% of patients, which is plausibly suggestive of chronic inflammatory conditions and nutritional inadequacies. Less common symptoms included chest pains 3.3%, myalgia 31.5%, and headaches 9.8%. Markedly, there was no patient who had skin lesions, thus suggesting that they are rare in this specific cohort.

Table 3 demonstrate Laboratory investigations refried high rate in inflammatory biomarkers, the average white blood cell (WBC) count was 12.91×10^9/L (SD=3.04) which is agreeable with an inflammatory process. The levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were also increased, with a mean of 50.25 mm/hr. (SD-11.57) and 63.31 mg/l (SD-20.11) respectively. These biological markers indicate the inflammatory load of the body in the whole family with Mediterranean fever (FMF).

Table 3. Laboratory characteristics of FMF patient

Value	Total	Minimum	Maximum	Mean	Std. deviation
WBC	92	6.00	22.00	12.9130	3.04058
ESR	92	29.00	70.00	50.2500	11.56883
CRP	92	24.00	112.00	63.3152	20.11392

Source: Compiled by the authors of this study

Table 4. Duration and frequency of FMF attacks per day and month respectively

Duration /hours /day	Mean	Std. deviation	Percent
(2-7) hours/day	3.77	1.46	
	Frequency/month	**No.**	
Frequency of FMF	1 attack/month	66	71.7
	2 attack/month	21	22.8
	3 attack/month	5	5.4

Source: Compiled by the authors of this study

Table 5. Distribution of MEFV gene mutations among FMF patients

Gene mutation	Gene type	Number	Total
Heterozygote	E148Q	18	46(50%)
	M694V	14	
	V726A	10	
	M680I	3	
	A744S	1	
Homozygote	M694V-M694V	6	16(17.4%)
	E148Q-E148Q	3	
	M680I-M680I	2	
	V726A-V726A	2	
	P396S-P396S	2	
	M694I-M694I	1	
Compound heterozygote	E148Q-M680I	4	24(26.1%)
	M680I-V726A	4	
	F4726A-E148Q	3	
	V726A-R761H	3	
	E148Q-G304R	3	
	M680I- T267I	3	
	M694V-K695R	2	
	R761H-M694V	2	
Complex Heterozygote	M694V-M680I-M694I-E148Q	3	6(6.5%)
	E148Q-P369S-M694V-V726A-M680I	2	
	M694V-M691V-M694I-V726A	1	

Source: Compiled by the authors of this study

The FMF attacks varied in length, typically lasting between two and seven hours a day, with an average duration of about 3.8 hours (SD=1.46). Most children 71.7% experienced these painful episodes roughly once a month, while others had them a bit more often—about 22.8% reported two attacks per month, and a smaller group 5.4% experienced as many as three monthly episodes (Table 4).

Genetic testing revealed a heterogeneous group of MEFV variants. The most common genotype in all identified alleles was heterozygous mutations, comprising 50% of all the observed allele with E148Q being the most frequent followed by M694V and V726A. The homozygous genotypes were found in 17.4% of the cohort of which M694V-M694V arrangement was the dominant homozygous form (Table 5).

Table 6. Joint involvement in FMF patient

Joints	Numbers	Percent
KNEE	39	42.4
Elbow	1	1.1
Ankles	5	5.4
both knee	34	37.0
Wrist	5	5.4
Poly	8	8.7

Source: Compiled by the authors of this study

The genetic complexity of familial Mediterranean fever was emphasized as the proportion of 26.1% of the total cases was compound heterozygosity. A subgroup of patients (6.5 percent) displayed complex heterozygosity, which was indicated by the presence of multiple allelic variations thus enhancing the subtle genotype-phenotype relationship that is relevant in the pathogenesis of FMF.

Table 6 showed that joint symptoms were frequent, with the knee joint being the most affected 42.4%. Other joints, such as the ankle and wrist, were less frequently involved 5.4%, and multi-joint involvement was noted in 8.7% of patients. These findings confirm that the musculoskeletal burden is significant for patients with familial Mediterranean fever.

Statistical correlations revealed significant associations between genotype and many clinical and laboratory markers (Table 7). Factors such as sex, family history, kinship, and residential background showed a strong influence on the negative phenotype P<0.0001. Similarly, the 40 markers (C-reactive protein, white blood cell count, and red blood cell clotting) and symptoms such as fever, arthritis, and abdominal pain were associated with specific genotypes. Interestingly, skin lesions and pain showed little to no association, suggesting they may be independent of the variability in this category. Attack duration and frequency also showed a strong association with the radial phenotype, indicating a significant influence on disease susceptibility.

The standard of care for FMF is colchicine therapy, which was well received by the majority of patients

Table 7. Correlation statistically between different variant clinical and laboratory with FMF genotype

No.	Variable	T test	P-value
1	gender - genotype	-4.524	0.0001
2	consanguinity - genotype	-6.208	0.0001
3	Family history - genotype	-4.377	0.0001
4	religion - genotype	-6.031	0.0001
5	residences - genotype	-4.506	0.0001
6	WBC - genotype	33.958	0.0001
7	ESR - genotype	38.863	0.0001
8	CRP - genotype	29.099	0.0001
9	FEVER - genotype	-8.461	0.0001
10	Abdominal pain - genotype	-6.516	0.0001
11	Arthritis - genotype	-3.032	0.003
12	State of appetite - genotype	-2.569	0.012
13	Stunted growth - genotype	-4.060	0.0001
14	Skin lesion- genotype	1.032	0.305
15	Joint involvement - genotype	4.790	0.0001
16	Chest pain - genotype	.732	0.466
17	Myalgia - genotype	-1.809	0.074
18	Frequency of attack- genotype	-4.338	0.0001
19	Duration of attack - genotype	9.777	0.0001

Source: Compiled by the authors of this study

Table 8. Follow up and response to treatment

Response to colchicine	Number	Percent
Good	87	94.6
Not well	5	5.4
Ultrasound finding no documented amyloidosis		

Source: Compiled by the authors of this study

(94.6%). The suboptimal response rate was only 5.4%. Crucially, no cases had ultrasound evidence of amyloidosis, a serious FMF complication, suggesting that the disease was effectively managed and that early intervention may have been possible (Table 8).

DISCUSSION

In similarity to another studies Turkey and Iraq, our pediatric patients with FMF, had mean of age 8.02 years [1], for example, similar to other Kurdish series in Iraq and Turkey, our pediatric FMF cohort had a mean age of 8.02 years. Eastern Turkish child had a mean age about 7.7 years with a ratio related sex 1:1, while Sulaymaniyah child had a mean age of 7.8 years with male prevalence ~64% [15]. In corresponding the line, some reports from Iraq, the researcher institute a greater male bias 65% male. According to [15] the group's parental consanguinity was a remarkable 79%, significantly higher than the rates in Turkey ~24% and even other Iraqi/Kurdish cohorts ~33% [1]. Similarly, a positive family history 63% was more common than reported elsewhere (e.g. 47% in [1]. These divergences likely reflect local marriage practices and genetic pooling in Duhok. Nearly all our patients were Muslim 91%, mirroring regional demographics; such details were not reported in most FMF series but align with the ethnic composition of northern Iraq. Two-thirds of our cases were urban residents. In sum, our demographic profile is broadly consistent with nearby regions, except for the much higher consanguinity and family history, which may amplify autosomal recessive FMF transmission in this population. The clinical presentation in Duhok pediatric FMF resembled that of other Middle Eastern cohorts. All our patients had recurrent fever 100% and most had abdominal pain ~85%, paralleling Turkish (fever ~85%, abdominal pain ~95%) [16]. Kurdish-Iraqi reports (95–100% fever, 75–80% pain). However, some manifestations varied. We found a high rate of arthritis 46.7%, substantially according to [15] more than the ~10% reported in Turkish children though similar to the 45% with arthralgia in a small Iraqi Kurdish series [17]. This may reflect younger age or ethnic differences (arthritis tends to be less common in Arab and Turk populations but can be high in pediatric-onset FMF). Other symptoms in our cohort – myalgia 32%, headache 10%, chest pain 3%, anorexia 59% and notably 61% with stunted growth – were within or above reported ranges. For example, according to [4, 16] the symptoms as anorexia/fatigue were common in an Iranian registry 64% anorexia, and [17] has been reported in about 5% of children with FMF in Turkey. Notably, we observed no erysipelas-like skin rash, whereas Turkish and Kurdish series report rash in 3–15% of patients. This absence according to [16]; it may be due to genetic or environmental factors; skin lesions in FMF often associate with the M694V mutation (which was less prevalent here). In summary, our patients' symptoms (fever and serositis) are largely consistent with FMF elsewhere, but the higher arthritis and growth failure rates suggest possible influences of genetic background, nutritional status, or delayed diagnosis in Duhok. As expected during FMF attacks, our patients showed elevated inflammatory markers (mean WBC~12.9×10^9/L, ESR~50 mm/h, CRP~63 mg/L). These findings align with [4] the pattern of acute-phase reactant elevation reported in FMF cohorts worldwide. For instance, [16] noted leukocytosis and raised ESR/CRP during attacks in Turkish children. We did not observe any routine laboratory anomaly unique to our group. The degree of inflammation (ESR/CRP levels) was comparable to published pediatric series as reported in previous studies [1, 16], suggesting similar attack intensity. Few studies quantify these values in children by region, but our results are in line with general FMF literature: all attacks produce pronounced Neutrophilic inflammation. No renal proteinuria or amyloiduria was found, consistent with the lack of amyloidosis in clinical follow-up. Thus, laboratory profiles in Duhok's FMF children are broadly concordant with findings from Turkey, reflecting the expected systemic inflammation of FMF. The MEFV mutation spectrum in our cohort both mirrors and diverges from other populations. In Duhok children, the E148Q variant was the single most frequent allele, followed by M694V, V726A and M680I. In contrast, [16] report that the large Turkish series typically find M694V as the top allele (e.g. ~27% in Eastern Anatolia), with E148Q often second as a common heterozygote 38% of heterozygotes had E148Q). Our distribution resembles the Kurdish Sulaymaniyah data, where E148Q and M680I were also very common [1], though even there M694V was more frequent than in Duhok. In [16] authors found the Iranian FMF patients typically carry M694V (~20%) at higher frequency than E148Q (~10%) opposite to our pattern. Similarly, as [18] and [19] report that the Armenian and many Middle Eastern cohorts are dominated by M694V (often 50–75%), in addition, [16] found the Italian patients also show M694V > E148Q > M680I. Thus, the prominence of E148Q in our sample is unusual and may reflect local ancestry (western Iranian Kurdish influences or high inbreeding can enrich particular alleles). Ethnic admixture likely explains these differences. Notably, population data show that Ashkenazi Jews (Israel) have high E148Q, whereas non-Ashkenazi Jews and Armenians carry mostly M694V. Our findings align more with the former pattern. In sum, while the presence of major FMF mutations (E148Q, M694V, V726A, and M680I) is consistent with global observations [4, 15, 18], the relative frequencies diverge: Duhok children have excess E148Q and fewer classic exon-10 mutations. These discrepancies likely stem from genetic background (found-

er effects, consanguinity) and possibly under-diagnosis of mild alleles in neighboring populations. We found significant associations between genotype and several disease features (Table 7). Specifically, severe genotypes (e.g. homozygous or compound heterozygous for exon 10 mutations) tended to have earlier onset, more frequent and longer attacks, and higher inflammatory markers, while milder genotypes (such as simple E148Q carriers) had comparatively attenuated disease. This pattern accords with the literature. For example, M694V homozygosis is well known to portend a severe FMF phenotype and amyloidosis risk, and even asymptomatic M694V homozygotes are often advised to be treated. The [20], similarly reported that M694V homozygotes have incomplete response to colchicine and more severe courses. In our data, patients with two exon-10 mutations had higher attack frequency and duration $P<0.0001$, mirroring such reports. Conversely, the E148Q variant, considered a low-penetrance allele, was over-represented in patients with milder attacks. The international FMF registries also show that M694V and M680I (exon 10) drive more severe disease, whereas E148Q and V726A tend to modulate or attenuate symptoms. Thus, our genotype-phenotype correlations are consistent with these global trends. Environmental or healthcare factors might further shape severity for instance, frequent respiratory or gastrointestinal infections (not measured) could trigger attacks but the strong statistical links we observed largely reflect the inherent impact of MEFV mutation type. Our treatment outcomes were excellent: 94.6% of patients responded well to colchicine, and none developed amyloidosis on follow-up. This closely matches the high efficacy reported elsewhere. In Baghdad, researcher found that all 23 FMF patients (adults) responded to colchicine with complete attack suppression and no amyloid complications. In Kurdish children, [17] noted only ~5% colchicine resistance and also no amyloidosis. Likewise, most Turkish pediatric series report >90% good control on colchicine. The consistently high remission rates likely reflect similar disease mechanisms and the universal use of colchicine prophylaxis across regions. The small fraction of non-responders (5.4% in our cohort) is within the 2–10% range described in major FMF series. Factors such as M694V homozygosis have been linked to colchicine resistance, but we did not find a significant difference in response by genotype - likely due to our sample size. Finally, we attribute the absence of amyloidosis to both effective colchicine uses and possibly a lower intrinsic risk in this population, as was suggested in Iraqi Arabs. In summary, our treatment response pattern is consistent with global experience: colchicine effectively prevents attacks and amyloidosis in the vast majority of FMF children [21] (Duman et al., 2025) and healthcare access in Duhok appears sufficient to maintain adherence.

CONCLUSIONS

A higher male preponderance, extreme consanguinity, and a noticeably high prevalence of the E148Q MEFV variation are among the distinctive features of this study on a juvenile FMF cohort from Duhok that show similarities with regional counterparts. Despite some inconsistencies, certain clinical findings, such as the high prevalence of arthritis, are consistent with other data from the Middle East. No unusual test results were recorded, and inflammatory markers reflected global patterns during the attacks. In line with broader research on FMF, genotype-phenotype associations exposed that severe genotypes were associated with more severe sickness. Accurate treatment consequences, including a 94.6% response to colchicine with no amyloidosis, demonstrated fruitful management performances. All things well thought-out, these results improve knowledge of FMF in a variety of groups and bolster the effectiveness of up-to-date therapeutic modalities.

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ORIGINAL ARTICLE

CONTENTS

Prevalence and structure of periodontal diseases in the Ukrainian population based on the AAP/EFP 2017 classification

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ABSTRACT

Aim: To determine the prevalence and structure of periodontal diseases among the population of Ukraine using the AAP/EFP 2017 Classification.

Materials and Methods: A retrospective analysis of electronic outpatient medical charts of dental patients aged 25 to 75 years was conducted; the patients were divided into 3 groups depending on age. According to the data contained in the charts, each patient was diagnosed according to the AAP/EFP 2017 Classification. Statistical methods were used to determine the associations between age, gender and periodontal tissue condition, prevalence of inflammation, stage and grade of periodontitis.

Results: There were 12.8% of patients with intact periodontal tissues, 54.4% of patients were diagnosed with gingivitis, and 32.8% of patients were diagnosed with periodontitis. The most common diagnosis among patients with periodontitis was generalized periodontitis of stage II, grade B (25.9%). Statistically significant relationships were found between age and the presence of periodontal pathology, its prevalence, stage and grade of periodontitis. In addition, associations between gender and the condition of periodontal tissues and the stage of periodontitis were found.

Conclusions: In patients of different age groups and genders, gingivitis was the most common diagnosis, and generalized moderate form prevailed in the structure of periodontitis. Age and gender affect the risk of occurrence and clinical course of periodontal diseases. The use of AAP/EFP 2017 Classification in clinical practice provides an individualized approach to treatment planning for patients with various periodontal tissue lesions.

KEY WORDS: risk factors, periodontitis, epidemiology, gingivitis, age distribution, AAP/EFP 2017 Classification

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INTRODUCTION

Periodontal tissue pathologies remain an important group of diseases that significantly affect the quality of life of patients of all age groups. There are numerous classifications that attempt to systematize all possible variants of periodontal lesions according to various criteria, including the severity of the clinical course, prevalence, pathomorphological features, etc. At the same time, the inconsistency of these criteria in different classifications leads to inconsistent results of epidemiological studies and a lack of clear understanding of the global burden of disease and the need for treatment of such patients [1].

In Ukraine, the classification of periodontal tissue diseases by M. F. Danilevsky is widely used [2, 3]. The main peculiarity of this classification is the differentiation of such diseases as localized periodontitis, generalized periodontitis and periodontosis into distinct nosological forms. This classification did not consider the intensity of periodontitis progression, and the criteria for determining the severity were the depth of periodontal pockets, which varied significantly from patient to patient depending on the severity of gingival edema, and radiographic bone resorption, which could also be assessed ambiguously, considering the angle of the radiographic tube relative to the film or the radiovisiograph sensor, the skills of the radiologist, the level of interpretation of radiographs by the dentist.

However, since 1999, the Armitage classification of inflammatory periodontal diseases has been widely used worldwide, which included four forms: necrotizing, chronic, aggressive, and periodontitis as a manifestation of systemic diseases, each of which had localized and generalized forms, while such a disease as periodontosis was not distinguished at all [4]. Most of the discussions were devoted to the differential diagnosis of aggressive and chronic forms of pathology, as there were no clear, reliable criteria. In addition, the course of the diseases could change over time, which, consequently, changed the diagnosis and required a change in treatment strategy. The use of these unclear criteria in clinical and scientific work made it difficult to

apply this classification, which led to the development and implementation of a new one.

Currently, the international community recognizes the classification of Periodontal and Peri-implant Diseases and Conditions, approved at the consensus congress of the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) in 2017 (AAP/EFP 2017 Classification) [4, 5]. During its approval, the absence of significant differences in the pathophysiology of aggressive and chronic forms of periodontitis was recognized, a gradation of stages and grades of periodontal tissue damage was proposed, clear criteria for diagnosing periodontal diseases and healthy periodontal condition were given, and the condition of peri-implant tissues was first considered [4].

In the context of mass migration of the population, it is important to match the accepted nosological forms of diseases among dentists from different countries in order to unify diagnostic criteria and approaches to the treatment and prevention of such pathologies. In addition, the use of a standardized classification of diseases contributes to the development of international scientific research on epidemiological indicators, specific clinical features of the course, effectiveness of various methods of treatment and prevention of periodontal pathology.

Currently, there are no prevalence rates of different stages and grades of periodontitis in the population of Ukraine according to the AAP/EFP 2017 Classification. Thus, the introduction of a modern classification of periodontal diseases in the country will allow to integrate the domestic field of periodontology into the global context, to supplement epidemiological knowledge on the prevalence of periodontal diseases in the region and to compare the effectiveness of the use of different criteria for classifying diseases.

AIM

To determine the prevalence and structure of periodontal diseases among patients of different age groups, considering gender differences and using the AAP/EFP 2017 Classification.

MATERIALS AND METHODS

A retrospective analysis of 3200 electronic dental charts of patients aged 25 to 75 years (1510 men and 1690 women) who visited the periodontal department of the Municipal Non-Profit Enterprise "City Dental Clinic" in Rivne, Ukraine, during 2024 was conducted. The selected patient charts were organized using the Cliniccards software, which contains tabs for periodontal chart and periodontal screening test with a description of the patient's periodontal status. Inclusion criteria were a detailed description of the patient's history, including existing systemic diseases, a correctly completed periodontal chart, the presence of at least four pairs of antagonist teeth. The study did not include medical records of people with complete absence of teeth, patients whose dentition was restored using implants, charts with incomplete periodontal examination results and in the absence of X-ray results.

The analyzed outpatient charts were divided into 3 groups depending on the age of the patients. Group I included medical records of 929 patients (404 men and 525 women) aged 25 to 44 years, Group II included 1632 patients (821 men and 811 women) aged 45 to 60 years, and Group III included 639 patients (285 men and 354 women) aged 61 to 75 years. In each periodontal chart, the clinical attachment loss, probing depths, and the number of areas with bleeding on probing were determined. We also studied the degree of radiological bone resorption, the furcation involvement, mobility and number of teeth, the need for comprehensive dental rehabilitation due to occlusal plane deformities, alveolar process defects, and other factors that required the involvement of related professionals to treat patients and determine the stage of periodontitis. Smoking and diabetes mellitus were considered modifying factors that influenced the grade of periodontitis progression. These parameters were entered into a Microsoft Excel spreadsheet for further analysis.

Based on the data obtained from the medical records, each patient was diagnosed according to the AAP/EFP 2017 Classification. The results were presented in absolute numbers and percentages for each age group of patients, considering their gender differences. Pearson's chi-squared test was used to determine the relationship between gender, age of patients and the nosological form, prevalence, stage and grade of the disease. Statistical processing of the results was performed using STATISTICA 12 (StatSoft Inc., USA). The relationship was considered statistically significant at $p<0.05$.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

RESULTS

According to the analyzed patient charts, the following data were obtained on the prevalence of periodontal diseases and conditions in patients of different age groups (Table 1).

Table 1. Prevalence of periodontal diseases and conditions among Ukrainian residents of different ages and genders

Condition of periodontal tissues	Group I		Group II		Group III		Total	
	1	2	1	2	1	2	1	2
Healthy periodontium	129 (31.9)	97 (18.5)	98 (11.9)	59 (7.3)	16 (5.6)	9 (2.6)	243 (16.1)	165 (9.8)
Gingivitis	158 (39.1)	299 (56.9)	573 (69.8)	594 (73.2)	80 (28.1)	38 (10.7)	811 (53.7)	931 (55.1)
Periodontitis	117 (29.0)	129 (24.6)	150 (18.3)	158 (19.5)	189 (66.3)	307 (86.7)	456 (30.2)	594 (35.1)
Total	404 (100)	525 (100)	821 (100)	811 (100)	285 (100)	354 (100)	1510 (100)	1690 (100)

Note: 1 – number of men, abs. (%), 2 – number of women, abs. (%)
Source: compiled by the authors of this study

Table 2. Distribution of periodontitis stages among Ukrainian residents of different ages and genders

Stage of periodontitis	Group I		Group II		Group III		Total	
	1	2	1	2	1	2	1	2
I	35 (29.9)	45 (34.9)	15 (10.0)	24 (15.2)	9 (4.8)	25 (8.1)	59 (12.9)	94 (15.8)
II	58 (49.6)	65 (50.4)	68 (45.3)	79 (50.0)	66 (34.9)	138 (44.9)	192 (42.1)	282 (47.5)
III	18 (15.4)	13 (10.1)	45 (30.0)	39 (24.7)	76 (40.2)	107 (34.9)	139 (30.5)	159 (26.8)
IV	6 (5.1)	6 (4.6)	22 (14.7)	16 (10.1)	38 (20.1)	37 (12.1)	66 (14.5)	59 (9.9)
Total	117 (100)	129 (100)	150 (100)	158 (100)	189 (100)	307 (100)	456 (100)	594 (100)

Note: 1 – number of men, abs. (%), 2 – number of women, abs. (%)
Source: compiled by the authors of this study

Table 3. Distribution of periodontitis grades among Ukrainian residents of different ages and genders

Grade of periodontitis	Group I		Group II		Group III		Total	
	1	2	1	2	1	2	1	2
A	12 (10.3)	16 (12.4)	8 (5.3)	11 (7.0)	4 (2.1)	12 (3.9)	24 (5.3)	39 (6.6)
B	76 (65.0)	90 (69.8)	90 (60.0)	103 (65.2)	104 (55.0)	184 (59.9)	270 (59.2)	377 (63.5)
C	29 (24.7)	23 (17.8)	52 (34.7)	44 (27.8)	81 (42.9)	111 (36.2)	162 (35.5)	178 (29.9)
Total	117 (100)	129 (100)	150 (100)	158 (100)	189 (100)	307 (100)	456 (100)	594 (100)

Note: 1 – number of men, abs. (%), 2 – number of women, abs. (%)
Source: compiled by the authors of this study

In total, 408 outpatient charts (12.8% of the total number of charts analyzed) with intact periodontal tissues, 1742 charts of patients (54.4%) diagnosed with gingivitis, and 1050 charts of patients (32.8%) diagnosed with periodontitis were analyzed. The largest number of patients without periodontal pathology, namely 31.9% of men (of the number of men in the group) and 18.5% of women, was recorded in age group I, while in group III the proportion of such patients was minimal, 5.6% and 2.6%, respectively. According to periodontal charts, gingivitis was diagnosed more often in patients of group II, in 69.8% of men and 73.2% of women, and was diagnosed much less often in patients of the corresponding sex of age group III, in 28.1% and 10.7%. The opposite situation was observed regarding the prevalence of periodontitis, the number of patients with this disease was the lowest in age group II with 18.3% of men and 19.5% of women, and the highest in the older age group with 66.3% and 86.7%, respectively. A statistically significant association was found between the condition of periodontal tissues and age (χ^2=147.7; p<0.001) and gender of patients (χ^2=24.5; p<0.001).

In the outpatient charts of all age groups, generalized periodontal lesions were more often recorded. In particular, localized gingivitis was diagnosed in only 389 patients (22.3% of the number of patients with gingivitis), and generalized gingivitis in 1353 patients (77.7%). A similar pattern was observed in patients with periodontitis: localized lesions were diagnosed in 346 patients (32.9%), and generalized lesions in 704 patients (67.1%). A significant relationship was found between the prevalence of the inflammatory process and the age of patients (χ^2=6.7; p<0.001), but not significant with respect to gender (χ^2=1.3; p>0.05).

Based on the results of the analysis of periodontal charts and radiographs of patients with periodontitis, the stage and grade of the disease were determined for each person (Table 2, Table 3).

According to the criteria of AAP/EFP 2017 Classification, stage I periodontitis was recorded in 153 patients

(14.6% of the number of patients with periodontitis), stage II was recorded in 474 patients (45.1%), stage III in 298 patients (28.4%), and stage IV in 125 patients (11.9%). The proportion of patients diagnosed with stages II and III periodontitis increased with age, reaching a maximum in the older age group, while the prevalence of cases of stage I periodontitis predictably decreased with age. Thus, a significant correlation (χ^2=127.8; p<0.001) was found between the age of patients and the stage of periodontitis. Although the most common stage of the disease in patients of both sexes was stage II, men of all age groups were more likely to have more severe stages of the disease than women, in particular, stage III periodontitis was diagnosed in 30.5% of men and 26.8% of women, and stage IV in 14.5% of men and 9.9% of women. The sex of the patients whose charts were analyzed also had a statistically significant (χ^2=8.8; p<0.05) effect on the stage of the disease.

Grade A of periodontitis progression was diagnosed in the smallest number of patients, namely 63 patients (6.0%), grade B was recorded much more often, in 647 patients (61.7%), and grade C was recorded in 340 patients (32.3%). The proportion of patients with grade B periodontitis was similar in all age groups, but with age, the number of patients with grade A decreased significantly and the number of patients with grade C increased. According to the results of statistical analysis, a significant (χ^2=36.6; p<0.001) association between patient age and periodontitis grade was determined. Both men and women of all groups more often had grade B disease progression, but men were diagnosed with grade C more often than women. At the same time, the relationship between gender and the grade of periodontitis was not significant (χ^2=3.9; p>0.05).

The most common diagnosis in patients of all age groups was generalized periodontitis of stage II, grade B, which was diagnosed in 272 patients (25.9% of the number of patients with periodontitis). The number of patients with generalized periodontitis of stage III, grade C was much lower, 206 patients (19.6%). In the electronic charts of Ukrainian residents with localized periodontitis, stage II, grade B of the disease was also more often recorded, namely in 193 patients (18.3%). The analysis revealed no cases of stage I, grade C and stage IV, grade A periodontitis, both for localized and generalized forms.

DISCUSSION

The prevalence of periodontal diseases is gradually increasing and today this group of pathologies ranks sixth in the world [6]. Epidemiological indicators of periodontal disease vary significantly from country to country, with the highest rates in Asia and the lowest in South Africa and Oceania [7]. According to a national study in the United States of America, the prevalence of periodontitis among adults was 93.1%, which was almost three times higher than the results obtained in our study [8]. According to the results of a systematic review of the literature in Latin America, reporting rates of gingivitis range from 28.0% to 96.2%, and periodontitis from 16.3% to 59.3% in residents of different ages and genders [9]. In a clinical study conducted in Kazakhstan, researchers found the prevalence of periodontitis to be 69.0%, with a significant association between patient age and periodontal tissue condition [10].

Generalized periodontitis of stage II, grade B was diagnosed more often in patients of all age groups, which is consistent with other results of similar studies [4, 8]. Based on the results of a similar retrospective analysis of outpatient charts of patients over 18 years of age, researchers found that the most common variant of generalized periodontitis was stage II (65.0%) and grade B (63.0%). In general, in this study, as well as in our study, stage II, grade B of generalized periodontitis was the most common diagnosis (32.0%), slightly less common were stage III, grade C of generalized periodontitis (23.0%) and stage IV, grade C of periodontitis (18.0%) [11]. In another study, patients with an average age of 45.5 years were more likely to have stage I (42.0%) and stage IV (28.0%) generalized periodontitis [12]. During a clinical examination of Portuguese residents with an average age of 49 years, stage III (51.2%) and stage IV (30.4%) of periodontitis were predominantly recorded, as well as the prevalence of generalized forms (66.5%) over localized forms (33.5%) [13].

Numerous studies are available in which the authors concluded that more severe forms of periodontitis are more common in men [12-14]. In contrast to our results, another study on the epidemiologic indicators of periodontal lesions found no statistically significant differences between the prevalence of periodontal pathology and the sex of patients of different age groups [15]. Such differences in indicators can be explained by different research methodology, failure to consider a number of regional factors, including access to dental care, income level, genetic predisposition of representatives of different ethnic groups to the development of periodontal diseases, etc.

Periodontal diseases have significant variability in clinical manifestations, etiologic factors of development and sensitivity to treatment, which leads to the existence of various classification systems for these pathologies [5]. The introduction of a unified and at the same time convenient for clinical practice classification will increase the relevance of epidemiological and clinical

studies. The AAP/EFP 2017 Classification systematizes all possible forms of periodontal pathology according to clear criteria that are understandable to both clinicians and researchers. The classification includes not only criteria of disease severity, such as loss of epithelial attachment and probing depth, but also factors that increase treatment complexity, namely tooth loss, occlusion disorders, and furcation involvement. These parameters help determine the competencies of specialists required for patient rehabilitation. Importantly, they also allow clinicians to predict the duration and cost of treatment already at the stage of initial diagnosis.

An important feature of the AAP/EFP classification is the introduction of a system of periodontitis grades that reflects the intensity of disease progression and possible response to treatment. Consideration of modifying factors, such as tobacco smoking and the concentration of glycosylated hemoglobin (HbA1c) in the patients' serum, allows to create individualized treatment plans for individuals and provide a reasonable prognosis for the success of rehabilitation.

Future research should focus on the development and implementation of improved treatment protocols for patients depending on the stage and grade of periodontitis development. In addition, it is necessary to consider other pathogenetic mechanisms of pathology, in particular the impact of certain generalized somatic diseases, stress and behavioral patterns of patients on the clinical course of periodontitis.

CONCLUSIONS

The results of a retrospective analysis of outpatient records of patients of different age groups and sexes revealed that the prevalence of gingivitis was 54.4%, that of periodontitis was 32.8%, and only 12.8% of patients had a healthy periodontal condition. Among patients of all age groups with periodontitis, the generalized form of stage II, grade B of this disease was more often diagnosed, namely in 25.9% of patients. A significant relationship was revealed between the age of patients and the condition of periodontal tissues, the prevalence of the inflammatory process, the stage and grade of periodontal disease. An association was also found between the sex of patients and the likelihood of developing periodontal disease. Consequently, applying the modern classification during routine clinical visits will allow to develop differentiated approaches to the treatment of patients, taking into account the pathogenetic peculiarities of periodontitis.

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CONTENTS

Rethinking disability assessment: Shift to a functioning-based model

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ABSTRACT

Aim: To analyze the development and implementation of the new framework for assessing the functional status of disability in Ukraine, and to evaluate the results of the first year of the new system's operation.

Materials and Methods: Sociological method was used. The Ministry of Health has published an analytical report on the results of the first year of work by the expert teams assessing a person's daily functioning from January 1, 2025. Before the reform, the system was based on 328 commissions and 1267 doctors. In contrast, after the reform, more than 7000 physicians were involved in all regions of Ukraine. More than 1,300 expert teams have been formed, making more than 554000 decisions in a yearStatistical analysis included descriptive statistics of indicators. Statistical processing and graphical visualisation of the data were performed using Microsoft Excel (Microsoft Excel for Microsoft 365 MSO, version 2603, build 16.0.19822.20086, 64-bit).

Results: A new system focused on assessing functioning has been introduced into clinical practice. A comprehensive legal framework was developed, and the Center for Assessment of the Functional State of a Person was established in 2025. The system includes over 1300 expert teams and approximately 7000 doctors, operates nationwide, and is highly digitized via the Diia platform. Initial results show increased transparency, accessibility, and user satisfaction.

Conclusions: The reform aligns with international standards and represents a systemic step toward rights-based disability assessment. However, further improvements are needed in regulatory support, institutional capacity, digital infrastructure, and consistent law enforcement.

KEY WORDS: disability, reform, functioning assessment

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INTRODUCTION

In the current context of the development of the rule of law and the implementation of international standards in the field of human rights, ensuring the rights of persons with disabilities is of particular importance, especially through the creation of effective mechanisms for assessing their functional status and implementing social guarantees. The relevance of this issue stems from the need to transition from outdated approaches, based mainly on the medical model of disability, to a comprehensive approach that accounts for both a person's health status and the influence of the social environment on their life. Reforming the system for assessing a person's functional state in Ukraine is part of the broader process of harmonizing national legislation with international standards and implementing the principles of the rule of law, equality, and non-discrimination. In this context, it is important to analyze the legal foundations of the relevant reform and its practical implementation, as well as to identify problematic aspects that arise during law enforcement.

Ukraine signed the UN Convention on the Rights of Persons with Disabilities (hereinafter referred to as the UN Convention) and the Optional Protocol thereto on September 24, 2008, in New York. The Verkhovna Rada ratified the above-mentioned international legal acts on December 16, 2009, and the document entered into force for Ukraine on March 6, 2010, thereby enshrining the obligation to ensure the protection of the rights and freedoms of persons with disabilities without dis-

crimination. The Convention obliges signatory states to align their national legislation with international standards, ensuring the accessibility of infrastructure, education, employment, and justice for persons with disabilities [1–3].

The Convention establishes a fundamentally new approach to understanding disability, which is based on a combination of medical and social factors and involves a transition from an exclusively medical model to a biopsychosocial one. In this context, disability is considered the result of the interaction between a person and environmental barriers that prevent their full and effective participation in public life on an equal basis with others. Of particular importance are the provisions on equality before the law, non-discrimination, accessibility, and the right to independent living and integration into society.

The European Union has adopted and implemented the European Code of Social Security [4], which defines the fundamental principles of social security. International experience in the legal regulation of social security is highly valuable for Ukraine, particularly for its prospects for development and improvement. Undoubtedly, the problem of developing new legislation on the rights of persons with disabilities remains particularly acute. As of the end of 2025, there were over 3.4 million persons with disabilities in Ukraine, which indicates a significant increase of approximately 600000 people since the beginning of the full-scale war (from 2.8 million in 2022). Due to hostilities and disease, the number of people in need of rehabilitation and prosthetics is increasing every day [5].

As is known, the Constitution of Ukraine, proclaiming Ukraine a democratic, social, and legal state, establishes that current international treaties, the consent to which has been given by the Verkhovna Rada of Ukraine, are part of the national legislation of Ukraine [6].

The implementation of the UN Convention on the Rights of Persons with Disabilities in Ukraine is being carried out through legislative changes in inclusive education, accessibility, employment, and deinstitutionalization. This necessitates transforming outdated approaches, based mainly on the medical model of disability, into a comprehensive approach that accounts for both the individual's health status and the influence of the social environment on their life activities through the reform of medical and social assessments.

AIM

To analyze the development and implementation of the new framework for assessing the functional status of disability in Ukraine, and to evaluate the results of the first year of the new system's operation.

MATERIALS AND METHODS

The concept of reform of medical and social expertise in Ukraine was developed by the authors based on contemporary approaches to disability, particularly the biopsychosocial model, which provides assessment of functioning in accordance with the International Classification of Functioning, Disability and Health (ICF). The proposed framework formed the basis of the Resolution of the Cabinet of Ministers of Ukraine No. 1338 dated November 15, 2024, "Some Issues of the Implementation of the Assessment of a Person's Daily Functioning".

Sociological method was used. The Ministry of Health has published an analytical report on the results of the first year of work by the expert teams assessing a person's daily functioning from January 1, 2025. Before the reform, the system was based on 328 commissions and 1267 doctors. In contrast, after the reform, more than 7000 physicians were involved in all regions of Ukraine. More than 1,300 expert teams have been formed, making more than 554000 decisions in a yearStatistical analysis included descriptive statistics of indicators. Statistical processing and graphical visualisation of the data were performed using Microsoft Excel (Microsoft Excel for Microsoft 365 MSO, version 2603, build 16.0.19822.20086, 64-bit).

ETHICS

The study was approved by the Bioethics Commission of the State Institution "Ukrainian State Scientific Research Institute of Medical and Social Problems of Disability of the Ministry of Health of Ukraine". It was conducted in accordance with the principles of bioethics outlined in the Declaration of Helsinki, "Ethical Principles of Medical Research Involving Humans," and the "Universal Declaration on Bioethics and Human Rights" (UNESCO).

RESULTS

The previous system of medical and social expertise (MSE) revealed systemic defects that made it ineffective. In particular, the definition of disability was based primarily on medical diagnosis, indicating the dominance of the so-called diagnosis-centered approach. Assessment procedures were formalized and did not account for the person's actual level of functioning. It failed to adequately assess functional capacity or rehabilitation needs. In addition, the system was characterized by excessive bureaucracy, paper-based documentation,

Table 1. Number of processed cases by regions of Ukraine in 2025

Region	Total received
Vinnytsia	2183
Volyn	706
Dnipropetrovsk	2875
Donetsk	428
Zhytomyr	914
Zakarpattia	559
Zaporizhzhia	1222
Ivano-Frankivsk	472
Kyiv region	1104
Kirovohrad	614
Luhansk	227
Lviv	1620
Mykolaiv	2995
Odesa	1603
Poltava	1501
Rivne	551
Sumy	781
Ternopil	651
Kharkiv	3421
Kherson	102
Khmelnytskyi	1804
Cherkasy	574
Chernivtsi	681
Chernihiv	715
Kyiv	2075
TOTAL	**30880**

Source: compiled by the authors based on [10]

and lengthy case processing times. Also, there was a high risk of corruption and limited transparency in decision-making.

All the above circumstances indicated a systemic crisis in the previous model, necessitating its radical reform. The first steps of the reform of medical and social expertise in Ukraine were made in 2016-2018, when more than 40 legislative acts were amended, replacing the incorrect term "disabled" with "person with a disability". This was done to shift the focus from the medical diagnosis to the individual and existing barriers in society. The next steps on this path were the approval of the National Action Plan for the Implementation of the Convention for the Period up to 2025 [7], which identified specific actions to ensure accessibility and inclusion, and the National Strategy for Creating a Barrier-Free Space [8], which focused on physical, digital, informational, and social accessibility. A recent step was the liquidation of the medical and social expertise service since January 1, 2025 [9].

The new approach to medical and social expertise is person-centered. The new model of disability views disability not only as a medical problem, but as the result of the interaction of a person's health status with society. This approach allows not only to state the presence of a disease, but also to determine what support is needed for maximum participation in social life.

Reducing bureaucracy is one of the key areas of the reform, which aims to significantly simplify citizens' interaction with the system. So, the functions of medical and social expert commissions (MSECs) have been transferred to expert teams in multidisciplinary hospitals. A digital process of document submission and data exchange between hospitals was implemented, based on Diia.Engine, which simplifies the expertise process and enables more effective coordination across all stages of rehabilitation and social assistance.

The reform also strengthened patients' rights. This includes access to information on the case, the possibility of obtaining copies of documents, the right to a representative, recording the assessment process, and appealing decisions in the Center for the Assessment of the Functional State of a Person or in court. Starting in 2026, mandatory audio recording of procedures has been introduced. There is no more need to collect numerous paper documents, as all necessary data will be automatically transferred between institutions. Thanks to online applications and electronic registries, document processing was accelerated, and decision-making time was significantly reduced to 19 days on average, whereas previously it took almost half a year. Patients also gained the right to independently choose a medical institution for assessment.

The Ministry of Health has published an analytical report on the results of the first year of work by the expert teams assessing a person's daily functioning from January 1, 2025 [10]. Before the reform, the system was based on 328 commissions and 1267 doctors. In contrast, after the reform, more than 7000 physicians were involved in all regions of Ukraine. More than 1,300 expert teams have been formed, making more than 554000 decisions in a year.

The number of cases processed by region of Ukraine is shown in Table 1.

The distribution of cases by the verification of previous MSEC decisions is shown in Fig. 1, and Table 2 shows the aim of referring patients for functional assessment.

The formats for completing the procedure have also changed: in addition to in-person, a remote format has been introduced for certain conditions and for patients abroad. Dozens of training events for doctors were held, and amendments were made to legislative acts, in particular to 32 laws and over 120 government resolutions.

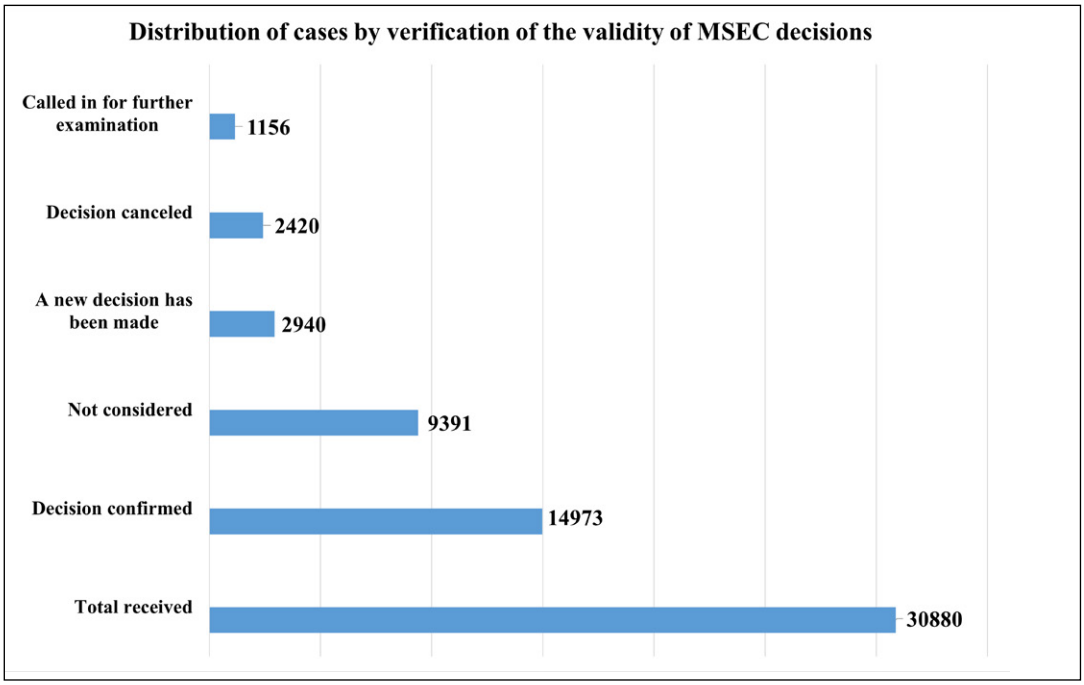


Fig. 1. Distribution of cases by the verification of previous MSEC decisions
Picture taken by the authors

Table 2. The aim of referring patients for the assessment of functioning

No.	Purpose of Referral	Number
1	Expiration of the period for which disability was established	293036
2	Establishment of disability	288742
3	Provision of assistive rehabilitation devices / medical devices	25681
4	Determination of the degree of loss of professional working capacity	24804
5	Re-assessment in case of changes in health condition	22926
6	Update of recommendations (part of the Individual Rehabilitation Program)	16028
7	Extension of temporary disability (sick leave)	14073
8	Determination of the need for permanent external care and other social services	8674
9	Need to change the cause of disability	7587
10	Determination of medical indications/contraindications for driving	1727
11	Establishing a causal link between disability and diseases suffered in childhood	1736
12	Referral to a residential care institution	879
13	Establishing a causal link between death and occupational disease/work injury/other health damage	162

Source: compiled by the authors of this study

In Table 3, you can see the number of cases reviewed via the electronic system, and in Fig. 2, the number of disability cases by nosological form.A patient survey conducted in late 2025 showed a generally positive perception of the changes. Most respondents noted that the procedure had become clearer, and almost half said that the new system worked better than the previous one. The significance of the reform is illustrated by the example of people who have undergone amputations. If, in the previous system, the key result was the establishment of a disability group, then in the new model, the level of functional limitations, the need for prosthetics and rehabilitation, and the possibility of further employment are determined, ensuring more effective integration of the person into society.

A comparative analysis of the previous and new systems indicates a radical transformation in approaches to assessment: from a medical model to a biopsychosocial one, from assessing the diagnosis to assessing functioning, from paper-based document flow to electronic, and from long review periods to significantly shorter ones. At the same time, there was a transition from a

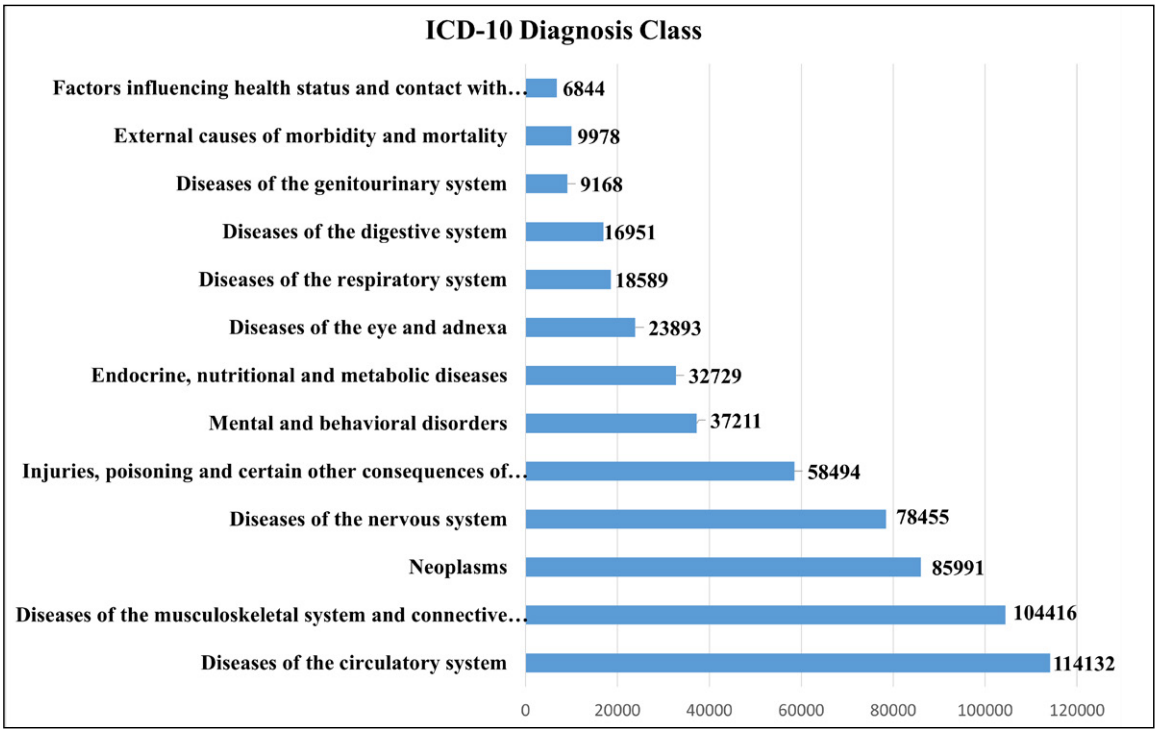


Fig. 2. Distribution of disability cases depending on nosology
Picture taken by the authors

Table 3. Number of cases reviewed in the electronic system

No.	Institution	Number of Cases
1	Center for Functional Status Assessment of Individuals	10845
2	MNPE "Vinnytsia Regional Clinical Hospital named after M.I. Pyrohov" of Vinnytsia Regional Council	9775
3	MNPE "Regional Clinical Hospital named after O.F. Herbachevskyi" of Zhytomyr Regional Council	9469
4	MNPE "Lviv Territorial Medical Association 'Multidisciplinary Clinical Hospital of Intensive Care and Emergency Medical Aid'"	8835
5	MNPE "City Clinical Hospital No. 11" of Odesa City Council	8150
6	ME "Poltava Regional Clinical Hospital named after M.V. Sklifosovskyi" of Poltava Regional Council	7530
7	MNPE "Zaporizhzhia Regional Clinical Hospital" of Zaporizhzhia Regional Council	6859
8	MNPE of Lviv Regional Council "Lviv Regional Clinical Hospital"	6820
9	MNPE "Regional Clinical Hospital of Ivano-Frankivsk Regional Council"	6648
10	MNPE of Lviv Regional Council "Lviv Regional Oncology Treatment and Diagnostic Center"	6629
11	MNPE "City Emergency and Ambulance Hospital" of Zaporizhzhia City Council	6607
12	MNPE of Lviv Regional Council "Lviv Regional Clinical Cardiology Treatment and Diagnostic Center"	5954
13	MNPE of Kharkiv Regional Council "Regional Clinical Hospital"	5338
14	MNPE "Khmelnytskyi Regional Hospital" of Khmelnytskyi Regional Council	5086
15	ME "Volyn Regional Clinical Hospital" of Volyn Regional Council	4888
16	MNPE of Lviv Regional Council "Lviv Regional Hospital for War Veterans and Repressed Persons named after Yu. Lypa"	4770
17	MNPE "Central City Clinical Hospital" of Chernivtsi City Council	4572
18	MNPE "Kyiv City Clinical Hospital No. 7" of the executive body of Kyiv City Council (Kyiv City State Administration)	4239
19	MNPE "Kyiv City Clinical Hospital No. 12" of the executive body of Kyiv City Council (Kyiv City State Administration)	4224
20	MNPE "Vinnytsia City Clinical Hospital No. 1"	4188

Source: compiled by the authors of this study

narrowly professional approach to a multidisciplinary one, which provides a more objective and comprehensive assessment of the person's condition.

The implementation of the reform demonstrates a significant increase in the role of the Center for the Assessment of the Functional State of a Person (CAFSO), which serves as a key element in quality control. During 2025, the Center received 31653 materials, of which 15806 were for validity verification, and 15349 were for appeal decisions, indicating a high level of system load. In total, about 66% of cases (21819) were processed. In comparison, the efficiency of considering appeals is higher (74%) than that of verifying validity (58%). An additional indicator of the legal load is the processing of 673 court cases, as well as thousands of lawyer requests (2474) and requests for information (2440), which form a significant amount of legal support for the Center's activities. At the same time, in 77% of cases, the previous expert teams' decisions remain unchanged. In 14% of cases, new decisions are made, confirming the significant role of the Center for the Review and Correction of Decisions as an institution.

DISCUSSION

Many countries have adopted the ICF as the basic framework for developing health and social policies and legislation on disability and related areas [11]. The ICF has wide application at the population, health, and social services levels [12]. However, in most countries worldwide, the ICF is used to determine the necessary rehabilitation measures for a patient, assess their effectiveness, and collect statistical information on the needs of people with disabilities. The use of the ICF as a tool for determining disability has been implemented only in Taiwan [13].

The reform of the functional assessment system in Ukraine establishes a new regulatory and methodological framework for assessing a person's functional status, integrating clinical, functional, and legal components. The integration of legal and regulatory, causal, and risk-based analytics increases decision quality and minimizes regulatory and judicial risks. The use of the International Classification of Functioning (ICF) provides a methodological basis for objectifying the functional state and establishing a transparent link between medical data and legal consequences. Thus, a new institutional model is being formed, within which the expert decision acquires the status of a legally significant document that determines the scope of social guarantees, rights, and responsibilities of the state towards an individual.

As noted by the Minister of Health, Viktor Lyashko, "Thanks to the joint work of doctors, medical institutions, and the state, we have managed to make a qualitative transition in approaches to assessing human functioning. What was previously declared at the level of regulatory and legal acts today actually works as a tool for determining the needs of a person with a disability. We are building a system that meets international standards for the rights of people with disabilities and is based not only on diagnosis but also on a person's everyday capabilities" [14].

It is worth noting that the development of a stable practice of judicial control over decisions in the new system remains in its early stages. In the future, it will contribute to increasing trust in the system and ensuring an appropriate balance between the discretionary powers of expert teams and the rights of individuals.

CONCLUSIONS

1. The reform of the assessment of a person's functioning in Ukraine took its first steps in 2016 and was finished on January 1, 2025, when the old system was canceled. The new model of disability views disability not only as a medical problem, but as the result of the interaction of a person's health status with society.
2. The new approach to medical and social expertise is person-centered, digitalized, transparent and allows to determine what support is needed for maximum participation of a person in social life. The reform of the assessment of a person's functioning is a comprehensive, systemic step towards implementing international human rights standards.
3. The reform involved a large number of physicians – more than 7000 doctors (1300 expert teams) take part in the assessment of a person's functioning, and during a year they made 554000 decisions.
4. The results of the first year of the implementation of the reform demonstrate the effectiveness of the new assessment system, while at the same time, further institutional and regulatory improvement is needed to achieve consistency and predictability of daily expertise practice.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

CONTENTS

Impact of legal guarantees on the mental health of law enforcement officers of Ukraine in the conditions of conducting military (combat) actions

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ABSTRACT

Aim: To conduct a comprehensive analysis of the legal guarantees for Ukrainian law enforcement officers performing their official duties in areas of military (combat) operations, and their impact on the preservation of mental and physical health. The research also aims to identify the relationship between the level of implementation of these guarantees, psycho-emotional state, occupational stress, and the risks of burnout among this category of personnel.

Materials and Methods: The study was designed as an interdisciplinary empirical legal study combining legal, medico-social, and statistical methods. It included comparative legal analysis, an anonymous survey, and statistical processing of the data. The study involved 48 law enforcement officers with experience of service in combat zones or other high-risk conditions. The main research instrument was an adapted questionnaire assessing psychological competencies and the perception of legal guarantees.

Results: The respondents highly rated the importance of psychological competencies for professional communication, while self-assessment of communicative skills was moderately high. At the same time, indicators of stress prevention, perception of legal guarantees, legal certainty, maladaptive behaviour risks, and mental health remained at an average level. The lowest scores were related to access to psychological assistance and access to rest and rotation. Correlation analysis showed that stronger legal guarantees were associated with lower occupational stress, while greater legal certainty was linked to better self-assessed mental health. Insufficient legal guarantees were significantly associated with emotional burnout.

Conclusions: Legal guarantees for law enforcement personnel in combat conditions should be regarded not only as a formal element of service status, but also as a practical mechanism for preserving mental and physical health. Strengthening legal certainty, improving access to psychological and medical support, and ensuring effective rest and rotation mechanisms are essential for reducing stress and burnout and for enhancing professional resilience.

KEY WORDS: legal guarantees; mental health; combat conditions

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INTRODUCTION

Ensuring the rights of Ukrainian law enforcement officers who perform their official duties in areas of military (combat) operations is a crucial condition for preserving their mental and physical health. Under such circumstances, the activities of Ukrainian law enforcement agencies are carried out under an increased risk to life, significant emotional strain, severe time constraints for decision-making, and the need for constant interaction with victims, witnesses, civilians, and military personnel [1, 2]. Therefore, the legal guarantees for Ukrainian law enforcement officers should be considered not only as an element of their official status but also as a factor in the prevention of occupational stress, burnout, and mental health disorders.

The constitutional basis for such an approach is the right to life and the right to health protection. According to Articles 27 and 49 of the Constitution of Ukraine, the state is obliged to ensure the protection of human life and create conditions for health protection, medical assistance, and rehabilitation [3]. During military (combat) operations, these provisions must have practical significance for Ukrainian law enforcement officers and encompass safe conditions of service, unimpeded access to medical and psychological assistance, rest, rotations, legal briefings, and mechanisms for responding to violations of legal guarantees [4, 5].

Legal certainty takes on particular importance under these conditions. A Ukrainian law enforcement officer is simultaneously a bearer of constitutional rights and an entity endowed with authoritative powers. This duality is particularly evident during operational-search measures (OSM) and covert investigative (search) actions

(CISA) in areas of military (combat) operations, where the necessity for a lawful, rapid, and proportionate response is coupled with an elevated risk of operational, procedural, or disciplinary evaluation of their actions. Ukrainian legislation on operational-search activities [6, 7] and the criminal procedural regulation of covert investigative (search) actions [7–10] establish the legal grounds and limits for such measures. However, a lack of clarity regarding procedures, the boundaries of lawful decisions for their execution, or potential legal consequences can exacerbate anxiety and occupational stress among Ukrainian law enforcement officers in areas of military (combat) operations.

In this context, the implementation of the strategic directions for reforming Ukraine's law enforcement system is of great importance. These directions are enshrined, in particular, in the Decree of the President of Ukraine No. 273/2023 of May 11, 2023 [11] and the Order of the Cabinet of Ministers of Ukraine No. 792-r of August 23, 2024 [12], which stipulate the improvement of the legal and regulatory framework for the activities of Ukrainian law enforcement agencies, the enhancement of the legal certainty of their functioning, and the provision of appropriate legal and social guarantees for Ukrainian law enforcement officers within the framework of Ukraine's integration into the European Union. These provisions hold conceptual significance for establishing a proper system of legal guarantees for Ukrainian law enforcement officers while they perform their assigned duties in areas of military (combat) operations.

The violation or insufficient implementation of legal guarantees under such conditions can negatively impact the mental and physical health of Ukrainian law enforcement officers. A lack of psychological support, the stigmatization of seeking help, excessive workload, disruption of rest regimens, a shortage of protective equipment, and the uncertainty of the legal boundaries of official actions increase the risk of emotional exhaustion, professional deformation, sleep disorders, somatic complaints, and maladaptive forms of coping with stress [13, 14].

Modern international standards confirm that an employee's mental health is a component of a safe professional environment. The World Health Organization's guidelines on mental health at work emphasize the need for organizational measures, training, support, and the early detection of risks [15]. The standards of the United Nations Office on Drugs and Crime/World Health Organization focus on evidence-based preventive approaches to risky behavior [16], while the documents of the North Atlantic Treaty Organization highlight the importance of psychological support for personnel throughout the entire cycle of task execution [17].

At the same time, the scientific literature lacks a comprehensive investigation into the relationship between the legal guarantees of the rights of Ukrainian law enforcement officers in areas of military (combat) operations, the legal certainty of operational-search measures (OSM) and covert investigative (search) actions (CISA), access to medical and psychological assistance, and indicators of mental and physical health. It is this specific gap that determines the relevance of the current study.

AIM

The object of the study is to conduct a comprehensive analysis of the legal guarantees for Ukrainian law enforcement officers performing their official duties in areas of military (combat) operations, and their impact on the preservation of mental and physical health. The research also aims to identify the relationship between the level of implementation of these guarantees, psycho-emotional state, occupational stress, and the risks of burnout among this category of personnel.

MATERIALS AND METHODS

The research was conducted as an interdisciplinary empirical-legal study employing legal, medical-social, and statistical methods. Its objective was to evaluate the relationship between the legal guarantees of the activities of Ukrainian law enforcement officers in areas of military (combat) operations and indicators of their mental and physical health.

The study was cross-sectional in nature. It included: a comparative legal analysis of international standards in the field of mental health under conditions of increased occupational risk; an anonymous survey of Ukrainian law enforcement officers; and statistical processing of the obtained data.

Inclusion criteria were affiliation with a Ukrainian law enforcement agency, age 18 and older, experience in performing official duties in areas of military (combat) operations or in high-risk environments, and voluntary informed consent. Exclusion criteria included refusal to participate, incomplete questionnaires, and the provision of answers that might contain restricted or classified information.

In accordance with the defined criteria, the empirical base of the study comprised the survey results of n=48 Ukrainian law enforcement officers who had experience performing official duties in areas of military (combat) operations or other high-risk conditions. The sample

Table 1. Results of the questionnaire of Ukrainian law enforcement officers regarding the assessment of psychological competencies and the perception of legal guarantees under conditions of military (combat) operations (n=48)

Questionnaire block	Indicator value (M±m), points	Comment on the indicator value
The importance of psychological competencies for professional communication	4.3±0.64	high level
Self-assessment of communication skills	3.7±0.72	moderately high level
Prevention of professional stress and burnout	2.8±0.9	average level
Perception of legal guarantees	3.1±0.84	average level
Legal certainty regarding operational and investigative measures (ORZ) and covert investigative (search) actions (CI(S)A)	3.0±0.82	average level
Risks of maladaptive behavior	2.9±0.88	average level
Self-assessment of mental health	3.2±0.78	average level
Self-assessment of physical health	3.6±0.74	moderately high level

Source: compiled by the authors of this study

Table 2. Correlations between legal guarantees and indicators of mental and physical health of Ukrainian law enforcement officers under conditions of military (combat) operations

Pair of variables	r	p
Legal guarantees and occupational stress	–0.46	0.01
Legal certainty and mental health	0.39	0.01
Legal guarantees and physical health	0.33	0.045
Psychological competencies and mental health	0.3	0.05
Psychological competencies and physical health	0.25	0.06
Legal certainty and burnout	–0.52	0.001

Source: compiled by the authors of this study

characteristics indicate significant professional experience among the respondents: their average age was 31.4±1.1 years, and their average length of service was 7.2±0.8 years. Notably, 100% of the surveyed individuals directly performed tasks in areas of military (combat) operations. The specifics of their activities encompassed both communicative and procedural components: 72.9% of the individuals (n=35) were involved in interactions with victims, witnesses, or the civilian population, while 85.4% (n=41) of the respondents had experience performing procedural or operational tasks.

The primary research instrument was an adapted questionnaire for assessing psychological competencies and the perception of legal guarantees, based on a five-point scale: 1-1.8 – very low level, 1.81-2.6 – low level, 2.61-3.4 – medium level, 3.41-4.2 – moderately high level, 4.3-5.0 – high level of indicator values [17]. It included blocks regarding the significance of psychological competencies, self-assessment of communication skills, prevention of occupational stress and burnout, perception of legal guarantees, legal certainty of covert investigative (search) actions (CISA), risks of maladaptive behavior, as well as socio-professional characteristics. The internal consistency of the questionnaire was evaluated using Cronbach's alpha, which was 0.87 (an adequate level of consistency), ensuring its validity.

Statistical processing was carried out using IBM SPSS Statistics v. 27.0 (Armonk, NY: IBM Corp., USA). Quantitative indicators were presented as the mean value and standard error of the mean (M±m). Spearman's correlation analysis (r) was performed to evaluate the relationships between variables. Differences were considered statistically significant at $p < 0.05$.

ETHICS

The study was conducted in compliance with the principles of the Declaration of Helsinki. Participation was voluntary; respondents were informed about the purpose of the study, its anonymous nature, and their right to withdraw from participation at any stage. The research protocol was approved by the local bioethics committee.

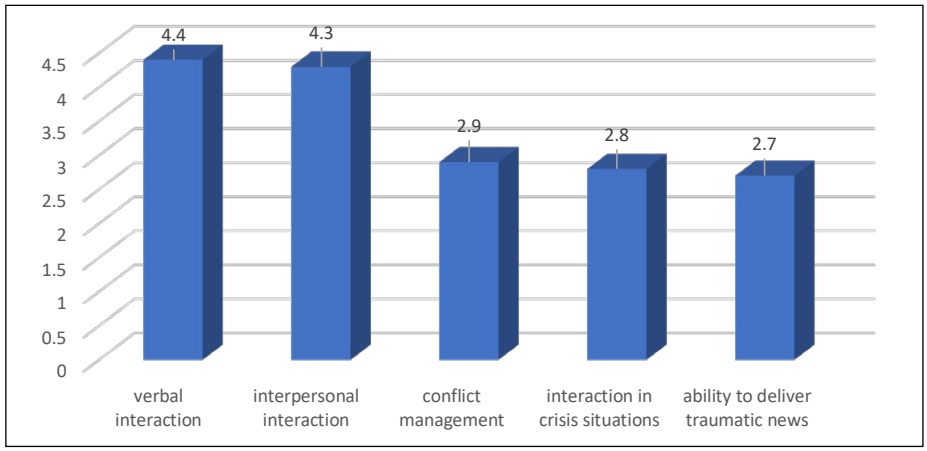


Fig. 1. In-depth self-assessment of existing psychological competencies among respondents (points) (n=48)
Picture taken by the authors

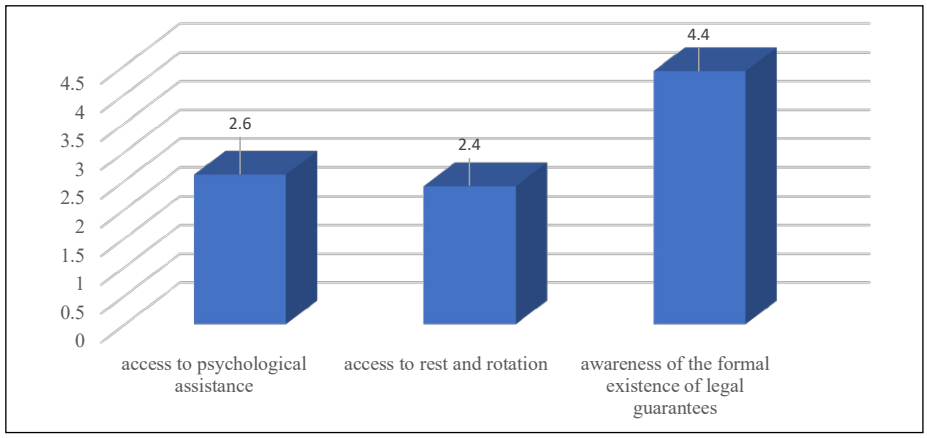


Fig. 2. In-depth self-assessment of the perception of legal guarantees by respondents (points) (n=48)
Source: compiled by the authors of this study

RESULTS

The results of the questionnaire regarding the assessment of psychological competencies and the perception of legal guarantees are presented in Table 1.

The majority of respondents highly evaluated the importance of psychological knowledge for professional communication – 4.3±0.64 points, whereas the self-assessment level of their communication capabilities was rated as moderately high (3.7±0.72 points) (Table 1). Notably, there were no respondents who rated the importance of psychological knowledge for professional communication at a low level (1.0–2.6 points); the proportion of those who rated it at a medium level (2.61–3.4 points) was 8.3% (4 out of 48 individuals), while at a sufficiently high level (4.3–5.0 points) it was 62.5% of the respondents (30 out of 48 individuals).

In turn, a more in-depth self-assessment of existing psychological competencies revealed a predominance of verbal and interpersonal interaction skills, which scored 4.4±0.62 points and 4.3±0.64 points among the respondents, respectively. Conversely, lower indicators, falling within the medium-level range, pertained to conflict management (2.9±0.88 points), interaction in crisis situations (2.8±0.9 points), and the ability to deliver traumatic news (2.7±0.92 points) (Fig. 1).

The average score for the block on the prevention of occupational stress and burnout was 2.8±0.9 points. The proportion of respondents who rated their own ability to prevent professional burnout at a low level (1-2.6 points) was 29.2% (14 out of 48 individuals), while only 33.3% (16 out of 48 individuals) demonstrated a high level (4.3-5 points).

The average indicator for the perception of legal guarantees was 3.1±0.84 points. The lowest scores pertained to access to psychological assistance – 2.6±0.92 points, and rest and rotation – 2.4±0.94 points, whereas the level of general awareness regarding the formal existence of legal guarantees was high and amounted to 4.4±0.62 points (Fig. 2).

The average indicator of legal certainty regarding operational-search measures (OSM) and covert investigative (search) actions (CISA) was 3.0±0.82 points. At the same time, the proportion of respondents who rated their own legal certainty at a low level (1–2.6 points) was 33.3% (16 out of 48 individuals), while only 16.7% (8 out of 48 individuals) rated it at a high level.

The average score on the scale of risk of maladaptive behaviour was 2.9±0.88 points, indicating that risks are already present among a noticeable portion of the respondents. Consequently, 37.5% (18 out of 48) of the respondents indicated a reluctance to seek psychological help due to stigmatization or fear of negative professional consequences. At the same time, 58.3% (28 out of 48) of the surveyed individuals were aware

of the potential legal consequences of maladaptive behaviour for their official activities.

Physical health was rated higher by the respondents (3.6±0.74 points), indicating that the majority of them feel physically relatively well, with occasional, but non-critical, limitations. Mental health (3.2±0.78 points) was at a lower level – a zone of moderate well-being, where there may be periodic emotional difficulties, stress, or a decrease in psychological comfort.

For a deeper analysis of the factors influencing the psycho-emotional and physical state of the respondents, a Spearman correlation analysis was conducted. The obtained results support the hypothesis that the level of legal certainty and the full implementation of guarantees are key determinants of the occupational health of law enforcement officers under combat conditions.

The generalized indicators of the relationships are presented in Table 2.

Upon further investigation of the correlations between the studied factors, the following was established:

- a negative correlation between the level of legal guarantees and occupational stress ($r = -0.46$, $p = 0.01$), reflecting the role of legal uncertainty as a psycho-emotional stressor;

- a positive correlation between legal certainty and self-assessment of mental health ($r = 0.39$, $p = 0.01$); better awareness of legal guarantees and normative certainty is associated with a higher self-assessment of mental well-being, reflecting reduced anxiety and an increased sense of control;

- a positive correlation between psychological competencies and self-assessment of physical health ($r = 0.33$, $p = 0.045$), which may be mediated through more effective coping strategies, stress regulation, and health behaviors.

Furthermore, an insufficient level of legal guarantees was associated with an increased risk of emotional exhaustion ($r = -0.52$, $p = 0.001$) (Table 2). This is the most pronounced correlation in the model, highlighting the critical nature of the legal factor as a determinant of professional burnout and a factor influencing the respondents' mental health.

DISCUSSION

The obtained results confirm that the guarantees of the rights of Ukrainian law enforcement officers in areas of military (combat) operations should be considered not only as a formal element of their official status but also as a practical mechanism for preserving mental and physical health. The identified relationship between the level of perception of legal guarantees, the availability of medical and psychological assistance, legal certainty, and the level of occupational stress indicates that legal protection in such conditions performs not only a regulatory but also a preventive function [3, 4].

The study results provide grounds to assert that legal certainty is an independent factor in the mental stability of a Ukrainian law enforcement officer. Insufficient clarity regarding the limits of a lawful order, procedural requirements, and potential legal consequences increases the level of occupational stress, which is consistent with the approach of the European Court of Human Rights, according to which a system of secret measures must be accompanied by clear and foreseeable safeguards against abuse [9].

An important result is the identified gap between awareness of the significance of psychological competencies and actual readiness to act in conflict, crisis, and traumatic communicative situations. This indicates that psychological competence in combat (military) conditions should be considered a component of occupational safety, rather than an optional individual quality [2, 5, 19].

The results regarding occupational stress and burnout are consistent with contemporary studies that indicate a high level of emotional exhaustion, anxiety, and operational stress among Ukrainian law enforcement officers, especially under conditions of organizational overload and insufficient support [1, 13, 15, 19]. In this context, the position of the World Health Organization, according to which mental health in the workplace requires systemic organizational measures, training, and support, is fully relevant to the performance of duties by Ukrainian law enforcement officers under conditions of military (combat) operations [16].

Special attention should be paid to the established link between the insufficient implementation of legal guarantees and the risks of maladaptive behaviour. Such risks are not only of an individual-psychological nature but also organizational-legal, as they can affect discipline, security, confidentiality, and the legality of professional actions [4, 20]. This also aligns with the approach of the North Atlantic Treaty Organization to the psychological support of personnel throughout the entire cycle of task execution [17, 21].

It is worth emphasizing that service in combat conditions is accompanied not only by a high level of stress but also by a significant gap between formally enshrined legal guarantees and their practical implementation. It is precisely this discrepancy that becomes a catalyst for emotional exhaustion and a decrease in professional effectiveness. Comparing the obtained results with modern international approaches (WHO, UNODC, NATO, ECHR) once again proves the necessity of transitioning to a systemic, preventive approach to protecting the mental health of law enforcement officers. Such an approach should integrate the improvement of legislation, clarity of procedures, enhanced psychological training, and barrier-free access to assistance within a unified logic of ensuring professional resilience and the humanisation of service.

At the same time, the results should be evaluated taking into account the limitations of the study. The cross-sectional design does not allow for the establishment of cause-and-effect relationships, and the use of self-assessment may lead to socially desirable responses or the underreporting of specific problems. Despite this, the study has scientific and practical value, as it demonstrates the need to integrate legal, organizational, and psychological mechanisms into a unified system of protection for Ukrainian law enforcement officers under conditions of military (combat) operations.

CONCLUSIONS

The study confirmed that the legal guarantees for law enforcement officers under combat conditions are a critical mechanism for preserving their mental and physical health. The realization of the constitutional rights to life and health protection requires practical implementation through the creation of safe service conditions, a clear rotation schedule, and unimpeded access to medical and psychological assistance.

It was established that the level of legal certainty during the conduct of operational-search measures (OSM) and covert investigative (search) actions (CISA) directly impacts psycho-emotional stability: clear regulatory frameworks reduce anxiety levels, whereas legal uncertainty acts as an additional occupational stressor.

Correlation analysis demonstrated a direct relationship between the comprehensive implementation of legal guarantees and the indicators of professional burnout and maladaptation. The survey results indicate an acute need to improve crisis interaction and conflict management skills within the professional training of officers.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

CONTENTS

Molecular docking analysis of the interaction between metformin/glimepiride combination and organic cation transporter in diabetic patients

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DEPARTMENT OF CHEMISTRY, COLLEGE OF SCIENCE FOR WOMEN, UNIVERSITY OF BAGHDAD, BAGHDAD, IRAQ

ABSTRACT

Aim: This study aimed to evaluate the interaction of glimepiride/metformin with organic cation transporter protein-1 (OCT-1) using molecular docking technology, as well as to determine the drug's effect on serum OCT-1 levels in patients compared to healthy individuals. This may contribute to understanding the efficacy of this treatment in controlling blood glucose levels.

Materials and Methods: Molecular docking technology was used to determine the interaction of the glimepiride/metformin combination with organic cation transporter 1 (OCT-1). The study included 50 women: 26 with type 2 diabetes and 24 healthy women as a control group. ELISA was used to determine the levels of organic cations in the participants' serum.

Results: The results showed a high binding energy of -10.2 kcal/mol between the glimepiride/metformin combination and the OCT-1 protein, indicating the drug's efficacy in treating diabetes. These results confirm the findings of the clinical trial on OCT-1, which showed that the protein level in patients was (511.6 ± 120.3), similar to the concentration in the control group (558.8 ± 39.2), indicating that most of the drug had entered the cells.

Conclusions: The results suggest that the glimepiride/metformin combination is a recommended treatment option for lowering blood glucose levels and treating type 2 diabetes.

KEY WORDS: organic cation, type 2 diabetes, molecular docking, glimepiride

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INTRODUCTION

The protein-protein interaction is important in explaining the actions of several molecules as well as the structure for identification. Molecular docking was used for the interaction; this method explains the association with the active site [1, 2]. The presented method is very important in knowing the action of drugs that are used for treating diseases; the most important model used is diabetes [3, 4]. Several parameters were used to identify it is relation to diabetes and drug that used in treated diabetes [5, 6]. Diabetes is also associated with metabolic syndrome [7]. Most people with type 2 diabetes are obese and have insulin resistance, which reduces the cells' response to insulin [8, 9]. At the onset of the disease, beta cells increase insulin secretion to compensate, but over time, they become unable to maintain this level, leading to disease progression [10]. Genetic factors also play a role in the development of the disease [9, 11]. Many drugs are used to treat diabetes, the first line of treatment being the diabetes drug metformin [12, 13]. Metformin works by preventing the liver from producing glucose, reducing glucose production, and increasing energy expenditure in fat, liver, and muscle cells by activating AMP-activated protein kinase, which helps these tissues absorb and utilize glucose well [12, 14, 15]. Glimepiride, a type of medication called a sulfonylurea, helps control type 2 diabetes by stimulating the pancreas to secrete more insulin [16]. Many medications require transporter or carrier proteins. They facilitate the transport of many drugs and natural substances across cell membranes and organelles. One such transporter protein is the organic cation transporter OCT1 (SLC22A1), which is primarily expressed in the liver [17]. OCT-1 facilitates the uptake of cationic metabolites and drugs in the liver and plays a role in their distribution and transport within hepatocytes [18, 19]. Glimepiride increases the number of glucose transporters on the surface of muscle and adipose tissue cells, helping these cells absorb glucose more efficiently. It also promotes insulin-mediated glycogen synthesis and lipogenesis, and reduces glucose production in the liver. Its blood glucose-lowering effect is based on increased insulin

secretion and improved glucose utilization by the body Glimepiride is rapidly and completely absorbed when taken orally [20]. Combination of drugs are important to lowering blood glucose, for example metformin which is long been used for treating diabetes can be combined with other medications [21, 22]. Also, sulfonylurea drug with metformin or Glimepiride with metformin [23-25]. Although patients use these drugs to manage diabetes, their effectiveness in lowering blood sugar levels varies. This study was conducted to examine the effectiveness of various drugs in treating diabetes by examining how strongly they bind to receptors and comparing predicted results with actual receptor levels.

AIM

This study aimed to evaluate the interaction of glimepiride/metformin with organic cation transporter protein-1 (OCT-1) using molecular docking technology, as well as to determine the drug's effect on serum OCT-1 levels in patients compared to healthy individuals. This may contribute to understanding the efficacy of this treatment in controlling blood glucose levels

MATERIALS AND METHODS

This study included 50 women aged between 40 and 60 years with a body mass index (BMI) between 25.55 and 30.53.

The study was divided into two groups:

Group G1: 26 women diagnosed with type 2 diabetes, taking metformin with glimepiride.

Group G2: 24 healthy women, as a control group.

Patients with diabetes were diagnosed in the Diabetes and Endocrinology Department at Baghdad Teaching Hospital – Medical City. Diabetologists diagnosed 26 women with type 2 diabetes after assessing their symptoms and measuring their glycated hemoglobin (HbA1c) levels. The study also included a control group with normal HbA1c levels and no prior history of diabetes. All necessary approvals were obtained from the hospital and university for the study protocol.

CRITERIA FOR EXCLUSION

Women with chronic conditions, including heart, kidney, liver, bone, and tumor diseases, gastrointestinal diseases, hypertension, metabolic disorders, type 1 diabetes, and smokers, were excluded. women taking medications that could affect the study results were also excluded, with the exception of metformin and glimepiride.

SAMPLE COLLECTION AND ANALYSIS

Ten milliliters of venous blood were collected from each participant. A whole blood sample was immediately placed in an EDTA tube for glycated hemoglobin (HbA1c) level determination. The isolated serum was aliquoted into tiny containers. On the same day, spectrophotometry assessments were done on lipid and FBS levels in a segment of the extracted serum. The researchers aliquoted the residual serum into labeled storage vials and refrigerated it at -20°C to further measure the OCT-1 protein using the enzyme-linked immunosorbent assay (ELISA).

STATISTICAL WORK

Graph pad prism 10 and SPSS version 26 were used. Confidence interval 95% was used, One Way ANOVA analysis in combined with Tukey's multiple comparison tests were used to assess the significance level among the studied groups. other statistical toles was used like Reserve operator characteristic

ETHICAL APPROVAL

The ethical have been approved by the committee of College of Science for Women according to the reference 5302/22 in 2024/8/21

RESULTS AND DISCUSSION

MOLECULAR DOCKING

The researchers obtained the three-dimensional structure of OCT1 at a crystal resolution of 3.57 Å from the Protein Data Bank (PDB ID: 8ET6), which represents the native, unmutated form of the protein. Structural and physicochemical data for the drug compounds were obtained from PubChem. These compounds were then converted into the PDBQT format suitable for docking simulations using Open Babel, integrated into the PyRx platform.

THE MOLECULAR BOND OF GLIMEPIRIDE WITH THE ORGANIC CATION TRANSPORTER 1

The AutoDock program was used to analyze the molecular docking of glimepiride with the OCT-1 transporter protein. AutoDock was used to evaluate its binding affinity and location within the active site. Table 1 shows the optimal binding pose with a binding energy of -8.8 kcal/mol, indicating a strong and stable interaction between glimepiride and OCT-1. Other docking poses showed binding energies between -8.6 and -8.0 kcal/mol, supporting the stability of the molecule within the

Table1. Results of molecular docking of glimepiride with OCT1 protein

Ligand	Binding Affinity kcal/mol	RMSD	Interaction type	Amino Acids Residue
Glimepiride	-8.8	0	hydrogen bonds	SER-382
			carbon-hydrogen bonds Interaction	PHE-379
			van der Waals interactions	VAL-385, TYR-361, ARG-439, ILE-248, ILE-365, CYS-436, PHE-380, VAL -40 and LEU-248
			π-interactions such as π-sigma interactions	MET-368, and TYR -381
			π-alkyl interactions	TYR - 36, VAL-37,and LEU-384
			bi-anion interacts	ASP-378

Source: Compiled by the authors of this study

Table 2. Results of molecular docking of metformin and glimepiride with OCT-1 protein

Ligand	Binding affinity	RMSD/ lower and upper bound	Interaction type	Amino acids residue
Metformin + Glimepiride	-10.2	0	hydrogen bonds interactions	TYR-36, VAL-37, SER-358, ASP-474, and TYR-361
			Pi-sigma interactions	PHE-446
			van der Waals interactions	GLY-38, VAL-40, LYS-214, GLN-362, GLN-447, PHF-159, CYS-473, GLY-477, GLN-241, ALA-383, SER-382, ILE-365, ARG-439, and TRP-354
			Pi-alkyl interactions	PHE-379, LEU-248, and CYS -450
			alkyl interactions	PHE-379

Source: Compiled by the authors of this study

Table 3. Clinical data in patients having diabetes mellitus and control group

Parameter	G1:N=26 (Mean±SD)	G2:N=24 (Mean±SD)	P- Value
Age	49.3±7.2	44.6±6.2	0.7
BMI	29.9±3.1	26.2±1.8	0.005
FBG (mg/dl)	150.9±48.08	86.56±10.61	0.0001
HbA1C	8.361±1.568	5.246±0.388	0.0001
TG(mg/dl)	189.6±86.18	138.4±81.96	0.09
Cholesterol (mg/dl)	212.9±40.93	184.6±41.51	0.05
LDL(mg/dl)	125.7±36.45	110.6±40.75	0.2
HDL(mg/dl)	48.42±9.222	46.28±5.418	0.4
VLDL(mg/dl)	37.91±17.24	27.67±16.40	0.09

*Note: *For groups and presenting them with the symbols below:*
G1: Diabetic patients taking metformin with glimepiride;
G2: control group
Source: Compiled by the authors of this study

Table 4. Mean ± SD value of 1-OCT for studied groups

Parameters		G1	G2
OCT-1 (Pg/ml)	Mean± Std. deviation	511.6± 120.3	558.8± 39.2
	Lower 95% CI of mean	459.6	535.1
	Upper 95% CI of mean	563.6	582.5
	P Value	P= 0.1	

*Note: *For groups and presenting them with the symbols below:*
G1: Diabetic patients taking metformin with glimepiride;
G2: control group
Source: Compiled by the authors of this study

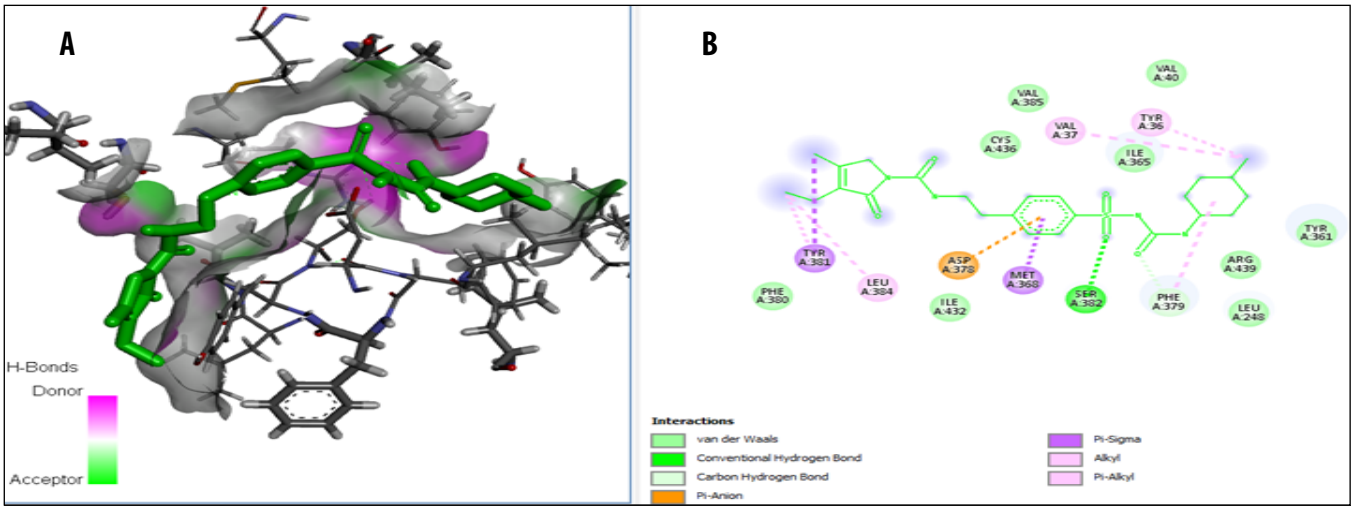


Fig. 1. A: Three-dimensional representation of the glimepiride interaction within the active site of the OCT-1 protein.
B: Two-dimensional representation of the glimepiride interactions with amino acid residues in the active site
Source: Own materials

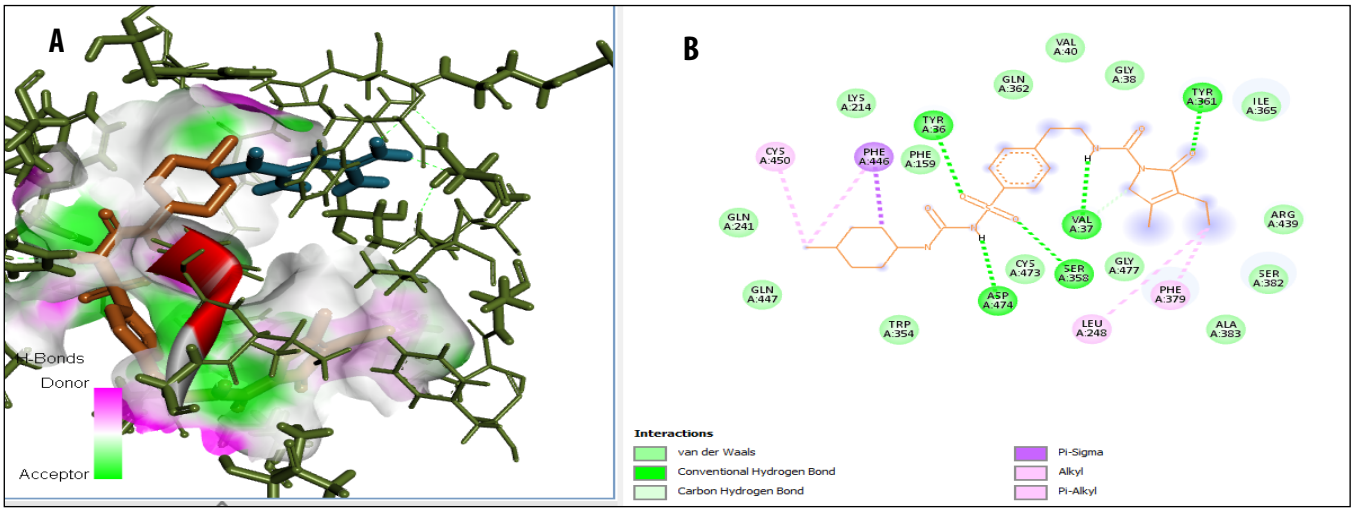


Fig. 2. A: 3D representation of metformin (shown in blue) and glimepiride (shown in red) interaction within the active site of OCT-1 protein.
B: Two-dimensional representation of the interactions of metformin and glimepiride with amino acid residues in the active site
Source: Own materials

active site. The optimal pose yielded an RMSD value of 0.0, confirming it as the reference structure. Figure 1. A-B shows that glimepiride localizes well within the protein's active pocket and identifies a set of key interactions with the surrounding amino acid residues. These include hydrogen bonds with SER-382, carbon-hydrogen bonds with PHE-379, and van der Waals interactions with VAL-385, TYR-361, ARG-439, ILE-248, ILE-365, CYS-436, PHE-380, VAL-40, and LEU-248. Interactions that contribute to enhancing the stability of glimepiride within the active site were observed: bi-sigma interactions with MET-368 and TYR-381, bi-alkyl interactions with TYR-36, VAL-37, and LEU-384, and a dianionic interaction with ASP-378. These results suggest that glimepiride exhibits a potent and effective binding to the OCT1 transporter protein, demonstrating its ability to influence protein function.

Molecular docking of metformin and glimepiride to the transporter protein OCT1, Using a molecular docking program, significant differences were found when the carrier protein was bound to metformin alone and then to both metformin and glimepiride. As previously demonstrated, the binding results with metformin were relatively weak, while the binding of glimepiride and metformin showed stronger results or binding forces of -8.5 and -10.2 kcal/mol. This improvement is likely due to the enhanced interactions facilitated by the presence of glimepiride with metformin, as the two molecules formed a network of interactions that included traditional hydrogen bonds with amino acids (such as TYR-36, VAL-37, SER-358, ASP-474, and TYR-361). Pi-sigma interactions were also evident with the amino acid PHE-446. In addition, van der Waals

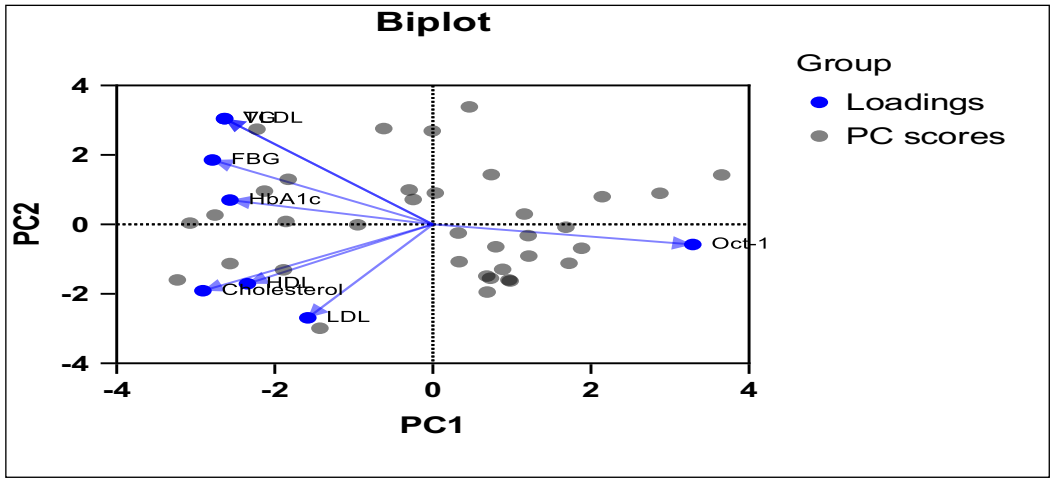


Fig. 3. Principle component analyses of metabolic parameters
Source: Own materials

interactions were recorded with (GLY-38, VAL-40, LYS-214, GLN-362, GLN-447, PHF-159, CYS-473, GLY-477, GLN-241, ALA-383, SER-382, ILE-365, ARG-439, and TRP-354), Pi-alkyl interactions were observed with (PHE-379, LEU-248, and CYS-450), and alkyl interactions occurred with the amino acid (PHE-379) as shown in Table 2 and Figure 2. A-C. These diverse and overlapping interactions reflect the compound's ability to stabilize itself within the binding site, enhancing the drug's interaction with the OCT-1 protein. This also suggests a potential synergistic effect on the transport or cellular uptake of the two drugs when used together, supporting their combined use in the clinical treatment of type 2 diabetes patients

In review patients with type 2 diabetes can receive glimepiride alone or in combination with other antidiabetic drugs. It can also be used as adjunctive therapy with insulin [26]. other study confirmed the clinical significance of glimepiride as a stimulant for insulin secretion from the pancreas, thereby improving blood glucose control [27]. A previous study evaluated the use of oral hypoglycemic medications to improve treatment practices. The results of this study showed that glimepiride was the optimal choice due to its superior pharmacokinetic properties in terms of safety and efficacy. However, its use was less common (28%) compared to glibenclamide, which was more commonly used (42.1%). Furthermore, the study found that the glibenclamide dosage was inadequate, and two cases of hypoglycemia were reported after prolonged use[28]. A recent computational study has shown that glimepiride has a high affinity for binding to human glucose transporter inhibitors and human aldose reductases, supported by molecular docking analysis and molecular dynamics simulation[29].

BIOCHEMICAL PARAMETERS

The clinical data of patients with diabetes mellitus and the control group are presented in Table 3. Age distribution ensured that age-related factors did not influence any statistically significant differences in the other variables. The results of the statistical analysis showed that age is not a statistically significant variable, due to the homogeneity of ages among the sample members. study results showed clear and statistically significant differences between groups G1 and G2 with regard to body mass index (BMI). indicating that individuals in group G1 experienced greater weight gain than individuals in groups G2. However, one study supports the idea that the drug has anti-obesity effects because it found that patients with type 2 diabetes who take metformin have a lower body mass index[30]. However, the results of this study showed the opposite: the mean body mass index (BMI) of patients using metformin with glimepiride (G1) was higher than the mean BMI of the healthy control group (G2). The lower BMI in the G2 group was an expected outcome, as these individuals did not suffer from any metabolic disorders and were likely to have followed healthy lifestyles that contributed to maintaining a normal weight. The higher BMI in the G1 group may be attributed to other factors, including poor adherence to treatment, lower levels of physical activity, or a difference in treatment duration.

Clinical parameters like HbA1c and FBG have been studied. The level of both studied parameters showed significant elevation in the patient group as compared to the control group. Use The combination treatment demonstrated the ability to control blood glucose and enhance cellular sensitivity to insulin. A previous study confirmed that glimepiride had a significant effect on blood glucose control [31]. Also, using the combination drugs improved blood glucose level [32]. A previous

study involving 76 patients compared the metformin/glimepiride and metformin/glibenclamide groups. The metformin/glimepiride group demonstrated greater effectiveness in controlling blood sugar levels, with a reduction in the number of hypoglycemic episodes among patients with uncontrolled type 2 diabetes[33]. According to a previous study that found individual patient responses to glimepiride vary, the ABCC8 gene polymorphism (rs757110) may affect insulin and glucose levels throughout the treatment period, underscoring the importance of tailoring treatment to each individual patient to maximize effectiveness and minimize risks [34]. The study did not show significant differences in lipid profile between the two groups, suggesting that the treatment did not significantly affect these parameters, as its effect depends on individual factors such as body weight and blood sugar control.

OCT1 protein levels were determined in the volunteer subject, as shown in Table 4. Molecular docking analysis revealed that glimepiride exhibited a good affinity for the OCT1 transporter protein's site, indicating a stronger binding affinity for this protein. A decrease in serum OCT1 concentrations was observed in diabetic patients receiving metformin-glimepiride, supporting the hypothesis of its important role in extracellular insulin transport via the OCT1 transporter protein. Its lower serum levels, compared to normal levels in healthy individuals, suggest increased cellular uptake. These results indicate that glimepiride possesses pharmacological properties that make it more effective in influencing insulin uptake via this protein. Previous research has shown that the OCT1 transporter protein facilitates the pharmacological efficacy of metformin by transporting it from intestinal cells to the portal circulation and allowing it to enter liver cells [25, 31]. These data underscore the importance of studying the properties and functions of the OCT1 transporter to understand the mechanisms of different drug responses in patients with type 2 diabetes.

Principle component analyses have been done to identify the contribution of the metabolic parameters in the disease Figure 3, Lipid profile, FBG, and HbA1c contributed toward the negative side of PC1 that indicates their association to the diabetic group; in contrast, OCT-1 loaded in the positive direction, which is related to the control group, and it is level related to the drug used.

CONCLUSIONS

The results of the molecular docking study indicate that glimepiride treatment, particularly when used in combination with metformin, exhibits high binding energy to the OCT1 protein, suggesting a stronger interaction that may contribute to improved drug uptake and intracellular efficacy. These biochemical findings support this hypothesis, as the group of patients receiving the glimepiride-metformin combination showed OCT1 protein levels similar to those observed in healthy individuals in the control group. Overall, these results highlight the importance of integrating clinical analysis with molecular docking techniques to better understand patient response to treatment and pave the way for designing personalized treatment plans based on each patient's molecular and physiological characteristics.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Impact of hormonal disorders after surgical treatment of endocrine pathology on dermatologic status and the need for aesthetic rehabilitation

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ABSTRACT

Aim: To evaluate the impact of postoperative hormonal disorders on dermatologic status and to determine the need for aesthetic rehabilitation in patients after surgical treatment of endocrine pathology.

Materials and Methods: A prospective cohort study included 128 patients aged 19–76 years after endocrine surgery. The sample comprised 54 patients after thyroidectomy, 61 after parathyroidectomy, 3 after adrenalectomy, and 10 after combined procedures. Dermatologic examination, scar assessment, hormonal profiling, and quality-of-life evaluation using SF-36 and DLQI were performed. Quantitative variables were summarized as mean ± standard deviation or median and interquartile range; qualitative variables as absolute and relative frequencies. Comparative analysis used the chi-square test, relative risk (RR) with 95% confidence interval (CI), and Pearson correlation (r).

Results: Hormonal dysfunction was identified in 93 patients (72.7%). Dermatologic changes were found in 101 patients (78.9%), most commonly xerosis (50.0%), pathological scarring (40.6%), alopecia (28.9%), and pigmentation disorders (24.2%). Patients with hormonal imbalance had a significantly higher risk of dermatologic complications than those without endocrine dysfunction (88.2% vs 55.6%; RR = 1.59; 95% CI 1.21–2.08; $p < 0.01$). Aesthetic defects requiring correction were identified in 76 patients (59.4%). Scar severity correlated with impaired dermatology-specific quality of life ($r = 0.61$; $p < 0.001$).

Conclusions: Hormonal disorders after endocrine surgery are significantly associated with dermatologic complications and reduced quality of life. Integration of dermatologic surveillance and aesthetic rehabilitation into postoperative care is clinically justified.

KEY WORDS: thyroid gland, skin diseases, quality of life

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INTRODUCTION

Endocrine surgical interventions, including thyroidectomy, parathyroidectomy, and adrenalectomy, are widely used in the treatment of endocrine pathologies. Despite advances in surgical techniques, postoperative hormonal imbalance remains a frequent and clinically relevant outcome [1, 2]. These disturbances have systemic effects involving metabolism, connective tissue, and reparative processes.

The skin is recognized as a hormonally responsive organ, sensitive to fluctuations in thyroid hormones, glucocorticoids, and calcium-regulating pathways [3–5]. Such changes may lead to xerosis, impaired elasticity, alopecia, dyschromia, and abnormal scar formation [6–9].

Thyroid dysfunction, in particular, has been associated with altered epidermal turnover, reduced hydration, and impaired dermal remodeling [8, 10]. Disorders of calcium metabolism and adrenal function may further contribute to structural and functional skin alterations [11, 12].

In addition to biological effects, dermatologic manifestations have a significant psychosocial impact. Visible scars and skin changes, especially in exposed areas, may negatively affect self-esteem and quality of life [13, 14]. Studies on thyroidectomy outcomes have shown that scar-related dissatisfaction remains clinically relevant even in cases of successful treatment [15, 16].

However, most available studies focus on isolated aspects of endocrine dermatology or scar outcomes. Comprehensive evaluation of the relationship between hormonal imbalance, dermatologic status, and the need for aesthetic rehabilitation remains limited. Therefore, further investigation of these interactions is necessary to improve postoperative management and support multidisciplinary care approaches [17–20].

AIM

To evaluate the impact of hormonal disorders after surgical treatment of endocrine pathology on dermatologic status and to determine the need for aesthetic rehabilitation.

MATERIALS AND METHODS

The study was designed as a prospective cohort clinical investigation with an analytical component. A total of 128 patients who underwent surgical treatment for endocrine pathology were consecutively included in the study. The observation period after surgery ranged from 3 to 24 months, which allowed assessment of both early and intermediate postoperative changes in hormonal status, skin condition, scar maturation, and patient-reported quality of life.

The study was conducted during 2024–2025 and was based at the State Institution of Science «Center of innovative healthcare technologies» State Administrative Department (Kyiv, Ukraine) and Kyiv City Clinical Hospital № 1 (Kyiv, Ukraine). Patient recruitment was performed prospectively, with consecutive inclusion of eligible participants, while clinical examination and data collection were carried out at both institutions according to a unified study protocol, ensuring methodological consistency and comparability of results.

The age of the patients ranged from 19 to 76 years. The mean age was (mean [M] ± standard deviation [SD]) 48.6±12.4 years; the median (Me) age was 49 years, with an interquartile range (IQR) of 39–58 years. The sex distribution showed a slight predominance of women: 70 women (54.7%) and 58 men (45.3%), corresponding to a female-to-male ratio of 1.21:1.

According to the type of surgical intervention, the cohort included 54 patients after thyroidectomy, 61 after parathyroidectomy, 3 after adrenalectomy, and 10 after combined surgical procedures. Combined procedures included cases in which the volume of intervention involved more than one endocrine anatomical region or required extended operative management with a potentially greater systemic hormonal impact.

Inclusion criteria were as follows: age over 18 years, history of endocrine surgical treatment, postoperative follow-up from 3 to 24 months, and the patient's ability to provide informed consent and complete questionnaires. Exclusion criteria comprised severe primary dermatologic diseases unrelated to endocrine dysfunction, decompensated systemic inflammatory disease, severe psychiatric conditions impairing questionnaire completion, active generalized infection, and terminal oncologic status.

Clinical evaluation included a structured dermatologic examination with attention to skin hydration, elasticity, desquamation, pigmentation changes, vascular manifestations, appendageal disorders, and characteristics of postoperative scars. The scar assessment was based on routine clinical criteria reflecting elevation, density, color, and subjective symptoms, and was additionally supported by standardized photographic documentation. For analytical purposes, clinically significant scarring was defined as a visible postoperative scar with one or more of the following features: hypertrophy, irregular contour, persistent erythema, adhesiveness, subjective discomfort, or clear cosmetic dissatisfaction.

Hormonal status was assessed according to the type of surgical intervention. In thyroidectomy patients, serum thyroid-stimulating hormone and free thyroxine were analyzed. In parathyroidectomy patients, parathyroid hormone and calcium-phosphate metabolism parameters were considered. In adrenalectomy patients, cortisol-related postoperative status was assessed. Hormonal dysfunction was defined as laboratory-confirmed deviation from reference values accompanied, where relevant, by clinical or treatment-related significance.

Quality of life was assessed using two validated instruments. General health-related quality of life was evaluated by the SF-36 questionnaire, while skin- and appearance-related burden was assessed using the Dermatology Life Quality Index (DLQI). A DLQI score above 6 was interpreted as reflecting at least moderate impact on dermatology-specific quality of life.

Statistical analysis was performed using standard biostatistical approaches. Quantitative variables were presented as M ± SD or as Me and IQR, depending on data distribution. Qualitative variables were described using absolute and relative (%) frequencies (with 95 % confidence interval [CI] provided where appropriate). Differences in categorical variables between groups were assessed using the chi-square test. Relative risk (RR) and 95% CI was calculated for major clinical associations. Pearson correlation (r) analysis was used to determine the relationship between continuous or ranked clinical indicators, including the association between scar severity and DLQI, as well as between thyroid-related indicators and xerosis severity. A p-value of less than 0.05 was considered statistically significant.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Table 1. Baseline characteristics of the study cohort (n=128)

Parameter	n	% / Descriptive indicator
Type of surgery		
Thyroidectomy	54	42.2
Parathyroidectomy	61	47.7
Adrenalectomy	3	2.3
Combined procedures	10	7.8
Sex		
Women	70	54.7
Men	58	45.3
Age		
Range	—	19–76 years
M ± SD	—	48.6±12.4
Me (IQR)	—	49 (39–58)

Source: compiled by the authors of this study

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki and the standards of good clinical practice. All patients were informed about the purpose of the study, the character of the examinations performed, and the anonymous use of aggregated data for scientific analysis. Written informed consent was obtained from all participants prior to inclusion. The study protocol was approved by the local bioethics committee of the participating institution.

FRAMEWORK

The study was conducted as a fragment of the Scientific Department of Minimally Invasive Surgery scientific project (State Institution of Science «Center of innovative healthcare technologies» State Administrative Department) «Optimization of approaches to providing specialized medical care for surgical patients using personalized anesthetic support» (state registration number 0125U000315; term: 2025-2029).

RESULTS

A total of 128 patients were examined. The structure of the cohort by surgery type, sex distribution, and age characteristics is presented in Table 1.

The analysis of Table 1 demonstrates that the largest subgroup consisted of patients after parathyroidectomy (47.7%), followed by thyroidectomy (42.2%). Adrenalectomy was markedly less frequent, which should be taken into account when interpreting subgroup-specific findings. The sex structure was relatively balanced, although women predominated slightly, which is consistent with the epidemiological distribution of several endocrine conditions. The age profile indicates that a considerable proportion of the sample belonged to working-age groups, underscoring the social and rehabilitative relevance of postoperative aesthetic outcomes.

Postoperative hormonal dysfunction was identified in 93 of 128 patients (72.7%; 95% CI 64.3–80.0). The frequency of endocrine imbalance according to surgery type is shown in Table 2.

Table 2 shows that combined surgical procedures were associated with the highest proportion of postoperative hormonal dysfunction (80.0%), followed by thyroidectomy (72.2%). Although adrenalectomy demonstrated a high relative proportion (66.7%), this subgroup was too small for robust isolated inference. The lowest frequency of hormonal disturbances was observed after parathyroidectomy (55.7%), yet even in this group, more than half of the patients had clinically relevant biochemical imbalance. These findings suggest that postoperative endocrine instability is common across endocrine surgical categories but appears particularly pronounced in interventions with a larger or more complex endocrine impact.

Dermatologic changes of varying severity were recorded in 101 of 128 patients (78.9%; 95% CI 71.0–85.4). Their structure is summarized in Table 3.

According to Table 3, xerosis and reduced elasticity constituted the most frequent dermatologic complaints, affecting half of the study population. Pathological scarring was the second most prevalent manifestation and occurred in 40.6% of patients, which is clinically meaningful given the visibility of cervical and upper thoracic postoperative areas. Hair-related changes and pigmentary disturbances were also common, while vascular manifestations occurred less frequently but contributed to the aesthetic burden in a subset of patients. Overall, the pattern indicates that endocrine

Table 2. Postoperative hormonal dysfunction according to the type of surgery

Type of surgery	Patients with hormonal dysfunction, n	Total in subgroup, n	%
Thyroidectomy	39	54	72.2
Parathyroidectomy	34	61	55.7
Adrenalectomy	2	3	66.7
Combined procedures	8	10	80.0
Total	**93**	**128**	**72.7**

Source: compiled by the authors of this study

Table 3. Structure of dermatologic manifestations in the study cohort

Dermatologic manifestation	n	%
Xerosis / reduced skin hydration and elasticity	64	50.0
Pathological scarring	52	40.6
Alopecia / hair thinning	37	28.9
Pigmentation disorders	31	24.2
Vascular changes / telangiectatic component	19	14.8

Source: compiled by the authors of this study

Table 4. Association between hormonal dysfunction and dermatologic complications

Group	Dermatologic complications, n	No dermatologic complications, n	Total, n	% with dermatologic complications
Hormonal dysfunction present	82	11	93	88.2
Hormonal dysfunction absent	19	16	35	54.3

Source: compiled by the authors of this study

Table 5. Main dermatologic manifestations according to type of surgery, % within subgroup

Type of surgery	Xerosis	Pathological scarring	Alopecia	Pigmentation disorders
Thyroidectomy (n=54)	61.1	63.0	40.7	29.6
Parathyroidectomy (n=61)	44.3	27.9	18.0	19.7
Adrenalectomy (n=3)	66.7	33.3	33.3	33.3
Combined procedures (n=10)	70.0	70.0	50.0	40.0

Source: compiled by the authors of this study

surgical patients experience not a single isolated cosmetic symptom, but rather a complex combination of texture, appendageal, and scar-related changes.

To determine whether hormonal imbalance was associated with a higher burden of skin pathology, the prevalence of dermatologic manifestations was compared between patients with and without postoperative hormonal dysfunction (Table 4).

The comparison presented in Table 4 revealed a marked difference in dermatologic burden between the groups. Among patients with hormonal dysfunction, 88.2% had clinically relevant dermatologic manifestations, whereas among patients without hormonal imbalance this proportion was 54.3%. The calculated relative risk of dermatologic complications in the presence of postoperative hormonal dysfunction was RR=1.62 (approximately; 95% CI 1.18–2.22), and the group difference was statistically significant (χ^2, $p<0.01$). This confirms that hormonal imbalance is not merely an accompanying postoperative finding, but a clinically important determinant of skin pathology.

Further subgroup analysis by type of surgery demonstrated distinct dermatologic profiles (Table 5).

Table 5 indicates that the most unfavorable dermatologic pattern was observed after combined procedures, in which xerosis and pathological scarring each reached 70.0%. Thyroidectomy patients also showed a high burden of xerosis and scarring, supporting the relevance of thyroid hormone regulation for skin hydration, repair, and scar remodeling. By contrast, parathyroidectomy patients had comparatively lower rates of scar and hair involvement, although dermatologic complications remained clinically important in this group as well. Because the adrenalectomy subgroup was very small, these data are best interpreted descriptively.

Aesthetic defects considered sufficient to justify medical correction or specialized counseling were identified in 76 patients (59.4%). The most common aesthetically significant abnormalities included visible cervical scar deformation, contour irregularity of the anterior neck region, persistent discoloration within the scar zone, and combined skin-hair changes contributing to dissatisfaction with appearance.

The quality-of-life assessment showed that 63 of 128 patients (49.2%) had DLQI values above 6, corresponding to moderate or more pronounced negative dermatologic impact on daily life. Correlation analysis demonstrated a strong positive association between scar severity and DLQI ($r=0.61$; $p<0.001$), indicating that worsening scar characteristics were accompanied by progressive impairment in dermatology-specific quality of life. In thyroidectomy patients, a moderate positive relationship was also found between thyroid-related hormonal imbalance and xerosis severity ($r=0.52$; $p<0.01$), supporting the biological plausibility of the observed cutaneous changes.

In summary, the Results section shows that postoperative hormonal dysfunction was common, dermatologic complications affected the majority of patients, and the burden of these changes was significantly greater in hormonally unstable individuals. The combination of frequency data, comparative risk estimates, and quality-of-life correlations provides a consistent basis for considering dermatologic surveillance and aesthetic rehabilitation as clinically meaningful elements of postoperative care in endocrine surgery.

DISCUSSION

The results of this study confirm that hormonal disturbances after endocrine surgery are significantly associated with dermatologic complications and reduced quality of life. These findings support the concept of the skin as a hormonally regulated organ whose structure and function depend on systemic endocrine balance [5–7].

The high prevalence of xerosis and decreased skin elasticity observed in this cohort, particularly after thyroidectomy, is consistent with previous reports demonstrating the role of thyroid hormones in epidermal turnover and dermal hydration [8, 10]. Similarly, endocrine dysfunction has been shown to impair barrier function and connective tissue metabolism, contributing to clinically significant skin changes [9].

The association between hormonal imbalance and pathological scarring identified in this study aligns with evidence that systemic factors, including endocrine status, influence wound healing and collagen remodeling [17]. Studies of thyroid surgery outcomes have also shown that scar characteristics significantly affect patient satisfaction and quality of life [13, 15, 16].

The observed correlation between scar severity and DLQI confirms the importance of dermatologic manifestations in shaping psychosocial well-being. Previous research has demonstrated that visible scars may impair social functioning and self-perception, particularly in anatomically exposed regions [14, 18].

From a clinical perspective, the high prevalence of aesthetic defects indicates that postoperative care should not be limited to endocrine and surgical outcomes. Instead, early dermatologic assessment and integration of aesthetic rehabilitation should be considered essential components of patient management.

These findings are consistent with modern patient-centered approaches and international recommendations emphasizing multidisciplinary rehabilitation strategies [19, 20].

Despite certain limitations, including a small adrenalectomy subgroup and an observational design, the study provides evidence supporting a comprehensive approach to postoperative care in patients undergoing endocrine surgery.

CONCLUSIONS

The present study demonstrates that postoperative hormonal disorders following surgical treatment of endocrine pathology are highly prevalent and represent a significant factor contributing to dermatologic complications. The findings confirm a statistically significant association between endocrine imbalance and the development of clinically relevant skin changes, including xerosis, pathological scarring, alopecia, and pigmentation disorders. This underscores the systemic nature of postoperative endocrine dysfunction and its direct impact on skin homeostasis and reparative processes.

A substantial proportion of patients exhibited aesthetic defects requiring medical attention, and nearly half demonstrated impaired dermatology-specific quality of life. The strong correlation between scar severity and DLQI indicates that dermatologic manifestations are not merely cosmetic concerns but constitute an important determinant of psychosocial well-being and patient-reported outcomes. These results highlight the necessity of incorporating dermatologic assessment into routine postoperative evaluation.

Overall, the data support the implementation of a multidisciplinary approach to postoperative care in patients undergoing endocrine surgery, integrating endocrine management, dermatologic monitoring, and aesthetic rehabilitation. Such an approach has the potential to improve both functional recovery and quality of life and should be considered in the development of standardized clinical pathways for this patient population.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Current issues in the vaccination of healthcare workers

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ABSTRACT

Aim: To assess healthcare professionals' attitudes toward vaccination, evaluate vaccination coverage, and perform a SWOT analysis of immunoprophylaxis to identify strengths, weaknesses, opportunities, and threats.

Materials and Methods: A structured, anonymous 23-item questionnaire assessed knowledge and attitudes toward immunoprophylaxis among healthcare workers (HWs), covering demographics, vaccination awareness, infection prevention practices, attitudes, and professional motivation. The online survey (Google Forms) was conducted from May to December 2025 with ensured anonymity. Vaccination coverage was assessed using records of 1060 HWs from two public healthcare facilities, with comparative analysis across departments. A SWOT analysis was performed. For relative indicators, 95% confidence intervals (CIs) were calculated, accounting for sampling error associated with sample size (MedStat v.5.2).

Results: The majority of study participants demonstrated a positive attitude towards immunoprophylaxis: 72.4% (CI: 63.8–81.0) rated it as absolutely positive. However, gaps were identified: correct understanding of current COVID-19 vaccination recommendations was 28% (CI: 19.4–36.6), while 74% (CI: 65.6–82.4) correctly assessed continuation of vaccination schedules. The SWOT analysis showed generally positive attitudes toward vaccination and potential for improving coverage through education and management interventions.

Conclusions: Despite positive attitudes (72.4%) and satisfactory self-assessed knowledge, vaccination coverage among healthcare workers remains low (<30%): 29.7% for tetanus-diphtheria and 27.5% for hepatitis B. This reflects a clear gap between knowledge, motivation, and practice, indicating the need for integrated interventions, including education, communication skills development, and strengthened institutional vaccination policies.

KEY WORDS: immunoprophylaxis, healthcare workers, infection control, communication

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INTRODUCTION

Immunoprophylaxis is one of the most effective measures for preventing infectious diseases and an important component of the infection control system in healthcare facilities. Vaccination of healthcare workers (HWs) is one of the key tools of modern preventive medicine, ensuring the safety of healthcare provision, reducing the spread of infections in healthcare facilities (HCFs), and protecting both staff and patients [1, 2]. HWs belong to groups at increased occupational risk of infection. Their immunization plays an important role not only in the prevention of vaccine-preventable diseases but also in combating antibiotic resistance, as a reduction in morbidity helps reduce the inappropriate use of antibacterial drugs and, consequently, slows the development of resistant strains of microorganisms [1].

In Ukraine, the importance of immunoprophylaxis among the general population is determined by several key factors. First and foremost, there remains a risk of the spread of vaccine-preventable infections such as measles, diphtheria, and viral hepatitis B. At the same time, vaccination coverage among the adult population, including HWs, remains insufficient in some cases and stands at around 60–80%.

Although most HWs generally have a positive attitude toward immunoprophylaxis, their actual vaccination rates are often lower than the recommended levels. In particular, the rate of hepatitis B vaccination among HWs varies across countries, ranging from 60% to 90%, depending on the availability of relevant programs and the effectiveness of monitoring their implementation [3]. This highlights a gap between a positive attitude toward immunoprophylaxis and actual vaccination coverage, which does not always meet immunization targets.

In the context of these challenges, the issue of effective interaction between healthcare professionals and patients takes on particular importance, as the quality of communication directly influences the level of trust and acceptance of vaccination. Problems in healthcare professionals' communication with patients regarding immunoprophylaxis are linked to inadequate commu-

nication skills, a lack of time for consultation, the use of complex medical terminology, and reduced trust in vaccination due to the influence of misinformation [1, 4, 5]. These factors complicate the building of patient trust and acceptance of vaccination, reducing the effectiveness of preventive measures, which requires both thorough analysis and targeted intervention. Consequently, improving healthcare professionals' communication skills is one of the key areas for enhancing the effectiveness of immunoprophylaxis.

In view of the above, it is advisable to apply strategic assessment tools, in particular SWOT analysis. SWOT analysis is widely used to evaluate immunoprophylaxis programs at both national and global levels, enabling the identification of internal and external factors influencing the effectiveness of vaccination [6, 7].

AIM

To assess the attitudes of healthcare professionals from various disciplines towards vaccination, determine their vaccination coverage rates, and conduct a SWOT analysis of immunoprophylaxis among healthcare staff to identify strengths, weaknesses, opportunities, and potential threats.

MATERIALS AND METHODS

To assess knowledge and attitudes towards immunoprophylaxis among healthcare workers, a structured anonymous questionnaire was developed, consisting of 23 questions and comprising the following sections: general information about the respondent (age, gender, field of professional activity) – three questions; awareness of vaccination (vaccinations in accordance with the national schedule, vaccination against influenza, COVID-19 and other infections) – five questions; assessment of practical skills and behavioral aspects of infection prevention – five questions; attitudes towards vaccination (assessment of vaccine efficacy and safety, level of trust) – four questions; professional motivation and communication skills – six questions

During the study, primary data obtained through a survey of healthcare workers were used, as well as documentary materials containing information on vaccinations administered. The survey was conducted between May and December 2025. Data were collected using an online questionnaire (Google Forms) distributed via Google Drive.

A SWOT analysis [6, 7] was used to assess healthcare professionals' attitudes towards vaccination, vaccination coverage rates, and awareness of immunoprophylaxis. This enabled the identification of internal and external factors influencing vaccination status and staff awareness, as well as an analysis of strengths, weaknesses, opportunities, and threats. The SWOT analysis included: strengths: medical training, access to evidence-based information, a high level of professional responsibility; weaknesses: lack of time, insufficient knowledge regarding certain aspects of vaccination, mistrust of certain vaccines, low motivation; opportunities: implementation of educational programs, national and local immunization campaigns, expanded access to free vaccines; threats: spread of misinformation, professional burnout, increased epidemiological risks.

The elements of the SWOT analysis were developed based on the results of the questionnaire and data on the actual vaccination coverage among the target population, which made it possible to assess both the vaccination rate and the target population's awareness.

To assess vaccination coverage, an analysis was conducted of records regarding preventive vaccinations received by 1060 HWs in two public healthcare facilities. A comparative analysis was carried out between different departments of multi-specialist hospitals to identify differences in vaccination rates.

Statistical data processing was carried out using the MedStat v.5.2 software. For relative indicators, 95% confidence intervals (CIs) were calculated, taking into account the sampling error associated with sample size.

ETHICS

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Participation was voluntary, and no personal data were collected. Prior to participation in the study, all respondents were duly informed about the purpose of the survey, its design, and the assurance of anonymity and confidentiality regarding their personal data and the information provided.

FRAMEWORK

The study was conducted as a fragment of the scientific project of the Department of_Epidemiology and Evidence-Based Medicine, Bogomolets National Medical University, «Studying the impact of the Russian-Ukrainian armed conflict and the COVID-19 pandemic on the morbidity and mortality of the population of Ukraine» (state registration number 0125U001645; term: 2025-2027).

RESULTS

As part of the study, 104 questionnaires completed by healthcare workers were analyzed to assess their atti-

tudes towards immunization, level of awareness, and practical involvement in its implementation. Women predominated among the respondents – 86.5% (CI: 79.9–93.1), which corresponds to the gender structure of the healthcare system [8]. In terms of professional activity, 61% (CI: 51.6–70.4) of respondents were involved in clinical practice, whilst 39% (CI: 29.6–48.4) worked in healthcare management and organizational structures. The majority of study participants viewed immunoprophylaxis positively: 72.4% (CI: 63.8–81.0) classified their attitude as unambiguously positive. At the same time, 62.0% (CI: 52.7–71.3) of respondents reported being vaccinated against seasonal influenza annually. The vaccination rate was higher among representatives of healthcare management structures – 70% (95% CI: 56.0–84.0) – compared with healthcare practitioners in the clinical sector – 57% (95% CI: 44.8–69.2). Among those surveyed, 59% (CI: 49.6–68.4) of healthcare professionals were directly involved in organizing or conducting vaccination sessions.

Respondents generally rated their colleagues' awareness of vaccination and their own knowledge of current recommendations highly. At the same time, only 28% (CI: 19.4–36.6) answered questions on current COVID-19 vaccination recommendations correctly. In contrast, 74% (CI: 65.6–82.4) correctly identified the possibility of continuing the vaccination course without loss of efficacy. Awareness of the Immunoprophylaxis Development Strategy up to 2030 [9] was reported by 73% (CI: 64.5–81.5) of study participants.

When assessing communication aspects, it was found that 71% (CI: 62.3–79.7) of respondents frequently or occasionally encounter individuals who are skeptical about vaccination. In such situations, 88% (CI: 81.7–94.3) attempt to explain the benefits of vaccination, whilst 75% (CI: 66.7–83.3) use arguments based on the principles of evidence-based medicine. At the same time, 55% (CI: 45.4–64.6) reported difficulties in communicating with individuals who hold strong anti-vaccination beliefs.

Among the factors negatively affecting vaccination coverage, the most frequently cited were misinformation in the media – 61% (CI: 51.6–70.4), fear of possible side effects – 54% (CI: 44.4–63.6), and the influence of one's social circle – 32% (CI: 23.1–40.9). According to respondents, the views of family, friends, or colleagues can significantly influence an individual's decision regarding vaccination. The vast majority of respondents, namely 62% (CI: 52.7–71.3), believe that information campaigns alone are insufficient to significantly increase vaccination rates.

Thus, analysis of the data shows that the key barriers are predominantly informational and communication-related, which underscores the need to strengthen systematic educational efforts and develop effective strategies to counter misinformation.

For a significant proportion of respondents – 79% (CI: 71.2–86.8) – the opportunity to influence vaccination rates by educating others is an important motivating factor.

Respondents rated their colleagues' awareness of vaccination highly – 84% (CI: 76.4–91.8), and their own knowledge of current recommendations – 80% (CI: 72.6–87.8), which demonstrates a general confidence in their professional competence regarding immunoprophylaxis.

The following key aspects can be identified based on the survey results:

– Correct understanding of current recommendations regarding COVID-19 vaccination – 28% (CI: 19.4–36.6). This figure indicates significant gaps in knowledge regarding current approaches;

– Correct assessment of the possibility of continuing the vaccination course without loss of efficacy – 74% (CI: 65.6–82.4). The majority of respondents demonstrated a correct understanding of the principles of immune response formation;

– Awareness of the Immunoprophylaxis Development Strategy up to 2030 – 73% (CI: 64.5–81.5). This indicates a sufficient level of awareness regarding the strategic directions for the sector's development.

The results obtained, taking into account the margin of error, indicate a generally positive attitude among healthcare professionals towards immunoprophylaxis and their active professional engagement. At the same time, the widening of CIs compared to a larger sample size points to increased statistical uncertainty and highlights the need for further research and systematic updating of educational programmes.

To assess vaccination coverage in healthcare facilities, data from 1,060 HWs were analyzed, divided into four groups: inpatient units for adults, inpatient units for children, outpatient units, and paraclinical units. Vaccination coverage against hepatitis B (HBV) and tetanus and diphtheria (TD) in various units was analyzed. Mandatory vaccination of HWs is regulated by regulatory and legal documents and relevant orders of the Ministry of Health of Ukraine [10]. In total, 292 individuals were vaccinated against HBV, representing 27.5% (CI: 24.8–30.2), and 315 individuals against TD, representing 29.7% (CI: 26.9–32.5).

Among the target population in inpatient units for adults, the highest number of vaccinations was recorded: 222 individuals against TD, accounting for 38.8% (CI: 34.8–42.8), and 201 individuals against HBV – 35.1% (CI: 31.2–39.0). In inpatient units for children, the proportion vaccinated against TD was 33.3% (CI: 21.9–44.7) and against HBV – 25.7% (CI: 15.2–36.4). In outpatient units,

Table 1. SWOT analysis of immunization (coverage and knowledge) among healthcare professionals

Strengths	Weaknesses
Higher vaccination rates in inpatient departments: tetanus/diphtheria 38.8% (CI: 34.8–42.8); positive attitude towards vaccination: 72.4% (CI: 69.6–75.2); personal practice of flu vaccination: 70% (CI: 56.0–84.0); self-assessment of knowledge: colleagues' awareness – 84%, own knowledge – 80%; active participation in organizing vaccination sessions – 59% (CI: 56–62).	Overall vaccination coverage against tetanus/diphtheria: 29.7% (CI: 26.9–32.5); low hepatitis B vaccination coverage: 27.5% (CI: 24.8–30.2); vaccination coverage among primary care practitioners seeing outpatients: tetanus/diphtheria – 14.5% (CI: 10.1–18.9); discrepancy between positive attitudes and actual vaccination; low awareness of current recommendations regarding COVID-19 – 28% (CI: 23.9–32.1); ambiguity in regulatory documents regarding the reporting of adverse events
Opportunities	**Threats**
Motivation to educate others: 79% (CI: 76.5–81.5); increasing vaccination coverage to ≥80%; training on communicating with sceptics: 55% (CI: 52–58); use of evidence-based practices: 75% (CI: 72.2–77.8); educational campaigns on current vaccination schedules; integration of vaccination into the infection control system; strengthening the role of managers as agents of change	High percentage of people not vaccinated against tetanus/diphtheria: 70.3% (CI: 67.5–73.1); not vaccinated against hepatitis B: 72.5% (CI: 69.7–75.3); risk of occupational infection (HBV, tetanus, diphtheria); risk of spreading nosocomial infections (HAI); misinformation in the media – 61%; fear of side effects – 54%; influence of peers – 32%; comments during inspections/audits

Source: compiled by the authors of this study

vaccination coverage was lower, at 14.5% (CI: 10.1–18.9) against TD and 23.4% (CI: 18.3–28.5) against HBV. In paraclinical units, vaccination coverage against TD was 20.9% (CI: 14.5–27.3) and against HBV was 4.1% (CI: 2.0–6.2).

A SWOT analysis was conducted based on the obtained data on vaccination coverage rates among the target population and the results of a survey on attitudes towards immunization. This made it possible to systematize the identified strengths and weaknesses, as well as to identify key opportunities and threats for increasing vaccination rates. The results of the SWOT analysis are presented in Table 1.

The SWOT analysis revealed that healthcare workers generally have a positive attitude towards vaccination and significant potential to improve immunization coverage through educational initiatives and proactive management decisions. At the same time, there remains a substantial gap between attitudes towards vaccination and actual vaccination practices, exacerbated by insufficient knowledge and the influence of misinformation. Therefore, increasing vaccination coverage requires a comprehensive approach that combines training, clear regulatory frameworks, and a strengthened role for managers as a key tool for improving vaccination rates among HWs.

DISCUSSION

According to the literature, critically low immunization rates were observed in Middle Eastern countries between 2020 and 2024: only 16.75% for hepatitis B virus (HBV) and 12.87% for tetanus/diphtheria [11]. These figures are consistent with earlier studies in the United States, where tetanus/diphtheria coverage among HWs in 2011 was only 26.9%, although this figure was higher than that in the general population (11.1%) [12].

In 2018–2019, a sociological survey was conducted involving 1,384 healthcare professionals from four regions of Ukraine. The results revealed gaps in healthcare professionals' knowledge and perceptions regarding the organization of vaccination. The highest level of awareness regarding immunoprophylaxis was demonstrated by healthcare facility managers and specialists who had undergone specialized training in vaccination, whilst the lowest level of awareness was observed among clinical healthcare practitioners [13].

A study conducted in Poland in 2021 among 2,300 healthcare workers using a questionnaire assessed their attitudes and behavioral intentions regarding vaccination against COVID-19. It was found that 82.95% of respondents expressed willingness to be vaccinated against SARS-CoV-2. At the same time, HWs represent a group at increased biological risk due to their daily professional activities. Despite the relatively high level of declared willingness to be vaccinated, the overall proportion of HWs intending to be vaccinated against COVID-19 is considered insufficient [14]. COVID-19 infection among HWs affects the provision of healthcare services to the population [15].

In a study conducted in the United States in 2021, 1257 HWs were surveyed via a questionnaire. The study assessed COVID-19 vaccination status, professional contact with COVID-19 patients, reasons for deciding to get vaccinated or refusing the vaccine, and the main sources of information about vaccination. The results showed that the level of support for vaccination among HWs in the United States was only 60–67%. The main reasons for low uptake were low levels of trust in vaccines, a lack of reliable information, and the influence of personal beliefs [14]. The Centers for

Disease Control and Prevention (CDC) recommends that healthcare professionals actively encourage the public to get vaccinated against COVID-19. To increase the effectiveness of such measures, it is important to understand the general perception of vaccines among healthcare workers and other healthcare professionals [5].

The results of studies conducted in China in 2022 indicate that HWs generally demonstrate a high level of vaccine acceptance, which, however, varies depending on socio-demographic and professional characteristics. According to a meta-analysis, the level of willingness to be vaccinated among healthcare workers in China is around 78%, highlighting the need for targeted educational programmes. The implementation of these programmes may help increase vaccination coverage and support the development of herd immunity [16].

The use of SWOT analysis in conjunction with data from a healthcare professional survey allows for the systematization of factors influencing vaccination adherence, including organizational barriers and behavioral aspects [17]. The SAGE working group defines vaccine hesitancy as a delay in acceptance or refusal of vaccination despite its availability. Recognizing this phenomenon is important for developing a coordinated approach among specialists and allows for clearer identification of factors contributing to lower vaccination rates. At the same time, low vaccination coverage is not always due to hesitancy alone, a fact that must be taken into account when planning relevant measures [18].

LIMITATIONS OF THE STUDY

The authors of the manuscript acknowledge that the limitations of this review stem from the fact that the results reflect the views of the sample rather than the entire population of healthcare workers in Ukraine; the margin of error does not account for possible self-selection bias associated with voluntary participation in the survey; the data are sufficient for analytical conclusions but require caution when extrapolated to the national level.

PROSPECTS FOR FURTHER RESEARCH

Future research will focus on analyzing the level of awareness among medical students regarding immunoprophylaxis. It is important to assess the effectiveness of educational programs in fostering professional knowledge and a responsible attitude towards vaccination. It is also advisable to compare the level of awareness among students from different years and faculties, which will help identify existing gaps and determine areas for improving the educational process, thereby positively influencing the training of future healthcare professionals.

CONCLUSIONS

Despite a positive attitude towards immunoprophylaxis (72.4%) and a satisfactory level of self-assessed knowledge among healthcare workers, actual vaccination coverage remains critically low (<30%). Specifically, 29.7% of HWs have been vaccinated against tetanus and diphtheria, and 27.5% against hepatitis B. This highlights a gap between knowledge, motivation, and practice and points to the need for systematic managerial and educational measures. The identified discrepancy underscores the need for comprehensive interventions combining educational programmes, the development of communication skills, and adherence to institutional policies to increase vaccination coverage among healthcare workers.

Therefore, an adequate level of vaccination among HWs is a vital component of Ukraine's public health system. Immunisation provides individual protection, reduces the risk of healthcare-associated infections (HAIs), enhances patient safety, and helps build trust in vaccination.

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ORIGINAL ARTICLE

CONTENTS

Communication strategies in ensuring the quality of obstetric and gynecological care

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ABSTRACT

Aim: To substantiate measures for improving the quality of obstetric and gynaecological care by enhancing communication among participants in the healthcare delivery process.

Materials and Methods: Bibliographic, sociological, medical-statistical, and information-analytical methods were used. Sources included scientific literature, sociological survey results, and international and national healthcare quality strategies and programmes. The survey involved 202 healthcare professionals from a maternity hospital and an antenatal clinic in Kyiv and Kyiv Oblast (2021), and 108 healthcare managers who completed a custom-designed Google Forms questionnaire (2025–2026).

Results: The medical and social study identified current communication problems among participants in obstetric and gynaecological care delivery. Despite declared principles of openness, systemic barriers persist in healthcare facilities, including interstructural dysfunction and hierarchical dependence. According to managers, non-compliance with care standards is partly related to insufficient communication between medical personnel and patients, as well as between administration and staff. Key obstacles to implementing a patient-oriented approach included formal monitoring of satisfaction, resource deficits, and weaknesses in internal interaction at different management levels.

Conclusions: Analysis of organisational culture in obstetric and gynaecological facilities revealed significant communication problems and hierarchical barriers that complicate adherence to care standards and may increase patient safety risks. System improvement should focus on strengthening horizontal communication, encouraging open discussion of professional risks, and expanding document management automation to reduce the influence of the human factor.

KEY WORDS: communication, organization of medical care, obstetric and gynecological profile, quality, safety, strategies

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INTRODUCTION

Research on communication issues in obstetrics and gynaecology under modern conditions is a critically important component of healthcare practice. The quality of medical care in this field is measured not only by successful surgical interventions or the absence of complications, but also by the psychological state of women and their trust in the healthcare system.

Effective communication between medical personnel and patients directly affects the safety of medical care. In obstetrics and gynaecology, decisions are often made under conditions of limited time and increased risk. Misunderstandings, insufficient information, or ignoring complaints can lead to medical errors, complications, and even threats to the life of the mother and child [1]. Under such conditions, empathy, prevention of obstetric violence, and the implementation of ethical communication become decisive. WHO documents emphasise effective communication, respect, preservation of dignity, and emotional support as key components of quality care in maternal and newborn health [2].

It is well known that communication is the foundation of a patient-centred approach. High-quality obstetric and gynaecological care involves taking into account the individual needs, emotional state, and cultural and social characteristics of patients. Effective communication directly influences adherence to treatment. Open dialogue contributes to building trust, increases adherence to treatment, and improves compliance with medical recommendations [3, 4].

In modern conditions, the importance of informed consent and medical ethics is increasing. Patients have the right to actively participate in decision-making regarding their health. This is not possible without a clear

and accessible explanation of the diagnosis, treatment options, risks, and alternatives [5, 6].

The role of interprofessional communication should be highlighted separately. The quality of care depends not only on the interaction between the doctor and the patient, but also on the coordinated work of the entire medical team, including obstetrician-gynaecologists, anaesthesiologists, neonatologists, and nursing staff. According to WHO data, most critical errors in medicine occur not due to a lack of knowledge, but due to communication gaps caused by inaccurate transmission of information between shifts and insufficient teamwork. Clear transmission of information between specialists reduces the risk of errors and increases the effectiveness of medical services [7, 8].

The relevance of the topic is also due to the implementation of modern standards of healthcare quality and international recommendations that emphasise the importance of communication skills as a component of the professional competence of medical workers [9, 10].

In the context of the transformation of the national healthcare system, digitalisation of medicine, and the development of telemedicine, the forms of interaction with patients are changing, which requires new approaches to communication, preservation of confidentiality, and accuracy of information transfer [11]. At the same time, the issue of communication in obstetric and gynaecological practice is insufficiently covered in the scientific literature. The vast majority of publications concern general rules of communication in medicine, communication models, communication techniques, and educational aspects [12–18]. The organisational aspects of communication in the provision of obstetric and gynaecological care, as an important component of ensuring healthcare quality, remain insufficiently studied, which determines the relevance of this study.

Thus, studying the state and problems of communication in the process of providing obstetric and gynaecological care is an urgent task that allows transformation of the "doctor–patient" model from paternalistic to partnership-based, which is the foundation for implementing the principles of evidence-based medicine and ensuring high standards of healthcare quality and patient safety.

AIM

The aim of the study is to substantiate measures to ensure the quality of obstetric and gynecological care for the population by improving communication between participants in the service delivery process.

MATERIALS AND METHODS

The research methodology involved bibliographic, sociological, medical-statistical, and information-analytical methods. The source base consisted of scientific literature, results of sociological surveys of various respondent groups regarding the quality of obstetric and gynecological care in healthcare institutions, as well as international and national strategies and programmes for ensuring the quality of healthcare services.

The first survey was conducted in 2021 and involved 202 healthcare professionals from a maternity hospital and an antenatal clinic in Kyiv and Kyiv Oblast. The second survey, carried out in 2025–2026, targeted healthcare managers (n = 108) and used a custom-designed Google Forms questionnaire. Based on the data obtained, intensive indicators per 100 respondents were calculated together with their standard errors.

The opinions of medical personnel regarding the state of communication in obstetric and gynaecological healthcare facilities were analysed, as well as the views of specialists in healthcare organisation and management regarding the levels of communication between participants in the obstetric and gynaecological care delivery process. To assess the communication aspects of care quality and safety, a specially developed questionnaire by the facility's quality team for medical staff was used. The questionnaire covered key aspects of internal interaction, from the level of team support and openness of communication to the systematic reporting of incidents and errors in work.

The survey of healthcare managers aimed to provide a comprehensive assessment of the quality management system in obstetric and gynaecological facilities and to identify key factors influencing the effectiveness of care, with an emphasis on communication processes. Recommendations of the WHO and national strategic documents were analysed in the context of communication as a component of quality assurance.

ETHICS

The study complied with the basic principles of the Council of Europe Convention on human Rights and Biomedicine, World Medical association declaration of helsinki on the ethical principles for medical research involving human subjects, and current national regulations. as the surveys were anonymous, the respondents' participation was assumed to be voluntary, the principles of medical ethics were not violated.

FRAMEWORK
The article was prepared within the framework of research works of Bogomolets National Medical University "Scientific substantiation of improving the organizational foundations of the health care system under conditions of modern transformational changes" (2023-2025, state registration number 0123U101432).

RESULTS

Analysis of surveys of specialists from obstetric and gynaecological healthcare facilities regarding communication aspects of care provision showed that 79.0±2.9 out of 100 respondents confirmed regular informing by facility management about changes in its work. Opportunities for the open expression of opinions regarding deficiencies in the patient care process were reported by 77.0±3.0 out of 100 respondents, regarding errors in work by 84.0±2.6 out of 100 respondents, and regarding other problems.

At the same time, almost two-thirds of the personnel (63.0±3.4 out of 100 respondents) indicated that they are afraid to speak up when they observe that something is being done incorrectly. Only slightly more than one-third of respondents (36.0±3.4 out of 100) noted that they can freely question the decisions and actions of more authoritative colleagues.

In this context, the frequency of reporting incidents occurring in the work process is of particular importance. 60.0±3.4 out of 100 respondents gave affirmative answers to the question on reporting errors when no effect reached the patient. If an error occurred and had a negative effect on the patient, 70.0±3.2 out of 100 respondents stated that they would report it.

A positive finding is the medical personnel's confidence in the administration's creation of a favourable climate for patient safety within the team, reported by 88.0±2.3 out of 100 respondents. The vast majority of respondents are convinced of good interaction between structural subdivisions of the healthcare facility; however, 31.0±3.3 out of 100 respondents question this assessment. Half of the respondents (51.0±3.5 out of 100) indicated that information important to the patient may be lost during shift changes or during transfer of patients between departments. In addition, 73.0±3.1 out of 100 respondents reported satisfaction with teamwork with colleagues from other departments.

The study of the opinions of healthcare organisers from various regions of the country showed that 33.3 ± 4.5 out of 100 respondents identified insufficient communication between medical personnel and patients as a reason for non-compliance of obstetric and gynaecological services with current standards, while 16.7 ± 3.6 out of 100 identified insufficient communication between facility administration and medical personnel. Managers believe that communication with patients should be among the priority training topics for medical personnel, an opinion supported by 30.6 ± 4.4 out of 100 respondents.

Significant attention in the managers' survey was paid to barriers to the implementation of a patient-oriented quality management model. Among the key barriers, respondents highlighted low quality of feedback and a formal approach to patient surveys (44.4 ± 4.8 out of 100 respondents); communication difficulties, such as language and cultural barriers between personnel and patients (25.0 ± 4.2 out of 100); resource deficits, particularly lack of finances and staff for developing partnerships with patients (22.2 ± 4.0 out of 100); and information and organisational gaps, primarily insufficient patient awareness of their rights (16.7 ± 3.6 out of 100), lack of clear local protocols or responsible persons (16.7 ± 3.6 out of 100), and irregular analysis of satisfaction results (8.3 ± 2.7 out of 100).

Other problems received lower support, including sceptical attitudes of patients toward their own ability to initiate changes, lack of knowledge about the significance of the patient-oriented approach, difficulties in obtaining informed consent due to terminological barriers or unwillingness to study documentation, and a general lack of systematisation in involving patients. Ineffective communication between participants in the medical care quality control system, according to managers, creates difficulties when implementing changes or new approaches to quality control.

Analysis of WHO strategic and programme documents indicates the key role of communication aspects in ensuring the quality of medical care.

The WHO document "WHO recommendations: intrapartum care for a positive childbirth experience" emphasises the need for effective communication between healthcare providers caring for pregnant women and women in labour, using simple and culturally acceptable methods. However, in many settings, non-clinical intrapartum practices such as emotional support through companionship during labour, effective communication, and respectful care—although simple and inexpensive to implement—are not prioritised. Effective communication and interaction between health workers, health service managers, women, and representatives of women's groups and movements are important to ensure that care meets the needs and preferences of women in all contexts and conditions [2].

The need for interaction with facility management and regular communication between quality control teams and facility administration is emphasised in the WHO publication *Improving the quality of care for mater-*

nal, newborn and child health: implementation guide for national, district and facility levels. Such communication ensures the exchange of information regarding quality control and facilitates engagement of stakeholders in solving quality improvement problems [18].

WHO emphasises that all health workers are expected to provide information, education, and communication to patients. All midwives are expected to provide individual counselling. As part of a quality improvement strategy, stakeholders can develop communication plans for dissemination among health workers [10].

The need for private physical space to ensure effective communication between women and health workers is highlighted in the WHO Labour Care Guide Implementation Resource Package [19].

In many health systems, effective information management remains a weak point in quality assurance. The use of personal medical data for monitoring and improving medical services serves an important public purpose but must always ensure confidentiality. Every country should have national legislation that protects patient confidentiality while enabling the appropriate use of data and transparent communication with the public regarding data use, as well as establishing global standards for improving data quality and comparability.

An important measure for uniting clinical personnel is joint morbidity and mortality reviews, which are used to examine adverse events and improve clinical competencies. They promote active recognition of errors or misjudgements and provide opportunities for learning, as well as for identifying measures to improve processes, strengthen cooperation, and enhance communication [20].

Continuous advocacy is important for improving understanding of midwifery care models and the role of midwives through clear, evidence-based communication, intersectoral discussions, joint seminars, and training activities.

Interdisciplinary communication is facilitated by the development and strengthening of coordination mechanisms between health workers, particularly in emergency situations. This is supported by regular interdisciplinary meetings to review cases, address problems, and strengthen teamwork, as well as the implementation of effective conflict-resolution systems between health workers to enhance cooperation and professional respect [21].

The Strategy for the Development of the Healthcare System until 2030 [11] aims to improve the communication component of healthcare quality assurance. The document defines one of its strategic goals as ensuring universal access of the population to quality medical services. At the same time, the key values and guiding principles of the Strategy are efficiency and accountability, which involve establishing clear communication between all levels of management and resource utilisation. The tasks for implementing the Strategy include strengthening communication and clarification regarding the development, expansion, and approval of state financial guarantees for healthcare services; development of infrastructural and technical conditions for providing quality medical services using information and communication systems at all levels; and promotion of the availability of information and communication technology products and services in the electronic healthcare system and other key information systems and registries in the healthcare sector.

DISCUSSION

Analysis of the opinions of medical personnel and specialists in healthcare organisation and management regarding the state of communication in obstetric and gynaecological healthcare facilities and the levels of communication between participants in the obstetric and gynaecological care delivery process allowed for a comprehensive assessment of the situation and identification of strengths and weaknesses.

Positive findings include proper informing of medical personnel by facility management regarding changes in work, the opportunity for medical workers to openly discuss problems and express opinions on deficiencies in the patient care process, and ways to improve medical care.

However, although medical personnel generally assessed working conditions and interaction with the administration positively, the survey results revealed a number of problem areas. In particular, 14.0 ± 2.4 out of 100 respondents noted a lack of information about the facility's current activities. The most critical challenge was deficiencies in internal communication: 32.0 ± 3.3 out of 100 respondents noted difficulties in interaction between subdivisions, and 19.0 ± 2.8 indicated an insufficiently favourable working environment. Such communication gaps may lead to the loss of strategically important data during information transfer between structural units.

It is noteworthy that some medical personnel are afraid to point out actions they consider incorrect. The main negative factors include excessive hierarchisation, where fear of management replaces professional dialogue, which prevents personnel from critically assessing managerial decisions. This leads to the risk of systemic problems in patient care remaining unreported by both sides.

Healthcare managers confirmed the importance of the communication component in ensuring the quality of

obstetric and gynaecological care. One-third attributed non-compliance with medical care standards specifically to insufficient communication between medical personnel and patients, and one-sixth to insufficient communication between facility administration and medical personnel. They identified key barriers to achieving high-quality medical care for pregnant women, women in labour, postpartum women, and women in general as: inadequate quality of feedback and a formal approach to patient surveys, language and cultural communication barriers between personnel and patients, resource constraints for developing partnerships with patients, insufficient patient awareness of their rights, and irregular analysis of satisfaction results, among others.

To eliminate the identified shortcomings and build a mature culture of quality and safety within the facility, primary attention should be paid to implementing a culture of openness that encourages staff to freely report risks. Key strategic steps should include strengthening feedback mechanisms, including the regular collection of staff proposals for improving the quality of care; democratisation of management through the creation of direct communication channels between frontline specialists, quality and safety managers, and senior management; and technological modernisation, including reducing the risk of errors through maximal automation of medical documentation processes [2, 10].

The communication strategy should be integrated into the overall quality management strategy for obstetric and gynaecological care within the facility [18]. Ensuring multilevel information exchange and developing internal audit mechanisms will increase staff awareness of strategic quality objectives and promote sustainable adherence to the principles of medical ethics and deontology.

The implementation of standardised information transfer techniques, training in conflict management and empathy, the formation of multidisciplinary teams, the improvement of visual communication and comprehensive information delivery, and the establishment of crisis communication systems will enable the achievement of high standards of obstetric and gynaecological care quality.

PROSPECTS FOR FURTHER RESEARCH

Promising areas for further research include the development and implementation of standardized protocols for interdisciplinary interaction to ensure continuity of obstetric care at all stages of the treatment process. Separate attention should be paid to studying digital communication strategies and their impact on the formation of partnership relations between medical personnel and patients. It is also important to provide scientific substantiation of methods for integrating feedback from women into the system of monitoring the quality of medical services to increase the patient orientation of the facility.

CONCLUSIONS

The conducted analysis of the communication environment in obstetric and gynaecological facilities demonstrated the contradictory nature of organisational culture. Despite established principles of comprehensive informing of personnel about implemented changes and open discussion of problems, systemic barriers persist within facilities, in particular manifestations of interdepartmental dysfunction and hierarchical dependence. This may create certain threats to patient safety and hinder the achievement of appropriate care quality, which requires transformation of the internal communication system from a rigid vertical model to one oriented towards quality, safety, and openness.

The results of the survey of healthcare managers confirm that communication deficits are one of the determining factors in non-compliance with obstetric and gynaecological care standards. It has been established that a negative impact on the quality of medical services is exerted not only by communication gaps in the "staff–patient" system, but also by deficiencies in internal interaction within the "administration–staff" system. The key barriers to the development of a patient-oriented approach were identified as a formal approach to monitoring patient satisfaction, language and cultural barriers, and resource constraints, which together hinder the implementation of partnership principles and effective feedback.

For the transformation of the culture of quality and safety in healthcare facilities, the following strategic directions are proposed: building trust, including the transition to a policy of reporting risks without fear of sanctions and ensuring direct access of staff to senior management; active involvement of the team, including the systematic collection and implementation of innovative proposals from employees in the field of quality and safety; and digitalisation and minimisation of the human factor through the introduction of automated documentation systems. The foundation for improving the safety culture should be the development of horizontal communication and technological optimisation. In particular, stimulating open dialogue regarding professional risks, establishing direct interaction between staff and administration, and relieving healthcare workers of routine documentation tasks through automation are critically important.

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CONTENTS

Interplay between p53 dysfunction and inflammatory cytokines in colorectal cancer pathogenesis

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ABSTRACT

Aim: The present research set out to investigate the relationship between F53 and interleukins as well as the possible relationship between p53 with the emergence of malignant lesions, specifically colorectal cancer (CRC).

Materials and Methods: Patients at Baghdad's Medical City Hospital provided the colorectal cancer samples, Forty colorectal patients and forty control samples from healthy individuals between the ages of 35 and 75and cancer specimens made up the eighty samples that were gathered.

Results: This work employed a quantitative real-time polymerase chain reaction (RT-PCR) to accurately assess the expression levels of the p53 gene expression, namely the fold change calculated using the $2^{-}\Delta\Delta Ct$ method, as well as ELISA to detect the levels of IL-6 and IL-8. According to the data, colorectal cancer patients had higher levels of IL-6 and IL-8 (25.8± 7.6 pg/ml, 119.9± 76.7 pg/ml) than control (8.7± 2.3 pg/ml, 43.2± 12.1 pg/ml), instead P53 levels were lower in patients (130.5 ± 65.8 pg/ml) than control (182.4 ± 93.7 pg/ml). The expression of the p53 gene was dramatically reduced in 15 of the 40 colorectal cancer (CRC) samples that were used for RT-PCR. These results point to a possible link between the development of colorectal cancer (CRC) and downregulated p53 expression. With a P value < 0.02, the results indicated a substantial variation in the expression of P53titer among patients and controls.

Conclusions: The cytokines in issue are definitely higher in cancer patients' blood, and due to their critical involvement in the etiology of the disease, they would be appealing targets for novel therapeutics meant to treat colorectal cancer.

KEY WORDS: p53 gene, IL-6, IL-8, colorectal cancer (CRC), real-time polymerase chain reaction, ELISA

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INTRODUCTION

Another of the deadliest and third most prevalent cancers worldwide is colorectal cancer (CRC)., is a serious threat to the world's health. One The illness makes more than just 900,000 deaths every year, and its prevalence shows a concerning increase in groups that are typically thought to be at reduced risk [1]. Increasing epidemiologic impact emphasizes how urgently an extensive comprehension of the pathogenesis of CRC as well as the creation of novel treatment approaches are needed. Despite its ability to combat tumor cells, cellular immunity is essential [2]. T lymphocytes (T-helper 1) produce the lymphokine interleukin-6 (IL-6) and IL-8 which is produced by Th cells. Interleukin-8 (IL-8) is a cytokine that offers significant promise as a predictive and/or prognostic biomarker for cancer. It either autocrinely or paracrinely influences the occurrence of cancers. IL-8 may have a special involvement in breast cancer since the disease is mostly brought on by the production of the estrogen receptor (ER) and the human epidermal growth factors receptor 2 (HER2) [3]. Endothelial cells and macrophages respond by releasing interleukin-8, which was produced by both malignant and stromal cells, respectively. Prior studies have shown that IL-8 accelerates the formation of colorectal cancer malignancies by promoting angiogenesis, metastasis, and invasion by cells [4]. The cellular protein p53 was first discovered to bind to the SV40 large T antigen [5]. A new phase in cancer research is ushered in by this revelation. research that is expected to have a big impact on clinical practice. Stress triggers the transcription factor p53, which controls a large number of genes downstream in order to carry out regulatory tasks in multiple pathways of signaling. Approximately 40–50% of sporadic colorectal cancers have a p53 mutation [6]. The course and result of sporadic CRC are strongly correlated with the presence of p53 mutations. A number of small molecule drugs have been the subject of extensive research in recent years for their potential to restore and reactivate p53 through various ways.

Clinical trials are being conducted on these promising chemicals, which could eventually be authorized for use in the treatment of people with colorectal cancer [7]. The pathophysiology of colorectal cancer involves complicated interactions between inflammatory cytokines and dysfunctional p53. Intestinal cytokine networks are influenced by inflammatory cytokines, which are crucial to the growth of this cancer [8]. Research shows that attempts to counteract abnormal signaling and its role in cancer etiology interact dynamically. They draw attention to the control of cytokines that trigger inflammation and inflammatory/oncogenic pathways. This intricate relationship emphasizes how crucial it is to comprehend these mechanisms in order to create successful treatments. The pathogenesis of colorectal carcinoma and the impact of p53 mutations on clinical outcomes are the main topics of this investigation [9]. Furthermore, this article discusses the recent accomplishments in Reactivating this transcriptional pathway in colorectal cancer (CRC) with p53 modulators may be a promising alternative anti-cancer treatment.

AIM

The present research aims to investigate the regulation of the p53 gene in patients with colorectal cancer. As well as the levels of immunological parameters and the relationships between them.

MATERIALS AND METHODS

ETHICAL APPROVAL

This study protocol approved by Ethical and research committee College of Medical and Health Technologies / Gilgamesh University (number: 343 date: 12/12/2025). Before enrollment in the study, the research concept was verbally explained to the patients and each patient signed consent. The Helsinki Declaration and later amendments for human research were applied for all procedures in this research.

COLLECT THE SAMPLES

To find any genetic variations, blood samples were taken from individuals with colon cancer at the Baghdad's Medical City Hospital from January 2025 to March2025, The patients were between the ages of 35 and 75. The blood's five milliliters taken from each subject were split into two milliliters of in an anticoagulant-free gel tube and left to clot at the temperature of the room. After that, the blood was centrifuged at 2000x for 10 minutes. Serum samples were then kept at -20°C until they were needed for an ELISA test and 3 ml were stored in a tube of EDTA with anticoagulation at -20°C for extraction of RNA. As directed by the kit instructions, the ELISA test (SUNLONG, China) was used to examine the immunological assays for IL-6 and IL-8. TRIzolTM-assisted RNA extraction followed by targeted gene cDNA synthesis. A Korean company called Bioneer supplied the cDNA ready-to-use kit, which was used to create the cDNA for genomic investigation of p53 (Table 1).

CALCULATING THE GENE EXPRESSION FOLD

By implementing these steps, the Levak equation was used to evaluate the fold expression in comparison to the housekeeping gene and control.

Ct (control) - Ct (control over housekeeping) = Δ Ct (control) ΔCt (sample) = Ct (sample) - Ct (housekeeping sample) Δ Ct (control) minus Δ Ct (sample) equals ΔΔ Ct Gene expression foldof = (2^{-}Δ Δ Ct).

CRITERIA FOR INCLUSION AND EXCLUSION

Age over 35 with colorectal cancer confirmed by histology was one of the inclusion requirements readiness to participate in the genomic investigation of p53.

Among the exclusion criteria were further cancers.

PRIMER SEQUENCE INCLUSION

Table 2 lists the sequences, their positions within the gene.

ANALYSIS OF STATISTICS

SPSS version 20, an analytical statistical program, was used to examine the information. The mean ±SD is used to display the data. The data was statistically analyzed using correlation and the t-test. The statistical meaningful level were established at $P < 0.05$.

RESULTS

There were 80 participants in all, 40 of whom were patients and 40 were controls. According to table 3, 10 patients (13%) were in the 35–45 age range, 27 patients (34%) were in the 46–55 age range, 20 patients (25%) were in the 56–65 age range, and 23 patients (28%) were in the 55–75 age range.

When comparing patients with colorectal cancer to the healthy group, the results in table 4 revealed a statistically significant elevation of both IL-6 (25.8± 7.6pg/ml, 8.7± 2.3 pg/ml) and IL-8 (119.9± 76.7p g/m L vs. 43.2± 12.1p g/m L) levels (p=0.003, p=0.001).

Table 5 shows that the p53 titer was lower in colorectal cancer patients than in the unaffected population.

Table 1. The PCR circumstance is revealed

Step	Temperature (°C)	Duration	Cycles
Initial Denaturation	96	3 min	1
Denaturation	94	15 s	40
Annealing	55	45 s	
Extension	74	60 s	

Source: Compiled by the authors of this study

Table 2. The P53 gene primer sequences employed in this investigation

Gene	Primer	Sequence (5′→3′)	Location within sequence (nucleotide)
P53 Gene	Forward	5′-TGCAAAGAGGTGCGTGTAA-3′	702–720
	Reverse	5′-CTGAACCGTCCCTGTAGAT-3′	841–850

Source: Compiled by the authors of this study

Table 3. Age-specific the distribution of colorectal cancer (CRC)

Parameters		N=80	%
Age (years)	35-45	10	13%
	46-55	27	34%
	56-65	20	25%
	55-75	23	28%
Total		80 (100%)	

Source: Compiled by the authors of this study

Table 4. Interleukin means concentrations in patients with colorectal cancer relative to the control group

Interleukins	Patients	Controls	P-value
IL-6(pg/ml)	25.8± 7.6	8.7± 2.3	0.01
IL-8(pg/ml)	119.9± 76.7	43.2± 12.1	0.01

Source: Compiled by the authors of this study

Table 5. P53 titer mean among individuals with colorectal cancer relative to the control group

Parameter	BC Patients	controls	P-value
P53titer	130.5 ± 65.8	182.4 ± 93.7	0.02

Source: Compiled by the authors of this study

This study found that there was a positive correlation between P53 Titer and IL-6 Levels in the Serum of Participants with Colorectal Cancer compared with Control groups (R: 0.073) (Fig. 1).

This study found that there was a positive correlation between P53 Titer and IL-6 Levels in the Serum of Participants with Colorectal Cancer compared with Control groups (R0.1339) (Fig. 2).

DISCUSSION

Recently has been found that many tumor forms, particularly colorectal cancer, have elevated concentrations of IL 8, a cytokine that promotes inflammation with angiogenic properties [10]. It has been discovered that IL 8 acts on cancer cells through its receptors in order to stimulate angiogenesis in vivo as well as migration, invasion, and multiplication in colorectal cancer [11]. According to the current study, individuals with colorectal cancer had a considerably higher IL 8 content than did healthy people. There have been prior reports of increased levels of IL 8 in cancer samples and lines of cells; The findings showed that as contrasted with normal colon tissues, the amounts of IL 8 were higher in CRC tissue. The current study's genome sequencing results revealed seven alterations, one placement, one elimination. and one overexpression in the CRC tissues' IL 8. Tâlvan et al. [12] claim that IL 8 is associated with an increased risk of cancer of the colon. In addition, a higher sensitivity was associated with the heterozygous type of IL 8 to CRC in comparison to control in another earlier investigation including Malaysian patients suffer-

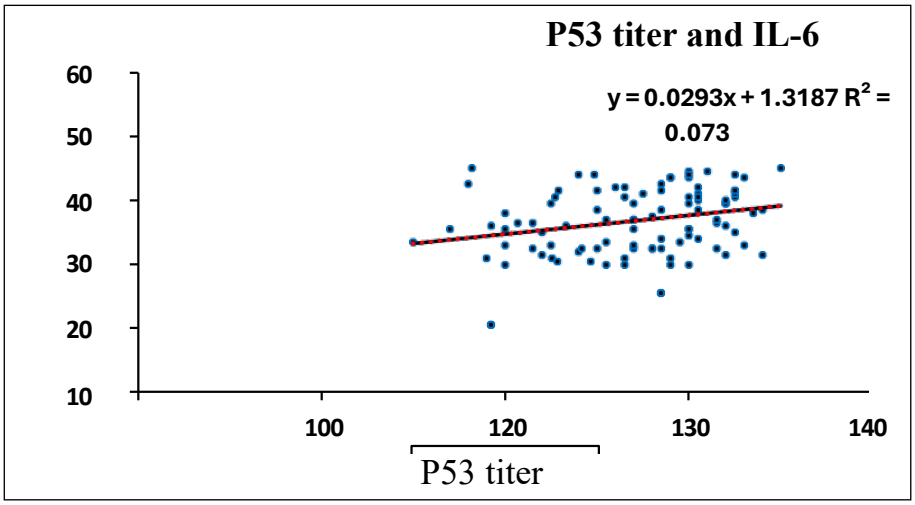


Fig. 1. The Association among P53 titer and IL-6 levels in the serum of participants with colorectal cancer
Source: Compiled by the authors of this study

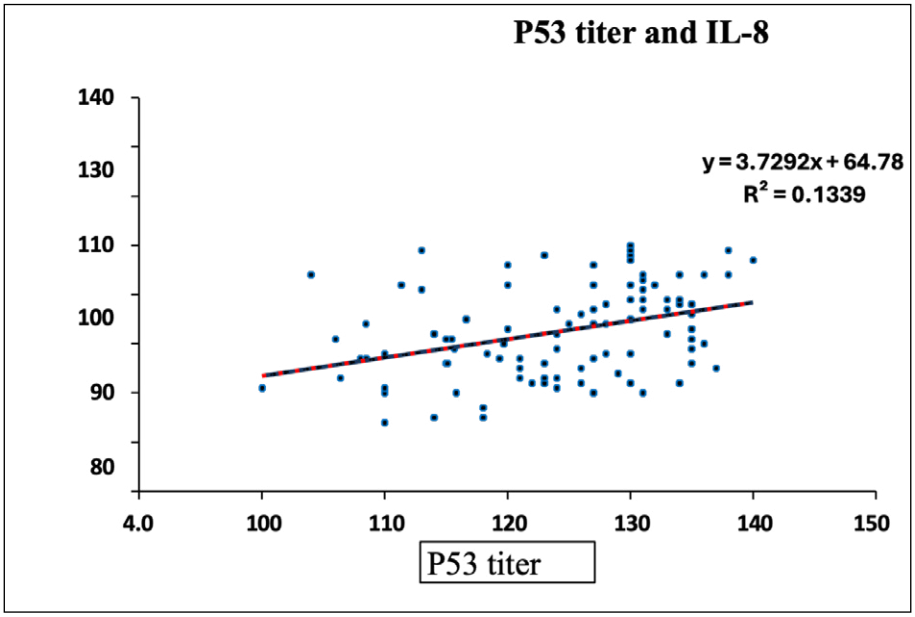


Fig. 2. The association between P53 titer and IL-8 levels in the serum of participants with colorectal cancer
Source: Compiled by the authors of this study

ing from CRC [13]. According to reports, IL 8 is linked to increased promoter activity, which raises IL 8 levels and encourages its proangiogenic actions, ultimately leading to an increase in the proliferation of tumor cells [14]. According to Ghazwan et al., the two groups' p53 levels differed significantly, with the patients' mean being lower than that of the control group [15]. This contrasts with the results of studies by Sofiani et al. [16], who found that, in comparison to control processes, the average circulating blood level of p53-in patients increased significantly.

Similar observations were made by Su et al. [17], who found revealed patients with established tumor phases prior to surgery had significantly greater serum IL-6 levels than healthy controls. The levels were noticeably lower on the 10th day following surgery, though. Furthermore, Pop et al. [18] and Pu et al. [19] made the interesting observation that the levels of IL-6 in the malignant tissue were significantly higher than those in the typical mucosa and that they were closely connected with the levels of IL-6 in the blood serum. The researchers therefore concluded that serum IL-6 concentrations mirror the IL-6 concentrations in the tumor tissue and demonstrate the tumor's capacity to proliferate. The elevated IL-6 levels in the samples of CRC patients undergoing treatment may be caused by the following factors: The CEA has been shown to trigger the production of several cytokines, including IL-6, from the liver's Kupffer cells, which may then promote the growth of tumor cells at metastatic sites [20]. Infected cells from the immune system may also be a source of IL-6. Using RT-PCR analysis, it has been found that p53 andIL-6 proteins are present in colorectal tumor tissue. Nonetheless, this cytokin may be produced by macrophages, which is consistent with other findings that support the idea that inflammatory substances in colorectal cancers originate from monocytosis [21].

CONCLUSIONS

The results showed that colorectal cancer is significantly influenced by IL-6 and IL-8. progression and constitute important biomarker for identification and prediction cancer. The cytokines in question are indeed elevated in cancer patients' blood, and due to their vital roles in the etiology of the disease, they would be desirable targets for innovative therapies intended to treat colorectal cancer. This protein is an excellent option for the treatment of cancer because p53 deficiency is commonly seen in human malignancies.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

CONTENTS

Medico-pedagogical aspects of preventing negative learning experiences as a factor in preserving students' health under martial law

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ABSTRACT

Aim: This article aims to analyze the medico-pedagogical aspects of negative learning experiences among university students during martial law in Ukraine, particularly in relation to personal initiative and cooperation; to explore the impact of these experiences on students' health and well-being; and to identify preventive teaching strategies aimed at reducing traumatization and supporting students' subjective well-being.

Materials and Methods: A total of 1650 participants took part in the study. The participants were future professionals studying at the bachelor's and master's levels of higher education at Bogomolets National Medical University, Borys Grinchenko Kyiv Metropolitan University, and Volodymyr Vynnychenko Central Ukrainian State University. The study was conducted over a period of three and a half years under the conditions of ongoing military aggression by Russian troops on the territory of Ukraine. The analysis incorporated the results of a 3.5-year study examining interaction styles among future professionals during learning under conditions of ongoing military aggression by Russian troops on the territory of Ukraine, with particular attention paid to the significant increase in passivity during group work. Correlation analysis was conducted to determine the relationship between increasing passivity in group activities during learning and increasing stress indicators.

Results: The findings indicate that learning may have both positive and negative effects on students' health, including sleep disturbances, eating disorders, decreased immunity, and exacerbation of chronic conditions. The negative effects of personal initiative were identified at three levels: self-perception, perception by others, and evaluation of outcomes. Negative experiences in collaborative activities were associated with rivalry, dominance, and neglect within group interactions.

Conclusions: Preventing negative learning experiences in higher education, particularly in the areas of personal initiative and collaboration for sustainable development, requires teaching approaches that support students' well-being, encourage conscious and balanced participation, and minimize the risks of traumatization and retraumatization during the educational process.

KEY WORDS: GreenComp, subjective well-being, health-preserving education, traumatization

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INTRODUCTION

The contemporary socio-political, socio-economic, and socio-cultural context highlights the growing importance of purposeful actions aimed at achieving sustainable development. In this regard, particular attention has been paid to the European Competence Framework for Sustainable Development (GreenComp), which identifies four key areas of competence development [1]. The present study focuses on the "Action for Sustainable Development" domain of GreenComp, which has become the conceptual basis of this research [1–4]. According to GreenComp, this domain includes three core competencies, two of which — cooperation and personal initiative — constitute the primary focus of the present study.

The selection of these competencies is explained by their potential influence on the psychological well-being and health of individuals involved in collaborative activities or demonstrating personal initiative during the educational process (Table 1).

Table 1. Competencies and descriptors within the "Action for Sustainable Development" domain were examined in this study

Competencies	Descriptors	Objects of our research
Political agency	Ability to navigate political systems, identify responsibility for unsustainable behavior, and advocate for effective sustainable development policies	No
Cooperation	Ability to promote change through collaboration with others	Yes
Personal initiative	Ability to recognize one's own potential in sustainable development and actively contribute to improving societal and environmental prospects	Yes

Source: compiled by the authors based on [1]

Previous studies [5, 6] define cooperation as a form of interaction based on mutual influence, interdependence, and coordinated activity between participants. Cooperation is viewed as an integrating factor that supports coherence in collective actions aimed at achieving shared goals.

Within the context of collaborative interaction, particular attention should be paid to its psychological dimension. Interaction during collaboration involves mutual influence, the development of shared approaches to joint activity, the exchange of ideas, knowledge, skills, and values, and the establishment of constructive interpersonal relationships. Such forms of interaction contribute to reducing rivalry and dominance within group work.

Researchers [6, 7] also describe personal initiative as an important competence that includes the ability to act independently, demonstrate creativity and responsible risk-taking, propose original ideas, recognize new opportunities, and consistently implement one's ideas despite potential difficulties.

According to previous studies [6, 8], personal initiative is associated with originality and the ability to address social or individual needs. It may be expressed both individually and collaboratively, particularly in situations where successful implementation depends on support from others and effective cooperation within a group.

AIM

The aim of this study is to examine the medico-pedagogical aspects of negative learning experiences among university students under martial law in Ukraine, using personal initiative and cooperation as examples; to determine the impact of these experiences on students' health; and to identify preventive teaching strategies aimed at reducing traumatization and supporting students' subjective well-being.

MATERIALS AND METHODS

A total of 1650 participants took part in the study. The participants were future professionals studying at the bachelor's and master's levels of higher education at Bogomolets National Medical University, Borys Grinchenko Kyiv Metropolitan University, and Volodymyr Vynnychenko Central Ukrainian State University. The study was conducted over a period of three and a half years under the conditions of ongoing military aggression by Russian troops on the territory of Ukraine.

The study employed a combination of general scientific methods, including analysis, comparison, systematization, and generalization, as well as empirical methods, including observation, individual interviews, anonymous questionnaires, and the interaction style identification method [9].

The anonymous questionnaire consisted of seven questions:

1. How does learning affect your health?
2. When do you notice a positive impact of learning on your health?
3. When do you notice a negative impact of learning on your health?
4. Under what conditions does demonstrating personal initiative during learning negatively affect your health?
5. Under what conditions does demonstrating personal initiative during learning positively affect your health?
6. Under what conditions does cooperation during learning negatively affect your health?
7. Under what conditions does cooperation during learning positively affect your health?

The interaction style identification method [9] was used to determine participants' tendencies toward specific interaction styles, including directive, collegial, business-oriented, and non-interference styles during cooperation. The method includes 20 statements that respondents evaluate according to how often they personally behave in the described manner during interaction with others.

Examples of the statements included:

1. I tell others what to do.
2. I listen to the opinions of others.
3. I give others the opportunity to participate actively in decision-making.

4. I give others the opportunity to act independently.
5. I persistently explain to others how they should act.
6. I teach others how to work.
7. I ask others for advice.
8. I do not interfere with the work of others.
9. I indicate when work needs to be completed.
10. I take into account the achievements of others.
11. I support initiative.
12. I do not interfere in activities and allow others to act independently.
13. I demonstrate how actions should be performed.
14. Sometimes I allow others to participate in discussing a problem.
15. I listen carefully to other participants.
16. If I interfere in a situation, I do so in a business-like manner.
17. I do not share the opinions of others.
18. I make efforts to resolve contradictions.
19. I try to take different points of view into account.
20. I believe that everyone should use their talents to the fullest extent possible.

Responses were evaluated using a five-point scale, where 5 indicated "always" and 1 indicated "never". To interpret the results, the following groupings were applied:

1. Statements 1, 5, 9, 13, and 17 indicated a tendency toward a directive interaction style.
2. Statements 3, 7, 11, 15, and 19 indicated a tendency toward a collegial interaction style.
3. Statements 4, 8, 12, 16, and 20 indicated a tendency toward a non-interference interaction style.
4. Statements 2, 6, 10, 14, and 18 indicated a tendency toward a business-oriented interaction style.

Each group could receive a maximum score of 25 points. Scores between 70 and 80 points indicated a tendency toward active interaction with others. Scores between 30 and 40 points indicated a tendency toward passivity in group activities. Scores of 20 points or more within a particular category indicated a pronounced tendency toward a specific interaction style, while scores between 12 and 14 points indicated that an individual was capable of demonstrating only that specific interaction style.

The analysis incorporated the results of a 3.5-year study examining interaction styles among future professionals during learning under conditions of ongoing military aggression by Russian troops on the territory of Ukraine, with particular attention paid to the significant increase in passivity during group work. Correlation analysis was conducted to determine the relationship between increasing passivity in group activities during learning and increasing stress indicators.

ETHICS

In this study, the authors adhered to the Ethical Principles for Medical Research Involving Human Subjects outlined in the World Medical Association's Declaration of Helsinki (WMA, 1964) and its subsequent amendments, as well as current Ukrainian regulations. The research protocol, which included anonymous questionnaires and interviews with 1650 students, was approved by the relevant institutional ethics committees (or scientific councils) of the participating universities: Bogomolets National Medical University, Borys Grinchenko Kyiv Metropolitan University, and Volodymyr Vynnychenko Central Ukrainian State University. All participants took part in the study voluntarily and were informed about the purpose of the research.

RESULTS

Analysis of the survey results revealed that training affects the health of future teachers both positively and negatively. Future professionals associate the positive impact of training on their health with obtaining positive results. They attributed the following to positive results (Fig. 1): 1) Learning outcomes that are directly reflected in the completion of a certain process (successfully passed exams and tests). 2) Learning outcomes that are perceived as personal changes (increased self-esteem; development of intelligence, thinking, stress resistance, knowledge, and skills; broadening of worldview). 3) Learning outcomes that are associated with positive feelings (a sense of progress, a sense of belonging to the educational community, and a sense of self-worth and self-realization). 4) Learning outcomes that are associated with pleasant mental states (states of elation, confidence, a surge of energy, and a positive mood). 5) Learning outcomes associated with enthusiasm.

Future professionals also emphasized that the positive impact of learning on health is connected not only with educational outcomes but also with the learning process itself. According to respondents, this occurs when lecturers demonstrate enthusiasm in teaching, provide practically meaningful knowledge and skills, stimulate interest in learning, explain new material in an engaging manner, support students' understanding of educational content, and use non-standard teaching approaches that help shift students' attention away from anxious thoughts toward the analysis and comprehension of new information.

The analysis of the survey results also identified the conditions under which future professionals perceive learning as non-harmful to their health. According to 100% of respondents, such conditions include the

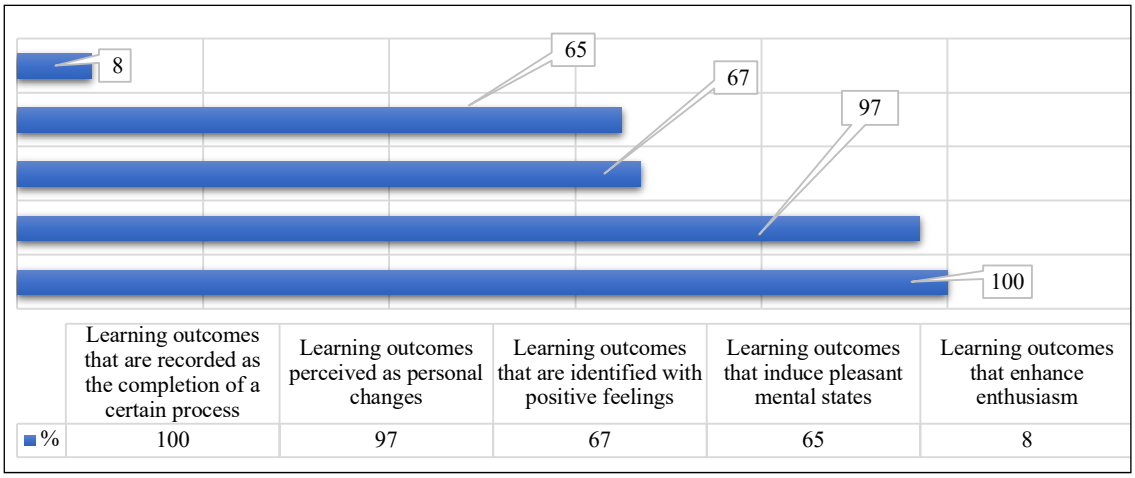


Fig. 1. The positive impact of learning on the health of future professionals in the context of positive learning outcomes
Picture taken by the authors

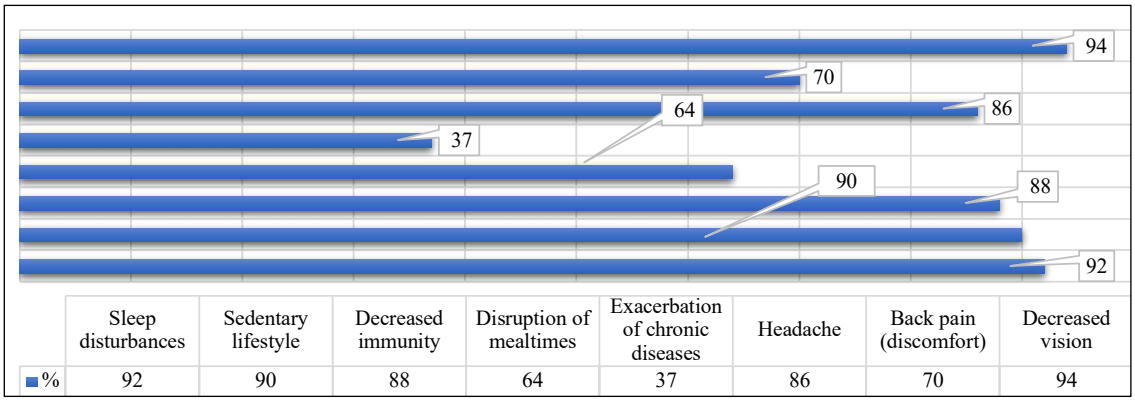


Fig. 2. Manifestations of negative influence on the learning of future professionals
Picture taken by the authors

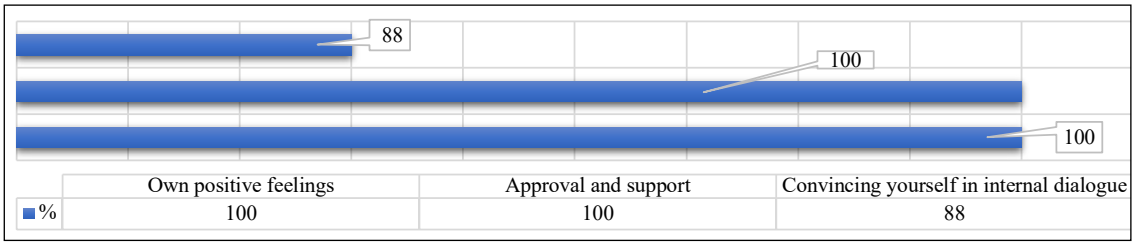


Fig. 3. Factors positively influencing personal initiative during learning without harming the health of future professionals
Picture taken by the authors

availability of favorable learning conditions and necessary educational resources, the prior clarification of assessment criteria, and the implementation of fair assessment practices. In 92% of cases, respondents emphasized the importance and value of the information being studied, while in 68% of cases, respondents indicated that lecturers ensured continuous exposure to new knowledge and learning experiences.

The findings suggest that health-preserving education is closely connected to the social well-being of future professionals. This includes:

• the degree of satisfaction with material well-being [10], nutrition, and the availability of resources necessary for learning;

• the degree of satisfaction with interaction with others, which depends on the perceived value of educational information, the acceptance of assessment criteria, and the implementation of fair assessment practices.

At the same time, learning may also negatively affect the health of future professionals (Fig. 2). Analysis of the survey data identified several factors contributing to the negative impact of learning on students' health. These factors include combining studies with employment,

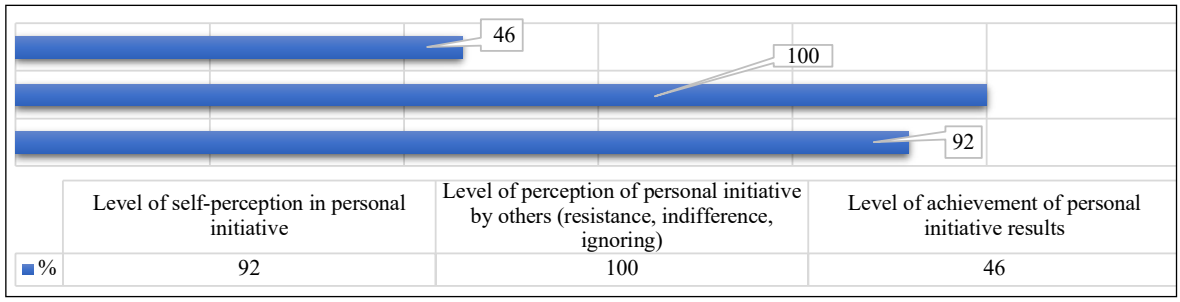


Fig. 4. Levels of manifestation of the negative impact of personal initiative on the health of future professionals during learning
Picture taken by the authors

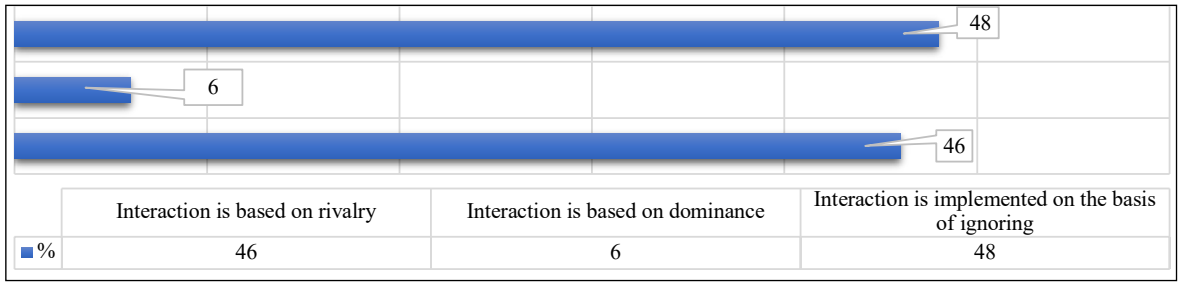


Fig. 5. Forms of interaction during collaboration associated with negative effects on the health of future professionals during learning
Picture taken by the authors

prolonged computer work and sedentary behavior, excessive intellectual workload combined with deadlines, stressful situations associated with failure, fear of evaluation, or personal and family-related difficulties, as well as sleep disturbances, irregular eating habits, decreased immunity, and exacerbation of chronic diseases.

Further analysis of the data presented in Fig. 2 showed that future professionals experience the negative impact of learning on their health during different stages of the educational process, in particular:

1. During face-to-face and distance learning. Respondents reported accumulated fatigue caused by combining studies with work, business trips, or volunteer activities. They indicated an imbalance between study and rest. In cases involving overly complex educational material, large numbers of assignments, or difficulties completing tasks, respondents experienced headaches. Prolonged computer work also caused back pain and physical discomfort. Students additionally reported emotional tension associated with unfair assessment or uncertainty regarding task completion.
2. At the beginning of examination periods. Before examinations or assessment sessions, respondents reported strong emotional tension accompanied by headaches. In 2% of cases, respondents described severe stress reactions accompanied not only by headaches but also by nervous tics, including involuntary physical reactions such as eye twitching or discomfort in the throat. Respondents also indicated that this period often coincided with the onset or exacerbation of illnesses, while continuous involvement in the educational process delayed recovery or rehabilitation.
3. During examination periods. Future professionals reported poor sleep quality, irregular eating habits, and constant nervous tension.

The study also examined how actions related to sustainable development implemented during learning affect the health of future professionals. In this context, particular attention was paid to personal initiative and cooperation.

According to respondents, demonstrating personal initiative during learning may have both positive and negative effects on health.

Personal initiative during learning was perceived as non-harmful to health only under the following conditions:

1. The initiative is recognized and supported by lecturers and other students.
2. The initiative contributes to positive thoughts, the emergence of new opportunities and skills, obtaining scholarships, participation in desired events, and the achievement of meaningful results. Respondents also emphasized that personal initiative should serve as a source of inspiration without overloading daily routines or disrupting the balance between studies, work, and rest.
3. The initiative is associated with positive emotional experiences, including internal motivation rather

Table 2. Results of research on the interaction style of future professionals during learning in conditions of aggressive military actions of Russian troops on the territory of Ukraine

Predisposition of the manifestation of inclination	Years			
	2022	2023	2024	2025 (until April)
Predisposition to interact with others while learning in various ways	89%	77%	64%	52%
Predisposition to be passive in group work while learning	11%	23%	36%	48%
Predisposition to a collegial style of interacting with others during learning	72%	84%	90%	86%

Source: compiled by the authors of this study

than coercion, a sense of unity, self-realization, success, personal growth, achievement of specific results, recognition from lecturers or scientific supervisors, and confidence in one's own abilities.

4. The initiative receives approval and support from others.
5. Individuals can regulate their internal dialogue, particularly negative expectations, memories of previous negative experiences, self-criticism, accusations, and negative emotions (Fig. 3).

The negative impact of personal initiative on students' health was identified at three levels (Fig. 4):

1. At the level of self-perception in personal initiative. Future professionals reported taking on excessive responsibility, including organizing events, implementing projects, and participating in additional educational activities. Respondents indicated that they often failed to realistically assess their own resources, awareness, family circumstances, workload, or time management abilities. Many participants described attempting to manage too many responsibilities simultaneously, turning personal initiative into what they referred to as a "personal catastrophe". Respondents also reported perfectionism, fear of criticism and condemnation, constant comparison with others, inability to refuse additional responsibilities, and excessive self-pressure to perform all tasks perfectly.
2. At the level of perception of personal initiative by others. Respondents indicated that personal initiative was sometimes not appreciated or supported by other participants in the educational process. Instead, it was accompanied by resistance, indifference, or being ignored by others. Under such conditions, personal initiative became an isolated burden of responsibility without support, often accompanied by conflict situations and the shifting of responsibility among participants.
3. At the level of the outcomes of personal initiative. Respondents associated negative experiences with situations in which personal initiative failed to produce positive results and was accompanied by unrealistic expectations regarding oneself and one's actions.

Like personal initiative, cooperation during learning may also have both positive and negative effects on the health of future professionals. According to the survey results, learning was perceived as health-preserving under the following conditions:

1. Humanization of relationships. During cooperation, future professionals emphasized mutual support, respect, trust, understanding, cohesion, motivation, mutual assistance, and the exchange of ideas and opinions within a supportive atmosphere characterized by a sense of synergy.
2. Teamwork. Respondents highlighted the importance of a clear distribution of responsibilities and tasks among participants. Positive experiences were associated with a supportive working atmosphere in which no participant felt overloaded compared to others, ideas were discussed collectively, all participants had the opportunity to express and discuss opinions, and responsibility for achieving planned outcomes was shared among group members.

At the same time, future professionals also identified situations in which cooperation negatively affected their health (Fig. 5).

Negative effects were reported when interaction during collaboration was based on rivalry, characterized by a lack of mutual understanding and agreement among participants, the emergence of misunderstandings and conflicts, and feelings of anxiety or tension caused by uncertainty in collective work and unfair distribution of responsibilities.

Negative experiences were also associated with dominance during collaboration, particularly in situations involving dishonesty, irresponsibility, or passivity among participants. Respondents described situations in which some participants performed tasks irresponsibly or only imitated participation, forcing others to complete the work on their behalf.

In addition, respondents reported negative effects when collaboration was based on ignoring, including the absence of active participation by certain group members and disregard for the time, resources, and capabilities of other participants.

Using the method for identifying interaction styles [9], we found that during the experimental study,

which lasted nearly 3.5 years, quantitative indicators underwent significant changes: the tendency to interact with others during learning decreased from 89% (2022) to 52% (2025); the tendency toward passive behavior in group work during learning increased from 11% (2022) to 48% (2025); and the tendency toward a collegial style of interaction with others during learning increased from 72% (2022) to 86% (2025) (Table 2).

DISCUSSION

Analysis of the results of the study examining interaction styles among future professionals during learning under conditions of ongoing military aggression by Russian troops on the territory of Ukraine revealed a significant increase in passive behavior during group work, reaching 48% of cases. These findings were compared with the results concerning the negative impact of cooperation on the health of future professionals (Figure 5). The analysis demonstrated that respondents experienced irritation when other participants remained inactive during collaborative activities. Such inactivity was often perceived by future professionals as ignoring collective responsibilities, which contributed to negative emotional reactions toward passive participants.

To develop preventive measures [11] to prevent the formation of negative learning experiences among future professionals, particularly in the context of personal initiative and collaboration related to sustainable development practices, the study also examined prior scientific research on the reasons for students' inactivity during educational activities.

Previous studies [12–14] indicate that psychological trauma caused by the stressful and destructive consequences of war continues to affect students until these traumatic experiences are processed and overcome. During this period, future professionals experience depressive states in 99% of cases, sudden mood changes in 92% of cases, increased irritability in 52% of cases, aggressiveness in 11% of cases, and outbursts of anger in 7% of cases [15].

Researchers also found that future professionals most frequently reported a constant desire to sleep in 97% of cases, a tendency to postpone educational tasks perceived as overly difficult in 79% of cases, and a desire for isolation and withdrawal in 56% of cases. The direct or indirect activation of psychological trauma during learning, particularly under conditions of high emotional tension and negative psychological states, contributes to various adverse effects on the health of future professionals [16].

Another study found that nearly half of the students participating in the research experienced anxiety [17], which significantly increased the risk of burnout. Up to 50% of students were either in the initial stage of burnout or had already progressed beyond it [18].

Comparative studies examining the pre-war period and the period of military operations on the territory of Ukraine [3] demonstrated a substantial increase in stress prevalence among Ukrainian students. In 2012, the prevalence of stress was 45%; in 2016, 50%; in March 2022, 53%; after the first year of the war, 80%; and after the second year of the war, the prevalence of stress reached 96% [19].

Based on the analysis of previous studies [1-19], it can be concluded that inactivity among future professionals during educational activities is largely associated with psychological trauma caused by prolonged military aggression by Russian troops on the territory of Ukraine and by the tragic consequences of war, including the destruction of cities and villages, the loss of relatives and friends, and constant shelling and insecurity.

Prospects for further research include the experimental investigation of factors that should be considered by lecturers when organizing health-preserving education for future professionals.

CONCLUSIONS

Preventing the formation of negative learning experiences among future professionals, with particular attention to personal initiative and cooperation in the context of sustainable development practices, should involve several important actions by lecturers during the organization of the educational process.

Lecturers should discuss students' subjective well-being and explain that effective personal initiative during learning depends on multiple factors, including external circumstances, workload, and individual resource capacities such as time management, level of awareness, personal resilience, planning skills, the ability to refuse excessive responsibilities, tendencies toward self-comparison, sensitivity to criticism and condemnation, and perfectionism.

It is also important to support the development of students' ability to recognize and evaluate their own potential in the field of sustainable development. Future professionals should be involved in forms of cooperation that minimize the risks of traumatization and retraumatization and instead promote positive experiences of self-realization through collaborative activities. Such cooperation should take into account the individual's available physical, emotional, and psychological resources.

Lecturers should also explain that passivity or lack of activity during cooperation may be associated with

internal psychological changes resulting from traumatic experiences. Understanding the psychological consequences of prolonged exposure to traumatic events may contribute to more supportive and health-preserving educational practices.

Overall, the organization of the educational process should be based on the principles of health-preserving education aimed at supporting students' psychological well-being under conditions of ongoing social stress and military conflict.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest.

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CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

CONTENTS

The impact of psychoemotional state on the intensity and nature of pain after hysteroscopic myomectomy

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ABSTRACT

Aim: To assess the impact of psychoemotional status indicators (state anxiety, trait anxiety, and depression) on the intensity and duration of postoperative pain syndrome in patients after hysteroscopic myomectomy, and to determine their prognostic value for optimising analgesic management under conditions of wartime stress.

Materials and Methods: Ninety reproductive-age patients with submucosal uterine fibroids were examined. Group 1 (n=62) included women living under wartime stress in Ukraine: subgroup 1.1 (n=32) internally displaced persons and subgroup 1.2 (n=30) residents of Kyiv. Group 2 (n=28) comprised Ukrainian women temporarily living abroad who returned to Kyiv for planned surgery. Psychoemotional status was assessed using the Spielberger–Hanin and Beck scales, and pain using the NRS scale. Statistical analysis used nonparametric methods and ROC analysis.

Results: Anxiety levels differed significantly between all groups ($p<0.001$), highest in internally displaced persons. Subgroups 1.1 and 1.2 had higher NRS pain scores and required the maximum daily dexketoprofen dose (150 mg) compared with group 2. ROC analysis showed state anxiety strongly predicts acute pain intensity (AUC=0.804), while depression predicts pain duration in the outpatient setting (AUC=0.860).

Conclusions: Wartime stress significantly modulates pain perception by lowering the pain threshold even during hysteroscopic myomectomy. State anxiety correlates with acute postoperative pain intensity, while depressive states are associated with prolonged pain and the risk of chronification. These findings support personalised analgesia that considers patients' psychoemotional profiles.

KEY WORDS: uterine fibroids, psychoemotional state, hysteroscopy, pain

Wiad Lek. 2026;79(6):1266-1272. doi: 10.36740/WLek/222586 DOI

INTRODUCTION

Contemporary concepts of pain have undergone significant changes over recent decades. Whereas pain was previously considered a direct consequence of tissue damage and a reflection of its intensity, this view has now been revised. The modern biopsychosocial model regards pain as a complex phenomenon shaped not only by physical tissue alterations but also by the patient's psychological characteristics and environmental factors [1, 2].

Despite advances in analgesia, the lowest level of satisfaction with postoperative pain management is observed among gynaecological patients [3]. This is particularly relevant for women after hysteroscopic myomectomy, as the intensity of postoperative pain in this cohort does not always directly reflect the extent of surgical intervention [4]. Despite the minimally invasive nature of the procedure, pain perception is largely modulated by individual psychoemotional characteristics, anxiety levels, expectations regarding surgery, as well as neuroendocrine mechanisms of the stress response [5]. Moreover, interventions involving the uterus as an organ that plays a key role in reproductive function may be associated with increased psychoemotional sensitivity in patients, which affects the subjective perception of pain [6, 7].

At the same time, this issue becomes particularly relevant for women in Ukraine under wartime conditions. Chronic stress associated with the prolonged psychotraumatic impact of war is accompanied by dysregulation of the neuroendocrine response, alterations in the hypothalamic–pituitary-adrenal axis, and increased anxiety, which may modulate the intensity and qualitative characteristics of pain syndrome [8–10].

As a result, even minimally invasive interventions may be associated with more pronounced and variable pain perception.

AIM

To assess the impact of psychoemotional status indicators (state anxiety, trait anxiety, and depression) on the intensity and duration of postoperative pain syndrome in patients after hysteroscopic myomectomy, and to determine their prognostic value for optimising analgesic management under conditions of wartime stress.

MATERIALS AND METHODS

A total of 90 patients of reproductive age with submucosal uterine fibroids who underwent hysteroscopic myomectomy were included in this pilot study. To assess the characteristics of postoperative pain syndrome under different psychosocial contexts, the patients were divided into groups: Group 1 (main group, n=62) included patients living under chronic wartime stress in Ukraine. Depending on living conditions, this group was subdivided into subgroup 1.1 (n=32) – internally displaced women from frontline territories, and subgroup 1.2 (n=30) – residents of Kyiv. Group 2 (comparison group, n=28) consisted of Ukrainian women temporarily residing abroad who arrived in Kyiv for planned surgical intervention.

Inclusion criteria: verified submucosal uterine fibroid accompanied by clinical symptoms (in particular, menstrual cycle disorders and pain syndrome) and constituting an indication for surgical treatment; feasibility of applying a unified postoperative analgesia protocol; provision of informed voluntary consent to participate in the study, including psychometric testing.

Exclusion criteria: regular use of psychotropic drugs (neuroleptics, tranquillizers) that could distort the assessment of pain and psychoemotional status; presence of chronic pain syndromes of other localisation; contraindications to the use of drugs included in the standard analgesic regimen (dexketoprofen, paracetamol); patient refusal to continue participation in the study or inability to complete assessment at the outpatient stage.

Assessment of psychoemotional status was performed in the preoperative period using validated psychometric instruments. Levels of state anxiety (SA) and trait anxiety (TA) were determined using the Spielberger–Hanin scale (1978). The results were interpreted as follows: up to 30 points – low anxiety; 31–45 points – moderate anxiety; 46–80 points – high anxiety.

Depressive symptoms were assessed using the Beck Depression Inventory (BDI). Scores were interpreted as follows: 0–9 points – no depression; 10–18 points – mild; 19–29 points – moderate; 30–63 points – severe depression.

Pain intensity was assessed using the Numeric Rating Scale (NRS). Patients subjectively rated pain severity from 0 (no pain) to 10 (maximum intensity pain).

Statistical analysis of the results was performed using non-parametric methods. Quantitative data are presented as the median (Me), interquartile range [Q1; Q3], and the 10th and 90th percentiles (P10–P90). Comparisons between three independent groups were conducted using the Kruskal–Wallis test. Pairwise comparisons were performed using the Mann–Whitney U test with Bonferroni correction. Categorical variables across three groups were compared using Fisher's exact test. Pairwise comparisons were pre-specified based on the study design and clinical rationale, therefore, no correction for multiple comparisons was applied. Pairwise post-hoc comparisons were performed using Fisher's exact test or Pearson's χ^2 test, depending on the expected cell frequencies (Fisher's exact test was applied when any expected cell count was less than 5). The predictive ability of psychoemotional indicators for pain intensity and duration was assessed using ROC analysis with calculation of the area under the curve (AUC) and determination of the 95% confidence interval (CI). A p-value <0.05 was considered statistically significant.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki and the standards of good clinical practice. All patients were informed about the purpose of the study, the character of the examinations performed, and the anonymous use of aggregated data for scientific analysis. Written informed consent was obtained from all participants prior to inclusion. The study protocol was approved by the local bioethics committee of the participating institution.

FRAMEWORK

The study was conducted during 2025–2026 within the framework of the research project "Optimization of approaches to providing specialized medical care for surgical patients using personalized anesthetic support" (state registration No. 0125U000315), based at the gynaecological department of the State Institution of Science «Center of innovative healthcare technologies» State Administrative Department. The study was also carried out in accordance with the research theme of the Department of Hospital Obstetrics at Bogomolets National Medical University, "Modern approaches to

Table 1. Indicators of Psychoemotional Status of Patients in the Study Groups Before Surgical Intervention

Parameters (points)	Subgroup 1.1		Subgroup 1.2		Group 2		p
	Me [Q1;Q3]	P10–P90	Me [Q1;Q3]	P10–P90	Me [Q1;Q3]	P10–P90	
State anxiety	62.5[51;75]	47 – 78	51[43.5;56]	36 – 64	42[35;46]	28 – 54	p_1<0.001 p_2<0.001 p_3<0.001
Trait anxiety	50[42;56]	29 – 66	34.5[30;39]	22 – 44	26.5 [22;34]	20 – 45	p_1<0.001 p_2<0.001 p_3=0.009
Depression	22.5[11;27]	8 – 38	11.5[8;14]	6 – 32	27.5 [17;41]	8 – 48	p_1=0.003 p_2=0.023 p_3<0.001

Notes: Data are presented as Me [Q1; Q3], as well as P10–P90 (10th and 90th percentiles). Statistical significance between groups was assessed using the Kruskal–Wallis test with subsequent pairwise comparisons using the Mann–Whitney U test; p_1 – level of significance for comparisons between subgroup 1.1 and 1.2; p_2 – between subgroup 1.1 and group 2; p_3 – between subgroup 1.2 and group 2

Source: compiled by the authors of this study

diagnosis, treatment, and prevention of obstetric and gynaecological diseases: perinatal and maternal aspects, immunology of women's health, homeostasis, reproductive potential, and the impact of somatic health on the condition of the mother, foetus, and newborn" (state registration No. 0125U000002), at the gynaecological department of the Municipal Non-Profit Enterprise "Kyiv Perinatal Centre".

RESULTS

The first stage of the study involved a comprehensive analysis of the baseline psychoemotional status of patients prior to surgery. Given that the modern concept of pain formation is based on the biopsychosocial model, verification of anxiety and depression levels was necessary to further determine their role in modulating postoperative pain perception. The summarised results of the comparative analysis of anxiety and depression indicators in the study groups are presented in Table 1.

The analysis between the study groups demonstrated statistically significant differences in the level of state anxiety (H=37.29; p<0.001), trait anxiety (H=37.59; p<0.001), and depression (H=21.19; p<0.001). According to pairwise comparisons, state and trait anxiety differed significantly between all study groups. Regarding depression levels, statistically significant differences were also observed between all groups; however, the least pronounced difference was found between groups 1.2 and 2 (Table 1).

The next stage of the study focused on evaluating the impact of the identified psychoemotional disturbances on pain levels in the postoperative period. Analysis of pain intensity using the NRS scale and the amount of analgesic consumption allowed assessment of the effectiveness of the standard analgesic regimen under different levels of stress load. Particular attention was paid not only to the subjective perception of pain during hospital stay, but also to the need for additional analgesia and the duration of pharmacological support after discharge to the outpatient rehabilitation stage.

The clinical characteristics of the pain syndrome and the structure of drug consumption in the study groups are presented in Table 2.

Analysis of the distribution of postoperative pain intensity according to the Numeric Rating Scale (NRS) between the study groups demonstrated statistically significant differences (χ^2=17.520; df=4; p=0.002). The obtained data indicate that the structure of pain intensity differed substantially between groups. In particular, in Group 2, the proportion of patients with mild pain was higher compared with subgroups 1.1 and 1.2, whereas these subgroups showed a higher proportion of patients with severe pain compared with Group 2. At the same time, in all groups, patients with moderate pain predominated, with no statistically significant differences observed between groups for this category. Thus, Group 2 demonstrated a shift in distribution towards lower pain intensity, whereas subgroups 1.1 and 1.2 were shifted towards higher NRS values.

Comparative analysis of the distribution of baseline analgesic doses on the first postoperative day revealed a statistically significant difference between the study groups (χ^2=20.091; df=4; p<0.001). In Group 2, a greater proportion of women achieved adequate analgesia with 50 mg dexketoprofen compared with subgroups 1.1 and 1.2. In contrast, subgroups 1.1 and 1.2 were characterised by a predominance of patients requiring a daily dose of 150 mg.

It was established that the frequency of additional analgesia requirements also differed significantly between

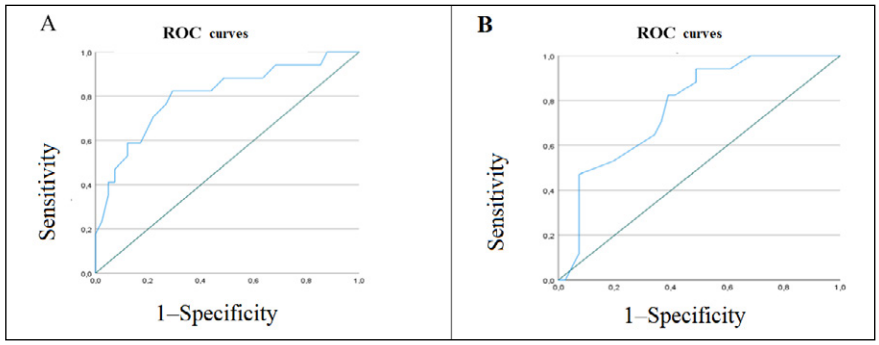


Fig. 1. ROC curves for assessing the predictive ability of anxiety regarding postoperative pain intensity: A – state anxiety; B – trait anxiety
Picture taken by the authors

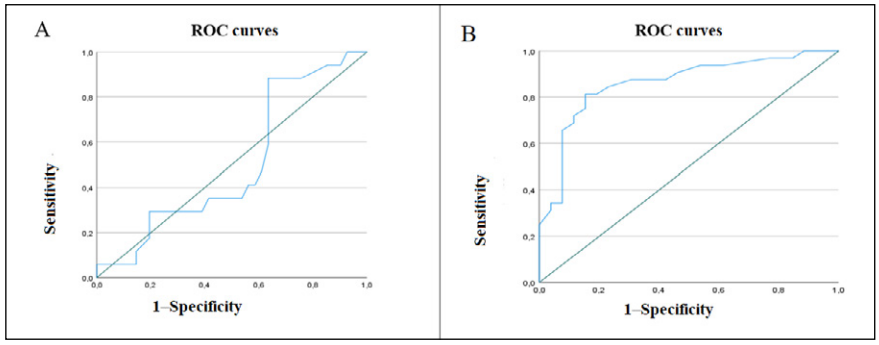


Fig. 2. ROC curves for assessing the predictive ability of depression level: A – for predicting postoperative pain intensity (AUC=0.506); B – for predicting the duration of postoperative pain syndrome (AUC=0.860)
Picture taken by the authors

groups (χ^2=12.857; p=0.02), with a consistent decrease from subgroup 1 to Group 2, confirmed by a significant linear trend (p<0.001). Thus, in subgroup 1.1, 37.5% (95% CI: 21.1–56.3) of patients and in subgroup 1.2, 30% (95% CI: 14.7–49.4) required additional analgesia during the first postoperative day. In Group 2, no need for additional analgesia was observed.

After discharge, the need for oral analgesia was present in almost all women; however, the requirement for additional analgesia during this period was observed in 18.8% (95% CI: 7.2–36.4) of patients in subgroup 1.1 and 17.9% (95% CI: 6.1–36.9) of patients in Group 2.

Analysis of the duration of analgesic use during the outpatient period demonstrated a between-group difference at a statistically significant level (H=50.5; p<0.001). Further pairwise analysis using the Mann–Whitney U test with Bonferroni correction showed that patients in subgroup 1.1 and Group 2 used analgesics for a longer period than those in subgroup 1.2 (Table 2).

Given the identified significant differences in pain intensity and duration of analgesic support between groups, the next stage of the study involved determining the prognostic significance of each component of psychoemotional status. Considering the modern pain model assumes a complex interaction between the psychological domain and the nociceptive system, it became necessary to objectify which indicators—anxiety or depression—have higher discriminative ability in predicting the severity of the postoperative course.

The results of the prognostic model evaluation for anxiety and depression indicators are presented in Fig. 1 and Fig. 2.

According to the ROC curve analysis, the level of state anxiety demonstrated good predictive ability for the development of severe postoperative pain (AUC=0.804; 95% CI: 0.673–0.935; p<0.001). The obtained results indicate that an increased level of state anxiety is associated with a higher probability of developing an intense pain syndrome in the postoperative period.

Additionally, ROC curve analysis showed that trait anxiety also has predictive value for the development of severe postoperative pain (AUC=0.770; 95% CI: 0.647–0.894; p=0.001). However, its discriminative ability was slightly lower compared with state anxiety, indicating a more pronounced influence of the current psychoemotional state on pain formation.

The ROC curve analysis showed that the level of depression does not have predictive value for the development of severe postoperative pain (AUC=0.506; 95% CI: 0.347–0.666; p=0.939). These findings indicate the absence of a statistically significant association between depressive symptoms and pain intensity in the postoperative period.

However, ROC curve analysis demonstrated a high predictive ability of depression level regarding the duration of postoperative pain syndrome (AUC=0.860; 95% CI: 0.761–0.959; p<0.001). It was found that depressive symptoms are associated with a prolonged pain course and may be considered a risk factor for pain chronification.

The conducted ROC analysis allowed for the mathematical confirmation of the role of the current emotional state in modulating the acute pain response, as well as the assessment of the impact of depressive states on

Table 2. Comparative characteristics of postoperative pain intensity and parameters of analgesic support in patients of the study groups

Parameters		Subgroup 1.1 (n=32)	Subgroup 1.2 (n=30)	Group 2 (n=28)	p
NRS (postoperative)	1	1 (3.1%)	1 (3.3%)	6 (21.4%)	p_1=1,000 p_2=0,043 p_3=0,048
	2	18 (56.3%)	14(46.7%)	20 (71.4%)	p_1=0,612 p_2=0,287 p_3=0,067
	3	13 (40.6%)	15(50%)	2 (7.1%)	p_1=0,610 p_2=0,003 p_3<0,001
Analgesic dose (dexketoprofen), 1st postoperative day	1	0 (0%)	1 (3.3%)	7 (25%)	p_1=0,484 p_2=0,003 p_3=0,023
	2	24 (75%)	20 (67.7%)	20 (71.4%)	p_1=0,759 p_2=0,778 p_3=0,780
	3	8 (25%)	9 (30%)	1 (3.6%)	p_1=0,778 p_2=0,029 p_3=0,013
Need for additional analgesia (paracetamol), 1st postoperative day		12 (37,5%)	9 (30.0%)	0 (0%)	p_1=0.522 p_2<0.001 p_3=0.002
Oral analgesia (outpatient period)		32 (100%)	22 (73.3%)	28 (100%)	p_1=0.001 p_2=1.000 p_3=0.005
Need for additional analgesia (outpatient period)		6 (18,8%)	0 (0%)	5 (17.9%)	p_1=0.024 p_2=1.000 p_3=0.021
Duration of analgesic intake (outpatient period)		2 [2;3]	1 [0;1]	2 [2;3]	p_1<0.001 p_2=0.519 p_3=0.002

Notes: NRS (Numeric Rating Scale) – numerical pain rating scale; 1 – score 0–3 (mild pain); 2 – score 4–6 (moderate pain); 3 – score 7–10 (severe pain). Analgesic dose: 1 – 50 mg; 2 – 100 mg; 3 – 150 mg. Statistical significance: Pearson's χ^2 and Fisher›s exact test were used for categorical data; for quantitative data (duration of intake), the Kruskal–Wallis test and Mann–Whitney U test were applied; p_1 – level of significance for comparisons between subgroups 1.1 and 1.2; p_2 – between subgroup 1.1 and group 2; p_3 – between subgroup 1.2 and group 2
Source: compiled by the authors of this study

the tendency toward prolongation of pain syndrome during the outpatient stage.

DISCUSSION

The results of the present study confirm the modern biopsychosocial model of pain, according to which the intensity of postoperative pain syndrome (PPS) is determined not only by the extent of surgical trauma but also by a complex interaction of psychoemotional and social factors.

Analysis of the psychoemotional profile of patients revealed a clear relationship between social context and anxiety levels. The highest levels of state and trait anxiety were observed in internally displaced persons (subgroup 1.1), reflecting the cumulative effect of prolonged psychotraumatic stress. The statistically significant differences between all groups (p<0.001) indicate that current living conditions in a war-affected environment are a dominant factor in the formation of an anxious psychoemotional background.

Establishing a cause-and-effect relationship between psychological status and pain intensity was a key objective of the study. Our findings demonstrate that patients with higher anxiety levels (subgroups 1.1 and 1.2) had statistically higher NRS scores compared with women residing abroad (group 2). This supports the hypothesis that elevated stress load lowers the pain threshold and modulates the neuroendocrine response of the organism [11, 12].

Pharmacological validation of the results showed that the pattern of analgesic consumption directly

correlates with the psychoemotional profile. In Group 2 (lower anxiety levels), a greater proportion of women achieved adequate analgesia with the minimal dose of dexketoprofen (50 mg) compared with subgroups 1.1 and 1.2, where a predominance of maximum daily doses (150 mg) was observed and additional administration of paracetamol was required in a subset of patients. This indicates that psychoemotional destabilisation necessitates intensified analgesic management despite an identical surgical intervention.

The prognostic significance of the identified factors was further analysed using ROC curves. The obtained results allow differentiation between the influence of anxiety and depression on different characteristics of pain. State anxiety proved to be the most powerful predictor of acute pain intensity. This is likely due to the fact that the current emotional state directly modulates the rapid nociceptive response, enhancing pain signal perception at the cortical level. Depression, while not directly affecting pain intensity, demonstrated high predictive value for the duration of pain syndrome in the outpatient period. This suggests that depressive disorders, associated with impaired central antinociceptive mechanisms, contribute to pain prolongation and increase the risk of chronification [13–15].

Thus, the obtained data indicate the necessity of a personalised approach to postoperative analgesia in patients, taking into account their psychoemotional status. The identified patterns suggest that preventive correction of state anxiety may reduce the peak intensity of postoperative pain syndrome, whereas treatment of depressive states is important for preventing prolonged pain and improving rehabilitation outcomes in patients living under conditions of chronic stress.

CONCLUSIONS

The study demonstrated that conditions of acute and chronic wartime stress in Ukraine significantly modulate pain perception even during minimally invasive surgical techniques such as hysteroscopic myomectomy.

Thus, according to our results, state anxiety is associated with the highest predictive ability for postoperative pain intensity, while depression shows high prognostic significance for pain duration (prolongation of pain). In contrast, trait anxiety is associated with somewhat lower postoperative pain intensity, and high levels of depression are not associated with pain intensity. These findings may indicate different mechanisms of influence of psychoemotional factors on the development of acute and prolonged pain after hysteroscopic myomectomy.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Determination of tongue pressure force: Experimental research

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ABSTRACT

Aim: To identify the zones of maximum contact force (F, N) of the tongue at 100% and 125% tongue volume on areas of the oral cavity in an experimental study, and to conduct a comparative analysis of the contact force indicators.

Materials and Methods: 3D prototypes of the patient's upper and lower jaws were created. Measurements were carried out using a FlexiForce film force sensor and an Arduino Nano microcontroller module. This allowed recording of the contact force applied by the tongue.

Results: The maximum values of contact force were recorded in the following areas: the marginal gingiva on the lingual surface of the lower central incisors, the marginal gingiva on the palatal surface of the upper central incisors, the middle third on the lingual surface of the lower central incisors, and the middle third on the palatal surface of the upper central incisors. An increase in values was noted in all studied zones when the tongue volume increased to 125%.

Conclusions: A comparative analysis of tongue contact force indicators obtained during the experimental study demonstrated an increase in values when the tongue volume was enlarged to 125% in the areas of the oral cavity of the upper and lower jaws, compared with the actual tongue volume.

KEY WORDS: maximum stress concentration, dentognathic anomalies and deformations

Wiad Lek. 2026;79(6):1273-1279. doi: 10.36740/WLek/222569 DOI

INTRODUCTION

The tongue has an important role in the functioning of the dentognathic apparatus [1, 2]. Excessive pressure of the tongue on surrounding structures – especially when its size increases, its habitual static position changes, or its function is impaired – leads to alterations in the anatomical and topographical relationships with adjacent tissues and is considered a primary aetiological factor in the development of pathological occlusions [2, 3].

Permanent tongue enlargement (macroglossia) can be attributed to muscular hypertrophy or hyperplasia (primary macroglossia) or to an underlying condition (secondary macroglossia). Secondary macroglossia may be associated with congenital or acquired factors (Down syndrome, Beckwith–Wiedemann syndrome, neurofibromatosis type I, idiopathic muscular hypertrophy, etc.), metabolic/endocrine disorders (hypothyroidism, myxoedema, acromegaly, amyloidosis), inflammatory/infectious, systemic, traumatic, and neoplastic factors (congenital lymphangiomas or vascular malformations). The distorted interrelations between a hypertrophied tongue and surrounding bony structures (maxilla, mandible, alveolar process, and dental arches) can significantly influence their growth and development, especially in childhood and early adolescence. At the same time, the exact mechanisms of tongue-associated maxillofacial and occlusal abnormalities are not yet well understood. The multifactorial nature of orthognathic pathology and limited data concerning the biomechanical influences of the enlarged tongue (contact pressure, functional force, and their influence on stress and strain distribution within the growing bone) cause significant uncertainty and controversy in treatment and prevention strategies. Due to the specific structure of the tongue, the diagnosis of macroglossia and the extent of its enlargement is quite complex [2, 4–6], with no clear evidence of a correlation between tongue dimensions and the severity of the resulting orthodontic pathology. In this context, experimental studies conducted through mechanical and mathematical modelling, modern computer technologies, and the construction of three-dimensional simulation models of the biomechanical system "tongue–dentognathic apparatus" are of particular importance [7–9].

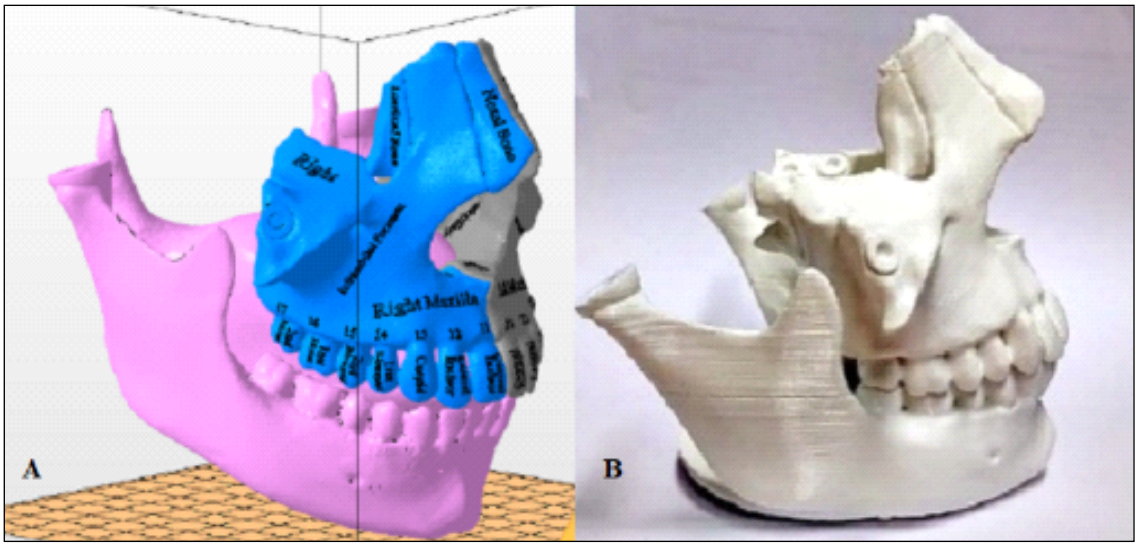


Fig. 1. 3D prototypes of the patient's jaws based on CBCT scans of the skull (A), 3D prototypes of the jaws printed on a 3D printer (B)
Picture taken by the authors

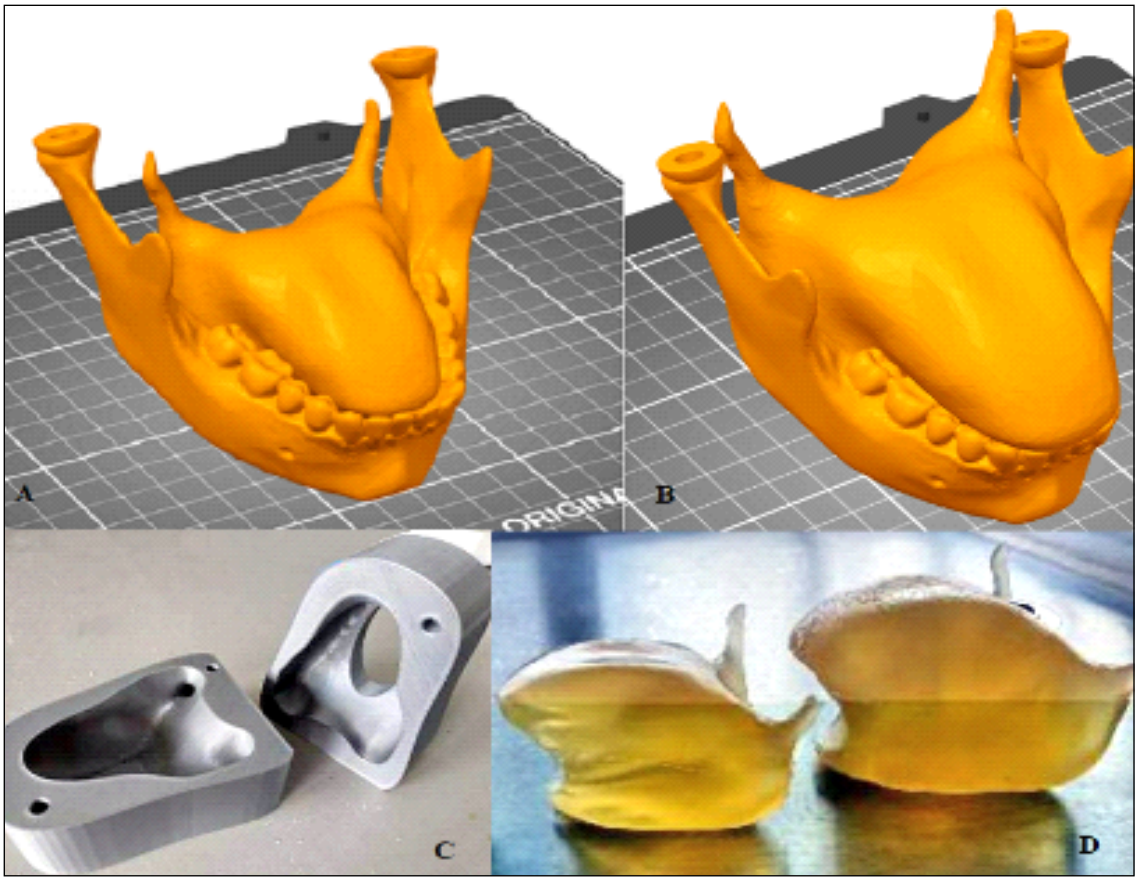


Fig. 2. 3D-printed tongue prototypes with 100% (A) and 125% (B) volumes in the mandibular space, a tongue mold made of PLA (Prusa PLA, Prusa Research a.s., Prag, Czech Republic) (C), and ballistic gel tongue models with 100% and 125% volumes (D)
Picture taken by the authors

AIM

To identify the zones of maximum contact force (F, N) of the tongue at 100% and 125% tongue volume in the areas of the oral cavity of the upper and lower jaws in an experimental study, and to conduct a comparative analysis of the contact force indicators.

MATERIALS AND METHODS

Cone-beam computed tomography (CBCT) and magnetic resonance imaging (MRI) were used in this study for patient M., aged 12, who sought care at Children's Clinical Hospital No. 7, Department of Surgical Dentistry and Maxillofacial Surgery of Paediatric Age, Bogomolets

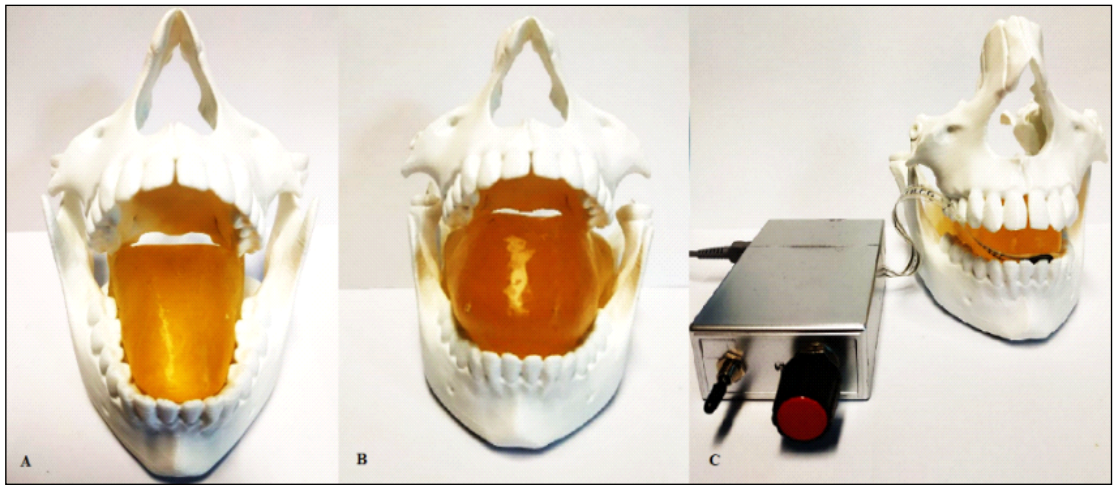


Fig. 3. Ballistic gel tongue models with volumes of 100% (A) and 125% (B) in the mandibular space, and an electronic device based on an Arduino Nano microcontroller module with a FlexiForce thin-film force sensor (C)
Picture taken by the authors

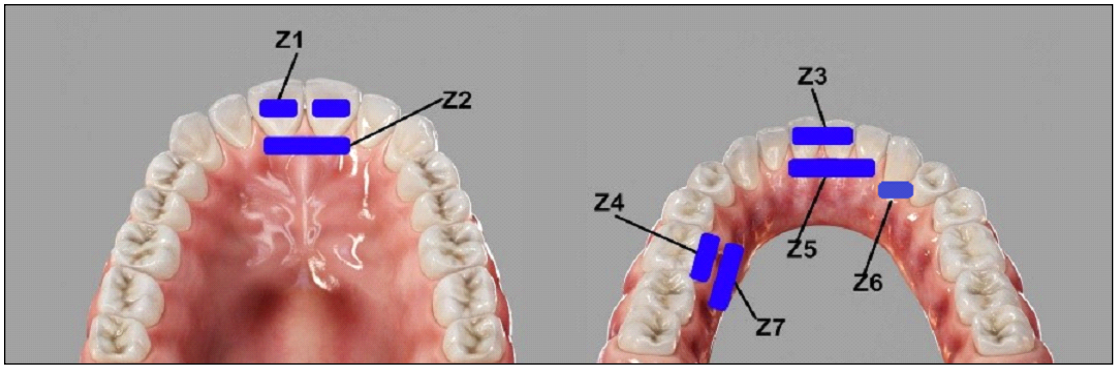


Fig. 4. Zones of maximum contact force (F, N) of the tongue fixation on areas of the oral cavity in the upper and lower jaws
Picture taken by the authors

National Medical University, for general medical indications. The patient was found to have a physiological (orthognathic) bite, with no functional disorders of the maxillofacial region.

The first step was the creation of 3D prototypes of the patient's upper and lower jaws based on CBCT scans of the skull. The base model was derived from a geometry obtained from Thingiverse, an open online repository of user-generated 3D models, provided under a Creative Commons licence for non-commercial use [10]. Since the model is modifiable, Boolean operations were applied in Siemens NX software (Ver. 2015, 2202) to connect the components of the upper jaw and to smooth the palatal fissure that had formed (Fig. 1A). The jaw prototypes were printed using an FDM 3D printer (Prusa Mk3S+, Prusa Research a.s., Prague, Czech Republic) and PETG filament FIL-A-GEHR PETG® (Gehr GmbH, Mannheim, Germany) (Fig. 1B).

The MRI scans of the tongue were segmented using 3D-Slicer (Ver. 4.13.0), and an STL file of its surface was created. Then, a two-component mold of a normal anatomical tongue model was designed using Siemens NX software (Ver.2015, 2202). The next step, also performed in Siemens NX, involved scaling the STL model of the tongue to 125% volume (Fig. 2A, B). Molds for 3D printing were fabricated from polylactic acid (PLA, Prusa PLA) using a Prusa MK3S+ 3D printer (Prusa Research, Co) (Fig. 2C).

Ballistic gelatin was selected as the tongue prototype material for the study [11, 12]. In terms of mechanical properties, this material closely approximates the actual density of the human tongue. The composition of ballistic gelatin is tailored to simulate the physical properties of living human tissues (viscosity, density, resistance) in experiments studying the impact of firearms, mines, or explosive devices. Human muscle tissue consists of approximately 75% water; ballistic gelatin enables the mechanical properties to be modelled with a high degree of similarity by binding the liquid phase into a form suitable for experimentation.

In addition to water and isopropanol (99,9%), glycerin and porcine gelatin were used to prepare the artificial tissue. Before adding the other ingredients, the porcine gelatin powder was mixed with water and left to swell

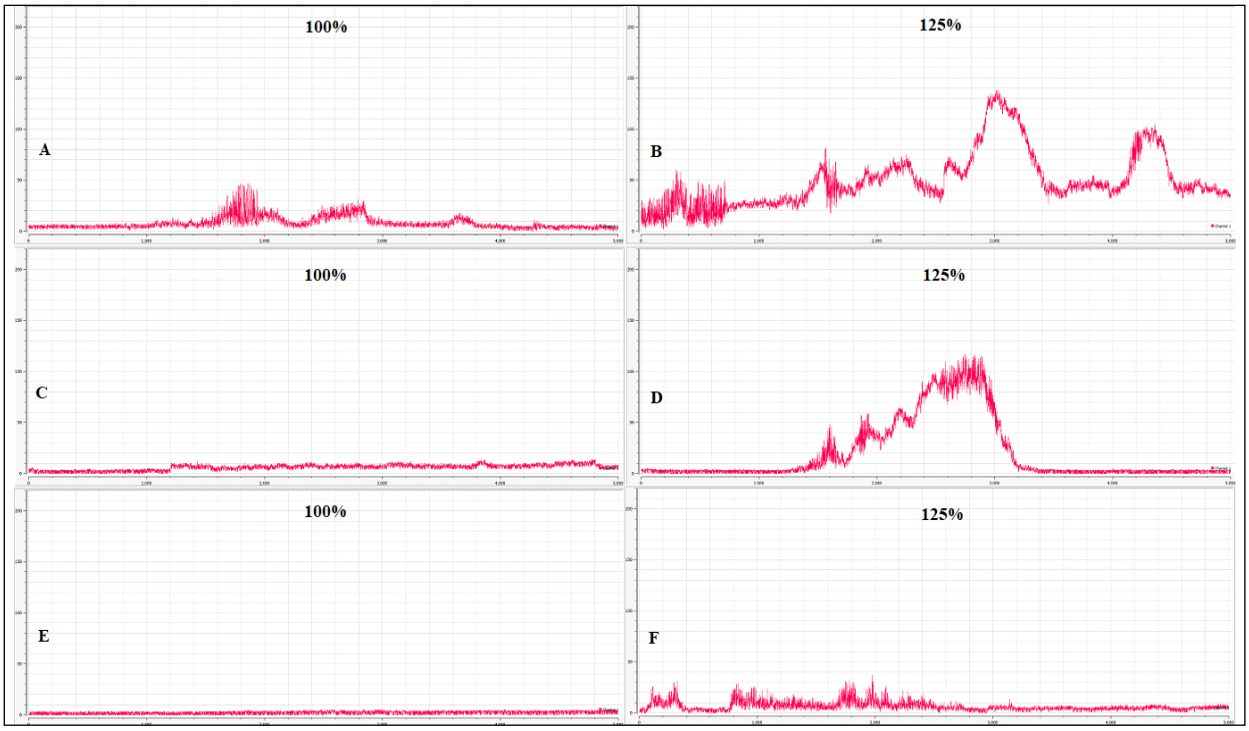


Fig. 5. Time-based registration of contact force (F, N) of the tongue using SerialPlot software graphs at tongue volumes of 100% and 125% in the zones of the marginal gingival on the lingual surface of the lower central incisors (A, B), marginal gingival on the palatal surface of the upper central incisors (C, D), and marginal gingival on the lingual surface of the lower canines (E, F)
Picture taken by the authors

for 10 minutes. The mixture was then heated in a water bath at 60 °C until fully dissolved, to obtain a clear fluid. One litre of ballistic gel was prepared using the following proportions: 500 ml of distilled water, 250 ml of isopropanol (99,9%), 250 ml of glycerin (>87%), and 162 g of porcine gelatin. Before slowly pouring the mixture into the moulds, both parts of the mould were joined together (Fig. 2D). Following the moulding process, the mould was placed in a temperature-controlled cooling chamber (4 °C) for 12 h to ensure uniform thermal dissipation. After reaching ambient temperature, the final step involved demoulding the specimen.

3D models of the tongue at 100% and 125% volume were obtained and subsequently placed, one at a time, within the space of the lower jaw (Fig. 3A, B). To perform the measurements, a FlexiForce thin-film force sensor was used, with a surface area (S, mm^2) of 78,5 mm^2, which enabled the recording of tongue pressure force values. An electronic device based on an Arduino Nano microcontroller module was used for data acquisition (Fig. 3C). The contact force (F) of the tongue was determined in N from the sensor readings.

Analog-to-digital conversion of the force sensor signal was performed using SerialPlot software after appropriate configuration in Arduino IDE. Following calibration with a 1 kg (9.81 N) reference weight, the FlexiForce thin-film force sensor was placed in the area between the tongue and both the middle third and marginal gingival part on the palatal surface of the upper teeth, as well as the lingual surface of the lower teeth. The model was closed manually with applied force until occlusion was achieved.

The following zones were chosen for sensor placement: Z1 – the middle third on the palatal surface of the upper central incisors; Z2 – the marginal gingival part on the palatal surface of the upper central incisors; Z3 – the middle third on the lingual surface of the lower central incisors; Z4 – the middle third on the lingual surface of the lower first molars; Z5 – the marginal gingival part on the lingual surface of the lower central incisors; Z6 – the marginal gingival part on the lingual surface of the lower canines; Z7 – the marginal gingival part on the lingual surface of the lower first molars (Fig. 4). These areas were chosen to distinguish the influence of macroglossia on different segments of the dental arches and alveolar bone, which are responsible for the development of certain types of occlusal anomalies.

ETHICS

In conducting this study, the authors complied with the ethical standards set forth in the World Medical Association's Declaration of Helsinki and current Ukrainian legislation, which regulate scientific research involving

Table 1. Contact force (F, N) of the tongue values in the corresponding zones of the upper and lower jaws in the experimental study

Zone	Model without restriction of distal tongue displacement		Model with restriction of distal tongue displacement	
	Contact force (F) of the tongue, N		Contact force (F) of the tongue, N	
	100%	125%	100%	125%
Z1	0	0	0.3	4.5
Z2	0	0	0.2	6.4
Z3	0.5	1.0	1.2	5.1
Z4	0.7	2.9	0.5	3.4
Z5	0.3	1.1	1.1	7.7
Z6	0.3	1.5	0.5	1.5
Z7	0.1	1.8	0.8	4.1

Source: compiled by the authors of this study

the use of medical records. The data used in the experiment were collected during additional examination after the patient was provided with clear, complete, and accessible information regarding the purpose, design, and methodology of the study, as well as the potential risks, benefits, and alternatives. The Commission on Bioethical Expertise and Ethics of Scientific Research of the Bogomolets National Medical University, Ministry of Health of Ukraine, reviewed the study materials and issued a recommendation for approval.

RESULTS

At 100% volume of the tongue, the values were insignificant. The maximum values of contact force (F, N) were recorded in the following areas: middle third on the lingual surface of the lower central incisors (Z3), marginal gingival part on the lingual surface of the lower central incisors (Z5), middle third on the lingual surface of the lower first molars (Z4) and marginal gingival part on the lingual surface of the lower canines, (Z6). An increase in contact force (F, N) of the tongue was observed in all studied zones of the upper and lower jaws when the tongue volume was increased to 125%. The maximum values of contact force (F, N) were recorded in the following areas: the marginal gingival on the lingual surface of the lower central incisors (Z5), the marginal gingival on the palatal surface of the upper central incisors (Z2), the middle third on the lingual surface of the lower central incisors (Z3), and the middle third on the palatal surface of the upper central incisors (Z1) (Fig. 5). Table 1 presents the contact force (F, N) applied by the tongue with and without restriction at the upper and lower jaw zones.

The highest values of contact force (F, N) at 100% and 125 % volume of the tongue were recorded in the following areas: the marginal gingival on the lingual surface of the lower central incisors (Z5) and the middle third on the lingual surface of the lower central incisors (Z3) (Table 1).

The quantity of established contact zones where the maximum pressure was determined at 100% and 125% volume of the tongue was higher on the lower jaw compared to the upper.

DISCUSSION

The majority of researchers agree that, despite its adaptive properties, the tongue has a significant role in the development of the dentognathic apparatus. The interaction between tongue force and the forces of the lips and cheeks is of particular interest when planning orthodontic treatment. Clear data on the distribution of maximum pressure gradients are lacking, as the tongue, situated within the oral cavity, can exert varying degrees of pressure on adjacent structures, thereby influencing the growth and development of the dentognathic apparatus [1, 2, 4–6].

Clinical studies on tongue pressure measurement are noteworthy. For example, Lee Y.S. and co-authors, using the Iowa Oral Performance Instrument, demonstrated possible differences in maxillofacial morphology depending on tongue muscle strength and lip pressure [13]. Tsujimoto K. and co-authors found that the greater the change in tongue mobility, the lower the pressure during protrusion and swallowing, and the worse the swallowing function in individuals with temporomandibular dysfunction [14]. Using a tongue pressure measurement device, Mizokami K. and co-authors established that occlusal contact area, maximum bite force, tongue pressure, and masticatory efficiency gradually increase with age, while lip pressure remains stable [15].

The most accurate data collection can be achieved by measuring tongue contact force in the anterior, posterior, and lateral areas of the oral cavity in both static position and during swallowing using flexible pressure sensors. For instance, Yu M. and Gao X. conducted an intraoral study to determine pressure in specific areas of the hard palate in individuals with various forms of

dentognathic deformities. Their findings revealed a relationship between contact force, type of deformation, and dental arch morphology: the wider the dental arch, the lower the pressure exerted during swallowing in the anterior and lateral regions [1]. Similarly, Valentim A.F. and co-authors examined the influence of tongue pressure on dental arches at rest and during swallowing. They identified a correlation between tongue pressure and both the width and length of the dental arch [4].

Studies involving 3D biomechanical tongue models have been described in both international and Ukrainian scientific publications. Finite element models considering the nonlinear biomechanical behaviour of its tissues for assessing the impact of glossectomy on patients' speech were presented by Gérardim J.-M. and co-authors [7]. Calka M. conducted research in the context of speech motor control [8]. Perrier P. and co-authors studied biomechanical models of speech articulators for speech motor control, including examples where biomechanics informs us about trajectory shapes, the relationship between velocity and trajectory, the connection between motor control accuracy and acoustic variability, and the influence of dynamic properties on the shaping of soft speech articulators [9, 16].

The results of our experimental study demonstrate a clear trend in the localisation of maximum contact force (F, N) of the tongue on surrounding oral cavity tissues. The location of the zones identified in the experiment corresponds with data presented in other scientific publications [1, 4, 5]. It was clearly shown that enlargement of the tongue by 25% results in a significant static load on the surrounding bony structures. According to Wolff's law, increased contact pressure and stress within bone significantly influence its growth and remodelling. It was found that the most intensive pressure of the tongue develops in the frontal area of the maxilla and mandible; thus, a tendency towards sagittal anomalies in patients with macroglossia can be expected. This finding is supported by clinical studies in Angle Class III patients.

Although the absolute values obtained in the experimental study should not be considered definitive due to the lack of reference normative values, the data obtained can be used for the development of prevention strategies in patients with enlarged tongue, through compensation of abnormal forces and increasing space for the tongue by maxillary expansion or similar approaches.

To prevent distal displacement of the tongue within the lower jaw space, a barrier was placed. Without this barrier, the experiment was unsuccessful, as the tongue "protruded distally" and failed to apply measurable force to the sensor.

The accuracy of in vivo measurements is highly dependent on the method and location of sensor placement. Even when mounted on ultra-thin, custom-made overlays, sensors may introduce distortion into the results. Conversely, measurements taken without stable fixation are also suboptimal, as sensors may shift from the intended measurement site. Another critical factor influencing data reliability is the sensitivity of the device.

PROSPECTS FOR FURTHER RESEARCH

It is planned to identify the contact force (F, N) of the tongue, investigate the level of stress and on the areas of the oral cavity in the upper and lower jaws in vivo and conduct comparative analysis of the contact force indicators.

CONCLUSIONS

A comparative analysis of tongue contact force indicators obtained during the experimental study demonstrated an increase in values when the tongue volume was enlarged to 125% in the areas of the oral cavity of the upper and lower jaws, compared with the actual tongue volume. The areas of the marginal gingiva on the lingual surface of the lower central incisors, the marginal gingiva on the palatal surface of the upper central incisors, the middle third on the lingual surface of the lower central incisors, and the middle third on the palatal surface of the upper central incisors were the zones where the values were highest.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Prevalence and distribution of malposed canines in young adults: A cross-sectional clinical study

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ABSTRACT

Aim: This study aims to evaluate the prevalence and distribution of malposed permanent canines in young adults according to gender, dental arch (maxillary and mandibular), position (buccal and lingual), laterality (right and left sides), and Angle's classification of malocclusion (class I, II, and III).

Materials and Methods: A cross-sectional clinical study was conducted on 302 undergraduate dental students (170 males and 132 females) aged between 19–24 years. Each participant underwent a careful intra-oral clinical examination to determine the malposed canines. Canine malposition was recorded, and data were analyzed using descriptive and inferential statistics.

Results: This study found that 113 participants had malposed canines, giving an overall prevalence 37.4%. Females showed a higher prevalence (47.0%) of canine malposition than males (30.0%). Slightly more malposed canines in the mandibular arch (51.3%) than in the maxillary arch (48.7%). Buccal canine malposition was the most frequent (95.6%) of cases. Also, right-side canine malposition (54.9%) was more frequent than left-side (45.1%). The majority of malposed canines were recorded in Class I malocclusion (73.45%).

Conclusions: Canine malposition is a common clinical finding among young adults. The strong association between Class I malocclusion and malposed canines indicates that canine malposition is mainly affected by local eruption factors rather than skeletal sagittal discrepancies. These findings showed the importance of early clinical examination and interceptive orthodontic treatments to decrease the complexity of future orthodontic treatment.

KEY WORDS: interceptive orthodontic treatments, orthodontic treatment, a cross-sectional clinical

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INTRODUCTION

Permanent canines had a distinctive position in the dental arch because of their important contribution to facial appearance, continuity of the arch, and normal occlusal function. Their situation at the junction between the anterior and posterior segments plays a visible role in lip support and smile harmony. In addition, their long roots and strong morphology allow them to participate effectively in canine guidance and in the regulation of occlusal forces during lateral mandibular movements [1,2]. The eruption of the permanent canine is a more complicated process than other teeth because the canine has a relatively high and deep developmental position within the arch, with a long and irregular eruption pathway. Their eruption occurs relatively late, exceeded only by third molars [2–4]. This makes the canines mostly subjected to local and environmental influences that may interfere with normal eruption, increasing the likelihood of positional disturbances, malposition, or impaction [5–7].

Generally, canine malposition is considered a multifactorial condition rather than a single identifiable cause. Tooth size–arch length discrepancy, arch crowding, prolonged retention or premature loss of deciduous teeth, disturbances in eruption pathways, and anomalies of adjacent teeth are among the most common factors associated with canine malposition. Maxillary lateral incisors play an important role in guiding the eruption pathway of permanent canines, and disturbances affecting these teeth may increase the risk of canine displacement [8–11]. Malposition may still occur in subjects with normal sagittal occlusal relationships, suggesting that local eruption disturbances and abnormalities in eruption guidance may have a greater influence on canine position than sagittal skeletal discrepancies [9, 12].

Recent epidemiological studies demonstrated that the prevalence and distribution of ectopic and malposed canines vary among different populations, genders, skeletal patterns, and dental arches [6, 13–15]. These variations

may be associated with differences in craniofacial morphology, eruption guidance mechanisms, environmental influences, and genetic background among different populations [14, 16]. For this reason, population-specific investigations are important for accurate diagnosis, early interception, and appropriate orthodontic treatment planning because local etiological and developmental factors may vary among different populations [14, 16].

Despite the clinical relevance of eruption problems involving permanent canines, information regarding their prevalence and characteristics among Iraqi young adults is still limited [13, 15]. Recent orthodontic literature has highlighted that ectopic and malposed canines represent a clinically significant eruption disturbance that may adversely affect occlusion, dental arch integrity, periodontal health, and orthodontic treatment complexity. Contemporary studies have demonstrated that canine displacement is associated with multiple interacting factors, including skeletal pattern, eruption guidance disturbances, arch length deficiency, and anomalies affecting adjacent teeth. Furthermore, early diagnosis and interceptive orthodontic management have been strongly recommended to minimize complications and improve treatment outcomes [6, 8, 9, 16].

Dental students represent an appropriate study group, as their age coincides with completion of permanent dentition and the stage at which eruption-related positional anomalies are most likely to be clinically apparent. Accordingly, the present study was performed to assess the prevalence and distribution of malposed canines among Iraqi dental students in Al-Najaf city and to evaluate their association with gender, dental arch, buccal or lingual position, laterality, and Angle's classification of malocclusion.

MATERIALS AND METHODS

STUDY DESIGN AND SETTING

This study was carried out as a cross-sectional clinical investigation at the College of Dentistry, University of Kufa, in Al-Najaf city, Iraq. Undergraduate dental students were selected because they represent a young adult group in which permanent dentition is complete and positional eruption problems can be clinically observed.

STUDY POPULATION

A total of 350 undergraduate students were initially examined. After applying the inclusion and exclusion criteria, 302 students were included in the final analysis. The sample consisted of 170 males and 132 females, with ages ranging from 19 to 24 years.

ELIGIBILITY CRITERIA

This study included undergraduate students aged between 19 and 24 years who had complete permanent dentition and no previous history of orthodontic treatment. Participants with systemic conditions or long-term medication that could affect craniofacial growth or tooth eruption were excluded. Also, participants with craniofacial anomalies such as cleft lip or palate, obvious facial asymmetry, or any history of orthognathic surgery were excluded.

CLINICAL EXAMINATION

In this study, each participant underwent a careful intra-oral clinical examination in an upright position with adequate light using a dental mirror and a portable light source. Standardized infection control measures were applied during the examination. The examination focused on the presence and position of permanent canines. Any deviation from the normal alignment within the dental arch was identified and recorded. Canine malposition was noted when the canine was either buccally or lingually in relation to the ideal arch configuration. Because the evaluation depended only on clinical examination, impacted canines that needed radiographic assessment were excluded from the study.

RECORDED VARIABLES

For each participant, the malposed canines were identified and recorded according to gender, dental arch (maxillary or mandibular), position (buccal or lingual), side (right or left), and Angle's classification of malocclusion (Class I, II, or III). All data were documented using a standardized case sheet.

STATISTICAL ANALYSIS

The collected data were analyzed using descriptive statistics, including frequencies and percentages to describe the prevalence and distribution of malposed canines. The Chi-square test and Fisher's exact test were used when appropriate to assess the associations between categorical variables. A p-value < 0.05 was considered statistically significant.

ETHICAL APPROVAL

The article has ethical approval of University of Kufa College of Dentistry (Ref: FKD/EC/114).

RESULTS

As shown in Table 1, this study included 302 participants who were examined clinically, and it was found that

Table 1. Association between gender and prevalence of malposed canines

Gender	Malposed canines n (%)	Normal canines n (%)	Total	P-value
Male	51 (30.0%)	119 (70.0%)	170	
Female	62 (47.0%)	70 (53.0%)	132	
Total	113 (37.4%)	189 (62.6%)	302	0.002

Source: Compiled by the authors of this study

Table 2. Distribution of maxillary and mandibular malposed canines according to gender

Gender	Total malposed canines	Maxillary malposed canines n (%)	Mandibular malposed canines n (%)	P-value
Male	51	32 (62.7%)	19 (37.3%)	
Female	62	23 (37.1%)	39 (62.9%)	
Total	113	55 (48.7%)	58 (51.3%)	0.007

Source: Compiled by the authors of this study

Table 3. Association between gender and direction of canine malposition (buccal versus lingual)

Gender	Buccally malposed canine n (%)	Lingually malposed canine n (%)	Total
Male	48 (94.1%)	3 (5.9%)	51
Female	60 (96.8%)	2 (3.2%)	62
Total	108 (95.6%)	5 (4.4%)	113

Source: Compiled by the authors of this study

Table 4. Association between gender and side of malposed canines (right versus left)

Gender	Right n (%)	Left n (%)	Total
Male	29 (56.9%)	22 (43.1%)	51
Female	33 (53.2%)	29 (46.8%)	62
Total	62 (54.9%)	51 (45.1%)	113

Source: Compiled by the authors of this study

Table 5. Distribution of malposed canines according to Angle's classification of malocclusion

Angle's classification of malocclusion	Malposed canine
Cl I	83 (73.45%)
Cl II	29 (25.66%)
Cl III	1 (0.88%)

Source: Compiled by the authors of this study

113 participants had malposed canines, giving a total prevalence of 37.4%. Statistical analysis using the Chi-square test revealed a significant association between gender and the presence of malposed canines ($p = 0.002$). The prevalence of malposed canines in females (47.0%) was higher than in males (30.0%).

As shown in Table 2, statistical analysis using the Chi-square test showed a significant association between gender and the distribution of malposed canines between the maxillary and mandibular arches ($p = 0.007$). In males, maxillary malposed canines (62.7%) were more frequent than mandibular malposed canines (37.3%), while in females, mandibular malposed canines (62.9%) were more frequent than maxillary malposed canines (37.1%).

Table 3 showed the distribution of malposed canines according to buccal and lingual position in relation to gender. Buccally malposed canine was the predominant presentation in both males and females. Among male subjects, 48 canines (94.1%) were buccally malposed. Similarly, in female subjects, 60 canines (96.8%) were buccally malposed. Statistical analysis using Fisher's exact test revealed no significant association between gender and the direction of canine malposition ($p = 0.656$).

Table 4 showed the association between gender and the side of malposed canines (right versus left). In males, right-side canine malposition was observed in 29 cases (56.9%). Similarly, in females, right-side canine malposition was observed in 33 cases (53.2%). Statistical analysis using the chi-square test revealed no significant association between gender and the side of canine malposition ($p = 0.699$).

According to Angle's classification, this study revealed that most of the malposed canines were associated with Class I malocclusion. In particular, 83 cases (73.45%) were noticed in Class I, followed by 29 cases (25.66%) in Class II. Only one case (0.88%) was noticed in Class III malocclusion as presented in Table 5.

DISCUSSION

This study showed that the overall prevalence of malposed canines in young adults was 37.4%, indicating that canine malposition is relatively common in this age group. Recent investigations also reported that ectopic and malposed canines are commonly observed among young adults, with variations according to gender, skeletal pattern, and dental arch distribution [6]. This is in agreement with previous epidemiological studies, although the reported prevalence varies among populations because of differences in craniofacial characteristics, genetic background, environmental influences, and dental developmental patterns [6, 13–15]. A significantly higher prevalence of malposed canines in female participants than in males has been found; this finding is consistent with several previous studies that reported a higher prevalence of canine eruption disturbances among females [6, 9, 15]. One possible explanation is the difference in growth and maturation patterns between genders. Generally, girls complete craniofacial growth and dental development earlier than boys, which may decrease the chance for spontaneous correction of eruption problems and increase the possibility of malposition [9,12]. Genetic and local developmental factors may contribute to variations in canine eruption disturbances among individuals [16].

In terms of dental arch distribution, a slight predominance of malposed canines was found in the mandibular arch. Although maxillary canine malposition has been more frequently highlighted in the literature, particularly because of its elevated impaction rate, mandibular canine malposition should not be disregarded. Small arch length, lower anterior teeth crowding, and limited adaptability of the mandibular arch may interfere with the normal canine eruption, resulting in malposition [10, 11]. The noticed variation between males and females further encourages the role of local dental factors rather than generalized skeletal discrepancies. Buccal canine malposition was the predominant pattern in the present study, while lingual canine malposition was rare. This is in agreement with other studies reporting that buccally malposed canines are more common, while palatal or lingual malposition is mostly associated with impaction [5, 7, 16]. Recent studies similarly demonstrated that labial or buccal displacement represents a frequent clinical presentation of ectopic canines, particularly in association with arch length deficiency and crowding [6]. Since the present study depended only on clinical examination and excluded canine impaction, the low frequency of lingual malposition is expected [8].

According to Angle's classification, most malposed canines were associated with Class I malocclusion. Similar findings were reported in recent epidemiological studies, which observed a greater prevalence of ectopic canines in subjects with skeletal and dental Class I relationships [6]. This finding supports the concept that canine malposition is mainly related to local eruption disturbances rather than sagittal skeletal relationships [9, 12]. Factors such as arch length discrepancy, prolonged retention or early loss of deciduous canines, and anomalies affecting adjacent teeth, particularly maxillary lateral incisors, may interfere with the normal eruption guidance pathway of permanent canines [8, 17, 18].

The distribution of malposed canines between the right and left sides did not show a significant difference. This is consistent with previous studies that reported that Canine malposition may be influenced by developmental and environmental factors affecting eruption pathways and dental arch morphology [6, 19]. The findings of this study showed that canine malposition is a multifactorial problem with local dental eruption factors rather than skeletal pattern alone. Early clinical examination during the mixed dentition stage is essential, and early interceptive orthodontic management, including space supervision, extraction of retained deciduous teeth, and monitoring of canine eruption pathways, may reduce the severity of canine malposition and simplify subsequent orthodontic treatment [1, 16, 20, 21].

Recent evidence has demonstrated that ectopic and malposed canines remain a significant orthodontic problem because of their association with eruption disturbances, adjacent root resorption, periodontal complications, and increased treatment complexity. Contemporary studies have emphasized the importance of early radiographic and CBCT-based assessment for accurate localization and evaluation of ectopic canines, particularly in cases associated with abnormal eruption pathways or skeletal discrepancies. Moreover, current orthodontic approaches support early interceptive management to reduce complications, facilitate canine eruption, and improve long-term treatment outcomes [22, 23]. Contemporary clinical guidelines also support careful monitoring of eruption pathways and appropriate space management during the mixed dentition stage to facilitate more favorable eruption outcomes and reduce the need for complex surgical-orthodontic interventions [24].

The findings of the present study support the concept that canine malposition represents a multifactorial eruption disturbance influenced by the interaction of

local dental, developmental, and possibly genetic factors rather than sagittal skeletal relationships alone. The observed variations in prevalence and distribution patterns among different populations reported in contemporary orthodontic literature further suggest that environmental influences, craniofacial characteristics, and eruption guidance mechanisms may contribute differently across populations. Therefore, population-based epidemiological investigations remain important for improving early clinical recognition and establishing more individualized orthodontic diagnostic and preventive strategies for eruption abnormalities involving permanent canines [25, 26].

LIMITATIONS

This study was limited by its cross-sectional design and dependence on clinical examination without radiographic confirmation, which may have resulted in underestimation of impacted or unerupted canines. In addition, the sample was restricted to dental students from a single institution, which may limit the generalizability of the findings to the wider Iraqi population.

CONCLUSIONS

Malposed canines were frequently observed in the investigated young adults. In this study, they occurred more frequently in females, exhibited a slight predominance in the mandibular arch, and were predominantly displaced buccally. The common correlation between canine malposition and Class I malocclusion suggests that the former is primarily influenced by local eruption conditions rather than sagittal skeletal discrepancies. These results emphasize the significance of early clinical assessment and prompt interceptive interventions to mitigate the complexity of subsequent orthodontic treatment.

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CONFLICT OF INTEREST

The Author declares no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Resilience and professional identity of medical students during wartime: The Ukrainian experience

Kateryna O. Hololobova, Lesya V. Lymar, Volodymyr S. Tytykalo, Olena I. Kefeli- Ianovska, Ganna S. Trepet, Tetyana V. Kolomiiets

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ABSTRACT

Aim: To conduct an empirical analysis of resilience self-assessment and professional intentions among medical students and PhD students in Ukraine under the conditions of full-scale war, and to determine the impact of crisis conditions on the formation of their professional identity.

Materials and Methods: The study is based on the results of an anonymous cross-sectional survey (2025) conducted among students at Bogomolets National Medical University (N=214). Statistical data processing included the calculation of proportions and the margin of error (MOE) for a 95% confidence interval. Empirical data were supplemented by a content analysis of 39 relevant publications from the PubMed and Scopus databases (2022-2026).

Results: The sample exhibited a distinct gender imbalance (75.2% female). Despite significant psychological pressure, a high level of resilience was recorded: 63.1% of respondents rated their adaptability above average (over 51%). Strong professional loyalty was observed, with 65.4% of participants planning to continue their activities in Ukraine. Conversely, 26.6% of students remain «undecided», indicating the vulnerability of human capital due to the erosion of traditional social support mechanisms. The war has accelerated professional maturation through engagement in volunteering and tactical medicine, signaling processes of post-traumatic growth.

Conclusions: The full-scale war has transformed the professional «ego» of future physicians toward practical readiness and social responsibility. Continuity of education in crisis conditions requires the integration of flexible distance models with enhanced psychosocial mentorship. The results underscore the necessity of institutional support for students to preserve the human capital of the Ukrainian healthcare system.

KEY WORDS: resilience, medical students, wartime, soft skills

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INTRODUCTION

On February 24, 2022, the Russian Federation escalated the military actions ongoing in Ukraine since 2014 into a full-scale military invasion. The Ukrainian healthcare system, which had only recently begun to recover from the global COVID-19 pandemic, was immediately confronted with severe, multi-dimensional challenges: the systematic destruction of medical facilities, the displacement of healthcare professionals, and an instantaneous surge in demand for trauma, emergency, and rehabilitative services [1].

The war has resulted in widespread collective trauma, affecting the psychological condition of the entire nation [2]. The younger generation, specifically «Generation Z» represented by medical students, was particularly ill-prepared for such cataclysmic shifts [3]. Many medical students and PhD students suffered direct exposure to violence, loss of personal property due to hostilities and looting, and the tragic loss of family members [4]. Nevertheless, the majority of students demonstrated remarkable fortitude, resumed their studies through adapted digital platforms, and even engaged extensively in volunteer activities, often on the front lines of humanitarian aid [5].

The impact of the full-scale war on medical educational institutions was profound and required an immediate pedagogical transformation. Universities were compelled to transition back to distance learning, which they had only recently moved away from post-COVID-19 -and rapidly adapt their curricula to address the clinical realities of wartime [6]. Some institutions suffered severe property damage, which led to subsequent power outages and internet disconnections that interfered with the educational process. International students were evacuated, with a low probability of resuming their studies given the volatile military situation [7].

Cumulatively, these factors led to increased anxiety regarding life, health, and property, alongside documented difficulties in concentration and a decrease in academic performance [8]. Traditional social mechanisms, such as peer support and clinical rotations, were disrupted, necessitating the emergence of new pathways for professional identity development [5].

Professional identity in medicine is regarded as a complex construct of characteristics: skills and functions; knowledge, values, and ethics; personal identity; and group identity [9]. The development of professional identity is a process through which individuals integrate medical knowledge and attitudes into their professional «ego» [10]. This process commences in medical school and continues throughout professional life, making a person part of the medical community. The full-scale war disrupted the routine mechanisms of this formation, requiring robust resilience for successful adaptation [11].

Resilience, the capacity to maintain or regain psychological well-being in the face of adversity, is a central concept in understanding how individuals cope with extreme stress [12]. Resilience theory emphasizes that it is a dynamic process involving the interaction of individual characteristics, social support systems, and environmental factors. In medical education, the scope of resilience extends beyond the management of academic stress to the maintenance of professional integrity under crisis conditions [12].

AIM

The aim of this study is to conduct an empirical analysis of resilience self-assessment and professional intentions among medical students and PhD students in Ukraine under the conditions of full-scale war, and to determine the relationship between crisis conditions and the process of professional identity formation.

MATERIALS AND METHODS

This study is based on the results of a cross-sectional questionnaire survey conducted in 2025 among students and PhD students of Bogomolets National Medical University (N=214). The survey was administered anonymously via Google Forms and disseminated through official university channels. Participation was strictly voluntary. Before completing the questionnaire, respondents were informed about the study's aim and the general purpose of data collection. Statistical processing included the calculation of proportions (%) and the margin of error (MOE) for a 95% confidence interval (Z=1.96). The theoretical framework of the study was supplemented by a content analysis of 39 relevant publications (2022–2026) from the PubMed and Scopus databases to provide a comparative analysis of the empirical data obtained.

ETHICS

The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki. All participants provided informed consent. The survey was entirely anonymous; no personal data identifying individuals was collected. Results were processed in a de-identified and aggregated format. Official permission for the survey was obtained from the Department of Science and the Bioethical Commission at Bogomolets National Medical University.

FRAMEWORK

The study was conducted within the framework of a research project of the Bogomolets National Medical University: 0124U001087 «Effective teaching techniques in postgraduate medical education»; 01.2024- 12.2026.

RESULTS

The full-scale war has fundamentally altered the perception of professional identity among medical students. While military aggression on Ukrainian territory began in 2014, and medical students have participated in defence efforts since then [13], the 2022 invasion shifted this participation from a voluntary, localised choice to a national professional imperative [10]. Despite severe disruptions, the majority of Ukrainian medical students have maintained their commitment to medical practice within Ukraine. Research by Kuchyn et al. found that 85% of medical PhD students planned their future careers as physicians or educators within Ukraine [4]. This reflects a profound sense of professional identity acting as a motivation to serve the country.

A distinct trend observed is the emphasis on clinical and tactical medical competencies. Medical institutions have adapted curricula towards primary care, emergency medicine, and wartime trauma management [5, 15]. These shifts necessitated a reconsideration of educational paradigms in both medical and military educational institutions [16].

To determine the resilience self-assessment of medical students and PhD students, a cross-sectional survey was conducted at Bogomolets National Medical University. A total of 214 responses were analysed. The sample was predominantly female: 161 respondents (75.2%), while

Table 1. Analysis of Resilience Self-Assessment and Future Intentions (N=214)

Data Analysis Categories	Number (n)	Proportion (%)	Margin of Error (±%)
Resilience Self-Assessment			
- Low (less than 25%)	21	9.8%	3.98%
- Moderately Low (25–50%)	58	27.1%	5.96%
- Moderately High (51–75%)	71	33.2%	6.31%
- High (more than 75%)	64	29.9%	6.13%
Intentions Regarding Work/Study in Ukraine			
- Definitely yes	67	31.3%	6.21%
- More yes than no	73	34.1%	6.35%
- Undecided	57	26.6%	5.92%
- More no than yes	13	6.1%	3.21%
- Definitely no	4	1.9%	1.83%

Source: compiled by the authors of this study

Table 2. Correlation Between Resilience Self-Assessment Levels and Professional Intentions

Resilience Self-Assessment Level	Plan to Remain in Ukraine (N, %)	Undecided / Planning to Leave (N, %)	Total (N)
High / Moderately High (>50%)	108 (80.0%)	27 (20.0%)	135
Low / Moderately Low (≤50%)	32 (40.5%)	47 (59.5%)	79
Total	140	74	214

Source: compiled by the authors of this study

53 (24.8%) were male; no participants selected the "another" option. Regarding age, the largest group consisted of respondents aged 20+ (128; 60.0%), followed by those under 20 (62; 28.9%). Smaller proportions were represented by categories 30+ (8; 3.7%), 40+ (12; 5.6%), and 50+ (4; 1.8%). This indicates a primarily younger student population, as expected in a university setting. However, age labels such as «20+», «30+», and «40+» should be interpreted cautiously, as they formally overlap; clearer age bands would improve precision in future surveys.

Curriculum changes have direct implications for professional identity formation. Students adopted professional roles from the earliest days of the invasion, performing clinical duties and providing first aid [6]. Persistent study, including self-directed learning, functioned as a means of purpose and a distraction from war-related chaos [17]. Our survey of 214 students provided a detailed demographic and psychological profile. The sample was predominantly female: 161 respondents (75.2%), reflecting the typical student body structure of medical universities. Regarding age, the largest group was respondents aged 20+ (128; 60.0%), followed by those under 20 (62; 28.9%) (Table 1).

RESILIENCE

A statistically significant majority of respondents (63.1% when combining the «51–75%» and «over 75%» groups) rate their adaptability as above average. The margin of error for these key groups is approximately ±6%, which is acceptable for socio-psychological studies of this scale.

PROFESSIONAL INTENTIONS

The cumulative proportion of individuals with a positive ambition toward staying in Ukraine (65.4%) significantly exceeds the proportion of those with negative intentions (8.0%). The "undecided" group (26.6% with a margin of error of ±5.92%) represents the primary reserve for psychological and institutional support aimed at retaining human capital potential.

Responses to the question about future intentions in Ukraine also reveal an important trend. The most frequent answers were "more yes than no" (73; 34.1%) and "definitely yes" (67; 31.3%). Together, this means that 140 respondents (65.4%) showed an overall positive orientation toward staying and studying or working in Ukraine. At the same time, 57 students (26.6%) remained undecided, 13 (6.1%) answered "more no than yes," and only 4 (1.9%) selected "definitely no." Thus, although a considerable proportion of students are uncertain, explicitly negative intentions were rare. This may suggest that, despite the ongoing war and instability, many students still see their academic and professional future as linked to Ukraine. The relatively

large undecided group, however, reflects the continuing impact of insecurity, social strain, and possible concerns about educational and career prospects.

Comparative analysis of the data (Table 2) revealed a direct correlation between the respondents' psychological resilience and their future professional intentions in Ukraine. Among students with a high level of resilience, the vast majority (80.0%) expressed readiness to continue their studies and work in their home country. Conversely, in the low-resilience group, the proportion of «undecided» individuals or those planning to emigrate increases significantly to 59.5%. This supports the hypothesis that resilience functions not only as a psychological defence mechanism but also as a critical factor in retaining human capital within the medical field during wartime.

Beyond cognitive factors, the war created practical barriers: academic disruptions, power and internet outages, financial hardships, and the infrastructural crisis of winter 2025/26 under severe frosts. Despite these challenges, Ukrainian medical students demonstrated remarkable resilience. Their medical training and professional responsibility fostered an analytical approach to the wartime situation. Peer networks and family connections remained vital coping resources, while faculty increasingly adopted mentor roles [5].

DISCUSSION

This study, supplemented by our empirical data, reveals a complex landscape of medical education during wartime in Ukraine, characterized by severe psychological challenges alongside remarkable resilience and adaptation [17]. Data demonstrate that the war has triggered a mental health crisis among students, with high rates of stress, anxiety, and depression [8, 18].

The high variability in responses within the 20+ age group (MOE ±6.56 %) reflects the diverse coping mechanisms of young specialists transitioning to professional responsibility under fire. A critical finding is the high level of self-assessed resilience. Despite the psychological toll, 63.1% of respondents rate their adaptability as above average. These results suggest that "Generation Z" medical students are undergoing a process of post-traumatic growth [17]. The wartime environment has transformed their professional «ego», shifting it toward practical clinical readiness and a proactive volunteer mindset.

The data regarding professional intentions provide a strategic outlook for the healthcare system. The cumulative proportion of students with positive intentions to remain in Ukraine (65.4%) far exceeds those with negative intentions (8.0%). This high level of professional loyalty, even amidst infrastructural catastrophes, proves that with adequate support, students can develop robust professional identities.

However, the «undecided» group (26.6%) highlights a significant vulnerability. This segment represents a primary reserve for human capital; their uncertainty is likely linked to the erosion of support systems and academic disruptions [8]. Medical education must transition from simple continuity to trauma-informed mentorship. As faculty members themselves navigate wartime stress [21], the development of digital and psychosocial interventions [22] becomes paramount to shield the professional identity of students from long-term erosion.

CONCLUSIONS

The full-scale war has accelerated the professional maturation of medical students, transforming their professional «ego» towards practical readiness, volunteerism, and high social responsibility.

Statistical analysis confirmed that 63.1% of respondents rate their resilience as high or moderately high, which indicates significant potential for post-traumatic growth. The majority of surveyed students (65.4%) plan to connect their future with Ukraine, demonstrating steadfast commitment despite security instability.

Approximately 26.6% of students remain «undecided» regarding their future, reflecting a vulnerability that requires targeted institutional support to preserve the nation's human capital. Continuity of medical education in wartime is possible only through a combination of flexible distance-learning models and intensified practical training in disaster medicine.

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ORIGINAL ARTICLE

CONTENTS

Artificial intelligence as a clinical tutor in telemedicine: Opportunities and challenges in medical education

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ABSTRACT

Aim: To analyze key aspects of the application of AI as a clinical mentor in telemedicine-based medical education, and to assess the related opportunities, challenges, and attitudes of pediatric students.

Materials and Methods: A cross-sectional study was conducted to assess the level of digital competence of future pediatricians regarding telemedicine and AI. A total of 251 students from the Faculty of Pediatrics at Bogomolets National Medical University (BNMU) participated in the survey. Participants were aged 17 to 26 years, of whom 17.9% were male and 82.1% were female. The questionnaire included items on demographic characteristics, knowledge and use of telemedicine and AI tools, self-assessment of digital competence, and attitudes toward the integration of AI in healthcare. Data were analyzed using descriptive statistics and presented as relative frequencies (%).

Results: The study assessed digital competence and the use of AI among 251 future pediatricians regarding telemedicine-based medical education. Survey results indicated active engagement with AI tools in educational and professional tasks (63.7% positive responses), moderate confidence in integrated digital devices (55.0%), and cautious self-assessment of clinical decision support systems (53.4%). These findings informed the development and revision of courses at BNMU, enhancing students' practical skills and digital competence.

Conclusions: Future pediatricians actively engage with digital tools and AI, although confidence is higher in AI tasks than in integrated devices or clinical decision systems. The findings guided the development of updated courses to strengthen digital competence, practical skills, and critical evaluation of AI. Successful telemedicine implementation requires addressing data security, regulation, human-centred care, and digital inclusion to ensure safe, effective, and equitable healthcare.

KEY WORDS: AI, telemedicine, medical education, Clinical Tutor

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INTRODUCTION

The Strategy for the Development of Telemedicine in Ukraine (2023–2025) aims to integrate digital solutions into the healthcare system to provide remote care, particularly in wartime conditions [1]. It focuses on creating a unified telemedical space, expanding teleradiology and teleconsultations, and overcoming barriers to healthcare access through digital technologies. State policy emphasizes regulatory updates, improved technical infrastructure, and enhanced digital skills among healthcare professionals.

The strategy also outlines key aspects of digitalisation, including data protection, evaluation of effectiveness, and international cooperation, forming the basis for a modern, accessible healthcare model. By March 2026, the outcomes of its implementation are to be evaluated and reported.

In parallel, the "Framework of Digital Competence of a Healthcare Worker in Ukraine" [2] defines strategic directions for healthcare digitalisation. Based on European DigComp standards and adapted to national conditions, it structures digital skills across key areas such as data management, cybersecurity, and innovation, supporting education reform and the effective implementation of telemedicine in Ukraine.

AIM

To analyze key aspects of the application of AI as a clinical mentor in telemedicine-based medical education and to assess the related opportunities, challenges, and attitudes of pediatric students.

MATERIALS AND METHODS

The empirical basis of the study consisted of survey responses collected from future pediatricians as part of an assessment of digital competence in the context of telemedicine and AI. A cross-sectional study design was applied. A total of 251 students from the Faculty of Pediatrics at Bogomolets National Medical University voluntarily participated in the study. The participants were aged 17 to 26 years, including 17.9% males and 82.1% females.

Data were collected using a structured questionnaire specifically developed for this study. The questionnaire included several key sections: socio-demographic characteristics (age, gender); knowledge and use of telemedicine and AI tools; self-assessment of digital competence; and attitudes toward the integration of AI into healthcare practice.

The study employed general scientific methods, including survey analysis and descriptive statistics. The collected data were processed and presented as relative frequencies (%), allowing for the evaluation of trends in digital competence and the use of AI technologies among future pediatricians.

In the context of ongoing digital transformation in healthcare, particular attention was given to the role of AI and telemedicine in shaping professional competencies. The aim of this study was to assess the level of digital competence among future pediatricians and to explore their experience, attitudes, and readiness to integrate AI-driven technologies into clinical practice.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki and generally accepted bioethical standards for conducting sociological research in the medical field. All participants (N=251) were informed about the purpose, objectives, and voluntary nature of the study and provided informed consent prior to participation. The survey was anonymous, ensuring the confidentiality of personal data and protecting the academic and professional integrity of respondents.

Data processing was carried out in a depersonalized manner, and the results are presented in aggregated form, which eliminates the possibility of identifying individual participants.

The research protocol and instrument (questionnaire) underwent peer review and received approval from the local Bioethics Committees of the Bogomolets National Medical University.

FRAMEWORK

The study was conducted as a part of the research project within the framework of the international ERASMUS+ UkraineDigiTrans project (GA number 101179494).

RESULTS

The survey revealed varying levels of digital competence among future pediatricians regarding telemedicine and AI use. For general digital tools in medical practice, 50.6% of respondents rated themselves positively, 39.0% negatively, and 10.4% were undecided. Competence in clinical decision support systems was slightly higher, with 53.4% positive, 35.8% negative, and 10.8% undecided responses. AI tool usage in educational and professional contexts was reported by 63.7% of students, while 33.1% reported non-use and 3.2% were undecided. Regarding integrated digital devices and applications, 55.0% considered themselves competent, 35.0% non-competent, and 10.0% were uncertain.

These findings informed the revision of the course "Features of Artificial Intelligence Application in Pediatric Practice" and the development of "Telemedicine in the Healthcare System" at Bogomolets National Medical University under the ERASMUS+ UkraineDigiTrans project. Overall, students demonstrate active engagement with digital tools and AI; however, gaps in confidence highlight the need for structured training and practical experience to strengthen digital competence in clinical practice.

Modern educational programs require continuous improvement and regular updating to meet current demands and employers' expectations. A key element in this process is the development of digital competence among higher education students, particularly future physicians. The Telemedicine Development Strategy in Ukraine (2023–2025) aims to integrate digital solutions into the healthcare system to ensure remote medical care, especially in the context of war [1–3]. The strategy envisages the creation of a unified telemedicine space and the implementation of teleradiology and teleconsultations, which by 2024 will cover more than 30 medical guarantee packages. The primary objective of the initiative is to overcome barriers to healthcare access caused by military aggression through the integration of remote technologies into a unified digital healthcare system.

State policy focuses on updating regulatory frameworks, improving technical equipment in hospitals, and enhancing the qualifications of medical personnel for working with innovative technologies. Furthermore, by 31 March 2026, those responsible for the telemedicine development direction are required to evaluate the outcomes of the Telemedicine Development Strategy in Ukraine and submit a report to the Cabinet of Ministers of Ukraine. At the same time, emphasis is placed on the development of telemedicine within the "Digital Competence Framework for Healthcare Workers in Ukraine" [2], which defines strategic approaches to healthcare digitalisation. This framework was developed based on

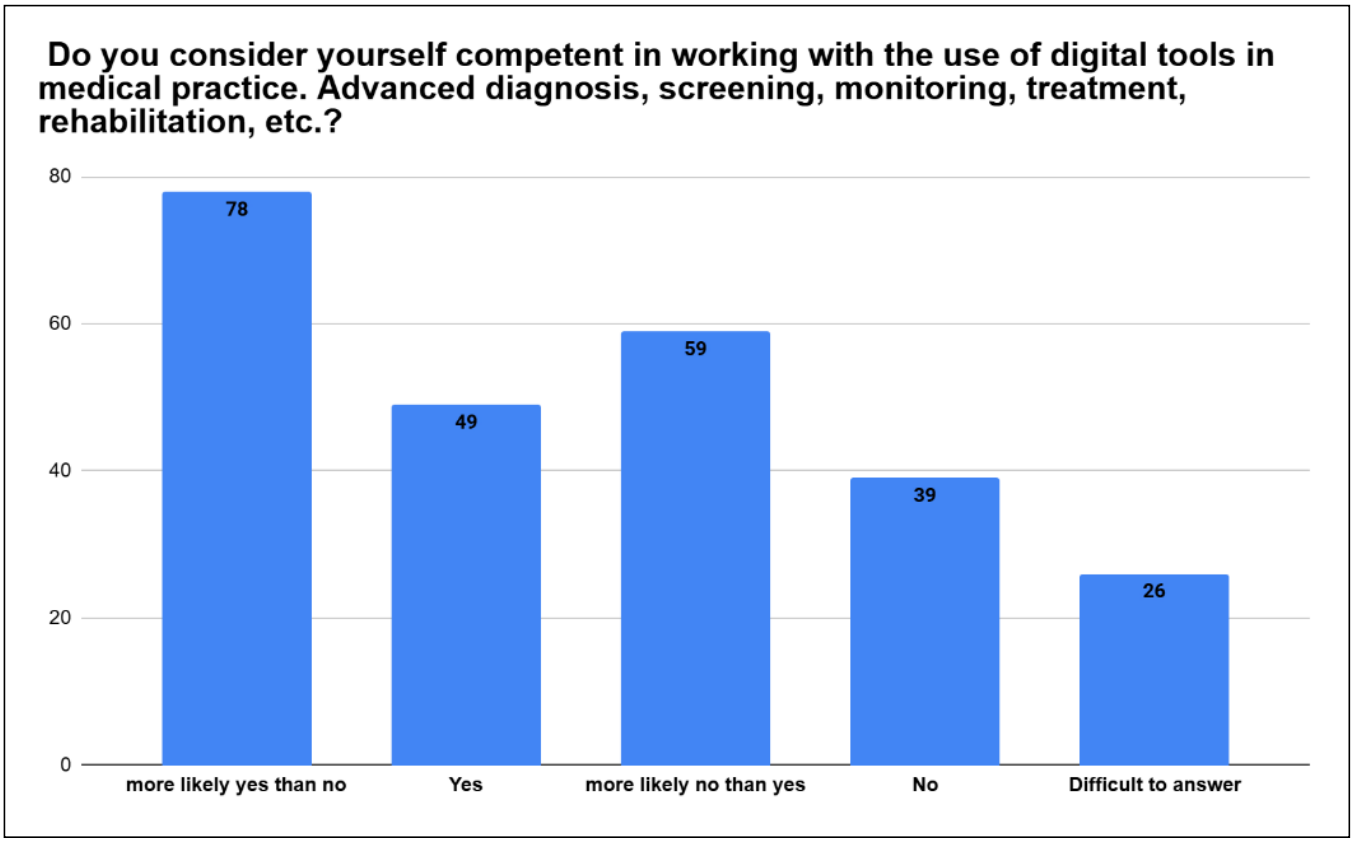


Fig. 1. Distribution of responses regarding the use of digital tools in medical practice
Picture taken by the authors

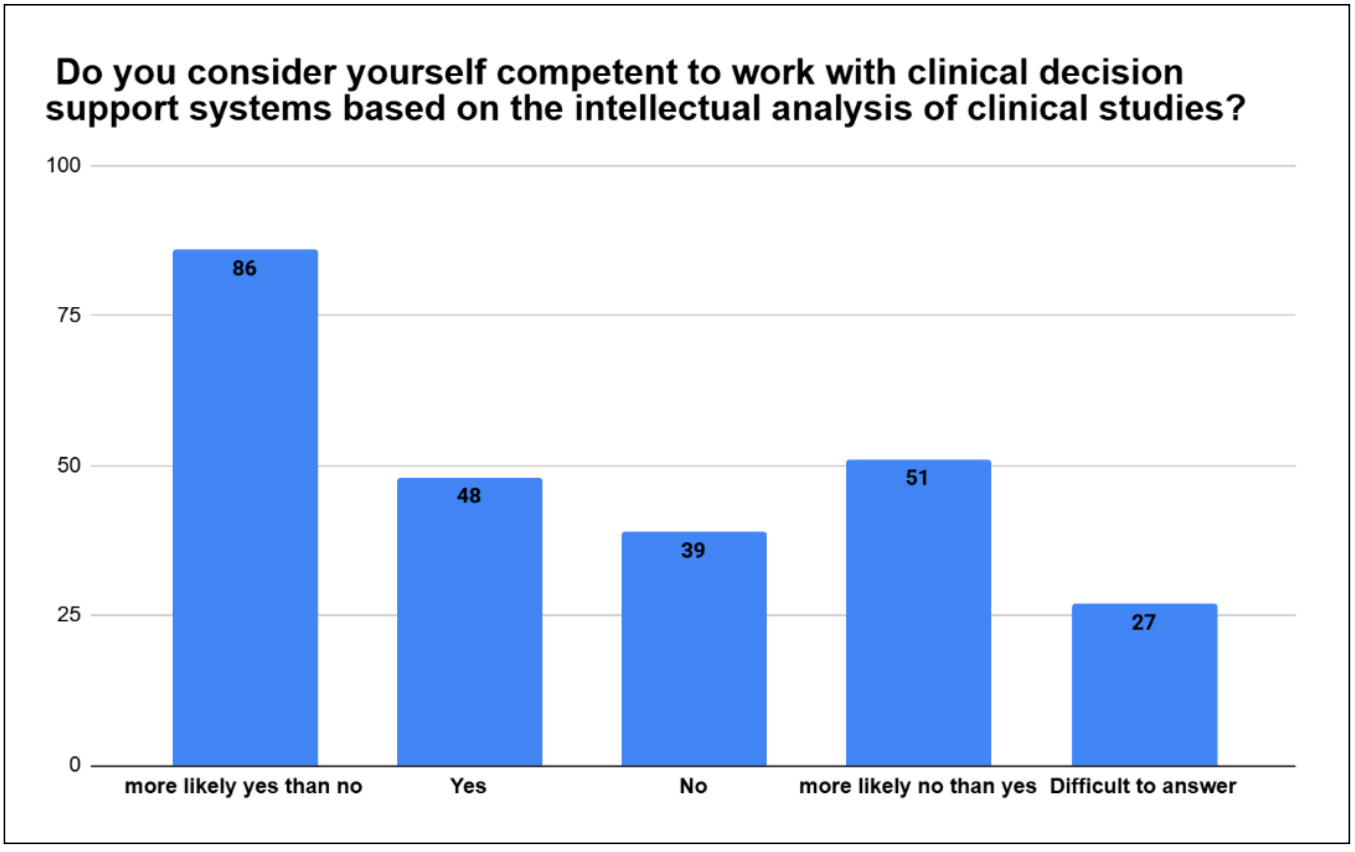


Fig. 2. Distribution of responses regarding the use of clinical decision support systems
Picture taken by the authors

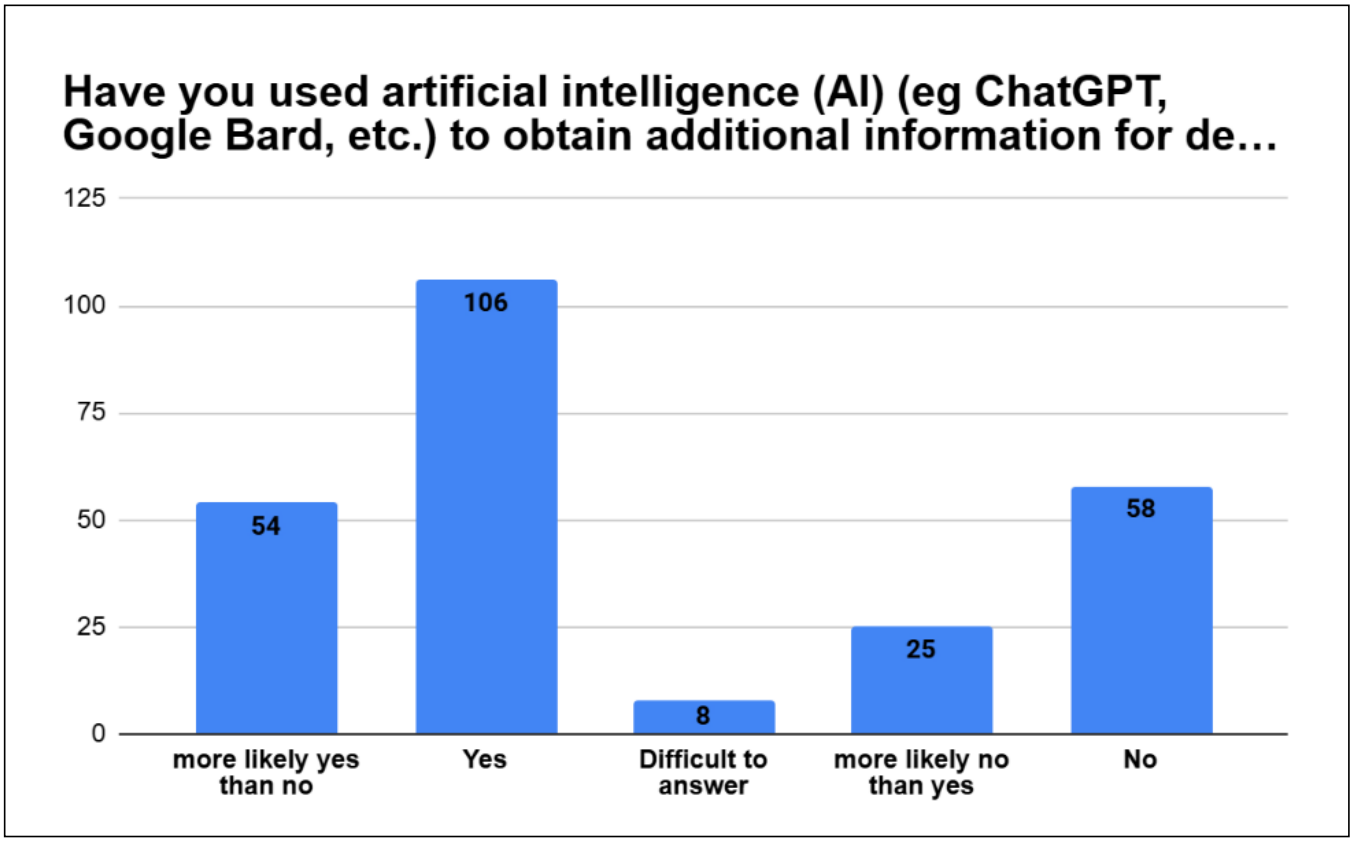


Fig. 3. Distribution of responses regarding the use of AI
Picture taken by the authors

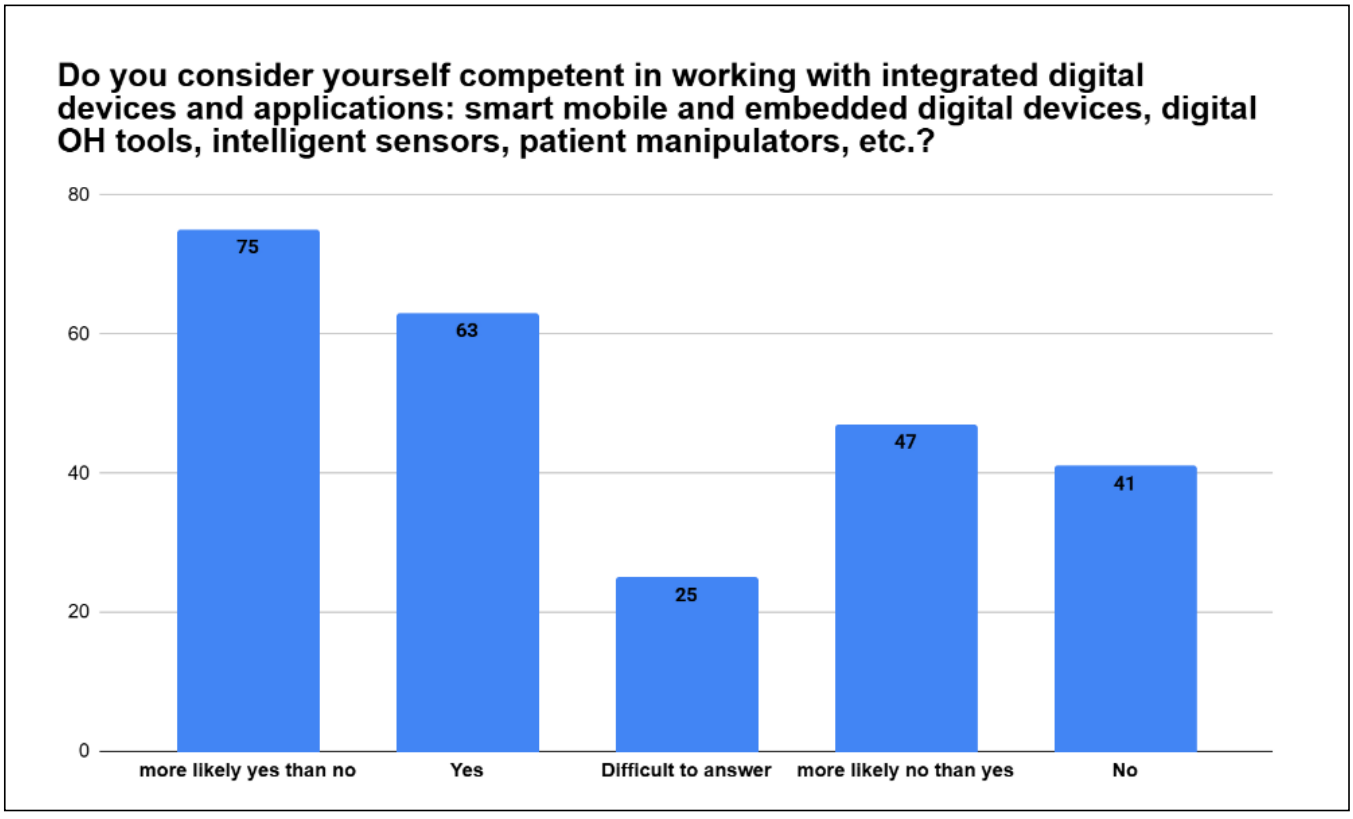


Fig. 4. Distribution of responses regarding the use of integrated digital devices and applications
Picture taken by the authors

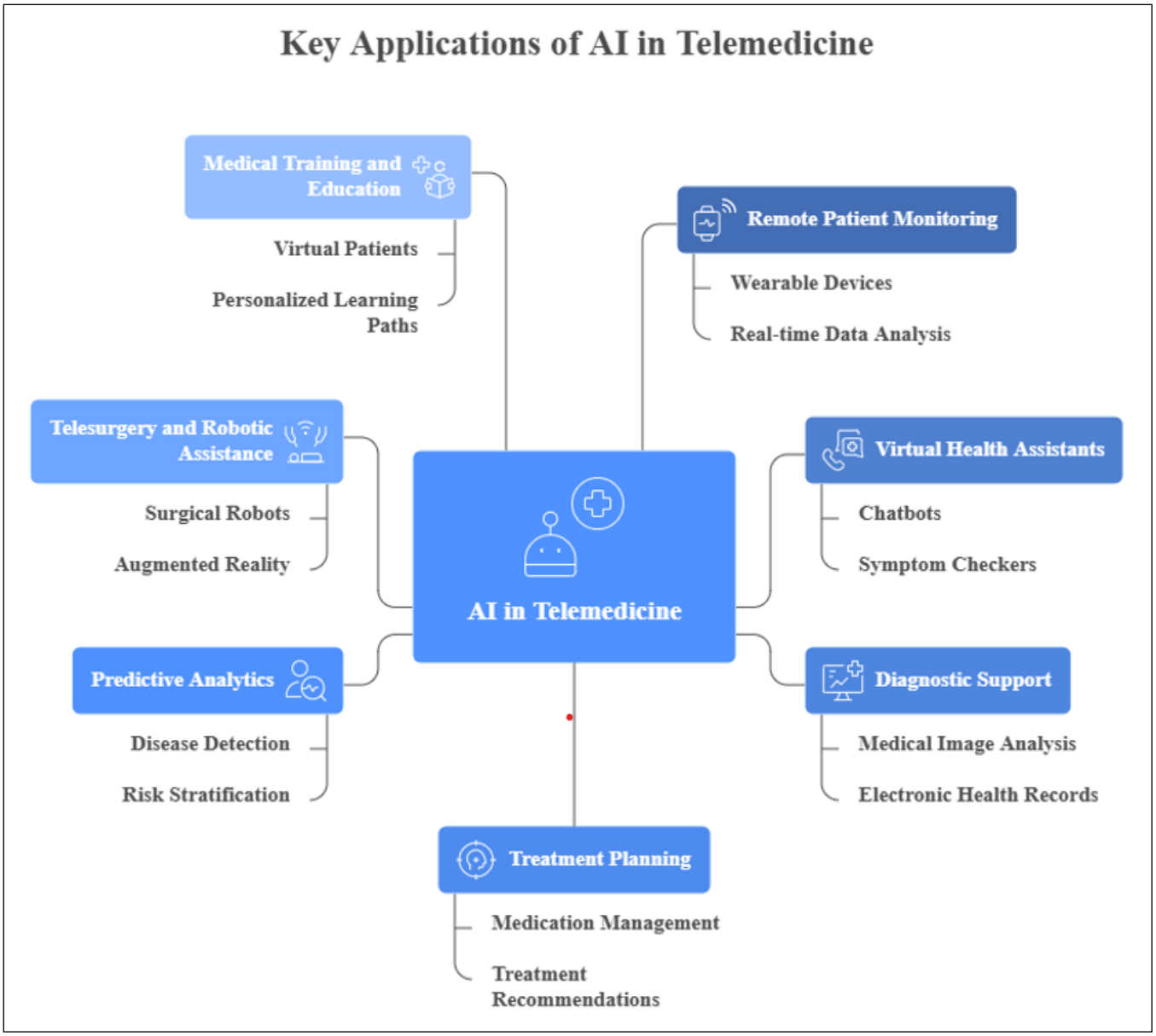


Fig. 5. Mental map of AI integration into telemedicine
Picture taken by the authors

European DigComp standards and adapted to national specifics, taking into account the challenges of martial law and the development of the electronic healthcare system (eHealth). Telemedicine is categorised under Sphere 3: Digital communication, interaction, and collaboration in the digital environment [4–6].

It is considered a critical component of a healthcare professional's digital competence, focusing specifically on the ability to participate in telemedicine consultations. Key aspects of telemedicine education include recommended resources, expected outcomes, and integration with other digital competencies. Recommended resources involve specialized courses on platforms like Prometheus and communication tools such as Zoom, Google Meet, and Microsoft Teams for simulations. The main educational goal is to gain practical experience in remote medical interaction. Telemedicine skills are closely connected with professional digital communication, secure clinical data exchange, electronic correspondence with patients and colleagues, and management of e-documents, including e-prescriptions and referrals within the eHealth system. In addition to these communication-related aspects, the sources emphasize that digital transformation in healthcare also involves understanding digital health interoperability and the strategic directions set by organizations such as the WHO to ensure that these remote systems function effectively within the broader healthcare landscape. The role of AI as a "clinical mentor" for medical students

is particularly relevant in telemedicine, where the combination of remote access, virtual patients, and AI analysis enables clinical training without physical presence [5–8]. Instructors can create scenarios for student learning, demonstrate telemedicine devices equipped with AI, and more. Within the scope of our study, students responded to questions regarding their proficiency in using telemedicine tools and AI.

Regarding competence in using digital tools in medical practice (e.g., diagnostics, screening, monitoring, treatment, rehabilitation), respondents reported moderate self-assessed competence. Positive responses accounted for 50.6%, negative responses for 39.0%, and 10.4% were undecided (Fig. 1).

Regarding competence in using clinical decision support systems based on intelligent analysis of clinical studies, respondents reported a generally cautious-positive self-assessment. Positive responses accounted for 53.4%, negative responses for 35.8%, and 10.8% were undecided, reflecting some uncertainty among students (Fig. 2).

Regarding the use of AI tools (e.g., ChatGPT, Gemini) for decision-making in professional or educational activities, respondents showed a high level of adoption and active integration. Positive responses accounted for 63.7%, negative responses for 33.1%, and 3.2% were undecided (Fig. 3).

Regarding the question on competence in using integrated digital devices and applications (e.g., smart mobile and embedded devices, digital health tools, intelligent sensors, patient simulators), respondents reported a moderately high level of self-assessed digital competence. Positive responses accounted for 55.0%, negative responses for 35.0%, and 10.0% were undecided, reflecting uncertainty or limited experience with these technologies (Fig. 4).

The survey results formed the basis for revising the syllabus of the course "Features of Artificial Intelligence Application in Pediatric Practice" and for creating a new educational course, "Telemedicine in the Healthcare System", at Bogomolets National Medical University within the framework of the ERASMUS+ UkraineDigiTrans project (GA number 101179494).

The course "Features of Artificial Intelligence Application in Pediatric Practice" develops students' knowledge and practical skills in AI technologies, including their application in diagnostics, treatment, telemedicine, and medical visualisation. It also promotes critical evaluation of AI, integration of digital tools into clinical reasoning, and adherence to ethical and data security standards.

The course "Telemedicine in the Healthcare System" provides future pediatricians with essential knowledge and practical skills for using telemedicine tools in clinical practice, supporting the digital transformation of healthcare in Ukraine.

The integration of AI into telemedicine (Fig. 5) offers significant opportunities for improving the accessibility and quality of healthcare services [9]. However, this process is accompanied by important challenges and considerations. A key aspect is ensuring data privacy and security. Telemedicine platforms handle large volumes of sensitive medical information and must ensure reliable protection against data breaches, unauthorised access, and cyberattacks. Adherence to international and national data protection standards, as well as the implementation of modern encryption and secure data transmission technologies, is essential for maintaining patient trust in digital healthcare services.

Another key challenge is regulatory compliance. Healthcare is highly regulated, and AI-based telemedicine must meet licensing, accreditation, and quality standards. Differences in regulations across regions may hinder scalability and slow innovation. Maintaining the human aspect of medicine remains critical. Despite AI efficiency, empathy and personal interaction are essential; therefore, telemedicine should complement rather than replace physicians, ensuring a balance between technology and human-centred care.

DISCUSSION

The high level of AI usage among respondents indicates its active integration into the educational and early professional activities of future physicians. This confirms the potential of AI as an effective tool for enhancing learning productivity, optimising routine tasks, and supporting clinical reasoning. The obtained results are consistent with global trends in the digitalisation of medical education, where AI is considered an important component in the formation of modern professional competencies [10, 11].

At the same time, the moderate level of confidence in using integrated digital devices and clinical decision support systems indicates a gap between the frequency of AI use and the depth of digital competence. This discrepancy may reflect superficial interaction with technologies without sufficient understanding of their clinical potential. This highlights the need to implement more structured, practice-oriented training aimed at developing skills in applying complex digital solutions in real clinical settings [12, 13].

A proportion of respondents demonstrated uncertainty or limited experience with digital tools, indicating insufficient practical training. These findings emphasise the importance of systematically integrating the development of digital competence into medical education curricula, particularly through simulation-based learning, the use of virtual patients, and clinical case analysis [5, 8].

The role of AI as a "clinical tutor" in telemedicine opens new opportunities for remote clinical training. The combination

of virtual patients, data analysis, and decision-support algorithms enables the simulation of clinical scenarios without physical presence, which is especially relevant in conditions of limited access to clinical practice. At the same time, the effective implementation of such approaches requires addressing several critical issues, including ensuring data privacy and security, compliance with regulatory requirements, and maintaining the principles of patient-centred care [14, 15].

Despite technological progress, the study results confirm that the human factor remains key in medical practice. Empathy, clinical reasoning, and interpersonal interaction cannot be fully replaced by algorithms. Thus, AI should be considered a complementary tool that enhances physicians' capabilities rather than replacing them. Maintaining a balance between technological innovation and humanistic values is critically important for the sustainable development of modern healthcare systems [16, 17].

CONCLUSIONS

These findings informed the revision of the course "Features of Artificial Intelligence Application in Pediatric Practice" and the development of a new course, "Telemedicine in the Healthcare System", at Bogomolets National Medical University within the ERASMUS+ UkraineDigiTrans project. These educational initiatives aim to develop students' theoretical knowledge and practical skills, enhance digital competence, foster critical evaluation of AI solutions, integrate digital tools into clinical reasoning, and ensure adherence to ethical and legal standards.

The integration of AI into telemedicine offers significant opportunities for improving healthcare accessibility and quality but is accompanied by several challenges. Key concerns include ensuring data privacy and security, compliance with regulatory requirements, maintaining the human aspect of patient interaction, and addressing digital inequality.

The successful realisation of the potential of digital medicine and AI in telemedicine requires a comprehensive approach that combines technological advancement with systematic support in education, regulation, security, and inclusivity. Only such a strategy can ensure the effective, safe, and equitable use of telemedicine in modern healthcare systems.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

CONTENTS

Soft tissues around the dental implants folowing mandibular segmental defect replacement: quantity and quality comparison assessment

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ABSTRACT

Aim: To compare the quantity and quality of surrounding soft tissues in patients after segmental mandibular defect reconstruction (SMDR) with bone grafts, before and after placement of implant-supported dental prostheses (ISDPs).

Materials and Methods: A total of 74 patients were included and divided into main (MG) and control (CG) groups. The MG consisted of patients after SMDR. The CG comprised 49 patients with a Kennedy Class II dental arch defect following tooth extraction. The width and area of attached gingiva (AG) were assessed before and after ISDP placement using intraoral scanning.

Results: After ISDP placement, the mean buccal width of AG at the medial implant was 0.94±0.90 mm in the MG and 2.18±0.95 mm in the CG ($p<0.01$). In the distal buccal region, the median values were 0 (IQR: 0–1) mm and 1.7 (IQR: 1–6) mm, respectively ($p<0.001$). The mean lingual width at the medial implant was 1.11±0.99 mm in the MG and 2.24±0.97 mm in the CG, whereas at the distal implant the median values were 0 (IQR: 0–0.6) mm and 2.1 (IQR: 1.5–2.75) mm, respectively ($p<0.001$). The median area of AG was 63.3 (IQR: 38.9–100.45) mm^2 in the MG and 233.9 (IQR: 186.75–295.75) mm^2 in the CG ($p<0.001$).

Conclusions: Patients after SMDR and placement of ISDP are characterized by lower quality and reduced volume of AG compared to conventionally rehabilitated patients with ISDP. To improve the long-term prognosis of treatment, soft tissue augmentation may be recommended.

KEY WORDS: mandibular reconstruction, dental implants, scanning, gingiva

Wiad Lek. 2026;79(6):1300-1305. doi: 10.36740/WLek/222564 DOI

INTRODUCTION

Reconstruction of mandibular defects remains one of the most challenging problems in maxillofacial surgery, particularly in cases of segmental mandibular defects (SMDR) caused by tumours, osteonecrosis, or high-energy trauma [1–3]. Such defects result in the loss of bone, teeth, and adjacent soft tissues, leading to impaired mastication, speech, swallowing, and social adaptation, with a marked negative impact on quality of life [4, 5]. Comprehensive rehabilitation is therefore required.

The main goal of treatment is the restoration of function and anatomical form, which depends on accurate reconstructive planning and the possibility of implant-supported dental prosthesis (ISDP) placement. SMDR are commonly reconstructed with vascularised bone grafts, particularly the fibular free flap (FFF), which also allows replacement of associated soft tissue loss [6, 7]. Dental implants placed in transplanted fibular bone have demonstrated integration rates of up to 98% [8, 9]. However, the condition of the surrounding soft tissues remains a major challenge, as peri-implant soft tissue quality and quantity are critical for long-term treatment success [10, 11].

AIM

The aim of this study was to compare the quantity and quality of the surrounding soft tissues in patients after reconstruction of SMDR with FFF, before and after placement of ISDP.

MATERIALS AND METHODS

A prospective, controlled, non-randomised study included 74 patients who underwent prosthetic rehabilitation at the Head and Neck Pathology Centre of Kyiv Regional Clinical Hospital, which is the clinical base of the Department of Maxillofacial Surgery, Bogomolets National Medical University. The study was conducted from October 2023 to December 2025. The inclusion criteria for the study were as follows:

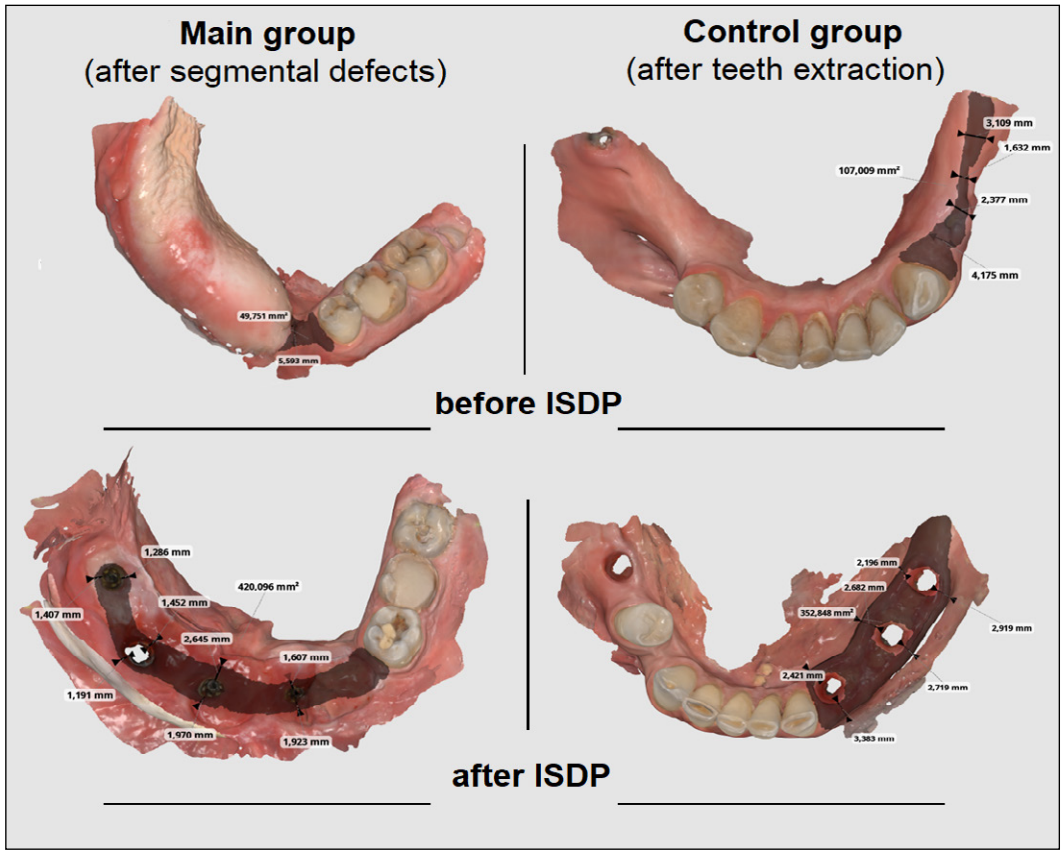


Fig. 1. Differences in the representation of intraoral scans between the two groups
Picture taken by the authors

1. Patients with SMDR (Brown Class I and II) who underwent surgical reconstruction using FFF [12];
2. CT-confirmed consolidation of the FFF bony component and the mandible (main group) or delayed dental implant placement after tooth extraction (control group);
3. Presence of a Kennedy Class II dental arch defect [13] corresponding to the reconstructed mandibular segment;
4. Placement of implant-supported dental prostheses in the area of mandibular reconstruction.

Twenty-five patients met the eligibility criteria and formed the main group after reconstruction of SMDR. The control group comprised 49 patients with a Kennedy Class II dental arch defect after tooth extraction for conventional reasons and no history of mandibular bone defects or discontinuity.

In both groups, the assessment of quantitative and qualitative characteristics was performed before and after placement of implant-supported dental prostheses (ISDP) (Fig. 1).

In both the main and control groups, the width and area of the attached gingiva were assessed before and after placement of ISDP. To this end, intraoral scanning of the prosthetic site was performed using a Medit i600 scanner (Medit Link) according to the manufacturer's recommended scanning protocol. The obtained scans were imported into Medit Link v3.4.7 (Korea) (Medit Design module), where the specified measurements were performed.

The intraoral scanning protocol was as follows:

1. The maxillary and mandibular arches were scanned, including the adjacent soft tissues.
2. The scan files were opened in Medit Design.
3. Measurement Mode was selected.
4. The width of the attached gingiva was determined based on the color differentiation provided by the software (lighter shade) and measured using the "Measure Distance by Two Points" tool.
5. The area of the attached gingiva was measured using the "Calculate Area by Selection" tool.

The boundary between the attached gingiva and the movable mucosa was identified using software-generated colour differentiation: a lighter shade for keratinised (attached) gingiva and a brighter shade for movable mucosa. In patients before placement of ISDP, the width of the attached gingiva was measured from the vestibular mucogingival junction (movable mucosa) to the lingual one. The area of the attached gingiva was measured along the crest of the alveolar ridge, including its buccal and lingual surfaces, from the gingival margin to the mucogingival junction. In patients after placement of ISDP, the width of the attached gingiva was measured

Table 1. Width and area of attached gingiva in distal extension defects before implant placement

Parameters	Main group (n = 16)	Control group (n = 24)	p*
Width of attached gingiva in the area of the medial aspect, mm	Me = 1.7 (IQR: 0.35-3.35)	Me = 3.9 (IQR: 2.65 - 6.1)	<0.01
Width of attached gingiva in the distal aspect mm	Me = 0.7 (IQR: 0-1.7)	Me = 3.9 (IQR: 2.05-5.4)	<0.001
Area of attached gingiva, mm^2	Me = 49.5 (IQR: 41.4-92.3)	Me = 185.3 (IQR: 94.6-207.85)	<0.001

Note: * — U-Mann-Whitney test
Source: compiled by the authors of this study

Table 2. Width and area of attached gingiva in distal extension defects after implant placement

Parameters	Main group (n = 9)	Control group (n - 25)	p
Buccal width at the medial implant, mm	M = 0.94±90	M = 2.18 ± 0.95	<0.01**
Buccal width at the distal implant, mm	Me = 0 (IQR: 0-1)	Me = 1.7 (IQR: 1-6)	<0.001*
Lingual width at the medial implant, mm	M = 1.11±0.99	M = 2.24±0.97	<0.001**
Lingual width at the distal implant, mm	Me = 0 (IQR: 0 - 0.6)	Me = 2 (IQR: 1.5 - 2.75)	<0.001*
Area of attached gingiva, mm^2	Me = 63.3 (IQR: 38.9 - 100.45)	Me = 233.9 (IQR: 186.75-295.75)	<0.001*

Notes: * — U-Mann-Whitney test; ** — T-test
Source: compiled by the authors of this study

Table 3. Comparison of the width and area of attached gingiva based on the location of the skin paddle in FFF after implant placement

Parameters	Extraoral skin paddle inset (n = 6)	Intraoral skin paddle inset (n = 4)	p*
Buccal width at the medial implant, mm	M = 0.82 ± 1.0	M = 1.01 ± 0.87	0.91
Buccal width at the distal implant, mm,	M = 0.87 ± 0.82	M = 0 ± 0	0.02
Lingual width at the medial implant, mm	M= 0.98 ± 1.10	M= 1.12 ± 0.83	0.83
Lingual width at the distal implant, mm	Me = 0 (IQR: 0 - 0.5)	Me = 0.35 (IQR: 0 - 0.95)	0.40
Area of attached gingiva, mm^2	M = 19.84 ± 57.27	M= 176.14 ± 161.47	0.17

Note: * — U-Mann-Whitney test
Source: compiled by the authors of this study

from the gingival margin to the mucogingival junction. All clinical stages of prosthetic treatment and all measurements were performed by a single prosthodontist.

For patients with distal extension edentulous defects prior to dental implant placement, the following parameters were assessed:

1. The width of the attached gingiva was measured at two points: in the distal part of the defect, 5 mm anterior to the retromolar triangle, and in the medial part, 5 mm distal to the tooth adjacent to (limiting) the defect.
2. The area of the attached gingiva was measured from the midpoint of the tooth adjacent to (limiting) the defect to the retromolar triangle.

For patients with a distal extension dental arch defect after implant placement, the following parameters were assessed:

1. The width of the attached gingiva on the buccal (vestibular) and lingual aspects along the midline of the mesial and distal implants.
2. The area of the attached gingiva from the midpoint of the tooth adjacent to (limiting) the defect to the retromolar triangle.

Statistical analysis was performed by a blinded investigator using EZR software (version 1.61) based on R version 4.2.2. Normality was assessed with the Shapiro–Wilk test. Normally distributed data were presented as mean ± SD and compared using the independent-samples t-test, whereas non-normally distributed data were presented as median and interquartile range (IQR) and compared using the Mann–Whitney U test. Statistical significance was set at $p<0.05$.

ETHICS

The study was approved by the Bioethics and Research Ethics Committee of Bogomolets National Medical University, which approves open publication of the study results. All procedures were conducted in accordance

with the Declaration of Helsinki [14]. Written informed consent was obtained from all participants.

FRAMEWORK

The study is a part of the research project of the Department of Maxillofacial Surgery at Bogomolets National Medical University titled "Clinical and experimental substantiation of new methods for rehabilitation of patients with maxillofacial defects and deformities using digital technologies and patient-specific solutions" (No. 0125U000004).

RESULTS

In 12 patients, the skin paddle was positioned intraorally, and in 13 patients extraorally. Before implant placement, the median width of attached gingiva in the main group was 1.7 (IQR: 0.35–3.35) mm medially and 0.7 (IQR: 0–1.7) mm distally, compared with 3.9 (IQR: 2.65–6.1) mm and 3.9 (IQR: 2.05–5.4) mm, respectively, in the control group ($p<0.01$). The median area of attached gingiva was 49.5 (IQR: 41.4–92.3) mm^2 in the main group and 185.3 (IQR: 94.6–207.85) mm^2 in the control group ($p<0.001$) (Table 1).

After implant placement, all attached gingiva measurements were lower in the main group than in the control group. Buccal width at the medial implant was 0.94±0.90 mm versus 2.18±0.95 mm ($p<0.01$). Buccal width at the distal implant was 0 (IQR: 0–1) mm versus 1.7 (IQR: 1–6) mm ($p<0.001$), lingual medial width was 1.11±0.99 mm versus 2.24±0.97 mm ($p<0.001$), and lingual distal width was 0 (IQR: 0–0.6) mm versus 2.1 (IQR: 1.5–2.75) mm ($p < 0.001$), respectively. The median area of attached gingiva was 63.3 (IQR: 38.9–100.45) mm^2 in the main group and 233.9 (IQR: 186.75–295.75) mm^2 in the control group ($p<0.001$) (Table 2).

After implant placement in the FFF group with an intraoral skin paddle, buccal medial width was 1.01±0.87 mm versus 0.82±1.00 mm in the group with an extraoral skin paddle ($p=0.91$), buccal distal width was 0±0 mm versus 0.87±0.82 mm ($p=0.02$), lingual medial width was 0.98±1.10 mm versus 0.98±1.10 mm ($p=0.83$), and lingual distal width was 0 (IQR: 0–0.5) mm versus 0.35 (IQR: 0–0.95) mm, respectively ($p=0.40$). The median area of attached gingiva was 19.84±57.27 mm^2 in the FFF group with an extraoral skin paddle and 176.14±161.47 mm^2 in the control group ($p=0.17$) (Table 3).

DISSCUSION

The importance of attached gingiva has long been recognised. Lang and Löe showed that a keratinized gingival width of <2 mm may predispose to inflammation [15], and recent studies confirm its role in peri-implant health [16, 17]. Patients after reconstruction of SMDR differ from those with intact jaws in both the quantity and quality of peri-implant soft tissues. In reconstructed areas, native mucosa may be replaced by skin tissue; therefore, although full restoration of natural gingiva is not possible, the formation of a stable band of keratinised soft tissue remains essential for long-term treatment success.

The absence of attached soft tissues complicates oral hygiene and may increase the risk of peri-implantitis. The incidence of peri-implant inflammation in reconstructed jaws ranges from 20.3% to 32.3% [18, 19]. Consequently, additional surgical procedures are often required to improve peri-implant soft tissue conditions. Hakim et al. reported that 62.2% of patients required additional surgical interventions to optimise soft tissue quality around implants [20]. Similarly, Shan et al. demonstrated that keratinised mucosa augmentation using an apically displaced flap with a free gingival graft can significantly increase keratinised tissue width after reconstructive surgery [21].

Our findings confirm that patients after mandibular reconstruction have significantly reduced levels of attached soft tissue compared with patients with secondary edentulism. Adequate keratinised tissue plays a crucial role in facilitating oral hygiene and reducing mechanical irritation from prosthetic constructions. In the present study, implant placement was associated with an increase in the amount of attached tissue; however, the overall volume of immobile tissue remained limited in reconstructed areas.

An important observation of this study is the evaluation of the area of attached tissue in addition to linear measurements. In reconstructed mandibles, the mucosa related to prosthetic construction often has a complex three-dimensional configuration, and linear width alone may not adequately reflect the soft-tissue support available for prosthetic rehabilitation. Therefore, assessing the area of attached tissue may provide a more comprehensive evaluation of peri-implant soft-tissue conditions.

Our results also showed no significant differences in the width and area of attached gingiva depending on whether the skin paddle of the fibular free flap was positioned intraorally or extraorally. At the same time, significant differences were observed between reconstructed patients and controls with conventional tooth loss.

Therefore, once the autotransplant has successfully integrated and postoperative healing has been completed without complications, optimal conditions must be established for prosthetic rehabilitation. Restoration of masticatory and speech function remains the ultimate goal of treatment, and adequate dental rehabilitation is necessary to prevent occlusal disorders and other functional disturbances [22].

It is evident that the condition of the soft tissues surrounding implants after mandibular reconstruction may depend on multiple factors. The choice of osseous flap for reconstruction (e.g., fibula free flap (FFF), scapula free flap, etc.) influences the characteristics of soft tissue formation around the bone graft, as well as the covering tissues within the oral cavity. At the same time, mucosal attachment may also depend on the positioning of the FFF, which can be either bone-driven or occlusion-driven fibular flap positioning [23].

Depending on the etiology of the defect, soft tissues may be subjected to various multifactorial influences. Patients who have undergone oncological treatment typically receive radiotherapy, followed by soft tissue atrophy and fibrosis [24]. Defects caused by combat trauma are associated with wound contamination, delayed primary surgical care, poorly defined wound boundaries, and extensive defects caused by high-energy weapons [25, 26]. Furthermore, multidrug-resistant infections have been reported in up to 84.6% of wounded patients [27].

In the present study, we did not investigate the impact of the aforementioned factors on the condition of the soft tissues surrounding implants, which can be considered a limitation of this study. At the same time, the cohort of patients included in the main group was heterogeneous with respect to these parameters, which may be considered an averaged sample in relation to the factors described above.

The present study has several strengths, including its prospective controlled design, the use of digital intraoral scanning for standardised soft-tissue assessment, and the performance of all measurements by a single prosthodontist. However, several limitations should be acknowledged, including the non-randomised design, the relatively small sample size, and the short follow-up period after implant placement. Further studies with larger cohorts and longer observation periods are required to clarify the influence of soft-tissue quantity and area on long-term peri-implant outcomes in reconstructed mandibles.

CONCLUSIONS

The obtained results revealed that patients after segmental mandibular reconstruction and placement of implant-supported dental prostheses are characterized by lower quality and a reduced volume of attached keratinised gingiva compared with conventionally rehabilitated patients with implant-supported prostheses. Management of such patients remains complex and often unpredictable. Therefore, optimal conditions for long-term treatment success should be established, including additional surgical procedures to augment attached soft tissues in the dental implant area after reconstructive surgery.

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ORIGINAL ARTICLE

CONTENTS

Certification of a patient's will in healthcare institutions: Medico-legal challenges and practical application

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ABSTRACT

Aim: To analyze medico-legal challenges and the practical application of patients' will certification in healthcare institutions during inpatient care.

Materials and Methods: A retrospective medico-legal analysis of court decisions from the Unified State Register of Court Decisions of Ukraine (2015–2026) was conducted. Of more than 450 identified cases, 60 met the inclusion criteria related to disputes over wills certified in healthcare institutions. Statistical analysis included Pearson's χ^2 test, Fisher's exact test, and odds ratios (OR) with 95% confidence intervals (CI). Additionally, a survey of 28 medical professionals assessed practical aspects and challenges of will certification in clinical settings.

Results: Wills certified by medical professionals and healthcare institution officials accounted for 60.0% of cases, while 40.0% were notarized. The proportion of wills declared invalid or void was significantly higher in the medical group (41.7%) compared to the notarial group (12.5%). A statistically significant association was identified between the certifying subject and court outcomes ($\chi^2 = 5.83$; p=0.016; Fisher's exact test p=0.031). Certification by medical personnel was associated with a fivefold increase in the likelihood of invalidation (OR=5.0; 95% CI: 1.24–20.15). Survey findings revealed insufficient legal knowledge and difficulties in assessing testamentary capacity and voluntariness.

Conclusions: Wills certified in healthcare settings demonstrate lower legal reliability compared to notarized wills. This may be attributed to clinical, organizational, and legal factors, including challenges in capacity assessment and limited legal training of medical staff. The findings highlight the need for improved interdisciplinary protocols.

KEY WORDS: public interest, legal validity, expression of will

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INTRODUCTION

Contemporary medical law doctrine and legal practice are increasingly confronted with issues related to the realization of patients' rights during inpatient care. One such right is the freedom to dispose of one's property upon death through the execution of a will. The Law of Ukraine "Fundamentals of Health Care Legislation" (1992) guarantees a patient undergoing inpatient care the right to be visited by, among others, medical professionals and a notary [1]. At the same time, a number of factors must be taken into account, as they may affect the patient's free and conscious expression of will [2]. These are medical, psychological, ethical, and ultimately legal factors [3-5].

Ukrainian legislation provides for a specific procedure for the certification of wills of persons undergoing treatment in hospitals or other inpatient healthcare institutions. According to Article 1252 of the Civil Code of Ukraine [6] and Article 40 of the Law of Ukraine "On Notariate" [7], wills of such persons may be certified by chief physicians, their deputies for medical affairs, or duty physicians of these institutions, as well as by heads of military hospitals, directors, or chief physicians of residential care institutions for the elderly and persons with disabilities [7]. Such wills are legally equated to notarized wills.

Certification of a will by these officials is permitted only in respect of individuals with full civil legal capacity and must be conducted in the presence of witnesses [8]. However,

determining the legal reliability of the testator's expression of will remains problematic. The patient's physical condition – due to pain, medication effects, cognitive impairment, psycho-emotional stress, delirium, depressive states – as well as potential influence from third parties, may call into question the authenticity and legal validity of the expressed will [9]. This refers to the ability of a person to understand the nature and consequences of making a will, to be aware of the extent of their property and the circle of potential heirs, and to make decisions without coercion. Otherwise, the will may be declared invalid or ineffective by the court.

From a medico-legal perspective, the certification of a patients will lie at the intersection of two fundamental values: individual autonomy and public interest. This is particularly important. A will is a unilateral legal act with a deferred legal effect, and therefore its authenticity and validity are often assessed posthumously in the context of legal disputes. Under such circumstances, medical professionals and healthcare institution officials are effectively required to perform functions that extend beyond clinical care and involve ensuring the legal reliability of the patient's expression of will. This necessitates a comprehensive analysis of the issue.

AIM

The aim of this study is to examine the legal nature of will certification in healthcare institutions, to identify the main medico-legal challenges associated with verifying the authenticity of the testator's expression of will and testamentary capacity, and to analyze approaches to addressing these challenges in practice.

MATERIALS AND METHODS

The study was conducted as a retrospective medico-legal analysis. The primary data source was the Unified State Register of Court Decisions of Ukraine [10]. The search was performed using the following keywords: "recognition of a will as invalid," "void will," "will certification by doctor," and "healthcare institution" for the period from January 1, 2015 to April 1, 2026.

The inclusion criteria were:

1) certification of a will in a healthcare institution;

2) the presence of a legal dispute concerning the recognition of the will as invalid or void;

3) identification of the certifying subject (medical professional, healthcare institution official, or notary); and

4) availability of the full text of the court decision in open access.

The exclusion criteria included:

1) absence of information regarding the place of will certification;

2) inability to identify the certifying subject;

3) appellate and cassation decisions; and

4) cases not related to disputes over the validity of wills.

Out of more than 450 identified court decisions, 60 cases met the inclusion criteria and were included in the analysis. Statistical analysis was performed using Pearson's chi-square (χ^2) test and Fisher's exact test in IBM SPSS Statistics (version 31.0.2.0, IBM Corp., Armonk, NY, USA). The strength of association was assessed by calculating the odds ratio (OR) with 95% confidence interval (95% CI). The level of statistical significance was set at $p<0.05$.

Additionally, a survey of 28 medical professionals from a healthcare institution in Kyiv was conducted between January and February 2026 to assess practical aspects of will certification. Participation in the survey was voluntary and anonymous. The questionnaire included items aimed at assessing:

1) respondents' awareness of the legal grounds for will certification in healthcare institutions;

2) their understanding of the range of authorized persons under current legislation;

3) their practical experience with will certification;

4) their attitudes toward performing such functions; and

5) their perception of legal liability risks, etc.

ETHICS

The authors declare that in preparing this article, all ethical principles and rules of academic integrity were observed. Bioethics: Study was conducted in accordance with the provisions of the Helsinki Declaration of the World Medical Association, Council of Europe Convention on Human Rights and Biomedicine, and Ukrainian legislation. Aggregated statistical data without disclosure of personal information was used. The survey was conducted on a voluntary and anonymous basis, in compliance with confidentiality principles. All respondents were informed about the purpose of the study and provided oral consent to participate.

FRAMEWORK

The study was conducted as a fragment of the complex scientific project of the Bogomolets National Medical University (state registration number 0125U000571 «Forensic medical assessment of the impact of subclinical alcohol intoxication on human cognitive functions»; term: 2025-2027); scientific project of the Department of Criminal Justice and Criminology at the V. M. Koretsky Institute of State and Law of the National Academy of Sciences of Ukraine: «Criminal Justice in the Context of Transitional Justice» (state registration number RK 0125U003191; term: I quarter 2026 – IV quarter 2028).

Table 1. Outcomes of wills certified in healthcare settings

Category	Medical professionals (n=36)	Notaries (n=24)
Declared void	7	1
Refusal to declare void	3	2
Declared invalid	8	2
Refusal to declare invalid	18	19

Source: compiled by the authors of this study

Table 2. Summary of will validity outcomes depending on the certifying subject (for statistical analysis)

Certifying subject	Will declared invalid / void	Claims dismissed	Total
Medical professionals	15 (41.7%)	21 (58.3%)	36
Notaries	3 (12.5%)	21 (87.5%)	24

Source: compiled by the authors of this study

RESULTS

A total of more than 450 court decisions issued between January 1, 2015 and April 1, 2026 were initially identified. Of these, 60 cases met the inclusion criteria and involved disputes concerning the recognition of wills certified in healthcare institutions as invalid or void.

The analysis showed that wills in healthcare settings were certified by medical professionals, healthcare institution officials, as well as notaries.

Although this category of disputes is relatively infrequent in judicial practice, the final sample comprised only 60 cases despite the extended study period. Nevertheless, the very existence of such disputes indicates the presence of medico-legal problems associated with the certification of wills in healthcare institutions, especially under the influence of clinical and psycho-emotional factors.

Among the analyzed cases:

- wills certified by medical professionals and healthcare institution officials accounted for 36 cases (60.0%);
- wills certified by notaries accounted for 24 cases (40.0%).

The corresponding results are presented in Table 1.

The summary of the results demonstrates substantial differences in court outcomes depending on the subject certifying the will. Among wills certified by medical professionals (n=36), 19.4% were declared void, 22.2% invalid, while in 58.3% of cases the claims were dismissed. Thus, the overall proportion of successfully challenged wills (declared void or invalid) in this group amounted to 41.7%.

In contrast, among wills certified by notaries (n=24), 4.2% were declared void and 8.3% invalid, whereas in 87.5% of cases the court rejected the claims. The overall rate of successful challenges in this group was 12.5%.

These findings indicate a significantly higher frequency of wills being declared invalid or void when certified by medical professionals or healthcare institution officials in a clinical setting compared to those certified by notaries. This may reflect the influence of medical, cognitive, and organizational factors on the adequacy of the certification procedure.

The aggregated results used for further statistical analysis are presented in Table 2.

Statistical analysis revealed a significant association between the certifying subject and court outcomes (χ^2=5.83; p=0.016). The results of Fisher's exact test also confirmed a statistically significant relationship between these variables (p=0.031). A higher proportion of wills declared invalid or void was observed among those certified by medical professionals and healthcare institution officials compared to those certified by notaries.

The assessment of the strength of association showed that certification of a will by a medical professional or healthcare institution officials was associated with substantially higher odds of it being subsequently declared invalid or void (OR=5.0; 95% CI: 1.24–20.15; p=0.031). The wide CI indicates limited precision of the estimate, likely due to the relatively small sample size.

The analysis of judicial practice indicates that wills in healthcare institutions are certified not only by notaries but also by medical professionals or healthcare institution officials. These include medical directors of public non-commercial enterprises, chief physicians, their deputies, acting heads of institutions, heads of departments, duty physicians, and general practitioners. Such a broad range of authorized persons may adversely affect the legal reliability of the testator's expression of will and contribute to inconsistencies in judicial practice.

To assess the practical aspects of exercising these powers, a survey of medical professionals, including general

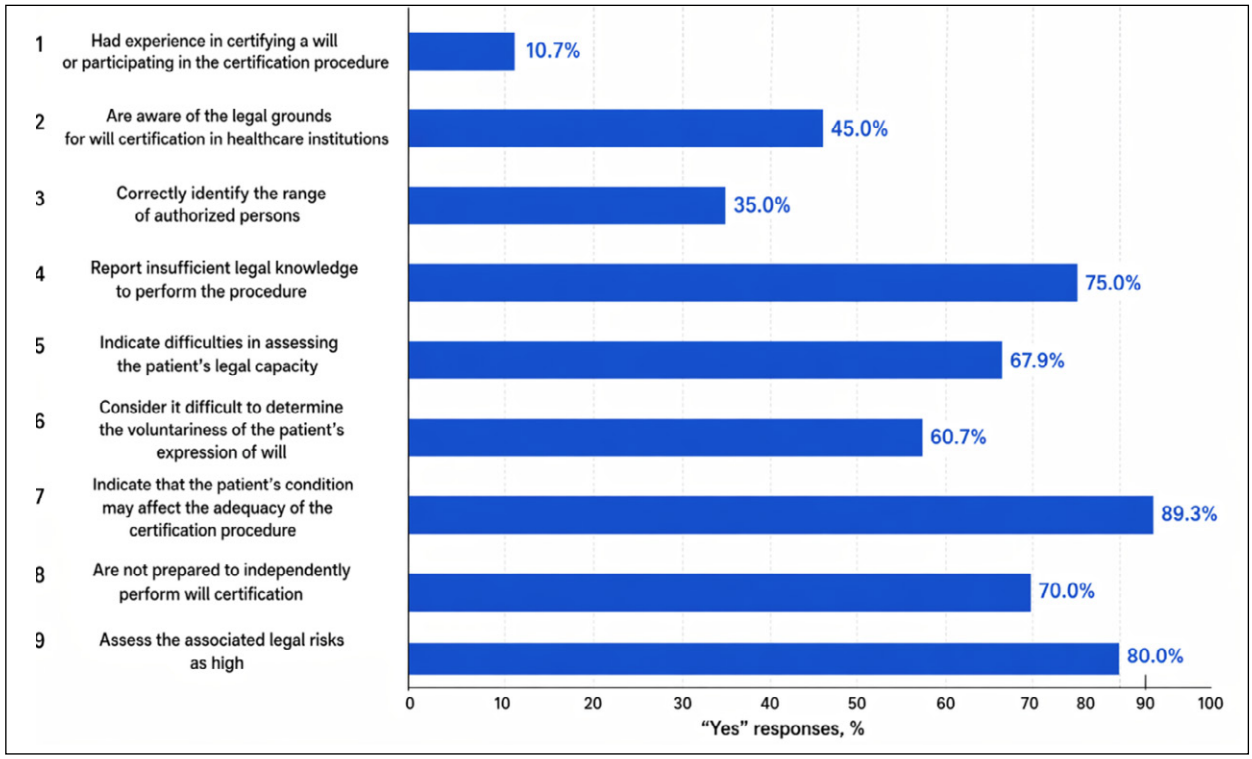


Fig. 1. Survey responses of medical professionals regarding will certification in healthcare settings (n=28)
Picture taken by the authors

practitioners (family physicians), surgeons, anesthesiologists, and healthcare administrators, from a healthcare institution in Kyiv was conducted. The study involved 28 respondents and was carried out between January and February 2026. The sample was created using a convenience sampling approach, driven by the specifics of access to respondents in the medical environment, including shift work, on-call duties, and clinical workloads. The survey results are presented in Fig. 1.

The survey results indicate substantial challenges in the practical implementation of will certification in healthcare institutions. Only 10.7% of respondents reported having experience in certifying a will or participating in such a procedure.

The majority of respondents reported significant professional and legal barriers. Specifically, 75.0% indicated insufficient legal knowledge, 67.9% reported difficulties in assessing the patient's legal capacity, 60.7% noted challenges in determining the voluntariness of the patient's expression of will, and 89.3% emphasized that the patient's physical and mental condition may affect the adequacy of the certification procedure.

The data also demonstrate a limited level of awareness among medical professionals regarding the legal grounds for will certification in healthcare settings. Only 45.0% of respondents were aware of the existence of such powers, while 35.0% correctly identified the range of authorized persons. Furthermore, 70.0% reported that they were not prepared to independently perform will certification, and 80.0% assessed the associated legal risks as high.

Taken together, these findings indicate the presence of significant organizational, legal, and clinical challenges in the implementation of legally prescribed powers. These results are consistent with the analysis of judicial practice, which demonstrated that wills certified by medical professionals or healthcare institution officials are significantly more likely to be declared invalid or void compared to those certified by notaries. These findings have substantial practical significance. They indicate a lower level of legal robustness of wills certified in clinical settings. This may be explained by insufficient legal training of certifying individuals.

DISCUSSION

Certification of a will is an intersectoral legal obligation arising from civil and notarial legislation, which is imposed on medical professionals in specific circumstances. It is a legally complex procedure requiring proper identification of the testator, verification of civil legal capacity, explanation of legal consequences, and strict compliance with formal requirements [11, 12]. Notaries perform these functions within a specialized legal framework. In contrast, medical professionals carry out will certification in the context of providing healthcare, where the primary focus is clinical care rather than ensuring legal validity. This difference increases the likelihood of procedural deficiencies.

In a comparative perspective, the medico-legal challenges identified in this study are consistent with global trends in the regulation of testamentary capacity and will execution in clinical settings. In many jurisdictions, including the United States, the United Kingdom, and EU countries, the assessment of testamentary capacity in hospitalized patients is recognized as a complex interdisciplinary issue involving both legal and medical expertise [9]. However, unlike the Ukrainian model, certification of wills is generally reserved for notaries or legal professionals, while physicians play a supporting role by providing clinical assessments of cognitive status and decision-making capacity rather than directly certifying legal acts.

Ukrainian legislation allows the certification of wills in healthcare facilities during inpatient treatment. Such wills are registered by authorized officials in a special register of wills and powers of attorney equivalent to notarized acts, the form of which is established by the Ministry of Justice of Ukraine [13]. Maintaining such a register constitutes a mandatory organizational requirement for healthcare institutions.

The clinical environment may influence the adequacy of will certification procedures [14, 15]. There are significant difficulties in assessing a patient's capacity to make a conscious decision regarding the execution of a will. Somatic and mental disorders may substantially influence this capacity. In many cases, a decisive factor is the limited legal knowledge of medical professionals in this area.

A limitation of this study is the lack of systematic official statistics in Ukraine on the invalidation or nullity of wills certified in healthcare institutions. Available data concern general categories of invalid transactions or wills without distinguishing between notarized and medically certified documents. This highlights the relevance of the present study in addressing this gap. The evidentiary value of medical documentation in subsequent litigation increases [16].

Medical professionals and healthcare institution officials effectively act as primary gatekeepers of legal capacity [4, 13]. However, survey results demonstrate that they often lack sufficient legal training, experience difficulties in assessing capacity and voluntariness, and perceive significant legal risks. This indicates a mismatch between delegated legal responsibilities and actual professional competencies.

Physicians are often the first to assess whether a patient's condition may impair their capacity for a valid legal expression of will. Evidence from Central European forensic practice further supports these findings. Studies indicate that expert evaluations in will disputes rely on a comprehensive analysis of the will's content, medical documentation, clinical history, witness statements, and behavioral characteristics of the testator near the time of execution [9]. Notably, a significant proportion of contested wills are made during periods of severe illness, often in hospital settings, underscoring the critical role of the clinical context.

CONCLUSIONS

1. The study identified a statistically significant association between the certifying subject and the likelihood of a will being declared invalid or void, based on a retrospective analysis of court decisions from the Unified State Register of Court Decisions of Ukraine (2015–2026). Wills certified by medical professionals and healthcare institution officials were invalidated significantly more often (41.7%) compared to notarized wills (12.5%), with approximately fivefold higher odds (OR = 5.0; 95% CI: 1.24–20.15; p=0.031).
2. These findings have important practical implications, indicating a lower level of legal robustness of wills certified in clinical settings. Survey data from medical professionals (n = 28) confirmed the presence of substantial professional, legal, and organizational barriers, including insufficient legal knowledge, limited awareness of legal grounds for certification, and difficulties in assessing testamentary capacity and voluntariness.
3. The findings reveal a gap between formal legal regulation and its practical implementation in healthcare institutions. Difficulties in assessing voluntariness and legal capacity–also noted in international practice–reflect a broader tension between patient autonomy and the legal validity of end-of-life decisions, highlighting the need for stronger safeguards, including interdisciplinary protocols and greater involvement of notaries.

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ORIGINAL ARTICLE

CONTENTS

Diagnostic value of lateral cephalometric parameters in determining vertical and horizontal maxillofacial growth patterns

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ABSTRACT

Aim: To assess the diagnostic value of qualitative and quantitative lateral cephalometric parameters in determining vertical, horizontal, and neutral maxillofacial growth patterns in patients with orthodontic pathology.

Materials and Methods: The study included 292 lateral cephalograms of patients aged 5 to 50 years who sought orthodontic consultation. Eleven quantitative cephalometric parameters were analysed in the full sample. In a randomised subgroup of 160 cephalograms, seven additional qualitative parameters were assessed. Growth pattern determination was performed using an integrated approach based on the absolute majority of diagnostic signs. In addition, 134 cephalograms were independently evaluated by 34 orthodontic trainees using qualitative characteristics only. The diagnostic performance of each parameter was assessed using balanced accuracy, sensitivity, specificity, and positive predictive value.

Results: Among 292 patients, 121 had a neutral growth pattern, 103 a vertical pattern, and 68 a horizontal pattern. Evaluation based only on qualitative signs resulted in correct classification in 60.45% of cases on average. Among quantitative parameters, ∠N-Go-Me demonstrated the highest diagnostic performance, with a positive predictive value of 82.9%, followed by ∠Ar-Go-Me and ∠Pn-MP. Among qualitative parameters, the mandibular angle, condylar process height, and contour of the lower mandibular border showed the highest diagnostic value.

Conclusions: Quantitative cephalometric parameters, particularly ∠N-Go-Me, are more diagnostically reliable than isolated qualitative assessment for determining maxillofacial growth patterns. A combined approach may improve diagnostic accuracy in orthodontic treatment planning.

KEY WORDS: orthodontics, cephalometry, craniofacial growth, vertical dimension

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INTRODUCTION

Orthodontic diagnostics is a fundamental basis for successful treatment [1]. In this context, cephalometric analysis is a unique method for accurately determining the differentiation of the level of pathology (skeletal or dentoalveolar) [2], the dimensions and relationships of the jaws to each other and to the anterior cranial base [3], as well as jaw convergence or divergence (maxillofacial growth pattern).

A correctly determined maxillofacial growth pattern not only influences the choice of treatment strategy but also helps prevent complications during orthodontic treatment and relapses afterwards [4–6].

When assessing facial aesthetics, vertical parameters are considered significant. The face is perceived as attractive when its upper, middle, and lower thirds are proportional. However, in cases of impaired development of the anterior cranial base [7, 8], taking into account hereditary factors [9], under the influence of general muscular [10] and postural imbalance [11], or abnormal functioning of oral cavity functions such as mastication [12, 13], swallowing [14], and breathing [15], the maxillofacial growth develops according to two pathological patterns: horizontal, leading to the formation of a short face, and vertical, leading to the formation of a long face.

The qualitative characteristics of the maxillofacial growth pattern were defined by A. Björk and J. Jarabak [16, 17]. However, in the early mixed dentition period or in doubtful cases of determining the growth pattern, it is impossible to base clinical decisions and orthodontic treatment objectives solely on qualitative features. Moreover, the accuracy of determining the growth pattern significantly depends on the clinician's qualification and experience, and is largely subjective. Therefore, a considerable number of

Table 1. Qualitative parameters analysed in the assessment of the maxillofacial growth pattern

Qualitative feature	Maxillofacial growth pattern	
	Vertical	Horizontal
Contour of the lower border of the mandible (lower jaw)	Concave in the region of the antegonial notch	Convex in the chin region
Shape of the mandibular symphysis	Elongated in the vertical plane	Elongated in the sagittal plane
Height of the mandibular condylar process	Greater height	Lower
Rotation of the dentoalveolar complex	Clockwise rotation	Counterclockwise rotation
Line connecting the mandibular head with the condylar process	Deviated from the midline	Deviation toward the midline
Mandibular angle	Increased	Markedly reduced
Height of the lower third of the face	Enlarged	Reduced

Source: compiled by the authors of this study

Table 2. Quantitative parameters analysed in the assessment of the maxillofacial growth pattern

Author	Parameter symbol	Parameter description
A.M. Schwarz [27]	∠B	Angle between the maxillary base (SpP) and the mandibular base (MP)
	∠Pn-MP	Angle between the perpendicular (Pn) to the anterior cranial base (NSe) and the mandibular base (MP)
	∠I	Angle between the perpendicular (Pn) to the anterior cranial base (NSe) and the maxillary base (SpP)
	∠Pn-OcP	Angle between the perpendicular (Pn) to the anterior cranial base (NSe) and the occlusal plane (OcP)
J.R. Jarabak [17]	∠NSAr	Angle between the NS and S–Ar planes
	∠Ar-Go – Me	Angle between the mandibular ramus and the mandibular base
	∠N-Go-Ar	Upper gonial angle
	∠N-Go-Me	Lower gonial angle
	(∠N-Go-Ar/∠N-Go-Me)×100	Ratio of the upper gonial angle to the lower gonial angle, reflecting not only the growth pattern type but also its degree
	∠NSGn	Y-axis angle
Downs W.B. [28], Arne Björk [16] – J.R. Jarabak [17].	S-Go	Posterior facial height
	N – Gn	Anterior facial height
	(SGo)/(NMe)×100	Ratio of posterior to anterior facial height

Source: compiled by the authors based on [16, 17, 27, 28]

prominent orthodontic researchers, in particular R. Ricketts [18], J. McNamara Jr. [19], and C. Steiner [20], have investigated quantitative parameters that allow for a more objective assessment of the maxillofacial growth pattern.

As a rule, the maxillofacial growth pattern is determined based on lateral cephalograms by considering the simple majority of qualitative and quantitative parameters [21–26]. However, in the available literature, there are no assessments of the degree of significance of each quantitative parameter's influence on the expert conclusion regarding the maxillofacial growth pattern. Moreover, there is no such analysis for partial combinations of qualitative and quantitative parameters, which would make it possible to substantially reduce the number of measurements required on lateral cephalograms for decision-making.

AIM

The aim of the study was to determine the diagnostic significance of qualitative and quantitative parameters of lateral cephalograms for assessing the maxillofacial growth pattern in patients with orthodontic pathology and to compare the results of an integrated assessment with expert determination of the maxillofacial growth pattern based solely on qualitative features.

FRAMEWORK

This study was conducted at the Department of Orthodontics of the P.L. Shupyk National Medical Academy of Ukraine as part of the research project "Develop and test an integrated approach in the diagnosis and treatment of orthodontic patients with comorbidities" (State registration number 0121U111023; duration: 2021–2025; extended to 2027).

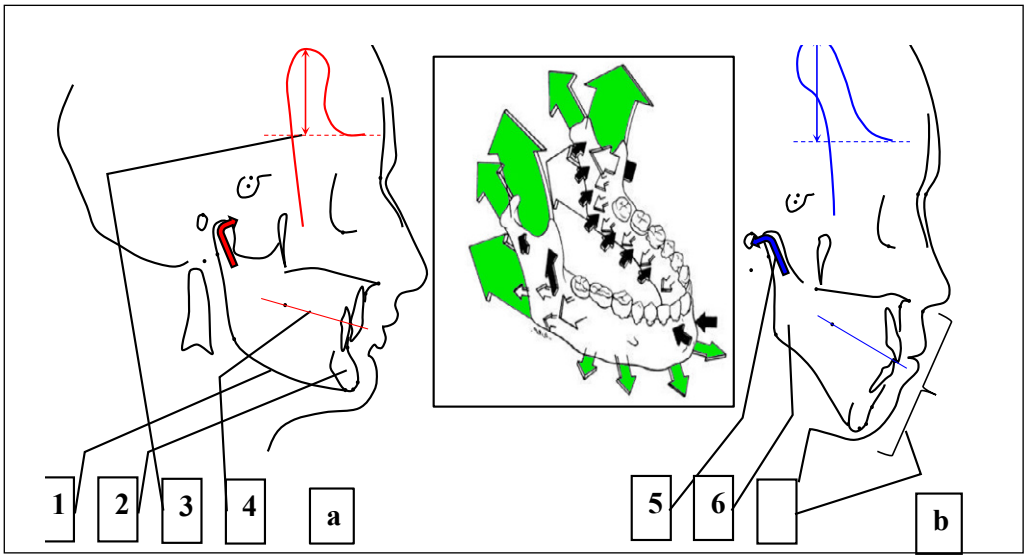


Fig. 1. Qualitative features of pathological types of maxillofacial growth (based on A. Björk and J. Jarabak [16, 17]): (a) horizontal maxillofacial growth pattern; (b) vertical maxillofacial growth pattern. 1) contour of the lower border of the mandible; 2) shape of the chin prominence; 3) height of the condylar process; 4) rotation of the dentoalveolar complex; 5) line connecting the mandibular head and condylar process; 6) mandibular angle; 7) height of the lower third of the face
Source: compiled by the authors based on [16, 17]

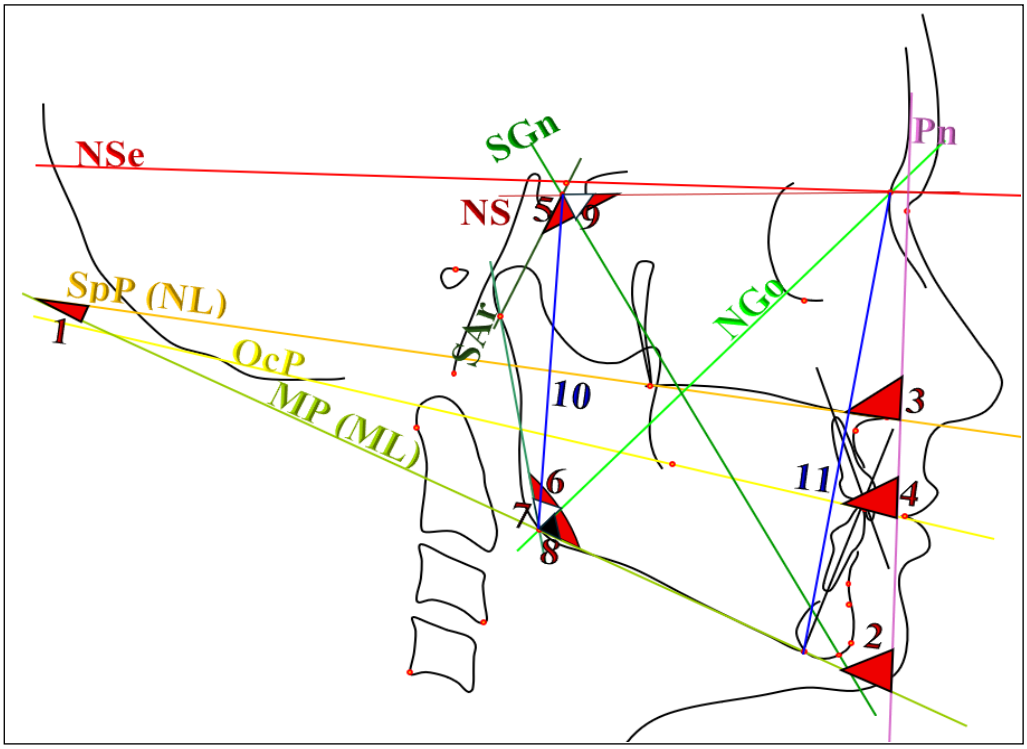


Fig. 2. Quantitative parameters analysed in the assessment of the maxillofacial growth pattern – cephalometric landmarks on lateral cephalograms (A. M. Schwarz [27]; J. R. Jarabak [17]; W. B. Downs [28]; A. Björk [16]): 1) ∠B; 2) ∠Pn–MP; 3) ∠I; 4) ∠Pn–OcP; 5) ∠NSAr; 6) ∠Ar–Go–Me; 7) ∠N–Go–Ar (upper gonial angle); 8) ∠N–Go–Me (lower gonial angle); 9) ∠NSGn (Y-axis angle); 10) posterior facial height (S–Go); 11) anterior facial height (N–Gn)
Source: compiled by the authors based on [16, 17, 27, 28.]

MATERIALS AND METHODS

Lateral cephalograms of patients with orthodontic pathology who sought consultation at the Department of Orthodontics, Shupyk National Healthcare University of Ukraine (Kyiv, Ukraine) were analysed. The maxillofacial growth pattern was determined in the vertical plane using an integrated method based on both qualitative and quantitative parameters (Table 1, Table 2, Fig. 1, Fig.2).

For the horizontal maxillofacial growth pattern (other terms: counterclockwise growth rotation, short face, low angle, anterior mandibular rotation, convergent type), the following features are characteristic: a convex contour in the chin region (mandible); an elongated symphysis in the sagittal (horizontal) plane; a low condylar process; counterclockwise rotation of the dentoalveolar complex; medial deviation of the mandibular head relative to the neck (towards the midline); an acute mandibular angle; and a reduced lower third of the face (Table 1, Fig. 1).

For the vertical maxillofacial growth pattern (clockwise growth rotation, long face, high angle, posterior mandibular rotation, divergent type), the following features are characteristic: a markedly concave contour in the antegonial notch region of the mandible; an elongated symphysis in the vertical plane; a high (elongated) condylar process; clockwise rotation of the dentoalveolar complex; distal deviation of the mandibular head relative to the neck (away from the midline); an obtuse mandibular angle; and an increased lower third of the face (Table 1, Fig. 1).

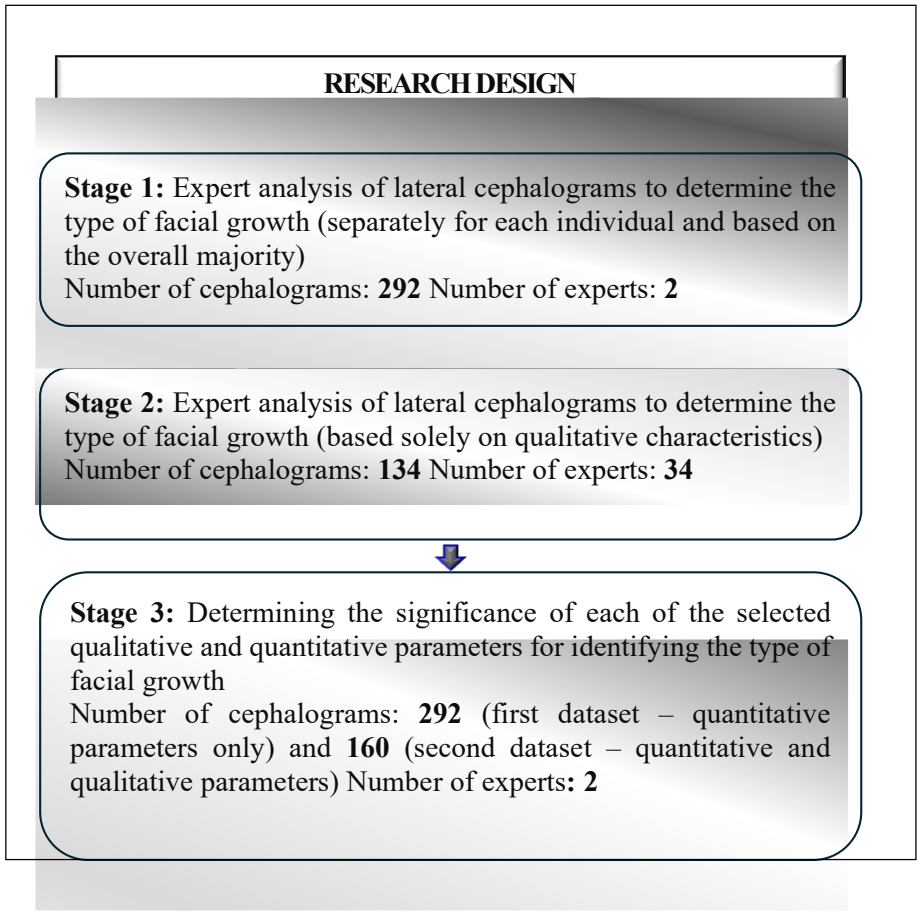


Fig. 3. Research design
Picture taken by the authors

For the neutral maxillofacial growth pattern, a balanced relationship between the vertical and horizontal components of growth is characteristic. The contour of the lower border of the mandible demonstrates a smooth, uniform course without a pronounced concavity in the antegonial notch region or excessive convexity in the chin region. The mandibular symphysis has a rounded, proportionate shape without a predominant deformation in either the vertical or sagittal plane. The height of the condylar process corresponds to average age-related and morphological characteristics.

Rotation of the dentoalveolar complex is balanced, without a pronounced tendency toward clockwise or counterclockwise rotation. The line connecting the mandibular head with the condylar process has a straight direction. The mandibular angle remains within normative values, approximating 123°, without a tendency toward marked reduction or increase. The height of the lower third of the face is proportional to the middle and upper thirds of the face. The quantitative parameters used for determining the maxillofacial growth pattern are presented in Table 2 and Fig. 2.

In the first stage of the study (Fig. 3), two datasets were formed. The full dataset included 292 lateral cephalograms of patients of both sexes: 124 males and 168 females (Fig.4a). For all these cephalograms, values of eleven quantitative parameters were obtained.

In the first (second) dataset, there were 70 (31) lateral cephalograms of patients aged 5 to 8 years (early mixed dentition period), 60 (24) cephalograms of patients aged 9 to 12 years (late mixed dentition period), and 162 (105) cephalograms of patients in both the developing permanent dentition and the fully established permanent dentition period, aged 13 to 50 years (Fig. 4b). All individuals with permanent dentition were grouped.

The second dataset is a random subset of the first and contains 160 lateral cephalograms (73 males and 87 females), for which qualitative parameters were additionally considered (a total of seven parameters).

In the first (second) dataset, there were 70 (31) lateral cephalograms of patients aged 5 to 8 years (early mixed dentition period), 60 (24) cephalograms of patients aged 9 to 12 years (late mixed dentition period), and 162 (105) cephalograms of patients in both the developing permanent dentition and the fully established permanent dentition period, aged 13 to 50 years (Fig. 4b). All individuals with permanent dentition were grouped.

In the second stage of the study (Fig. 3), 134 lateral cephalograms were randomly selected from the 292 cephalograms to compare the results of maxillofacial growth pattern assessment based on the absolute majority of qualitative (Table 1, Fig. 1) and quantitative (Table 2, Fig. 2) parameters with expert evaluation based solely on qualitative parameters.

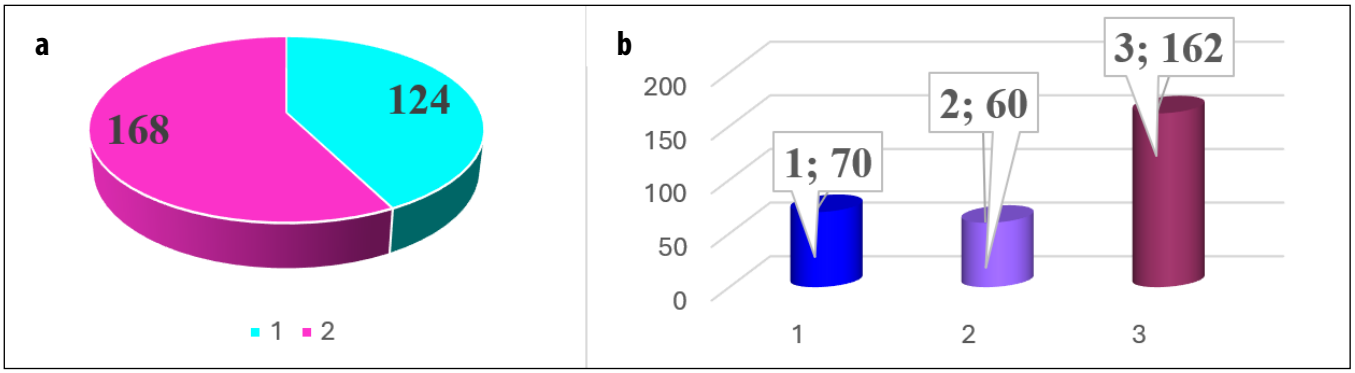


Fig. 4. Distribution of patients who's lateral cephalograms were analyzed according to: (a) sex (1 – male, 2 – female); (b) stage of dentition development (1 – early mixed dentition period, age 6–8 years; 2 – late mixed dentition period, age 9–12 years; 3 – developing and established permanent dentition period, age 13–50 years)
Picture taken by the authors

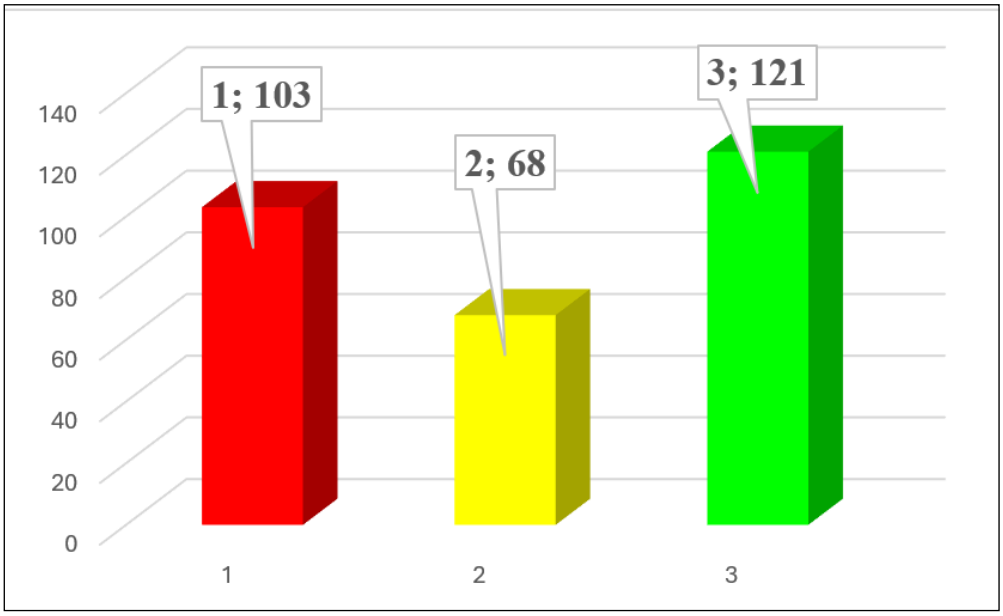


Fig. 5. Distribution of patients' lateral cephalograms according to the maxillofacial growth pattern: 1) vertical type, 2) horizontal type, 3) neutral type
Picture taken by the authors

The experts were 34 participants of an orthodontic specialization course. After studying the topic and acquiring practical skills, they were provided with links to complete a Google Form containing 134 tasks. Each task included a photographic image of one of the selected lateral cephalograms, and the respondents were required to assign one of three maxillofacial growth pattern types: neutral, vertical, or horizontal. The true growth pattern was defined as the one previously determined by the absolute majority of qualitative and quantitative parameters for each lateral cephalogram.

In the third stage of the study (Fig. 3), an analysis of 292 lateral cephalograms was performed to identify the parameters most significant for determining the maxillofacial growth pattern. The determination was based on the absolute majority of positive quantitative parameters (i.e., those corresponding to the values characteristic of a specific growth pattern). For 160 lateral cephalograms, qualitative parameters were also assessed.

Statistical data processing was performed by calculating diagnostic performance metrics for each qualitative and quantitative parameter of the lateral cephalograms. For each indicator, balanced accuracy, sensitivity, specificity, and positive predictive value were determined. Calculations were based on contingency tables using a one-vs-rest approach for each type of maxillofacial growth pattern, followed by averaging of the obtained values.

Accuracy is defined as the average probability of a correct (both positive and negative) test result across all types of maxillofacial growth patterns. Balanced accuracy accounts for the imbalance between the numbers of positive and negative cases in the overall dataset.

Sensitivity is defined as the average probability across all maxillofacial growth patterns of correctly classifying a case with a positive value of the tested parameter. Specificity is defined as the average probability across all maxillofacial growth patterns of correctly classifying a case with a negative value of the tested parameter. Positive predictive value is defined as the average probability of correct identification of the maxillofacial growth pattern among all cases classified as such based on a given cephalometric parameter.

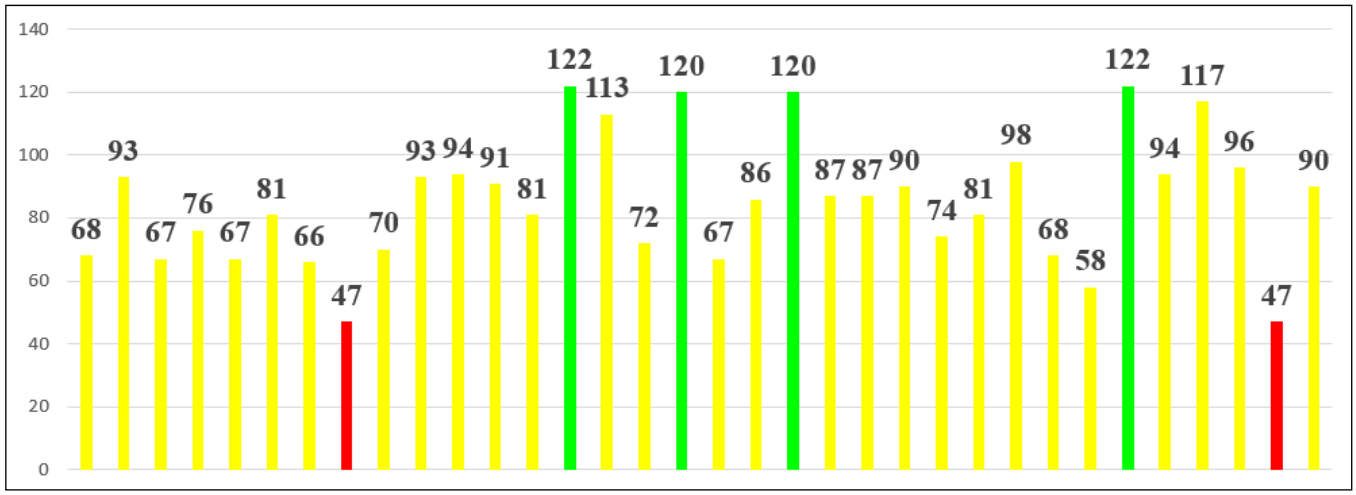


Fig. 6. Number of correctly identified maxillofacial growth patterns based on qualitative parameters. The assessment was performed by 34 experts (participants of a specialization course)
Picture taken by the authors

The 95% confidence interval (CI) limits were calculated using the Wald method; differences were considered statistically significant at $p<0.05$.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki. All patients or their legal representatives provided written informed consent for the use of diagnostic materials for scientific purposes. All lateral cephalograms included in the study were anonymised in advance; only the patients' age and sex were recorded in the database. The study protocol was reviewed and approved by the local bioethics committee.

RESULTS

As a result of the first stage of the study, it was established that, among 292 patients of both sexes aged 5 to 50 years, 121 had a neutral maxillofacial growth pattern, 103 had a vertical growth pattern, and 68 had a horizontal growth pattern (Fig.5).

The analysis of expert responses based solely on qualitative parameters (second stage) to the proposed tasks showed that the correct maxillofacial growth pattern was identified in an average of only 81 out of 134 cases, corresponding to 60.45% (Fig. 6).

The lowest number of errors in determining the maxillofacial growth pattern was made by four experts. They correctly identified the growth pattern in 120–122 out of 134 cases (89.6%–91.0%). The highest number of errors in determining the growth pattern based solely on qualitative features was made by two experts, who provided 47 correct answers each out of 134 (35.1%). The remaining 28 experts correctly identified the maxillofacial growth pattern in 47 to 120 cases (35.1% to 89.6%).

In the third stage of the study, the statistical agreement between the maxillofacial growth pattern determined by each quantitative or qualitative cephalometric parameter and the true value was analysed. The results are summarised in Table 3 (for quantitative cephalometric parameters) and Table 4 (for qualitative cephalometric parameters). The values in parentheses indicate the positive predictive value of the parameter in determining the corresponding maxillofacial growth pattern (i.e., the number of correctly identified cases among all cases classified as such based on the given parameter).

Tables 5 and 6 present the diagnostic performance indicators for the determination of the maxillofacial growth pattern by each cephalometric parameter, calculated based on the distributions obtained in Table 3 and Table 4, respectively.

As shown in Table 5, among the quantitative cephalometric parameters, the best diagnostic performance is demonstrated by ∠N–Go–Me, followed by ∠Ar–Go–Me, ∠Pn–MP, and ∠B, which show nearly identical values.

The least informative parameters are ∠I, ∠NSAr, and ∠N–Go–Ar, whose positive predictive value does not exceed 40%. When using ∠N–Go–Me as the sole parameter for determining the maxillofacial growth pattern, 17–18% misclassifications should be expected. This parameter demonstrates relatively high specificity (up to 90%) and slightly lower sensitivity (up to 82%).

It should be noted that some cephalometric parameters demonstrated an almost 100% positive predictive value for the identification of a specific maxillofacial growth pattern (e.g., ∠Pn–MP, ∠B, or ∠Pn–OcP for the identification of the horizontal growth pattern; see Ta-

Table 3. Distribution of maxillofacial growth patterns determined by each quantitative cephalometric parameter according to their agreement with the true types

Maxillofacial growth pattern		Vertical (v)	Horizontal (h)	Neutral (n)
Number of lateral cephalograms		103	68	121
Parameter				
∠N-Go-Me	v	**82 (80.4%)***	0	20
	h	0	**59 (92.2%)***	5
	n	21	9	**96 (76.2%)***
∠Ar-Go–Me	v	**38 (97.4%)***	0	1
	h	0	**35 (74.5%)***	12
	n	65	33	**108 (52.4%)***
∠Pn-MP	v	**99 (64.7%)***	2	52
	h	0	**19 (100.0%)***	0
	n	4	47	**69 (57.5%)***
∠B	v	**100 (64.5%)***	0	55
	h	0	**17 (100.0%)***	0
	n	3	51	**66 (55.0%)***
∠NSGnуголосиY	v	**40 (80.0%)***	0	10
	h	1	**14 (82.4%)***	2
	n	62	54	**109 (48.4%)**
(SGo)/(NMe)×100	v	**49 (75.4%)***	2	14
	h	5	**61 (51.3%)***	53
	n	49	5	**54 (50.0%)***
(∠N-Go-Ar)/ (∠N-Go-Me)×100	v	**60 (63.2%)***	4	31
	h	14	**37 (52.9%)***	19
	n	29	27	**71 (55.9%)***
∠Pn-OcP	v	101 (36.4%)	55	121
	h	0	**1 (100%)***	0
	n	2	12	0 (0,0 %)
∠I	v	41 (37.3%)	22	47
	h	0	0 (0.0%)	0
	n	62	46	74 (40.6%)
∠NSAr	v	24 (49.0%)	5	20
	h	7	11 (28.2%)	21
	n	72	52	80 (39.2%)
∠N-Go-Ar	v	30 (33.7%)	22	37
	h	34	23 (26.7%)	29
	n	39	23	55 (47.0%)

Note: * – cases where the positive predictive value of the parameter for the given maxillofacial growth pattern is not less than 50%
Source: compiled by the authors of this study

ble 3). However, this provides limited practical benefit, as among 68 truly horizontal cases, these parameters correctly identified only 1.5–28% of them.

Among the qualitative cephalometric parameters (Table 6), the best diagnostic performance was observed for the "mandibular angle", "height of the condylar process", and "contour of the lower border of the mandible". The least informative parameter was the "line connecting the mandibular head with the condylar process", although its positive predictive value remained not lower than 50%.

Overall, qualitative parameters demonstrated slightly lower performance compared to quantitative ones. The best-performing qualitative parameter, the "mandibular angle", when used as the sole criterion for determining the maxillofacial growth pattern, may result in up to

Table 4. Distribution of maxillofacial growth patterns determined by each individual qualitative cephalometric parameter according to their agreement with the true types

Maxillofacial growth pattern			Vertical (v)	Horizontal (h)	Neutral (n)
Number of lateral cephalograms			65	25	70
Parameter	Mandibular angle	v	**59 (77.6%)***	0	17
		h	0	**15 (83.3%)***	3
		n	6	10	**50 (75.8%)***
	Height of the condylar process	v	**34 (81.0%)***	0	8
		h	1	**16 (80.0%)***	3
		n	30	9	**59 (60.2%)***
	Contour of the lower border of the mandible	v	**49 (76.6%)***	0	15
		h	1	**15 (65.2%)***	7
		n	15	10	**48 (65.8%)***
	Rotation of the dentoalveolar complex	v	**58 (71.6%)***	0	23
		h	1	**17 (58.6%)***	11
		n	6	8	**36 (72.0%)***
	Height of the lower third of the face	v	**44 (81.5%)***	1	9
		h	1	18 (38.3%)	28
		n	20	6	**33 (55.9%)***
	Shape of the mandibular symphysis	v	**31 (75.6%)***	0	10
		h	2	12 (44.4%)	13
		n	32	13	**47 (51.1%)***
	Line connecting the mandibular head with the condylar process	v	**4 (50.0%)***	0	4
		h	4	**14 (53.8%)***	8
		n	57	11	58 (46.0%)

Note: * – cases where the positive predictive value of the parameter for the given maxillofacial growth pattern is not less than 50%
Source: compiled by the authors of this study

21–22% misclassifications. Nevertheless, this parameter shows relatively high specificity (over 87%) and slightly lower sensitivity (over 74%).

DISCUSSION

Research that exactly matches the aim and design of our work was not found, which underlines its relevance. However, individual qualitative cephalometric features, such as the contour of the lower border of the mandible [29] or the line connecting the mandibular head with the condylar process [30], are considered indicators of mandibular rotation. In contrast, recent studies confirm the importance of specific morphometric characteristics of the mandible, including the gonial angle, mandibular body angle, ramus height, and the ratio of anterior to posterior facial height, in differentiating hyperdivergent, normodivergent, and hypodivergent maxillofacial growth patterns [31].

Our results do not appear isolated; rather, they fit well within current trends. The existing literature most strongly supports three of our findings: (1) the high diagnostic value of mandibular angles; (2) the importance of condylar (ramus) height in identifying the vertical growth pattern of the maxillofacial complex [32].

What is most strongly supported in the current literature is the correlation between individual quantitative parameters and the determination of the maxillofacial growth pattern. For example, recent studies identify the mandibular angle and the inclination of the mandibular plane relative to the cranial base as the most informative parameters for distinguishing the hyperdivergent growth pattern [33]. In a large 2024 study employing machine learning (ML-NSL—an analogue of SN-GoMe / SN-GoGn in different analyses) with computer-based computation, this parameter was shown to be the most influential feature in the classification of anterior open bite and vertical skeletal imbalance [34].

Our finding regarding the high significance of angles such as ∠N–Go–Me and ∠Ar–Go–Me is well aligned with these recent data. Although contemporary authors more commonly use the notations SN-GoGn / SN-MP / ML-NSL / FMA / gonial angle rather than ∠N–Go–Me, the underlying concept remains consistent: the mandibular

Table 5. Statistical performance indicators for the determination of the maxillofacial growth pattern using different quantitative cephalometric parameters.

Parameter	Balanced accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)
∠N-Go-Me	0.859 (0.819-0.899)	0.819 (0.743-0.895)	0.899 (0.857-0.941)	0.829 (0.754-0.904)
∠Ar-Go-Me	0.691 (0.638-0.744)	0.592 (0.494-0.690)	0.789 (0.732-0.846)	0.748 (0.662-0.834)
∠Pn-MP	0.704 (0.652-0.756)	0.604 (0.507-0.701)	0.805 (0.749-0.861)	0.741 (0.654-0.828)
∠B	0.693 (0.640-0.746)	0.589 (0.491-0.687)	0.798 (0.742-0.854)	0.732 (0.644-0.820)
∠NSGnуголосиY	0.625 (0.569-0.681)	0.498 (0.399-0.597)	0.752 (0.691-0.813)	0.703 (0.612-0.794)
(SGo)/(NMe)×100	0.693 (0.640-0.746)	0.606 (0.509-0.703)	0.780 (0.722-0.838)	0.589 (0.491-0.687)
(∠N-Go-Ar)//(∠N-Go-Me)×100	0.676 (0.622-0.730)	0.571 (0.473-0.669)	0.780 (0.722-0.838)	0.573 (0.475-0.671)
∠Pn-OcP	0.497 (0.440-0.554)	0.332 (0.238-0.426)	0.662 (0.596-0.728)	0.455 (0.356-0.554)
∠I	0.502 (0.445-0.559)	0.337 (0.243-0.431)	0.668 (0.602-0.734)	0.390 (0.293-0.487)
∠NSAr	0.512 (0.455-0.569)	0.352 (0.257-0.447)	0.673 (0.607-0.739)	0.388 (0.291-0.485)
∠N-Go-Ar	0.521 (0.464-0.578)	0.361 (0.266-0.456)	0.681 (0.616-0.746)	0.358 (0.263-0.453)

Source: compiled by the authors of this study

Table 6. Statistical performance indicators for the determination of the maxillofacial growth pattern using different qualitative cephalometric parameters.

Qualitative feature (parameter)	Balanced accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)
Mandibular angle	0.807 (0.746-0.868)	0.741 (0.623-0.859)	0.874 (0.811-0.937)	0.789 (0.679-0.899)
Height of the condylar process	0.743 (0.675-0.811)	0.669 (0.543-0.795)	0.818 (0.745-0.891)	0.737 (0.619-0.855)
Contour of the lower border of the mandible	0.757 (0.691-0.823)	0.680 (0.555-0.805)	0.835 (0.765-0.905)	0.692 (0.568-0.816)
Rotation of the dentoalveolar complex	0.767 (0.701-0.833)	0.696 (0.573-0.819)	0.838 (0.768-0.908)	0.674 (0.548-0.800)
Height of the lower third of the face	0.710 (0.640-0.780)	0.623 (0.493-0.753)	0.797 (0.721-0.873)	0.586 (0.454-0.718)
Shape of the mandibular symphysis	0.652 (0.578-0.726)	0.543 (0.409-0.677)	0.761 (0.680-0.842)	0.570 (0.437-0.703)
The line connecting the mandibular head with the condylar process	0.594 (0.518-0.670)	0.483 (0.349-0.617)	0.704 (0.617-0.791)	0.500 (0.366-0.634)

Source: compiled by the authors of this study

plane angle and gonial angle are consistently increased in hyperdivergent patients and decreased in hypodivergent patients [35].

In our study, we did not confirm the high diagnostic significance of the Y-axis (parameter 9, Fig. 2). This finding may be addressed in future research, potentially involving larger sample sizes.

Further research perspectives include the analysis of partial combinations of the examined cephalometric parameters with the aim of potentially increasing their overall predictive value.

CONCLUSIONS

1. When assessing the maxillofacial growth pattern based exclusively on qualitative parameters, incor-

rect identification is possible in an average of 37.6% of cases (range: 10.4%–64.9%).
2. Among the qualitative parameters used for determining the maxillofacial growth pattern, the highest positive predictive value was observed for the following (in descending order): mandibular angle – 78.9%; height of the condylar process – 73.7%; contour of the lower border of the mandible – 69.2%. The lowest positive predictive value was observed for the "line connecting the mandibular head with the condylar process" – 50%.
3. Among the quantitative parameters used for determining the maxillofacial growth pattern, the highest positive predictive value was observed for the following (in descending order): ∠N–Go–Me – 82.9%, ∠Ar–Go–Me – 74.8%, ∠Pn–MP – 74.1%. The lowest positive predictive value was observed for the following (in ascending order): ∠N–Go–Ar – 35.8%; ∠NSAr – 38.8%; ∠I – 39.0%.

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CONFLICT OF INTEREST
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ORIGINAL ARTICLE

CONTENTS

Blastotrauma: Concept and development of the blast trauma severity scale (BTSS) for explosion-related injuries

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ABSTRACT

Aim: This study set out to develop and substantiate the concept of blastotrauma as a distinct category of traumatic pathology, to introduce the Blast Trauma Severity Scale (BTSS) for evaluating the severity of explosion-related injuries, and to show how the scale can be applied clinically in patients with combat-related trauma.

Materials and Methods: The study followed a retrospective observational design, drawing on archived clinical records of patients with combat-related injuries treated between 2023 and 2025. A total of 70 patients with blast and explosion-associated trauma qualified for inclusion. To enable consistent severity grading, the Blast Trauma Severity Scale (BTSS) was developed around five domains: soft tissue injury, bone injury, neurovascular injury, internal organ injury, and physiological response.

Results: The study introduces blastotrauma as a complex pattern of morphological and physiological damage arising when explosive energy is transferred to human tissues. The BTSS delivers an integrated severity score from 0 to 20 points, organised into four grades. Assessment can be further refined by appending the dominant blast-injury mechanism descriptor (P/S/T/Q). Applying the scale to the study cohort confirmed that consistent, standardized stratification of blast injuries is achievable in clinical practice.

Conclusions: The blastotrauma concept and the BTSS classification offer a practical framework for standardized description of explosion-related injuries, clinical stratification of patients, and continued research in trauma and military medicine.

KEY WORDS: combat trauma, military medicine, wound assessment

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INTRODUCTION

Modern armed conflicts have seen the extensive deployment of explosive devices, resulting in a large number of blast-related injuries. Such injuries are inherently complex, as they arise through several simultaneous mechanisms, including the pressure wave, fragmentation, blast wind displacement, and secondary environmental factors [1–3]. In clinical settings, they rarely present in isolation; combined injury patterns are the norm, resulting in diverse morphological changes and systemic disturbances. When explosive energy is transferred to human tissues, the resulting damage involves multiple organs and systems: barotrauma, fragment wounds, bone fractures, extensive soft tissue loss, internal organ injury, and systemic physiological compromise are all well documented [4–6]. This injury profile differs substantially from classical mechanical trauma, which necessitates classification and severity assessment approaches tailored specifically to blast injuries.

Injury severity in traumatology is commonly assessed using tools such as the Abbreviated Injury Scale (AIS) and the Injury Severity Score (ISS). However, these systems were developed for general trauma contexts and do not capture the specific mechanisms and pathophysiological features that define blast injuries [7–9].

Blast injuries have traditionally been grouped into four mechanisms: primary injuries from the pressure wave; secondary injuries caused by fragments; tertiary injuries from blast wind displacement of the body; and quaternary injuries such as burns and inhalation damage [2, 10–12]. When these forces act together, the resulting injury patterns are too complex for conventional scoring systems to adequately reflect. Given the distinctive mechanisms and specific clinical features of explosion-related trauma, treating these injuries as a separate category of traumatic pathology is well justified. Against this background, the present study pro-

poses the term "blastotrauma" to describe the complex injury spectrum produced by the transfer of explosive energy to human tissues. Without a unified severity assessment system, comparison of outcomes across studies of blast injury is difficult, and the development of standardised treatment protocols remains limited. To address this gap, the present study introduces the Blast Trauma Severity Scale (BTSS), a classification designed to improve consistency in the description of blast-related injuries and to support clearer clinical stratification of patients.

AIM

The study aimed to develop and substantiate the concept of blastotrauma as a distinct category of traumatic pathology, to introduce the Blast Trauma Severity Scale (BTSS) for grading the severity of explosion-related injuries, and to demonstrate its practical clinical application in a cohort of patients with combat-related trauma.

MATERIALS AND METHODS

The study used a retrospective observational design, analysing archived clinical records of patients who sustained combat-related injuries and received treatment between 2023 and 2025.

Data were obtained from electronic medical registries of patients with combat-related trauma. Each record contained information on the date of admission, mechanism of injury, clinical diagnosis, injury localisation, and therapeutic interventions performed.

Over the study period, 359 patients with combat-related injuries were recorded in the registry. From this cohort, 70 patients were identified whose records contained sufficient clinical detail to characterise injury type and severity and to apply the proposed classification system.

INCLUSION CRITERIA

Inclusion required all of the following:

1. presence of trauma sustained as a result of combat-related events;
2. availability of clinical information describing the injury;
3. sufficient data for the assessment of injury severity.

EXCLUSION CRITERIA

Patients were excluded if they had:

1. incomplete clinical data;
2. absence of information describing the injuries;
3. duplicated records within the registry.

TRAUMA SEVERITY ASSESSMENT

To bring consistency to blast injury evaluation, the Blast Trauma Severity Scale (BTSS) was developed. The scale covers morphological damage—soft tissue injuries, bone injuries, neurovascular injuries, and internal organ injuries—together with physiological disturbances, integrating both into a single assessment.

Each of the five domains is scored from 0 to 4 points, giving a maximum cumulative total of 20 points.

The total score maps onto four severity grades:

- Grade I (0-4 points) - mild injury;
- Grade II (5-8 points) - moderate injury;
- Grade III (9-13 points) - severe injury;
- Grade IV (14-20 points) - critical injury.

STATISTICAL ANALYSIS

Standard descriptive statistical methods were applied. Quantitative variables are reported as absolute values and relative frequencies (%). The analysis was designed to evaluate whether the proposed BTSS could be applied consistently and meaningfully to a real clinical cohort.

ETHICS

All work was carried out in compliance with the ethical principles of the Declaration of Helsinki of the World Medical Association for research involving human subjects. The study protocol was reviewed and approved by the Commission on Bioethical Expertise and Ethics of Scientific Research at Bogomolets National Medical University.

Because the study design was retrospective and relied entirely on archived clinical records, all patient data were fully de-identified and anonymised prior to analysis. No additional informed consent was required, as the study did not involve new interventions, prospective data collection, or the use of identifiable patient information beyond routine clinical documentation obtained during standard patient care.

RESULTS

CONCEPT OF BLASTOTRAUMA

Explosion-related injuries constitute a distinct and complex form of traumatic pathology arising from the transfer of explosive energy to human tissues. What distinguishes them from ordinary mechanical trauma is the concurrent action of multiple injury mechanisms, which together produce complex morphological and physiological damage patterns [1–3].

Four principal mechanisms are recognised: primary injuries from the blast wave; secondary injuries caused

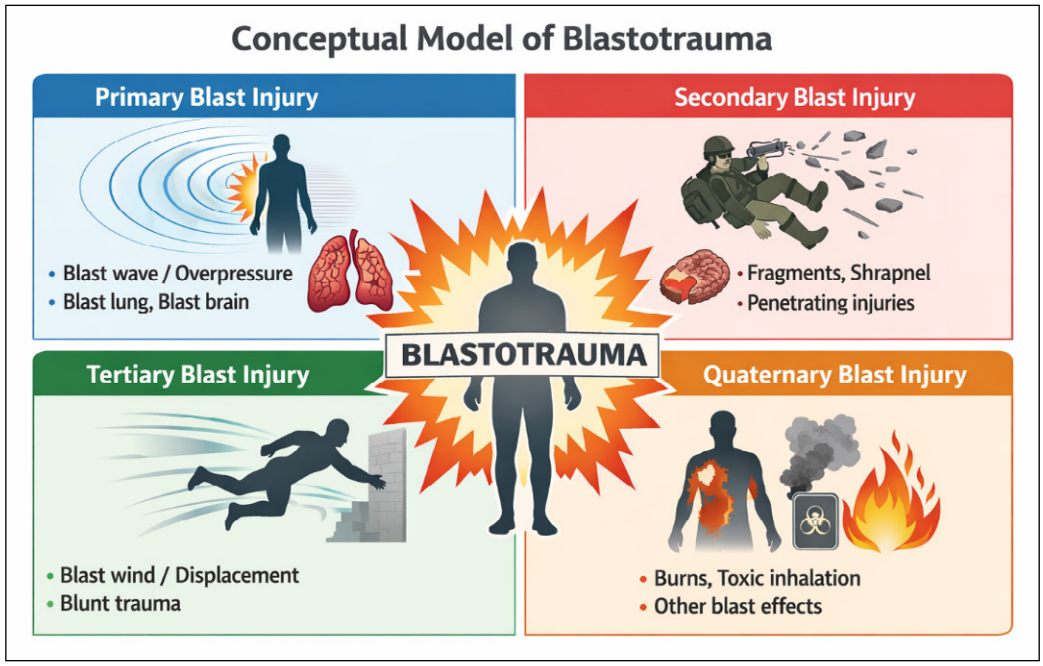


Fig. 1. Conceptual model of blastotrauma formation
Picture taken by the authors

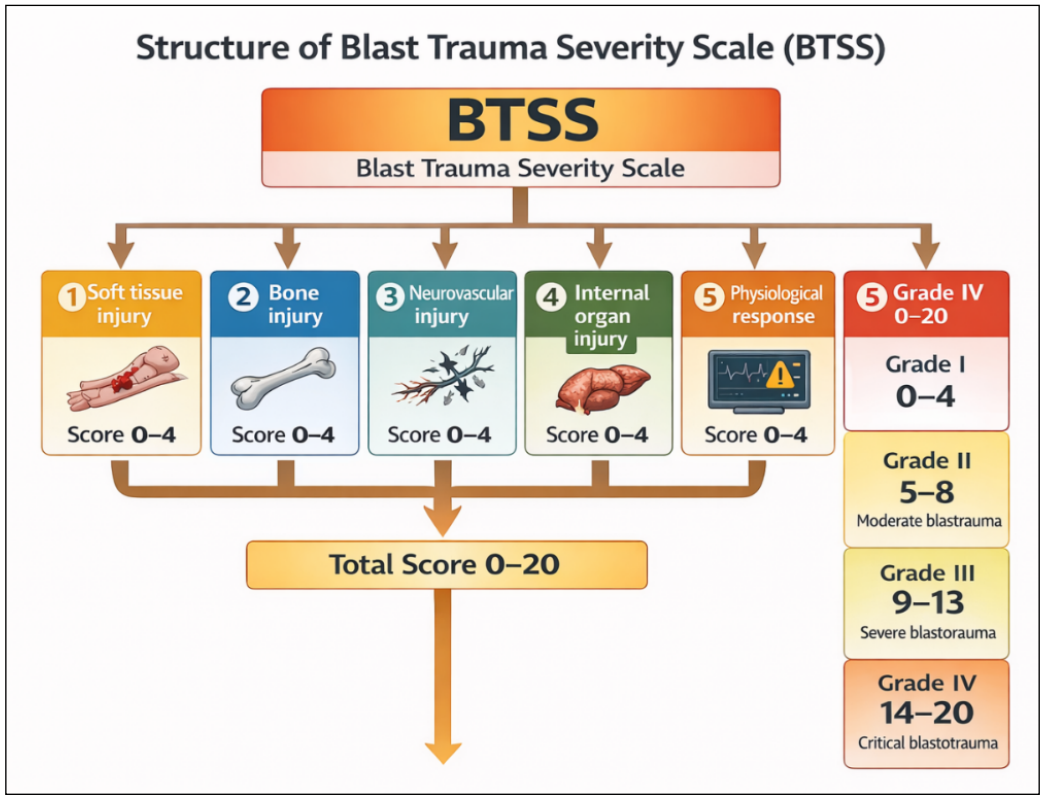


Fig. 2. Structure of the Blast Trauma Severity Scale (BTSS)
Picture taken by the authors

by fragments and debris; tertiary injuries resulting from body displacement by blast wind; and quaternary injuries, including burns, inhalation damage, and other environmental effects [2, 10–12].

Acting in combination, these mechanisms can produce virtually any combination of barotrauma, fragment wounds, bone fractures, extensive soft tissue defects, internal organ damage, and systemic physiological disturbance—a spectrum far broader than that observed in conventional trauma.

Given these specific mechanisms and the distinctive clinical presentation of explosion-related trauma, classifying such injuries as a separate category of traumatic pathology is well justified. The present study therefore introduces the term blastotrauma to denote the complex injury pattern produced when explosive energy interacts with human tissues through multiple simultaneous mechanisms.

Blastotrauma may accordingly be defined as a complex injury pattern arising from the interaction of multiple blast injury mechanisms, characterised by

Table 1. Blast Trauma Severity Scale (BTSS)

Domain	Score	Description
Soft tissue injury	0	No soft tissue injury
	1	Superficial wound
	2	Moderate soft tissue defect
	3	Extensive soft tissue damage
	4	Massive tissue destruction
Bone injury	0	No fracture
	1	Simple fracture
	2	Comminuted fracture
	3	Segmental fracture
	4	Critical bone defect
Neurovascular injury	0	No neurovascular injury
	1	Suspected injury
	2	Confirmed nerve injury
	3	Vascular injury
	4	Combined neurovascular injury
Internal organ injury	0	No internal organ injury
	1	Mild injury
	2	Moderate injury
	3	Severe injury
	4	Critical organ injury
Physiological response	0	Stable condition
	1	Mild physiological disturbance
	2	Moderate physiological disturbance
	3	Severe physiological compromise
	4	Critical physiological instability

Notes: Grade I - Mild blastotrauma (0-4); Grade II - Moderate blastotrauma (5-8); Grade III - Severe blastotrauma (9-13); Grade IV - Critical blastotrauma (14-20)

Source: compiled by the authors of this study

the coexistence of local morphological damage and a systemic physiological response.

Fig. 1 presents the conceptual model of blastotrauma formation.

BLAST TRAUMA SEVERITY SCALE (BTSS)

The Blast Trauma Severity Scale (BTSS) was developed to standardize the assessment of blast-related injuries. Rather than treating morphological damage and physiological disturbance as separate considerations, the scale combines both into a unified, integrated assessment.

The BTSS includes five domains:

1. soft tissue injury;
2. bone injury;
3. neurovascular injury;
4. internal organ injury;
5. physiological response.

Each domain is scored on a 0–4 scale, where 0 indicates the absence of the finding and 4 represents the most severe presentation. The scores across all five domains are summed, yielding a maximum possible total of 20 points.

Four severity grades are defined on the basis of the cumulative score:

- Grade I (0-4 points) - mild blastotrauma;
- Grade II (5-8 points) - moderate blastotrauma;
- Grade III (9-13 points) - severe blastotrauma;
- Grade IV (14-20 points) - critical blastotrauma.

To retain pathogenetic information about the blast event, the numerical score is supplemented with a descriptor identifying the dominant injury mechanism:

- P - primary blast injury;
- S - secondary blast injury;
- T - tertiary blast injury;
- Q - quaternary blast injury.

The combined notation brings both dimensions togeth-

Table 2. The dominant blast mechanism descriptors

Descriptor	Mechanism
P	Primary blast injury (blast wave)
S	Secondary blast injury (fragments and debris)
T	Tertiary blast injury (body displacement)
Q	Quaternary blast injury (burns, inhalation and other effects)

Source: compiled by the authors of this study

Table 3. Clinical characteristics of patients with combat-related blast and explosion-associated injuries

Variable	Value
Number of patients	70
Study period	2023–2025
Mechanism of injury	Blast and explosion-associated combat trauma
Combined injuries	Majority of patients
Soft tissue injuries	Frequently observed
Bone fractures	Common
Neurovascular injuries	Observed in part of patients
Internal organ injuries	Present in severe trauma cases
Physiological instability	Observed in severe trauma

Note: Data are presented as general characteristics of the studied cohort based on retrospective clinical records
Source: compiled by the authors of this study

Table 4. Distribution of patients according to Blast Trauma Severity Scale (BTSS) grades (n = 70)

BTSS Grade	Score Range	Severity of blastotrauma	Number of patients
Grade I	0–4	Mild blastotrauma	12
Grade II	5–8	Moderate blastotrauma	24
Grade III	9–13	Severe blastotrauma	22
Grade IV	14–20	Critical blastotrauma	12

Note: Severity grading is based on the cumulative score of the Blast Trauma Severity Scale (BTSS)
Source: compiled by the authors of this study

er in a single expression—for instance, S / 9 / Grade III indicates a secondary blast mechanism with a score of 9, classifying the injury as severe blastotrauma.

The full scoring structure of the BTSS is set out in Table 1.

MECHANISM DESCRIPTOR

Each BTSS score should be paired with the descriptor of the dominant blast mechanism (Table 2).

The structural overview of the BTSS is illustrated in Fig. 2.

CLINICAL CHARACTERISTICS OF PATIENTS

The cohort comprised 70 patients with combat-related blast and explosion-associated injuries treated during 2023–2025.

The injury profile was dominated by combined trauma involving varied combinations of soft tissue injuries, bone fractures, and internal organ damage.

The most common injury components were:

1. soft tissue injuries and defects;
2. fractures of long bones;
3. fragment-related wounds;
4. neurovascular injuries;
5. internal organ injuries.

Systemic physiological disturbances—most notably haemodynamic instability and respiratory compromise–were documented in a substantial proportion of patients.

The general characteristics of the study cohort are summarised in Table 3.

DISTRIBUTION OF PATIENTS ACCORDING TO BTSS GRADES

All 70 patients were assessed using the Blast Trauma Severity Scale (BTSS).

The distribution of injury severity across the cohort is presented in Table 4.

Table 5. Comparison of trauma severity scoring systems and the proposed BTSS classification

Characteristic	Abbreviated Injury Scale (AIS)	Injury Severity Score (ISS)	Trauma Score / TRISS	BTSS (proposed)
Type of assessment	Anatomical injury scale	Anatomical severity score	Physiological + anatomical prediction model	Integrated morphological and physiological assessment
Primary purpose	Classification of individual injuries	Overall trauma severity assessment	Prediction of survival probability	Assessment of blast-related trauma severity
Consideration of injury mechanism	No	No	Limited	Yes (P/S/T/Q descriptor)
Evaluation of soft tissue injury	Limited	Indirect	Limited	Direct assessment
Evaluation of bone injury	Yes	Yes	Indirect	Direct assessment
Evaluation of neurovascular injury	Limited	Limited	Limited	Direct assessment
Evaluation of internal organ injury	Yes	Yes	Yes	Direct assessment
Evaluation of physiological response	No	No	Yes	Yes
Applicability to blast injuries	Limited	Limited	Limited	Specifically designed for blastotrauma
Clinical simplicity	Moderate	Moderate	Complex	Simple

Source: compiled by the authors of this study

The use of the BTSS allowed clear stratification of all patients by injury severity. Patients with localised soft tissue injuries and limited fractures in the absence of significant physiological disturbance were typically assigned to Grade I or II. Those presenting with multiple fractures, extensive soft tissue damage, internal organ involvement, or neurovascular injury were classified as Grade III. Patients with massive combined injuries, marked physiological instability, or polytrauma were placed in Grade IV, corresponding to critical blastotrauma.

Appending the mechanism descriptor (P/S/T/Q) to the severity score integrates pathogenetic characterization of the blast event directly into the injury classification.

The BTSS can therefore support:

1. standardized assessment of blast injury severity;
2. clinical stratification of patients;
3. comparison of results between studies;
4. optimization of treatment planning.

DISCUSSION

Explosion-related injuries rank among the most complex forms of traumatic pathology, given the simultaneous action of multiple injury mechanisms and the resulting wide variability in clinical presentation. In contemporary armed conflicts, explosive devices are a leading cause of combat trauma, accounting for a growing proportion of patients with combined blast injuries [1–3, 17–20].

Blast injuries are defined by the concurrent action of several distinct mechanisms—the pressure wave, fragment wounds, blast wind displacement, and secondary environmental effects [2, 10–12]. When these forces combine, the resulting morphological and physiological injury patterns differ markedly from those observed in conventional mechanical trauma [21]. Against this background, the present study introduces the concept of blastotrauma as a distinct category of traumatic pathology. The concept reflects the complex nature of damage produced when explosive energy is transferred to human tissues through the simultaneous interaction of multiple blast injury mechanisms. A persistent challenge in traumatology is the lack of a severity assessment system specifically designed for blast injuries. Clinicians currently rely on instruments such as the Abbreviated Injury Scale (AIS) and the Injury Severity Score (ISS) [13–16], both of which were developed for general trauma and were not intended to capture the specific mechanisms of blast injuries [7–9].

Table 5 compares the most widely used trauma scoring systems with the proposed BTSS.

The BTSS introduced here bridges this gap by combining the evaluation of morphological damage with the assessment of systemic physiological responses in a single instrument. This integrated approach provides a more comprehensive picture of trauma severity than traditional scoring systems, which rely primarily on anatomical injury criteria. A notable strength of the scale is the P/S/T/Q mechanism descriptor: it preserves pathogenetic information about the blast event while simultaneously enabling severity-based patient stratification—an advantage not offered by existing general trauma scales.

In the study cohort, the BTSS successfully stratified blast injuries according to severity. The scale

demonstrates clear potential for standardised injury description, cross-study comparison of outcomes, and more structured clinical management of patients with blast trauma.

Certain limitations of this study must be acknowledged. The retrospective design and relatively small cohort size limit the generalisability of the findings. Prospective validation of the BTSS in larger and more diverse patient populations is required before wider clinical adoption can be recommended.

Despite these limitations, the blastotrauma concept and the BTSS classification represent an important initial step towards a standardised framework for describing and quantifying explosion-related injuries in both clinical and research settings.

CONCLUSIONS

1. Explosion-related injuries arise from a complex combination of injury mechanisms and produce a characteristic spectrum of morphological and physiological changes sufficiently distinct to justify recognition as a separate category of traumatic pathology, for which the term blastotrauma is proposed.
2. The study proposes a working definition of blastotrauma: a complex injury pattern produced when explosive energy is transferred to human tissues through the simultaneous interaction of multiple blast injury mechanisms.
3. The Blast Trauma Severity Scale (BTSS) introduced here integrates assessment of morphological damage and systemic physiological disturbances into a single instrument, enabling standardized grading of blast injury severity.
4. Pairing the BTSS numerical score with a dominant mechanism descriptor (P/S/T/Q) links severity grading to the pathogenetic characteristics of the blast event, adding clinical context that existing scales do not provide.
5. The BTSS classification is suitable for clinical stratification of patients with blast injuries, standardized documentation of injury patterns, and as a research instrument in trauma and military medicine.

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CONFLICT OF INTEREST
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CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

CONTENTS

Values of future healthcare specialists in wartime in Ukraine

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ABSTRACT

Aim: The aim of the study is to define the values typical for medical students by analysing the career choice motivations in wartime in Ukraine.

Materials and Methods: Overview, Data Retrieval and Thematic Analysis (Braun&Clarke) methods were used. The total of 45 students' essays were analysed in the study.

Results: The professional values of future healthcare specialists in Ukraine in wartime have been defined: restoring health, believing in recovery, recovering the joy of life, helping the military (rehabilitation students); alleviating suffering, respecting dignity, giving people hope, helping them overcome illness (medical students); supporting people who have experienced trauma, providing psychological support in life hardships (clinical psychology students); health and beauty care, volunteer dental care for the military (dentist students). It is established that the frequency of mentions in student essays about the *war* as a factor in the development of medicine in present Ukraine and the *military* who need assistance in restoring health/rehabilitation is quite the same as the frequency of mentions of the concept of "compassion" as an important professional value of future healthcare specialists.

Conclusions: To support and develop professional values of medical students (empathy, compassion), implementing courses that help improve awareness of the role of healthcare specialists in wartime into medical school curricula is recommended; as well as to cooperate with institutions that take care for socially vulnerable groups of the population and persons affected by war; and to expand the system of mental health support for students.

KEY WORDS: values, medical students, empathy, compassion, war, combat veteran

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INTRODUCTION

The characteristic features of the present development of the healthcare are the rapid development of innovative technologies in the field of reproductology, transplantology, genetics, the use of artificial intelligence, etc. on the one hand, and on the other hand, the need for a transparent quality control of professional medical care and the implementation of bioethical principles that ensure protection of dignity of an individual and their interests as a patient. In order to prevent abuse in healthcare and conflicts between a doctor and a patient/patient's relatives, the training process in medical universities should be managed according to the appropriate ideological principles and values.

The effectiveness of the formation of professional values of future healthcare specialists depends on the initial worldview priorities of medical students and proper modelling of their academic activity. The efforts of teachers of a medical university can influence the correction/formation/development of the values of students as individuals and as future healthcare specialists to some extent. Thus, the values already present in the context of career choice by the applicants for higher medical education should be defined in order to take these data into account when developing curricula and a system of educational activities. After all, each new generation of applicants is a "product" of a specific "era" that is expressed in the dominance of certain values, models of behaviour, individual and social ideals, lifestyle, principles of daily personal choice, as well as in the degree of awareness of the meaning of human life.

In this context, the issue of correlation of students' personal values and eternal moral values is urgent. World researchers emphasize the importance of moral values such as compassion and honesty in healthcare [1].

Using special reflective exercises, medical students can increase self-awareness/understanding and improve their ability to recognize situations in which conflicts may arise regarding their moral values and other personal values, which is likely to contribute to making moral decisions in clinical practice [1].

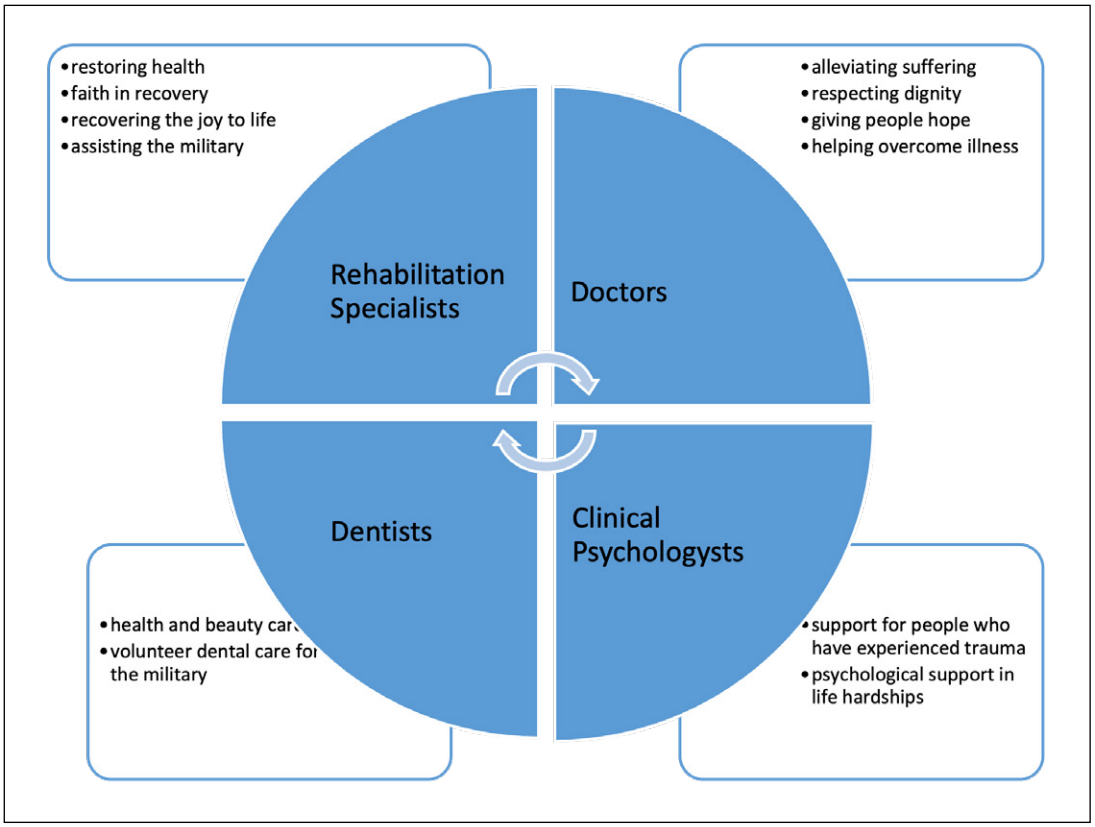


Fig. 1. Priority professional values of future healthcare specialists according to the results of the thematic analysis of student essays. *Figure designed by the authors*

Since medical university teachers work with the youth, "children of the time", there is a great need in understanding students and establishing cooperation with them to form a worthy personality of a future medical specialist. For Ukraine, which is currently fighting to protect its freedom and dignity in the war against the Russian aggressor, the issue of formation of professional values in medical students is really urgent. After all, the Ukrainian medical community faces a number of complex challenges that require rethinking approaches to medical care delivery in wartime. The basis for an adequate response to the needs of Ukrainian military and civilians in wartime is the hierarchy of professional values of medical specialists who save lives in the most challenging military settings. Considering that more than half a thousand doctors, nurses and other healthcare specialists died in the war against Russia [2], development of higher medical education and motivation of the young generation not to be afraid of military realities, but to choose a future career following their heart, as a form of service and a large part of the meaning of the life, is crucial for Ukraine.

AIM

The aim of the study is to define the values that are typical for medical students by analysing the motivations for their career choice in the wartime in Ukraine.

MATERIALS AND METHODS

To define the personal motivation of the career choice of future healthcare specialists, the research method of studying the written works (essays) of students justifying their individual choice in favour of the medical profession was used. The participants of the study were first-year students of the specialties of Medicine, Dentistry, Clinical Psychology, as well as second-year students of the specialty of Therapy and Rehabilitation, who entered Ternopil National Medical University during the third year of the full-scale war of Russia against Ukraine. Using the thematic analysis method (Braun & Clarke), 45 student essays have been studied and the priority professional values of future healthcare specialists have been defined that will contribute to the modification of curricula and modelling of educational tasks and activities for medical students.

RESULTS

According to the results of the thematic analysis of student essays, it has been established that the issue of personal career choice of young people living in Ukraine (with ongoing war) is much related to the challenges that the entire Ukrainian society is experiencing today. Substantiating their motivation to enter a medical university, the first-year students associate their future professional practice with the needs of their people,

who are defending their freedom and dignity in a war. Therefore, Ukrainian military and civilians do need professional medical care to save lives, as well as to restore physical and mental health. The main professional values of future healthcare specialists declared in students' essays have been defined and summarized (Fig. 1).

This is the way the future rehabilitation specialists expressed their desire to help patients restore their health, which, accordingly, recovers the joy of life. Since the war is ongoing in Ukraine, the first-year students defined giving a faith in recovery to those who suffered from military actions as a priority. In this context, helping the military after injuries/captivity is the most important. Please study a few quotes from the essays of future rehabilitation specialists:

"It was interesting for me to watch people recovering after injury and returning to a full life. I wish to be a rehabilitation specialist and help people. I chose Ukraine because medicine in Ukraine is also quite developed, and in wartime the efforts of a rehabilitation specialist is especially valuable because many people have injuries."

"My neighbour was seriously injured in the war, a broken pelvic bone. He is currently undergoing treatment, then rehabilitation. It is very valuable to me that he, like many of our soldiers, defends me, my family, my city. I also would like to be involved in some way in our victory over the enemy Russia, and this will be my professional assistance to wounded soldiers, to help them recover and have a more or less comfortable life again."

A sincere desire to help people restore their health motivated future rehabilitation specialists to enter a medical university:

"Since childhood, I have been interested in biology and studied well. In high school, I realized that I wished to help people. At first, I thought about being a psychologist, but when I studied human recovery, I first came across the specialty of Therapy and Rehabilitation. As it turned out, a physical therapist is a medical specialist, who helps restore and maintain the physical health of a patient.

When I decided on a career, I faced a question of choosing a university: medical or non-medical. I thought for a long time and researched the differences between institutions. It turned out that in some non-medical universities, physical therapist education is based mainly on sports training, not on the medical aspects of recovery, so I decided to choose a medical university. I hope that in the future I will become a physical therapist who helps people."

It is typical that future rehabilitation specialists do understand the problems which people with special needs face as if having been "in their shoes". A quote from the student's essay:

"My decision to enter a medical university was not made in one day. It was a long way of self-discovery and awareness of what I wish to do for the rest of my life. I have always been fascinated by the opportunity to help people by not only treating diseases, but also returning them the joy of full-fledged movement and active life. That is why I have chosen the specialty of Therapy and Rehabilitation. It combines profound medical knowledge with practical methods of patients' health restoration. I understood that this profession would require not only theoretical knowledge but also empathy, patience and constant self-development. Now, being a second-year student, I feel that I made the right choice. Every day brings new knowledge and confirms that medicine is my true calling. I dream of becoming a specialist who can restore people's faith in recovery and help them feel the joy of simple things that healthy people take for granted."

The results of the thematic analysis of essays written by future dentists demonstrate the students' desire to get a medical education in order to provide health and beauty care to their patients. The theses about the desire to provide volunteer (free) dental care to the military are really touching:

"A beautiful smile is very desirable by a modern person, especially women. And I wish to help people have such a beautiful and at the same time healthy smile. But this is not the only reason. It is unclear how long the war goes on, and the military need dental services and I would like to assist them professionally. I dream of contributing my share to volunteer activities as a dentist."

The analysis of the essays of future doctors has found out that students note several main values for which they strive to become a doctor. This is the desire to help a patient, alleviate their suffering, be attentive, compassionate and honest, respectful for the dignity of the patient, tolerant, and also give people hope, especially to the military, who have suffered as a result of military operations. In fact, many students associate their career choice with the desire to join the common cause of defending their native country.

Please see some quotes:

"I decided to become a doctor to be competent and able to help people. Firstly, I would like to give people joy in this way. Secondly, my goal is to contribute to the development of medicine in my country which suffers today due to war. I realize that it is challenging and even dangerous to be a doctor in our time, but my life will be meaningful about being able to help those defending us from the enemy."

"As for me, the profession of a doctor is the most important of all professions because only a doctor re-

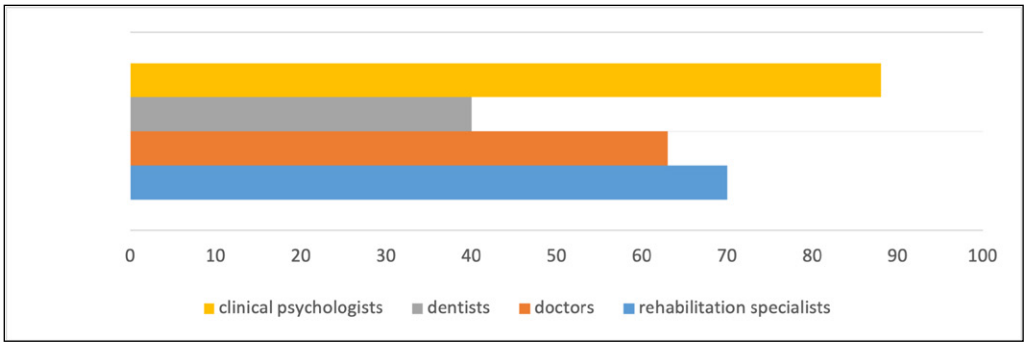


Fig. 2. Mentioning the value of "compassion" in student essays: quantitative analysis (%).
Figure designed by the authors

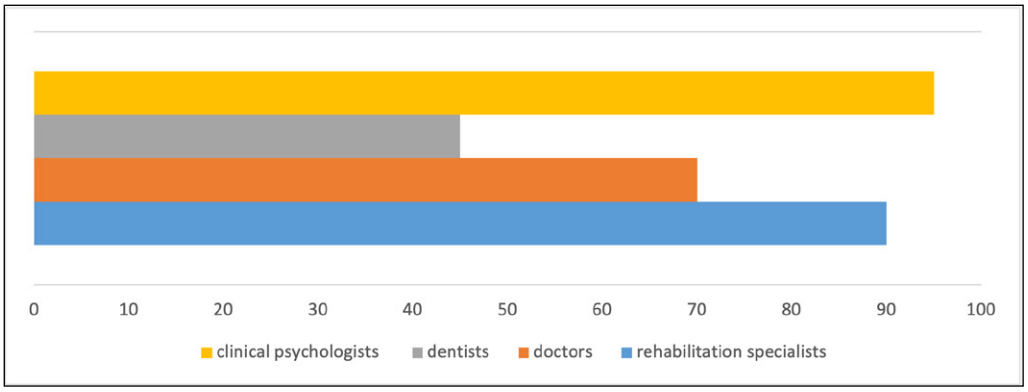


Fig. 3. Mentioning the concepts of "military"/"war" in student essays: quantitative analysis (%).
Figure designed by the authors

stores people's health and saves lives, especially now, during the war. I would like to contribute to the victory of Ukraine, to support the health of our defenders."

"I have decided to enter a medical university because I wish to help people and be valuable to society. I am interested in how the human body works, how diseases can be treated and pain can be alleviated. The profession of a doctor is a great responsibility, but at the same time an opportunity to save lives and support those in need. My motivation is to become an expert, constantly develop and do good to people."

"I have realized that I wish to dedicate my life to a meaningful profession that benefits people. I would like to learn not only to treat, but also to support, listen, explain and give faith in recovery to my future patients. Based on the example of my grandfather, who suffered from an illness for a long time and needed special care, I realize how important it is for our country to have doctors who are not only professionals, but also humanists. I will try to become one of them."

It should be noted that since 2025, an educational and professional program "Clinical Psychology" has been launched at I. Horbachevsky Ternopil National Medical University to train specialists in psychological counselling, diagnostics and mental health support. The results of the thematic analysis of student essays of future clinical psychologists indicate that the basic professional values for them are: support for people who have experienced trauma (primarily military personnel), and psychological care to people in life hardships.

Please study a few quotes:

"I would like to help those in hardships, support them in difficult situations and show that there is always light at the end of the tunnel. I would especially like to be beneficial to people who experienced stress, loss or other various challenges during the war, which has been going on for four years already. This is challenging, but my future profession of a clinical psychologist will help me deliver professional support for such people."

"I chose the career of a clinical psychologist but not a general practitioner because I believe that mental health is no less important than physical health. Clinical psychology allows understanding person's inner world more deeply, the causes of their anxiety, fear, stress, as well as psychosomatic disorders. My motivation involves the desire to support people in crisis situations, to heal with a word that can save the desperate."

"I decided to enter medical school because already in childhood I understood that helping people in difficult life situations is very important. Especially since my father is a military, and his service showed me what psychological burdens military personnel and their families face. This has prejudiced my career choice because I really wish to at least slightly reduce the pain that torments the souls of our defenders and their families after the war experience."

"My choice to become a clinical psychologist originates from my life experience. Nowadays, a lot of people in Ukraine need psychological support. Therefore, I think that I will be able to get a job and care for myself

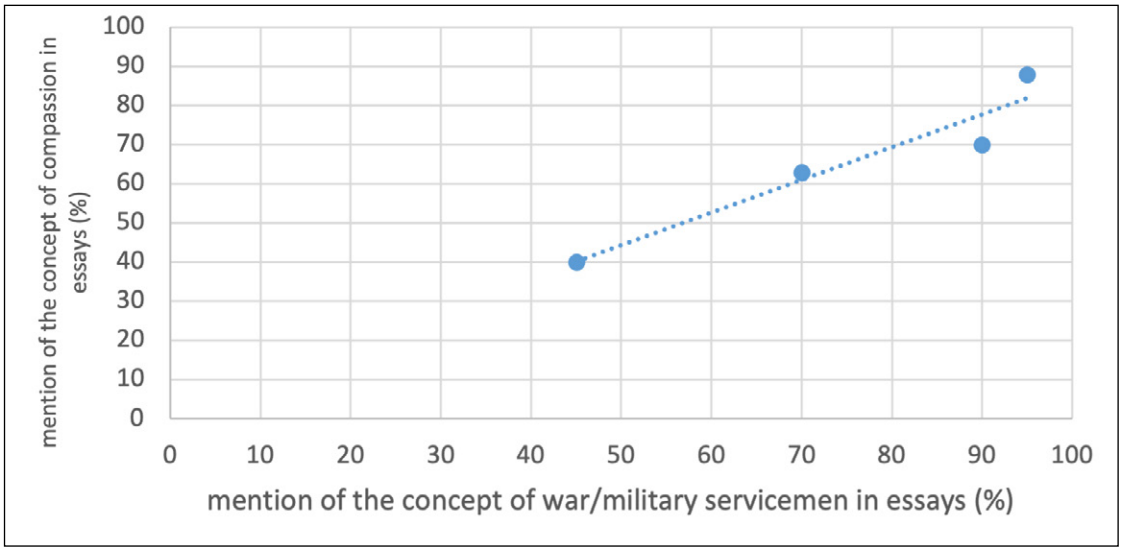


Fig. 4. Correlation between mention of the concepts of "war/serviceman" and "compassion". *Figure designed by the authors*

and my family in the future. I am already trying to support my relatives and friends, who often feel fear and anxiety because of the war. Studying at the university will help me do it professionally. The most important thing is our state of mind because our well-being depends on it."

"In my undergraduate studies, I plan to gain the necessary foundation so that in the future I can professionally recognise the causes of human internal conflicts and help resolve them. I believe that the profession of a clinical psychologist allows me becoming a reliable support for many people since mental health directly affects the quality of life and can even preserve it (I mean suicide prevention)."

Analysis of student essays was aimed at finding out whether they contain the concept of "compassion", which we interpret as one of the most important professional values of healthcare specialists, reflecting person's willingness and ability to feel and show emotions of understanding, benevolence and a desire to alleviate the pain/suffering of another person. The issue of studying this professional value is urgent owing to its increased significance as well as the frequent cases of a recent destructive model of behaviour of doctors, who show callousness/indifference rather than compassion for the patient (students spoke about such cases when studying the topic of "The rights of a patient" during the classes of Medical Law).

According to the results of the thematic analysis of student essays (Fig. 2), it was established that the most common meaning of the concept of "compassion" is found in the essays of future clinical psychologists (88%) that is explained by the high level of understanding of the specific features of the chosen profession. It implies compassion as an essential condition for the effective work of a clinical psychologist, who works with a delicate category, the human soul, which is extremely vulnerable. Future rehabilitation specialists (70%) are the second regarding the frequency of mentioning the concept of "compassion" that is associated with the acceptance of the fact of cooperation with patients with injuries, loss of limbs, impaired body functions due to war, and this involves compassionate attitude and sincere desire to help those affected.

A total of 63% of future doctors mentioned compassion in their essays as a value of the chosen profession that is explained by a decreased relevance of the compassionate attitude of general practitioners compare to clinical psychologists and rehabilitation specialists, who work mainly with socially vulnerable population. In addition, 40% of future dentists mentioned the concept of "compassion" in their assays usually drawing attention to the need for professional dental care for the military and internally displaced persons.

Actually, the aim was to find out how often the students participating in our study would mention the concept of "serviceman"/"war" in their essays taking into account that they chose the medical profession during the third year of the war of Russia against Ukraine,. The results of the thematic analysis are presented in Fig. 3.

Thus, it was found out that almost all clinical psychologists (95%) wrote in their essays about the war as an objective factor in the development of contemporary medicine in Ukraine and the increased demand for their chosen profession. Three students noted that the war directly affected their families (their father or other relatives were defenders of the Armed Forces of Ukraine) and this became the key motive for their desire to become a clinical psychologist. Almost the same number of rehabilitation specialists (90%) mentioned the concept of "serviceman"/"war" when justifying their career choice. They also gave examples of their friends

who had suffered in military operations and need professional rehabilitation. Apparently, such life stories were especially motivating for the students. Among the doctors who wrote essays, 70% of the authors mentioned servicemen as future patients whom they would like to help improve their health and "alleviate suffering". And less than half of dentists (45%) described their career choice mentioning the need to provide dental services to military personnel; 4 students expressed a desire to provide volunteer care to the servicemen of the Armed Forces of Ukraine.

The results of the thematic analysis indicate a correlation between the mention of the concepts of "war/serviceman" and "compassion" in student essays (Fig. 4).

The analysis of the data obtained has proved that the frequency of mentioning the war as a factor in the development of medicine in present Ukraine and military personnel who need help in restoring health/rehabilitation is almost the same as the frequency of mentioning the concept of "compassion" as an important professional value of future healthcare specialists. Thus, the students associate the concept of "compassion" with those future patients who defend the Ukrainian state with weapons in their hands today. This is facilitated, in particular, by the distribution of videos on social networks (students use them much today) about seriously wounded military personnel who are constantly admitted into military hospitals and clinics in various cities of Ukraine.

DISCUSSION

Our study reflects the characteristic features of future healthcare specialists training in Ukraine in wartime on the one hand, and on the other hand it is related to typical problems of the development of higher medical education in Europe and the world at the beginning of the 21st century. Thus, the issue of forming an adequate system of values for future healthcare specialists when human dignity and compassion are priorities for the doctor (including the clinician lecturer) regardless of the social status, nationality or religious beliefs of the patient/student, is urgent for contemporary healthcare. As reported by medical students, unprofessionalism and prejudice have significantly affected their wellbeing and trust in the medical profession. They felt demoralized, anxious or indifferent to the environment where they were exposed to unprofessional behaviour or prejudiced attitudes [3]. Comprehending this matter responsible institutions should create an environment where medical students are inspired to embody the values of diversity, equality and inclusion, and to manage the complex psychosocial factors and cultural influences in order to change the current culture of patient care [3].

According to the research results, Ukrainian medical students pay special attention to the needs of people with injuries, impaired body functions, loss of limbs due to war, etc. Mostly this is about military personnel, but in other countries, medical students also need to develop communication skills and form an inclusive culture. Present researchers emphasize it as well pointing to the need to cultivate respect for the dignity of people with disabilities. For example, a specific aim of teaching rehabilitation nursing is to help students respond to people with deformities and disabilities in a way that conveys belief in their dignity and value [4]. This educational objective specifically reflects the aims of contemporary medical education in Ukraine where a huge number of military personnel and civilians are victims of war not only physically but also mentally hurt.

To understand such patients, compassion for them and a desire to help them are essential. In the developed countries with no war, the desire to help another person decreases, as claimed by present researchers [5]. Therefore, they emphasize the indispensable role of the humanities and arts, which help in the formation of a humanistic worldview of physicians, since they allow doctors to understand patients in their holistic context. They also reflect a huge range of attitudes necessary for the formation of ethics and professionalism, and illustrate complex moral choices. Life stories and narratives enhance emotions and, thus, lay the foundation for the transmission of concepts [5]. These theses are confirmed by the results of our study: the students who wrote essays about examples from the lives of specific individuals, military personnel, noted their compassion and desire to help people, whose physical and mental health was affected due to the war.

One of the special methods of development of a humane personality of a doctor is to involve students in a ceremony in honour of body donors who altruistically donated their bodies that allows studying anatomy through dissection [6]. In this context, Ukrainian students develop the humanistic values, in particular, by paying tribute to fallen soldiers who died at the frontline. They do this every day at 9 a.m. during a minute of silence to give tribute to the soldiers, who gave their lives for Ukraine in the ongoing war.

Considering recent studies of changes in the level of empathy of medical students, which usually decreases during training (junior students show a higher level of empathy than senior students) [7], medical university teachers should improve the methodology for development of a system of professional values of students, among which empathy and compassion are prioritized.

In the era of digitalization of the training process, it

is important not to forget creative writing as a method of developing empathy and compassion. A number of present researchers confirm its effectiveness [8, 9]. Thus, Hatem et al. share the positive experience of introducing an elective course "Creative Writing for Medical Students", which gave students the opportunity to write and discuss the challenges and specific issues they face during their professional training as doctors (this involves the boundaries of medicine, death and dying, anticipating future challenges and identifying with a patient, etc.) [8]. By the way, the students of Ternopil National Medical University also have the opportunity for reflection within the framework of the elective course "Academic Writing", and teachers (in particular A. Vykhrushch, a co-author of this article) can thus find out students' concerns, followup their views on the current issues of student youth and medicine.

Indeed, reflective writing is effective for improving the ethical understanding of palliative care in the context of medical education. The results of the study by Lopane et al. have confirmed that nursing students (after watching a film about terminal illness and endoflife decision-making) show in their written reflections an increased awareness of ethical dimensions, such as patient autonomy, vulnerability, and the value of nonverbal communication [9]. The results of our study on the desire of Ukrainian medical students to serve people, in particular the victims of war, also confirm the effectiveness of creative writing for increasing the students' awareness of professional values already at the beginning of their training at a medical university.

In addition, modern researchers point to cinema as a separate pedagogical tool for development of empathy as a basic professional value of future health care specialists. Thus, Arora et al., studying the influence of cinema on the education of dental students, has found out that the results of film education are: increased understanding and practice of empathy, improved ability to recognize and respond to patients' emotions and appreciate different points of view [10]. The positive perception and acceptance of films with educational potential by students proves a high possibility of integrating this pedagogical tool into the curriculum. By the way, the students of Ternopil National Medical University are also periodically invited to watch films, in particular about doctors (i.e., "Giuseppe Moscatti: Love that Heals", "The Good Doctor"), the value of human support ("Train on December 31") that contribute to the development of empathy, compassion and selfsacrifice of future healthcare specialists, especially during the war in Ukraine. This is happening within the framework of the Cinema Evenings project initiated by the university student creative team in order to increase students' motivation to improve their professional development via the example of famous doctors.

In this context, the experience of developing a comprehensive program with an approach to compassion based on awareness that meets this need is very interesting [11] and the Compassionate University project, which informs, trains and mobilizes students and professionals to develop networks of care for people at the end of life [12], so that compassion as a value goes beyond professional competencies, and care for people spreads beyond the university. The students of Ternopil National Medical University also have the opportunity to develop their communication skills and improve empathy within the framework of the university's cooperation with the "House of Mercy of Saint Veronica", where elderly women left without care in difficult life circumstances receive care by nuns. Such experience is very relevant, because, as recent research shows, elderly people who are also a socially vulnerable group (poor, lonely, etc.) are in great need of support in obtaining medical information and forming health-promoting behaviour [13].

A specific aspect of this problem is the self-esteem of medical students and its development. We agree with researchers [14] who emphasize the need to develop the training programs and educational activities in a medical university that contribute to the development of professional values of self-compassion and moral courage, as well as the protection of mental health of future healthcare specialists. Such an approach is very important for organization of the training in medical universities in Ukraine in wartime. Thus, a Mental Health Center has been launched at Ternopil National Medical University, where students can receive group or individual professional support from psychologists and psychotherapists. Taking into account that crises may be an opportunity for the moral development of the individual [15], war as a global crisis is the external factor that prompts serious intrapersonal transformations of Ukrainian students. As future healthcare specialists they get a unique experience of moral self-development in order to survive and help other people stand, not break, in the tragic realities of war.

CONCLUSIONS

The results of the study show the need to support and develop the values of empathy and compassion in first-year and second-year medical university students with a high level of acceptance of these values in the context of their career choice motivation. The defined correlation between war as an external factor and compassion as a professional value of future doctors

encourages the implementation of courses into medical university curricula that contribute to improving awareness of the role of healthcare specialists in war. Since students, who mentioned the experience of their military relatives or friends in their essays, wrote more emotionally and empathetically, it is worth using these cases when teaching clinical and humanitarian disciplines in order to increase the compassionate attitude of future doctors. Cooperation with institutions that care for socially vulnerable groups of the population, as well as expanding the system of mental health support for students, especially in times of war, are promising areas of educational affairs of a medical university in Ukraine and other countries.

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CONFLICT OF INTEREST

The Author declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

The processing of pro-inflammatory cytokines in post-traumatic stress disorder: Inflammation as a central mechanism in PTSD pathophysiology

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ABSTRACT

Post-traumatic stress disorder (PTSD) is a severe psychiatric condition associated with persistent emotional dysregulation, cognitive impairment, and structural alterations in limbic and prefrontal brain regions. Growing evidence indicates that chronic inflammation and abnormal processing of pro-inflammatory cytokines are central components of PTSD pathophysiology. Activation of the NOD-like receptor family pyrin domain containing 3 inflammasome (NLRP3) and caspase-1 promotes the proteolytic maturation of pro-interleukin-1β (pro-IL-1β) and pro-interleukin-18 (pro-IL-18) into their active forms, amplifying neuroinflammatory signaling. Sustained microglial activation and disrupted neuron–microglia–astrocyte communication contribute to synaptic dysfunction and impaired neuroplasticity. In parallel, dysregulation of the hypothalamic–pituitary–adrenal axis (HPA axis) interacts with inflammatory pathways, leading to altered stress responses and persistent immune activation. Clinical studies have demonstrated associations between circulating inflammatory mediators, including IL-18 and IL-1β, and the severity of emotional inhibition, sleep disturbances, and maladaptive coping strategies in PTSD. Moreover, inflammatory activity has been linked to volumetric and microstructural changes in the hippocampus, amygdala, and prefrontal cortex observed in chronic PTSD. These findings support the concept that the processing of pro-inflammatory cytokines is a central mechanism in PTSD rather than a secondary consequence of stress exposure. Understanding the molecular pathways underlying cytokine maturation and neuroimmune signaling may contribute to improved biomarker-based diagnostics and the development of targeted therapeutic interventions.

KEY WORDS: inflammation; interleukin-1β; interleukin-18; microglia; NLRP3 inflammasome; post-traumatic stress disorder

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INTRODUCTION

Post-traumatic stress disorder (PTSD) is a chronic psychiatric condition that develops after exposure to severe traumatic events and is characterized by intrusive recollections, avoidance, negative changes in cognition and mood, and persistent hyperarousal. In addition to psychological symptoms, PTSD is associated with measurable neurobiological and immunological alterations. Increasing evidence indicates that chronic low-grade inflammation contributes to symptom maintenance and long-term disease progression [1].

Neuroimaging studies have demonstrated structural and functional abnormalities in the hippocampus, amygdala, and prefrontal cortex in individuals with PTSD. These regions are central to fear processing, memory consolidation, and emotional regulation. In parallel, elevated peripheral and central levels of pro-inflammatory cytokines, including interleukin-1β (IL-1β) and interleukin-18 (IL-18), have been reported. These findings support the concept that immune signaling pathways interact with stress-related neural circuits [2].

At the molecular level, activation of the NOD-like receptor family pyrin domain containing 3 inflammasome (NLRP3 inflammasome) has been proposed as a key mechanism linking psychological stress with immune activation. Assembly of this multiprotein complex leads to activation of caspase-1 and proteolytic maturation of pro-interleukin-1β and pro-interleukin-18 into their active forms, thereby amplifying inflammatory signaling. Sustained microglial activation and disturbed neuron–glia communication may impair synaptic plasticity and contribute to persistent symptoms [3, 4].

Furthermore, dysregulation of the hypothalamic–pituitary–adrenal axis (HPA axis) alters the balance between stress hormones and immune responses, potentially promoting glucocorticoid resistance and prolonged inflammation. Clarifying the mechanisms of cytokine processing and neuroimmune interaction is essential for understanding PTSD pathophysiology and for identifying clinically relevant biomarkers and therapeutic targets [5, 6].

AIM

The aim of this review is to critically summarize and integrate current evidence on the role of pro-inflammatory cytokine processing in the pathophysiology of PTSD, with particular emphasis on inflammasome activation, cytokine maturation, neuroimmune interactions, and their clinical relevance. Special attention is given to the NLRP3 inflammasome, caspase-1-dependent processing of interleukin-1β and interleukin-18, neuron–microglia–astrocyte crosstalk, and HPA axis dysregulation as interconnected mechanisms contributing to chronic neuroinflammation in PTSD. In addition, the review discusses the diagnostic and therapeutic implications of inflammatory biomarkers and highlights potential directions for future translational and biomarker-guided research.

MATERIALS AND METHODS

This article is a narrative review based on a structured analysis of the current literature concerning inflammatory mechanisms in post-traumatic stress disorder (PTSD), with particular emphasis on the processing of pro-inflammatory cytokines, inflammasome activation, neuroimmune signaling, and structural brain alterations associated with chronic stress exposure.

A literature search was conducted using major biomedical databases, including PubMed, Scopus, and Web of Science. The search strategy included combinations of the following keywords: "PTSD", "post-traumatic stress disorder", "inflammation", "neuroinflammation", "cytokines", "interleukin-1β", "interleukin-18", "NLRP3 inflammasome", "caspase-1", "microglia", "astrocytes", "HPA axis", "ER stress", "hippocampus", "amygdala", and "prefrontal cortex". Additional relevant articles were identified through manual screening of reference lists from selected papers.

Priority was given to peer-reviewed original studies, systematic reviews, meta-analyses, and high-quality review articles published in English, with particular focus on papers published between 2016 and 2025. Earlier studies were also included when they were considered fundamental for understanding the molecular and neurobiological basis of cytokine maturation and inflammasome signaling.

The inclusion criteria comprised studies addressing at least one of the following topics: (1) inflammatory and immune mechanisms in PTSD, (2) molecular pathways involved in the maturation of pro-inflammatory cytokines, especially IL-1β and IL-18, (3) activation and regulation of the NLRP3 inflammasome, (4) neuron–microglia–astrocyte interactions in stress-related neuroinflammation, (5) relationships between inflammatory markers and clinical manifestations of PTSD, and (6) structural or microstructural brain changes associated with inflammatory activity in PTSD.

Studies unrelated to PTSD or not directly addressing cytokine processing, neuroinflammation, or stress-related neuroimmune alterations were excluded. Non-peer-reviewed reports, conference abstracts without sufficient methodological detail, and articles lacking clear relevance to the topic were also omitted.

The selected literature was analyzed qualitatively and organized into thematic sections addressing molecular cytokine processing, glial and neuronal interactions, clinical correlates of inflammatory activation, chronicity-related brain alterations, and diagnostic or therapeutic implications. The purpose of this approach was to provide an integrative and clinically relevant overview of evidence supporting inflammation as a central mechanism in PTSD pathology.

REVIEW AND DISCUSSION

MOLECULAR MECHANISMS OF PRO-INFLAMMATORY CYTOKINE PROCESSING IN PTSD

Chronic psychological stress activates innate immune pathways that promote the production and maturation of pro-inflammatory cytokines. In PTSD, increasing evidence indicates that dysregulated cytokine processing contributes to persistent neuroinflammation and symptom maintenance. The maturation of IL-1β and IL-18 is a central event in this process [7].

One of the principal pathways responsible for cytokine maturation involves the NOD-like receptor family pyrin domain containing 3 inflammasome. This multiprotein complex is composed of the sensor molecule NLRP3, the adaptor protein apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC), and pro-caspase-1. Its activation generally requires two sequential signals. The priming signal is initiated by pattern recognition receptors, including Toll-like receptors, and leads to enhanced transcription of NLRP3 and pro-interleukin-1β (pro-IL-1β) through nuclear factor kappa B (NF-κB) signaling. The second signal is triggered by cellular stressors such as mitochondrial dysfunction, generation of reactive oxygen species, potassium efflux, or extracellular adenosine triphosphate release. These stimuli induce assembly of the inflammasome complex and subsequent activation of caspase-1 [8, 9].

Active caspase-1 cleaves pro-IL-1β and pro-IL-18 into their biologically active forms, enabling their secretion. These cytokines amplify inflammatory signaling,

enhance microglial activation, and influence neuronal function. IL-1β modulates synaptic plasticity and long-term potentiation, while IL-18 has been associated with stress reactivity and emotional regulation. Persistent activation of this pathway may therefore contribute to impaired fear extinction, heightened arousal, and cognitive disturbances observed in PTSD [10].

In addition to inflammasome signaling, endoplasmic reticulum stress pathways interact with inflammatory mechanisms. Activation of inositol-requiring enzyme 1 (IRE1) and activating transcription factor 6 (ATF6) may enhance inflammatory gene expression and further promote cytokine production. Crosstalk between cellular stress responses and immune signaling supports a sustained pro-inflammatory state within the central nervous system [3, 11].

Microglia play a central role in this process. Under chronic stress conditions, microglia shift toward a pro-inflammatory phenotype characterized by increased cytokine release and reduced support for synaptic remodeling. Disrupted communication between neurons, microglia, and astrocytes may impair neuroplasticity and structural integrity in stress-sensitive brain regions.

Together, these molecular mechanisms demonstrate how altered processing of pro-inflammatory cytokines can link psychological trauma with sustained neuroinflammation and functional brain changes in PTSD [12].

NEURON–MICROGLIA–ASTROCYTE CROSSTALK IN PTSD - RELATED NEUROINFLAMMATION

Post-traumatic stress disorder (PTSD) is associated with persistent alterations in communication between neurons and glial cells. The interaction between neurons, microglia, and astrocytes is essential for maintaining central nervous system (CNS) homeostasis. Under chronic stress conditions, this balance becomes disrupted, leading to sustained neuroinflammation and impaired synaptic function [13].

Microglia are the principal immune effector cells of the CNS. In response to stress-related signals and increased levels of pro-inflammatory cytokines, microglia shift toward a pro-inflammatory phenotype characterized by enhanced production of IL-1β, IL-18, and tumor necrosis factor-α (TNF-α). Activated microglia also release reactive oxygen species (ROS) and nitric oxide (NO), which may contribute to neuronal damage. Prolonged activation disrupts synaptic remodeling and reduces trophic support for neurons [14, 15].

Astrocytes regulate neurotransmitter clearance, maintain blood–brain barrier (BBB) integrity, and provide metabolic support. During inflammatory activation, astrocytes undergo reactive changes and increase secretion of cytokines and chemokines, which further amplify microglial activation. This process strengthens inflammatory signaling in limbic regions involved in fear processing and emotional regulation.

Neurons actively participate in immune signaling through the release of damage-associated molecular patterns (DAMPs) and neurotransmitters that modulate glial activity. Excessive glutamatergic transmission may enhance microglial activation and promote excitotoxicity, while reduced gamma-aminobutyric acid (GABA) signaling further destabilizes neural networks [16, 17].

Disrupted neuron–glia communication leads to impaired long-term potentiation (LTP), altered dendritic spine density, and reduced neuroplasticity in the hippocampus and prefrontal cortex. Elevated pro-inflammatory cytokines are also associated with decreased hippocampal neurogenesis. These changes contribute to memory disturbances, emotional dysregulation, and impaired fear extinction in PTSD.

Persistent dysregulation of neuron–microglia–astrocyte interactions sustains a self-perpetuating inflammatory environment within the CNS. Restoration of neuroimmune balance may represent an important therapeutic target in PTSD [18, 19].

PRO-INFLAMMATORY CYTOKINES AND CLINICAL MANIFESTATIONS OF PTSD

Pro-inflammatory cytokines play a significant role in linking immune activation with the clinical symptoms of PTSD. Elevated concentrations of IL-1β, IL-18, IL-6, and TNF-α have been reported in individuals with PTSD. These mediators influence neuronal signaling, synaptic plasticity, and neuroendocrine regulation, thereby contributing to emotional and cognitive disturbances [20, 21].

IL-1β is involved in the modulation of synaptic transmission and long-term potentiation. Excessive IL-1β activity impairs hippocampal plasticity and may disrupt memory consolidation and contextual processing. This mechanism may contribute to intrusive recollections and impaired fear extinction. IL-1β also interacts with the HPA axis, influencing cortisol secretion and stress responsiveness [22].

IL-18 has been associated with increased stress sensitivity and emotional dysregulation. Elevated IL-18 levels correlate with the severity of hyperarousal and avoidance symptoms. Through its interaction with inflammatory and stress-related signaling pathways, IL-18 may amplify neuroimmune responses and reinforce persistent symptomatology [23].

IL-6 exerts both pro- and anti-inflammatory effects but is frequently elevated in chronic stress conditions.

Table 1. Inflammatory pathways in PTSD: molecular mechanisms, neurobiological effects, and clinical correlates

Cytokine / pathway	Mechanism of activation	Neurobiological effect	Structural brain changes	Clinical correlates
IL-1β	NLRP3 inflammasome activation; caspase-1 cleavage	Impaired LTP; reduced neurogenesis	Hippocampal volume reduction	Intrusive memories; impaired fear extinction
IL-18	Inflammasome-dependent maturation	Increased stress sensitivity; microglial activation	Amygdala hyperreactivity	Hyperarousal; avoidance
IL-6	NF-κB-mediated transcription	Altered synaptic signaling; fatigue-related mechanisms	Limbic dysconnectivity	Sleep disturbance; cognitive impairment
TNF-α	Modulation of glutamatergic and GABAergic transmission	Increased excitatory tone; endothelial activation	Fronto-limbic imbalance	Emotional instability
HPA axis dysregulation	Glucocorticoid resistance; persistent immune signaling	Sustained inflammatory state	Prefrontal cortical thinning	Chronic symptom persistence
ER stress (IRE1, ATF6)	Amplification of inflammatory gene expression	Enhanced cytokine production	Microstructural alterations	Emotional dysregulation

Source: Compiled by the authors of this study

Increased IL-6 levels have been linked to sleep disturbances, fatigue, and cognitive impairment. Chronic exposure to IL-6 may alter synaptic function and contribute to reduced neuroplasticity in limbic structures [24].

TNF-α modulates glutamatergic and GABAergic neurotransmission. Elevated TNF-α levels may enhance excitatory signaling and reduce inhibitory control, leading to increased arousal and emotional instability. TNF-α also promotes endothelial activation and may affect blood–brain barrier integrity, further facilitating neuroinflammatory processes [25].

Inflammatory cytokines are not only peripheral markers but also active modulators of brain function. Their sustained elevation may contribute to structural changes observed in the hippocampus, amygdala, and prefrontal cortex. Chronic inflammatory signaling may therefore represent a biological substrate underlying symptom persistence and disease chronicity [26].

Associations between cytokine levels and clinical features such as emotional inhibition, maladaptive coping strategies, and sleep quality suggest that immune markers may have diagnostic and prognostic value. Understanding the relationship between pro-inflammatory cytokines and clinical manifestations may support the development of targeted interventions aimed at reducing inflammation and improving functional outcomes in PTSD [27].

The relationship between cytokine maturation, neurobiological alterations, and clinical manifestations in PTSD is summarized in Table 1.

CHRONICITY OF PTSD AND STRUCTURAL BRAIN ALTERATIONS

The duration of PTSD is associated with progressive neurobiological changes that may reflect sustained inflammatory and stress-related mechanisms. Chronic exposure to elevated pro-inflammatory cytokines and persistent dysregulation of the HPA axis can influence brain structure and microarchitecture, particularly in regions involved in memory, emotional regulation, and executive control [28].

Neuroimaging studies have consistently demonstrated volumetric reductions in the hippocampus in individuals with long-standing PTSD. The hippocampus is highly sensitive to stress hormones and inflammatory mediators. Prolonged exposure to IL-1β, IL-6, and IL-18 may impair neurogenesis and synaptic plasticity, leading to decreased dendritic complexity and neuronal loss. These changes are associated with deficits in contextual memory processing and impaired fear extinction [29, 30].

The amygdala, a key structure in threat detection and emotional reactivity, may show altered functional connectivity and, in some cases, volumetric changes depending on illness duration. Chronic inflammatory signaling can enhance excitatory neurotransmission and reinforce hyperresponsiveness within amygdala circuits, contributing to persistent hyperarousal and exaggerated stress responses [31].

The prefrontal cortex, particularly the medial and dorsolateral regions, plays a central role in top-down regulation of emotional responses. Structural and microstructural alterations in this region have been linked to impaired inhibitory control over limbic structures. Sustained neuroinflammation, microglial activation, and oxidative stress may disrupt white matter integrity and synaptic organization, further weakening regulatory circuits [32, 33].

Diffusion tensor imaging studies suggest that chronic PTSD is associated with reduced white matter coherence

Table 2. Potential therapeutic targets and intervention strategies related to neuroinflammation in PTSD

Therapeutic target	Proposed intervention	Expected biological effect	Current limitations
NLRP3 inflammasome	Direct or indirect inhibition of NLRP3 signalling	Reduced maturation of IL-1β and IL-18 and attenuation of downstream inflammatory responses	Limited evidence from PTSD-specific clinical studies
Oxidative stress and mitochondrial dysfunction	Antioxidant strategies and interventions supporting mitochondrial function	Reduced generation of reactive oxygen species and decreased inflammasome activation	Variable efficacy and limited biomarker-guided evidence
HPA-axis dysregulation	Interventions aimed at restoring glucocorticoid sensitivity and neuroendocrine balance	Improved regulation of stress responses and reduced immune activation	Considerable heterogeneity in endocrine profiles among patients with PTSD
Microglial activation	Modulation of pro-inflammatory microglial activity	Reduced neuroinflammatory signalling and improved synaptic support	Lack of selective, microglia-specific therapeutic approaches
Sleep disturbance	Behavioural and pharmacological interventions aimed at improving sleep quality	Reduced inflammatory burden and improved neuroplasticity	Bidirectional relationship between sleep disturbance and PTSD severity
Physical inactivity	Structured physical activity and exercise-based programmes	Improved inflammatory regulation, neuroplasticity, and stress resilience	Differences in adherence, intensity, and treatment response
Glutamatergic and GABAergic imbalance	Restoration of excitatory–inhibitory neurotransmitter balance	Reduced excitotoxicity and secondary inflammatory amplification	Underlying mechanisms remain incompletely understood
ER stress pathways	Modulation of IRE1- and ATF6-dependent signalling	Reduced expression of inflammatory genes and cytokine production	Predominantly preclinical evidence and limited treatment specificity

Source: Compiled by the authors of this study

in fronto-limbic pathways. These microstructural abnormalities may reflect long-term inflammatory effects on axonal integrity and myelination. The interaction between inflammatory mediators and stress hormones likely accelerates these structural changes over time.

Importantly, the severity and duration of PTSD symptoms appear to correlate with both biomarker levels and neuroimaging findings. This relationship supports the hypothesis that chronic immune activation contributes to progressive brain alterations rather than representing a transient response to trauma [34].

Understanding the link between inflammatory processes and structural brain changes may provide clinically relevant information regarding prognosis and therapeutic timing. Early modulation of inflammatory pathways may reduce the risk of long-term neurobiological consequences in PTSD.

DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS OF NEUROINFLAMMATION IN PTSD

Recognition of neuroinflammation as a central component of PTSD has important diagnostic and therapeutic implications. Elevated levels of pro-inflammatory cytokines, including IL-1β, IL-18, IL-6, and TNF-α, may serve as measurable biological indicators of immune activation. When interpreted alongside clinical assessment, these biomarkers may improve risk stratification and support a more precise characterization of disease subtypes [35].

Peripheral inflammatory markers may reflect central immune processes, particularly when associated with microglial activation and BBB alterations. Combined evaluation of cytokine profiles, stress-related hormones, and markers of oxidative stress may provide a more comprehensive understanding of the neuroimmune state in individual patients. Such an approach may help identify patients at risk of chronicity, cognitive decline, or poor response to conventional therapy [36].

Therapeutically, modulation of inflammatory pathways represents a potential strategy in PTSD management. Targeting the NLRP3 and related signaling cascades may reduce maturation of IL-1β and IL-18 and attenuate downstream inflammatory effects. Although specific inflammasome inhibitors are still under investigation, indirect strategies such as reducing oxidative stress and stabilizing mitochondrial function may decrease inflammasome activation [37, 38].

Regulation of the HPA axis is also relevant. Interventions aimed at restoring glucocorticoid sensitivity may limit excessive immune activation. In addition, non-pharmacological strategies, including structured physical activity and sleep normalization, have been shown to influence inflammatory markers and improve neuroplasticity.

Understanding the interaction between inflammatory signaling and neurotransmitter systems, including glutamatergic and GABA pathways, may further refine treatment approaches. Reducing excessive excitatory activity and supporting inhibitory balance may indirectly limit neuroinflammatory amplification.

A biomarker-guided approach could facilitate personalized treatment planning, integrating psychotherapeutic, pharmacological, and lifestyle interventions. Continued investigation of neuroimmune mechanisms is necessary to clarify which patients may benefit most from anti-inflammatory strategies and to determine optimal timing of intervention in the course of PTSD [39, 40].

Potential therapeutic targets related to inflammatory signaling pathways in PTSD are presented in Table 2.

CONCLUSIONS

Current evidence indicates that the processing of pro-inflammatory cytokines is a central mechanism in the pathophysiology of PTSD. Activation of the NOD-like receptor NLRP3 and subsequent maturation of IL-1β and IL-18 contribute to sustained neuroinflammatory signaling. This process interacts with dysregulation of the HPA axis, microglial activation, and impaired neuron–glia communication.

Persistent inflammatory activity influences synaptic plasticity, neurogenesis, and structural integrity in the hippocampus, amygdala, and prefrontal cortex. These alterations provide a biological substrate for emotional dysregulation, intrusive memories, hyperarousal, and cognitive impairment. The association between cytokine levels and clinical features supports the relevance of immune markers in understanding disease heterogeneity and chronicity.

Neuroinflammation in PTSD should not be considered a secondary epiphenomenon but rather an integral component of disease mechanisms. The interaction between cellular stress pathways, inflammatory mediators, and neuroendocrine regulation forms a complex network that sustains symptom persistence.

Integration of inflammatory biomarkers with clinical and neuroimaging findings may improve diagnostic precision and facilitate individualized treatment strategies. Targeting inflammatory signaling pathways, restoring neuroimmune balance, and modulating stress-related mechanisms may represent promising directions for future therapeutic development.

Further translational and longitudinal studies are necessary to clarify causal relationships, identify reliable biomarkers, and determine whether early intervention in inflammatory pathways can prevent long-term structural and functional brain changes in PTSD.

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CONFLICT OF INTEREST

The Author declares no conflict of interest

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CREATIVE COMMONS 4.0

REVIEW ARTICLE

CONTENTS

Assessment of the potential for the implementation of geographic information systems in the public health system of Ukraine

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ABSTRACT

Aim: To synthesize current evidence on the use of Geographic Information Systems (GIS) in public health surveillance, with emphasis on digital health integration, spatial epidemiology, and decision support for infectious disease monitoring.

Materials and Methods: A narrative review approach was applied based on the analysis of recent peer-reviewed studies, policy documents, and reports from international health organisations. Sources included research on spatiotemporal disease mapping, digital epidemiology, and GIS-based surveillance systems. The review focused on applications of GIS in infectious disease tracking, health system planning, data integration platforms, and the digital transformation of public health infrastructure. A comparative analysis of methodological approaches and technological frameworks was conducted to identify trends, strengths, and limitations in current practice. The analysis utilized data from the international bibliographic database Scopus, PubMed, international repositories and public health atlases (Global Health Observatory, ECDC Surveillance Atlas of Infectious Diseases), the central eHealth database, as well as relevant regulatory and legal documents. Particular attention was given to publications and reports covering the period 2020-2025.

Conclusions: GIS technologies significantly enhance public health surveillance by enabling real-time visualization, improved spatial analysis, and better-informed decision-making. Integration of GIS with digital health systems and data infrastructures strengthens early warning capabilities and supports evidence-based interventions. However, challenges remain regarding data quality, interoperability, privacy protection, and unequal technological capacity across regions. Further development of standardized frameworks and ethical guidelines is required to ensure the effective and sustainable implementation of geospatial technologies in public health systems.

KEY WORDS: Geographic Information Systems; Public Health

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INTRODUCTION

In the context of the ongoing transformation of Ukraine's public health system, driven both by global challenges (including the rising prevalence of chronic non-communicable diseases, the impact of climate change, and the threat of emerging infectious diseases) and the consequences of the full-scale war, there is an increasing demand for tools capable of providing comprehensive, timely, and evidence-based monitoring of population health status and associated risk factors. Among such tools, Geographic Information Systems (GIS) play a pivotal role. In leading countries worldwide, GIS have long been integrated into epidemiological surveillance, population health analysis, healthcare service planning, and public health risk management [1, 2].

GIS enable the integration of medical, demographic, socio-economic, and environmental data within a spatial framework, thereby facilitating the identification of disease distribution patterns, high-risk population groups, territorial inequalities in access to healthcare services, and the influence of external determinants on population health. Spatial analysis, which underpins GIS methodology, provides significant opportunities for the early detection of health threats, forecasting disease dynamics, and optimizing decision-making processes in prevention and response strategies [3].

International experience demonstrates that GIS constitutes a core component of modern epidemiological surveillance and population health monitoring systems. For instance, in the United States, GIS technologies are integrated into the programs of the Centers for Disease Control and Prevention (CDC); in the European Union, they are applied within the European Centre for Disease Prevention and Control (ECDC); and in Canada, Australia, and South Korea, GIS are embedded in national digital platforms for risk assessment and public health

emergency management [4-6]. Most of these systems combine geospatial data with electronic health records, environmental information, and social determinants of health, significantly enhancing the accuracy and timeliness of public health responses.

For Ukraine, which is actively developing its public health system in accordance with World Health Organization (WHO) and European Union (EU) standards [7, 8], the integration of GIS into national health monitoring is not only a promising direction but also a necessity. The combination of geospatial technologies with existing state health registries, eHealth data, the National Geospatial Data Infrastructure, and information on risk factors creates a foundation for an effective, analytically oriented disease prevention system. This, in turn, can substantially improve the quality of public health decision-making, enhance preventive planning, and ensure evidence-based management of healthcare resources.

AIM

The aim of the study is to provide a comprehensive assessment of the potential for implementing GIS in the national public health system of Ukraine as a critically important tool for transforming the health monitoring framework and transitioning toward a risk-based model of disease prevention.

To achieve this aim, the following objectives were set:

1. To analyse the national needs of Ukraine and identify systemic limitations of the current population health monitoring model that could be addressed through a GIS component.
2. To examine the regulatory and legal framework governing the implementation of spatial technologies in Ukraine and assess its alignment with international standards.
3. To evaluate the existing technological capacity, including an analysis of available medical and environmental data sources suitable for integration into a Health GIS.
4. To conduct a comprehensive assessment of the technical feasibility, financial viability, and organizational readiness of the national healthcare system for GIS implementation.
5. To identify key implementation risks of GIS (in particular, issues of geoprivacy and data fragmentation) and develop evidence-based recommendations for their mitigation.

MATERIALS AND METHODS

The study is based on an analytical review and assessment of the scientific and technical potential for implementing GIS in the public health system. The analysis utilized data from the international bibliographic database Scopus, PubMed, international repositories and public health atlases (Global Health Observatory, ECDC Surveillance Atlas of Infectious Diseases), the central eHealth database, as well as relevant regulatory and legal documents. Particular attention was given to publications and reports covering the period 2020-2025.

ETHICS

This study represents an analytical assessment of the potential implementation of technologies based on a systematic review of publicly available scientific data published in peer-reviewed journals, international strategic guidelines, and official databases. The review is grounded in the analysis of verified sources and the applicable regulatory framework. All sources of information are appropriately cited and properly listed in the references. No patient-identifiable data were used, no new clinical interventions were conducted, and no primary collection of personal data was performed. Therefore, approval from a local ethics committee was not required.

FRAMEWORK

This study was conducted using state budget funding under Contract No. DZ/166-2025 dated 12.02.2025 between the Ministry of Education and Science of Ukraine and the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute", within the framework of the research and development project under the state order entitled "Development of a Methodology for Disease Prevention Based on Population Health and Risk Factor Monitoring" (State Registration No. 0125U001020, term: 2025-2026).

REVIEW AND DISCUSSION

The establishment of a modern public health system in Ukraine in accordance with the Law of Ukraine "On the Public Health System" No. 2573-IX dated 06.09.2022 [9] envisages a transition from predominantly descriptive morbidity statistics to analytical, risk-oriented monitoring focused on inequalities and territorial variations. The Law explicitly defines population health monitoring, assessment of risk factors, and early detection of threats as core functions of the public health system. However, it does not provide detailed methodological guidance regarding spatial analysis tools or the integration of geospatial data into routine epidemiological surveillance.

In parallel, the Law of Ukraine "On the National Geospatial Data Infrastructure" No. 554-IX (2020) [10] establishes the legal foundation for the development of a unified national geospatial infrastructure. Nevertheless, the healthcare sector currently utilises these capabilities only fragmentarily. As a result, there remains a significant gap between the needs of the public health system and the actual level of implementation of geoinformation technologies, which highlights the substantial potential for GIS adoption.

The systemic limitations of the current population health monitoring model in Ukraine include the following:

1. Fragmentation of medical and statistical data. Data on morbidity, mortality, risk factors, and socio-demographic characteristics are stored across multiple information systems (eHealth, MoH registries, National Health Service of Ukraine databases, Public Health Centre systems, State Statistics Service, and departmental geoportals). This fragmentation complicates integrated analysis. Spatial referencing (address, coordinates, administrative unit) is often missing or inconsistent, which prevents the construction of comprehensive risk maps.
2. Lack of a systematic spatial component in morbidity analysis. Individual studies in Ukraine have demonstrated the high informativeness of spatial-temporal analysis – for example, research on territorial differences in cause-specific mortality, which revealed significant regional and subregional disparities [11]. However, such approaches are not integrated into routine national surveillance systems.
3. Insufficient spatial resolution of risk assessment. Existing statistical reports are mainly aggregated at the regional level, and less frequently at the community level. This masks local "hotspots" characterized by elevated disease incidence or concentration of risk factors. International evidence emphasizes that without GIS-based approaches, it is not possible to adequately assess the spatial heterogeneity of epidemic processes and health determinants [12, 13].
4. Limited timeliness of outbreak response. Modern surveillance systems in the EU and WHO member states rely on near real-time monitoring with dynamic spatial visualization of infectious diseases (e.g., ECDC Surveillance Atlas of Infectious Diseases; WHO global platforms) [4, 14, 15]. In Ukraine, outbreak information is often disseminated in textual reports without interactive cartographic representation, which delays the localisation and targeted response measures.
5. Insufficient integration of health data with environmental and socio-economic indicators. Although geospatial infrastructure for environmental monitoring is being developed (including air pollution maps and agricultural burden assessments), these datasets are rarely integrated with health indicators within a unified analytical environment [13].
6. New challenges associated with the full-scale war. The WHO emphasizes that in emergency and conflict settings, rapid spatial analysis of risks, population displacement, infrastructure damage, and healthcare accessibility is critical [16]. In Ukraine, such approaches are applied only sporadically (e.g., in projects assessing damaged healthcare facilities), despite the systemic need for comprehensive implementation.

Key needs that can be addressed by GIS include the following:

1. Real-time monitoring of infectious diseases. International reviews covering 2020–2025 demonstrate that GIS became a fundamental tool of epidemiological surveillance during the COVID-19 pandemic, enabling visualization of disease spread, modelling of spatiotemporal dynamics, and assessment of intervention effectiveness [13, 17]. Spatial analysis is applied both to conventional disease mapping and to more advanced approaches, such as wastewater-based epidemiology, where GIS is integrated with mathematical models for early detection of viral circulation [18].

In study [19], the application of GIS for COVID-19 monitoring in Morocco enabled the identification of high-risk spatial clusters and the delineation of priority zones for public health interventions. Such approaches are directly relevant for Ukraine, where seasonal and emerging infectious disease threats persist (influenza, measles, poliomyelitis, zoonoses, and infection patterns associated with population displacement).

For Ukraine, the GIS potential in this area includes the development of national outbreak maps with real-time updates based on eHealth and laboratory information systems, spatiotemporal analysis, and integration of infectious disease data with population mobility and infrastructure indicators.

2. Spatial analysis of non-communicable diseases (NCDs). A range of studies from 2020–2025 highlights the effectiveness of GIS in examining spatial patterns of non-communicable diseases, particularly cardiovascular, oncological, and respiratory conditions [13]. In Ukraine, a notable example is the analysis of spatial variation in cause-specific mortality, which revealed substantial differences in risk across regions and subregional territories [11].

GIS enables the identification of territorial clusters with elevated NCD incidence or mortality; the analysis

of associations between NCDs and socio-economic determinants (income, employment, urbanization) as well as environmental factors; and the targeting of preventive interventions (screening programs, smoking cessation initiatives, blood pressure control, etc.).

The development of Health Inequality Data Repositories and WHO global platforms further emphasizes the importance of a spatial dimension in health inequality assessment, which is highly relevant for adaptation in Ukraine [14, 15].

3. Mapping environmental risks (air, water, radiation) and their health impacts. Geospatial technologies are widely used to assess the effects of air, water, and soil pollution on population health, including the analysis of strong associations between pollutant concentrations and hospitalization or mortality rates [13, 17]. In Ukraine, regional air quality mapping initiatives already exist; however, these data are rarely integrated with health statistics.

GIS enables the overlay of environmental pollution layers (air quality, water contamination, radiation levels) with disease distribution maps; the assessment of spatial associations between environmental risks and specific nosological entities; and the consideration of consequences of industrial accidents and military activities (destruction of chemical facilities and water supply infrastructure).

4. Healthcare infrastructure planning and service accessibility. The application of GIS in analysing healthcare accessibility (distance- and time-to-care) is a well-established practice in EU countries. For example, study [20] demonstrates how spatial analysis of healthcare facility distribution and transport accessibility can optimize service placement and identify underserved areas.

For Ukraine, this is particularly relevant due to the uneven distribution of the healthcare infrastructure between urban and rural areas; the destruction of healthcare facilities as a result of armed conflict; and the large-scale internal population displacement.

GIS can support the modelling of the optimal placement of primary care units, hospitals, and mobile medical points; the analysis of transport accessibility using isochrone-based travel time mapping; and the assessment of workload distribution across healthcare facilities.

5. Support for biosafety and biosecurity systems. Reviews of geospatial technologies in infectious disease surveillance indicate that GIS is a key tool not only for routine epidemiological monitoring but also for managing biological threats, including emerging and re-emerging infections [12, 13]. Geovisualization of national infectious disease alert systems, as demonstrated in European interactive tools (European Notifiable Diseases Interactive Geovisualization, ENDIG), facilitates system readiness assessment, identification of surveillance gaps, and simulation of response scenarios [21].

For Ukraine, which is developing its national biosafety system in line with European integration priorities and the International Health Regulations, the implementation of GIS-based modules in early warning systems represents a logical step.

6. Analysis of war-related health impacts and territorial inequalities in healthcare access. In the context of prolonged military aggression, the ability to map damaged and destroyed healthcare facilities, assess accessibility of services in frontline and de-occupied areas, and analyse spatial patterns of trauma, psychosocial consequences, and war-related morbidity becomes critically important.

WHO-recommended approaches for surveillance in emergency settings explicitly emphasize the use of geospatial data for risk assessment and intervention planning [15, 17]. When combined with the National Geospatial Data Infrastructure, this provides a foundation for developing specialized GIS modules for monitoring the public health consequences of war.

The analysis of Ukraine's public health needs demonstrates that the implementation and development of a GIS component is not merely a technological innovation but a necessary condition for transitioning towards a risk-oriented, spatially sensitive system of population health and risk factor monitoring. This is consistent with both national regulatory frameworks [9, 10] and contemporary international approaches of WHO, the EU, and leading countries to data-driven, geospatially enabled public health systems.

REGULATORY AND LEGAL FRAMEWORK FOR GIS IMPLEMENTATION IN UKRAINE

The development of Geographic Information Systems (GIS) in the field of public health in Ukraine is based on both national legislation and international strategic frameworks of digital health transformation. The regulatory and legal environment defines the legitimacy of data collection, processing, integration, and spatial visualization of medical and related datasets, while also establishing requirements for personal data protection, interagency interoperability, and data standardization [9, 10, 22-24].

A comparison of Ukrainian legislation with international frameworks indicates substantial potential, but also reveals existing gaps in the formal institutionalization of GIS as a core public health instrument. At the

Table 1. Comparative analysis of international frameworks and the Ukrainian regulatory environment in relation to digital health and GIS

Aspect	WHO: Global Strategy on Digital Health 2020–2025	EU: INSPIRE and related directives	Ukraine: current legal framework
Vision of digital health	Comprehensive strategy integrating digital technologies, including surveillance, data analytics, and decision support; emphasis on governance, ethics, and infrastructure	Creation of a unified spatial data infrastructure ensuring interoperability of geospatial data across sectors, including environment and health	Separate legal acts on public health, geospatial data, and eHealth; partial strategic elements exist, but no dedicated national digital health strategy with a clearly defined GIS component
Regulation of geospatial data	Emphasis on data as a shared resource; recommendations for integration of spatial data into monitoring systems without detailed technical specifications	Clearly defined data sets, metadata standards, and data access services applied across multiple sectors	The Law on the National Geospatial Data Infrastructure establishes general principles; however, sector-specific (health) geospatial standards and integration protocols remain insufficiently developed
Ethical and legal aspects of digital surveillance	Specific guidance on ethical issues in public health surveillance, including GIS use; focus on balancing public benefit and privacy protection	Regulatory focus primarily on technical and organizational standards; ethical aspects addressed in complementary policy documents	Personal data protection is regulated by general legislation; specific ethical frameworks for spatial epidemiological surveillance have not yet been codified
Integration of GIS into public health	Recommended as an effective tool for epidemiological surveillance, outbreak control, risk assessment, and inequality analysis	Widely applied in environmental monitoring, food safety, and One Health risk assessment systems	GIS use in public health remains largely project-based and fragmented; legislation does not formally establish GIS as a mandatory component of health monitoring systems

Source: compiled by the authors of this study

international level, key reference frameworks include the WHO Global Strategy on Digital Health 2020–2025, the INSPIRE Directive 2007/2/EC, and various guidelines on the use of digital technologies in epidemiological surveillance [24-26]. A comparative overview is presented in Table 1.

Thus, the current regulatory and legal framework in Ukraine provides the general enabling conditions for the implementation of GIS in public health; however, further harmonisation with international standards is required. Priority directions for improvement include the formalisation of spatial data requirements within sectoral health standards; the development of protocols for geocoding, anonymisation, and aggregation of health-related geodata for surveillance and analytics; the integration of medical data into the National Geospatial Data Infrastructure using INSPIRE-compliant standards; and the incorporation of GIS as a core component of national digital health strategies in line with WHO, EU, and other leading international recommendations.

THE ASSESSMENT OF THE POTENTIAL FOR GIS IMPLEMENTATION IN THE NATIONAL PUBLIC HEALTH SYSTEM

The assessment of the technical feasibility of implementing GIS in Ukraine's public health system should be based on the analysis of three key components: availability of digital data, the capacity for their integration into a geoinformation environment, and human resource potential.

First, in recent years, Ukraine has developed an extensive digital healthcare infrastructure. The Electronic Health System (eHealth) accumulates billions of electronic medical records, registries of healthcare facilities, physicians, medical services, and contracts with the National Health Service of Ukraine. Its architecture, data standards, and regulatory framework are described in detail in [27]. This indicates that a substantial volume of primary data suitable for spatially oriented analytics already exists in digital form.

Second, the Law of Ukraine "On the National Geospatial Data Infrastructure" No. 554-IX (2020) and the development of the national geoportal provide both legal and technical prerequisites for integrating health-related data into a standardized geospatial data infrastructure [10]. The concept of Spatial Data Infrastructure (SDI) for healthcare, presented in [28], demonstrates that linking electronic health records with SDI frameworks is a logical direction for the evolution of public health systems in many countries.

Third, international literature emphasises that effective use of GIS in public health requires interdisciplinary teams, including epidemiologists, biostatisticians, GIS analysts, and software developers. Reviews of GIS applications in surveillance highlight the institutionalization of the role of spatial epidemiologists within modern public health systems [12]. In Ukraine, human capacity in digital medicine and geoinformatics exists,

as evidenced by publications on spatial health analysis and digital transformation of healthcare [29, 30]; however, this expertise remains fragmented and is not yet concentrated within a unified institutional framework.

Overall, the technical feasibility of GIS implementation in Ukraine's public health system is assessed as high, due to the existing digital and geospatial infrastructure, provided that targeted investments are made in medical data geocoding and workforce development.

The financial feasibility of GIS implementation in public health is considered through the balance between system development and maintenance costs and the potential savings achieved through improved prevention efficiency, reduced outbreak scale, and optimised infrastructure utilization.

Several studies have demonstrated that GIS-based approaches in immunization programme planning and mobile healthcare delivery can be cost-effective. Reviews of digital tools for surveillance and outbreak response in African countries [31] show that well-designed digital surveillance systems, including GIS components, can be scalable and relatively low-cost, particularly when based on open-source software and cloud-based solutions [32]. Furthermore, study [33] emphasizes that GIS provides a structured and cost-efficient framework for managing complex surveillance datasets, thereby improving the overall performance of public health systems.

For Ukraine, where the public health regulatory framework is defined by the Law "On the Public Health System" No. 2573-IX and the digital transformation of healthcare has already been implemented on the basis of the eHealth system, GIS implementation can be viewed as an investment in more efficient resource allocation, including reducing excess hospital-bed capacity, targeting preventive programmes to high-risk areas, and optimising patient referral pathways [9, 27, 29].

Organizational readiness for GIS implementation is determined by the degree of institutional capacity to integrate spatial analytics into routine monitoring and management processes.

At the regulatory level, the Law of Ukraine "On the Public Health System" establishes population health monitoring, risk assessment, and early threat detection as core functions, thereby providing a legitimate framework for the use of analytical tools, including GIS [9]. The Law "On the National Geospatial Data Infrastructure" defines principles of openness, interoperability, and accessibility of geospatial data, which are essential for intersectoral collaboration in the health domain [10].

The WHO Global Strategy on Digital Health 2020–2025 emphasizes that successful implementation of digital technologies requires alignment of financial, organizational, human, and technological resources [25]. Analysis of Ukraine's digital health system shows that coordination mechanisms for eHealth governance have already been established; however, the integration of spatial data has not yet been defined as a distinct policy priority [27, 29].

Accordingly, organizational readiness can be assessed as partial, since:

- basic institutions (the Public Health Centre of the Ministry of Health, the Ministry of Health of Ukraine, and the National Health Service of Ukraine) exist and can act as both users and commissioners of GIS solutions;
- a regulatory framework supporting digitalization and geospatial infrastructure is in place;
- however, there is no dedicated national strategy or roadmap for Health GIS development, and no designated leading institution responsible for coordinating spatial epidemiology and analytics.

The implementation of GIS in public health is associated with several risks that must be systematically assessed and mitigated:

1. Confidentiality and geoprivacy. Contemporary studies on GIS ethics and digital surveillance highlight increasing risks of privacy breaches when publishing or sharing georeferenced health data. Research [34, 35] and systematic reviews on medical data privacy [36, 37] demonstrate that even anonymized datasets can be re-identified through spatial attributes, and that patients exhibit high sensitivity regarding privacy concerns. Modern geomasking approaches offer technical solutions for protecting geoprivacy while preserving analytical utility [38].
2. Data fragmentation and quality issues. Reviews of GIS applications in epidemiological surveillance indicate that heterogeneity of formats, lack of geocoding standards, and inconsistent data quality represent key barriers to GIS implementation, particularly in health systems undergoing transition [12, 39]. In Ukraine, where health, environmental, and infrastructure data are stored across multiple institutions, the risk of fragmentation is particularly pronounced.
3. Lack of standardization and intersectoral interoperability. Although the National Geospatial Data Infrastructure law formally establishes unified geodata principles, their practical implementation in the health sector remains limited. The absence of standardized data exchange protocols between the Ministry of Health, the Public Health Centre, the National Health Service, the Ministry of Environmental Protection, the State Emergency Service, and other agencies significantly restricts the analytical value of GIS for population health monitoring [10, 28].

4. Organizational inertia and workforce limitations. The introduction of spatial analytics requires transformation of governance processes—from static reporting to interactive dashboards and from episodic analytical reports to continuous spatiotemporal monitoring. Digital health transformation studies emphasize that without investment in user training and changes in organizational culture, digital tools remain underutilized [25, 29, 30].

In summary, the potential for GIS implementation in Ukraine's national public health system can be assessed as high in terms of technical and financial feasibility, and moderate in terms of organisational readiness. The main risks—primarily confidentiality, data fragmentation, and lack of standardisation—are manageable provided that targeted regulatory and institutional support is introduced, in line with WHO recommendations on digital health development and international approaches to Public Health SDI frameworks.

CONCLUSIONS

Based on the results of the conducted study on the potential for implementing Geographic Information Systems (GIS) in the national public health system of Ukraine, the following conclusions were formulated:

1. A critical need for GIS technologies has been identified to address systemic limitations of the current monitoring model, primarily data fragmentation and the lack of systematic spatial analysis. It has been established that the transition to risk-based epidemiological surveillance is not feasible without geovisualisation tools that enable the identification of disease "hotspots" and ensure timely response to public health threats, particularly under conditions of martial law.
2. The analysis of the regulatory and legal framework confirmed the existence of an adequate legal basis (Laws No. 2573-IX and No. 554-IX) for the development of a digital health ecosystem. However, the need for further harmonisation of national standards with international frameworks (WHO, INSPIRE) has been identified, particularly regarding the formalisation of requirements for medical data geocoding.
3. The assessment of technological capacity demonstrated the readiness of the national digital infrastructure for integration. The availability of a substantial dataset within the Electronic Health System (eHealth), together with the gradual development of the National Geospatial Data Infrastructure (NGDI), forms a necessary core for the establishment of an integrated GIS module.
4. The comprehensive feasibility assessment showed that, despite high technical and financial viability, the organisational readiness of the system remains partial. The main barrier is the absence of a unified national roadmap and a designated lead institution responsible for coordinating spatial analytics at the state level.
5. The study identified that the key risks related to geoprivacy and data fragmentation are manageable. The implementation of geomasking techniques, the establishment of interagency data-sharing agreements, and the development of human resources in spatial epidemiology are priority steps for the successful transformation of the public health system.

Thus, the implementation of a GIS component represents not only a technological upgrade but also a strategic prerequisite for establishing a modern, spatially sensitive healthcare system capable of effectively minimising population health risks.

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CONFLICT OF INTEREST
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REVIEW ARTICLE

CONTENTS

An indicative model of compulsory health insurance

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ABSTRACT

Aim: To propose an indicative model of compulsory health insurance in the context of a significant deficit in budget financing of the healthcare sector and a decrease in the population's financial access to medical care.

Materials and Methods: The search strategy involved the use of the keywords "health insurance", "health financing", "affordability", "patients", "healthcare", "insurance companies".The primary selection of materials was based on the analysis of the titles and abstracts of publications in accordance with the previously defined inclusion and exclusion criteria, formed according to the research topic. Of the 69 publications found, 21 were used. Methods used in the study: bibliographical, medical-statistical, analytical, graphical, functional-structural modelling, generalisation. The average salary "in hand" was calculated by subtracting from the average salary, according to official Ukrainian government sources (gov.ua, Ministry of Finance of Ukraine), personal income tax – 18.0% and military levy – 1.5% for the period until 01.12.2024; from 01.12.2024 the military levy increased to 5.0%. The real wage index, taking into account tax payments, was calculated according to the Methodology for calculating real wage indices

Conclusions: The proposed model is aimed at increasing the financial accessibility of medical care for the population, minimising the risks of inefficient use of resources, and strengthening the preventive component in health care. Its implementation requires further regulatory and organisational support.

KEY WORDS: patients, healthcare, insurance companies, payers, financing

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INTRODUCTION

Achieving the Sustainable Development Goals by 2030 includes, among other things, ensuring universal health coverage, financial risk protection, access to quality essential health services, and safe, effective medicines and vaccines. These targets are set out in Target 3.8. Coverage of the population with essential health services and the proportion of the population with high household expenditure on health are indicators of achievement of the goal [1].

Billions of people in the world are not covered by basic medical services and do not have full financial access to them. The prerequisites exist for catastrophic direct healthcare costs under the "out-of-pocket" model. It is typical for most countries in the world with low and medium levels of economic development. Other models are financed by taxes, such as the Beveridge model. It provides free medical care at the point of delivery. This model operates only in some economically developed countries – the United Kingdom, New Zealand, Spain. Insurance models are most consistent with Goal 3.8. This is the Bismarck model, when financing is provided by contributions from employees and employers to insurance funds. It is supplemented by tax payments. This model has been introduced in Germany, France, the Netherlands, Japan, and Switzerland. The national health insurance model is provided through payments from state insurance programmes (Canada, South Korea). The USA combines elements of different models [2].

Thus, insurance-based health financing models are operational in a small number of countries, and despite some progress, the achievement of Target 3.8 remains at risk [3].

In Ukraine, the right to medical care and health insurance is guaranteed by law [4]. However, the healthcare system is characterized by insufficient financial support and a significant share of out-of-pocket expenditures over a long period of time, which has intensified since the outbreak of the war in 2022 [5].

The authorities considered the issue of introducing compulsory health insurance in Ukraine at the legislative level as one of the mechanisms for improving the

financial access of the population to medical care even in peacetime, but this did not happen. O. V. Brezhneva-Yermolenko, A. O. Baiduzh (2019) [6]; I. Mishchuk, I. Vinnichuk (2019) [7]; N. V. Filipova (2021) [8]; D. V. Krylov (2023) [9]; B. Shevtsiv (2024) [10] and other scientists conducted scientific research on this topic. Separate directions for solving the problem of financing medical care by introducing various forms of medical insurance were identified. The topic of compulsory health insurance remains relevant and requires further development, as the war continues, the health of the population is deteriorating, the pressure on the healthcare system is increasing, and there is a deficit in healthcare funding.

AIM

The aim of the study was to propose an indicative model of compulsory health insurance in the face of a significant deficit in budget financing of the healthcare sector and a decrease in the population's financial access to medical care.

MATERIALS AND METHODS

The research materials were used at the stage of substantiating the relevance of the topic and discussing the results. The materials included domestic scientific publications posted on the websites of higher education institutions and on the ResearchGate platform, domestic regulatory and legal acts located on the Official Web Portal of the Verkhovna Rada of Ukraine (https://www.rada.gov.ua), and foreign scientific sources from the scientometric database PubMed; a total of 21 units. The review included publications that met the following criteria: thematic relevance to the study of health insurance; original research; reviews, studies, and recommendations of international organizations; domestic regulatory acts in force at the time of the study; publications from the past 5–7 years; availability of full text of publications.

The exclusion criteria included publications that did not correspond to the topic of the study, with no full text, not indexed in PubMed, without DOI (if there were other signs of low quality), with a publication period of more than 7–10 years; journalistic and popular science sources.

The search strategy involved the use of the keywords "health insurance", "health financing", "affordability", "patients", "healthcare", "insurance companies".

The primary selection of materials was based on the analysis of the titles and abstracts of publications in accordance with the previously defined inclusion and exclusion criteria, formed according to the research topic. Of the 69 publications found, 21 were used.

METHODS

Bibliographical, medical-statistical, analytical, graphical, functional-structural modelling, generalisation. The average salary "in hand" was calculated by subtracting from the average salary, according to official Ukrainian government sources (gov.ua, Ministry of Finance of Ukraine), personal income tax – 18.0% and military levy – 1.5% for the period until 01.12.2024; from 01.12.2024 the military levy increased to 5.0%. The real wage index, taking into account tax payments, was calculated according to the Methodology for calculating real wage indices [11].

ETHICS

The principles of bioethics were observed during the preparation of the article in accordance with the requirements of the Declaration of Helsinki and the legislation of Ukraine, which was confirmed by the conclusion of the commission on bioethics of the State Institution of Science «Center of innovative healthcare technologies» State Administrative Department.

FRAMEWORK

The study was conducted as a fragment of the scientific project of the Scientific Department of Healthcare Organization of the State Scientific Institution «Center for Innovative Healthcare Technologies» State Administrative Department on the topic «Medical and social justification, development and implementation of the «Center of innovative healthcare technologies» model based on the trinity of science, education and practice in the work of a multidisciplinary healthcare institution and determining its role in the formation of a single medical space» (state registration number 0125U000318; term: 2025-2029).

REVIEW AND DISCUSSION

The reform of the healthcare financing system began in Ukraine in 2017. The Law was adopted [12]. It provided for the allocation of 5.0% of funds as a share of the gross domestic product from the State Budget for the implementation of the medical guarantees programme. The programme represents a model of strategic procurement of medical services in its content. This is carried out through the National Health Service of Ukraine. The state hereby guarantees citizens, foreigners, stateless persons permanently residing in the territory of Ukraine, and persons recognised as refugees, full payment from the State Budget for necessary medical services and medicines. Payment is provided

Table 1. Expenditures on the medical guarantee program as a percentage of gross domestic product in 2022-2025 (according to gov.ua State websites of Ukraine, Ministry of Finance of Ukraine)

Years	Amount of financing for the medical guarantee program, billion UAH	Gross domestic product (GDP), billion UAH	Percentage of funding for the medical guarantee program from GDP
2022	143.9	5191.0	2.77
2023	139.4	6537.8	2.13
2024	157.3	7658.6	2.05
2025	172.8	8931.2	1.93

Source: compiled by the authors of this study

Table 2. Consumer price index (inflation index), average salary and purchasing power of citizens in Ukraine in 2022-2025 (according to gov.ua State websites of Ukraine, Ministry of Finance of Ukraine and authors' own calculations)

Years	Consumer Price Index (Inflation Index)	Average Nominal Wage (UAH)	Average Wage (UAH) after Taxes	Real Wage Index, including Taxes
2021	-	12993.56	10511.79	-
2022	126.6	13376.21	10822.21	81.3
2023	105.1	14308.46	11575.54	101.8
2024	112.0	17486.6	14146.66	109.1
2025	108.0	20653.55	15903.0	104.1

Source: compiled by the authors of this study

for emergency, primary, specialised, palliative medical care, medical rehabilitation, medical care for children under 16 years of age, and medical care in connection with pregnancy and childbirth.

However, almost half of healthcare spending was financed through out-of-pocket expenditures, and the level of household healthcare spending was 17.0% in 2021, before the full-scale invasion. This was one of the highest rates among 40 countries in the European Region [13].

Dynamic analysis showed that funding levels for the health guarantee programme did not meet legal obligations and decreased significantly – from 2.77% in 2022 to 1.93% in 2025 – during the war (Table 1).

At the same time, inflationary processes were taking place, as confirmed by the consumer price index, changes in wages, and purchasing power of citizens. There was significant tax pressure on the population, which continues to this day (personal income tax – 18.0% and military levy – 1.5% for the period until 01.12.2024; from 01.12.2024 the military levy increased to 5.0%; total taxes to the budget amounted to 19.5% from 2016 to 01.12.2024, and from 01.12.2024 to the present – 23.0%). Wages were growing but noticeably lagging behind inflationary processes (Table 2).

Therefore, financial access to medical care for citizens is constantly decreasing, although under the programme it is guaranteed by the state free of charge. This is leading to out-of-pocket expenditures when they need medical care. Expenses for medical care mean giving up some food and non-food products, incurring debt for housing and communal services and other socially necessary services that do not include medical care.

That's why, the author's model of compulsory health insurance provides for the collection of insurance funds on the principle of a balanced financial burden between several insurers (payers), but without the participation of citizens. Payments can be made by the state as deductions of insurance contributions for certain population groups (children, pregnant women), by employers from the employee compensation fund, by individual entrepreneurs, by the pension fund for persons with disabilities, the unemployed, pensioners, and other payers not prohibited by law. Insurance contributions supplement funds from the state budget allocated for health care. Payments of insured persons are credited to single centralized accounts of the Fund (insurer) of compulsory health insurance (hereinafter referred to as the Fund) - a non-profit self-governing organization - in authorized state banks. The main functions of the Fund are the accumulation of financial resources, maintaining a register of insurers, personalized accounting of all insured persons, receipts of funds. Part of the accumulated funds (in the amount of a two-month or monthly budget) is directed to the Fund's reserve to ensure its financial stability.

The Fund's responsibilities include developing standard forms of contracts with providers and consumers of medical services, which stipulate their rights and obligations, coding the insured person's insurance policy, forming standards for exchanging information

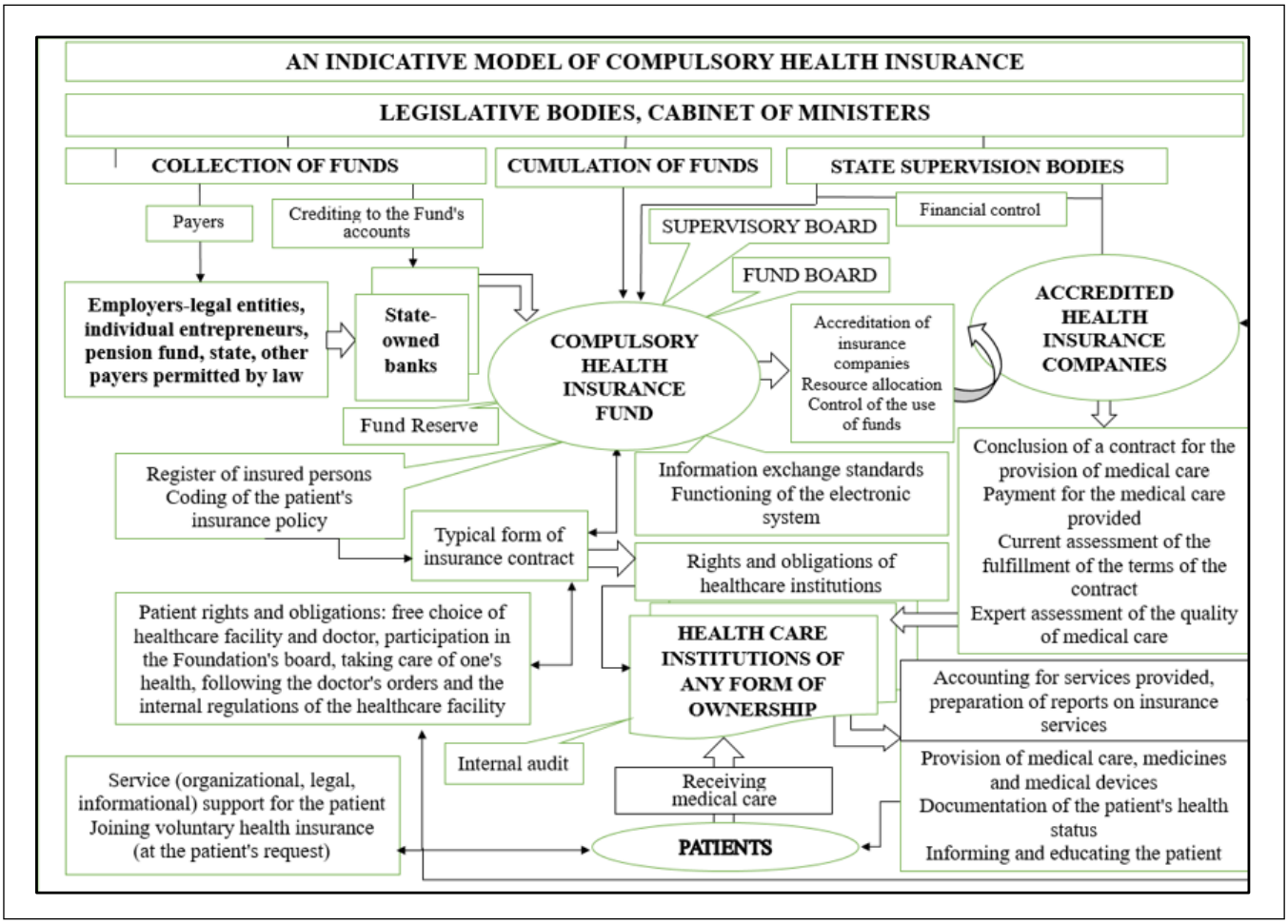


Fig. 1. An indicative model of compulsory health insurance
Picture taken by the authors

with participants in insurance relations using an electronic system, and ensuring confidentiality, use, and storage of data.

Insurance companies - other subjects of the compulsory health insurance model. The obligations to conclude contracts for the provision of medical services with their providers are assigned to them. Licensed/accredited healthcare institutions of any form of ownership may be providers of medical care. The Fund accredits insurance companies for compliance with the requirements for conducting activities in the compulsory health insurance system, namely: maintaining personalized records of insured persons who use medical services in healthcare institutions with which contracts have been concluded; making payments for medical services provided using an advance payment system (for example, not less than 50–70% of the cost); conducting an ongoing assessment of the fulfillment of the terms of the contract and an expert assessment of the quality of medical care provided in accordance with standards; providing service support to the patient in the event of an insured event, i.e., organizational, legal, and informational support; joining voluntary medical insurance at the patient's request. A prerequisite for the operation of such companies is not to receive profit from financing medical services in the compulsory health insurance system.

Providers ensure the provision of medical care to insured persons in accordance with the requirements of medical and technological documents and the terms of the contract. The list of services necessarily includes prevention, diagnostics, treatment, rehabilitation, palliative care, medical care during pregnancy and childbirth. They provide patients with medicines and medical devices; issue disability certificates, extracts from medical records and other documents necessary for receiving social benefits; provide patient information (providing complete information about the state of health, treatment methods, risks and cost of services provided); provide counseling and training of the patient in self-help methods; keep records of services provided; draw up insurance certificates and cost estimates to receive payments for services; provide access to external experts to verify compliance with the terms of the contract.

The insured person acts as an active subject of the compulsory health insurance system. He has certain

guarantees from the state/insurer and bears responsibility to them, determined by the contract. The insured person-patient has the right: to freely choose health care institutions and doctors (in particular primary health care) among those operating in the system; the right to medical care without out-of-pocket expenditures at the time of receiving services within the insurance program; participation in the Fund's board through representatives (trade unions, public associations); legal protection and confidentiality of information. A typical contract stipulates the obligations of the insured person/patient: taking care of their health (adhering to a healthy lifestyle, timely passing of preventive examinations, screening tests, receiving vaccinations); compliance with the internal regulations of the healthcare facility and the treatment regimen, providing reliable information about your status, and compulsory presentation of the insurance certificate (policy/card) code when seeking help.

The proposed an indicative model of the compulsory health insurance system provides for a system of risk management of irrational and inappropriate use of funds, abuse and corruption, and poor-quality provision of medical care. The subjects of external risk management are the Ministry of Finance of Ukraine, the Ministry of Health of Ukraine, the Accounting Chamber, the Supervisory Board of the Fund, patients, and the internal management is carried out by professional experts of the Fund, experts of insurance companies, and internal auditors of healthcare institutions (Fig. 1).

The authors of studies in the field of health insurance recommend that state authorities consider universal health insurance as a priority of healthcare, which corresponds to the purpose and results of the authors' study [14].

The principal approach that distinguishes the authors' model from health insurance models in draft domestic legislative acts of 2002–2016 and insurance models of European countries is a mechanism for collecting funds in which citizens do not participate. Unlike the proposed model, in Germany and the Czech Republic the insurance model operates due to an approximately parity distribution of the insurance burden between the employee and the employer [15, 16]. In Poland, the main sources of insurance contributions are taxes of employees and self-employed persons; the employer does not participate in financing medical care [17]. In France, employers, self-employed persons, and employees pay insurance contributions, but the amount of employee contributions is minimal. Also, all participants pay taxes from which funds for medical care are allocated [18].

In the considered models of health insurance of European countries, the Insurance Fund directly concludes contracts with health service providers, controls the quality of medical care, and manages risks without the participation of insurance companies. However, in Switzerland a health insurance model has been introduced based on a basic programme that is mandatory for all citizens, and more than 40 private insurance companies provide its implementation. The latter are not entitled to receive profit from the sale of compulsory health insurance plans [19]. A similar approach has been introduced in the Netherlands, where the basic package is implemented through insurance companies whose activities are strictly controlled by the state [20].

The authors see the advantages of including insurance companies in the proposed model in their ability to provide patient service support and expert functions in relation to healthcare institutions, in order to eliminate corruption risks and inappropriate use of insurance funds. Given the geographical extent of Ukraine, with full-fledged state administration in the territories of 23 regions and the city of Kyiv, insurance companies can relieve the Fund of work related to direct interaction with patients and healthcare providers.

In the proposed model, preventive services are added to the guaranteed list. These should be structured by procedures, interventions, and manipulations for a clear definition of cost, which is not observed in the medical guarantee programme. Positioning them only by name within the framework of primary and outpatient medical care services shifts the emphasis to diagnostic and therapeutic interventions, which leads to a reactive response of the healthcare system to changes in the patient's health status, rather than a proactive approach to health maintenance, prevention, and early detection of diseases [21]. The inclusion of structured preventive services in the list corresponds to the patient's obligation to take care of their health.

Methodological limitations of the study should be considered to include the use of theoretical data analysis to substantiate the model, which requires further empirical verification of its effectiveness. The dynamic nature of inflation, income levels, and the tax burden on the population may also affect the reliability of the proposed financial mechanisms.

Further research should focus on assessing the results of pilot implementation of the model in individual regions of Ukraine according to specified indicators of financial sustainability and quality of medical care, the development of digital infrastructure and information systems as structural components of the model, the impact of the system's functioning on the preventive activity of the population, and strategies for managing financial and corruption risks.

CONCLUSIONS

The proposed model of compulsory health insurance provides patient-oriented medical care, increases the financial accessibility of medical care for the population, is proactive in nature, motivates the population to maintain health and prevent diseases, does not create an additional financial burden on the population, whose taxes will not include additional costs for medical care, minimizes the possibility of abuse and irrational use of healthcare resources, and contributes to improving relations between the state, patients, the population, and healthcare providers.

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CONFLICT OF INTEREST
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CREATIVE COMMONS 4.0

REVIEW ARTICLE

CONTENTS

Clinical evaluation of custom-made 3d-printed ankle-foot orthoses: Effectiveness, safety, and clinical implications

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ABSTRACT

Aim: To review clinical evidence regarding the effectiveness, safety, and practical implications of custom-made 3D-printed ankle-foot orthoses in individuals with lower limb impairments.

Materials and Methods: A structured literature review was conducted through PubMed and the MAUDE adverse event database. Studies were included if they investigated custom-made 3D-printed mechanical AFOs and reported outcomes related to clinical effectiveness or safety. A total of 278 records were identified; after two-stage screening, 17 studies met the inclusion criteria.

Conclusions: Custom-made 3D-printed AFOs represent an effective and safe solution for individualized management of lower limb impairments. Evidence from 17 studies demonstrates improvements in gait kinematics, plantar pressure distribution, spatiotemporal parameters, and patient satisfaction, with outcomes equivalent to conventionally manufactured devices. No serious adverse events were identified. Future research should prioritize large-scale randomized controlled trials with standardized outcome measures and longer follow-up periods.

KEY WORDS: ankle-foot orthosis, 3D printing, additive manufacturing

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INTRODUCTION

Individuals with various neuromuscular and musculoskeletal ankle disorders, including weakness of dorsiflexors, motor control deficiencies, spasticity, and foot drop, frequently experience foot and ankle instability during daily activities [1, 2]. Ankle-foot orthoses (AFOs) are among the most commonly prescribed conservative interventions for individuals with lower limb impairments. They are designed to assist with foot clearance during the swing phase of gait and to stabilise the ankle during the stance phase, thereby improving mobility, independence, and quality of life [3, 4].

Traditional custom-made AFOs are typically manufactured from thermoplastic materials using plaster casting and moulding techniques. This process is labour-intensive, requires several hours of hands-on work, and is associated with significant health and safety concerns for orthotists [5]. Furthermore, conventional mass-produced prefabricated AFOs often lack the customisability and anatomical precision required for optimal clinical outcomes [6].

In recent years, additive manufacturing, commonly referred to as 3D printing, has emerged as a transformative technology in orthotics and prosthetics. This approach enables the production of highly individualised devices based on digital scans of the patient's anatomy using computer-aided design (CAD) software, offering significant advantages: reduced fabrication time, lower material waste, greater design freedom, and the ability to create complex structures that optimise weight, stiffness, and energy dissipation [7, 8].

Powers et al. evaluated the reliability and validity of low-cost 3D limb scanning for AFO fitting in 30 healthy participants using the Structure Sensor (Occipital Inc.) with Design Studio software. All Pearson correlation coefficients between physical and scan-based measurements were ≥0.80, and the majority of intraclass correlation coefficients exceeded 0.95. Minimal detectable change values for foot and ankle measures were below 4 mm for intrarater reliability and below 6 mm for circumferential and length measures. The authors concluded that low-cost 3D limb scanning provides valid

and reliable measurements of lower limb geometry for the purpose of AFO fitting under clinically standardised conditions [9].

Farhan et al. compared the accuracy and speed of seven commercially available 3D scanners for capturing foot, ankle, and lower leg morphology in 10 healthy participants. The Artec Eva (mean accuracy 2.5%, standard deviation 4.5), Structure Sensor I (-1.1%, standard deviation 6.8), and Structure Sensor Mark II (-1.7%, standard deviation 7.5) were the only devices within the predefined acceptable accuracy threshold of ≤5%. The Structure Sensor I was the fastest scanner (mean 20.8 s), while the Spectra required the longest scanning time (329.6 s). Mobile photogrammetry-based applications (Trnio 11 and Trnio 12) demonstrated the lowest accuracy and are not recommended for AFO fabrication. The authors concluded that the Artec Eva, Structure Sensor I, and Structure Sensor Mark II provide the most accurate and fastest digital acquisition of limb morphology for 3D-printed AFO production [10].

The 3D-printed orthoses are usually custom-made medical devices that are manufactured from different materials such as thermoplastic polyurethane (TPU), polyamide (PA), polypropylene (PP), and polylactic acid (PLA). These materials are selected according to their mechanical properties, including plasticity. Despite the fact that the device is used for a specific patient, modern 3D printers provide the possibility of mass manufacturing. According to the European Medical Device Regulation, custom-made devices of lower classes are not subject to mandatory certification by Notified Bodies [11]. Therefore, it is important to confirm the efficiency and safety of 3D-printed orthoses due to the presence of health risks for the patient associated with their use, especially falls.

AIM

The aim of this review was to synthesize current evidence regarding the clinical effectiveness, safety profile, and practical implications of custom-made 3D-printed AFOs for individuals with lower limb impairments.

MATERIALS AND METHODS

A structured literature review was conducted in accordance with the clinical evaluation requirements of Medical Device Regulation No 2017/745. The search was performed in PubMed and complemented by adverse event searches in the MAUDE database (FDA, USA). The search terms were: "ankle foot orthosis 3D", "AFO 3D", "ankle foot orthosis PA12", and "AFO PA12". The last 2 were used as PA material that complies with ISO 10993 biocompatibility requirements. The updated systematic review by Wang et al. was also consulted to identify additional relevant primary studies [12].

INCLUSION AND EXCLUSION CRITERIA

Studies were included if they: (1) investigated 3D-printed or additively manufactured mechanical AFOs; (2) addressed custom-made orthoses; (3) reported outcomes related to safety and clinical effectiveness; and (4) were published in English. Studies were excluded if they: concerned non-AFO orthoses, investigated serially manufactured (non-custom) devices, used other fabrication methods, or were duplicates identified across searches.

QUALITY ASSESSMENT

The methodological quality of included studies was assessed using criteria defined in MEDDEV 2.7.1 Appendix D, evaluating the appropriateness of device, clinical application, patient population, and reporting quality (R1–R3 scale). The modified Downs and Black checklist was also applied [13].

STUDY SELECTION

The initial database search identified 278 potentially relevant publications. Following title and abstract screening, 254 articles were excluded: different research focus (n=135), other orthosis type (n=34), duplicate results (n=82), retracted article (n=1), not in English (n=1), and not related to orthoses (n=1). Full texts of 24 articles were retrieved and evaluated, resulting in the exclusion of 7 further studies: other orthosis types (n=3), different research focus (n=1), focus on scanning methodology (n=1), unspecified orthosis type (n=1), and absence of clinical results (n=1). A total of 17 studies were included in the final analysis. The literature selection process is presented in Fig. 1.

STUDY CHARACTERISTICS

The 17 included studies covered a broad range of clinical populations, sample sizes, and methodological designs. Sample sizes ranged from 1 to 124 participants. The most represented clinical conditions were post-stroke drop foot (~25%), Charcot-Marie-Tooth disease (CMT), cerebral palsy, plantar fasciitis, and mechanical trauma. Other studies by Xu et al. (n=60, RCT) [14] and Pollen et al. (n=104 across 10 studies, systematic review) [15] also represented significant evidence contributions.

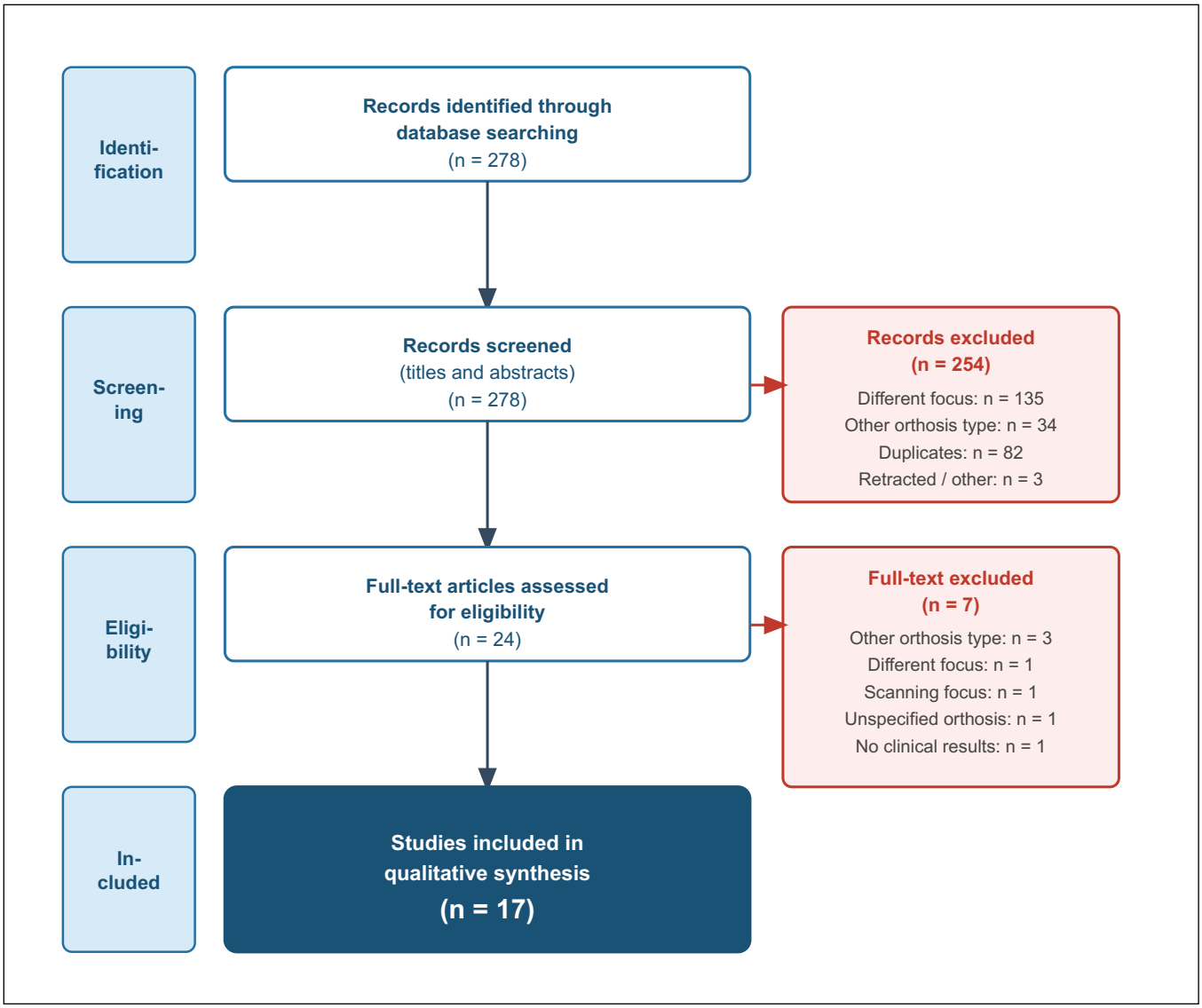


Fig. 1. PRISMA flow diagram of the literature selection process. The search was performed in PubMed with no restriction on the start date, up to January 2026
Picture taken by the authors

ETHICS

This review is based exclusively on the analysis of publicly available scientific data published in peer-reviewed journals, clinical guidelines, and databases. No patient-identifiable data were used, no new clinical interventions were performed, and no primary data collection from patients was conducted. Accordingly, approval from a local ethics committee was not required.

The authors affirm adherence to the ethical principles of the Declaration of Helsinki of the World Medical Association and to international standards of publication ethics, including the recommendations of the International Committee of Medical Journal Editors (ICMJE). No elements of this work contain plagiarism, fabrication, or falsification of data. All sources of information are correctly cited and properly formatted.

REVIEW AND DISCUSSION

The 3D printing techniques utilized included selective laser sintering (SLS), fused deposition modelling (FDM), fused filament fabrication (FFF), stereolithography (SLA), and multi-jet fusion (MJF). The most frequently used materials were polyamide Nylon 12 (PA12), polylactic acid (PLA), polyamide (PA), and carbon fibre composites. Outcome measures included gait kinematics, kinetics, plantar pressure, spatiotemporal parameters, patient-reported satisfaction, and functional assessments.

GAIT KINEMATICS AND KINETICS

The effects of 3D-printed AFOs on gait kinematics were consistently reported across included studies. Compared to the no-AFO condition (barefoot or shoe-only), 3D-printed AFOs significantly reduced ankle

plantarflexion at heel strike, push-off, and during the swing phase, indicating effective control of foot drop and improved foot clearance [15,16]. Ankle dorsiflexion during the swing phase was increased, supporting the primary functional goal of AFO application.

Hip flexion at heel strike was increased with 3D-printed AFOs compared to the no-AFO condition, suggesting enhanced proximal joint stability. The knee flexor moment between 35% and 60% of the stance phase was increased [15, 17]. Wojciechowski et al. demonstrated that 3D-printed AFOs made from PA12 were biomechanically comparable to conventional AFOs for children with Charcot-Marie-Tooth (CMT) and were approximately one-third lighter, a significant practical advantage [18].

When compared directly with conventionally manufactured AFOs, the 3D-printed devices demonstrated equivalent kinematic outcomes across most parameters, including peak hip flexion, hip joint moments, knee flexion, and ankle plantarflexor moment [15, 18]. Some studies reported that redesigned 3D-printed AFOs with modified geometry provided superior ankle dorsiflexion at heel strike and during swing, attributed to design innovations enabled by additive manufacturing [18].

Cha et al. described the design and clinical application of a 3D-printed AFO manufactured using automated CAD software (MediACE3D®, SolidEng Corp.) combined with 3D scanning (Artec Eva) in a single patient — a 68-year-old woman with foot drop secondary to common peroneal neuropathy. The AFO was fabricated using a fused filament fabrication (FFF) printer with thermoplastic polyurethane (TPU) filament. A mechanical durability test of 300,000 loading cycles (simulating approximately 4 months of use) demonstrated no cracking or structural deformation. Gait analysis showed that both the conventional polypropylene AFO and the 3D-printed AFO equally improved walking speed from 42.2 cm/s (without AFO) to 56.5 cm/s. Single stance symmetry was highest with the 3D-printed AFO (80.4%), followed by the conventional AFO (79.7%), and lowest without an AFO (69.7%). The conventional AFO provided slightly greater ankle dorsiflexion during swing phase due to higher rigidity. According to the Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST), the patient was more satisfied with the 3D-printed AFO in terms of weight and ease of use (total QUEST score: 4.5 vs. 4.1), while rating the conventional AFO as more effective due to the flexible material of the 3D-printed device causing some foot drop during swing [19].

PLANTAR PRESSURE DISTRIBUTION

The customization of AFOs using 3D printing was associated with improved plantar pressure distribution. Studies reported significant reductions in peak plantar pressure at the rearfoot, forefoot, and total plantar surface when wearing 3D-printed AFOs compared to shoe-only conditions [15, 18, 20]. In a well-powered RCT by Xu et al. (n=60, plantar fasciitis), 3D-printed AFOs led to significantly lower peak plantar pressure in the heel and midfoot regions and substantially reduced pain compared to standard orthoses, confirming the biomechanical benefits of individualized 3D-printed design [14].

SPATIOTEMPORAL PARAMETERS

Spatiotemporal gait parameters, including stride length, walking velocity, cadence, and stance time, were consistently improved with 3D-printed AFOs compared to the no-AFO condition across multiple studies [14, 16, 21, 22]. The spatiotemporal parameters measured with 3D-printed AFOs were generally equivalent to those achieved with conventional AFOs, with no statistically significant differences in stride length, cadence, stance time, or gait velocity in the majority of comparative studies [16, 18].

Qin et al. conducted a retrospective cohort study at Guigang People's Hospital (China), reviewing medical records of 124 children (aged 3–6 years) diagnosed with spastic cerebral palsy (GMFCS level I–II), treated between January 2022 and June 2024. Sixty-two children received customized 3D-printed AFOs (aluminum alloy upper combined with TPU95A sole), and 62 received traditional polyethylene AFOs. Both groups underwent identical 3-month standardized rehabilitation programmes. At 3-month follow-up, the 3D-printed AFO group demonstrated significantly superior outcomes: Gross Motor Function Measure (GMFM) scores (74.98±3.42 vs. 69.08±2.95, p=0.001), step length (31.15±4.18 vs. 28.68±4.32 cm, p=0.01), walking speed (0.56±0.10 vs. 0.52±0.12 m/s, p=0.022), and step width (14.52 ± 2.36 vs. 15.82±2.40 cm, p=0.011). Passive ankle dorsiflexion angle also showed greater improvement in the treatment group (p=0.027). The 3D-printed AFOs were significantly lighter (123.6±36.15 g vs. 183.2±65.78 g, p<0.001) and thinner (1.71±0.17 mm vs. 3.00 mm), which the authors attributed to the use of aluminum alloy and structural optimization, including ventilation holes. No adverse events were reported in either group [23].

FUNCTIONAL MOBILITY AND COMMUNITY AMBULATION

Cho et al. evaluated 3D-printed AFOs in three stroke survivors over a 4-week community ambulation training

programme. The orthoses improved step length, gait symmetry, ankle range of motion, and muscle activation efficiency. Patients also demonstrated improved balance, walking endurance, and reduced depressive symptoms [24]. Chae et al. reported that in three clinical cases, 3D-printed orthoses improved functional outcomes, including the 6-minute walk test and daily activity performance, compensating for lost motor function [25].

Amitrano et al. assessed 8 patients and noted that while passive orthoses partially corrected compensatory biomechanical patterns, physical training and gait training with the orthosis remained important complements to device prescription [26].

Chae et al. presented three case reports of patients with peripheral nerve injuries treated with individualized 3D-printed orthoses. The orthoses were designed using MIMICS Medical v17 and Geomagic Freeform software and printed on a FINEBOTZ420 machine. Case 3 involved a patient with right lower lumbar radiculopathy and foot drop, who received a 3D-printed AFO. Following orthotic application, the patient demonstrated improvement in the 6-minute walk test (6MWT) distance, improvement in the modified Emory Functional Ambulation Profile (mEFAP) score, and improved stability assessment scores. Patient satisfaction assessed by the QUEST questionnaire was rated as a perfect score. The authors highlighted that the advantages of 3D-printed orthoses over conventional ones include lower cost, easier modification, and faster fabrication, enabling physicians to create individually tailored products [25].

MECHANICAL PROPERTIES AND STIFFNESS

Choi et al. demonstrated in 8 healthy volunteers that 3D-printed AFOs at varying stiffness levels consistently optimized muscle-tendon function and reduced estimated energy cost during walking [27]. Raj et al. showed that 3D-printed PLA-CF AFOs exhibit higher stiffness and load-bearing capacity compared to standard PLA constructs, confirming mechanical reliability [28]. Ielapi et al. validated a protocol for assessing stiffness and stress distribution in two 3D-printed AFO designs, with modelling accuracy within approximately 10% of experimental results [29].

Swesi et al. investigated the process parameter optimization and mechanical properties of ankle–foot orthoses manufactured by fused filament fabrication (FFF) 3D printing using polypropylene (PP) filament. The study addressed the primary manufacturing challenge of PP — limited bed adhesion and high shrinkage, which is especially problematic for large parts such as AFOs. Through systematic optimization of printing parameters (nozzle temperature, print speed, layer height, infill pattern, and bed adhesion strategies), the authors achieved specimens meeting structural requirements for orthotic applications. PP was identified as a particularly suitable material for AFO fabrication due to its light weight, superior flexibility, chemical resistance, biocompatibility, and long-term durability properties that combine to offer an excellent balance between rigidity and energy return during gait. The findings provide a validated manufacturing framework for producing PP-based custom AFOs using accessible desktop FFF printers [30].

PATIENT SATISFACTION

Patient-reported satisfaction was assessed across several included studies. Lin et al. (2021) reported significantly higher satisfaction with 3D-printed AFOs compared to conventional ones in dimensions of fit, ease of use, comfort, and effectiveness ($p<0.001$) [17]. Fu et al. and Wojciechowski et al. found no statistically significant differences in satisfaction between 3D-printed and conventionally manufactured AFOs, with both types rated comparably in weight, comfort, and ease of use [18, 20]. Cho et al. noted positive qualitative feedback from stroke survivors, who appreciated the lighter weight, thinner profile, and improved gait adjustability [24].

SAFETY PROFILE

Among all 17 studies included in this review, no serious adverse events related to the use of 3D-printed AFOs were reported. Minor issues included transient discomfort during the initial fitting period and one instance of device cracking observed after 6 weeks of use in an SLS-manufactured segmented orthosis [31]. The search of the MAUDE database for the equivalent device manufacturer, Protect 3D Inc. (USA), identified zero adverse events. These findings support a favourable safety profile, with identifiable risks being manageable through clinical monitoring and individualized fitting.

GENERAL DISCUSSION AND CLINICAL IMPLICATIONS

This review synthesizes evidence from 17 clinical and biomechanical studies on custom-made 3D-printed AFOs. The overall findings indicate that these devices are effective, safe, and clinically acceptable for individuals with ankle impairments. The improvements in ankle kinematics, spatiotemporal gait parameters, plantar pressure distribution, and patient-reported

satisfaction are consistent with established evidence on conventional AFO efficacy [3, 15, 32].

A key finding of this review is the functional equivalence of 3D-printed AFOs to conventionally manufactured devices across the majority of gait parameters. This equivalence has important clinical implications: 3D-printed AFOs can replace conventional devices without compromising functional outcomes while offering additional advantages, including design flexibility, reduced fabrication time, and improved patient customization. The study by Wojciechowski et al. is particularly noteworthy in this regard, demonstrating that 3D-printed PA12 replicas of traditional AFOs produced equivalent biomechanical outcomes and self-reported satisfaction among children with CMT [18].

The large-sample study by Qin et al. (n=124 children) represents one of the most robust contributions to date in paediatric AFO research, demonstrating significant superiority of 3D-printed AFOs over conventional ones in GMFM scores, stride parameters, and user comfort [23]. Similarly, the RCT by Xu et al. (n=60) provides high-quality evidence for the effectiveness of 3D-printed orthoses in pain management and plantar pressure redistribution [14]. These two studies significantly strengthen the evidence base and should be considered central to future clinical guideline development.

The design-specific benefits of 3D printing deserve particular attention. The ability to precisely control AFO stiffness through strut design has been demonstrated to influence ankle kinematics and kinetics [2, 28, 29]. Stiffer struts reduce both plantarflexion and dorsiflexion ranges of motion, while more compliant struts allow greater ankle mobility with reduced push-off energy loss. These findings highlight the potential for 3D printing to enable evidence-based customization of mechanical properties, a capability practically limited with conventional thermoplastic fabrication.

The material PA12 (Nylon 12), used by the Scientific Park of Additive Technologies, is the most widely tested and clinically validated material for 3D-printed AFOs in the reviewed literature [7, 18]. It offers a favourable combination of mechanical strength, biocompatibility, and patient comfort, and has not been associated with adverse tissue reactions in any included study.

Leith et al. conducted a mixed-methods cross-sectional study investigating the usability of performing clinical adjustments on 3D-printed (PA12, HP Multi Jet Fusion technology) versus traditionally fabricated AFOs. Ten certified orthotists completed 10 standardized adjustment tasks (including strap relocation, cork wedge addition, grinding, flaring, volume reduction, and easing) on 3D-printed AFOs and evaluated usability using the Single Ease Question (SEQ) and System Usability Scale (SUS). Task completion rate was 99%; however, the professional standard completion rate was only 71%, primarily due to aesthetic concerns (discoloration of PA12 after heating or grinding). SEQ scores were significantly lower for the 3D-printed condition in 5 of 10 tasks. The mean SUS score for 3D-printed AFOs was significantly lower than for traditional AFOs (52.25±11.8 vs. 85.50±10.4, $p<0.001$), indicating low perceived usability for adjustment. Thematic analysis identified five main challenge areas: aesthetics, grinding difficulties, heating behaviour (requiring longer heating and more cautious technique), time-consuming adjustments, and concerns about brittleness/microfracture risk. Despite these challenges, orthotists were optimistic about future clinical adoption and proposed solutions, including optimized heat gun techniques, appropriate grinding protocols, postprocessing (dyeing, vapor smoothing, surface coating), and a learning curve with the new material. The authors concluded that current 3D-printed materials require further development in adjustability to be fully equivalent to traditional thermoplastics in clinical practice [33].

LIMITATIONS OF THE CURRENT EVIDENCE

Several limitations must be acknowledged. The majority of included studies had small sample sizes, with 8 of 17 studies including fewer than 5 participants. Heterogeneous patient populations, diverse AFO designs, and varied outcome measures across studies precluded meta-analytic pooling of data. Most studies evaluated immediate gait effects rather than long-term functional outcomes and device durability. Methodological quality was generally rated as "fair" using the Downs and Black checklist, with deficiencies in blinding, allocation concealment, and a priori power calculations [12]. Future research should prioritize large-scale RCTs with standardized outcome measures and follow-up periods of at least 6 months.

CONCLUSIONS

Custom-made 3D-printed ankle-foot orthoses represent an effective, safe, and clinically viable solution for individualized orthopedic management of lower limb impairments. Evidence from 17 reviewed studies demonstrates that 3D-printed AFOs improve lower extremity kinematics and kinetics, plantar pressure distribution, spatiotemporal gait parameters, and patient satisfaction compared to no-AFO conditions, with outcomes equivalent to conventionally manufactured devices.

The material polyamide PA 12, used by the Scientific Park of Additive Technologies (Kyiv, Ukraine), is

the most clinically validated material for 3D-printed AFOs, offering excellent biocompatibility, mechanical performance, and user comfort. No serious adverse events were identified in the reviewed clinical literature or in the MAUDE and Derzhliksluzhba adverse event databases.

Future research should prioritize large-scale randomized controlled trials in specific clinical populations, standardized outcome measures, and longer follow-up periods. Establishing consensus reporting standards for 3D-printed AFO studies would enhance the comparability and synthesis of evidence across studies.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Neuromolecular biomarkers of traumatic stress: Refining diagnostic criteria and personalizing treatment for core biological symptoms in PTSD

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ABSTRACT

Aim: The aim of this review is to assess the role of neuromolecular biomarkers in post-traumatic stress disorder (PTSD) and their usefulness in improving diagnostic accuracy and supporting personalized treatment strategies.

Materials and Methods: A narrative review of studies published between 2015 and 2025 was performed using databases such as PubMed, Scopus, and Web of Science. The analysis included clinical and experimental studies focusing on neuroinflammation, oxidative stress, endoplasmic reticulum stress, and markers of neuronal damage in PTSD. Special attention was given to associations between biomarkers and symptom severity, duration of illness, and treatment outcomes.

Results: PTSD is associated with disturbances in neuroimmune and neuroendocrine pathways. Increased levels of pro-inflammatory cytokines, including interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-18 (IL-18), are frequently observed. Activation of the NLR family pyrin domain containing 3 inflammasome (NLRP3 inflammasome) and elevated oxidative stress markers, such as malondialdehyde (MDA), indicate ongoing inflammatory and oxidative processes. Changes in neuronal injury markers, including ubiquitin carboxyl-terminal hydrolase L1 (UCHL1), suggest neurodegenerative mechanisms. Altered chemokine signaling, particularly fractalkine (chemokine C-X3-C motif ligand 1, CX3CL1), and activation of endoplasmic reticulum stress pathways, such as inositol-requiring enzyme 1 (IRE1) and activating transcription factor 6 (ATF6), are linked to impaired neuronal function and reduced synaptic plasticity. These findings indicate biological heterogeneity within PTSD.

Conclusions: Neuromolecular biomarkers may improve the current symptom-based diagnostic model of PTSD. Their integration with clinical assessment tools may support identification of biologically defined subgroups and enable more targeted treatment.

KEY WORDS: biomarker-based diagnostics, CX3CL1, neuroinflammation, NLRP3 inflammasome, oxidative stress, post-traumatic stress disorder

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INTRODUCTION

Post-traumatic stress disorder (PTSD) is increasingly understood as a disorder with a complex neurobiological basis, rather than only a psychological reaction to trauma. Exposure to traumatic stress induces persistent alterations in central and peripheral systems, including the hypothalamic–pituitary–adrenal axis (HPA axis), the immune system, and neural circuits involved in emotion regulation. Functional and structural changes within the amygdala, hippocampus, and prefrontal cortex are associated with heightened threat processing, impaired memory integration, and reduced top-down control. These alterations contribute to the development and maintenance of core PTSD symptoms such as hyperarousal, intrusive recollections, and avoidance [1].

Current diagnostic frameworks, including the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), and the International Classification of Diseases, Eleventh Revision (ICD-11), rely on symptom-based criteria. Although clinically useful, these classifications do not reflect underlying biological mechanisms and do not capture inter-individual variability. Patients presenting with similar symptom profiles may differ in terms of neuroendocrine regulation, inflammatory activity, and neuronal integrity. This limitation reduces diagnostic precision and may contribute to inconsistent treatment outcomes [2].

PTSD demonstrates considerable clinical and biological heterogeneity. Variability in symptom severity, duration of illness, and comorbid conditions indicates the involvement of multiple interacting biological pathways. These include chronic activation of neuroinflammatory processes, increased oxidative stress, dysregulation of the HPA axis, and disturbances in

synaptic plasticity. Such mechanisms may operate differently across individuals, suggesting the presence of biologically distinct subtypes [3, 4].

Integration of biological markers with psychometric assessment may improve the current diagnostic approach. The identification of neuromolecular biomarkers, including cytokines, markers of neuronal injury, and indicators of cellular stress, provides an opportunity to better characterize disease mechanisms.

Integration of biological markers with psychometric assessment may improve the current diagnostic approach and support more precise patient stratification within the framework of precision psychiatry [5].

AIM

The aim of this review is to analyze the role of neuromolecular biomarkers in PTSD in the context of its underlying neurobiological mechanisms. Particular attention is given to biomarkers associated with neuroinflammation, oxidative stress, neuroendocrine regulation, and neuronal injury, which may reflect core pathophysiological processes.

An additional objective of this work is to organize and critically evaluate the available literature regarding the potential diagnostic relevance of these biomarkers. In particular, their associations with symptom severity, duration of illness, and clinical presentation are examined, with consideration of methodological limitations and the lack of full standardization across studies. It is also emphasized that their potential to improve the accuracy of current diagnostic systems, such as DSM-5 and ICD-11, remains preliminary and requires further validation.

The review also aims to highlight the possibility of biological heterogeneity within PTSD. Variability in biomarker profiles may suggest the presence of distinct pathophysiological pathways; however, interpretation of these findings should be approached with caution due to inconsistencies in the available data and the need for further research using standardized methodologies.

Furthermore, the review discusses the potential implications of biomarker research for future diagnostic and therapeutic strategies in PTSD. While the identification of specific biological patterns may, in the future, support the development of personalized approaches, this application currently remains largely conceptual and requires further investigation, validation, and methodological standardization [6].

MATERIALS AND METHODS

This narrative review was conducted based on a structured search of the literature published between 2015 and 2025 using the PubMed, Scopus, and Web of Science databases. The search strategy included combinations of keywords related to PTSD, neuroinflammation, oxidative stress, endoplasmic reticulum stress, neurodegeneration, and biomarkers.

Eligible studies included original clinical and experimental research articles as well as relevant review papers published in English. Studies focusing on molecular and cellular mechanisms associated with PTSD were prioritized. Particular emphasis was placed on biomarkers related to neuroinflammatory processes, oxidative imbalance, endoplasmic reticulum stress pathways, and markers of neuronal injury.

Articles were selected based on their relevance to the objectives of the review, including the association of biomarkers with symptom severity, duration of illness, and treatment response. Studies lacking clear relevance to PTSD pathophysiology or biomarker assessment were excluded.

NEUROBIOLOGICAL BASIS OF PTSD

Post-traumatic stress disorder is associated with complex and interacting neurobiological mechanisms involving neuroendocrine regulation, structural and functional brain alterations, neuroimmune activation, oxidative imbalance, and impaired neuroplasticity.

Dysregulation of the HPA axis represents a central component of the stress response disturbance observed in PTSD. Under physiological conditions, activation of this axis begins with the release of corticotropin-releasing hormone (CRH) from the hypothalamus. CRH stimulates the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH), which in turn induces cortisol release from the adrenal cortex. Cortisol exerts regulatory effects through negative feedback mechanisms acting on both the hypothalamus and the pituitary gland. In PTSD, this regulatory system is altered [7]. Reduced basal cortisol levels and disruption of circadian rhythm are frequently observed. At the same time, increased sensitivity of glucocorticoid receptors enhances negative feedback, which may lead to an attenuated endocrine response despite persistent activation of limbic structures. This dysregulation contributes to abnormal stress reactivity and facilitates maintenance of inflammatory processes.

Structural and functional changes in the brain further contribute to PTSD pathophysiology. The amygdala shows increased activity, which is associated with enhanced threat detection and exaggerated emotional responses. This hyperactivation is linked to symptoms such as hypervigilance and persistent fear. The hippocampus, which is responsible for contextual memory

processing, demonstrates reduced volume and functional impairment. These alterations interfere with proper discrimination between safe and threatening stimuli and contribute to intrusive recollections. The prefrontal cortex, particularly its medial region, exhibits reduced activity, leading to impaired top-down regulation of limbic responses. The imbalance between hyperactive limbic structures and reduced cortical control forms a neurofunctional substrate of PTSD symptoms.

Neuroinflammatory processes play an important role in sustaining these alterations. Chronic stress leads to activation of microglia, the primary immune cells of the central nervous system. Activated microglia release pro-inflammatory cytokines, including interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-18 (IL-18) [8-10].

The activation of the NLR family pyrin domain containing 3 inflammasome (NLRP3 inflammasome) promotes maturation and release of these cytokines, amplifying inflammatory signaling. Persistent neuroinflammation disrupts synaptic transmission and contributes to neuronal dysfunction. In addition, impaired signaling between neurons and microglia, partly mediated by fractalkine (chemokine C-X3-C motif ligand 1, CX3CL1), alters neuroimmune communication [11, 12].

Oxidative stress and mitochondrial dysfunction represent another critical mechanism. Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and antioxidant defenses. Excess ROS leads to damage of lipids, proteins, and nucleic acids. Malondialdehyde (MDA), a product of lipid peroxidation, reflects membrane damage and neuronal vulnerability. Mitochondria, as the main source of cellular energy, become dysfunctional under chronic stress conditions, leading to increased ROS generation and reduced metabolic efficiency. Antioxidant systems, including glutathione (GSH) and enzymes such as superoxide dismutase (SOD), are often impaired, which further enhances oxidative damage. These processes contribute to neuronal injury and are closely linked to neuroinflammation [13, 14].

Disturbances in neuroplasticity further exacerbate the condition. Neuroplasticity refers to the ability of the nervous system to adapt through structural and functional changes in synapses. In PTSD, reduced levels of brain-derived neurotrophic factor (BDNF) impair neuronal survival and synaptic formation. Alterations in glutamatergic signaling, particularly involving the N-methyl-D-aspartate receptor (NMDA receptor), lead to excitotoxicity and synaptic dysfunction. Chronic stress also reduces synaptic density and disrupts neural connectivity. These effects are intensified by concurrent inflammatory and oxidative processes.

Together, these mechanisms form an interconnected network of neurobiological alterations that underlie the development and persistence of PTSD [15-17].

These neurobiological mechanisms are reflected in measurable neuromolecular biomarkers, which provide a link between underlying pathophysiology and clinical presentation in PTSD.

NEUROMOLECULAR BIOMARKERS IN PTSD: INFLAMMATION, OXIDATIVE STRESS AND NEURODEGENERATION

Neuromolecular biomarkers provide important insight into the biological mechanisms underlying post-traumatic stress disorder. Evidence indicates that PTSD is associated with persistent activation of inflammatory pathways, increased oxidative stress, and progressive neuronal damage. These processes are closely interconnected and contribute to the development and maintenance of clinical symptoms [18, 19].

Inflammatory markers represent one of the most consistently observed biological alterations in PTSD. Increased levels of pro-inflammatory cytokines, including IL-1β, IL-6 and IL-18, reflect activation of the immune response within both the peripheral and central nervous systems. These cytokines influence neuronal function by modulating synaptic transmission and plasticity. Tumor necrosis factor alpha (tumor necrosis factor alpha, TNF-α) further contributes to inflammatory signaling by affecting blood–brain barrier permeability and promoting microglial activation. Elevated levels of C-reactive protein (CRP) indicate systemic inflammation and are associated with increased risk and severity of PTSD. In contrast, interleukin-10 (IL-10), an anti-inflammatory cytokine, is often reduced, suggesting impaired regulation of the inflammatory response [20-22].

Together, these changes indicate a chronic low-grade inflammatory state. A central component linking inflammation with cellular stress is the NLRP3 inflammasome. This multiprotein complex is activated in response to cellular damage and stress signals. Its activation leads to stimulation of caspase-1 (caspase-1), which converts inactive cytokine precursors into active forms, including IL-1β and IL-18. In PTSD, activation of the NLRP3 inflammasome is associated with chronic stress exposure, mitochondrial dysfunction, and increased production of reactive oxygen species. This pathway amplifies inflammatory signaling and contributes to neuronal injury, making it a potential biomarker of disease activity and a therapeutic target [23-25].

Oxidative stress represents another major mechanism involved in PTSD. It results from an imbalance between the generation of reactive oxygen species ROS and antioxidant defenses. Excessive ROS production leads to damage of cellular components, including lipids, proteins, and nucleic acids. Malondialdehyde,

a product of lipid peroxidation, is widely used as a marker of oxidative damage and reflects disruption of cell membrane integrity. Antioxidant systems are often impaired in PTSD, as indicated by reduced levels of GSH, a key intracellular antioxidant. Enzymes such as superoxide dismutase SOD and catalase, which are responsible for neutralizing reactive oxygen species, may also show altered activity. These disturbances enhance oxidative damage and contribute to neuronal vulnerability [26-28].

Markers of neurodegeneration provide evidence of structural neuronal damage in PTSD. Ubiquitin carboxyl-terminal hydrolase L1 (UCHL1) is a neuron-specific protein involved in protein turnover and cellular homeostasis. Increased levels of UCHL1 indicate neuronal injury and disruption of proteostasis. Neuron-specific enolase (NSE), a glycolytic enzyme released during neuronal damage, serves as a marker of neuronal cell loss. Tau protein, which is responsible for stabilizing microtubules in neurons, may undergo pathological changes leading to impaired axonal transport and accumulation of abnormal protein aggregates. Alterations in tau protein levels suggest the presence of neurodegenerative processes [29, 30].

NEUROMOLECULAR BIOMARKERS IN PTSD: NEUROIMMUNE COMMUNICATION, ENDOPLASMIC RETICULUM STRESS, NEUROENDOCRINE AND NEUROTRANSMITTER ALTERATIONS

Neuromolecular biomarkers associated with post-traumatic stress disorder extend beyond classical inflammatory and oxidative pathways and include mechanisms related to neuroimmune communication, cellular stress responses, neuroendocrine regulation, and neurotransmitter systems. These interconnected processes contribute to the complexity and heterogeneity of the disorder.

Chemokines play a key role in the interaction between neurons and microglial cells. Fractalkine, is primarily expressed by neurons, while its receptor is located on microglia. Under physiological conditions, this signaling pathway maintains microglia in a regulated state and supports synaptic stability. In PTSD, altered CX3CL1 signaling leads to excessive microglial activation, increased production of pro-inflammatory mediators, and disruption of synaptic function. This imbalance contributes to impaired neuronal communication and may enhance neuroinflammatory processes [31].

Endoplasmic reticulum stress represents another important mechanism of cellular dysfunction. The endoplasmic reticulum is responsible for protein folding and cellular homeostasis. Under conditions of chronic stress, accumulation of misfolded proteins activates the unfolded protein response. This response is mediated by three main pathways: inositol-requiring enzyme 1 (IRE1), activating transcription factor 6 (ATF6), and protein kinase RNA-like endoplasmic reticulum kinase (PERK). Although initially adaptive, prolonged activation of these pathways may lead to pro-apoptotic signaling. C/EBP homologous protein (CHOP) is a key mediator of this process and promotes cell death when stress persists. These mechanisms are closely linked to neuroinflammation and oxidative stress, further contributing to neuronal damage [32, 33].

Neuroendocrine biomarkers reflect disturbances in the regulation of the stress response. Cortisol, the primary glucocorticoid, often shows reduced basal levels and altered circadian rhythm in PTSD. Adrenocorticotropic hormone secretion may also be dysregulated, indicating impaired signaling within the stress axis. Dehydroepiandrosterone and its sulfated form (DHEA/DHEA-S) exert neuroprotective effects and counterbalance glucocorticoid activity. An imbalance between cortisol and DHEA/DHEA-S may reflect reduced resilience and impaired stress adaptation.

Neurotransmitter systems are also significantly altered in PTSD. Reduced activity of serotonin (5-hydroxytryptamine, 5-HT) is associated with mood disturbances and anxiety. Increased noradrenaline (norepinephrine) activity contributes to hyperarousal and heightened stress responses. Dopamine dysregulation affects reward processing and cognitive function. Alterations in glutamatergic signaling, particularly involving the NMDA receptor, may lead to excitotoxicity and impaired synaptic plasticity. In contrast, reduced gamma-aminobutyric acid (GABA) activity results in diminished inhibitory control over neural circuits [34].

NEUROMOLECULAR BIOMARKERS IN PTSD: NEUROPLASTICITY, APOPTOSIS, EPIGENETIC AND METABOLIC ALTERATIONS

Neuromolecular biomarkers in post-traumatic stress disorder include a wide spectrum of processes reflecting impaired neuroplasticity, activation of apoptotic pathways, epigenetic regulation of gene expression, and systemic metabolic disturbances. These mechanisms are closely interconnected and contribute to both functional and structural alterations in the central nervous system.

Neuroplasticity is essential for adaptive responses to environmental stimuli and involves dynamic changes in synaptic structure and function. In PTSD, impairment of neuroplastic processes is associated with persistent emotional dysregulation and deficits in memory

processing. Brain-derived neurotrophic factor plays a central role in supporting neuronal survival and synaptic formation. Reduced levels of BDNF observed in PTSD are linked to decreased synaptic plasticity and impaired neural adaptation. Insulin-like growth factor 1 (insulin-like growth factor 1, IGF-1) also contributes to neuronal growth, neurogenesis, and cellular repair. Alterations in IGF-1 levels may reflect reduced regenerative capacity and diminished resilience of neural networks. These changes are influenced by chronic stress and interact with inflammatory and neuroendocrine pathways [35].

Apoptotic mechanisms represent another important aspect of neuronal damage in PTSD. Caspase-3 functions as a key executioner enzyme responsible for the final stages of programmed cell death, while caspase-9 is involved in the initiation of the intrinsic mitochondrial apoptotic pathway. Activation of caspase-9 leads to downstream activation of caspase-3, resulting in cellular degradation. Increased activity of these enzymes suggests that chronic stress may induce neuronal loss through mitochondrial-dependent mechanisms. Apoptosis is closely linked to oxidative stress and inflammation, which enhance cellular vulnerability and contribute to cumulative neuronal damage [36, 37].

Epigenetic mechanisms provide an additional layer of regulation by modifying gene expression without altering DNA sequence. DNA methylation, particularly in genes related to stress regulation such as the glucocorticoid receptor gene (NR3C1), can influence sensitivity to cortisol and alter HPA axis function. FK506 binding protein 5 (FKBP5) is another critical regulator of glucocorticoid receptor activity, and its genetic and epigenetic modifications have been associated with altered stress responses and increased susceptibility to PTSD. MicroRNAs, including microRNA-124 and microRNA-146a, regulate gene expression at the post-transcriptional level and are involved in controlling inflammatory and neuronal processes. Alterations in microRNA expression contribute to dysregulation of neuroimmune signaling and synaptic function [38, 39].

Metabolic biomarkers reflect systemic alterations associated with PTSD and link central nervous system dysfunction with peripheral physiology. The kynurenine pathway, responsible for tryptophan metabolism, is activated under inflammatory conditions and leads to the production of neuroactive metabolites. Quinolinic acid, one of these metabolites, has neurotoxic properties and can enhance excitotoxicity through activation of the N-methyl-D-aspartate receptor. Disturbances in lipid metabolism may affect membrane integrity and inflammatory signaling, while alterations in glucose metabolism can impair neuronal energy supply. Chronic stress may promote insulin resistance and disrupt metabolic homeostasis, further contributing to cognitive and emotional dysfunction.

Taken together, these biomarker groups suggest that PTSD involves interacting inflammatory, oxidative, neuroendocrine, neuroplastic, and metabolic mechanisms that may contribute to symptom persistence and clinical heterogeneity.

The main groups of neuromolecular biomarkers involved in PTSD, along with their underlying mechanisms and functional significance, are summarized in Table 1.

DIAGNOSTIC IMPLICATIONS

Neuromolecular biomarkers provide important information regarding the biological basis of post-traumatic stress disorder and may enhance current diagnostic approaches. One of the key aspects is their association with symptom severity. Increased levels of pro-inflammatory cytokines, oxidative stress markers, and indicators of neuronal injury have been linked to more severe clinical manifestations, including heightened anxiety, intrusive symptoms, and impaired cognitive function. Similarly, alterations in neuroendocrine markers, such as cortisol and ACTH, may reflect dysregulated stress responses corresponding to symptom intensity [40].

Biomarkers are also related to the duration of PTSD. Chronic forms of the disorder are often characterized by sustained activation of inflammatory pathways, persistent oxidative imbalance, and progressive neuronal damage. In contrast, early stages may involve more dynamic and potentially reversible changes. This suggests that biomarker profiles may differ depending on the stage of the disorder and could be used to monitor disease progression [2, 12, 18].

The variability in biomarker expression supports the concept of biologically distinct subtypes of PTSD. Differences in inflammatory activity, neuroendocrine regulation, and neuroplasticity may define subgroups of patients with specific pathophysiological mechanisms. Identification of such subtypes may improve classification systems and facilitate more precise clinical characterization.

Integration of biomarker data with psychometric tools represents an important step toward improving diagnostic accuracy. Instruments such as the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) and the PTSD Checklist for DSM-5 (PCL-5) provide standardized assessment of symptom severity. Combining these tools with biological measures may allow for a more comprehensive evaluation that reflects both clinical presentation and underlying biological processes [21, 25, 34].

Table 1. Neuromolecular biomarkers in PTSD: mechanisms and functional significance

Biomarker group	Example biomarkers	Mechanism	Functional significance in PTSD
Inflammatory markers	IL-1β, IL-6, IL-18, TNF-α, CRP	Activation of immune response, cytokine signaling	Chronic inflammation, synaptic dysfunction
Inflammasome	NLRP3 inflammasome	Caspase-1 activation, cytokine maturation	Amplification of neuroinflammation
Oxidative stress	ROS, MDA, GSH, SOD	Redox imbalance, lipid peroxidation	Cellular damage, neuronal vulnerability
Neurodegeneration	UCHL1, NSE, tau protein	Protein degradation dysfunction, neuronal injury	Neurodegenerative changes
Chemokines	CX3CL1	Neuron–microglia signaling	Dysregulated neuroimmune communication
Endoplasmic reticulum stress	IRE1, ATF6, PERK, CHOP	Unfolded protein response, apoptosis	Cellular stress, neuronal death
Neuroendocrine markers	Cortisol, ACTH, DHEA/DHEA-S	Stress axis dysregulation	Altered stress response
Neurotransmitters	Serotonin, dopamine, glutamate, GABA	Neurotransmission imbalance	Emotional and cognitive symptoms
Neuroplasticity markers	BDNF, IGF-1	Synaptic remodeling, neurogenesis	Impaired adaptation and memory
Apoptosis markers	Caspase-3, caspase-9	Programmed cell death	Neuronal loss
Epigenetic markers	NR3C1, FKBP5, microRNA	Gene expression regulation	Stress sensitivity, vulnerability
Metabolic markers	Kynurenine pathway, lipids, glucose	Metabolic dysregulation	Neurotoxicity, systemic effects

Source: Compiled by the authors of this study

Table 2. Clinical implications of neuromolecular biomarkers in PTSD

Clinical domain	Biomarker relevance	Potential application
Symptom severity	Cytokines, cortisol, oxidative markers	Correlation with clinical intensity
Disease duration	Inflammation, neurodegeneration markers	Monitoring progression
Biological subtypes	Multi-pathway biomarker profiles	Stratification of patients
Early detection	Neuroendocrine, inflammatory markers	Identification of at-risk individuals
Treatment selection	Neurotransmitters, inflammation, oxidative stress	Targeted therapy
Treatment response	BDNF, cytokines, cortisol	Monitoring effectiveness
Precision psychiatry	Integrated biomarker panels	Personalized treatment planning

Source: Compiled by the authors of this study

Neuromolecular biomarkers also have potential in early detection of PTSD. Changes in inflammatory, neuroendocrine, and metabolic markers may occur before the full development of clinical symptoms. Early identification of individuals at risk could enable timely intervention and reduce the likelihood of chronic disease progression.

PERSONALIZED TREATMENT APPROACHES

The growing understanding of neuromolecular mechanisms underlying post-traumatic stress disorder has created the basis for more targeted and individualized therapeutic strategies. Personalized treatment approaches aim to address specific biological disturbances, including inflammation, oxidative stress, neuroendocrine dysregulation, neurotransmitter imbalance, and impaired neuroplasticity. Such strategies move beyond symptom-based treatment and focus on underlying pathophysiological processes [18, 22, 26].

Anti-inflammatory therapies represent a promising direction, given the consistent evidence of chronic low-grade inflammation in PTSD. Modulation of inflammatory pathways may involve pharmacological agents targeting cytokine signaling, as well as interventions that reduce microglial activation. By decreasing levels of pro-inflammatory mediators, such approaches may improve neuronal function and reduce symptom severity.

Targeting pathways associated with the NLR family pyrin domain containing 3 inflammasome may further limit the amplification of inflammatory responses.

Oxidative stress is closely linked to inflammation and neuronal damage, making antioxidant therapies another important component of treatment. Strategies aimed at restoring redox balance include the use of compounds that enhance antioxidant capacity, such as glutathione precursors or agents supporting mitochondrial function. Reduction of reactive oxygen species may protect cellular structures, improve neuronal viability, and support functional recovery [16, 23, 34].

Modulation of the hypothalamic–pituitary–adrenal axis is also of therapeutic interest. Interventions targeting cortisol regulation and glucocorticoid receptor sensitivity may help normalize stress responses. Balancing the interaction between cortisol and dehydroepiandrosterone may further improve resilience to stress and reduce maladaptive physiological responses.

Therapies targeting neurotransmitter systems remain a central component of PTSD treatment. Modulation of serotonergic, noradrenergic, and dopaminergic pathways may improve mood regulation, reduce hyperarousal, and enhance cognitive function. Additionally, targeting glutamatergic signaling, particularly through the N-methyl-D-aspartate receptor, may influence synaptic plasticity and facilitate extinction of traumatic memories. Enhancing gamma-aminobutyric acid activity may further support inhibitory control within neural circuits [17, 19, 24, 34].

Neuroprotective strategies and interventions supporting neuroplasticity are increasingly recognized as essential. Enhancing levels of brain-derived neurotrophic factor and other growth factors may promote synaptic remodeling and neuronal survival. Such approaches may improve cognitive flexibility and facilitate adaptive processing of traumatic experiences. Interventions that support neurogenesis and synaptic connectivity may contribute to long-term recovery.

The integration of biomarker profiles with clinical phenotypes represents a core principle of precision psychiatry, enabling the identification of biologically distinct subgroups of PTSD. This approach may facilitate the selection of targeted interventions based on dominant pathophysiological mechanisms, such as inflammation-driven, neuroendocrine-dysregulated, or neuroplasticity-impaired subtypes.

The concept of precision psychiatry integrates these approaches by tailoring treatment to individual biological profiles. Biomarker-based stratification may enable the identification of dominant pathological mechanisms in each patient, allowing for the selection of targeted interventions. This approach has the potential to improve treatment effectiveness, reduce variability in outcomes, and support more efficient management of PTSD [11, 18, 33, 38, 40].

Overall, personalized treatment strategies based on neuromolecular biomarkers represent a promising direction in the management of PTSD, linking advances in neurobiology with clinical practice.

FUTURE DIRECTIONS

Future research on neuromolecular biomarkers in post-traumatic stress disorder should focus on several key areas that may improve understanding of disease mechanisms and support translation into clinical practice. One of the most important directions involves longitudinal studies. Most available data are derived from cross-sectional designs, which limit the ability to determine causal relationships and temporal dynamics. Longitudinal studies would allow for the assessment of biomarker changes over time, including the transition from acute stress responses to chronic PTSD. Such approaches may help identify early biological predictors of disease onset, progression, and remission, as well as factors associated with treatment response [15, 23].

Another critical area is the validation of biomarker panels. Single biomarkers often lack sufficient specificity and sensitivity to serve as reliable diagnostic tools. Therefore, combining multiple biomarkers representing different biological pathways, such as inflammation, oxidative stress, neuroendocrine regulation, and neuroplasticity, may provide a more accurate representation of the disorder. Standardization of measurement methods, population characteristics, and analytical approaches is necessary to ensure reproducibility and comparability across studies. Large-scale, multicenter investigations are particularly important for establishing clinically relevant biomarker profiles [18, 37].

Integration of multi-omics approaches represents a further step toward a comprehensive understanding of PTSD. Combining data from genomics, epigenomics, transcriptomics, proteomics, and metabolomics may reveal complex interactions between biological systems and identify key regulatory networks involved in stress responses. Such integrative analyses may also facilitate the identification of novel therapeutic targets and improve the ability to classify biologically distinct subtypes of PTSD [12, 22, 36].

Translation of biomarker research into clinical practice remains a major challenge. For biomarkers to be clinically useful, they must be accessible, cost-effective, and easy to interpret. Development of standardized protocols for biomarker assessment, including sample collection, processing, and analysis, is essential. In addition, clinical guidelines are needed to define how

biomarker data should be integrated with existing diagnostic tools.

The development of biomarker-based diagnostic systems may ultimately improve the current symptom-based classification of PTSD. Such systems could support early identification of individuals at risk, enable more precise diagnosis, and guide personalized treatment strategies. Continued research integrating biological and clinical data will be necessary to achieve these goals and to fully implement biomarker-driven approaches in psychiatry [11, 18, 22, 36].

The clinical relevance of neuromolecular biomarkers in PTSD extends beyond pathophysiological insight and includes their potential application in diagnosis, patient stratification, and personalized treatment planning, as summarized in Table 2.

LIMITATIONS

Several limitations should be considered. Most studies on neuromolecular biomarkers in PTSD are cross-sectional, limiting causal interpretation. There is also significant variability in measurement methods, sample types, and study populations, which reduces comparability. In addition, many biomarkers lack standardized thresholds, limiting their current clinical applicability. Finally, comorbid conditions may influence biomarker levels and complicate interpretation.

CONCLUSIONS

Post-traumatic stress disorder should be understood as a biologically complex and multidimensional condition involving interactions between neuroendocrine, immune, metabolic, and neurodegenerative mechanisms. The evidence presented in this review indicates that processes such as neuroinflammation, oxidative stress, dysregulation of the HPA axis, impaired neuroplasticity, and cellular damage collectively contribute to the development and persistence of PTSD symptoms. These findings support the view that PTSD extends beyond a purely psychological framework and involves measurable biological alterations.

Neuromolecular biomarkers may complement symptom-based diagnostic systems by providing objective information on underlying biological processes and, in the future, may help identify clinically relevant biological subgroups of PTSD. Their clinical application, however, still requires further validation and standardization.

Despite these promising perspectives, further translational research is required. Future studies should focus on validating biomarker panels, standardizing measurement methods, and establishing their clinical utility. Bridging the gap between experimental findings and clinical application remains a critical step in advancing biomarker-based approaches in psychiatry. Future advances in biomarker standardization and multi-modal integration may enable the transition from symptom-based classification toward biologically informed diagnostic systems in PTSD.

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CONFLICT OF INTEREST
The Author declares no conflict of interest

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REVIEW ARTICLE

CONTENTS

Adaptation of approaches to ensuring the availability of medicines for the population of Ukraine under martial law

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ABSTRACT

Aim: To analyze the availability of medicinal products for the Ukrainian population under martial law, identify key challenges in the pharmaceutical sector, and substantiate adaptive approaches for ensuring continuous pharmaceutical provision.

Materials and Methods: A systematic analysis of regulatory, legal, and empirical data (2022–2025) was conducted using sources from the Ministry of Health of Ukraine, the Ministry of Digital Transformation of Ukraine, the State Service of Ukraine on Medicines and Drugs Control, and international organizations. The search covered the period from February 2022 to early 2026, corresponding to the duration of full-scale war and martial law in Ukraine. Sources were included if they addressed pharmaceutical provision, access to medicines, or pharmacy services; reflected the functioning of healthcare or pharmaceutical systems under crisis or wartime conditions; provided empirical data, regulatory information, or analytical insights; and were published in peer-reviewed journals, official reports, or credible professional and industry platforms in English or Ukrainian. Sources were excluded if they were not relevant to pharmaceutical accessibility or healthcare delivery, lacked analytical or factual content, duplicated previously identified sources, or originated from unverified platforms. The initial search and screening resulted in 68 sources. After preliminary screening and relevance assessment, 32 sources were selected for full-text review. Ultimately, 21 sources were included in the final analysis, forming the evidence base of this study.

Conclusions: The pharmaceutical sector in Ukraine demonstrated high adaptive capacity under martial law. Despite infrastructural damage, workforce shortages, disrupted supply chains, and reduced affordability, the implementation of adaptive mechanisms improved access to essential medicines. Alternative delivery models (mobile pharmacies and "Ukrposhta. Pharmacy"), digital monitoring tools, regulatory simplification, and financial support programs enhanced both physical and economic accessibility. The integrated approach combining regulatory flexibility, digitalization, and alternative distribution systems ensures continuity of pharmaceutical provision and strengthens long-term resilience under crisis conditions.

KEY WORDS: pharmacies, accessibility, costs, pharmaceutical security

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INTRODUCTION

The full-scale military aggression against Ukraine, initiated in 2022, has caused significant destabilization of the national healthcare system, posing a critical threat to the state's pharmaceutical security [1, 2]. Under martial law, ensuring the accessibility of medicinal products has transformed from a purely logistical challenge into a vital component of humanitarian resilience. A confluence of destructive factors, including the disruption of supply chains [3–5], infrastructure damage [1, 3, 5], workforce shortages [7], and declining economic affordability [6, 8], has created a complex set of challenges for the pharmaceutical sector that necessitates rigorous scientific analysis [8, 9]. These aspects underscore the need to systematize the emerging adaptive strategies for pharmaceutical provision to the Ukrainian population amid the military conflict.

AIM

The aim of this study is to conduct a systematic analysis of the state of medicinal product availability for the population of Ukraine under martial law, identify critical challenges facing the pharmaceutical sector, and substantiate adaptive approaches to ensuring continuous pharmaceutical provision.

MATERIALS AND METHODS

This study was conducted as a targeted analytical review combined with document and regulatory analysis to assess pharmaceutical accessibility in Ukraine during martial law.

DATA SOURCES AND SEARCH PLATFORMS

The study utilized a combination of scientific databases and targeted searches of official and sector-specific

sources. Scientific publications were identified using Scopus, PubMed, Google Scholar. In addition, due to the limited availability of peer-reviewed evidence on wartime pharmaceutical systems, primary data sources were systematically included. These comprised: official governmental sources, international organizations, industry and professional platforms, official digital services and programs.

SEARCH STRATEGY

A combined search approach was applied, including database keyword search and targeted retrieval of relevant documents. The following keywords and their combinations were used: *"pharmaceutical accessibility", "medicine supply", "pharmacy services", "healthcare resilience", "war", "armed conflict", "Ukraine", "martial law", "mobile pharmacies", "drug availability", "humanitarian aid".* Boolean operators AND/OR were applied where appropriate. For primary data sources, a purposive search strategy was used, focusing on key institutions, pharmaceutical stakeholders, and policy documents relevant to the Ukrainian healthcare system during wartime.

TIME FRAME

The search covered the period from February 2022 to early 2026, corresponding to the duration of full-scale war and martial law in Ukraine.

ELIGIBILITY CRITERIA

Sources were included if they addressed pharmaceutical provision, access to medicines, or pharmacy services; reflected the functioning of healthcare or pharmaceutical systems under crisis or wartime conditions; provided empirical data, regulatory information, or analytical insights; and were published in peer-reviewed journals, official reports, or credible professional and industry platforms in English or Ukrainian.

Sources were excluded if they were not relevant to pharmaceutical accessibility or healthcare delivery, lacked analytical or factual content, duplicated previously identified sources, or originated from unverified platforms.

STUDY SELECTION

The initial search and screening resulted in 68 sources. After preliminary screening and relevance assessment, 32 sources were selected for full-text review. Ultimately, 21 sources were included in the final analysis, forming the evidence base of this study.

ETHICS

This review study was based exclusively on the analysis of publicly available scientific literature, official regulatory documents, institutional reports, and data published in peer-reviewed journals, clinical guidance documents, and open-access databases. The authors confirm that the manuscript contains no plagiarism, data fabrication, or data falsification. All sources of information were appropriately cited and referenced in accordance with academic integrity standards.

FRAMEWORK

The study was conducted within the framework of a research project of the Bogomolets National Medical University 2022–2025: Integrated scientific and practical approaches to improving the functioning of pharmaceutical market entities and pharmaceutical care in Ukraine (state registration № 0122U000488), carried out at the Department of Organization and Economy of Pharmacy.

REVIEW AND DISCUSSION

The pharmaceutical sector of Ukraine has encountered unprecedented challenges as a result of the full-scale military conflict that has persisted since February 24, 2022. Entering the fifth year of the war, the country has witnessed a record number of attacks on its healthcare system; in 2025, the frequency of such incidents increased by nearly 20% compared to 2024 [1]. According to World Health Organization data, at least 2881 attacks on healthcare facilities have been documented since the onset of the war. These hostilities have resulted in extensive damage to medical institutions, specialized transport vehicles, and pharmaceutical warehouses, as well as significant casualties among healthcare professionals [2].

Such repercussions have triggered a cascading effect across all segments of the pharmaceutical sector, severely complicating the provision of medicines and medical devices to the population. Manufacturers have sustained profound losses due to the destruction of production facilities and storage infrastructure. For instance, in 2022, a warehouse belonging to the pharmaceutical company "Farmak" was destroyed, leading to estimated losses of approximately 1.5 billion UAH (≈ 51 million USD at the 2022 exchange rate) [3].

Pharmaceutical distributors, responsible for supplying medicinal products to thousands of pharmacies and healthcare facilities, have also sustained substantial impacts. For instance, the national distributor BaDM lost 45% of its warehousing capacity during the 2022-2023 period; furthermore, in 2025, a third warehouse

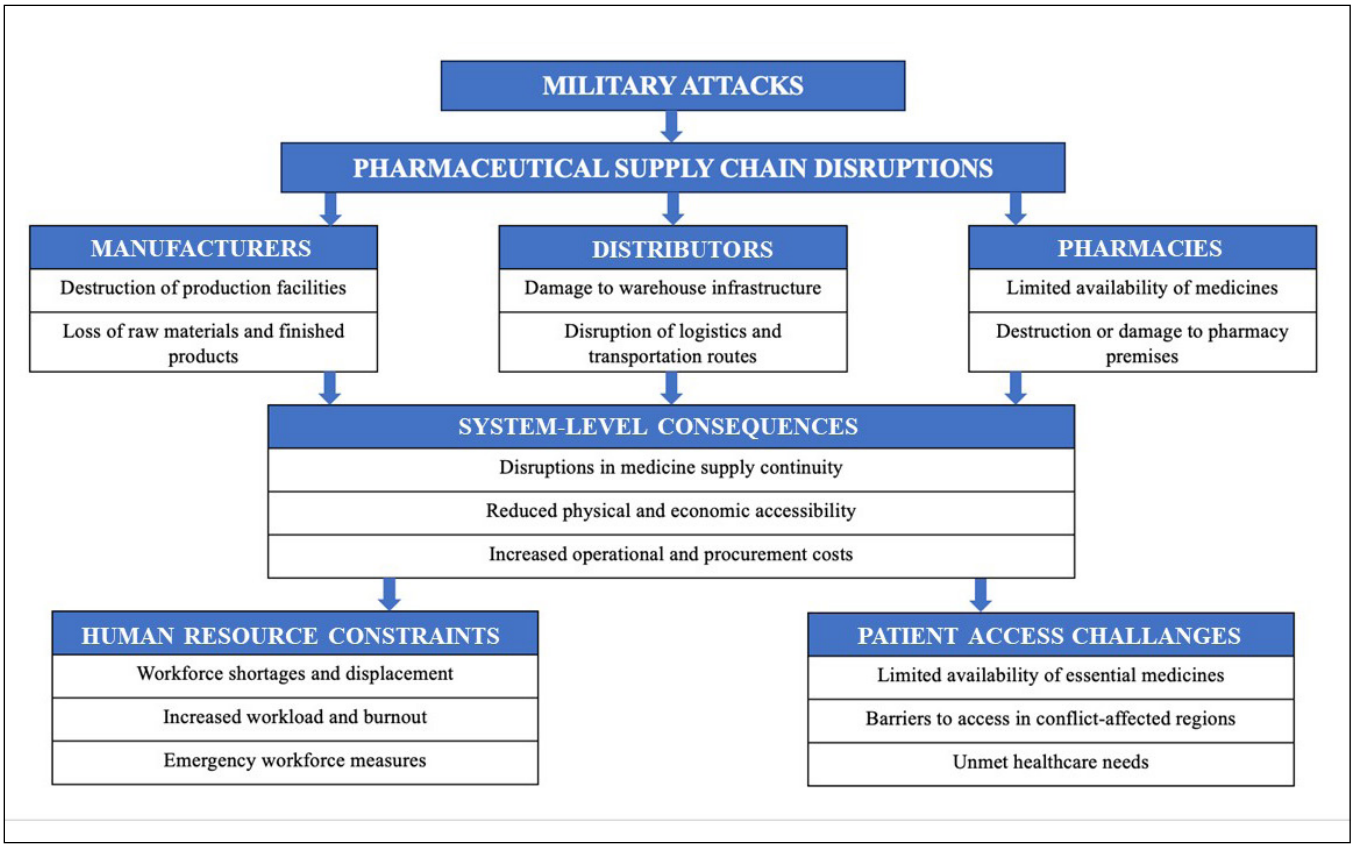


Fig. 1. Impact of the war on the pharmaceutical sector in Ukraine.
Source: compiled by the authors based on [1–6, 8, 19]

with an area of 43000 m^2 was completely destroyed [4]. Ukraine's second-largest distributor, Optima-Pharm, suffered damage to its warehouse complex and corporate offices twice in 2025, affecting over 29000 m^2, with company losses exceeding 100 million USD [5].

These disruptions in supply chains have resulted in depleted pharmaceutical inventories, significant delivery delays, and rising prices for the end consumer. Consequently, these factors have led to a marked decline in both the physical and economic accessibility of essential medicines.

Pharmacy networks have likewise sustained severe damage due to military operations. As of August 2022 alone, more than 500 pharmacies in eastern Ukraine were damaged, with 47 of them completely destroyed [6]. Furthermore, the war has precipitated critical staffing challenges within the retail pharmacy segment, which serves as a cornerstone of national pharmaceutical security. Currently, approximately 40% of vacancies in the pharmaceutical sector are for pharmacist positions, while an additional 15% consist of pharmacy manager roles [6-7].

The ongoing hostilities have triggered complex repercussions that create a ascading effect, progressively impacting all critical components of the pharmaceutical sector – from the manufacturing and distribution of medicinal products to the operational stability of pharmacies and the preservation of human resource potential. This systemic impact is visually represented in Fig 1.

In the context of martial law, Ukraine's healthcare system has faced unprecedented challenges that necessitated rapid and adaptive approaches to ensure stable pharmaceutical provision and maintain the population's pharmaceutical security [9]. To address these critical exigencies, a comprehensive suite of regulatory, legal, and organizational measures was developed and implemented. These initiatives were aimed at facilitating flexible crisis response, optimizing pharmaceutical supply chains, supporting the operational continuity of pharmacies, and safeguarding economic affordability for the public. The results of the systematization and visual representation of the primary approaches to adapting pharmaceutical provision under martial law are summarized in Table 1, which illustrates key interventions and their anticipated impact on the resilience of the pharmaceutical sector.

The implementation of these strategic directions is characterized by a systemic and complementary nature. The proposed mechanisms are designed not only for rapid response to immediate crisis challenges but also to establish a foundation for the long-term resilience of

Table 1. Primary Strategic Directions for the Adaptation of Pharmaceutical Provision Under Martial Law

Adaptation Pillar	Core Measures and Interventions	Anticipated Impact on Pharmaceutical Sector Resilience
Accelerated Regulatory Reform and Procedural Simplification	Temporary legislative amendments; expedited registration protocols for medicinal products [9, 10, 12]	Ensuring timely access to essential medicines under crisis conditions; minimization of bureaucratic barriers
Human Resource Management Adaptation	Implementation of temporary mechanisms for the substitution of vacant pharmacist and pharmacy manager positions [7, 8]	Maintenance of workforce stability and continuity of pharmaceutical provision
Implementation of Alternative Supply Channels	Deployment of mobile pharmacy units (MPU); the "Ukrposhta. Pharmacy" logistics project [6, 13-18]	Enhancement of physical accessibility in frontline and remote regions; ensuring uninterrupted pharmaceutical services
Digitalization and Inventory Monitoring	Integration of the "Affordable Medicines" (reimbursement) and "National Cashback" programs within the "Diia" digital ecosystem [20, 21]	Prevention of pharmaceutical shortages; optimized resource allocation; safeguarding economic accessibility
Financial and Economic Support Mechanisms	Social support initiatives, including "National Cashback" and "Winter Thousand" subsidy programs [20, 21]	Offsetting healthcare expenditures for the population; preservation of the economic affordability of medicines

Source: compiled by the authors based on [6-10, 12-18, 20, 21]

the pharmaceutical sector. Specifically, the integration of regulatory flexibility, digital monitoring tools, alternative supply channels, and financial-economic incentives facilitates the continuity of pharmaceutical provision, even amidst significant infrastructural and logistical constraints.

A pivotal role in shaping these adaptive mechanisms was played by the rapid updating of the regulatory and legal framework. Notably, one of the foundational regulatory decisions was the adoption of the Resolution of the Cabinet of Ministers of Ukraine № 471 (April 15, 2022), which established a specialized regime for expedited market access for medicinal products under martial law.

This normative act introduced the possibility of emergency (conditional) registration of medicines tailored to the urgent needs of the healthcare system. Key provisions included a substantial reduction in regulatory lead times and the extension of registration certificates for pharmaceuticals procured through state funds. Furthermore, a critical provision authorized the import of medicinal products in foreign-language labeling. This measure significantly expanded the capacity to rapidly supply the market with high-demand or scarce items and enhanced the flexibility of logistical solutions [10].

Simultaneously, alongside the transformation of regulatory mechanisms for medicinal product circulation, ensuring the human resource capacity of the pharmaceutical sector emerged as an equally vital adaptation priority. The conditions of martial law exacerbated the shortage of qualified personnel, necessitating an urgent revision of workforce regulation strategies. In response to these challenges, the competent regulatory authority, the State Service of Ukraine on Medicines and Drugs Control, implemented temporary regulatory solutions aimed at streamlining professional licensing and access to pharmaceutical practice. These measures facilitated a partial mitigation of workforce losses and maintained the continuity of pharmaceutical provision for the population [11].

Another pivotal dimension of adaptation under martial law was the implementation of alternative pharmaceutical supply channels. Amidst large-scale infrastructure destruction, the disruption of transport routes, and the impaired functionality of traditional pharmacy networks, the development of alternative delivery mechanisms became critical for sustaining the supply of medicines, particularly in rural areas and frontline regions. The legal framework for these mechanisms was formalized by the Resolution of the Cabinet of Ministers of Ukraine № 809 (August 4, 2023), which amended the Licensing Conditions for the Retail Trade of Medicinal Products.

This normative document introduced the concept of the MPU – a specialized vehicle utilized by a licensee to provide medicines to the population. The operation of MPUs is permitted under strictly defined circumstances: in rural localities lacking stationary pharmacies; in territories under a state of emergency; and within active combat zones or temporarily occupied areas, for the duration of martial law [12].

To ensure pharmaceutical quality standards, MPU vehicles are equipped with appropriate branding, point-of-sale systems, refrigeration units for thermolabile products, and integrated temperature and humidity monitoring systems, thereby guaranteeing compliant

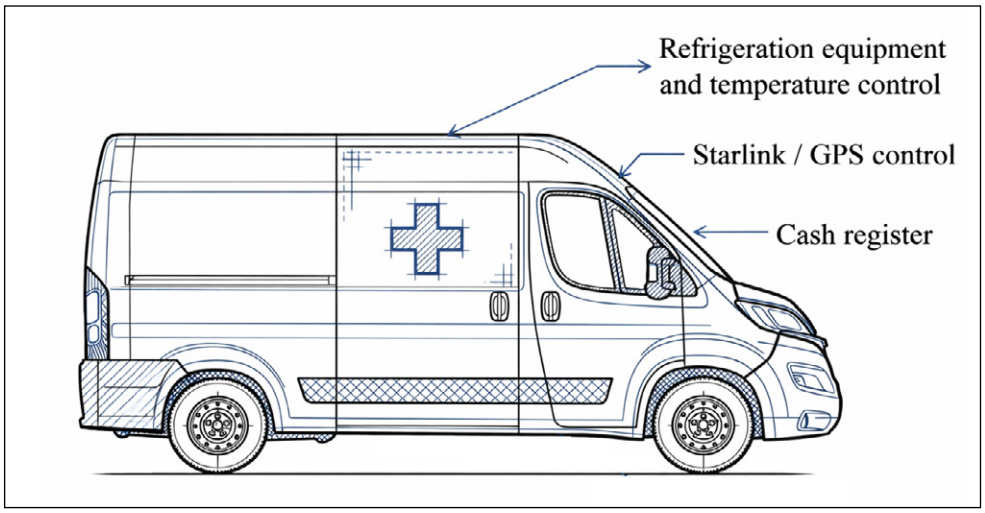


Fig. 2. Design and Equipment Specifications of a MPU.
Source: compiled by the authors based on [12]

storage conditions for medicinal products (Fig. 2).

The practical implementation of this mechanism reached fruition in 2024 through a pilot project in the Kharkiv region, where the route of a MPU covered 80 settlements lacking stationary pharmacies [13, 14]. As of 2025, 29 MPUs are operational across 17 regions of Ukraine, providing pharmaceutical services to over 1000 settlements [15]. MPU pharmacists provide not only the dispensing of medicinal products but also essential consultations and pharmaceutical care for patients. However, the deployment of MPUs has revealed several organizational challenges, notably the degraded state of road infrastructure, inconsistent internet connectivity, and insufficient public awareness regarding operating schedules.

Parallel to the expansion of the MPU network, another initiative aimed at enhancing medicinal accessibility was launched: the "Ukrposhta. Pharmacy" project. This state-led initiative, implemented with the support of the Ministry of Health and the Ministry for Reintegration of the Temporarily Occupied Territories of Ukraine, leverages the extensive logistical network of the national postal service, Ukrposhta. The project's primary objective is to ensure the delivery of medicines to settlements where stationary pharmacies are either absent or were destroyed due to hostilities [16].

The pilot phase of this initiative commenced in February 2024 in the de-occupied districts of the Donetsk region and the border communities of the Sumy region, where the pharmacy network had significantly contracted due to combat operations and temporary occupation. Initial medicinal deliveries were facilitated by mail from centralized warehouses, allowing patients to receive products either free of charge or with a partial co-payment under the state "Affordable Medicines" reimbursement program. By 2025, this project had expanded its reach to over 21000 rural settlements [17].

The "Ukrposhta. Pharmacy" project entails a comprehensive organizational workflow: patients can place orders via a dedicated web portal, a mobile application, or the national postal service's contact center. The system enables real-time order tracking, flexible delivery options, and remote pharmaceutical consultations. This approach provides not only logistics but also pharmaceutical monitoring and support, which is particularly vital for the elderly population – a demographic that heavily utilizes Ukrposhta for pension disbursements and utility payments [16, 18].

A subsequent logical progression in developing adaptive mechanisms was the enhancement of the economic affordability of medicinal products. This became critically relevant against a backdrop of significant inflation, active hostilities, and the deteriorating financial status of the population, specifically vulnerable groups such as the elderly, patients with chronic conditions, and low-income individuals. By the end of 2023, the weighted average cost per unit of the "pharmacy basket" had increased by 25.4% compared to 2022, imposing a severe financial burden on households and highlighting the necessity for state-led cost-offsetting mechanisms [19].

A key instrument in this regard is the state financial incentive program known as "National Cashback", designed to support both consumers and domestic pharmaceutical manufacturers. The program provides a 10% reimbursement on the purchase of Ukrainian-made goods and services, including medicines and medical devices, with a maximum monthly cap of 3000 UAH per user (≈ 82 USD). Upon registration, users accumulate funds from the purchase of domestic pharmaceuticals, which can subsequently be used for further essential expenditures, thereby mitigating financial pressure on families [20, 21].

A specific social initiative integrated within the digital ecosystem was the "Winter e-Support" program

– a one-time state payment of 1000 UAH (≈ 27 USD) intended to help citizens cover basic expenses, including medication. Statistical data from 2025 indicate that over 14 million Ukrainians utilized this program. Notably, expenditures on medicines ranked as the second most frequent use of these funds, following utility payments, confirming the program's efficacy in bolstering pharmaceutical security and social resilience.

To ensure the effective execution of these state support programs, pharmacies integrated specialized digital services, configured point-of-sale systems for automated cashback calculations, and conducted staff training. Furthermore, for patient convenience, an interactive digital map was developed, allowing users to locate the nearest pharmacies participating in the "Winter e-Support" and "National Cashback" programs.

CONCLUSIONS

Ukraine demonstrates remarkable agility and adaptive capacity within its pharmaceutical sector under martial law, consistently developing and implementing integrated approaches to ensure both the physical and economic accessibility of medicinal products. The synergy of alternative supply channels, digital monitoring tools, organizational innovations, and financial-economic mechanisms facilitates the continuity of pharmaceutical provision, even under extreme crisis conditions.

A significant factor in this process is the rapid evolution of the normative and legal framework, which establishes a flexible regulatory environment capable of responding to a highly volatile landscape. Consequently, these implemented adaptive strategies not only bolster the current resilience of the pharmaceutical sector but also form a robust structural foundation for ensuring medicinal accessibility during prolonged periods of systemic crisis.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

The video head impulse test in routine otorhinolaryngology practice: A scoping review

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ABSTRACT

Aim: To evaluate the role of the video head impulse test (vHIT) in routine otolaryngological practice and to summarize its combined use with other methods.
Materials and Methods: The study was conducted in accordance with the PRISMA-ScR guidelines. The literature search was conducted in PubMed, Scopus, Web of Science, Google Scholar, and the Inventis manufacturer's website using the following keywords: ("video head impulse test" OR vHIT) AND (vestibular OR vertigo OR otolaryngology OR "vestibulo-ocular reflex"), covering the period 2008–2026. Inclusion criteria: original and review articles on the clinical application of vHIT in otorhinolaryngology, combinations with other tests, nosological forms, and subjective scales. Out of 92 sources, 26 publications were selected.
Conclusions: The analysis showed that vHIT outperforms clinical HIT due to the detection of latent saccades and subclinical disturbances of the vestibulo-ocular reflex (VOR). The highest diagnostic value is achieved in combination with cVEMP/oVEMP, HRCT of the temporal bones, and caloric testing. vHIT is informative in cases of acute unilateral vestibulopathy, Meniere's disease, bilateral vestibulopathy, ototoxicity, vestibular schwannoma, and blast-induced vestibulopathy. It is recommended to use vHIT as the primary objective test in standardized algorithms for vestibular diagnosis to improve the accuracy of differential diagnosis, monitor rehabilitation, and standardize clinical practice.

KEY WORDS: vestibulo-ocular reflex, vertigo symptom scale

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INTRODUCTION

Dizziness and vertigo are common complaints in ear, nose, and throat clinics, making up 25-30% of visits. Recent studies show that vestibular disorders have increased, partly due to blast trauma from conflicts, which can damage the semicircular canals, otoliths, and other parts of the vestibular system, including both peripheral and central components [1, 2].

The vestibulo-ocular reflex (VOR) stabilizes the image on the retina during head movement by generating compensatory eye movements that are equal in speed and opposite in direction to the head impulse. The reflex arc is made up of the receptors in the semicircular canals, the vestibular nerve, the brainstem's vestibular nuclei, and the oculomotor nuclei. Normally, the vestibulo-ocular reflex, or VOR, has a gain of about 1.0 - this means the eyes move exactly as much as the head, keeping your gaze steady. But if the vestibular system is damaged, either in the peripheral or central parts, the gain drops. To keep your gaze fixed, the brain sends corrective signals to the eyes, making quick adjustments [2, 3].

The head impulse test (HIT), described by Halmagyi and Curthoys in 1988, allows for the detection of gross VOR asymmetry when evaluating the horizontal semicircular canals. However, the subjectivity of the assessment, the inability to quantitatively measure gain, and insensitivity to latent saccades significantly limit the diagnostic capabilities of the clinical HIT. vHIT has overcome these limitations by providing objective quantitative recording of VOR in the high-acceleration range (1500–4000°/s^2, peak velocity 150–300°/s) across all six semicircular canals [2–4].

Most commercial vHIT systems rely on goggles with built-in video cameras and accelerometers, which cause tracking artifacts and discomfort in children, elderly patients, and individuals with neck injuries. Systems with a remote infrared camera that does not physically contact the orbital region have offered an alternative approach that potentially reduces these artifacts and expands the range of testing options available [5].

Despite the growing number of publications on vHIT, there remains a lack of systematic data regarding its

clinical application in combination with other diagnostic methods and the correlation between the test's objective parameters and subjective scales, particularly the Ukrainian version of the Vertigo Symptom Scale [6]. This necessitates a scoping review to synthesize the available evidence and determine the prospects for implementing the method in routine practice [7].

AIM

This scoping review aimed to evaluate vHIT's role in everyday ear, nose, and throat practice. It looked at how vHIT works with other diagnostic tools, which conditions it's best at identifying, and how its results - like compensatory saccades - relate to patients' symptoms.

MATERIALS AND METHODS

This study was conducted as a scoping review in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) methodological guidelines [8].

The literature search was conducted from January to March 2026 in the following electronic databases and platforms: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search strategy included the following combinations of keywords and logical operators: ("video head impulse test" OR vHIT) AND (vestibular OR vertigo OR otolaryngology OR "vestibulo-ocular reflex" OR VEMP OR "computed tomography" OR "temporal bone"). The search time frame was 2008–2026. There were no language restrictions on the publications; however, only works with full-text versions in English or Ukrainian were selected for analysis.

Inclusion criteria: original studies and reviews dedicated to the clinical application of vHIT in otorhinolaryngological practice; publications containing data on the combination of vHIT with other diagnostic methods for the vestibular system; studies analyzing nosological forms of vestibular disorders or subjective symptom assessment scales. Exclusion criteria: conference abstracts, letters to the editor; publications without the full text.

The initial search identified 92 sources. After removing duplicates and screening by title and abstract, 47 publications were selected for full-text review. After a detailed analysis of the full texts, the final set consisted of 26 scientific papers. (Fig. 1.) In addition, the Ukrainian version of the Vertigo Symptom Scale [6] with the full text of the questionnaire was included in the analysis.

This study is a scoping review and is based exclusively on an analysis of publicly available scientific data published in peer-reviewed journals, clinical guidelines, and official manufacturer sources. No primary collection of patient information was conducted, no personally identifiable data were used, and no new clinical interventions or experiments were performed.

The vHIT SYNAPSYS system by Inventis, Italy, was selected as the glasses-free vHIT registration system.

ETHICS

The authors fully adhered to the ethical principles of the World Medical Association's Declaration of Helsinki, as well as the international standards of publication ethics recommended by the International Committee of Medical Journal Editors (ICMJE, 2024). No part of this work contains plagiarism, fabrication, or falsification of data. All sources of information used are correctly cited and formatted in accordance with the journal's requirements. Consequently, approval from a local bioethics committee was not required.

REVIEW AND DISCUSSION

The vHIT method measures the vestibulo-ocular reflex (VOR) at high-frequency acceleration, something the caloric test and Barani chair rotation test cannot do. It works by rotating the head briefly and passively, with an acceleration of 1500–4000°/s^2. A healthy vestibulo-ocular reflex will generate an eye movement that is equal in speed and opposite in direction. If the reflex is damaged, the eyes cannot keep up, and the brain has to make corrective movements to get the gaze back on track. These movements, called saccades, can happen after the stimulus is over or during it. The ones that happen after are visible, but the ones during are almost invisible to the clinician. The detection of covert saccades is a key advantage of vHIT over the clinical head impulse test (HIT): they appear earlier, often under conditions of sub- or pseudonormal gain, and indicate active central compensation for peripheral vestibular deficits. Traditional vHIT systems rely on the use of goggles with built-in cameras and accelerometers, which can lead to goggle slippage, patient discomfort, and limitations in certain populations.

Comparative studies of vHIT systems with and without glasses demonstrate that contactless systems with a remote infrared camera provide greater reproducibility of results and better tolerability in patients with neck injuries and post-traumatic stress disorder [10]. Remote recording technology eliminates one of the key technical artifacts of traditional vHIT, making the method more widely applicable in routine otolaryngological practice, including in children and patients affected by mine-blast injuries [11].

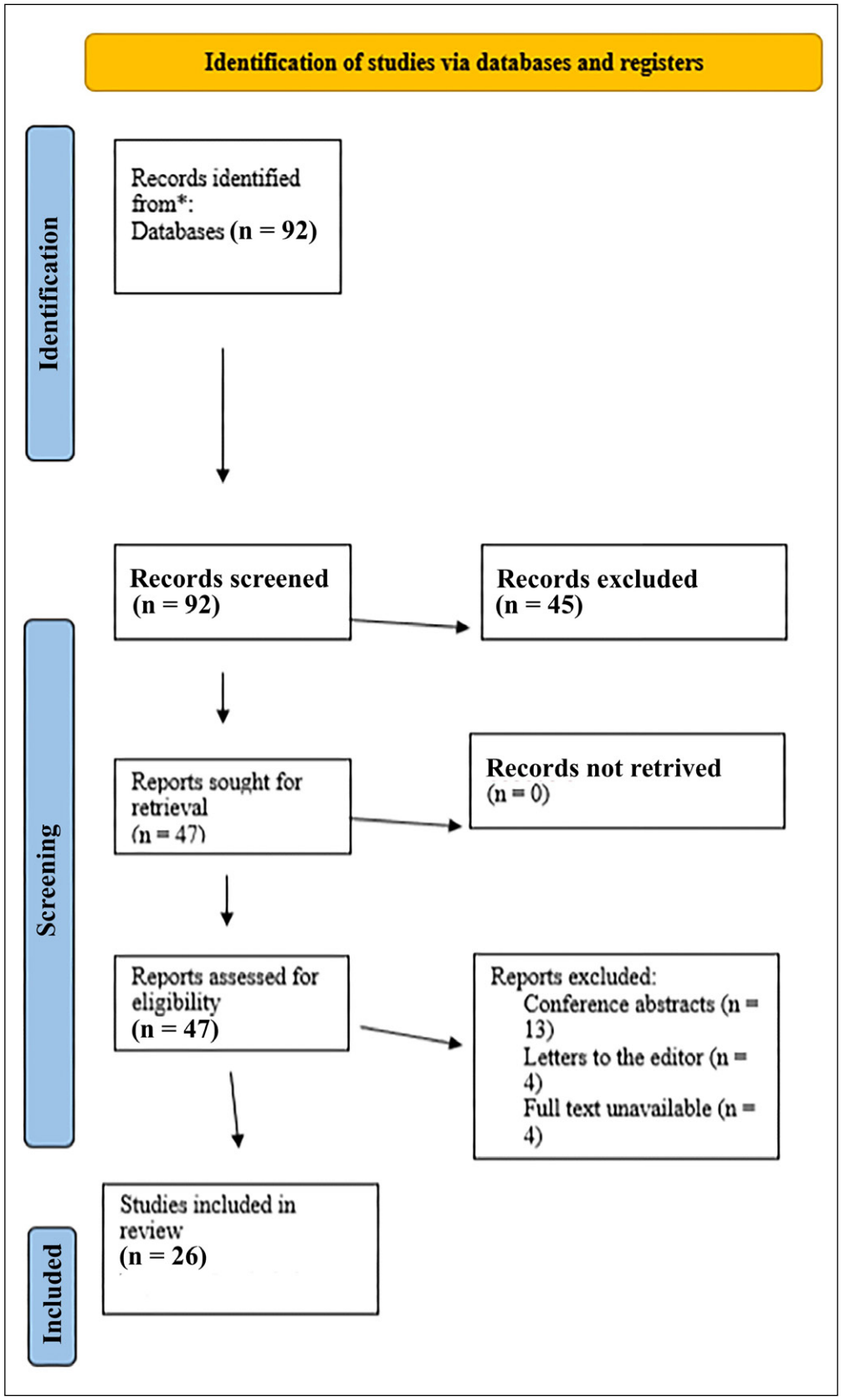


Fig. 1. PRISMA flow diagram
Compiled by the authors

The standard vHIT procedure involves the following position: the patient sits 1–1.5 m away from a stationary visual target at eye level. The physician stands behind or to the side of the patient, holding the patient's head with both hands at the temporal region. To test the horizontal semicircular canals, the head is tilted forward 30° from the horizontal. To test the vertical canals in the RALP and LARP planes, the head is tilted 45° toward the corresponding plane from the sagittal axis (Fig. 2).



Fig. 2. Demonstration vHIT in a seated patient. The examiner holds the patient's head firmly at the temples and performs rapid, unpredictable horizontal head rotations while the patient fixates on a stationary target
Picture taken by the authors

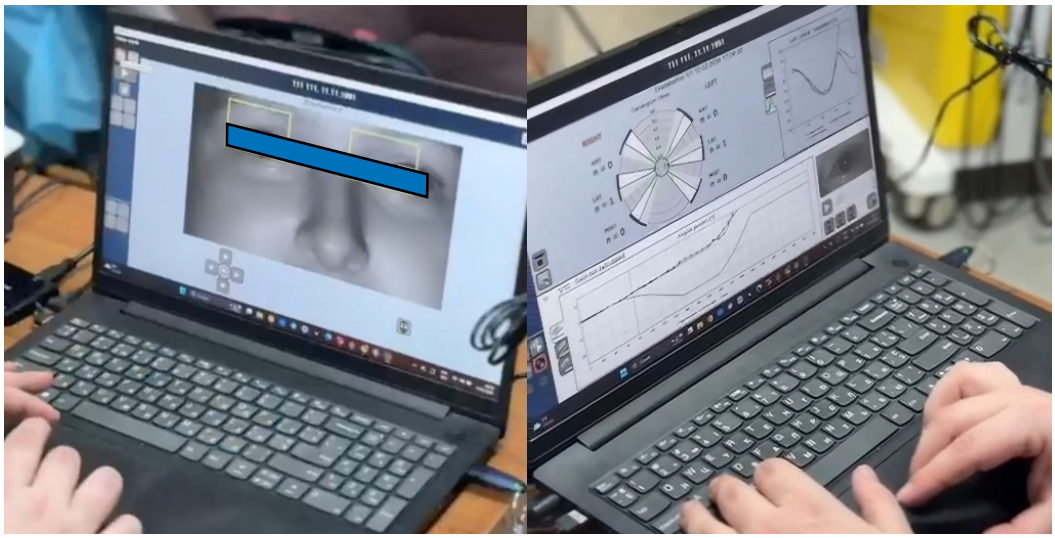


Fig. 3. Demonstration of eye-tracking module in the vHIT system. Live feed (center) shows pupil tracking with calibration cross; side panels present synchronized head and eye velocity traces, highlighting the software's capability to capture high-frequency VOR responses and latent saccades
Picture taken by the authors

The impulse is applied suddenly, with no warning, at 1500–4000°/s^2 and reaches a top speed of 150–300°/s. It should only move 10–20° at most. For accurate results, the patient must not know which way they'll be turned and should keep their eyes still before the impulse starts. Aim for 10-20 good impulses per channel, but any with interference, poor focus, or calibration issues are automatically dismissed by the software and don't factor into the gain calculation.

To calculate gain, we look at the ratio of eye velocity to head velocity during the first 40-60 milliseconds of a saccade. We consider it a compensatory saccade if the peak eye velocity deviates from the baseline. Covert saccades happen within 0-200 milliseconds of the stimulus, while overt saccades occur after 200 milliseconds. (Fig. 3) If a person has spontaneous nystagmus greater than 4°/s during testing, we need to correct for it or be cautious when interpreting the results, since nystagmus can hide or mimic abnormal saccades. Interpretation of vHIT results is based on two main parameters: VOR gain and the number of compensatory saccades (overt and covert). To standardize the assessment, data from an open dataset [12] and generalized values from the literature are used (Table 1).

Low VOR gain values, combined with compensatory saccades, are a sign of a problem. Covert saccades,

Table 1. Normal VOR gain values for vHIT systems (from the Figshare dataset)

Semicircular canal	Average gain (±SD)	Lower limit	Notes
Horizontal right	0.98 ± 0.08	≥ 0.85–0.90	The most stable parameter
Horizontal left	0.97 ± 0.09	≥ 0.85–0.90	Asymmetry < 0.15 is considered normal
Anterior right (RALP)	0.95 ± 0.10	≥ 0.75–0.80	Higher risk of artifacts
Posterior left (RALP)	0.94 ± 0.11	≥ 0.75–0.80	—
Front left (LARP)	0.96 ± 0.10	≥ 0.75–0.80	A decrease of 0.05–0.10 after age 70
Rear right (LARP)	0.95 ± 0.11	≥ 0.75–0.80	Physiologically lower values in children under 7 years of age

Source: compiled by the authors based on [4]

which can't be seen during a clinical test, are particularly useful for diagnosis. Normal gain values change with age: in babies, horizontal VOR gain is around 0.6 to 0.7, and it takes until age 7 to reach adult levels. After 65, gain values naturally drop due to muscle and hair cell loss. Using adult standards for children and older adults can lead to misdiagnosis. If the difference in VOR gain between the right and left canals is more than 0.15, it's a problem, no matter what the actual values are. This is a better way to spot one-sided damage than just looking at low gain values.

The HINTS Protocol is the only validated way to tell peripheral vestibular syndrome from central vestibular syndrome in patients with acute vestibular syndrome. It has three parts: checking the vestibulo-ocular reflex, looking at the type of nystagmus, and doing a skew deviation test. If the vestibulo-ocular reflex test is abnormal, the patient has unilateral horizontal nystagmus, and no skew deviation, it points to a peripheral problem - a result doctors consider safe. But a normal test result can be alarming, especially in cases of ischemia in certain brain areas, where the vestibular nerve might still be intact. The HINTS Protocol's accuracy depends on the doctor's expertise - non-specialists tend to get lower sensitivity scores [13].

Using vHIT to assess the HIT component makes the evaluation less subjective and more reliable. In otolaryngology, HINTS is most useful for cases of acute vestibular syndrome that last more than 24 hours and cause persistent vertigo and nystagmus. This is different from episodic vertigo, where HINTS doesn't apply.

The highest diagnostic accuracy of vestibular testing is achieved with a comprehensive approach (Table 2). No single test provides a complete picture of labyrinth function, as different tests cover different frequency ranges and different structures of the vestibular system.

One of the key aspects of modern vestibular diagnostics is the comparison of objective instrumental data with the patient's subjective perception. Clinical experience and a review of the literature indicate a well-known discrepancy between the objective degree of vestibular deficit and the severity of symptoms: some patients with a significant reduction in gain have minimal complaints due to successful central compensation, while others with normal or subnormal gain subjectively experience a pronounced functional deficit. A synthesis of the data shows that the traditional VOR gain parameter often does not correlate sufficiently with symptom severity, whereas compensatory saccades (overt and covert) are a more sensitive marker of subclinical vestibular dysfunction that persists despite normal gain [20].

Based on a synthesis of the included publications and similar correlational studies using validated vertigo scales (the Vertigo Symptom Scale in its international versions), a statistically significant association is predicted between the frequency of compensatory saccades on the vHIT and scores on the Ukrainian-language version of the VSS [6]. Verification of these correlations in our own patient cohort is the subject of a planned prospective study by the authors. For comparison, we present data from similar studies that used the original version of the VSS [20–22].

vHIT has limitations, mainly operator dependence, which requires precise stimulus delivery. It is also prone to false positives in patients with severe eye movement disorders. The results can differ from caloric tests in 30–50% of cases, as they measure different parts of the vestibulo-ocular reflex. Patients with blast trauma pose specific challenges, including neck injuries and PTSD, which demand adjustments to the testing protocol.

Prospects for Further Research. Expanding the use of vHIT in pediatric otolaryngology: the method has been proven effective in children as young as 3 months, opening up opportunities for early, objective diagnosis of congenital and acquired vestibulopathy in pediatric patients for whom subjective tests are not applicable.

Development of standardized protocols combining digital vestibular examinations, particularly for a cohort of patients affected by mine-blast injuries. It is critically important to have a validated multimodal algorithm that allows for the objective documentation of vestibular deficits for medical, social, and forensic medical examinations [20].

Table 2. vHIT in modern diagnostic algorithms: clinical scenarios, expected patterns, and clinical decisions

Clinical scenario	The Role of vHIT	Diagnosis (Bárány Society / ICD-11)
Persistent dizziness + nystagmus ≥ 24 hours; symptoms > 3 hours but < 24 hours at the time of examination	H-component of HINTS: horizontal channel VOR gain + presence of corrective saccades. A normal vHIT during the acute vestibular syndrome (AVS) is considered a 'red flag', as the peripheral vestibulo-ocular reflex (VOR) may be preserved in strokes involving the anterior inferior cerebellar artery (AICA) territory [14]. Diagnostic accuracy of HINTS among specialists: sensitivity 97–100%; among emergency physicians and non-specialists — 21–59% (κ = 0.10) [7–9].	AVS acute unilateral vestibulopathy (AUVP) ICD-11: AB31.0 Diff.: ischemic stroke (posterior fossa), AICA infarct
Intermittent vestibular syndrome (episodes lasting 20 minutes to 12 hours, plus fluctuating sensorineural hearing loss, tinnitus, and a sensation of fullness in the ear)	Caloric–vHIT dissociation: abnormal caloric test (canal paresis ≥ 22–34%, depending on the protocol) + normal vHIT gain = a sign of low-frequency damage with preserved VOR [10]. Critical note: vHIT gain alone does not distinguish Menière's disease (MD) from VM—the mean difference in gain between the groups is statistically insignificant (p = 0.497) [15]. It is the caloric–vHIT dissociation and the presence of saccades that have diagnostic value. A decrease in gain between attacks indicates progression and transition to stage II–III	MD ICD-11: AB31.1 Diff.: vestibular migraine (VM), VM-MD overlap
Oscillopsia during movement, unsteadiness in the dark and on uneven surfaces	Bilateral reduction in VOR gain is the primary diagnostic criterion [16]. Testing all 6 channels increases the sensitivity of the method and detects isolated lesions in the vertical channels [17]. vHIT is the priority test and should be performed first [12–13] The Suppression Head Impulse Paradigm (SHIMP protocol) should be used when results are inconclusive	BVP ICD-11: AB30 Diff.: neurodegeneration, ototoxicity
Subacute unilateral vestibulopathy + SNHL and/or tinnitus	Reduced gain + compensatory saccades on the affected side. The posterior canal is affected first due to the specific blood supply of the inferior branch of the vestibular nerve. A normal vHIT does not rule out a tumor: central compensation may mask the deficit [14–16]	Vestibular schwannoma (VS) ICD-11: 2A00.0 Diff.: AUVP, meningioma, bilateral vestibular schwannoma (neurofibromatosis type 2), posterior semicircular canal dehiscence [15–16]
Vestibular disorders following blast trauma (combat injury, primary–tertiary blast, mTBI)	Dissociative pattern: normal or subnormal gain with an increased number of covert saccades—reflects active central compensation in the presence of an unstable VOR [2]. The vertical canals are affected more frequently than in other forms of vestibulopathy. Covert saccades are the key parameter; it is they, rather than gain, that document the deficit	Blast-induced vestibulopathy ICD-11: AB31.Y Diff.: AUVP, PPPD, central vestibular syndrome (TBI)
Transient positional vertigo (< 1 min) triggered by a change in head position; without auditory symptoms	In typical benign paroxysmal positional vertigo (BPPV), vHIT is normal: canalolithiasis does not disrupt the VOR reflex arc. Abnormal posterior canal gain is found in ~55% of mixed posterior semicircular canal -BPPV cohorts and up to 73–88% in atypical forms (cupulolithiasis, short-arm); in typical first episodes, it is significantly less common. Abnormal vHIT in the presence of positional symptoms indicates a central origin or concomitant vestibulopathy. vHIT is not mandatory in a typical first episode	BPPV ICD-11: AB31.2 posterior canal (80%), horizontal canal (15%) Diff.: central positional nystagmus (posterior fossa tumor/stroke)
Occasional vertigo with a history of migraine (episodes lasting from 5 minutes to 72 hours; headache or photophobia; no persistent sensorineural hearing loss)	vHIT values are typically normal between attacks—there is no structural damage to the VOR. During an attack, a transient decrease in gain may occur in ≤ 30% of patients. Abnormal vHIT values between attacks warrant investigation for Menière's disease (MD) or a history of AUVP [1–3, 11]	Vestibular migraine (VM) ICD-11: 8A80.3 Diff.: MD (VM-MD overlap ~20 %), PPPD, transient ischaemic attack (vertebrobasilar)
Chronic non-systemic dizziness and unsteadiness lasting ≥ 3 months; (worsens when standing, during movement, and in visually stimulating environments; often following a vestibular episode)	vHIT is typically normal—PPPD is a functional disorder without structural damage to the VOR. Abnormal vHIT in PPPD indicates an organic trigger that caused the disorder. Gain does not correlate with symptom severity [21, 23]	PPPD ICD-11: 8A85 Diff.: VM, compensated AUVP, MD (interictal)
Changes in VOR during treatment (serial assessment during vestibular rehabilitation and pharmacotherapy)	The dynamics of corrective saccades are the primary marker of central vestibular compensation; they correlate more strongly with subjective scales than gain [15, 16]. Gain is a secondary parameter: it may normalize before symptoms resolve. The combination of vHIT + VEMP + posturography + subjective scales provides the highest diagnostic accuracy [17–19]. The absence of saccade dynamics after ≥ 3 months of vestibular rehabilitation therapy (VRT) requires a review of the program [23]	AUVP — monitoring of central compensation BVP — effect assessment VRT MD — follow-up intratympanic therapy blast traumatic brain injury/ documentation [24–26]

Source: compiled by the authors based on [1-3, 7-26]

Conducting prospective cohort studies on the correlation of compensatory saccades with the Ukrainian VSS in patients with concussion: existing data have limitations related to retrospective design and heterogeneity of groups; prospective studies will allow determining the prognostic value of vHIT parameters regarding vestibular function recovery [21, 26].

Standardization and validation of mobile software for vHIT screening, which is particularly relevant for primary care in resource-limited settings.

Integration of artificial intelligence for the automatic detection and classification of saccades: machine learning algorithms can reduce the variability of manual identification of covert saccades, which is one of the main causes of interlaboratory discrepancies in vHIT results [23, 25, 26].

CONCLUSIONS

The scoping review answered our three research questions. Otolaryngologists can use vHIT in their daily practice. It is an objective and efficient way to assess the vestibulo-ocular reflex, covering all six semicircular canals at high frequencies that the caloric test cannot match. vHIT also detects hidden eye movements that help diagnose vestibular problems that are not immediately apparent. This makes it useful for a broad range of patients, from children to the elderly and those with combat injuries.

Nosological forms with the highest diagnostic value for vHIT: The method demonstrates the clearest and most reproducible results in acute unilateral vestibulopathy, Meniere's disease, bilateral vestibulopathy and ototoxicity, vestibular schwannoma, and vestibulopathy resulting from blast trauma.

vHIT can be recommended as an objective instrumental test in standardized diagnostic algorithms for vestibular disorders in otorhinolaryngological and neurological practice. The implementation of this method in combination with other instrumental and subjective methods will improve the accuracy of differential diagnosis, ensure objective monitoring of the effectiveness of therapy and rehabilitation, and contribute to the standardization of vestibular practice in Ukraine.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Experience of resocialisation policy for veterans with post-traumatic stress disorder as a factor of security and socio-economic stability of Ukraine and the European Union

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ABSTRACT

Aim: To substantiate the strategic role of the resocialisation of veterans with PTSD as a critical factor in the security of Ukraine and the EU; to analyse the clinical specificity of contemporary combat-related disorders; and to demonstrate the necessity of implementing inclusive governance models of rehabilitation at the community level to prevent cross-border social risks.

Materials and Methods: A comprehensive approach was applied, including statistical, comparative, and clinical-diagnostic analyses. The source base consisted of a secondary analysis of data from international organisations (GPI, GLOBSEC, UNODC) and departmental statistics for the period 2008–2025. A systematic selection of publications was carried out in the Web of Science Core Collection, Google Scholar, and the electronic catalogues of the V. I. Vernadskyi National Library of Ukraine using the keywords: resocialisation, veterans, PTSD. Of 68 identified sources (including 34 articles), 22 studies that fully met the criteria of scientific validity were included in the final analysis.

Conclusions: It has been demonstrated that Ukraine's resocialisation policy represents a unique precedent for EU and NATO countries. It shows that the stability of the veteran community serves as an instrument for mitigating cross-border crime and social destabilisation in the region. Public administration bodies and local self-government play a decisive role in creating multi-level interventions. The transition from a punitive to a rehabilitative model proves its economic efficiency. Clinical advances by Ukrainian physicians in PTSD are fundamental for the European healthcare system, particularly in the context of rehabilitating foreign volunteers and preparing medical professionals for the challenges of modern conflicts.

KEY WORDS: policy, resocialisation of veterans, PTSD

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INTRODUCTION

The modern world is characterised by an extremely high level of conflict: according to the Global Peace Index (GPI) 2025 report, 59 active state-based conflicts and more than 180 regional armed confrontations have been recorded. This intensity has tragic consequences: data for 2024 indicate approximately 152 thousand war-related deaths [1]. Given Ukraine's status as an immediate neighbour of EU countries and a strategic partner of NATO, Ukrainian practices of veterans' resocialisation acquire critical importance for the European system of security and healthcare. Notably, foreign nationals from 75 countries serve in units of the Land Forces of the Armed Forces of Ukraine, participating in the defence of Ukraine against Russian aggression [2].

As of 2025, the number of veterans in Ukraine amounts to 1,3 million individuals [3], and according to projections, this figure may increase to 5 million after the end of hostilities [4]. According to the Department of Healthcare of the Ministry of Defence of Ukraine, 29% of diseases among military personnel are PTSD-spectrum disorders, and this figure continues to rise [5]. Studies published in *Psychiatry Research* indicate a high prevalence of PTSD among medical personnel and paramedics (up to 14.5%), while among veterans this показатель reaches 15–20% or higher, with a risk of symptom chronicity lasting for decades [6]. Data from the analytical center GLOBSEC confirm that in 25% of cases combat stress transforms into PTSD of varying severity [7].

The formation of a million-strong veteran community in the center of Europe requires not only local solutions but also synchronization with the medical standards of the North Atlantic Alliance. The experience of Ukrainian physicians in treating veterans and implementing multidisciplinary models of rehabilitation governance

represents a unique contribution for EU countries facing emerging mental health challenges. Thus, the development of an effective resocialisation policy in Ukraine is a shared interest of the EU security space, as the stability of the veteran community directly affects the social and economic resilience of the entire region.

AIM

To substantiate the role of the resocialisation of veterans with PTSD as a critical factor in the security of Ukraine and the EU; to analyse the clinical specificity of contemporary combat-related disorders; and to demonstrate the economic efficiency of investments in rehabilitation for preventing cross-border social risks.

MATERIALS AND METHODS

The study is based on a comprehensive analysis combining clinical-diagnostic, medico-economic, and statistical methods for the period 2008–2025. The empirical base consisted of a secondary analysis of reports from international organizations (GPI, GLOBSEC, UNODC, World Bank), as well as departmental statistics from the Ministry of Health of Ukraine and the Ministry of Defence of Ukraine. A systematic search for relevant publications was conducted in the Web of Science Core Collection, Google Scholar, and the electronic catalogues of the V. I. Vernadskyi National Library of Ukraine using the key descriptors: resocialisation, veterans, PTSD. Of 68 identified sources (including 34 articles), 22 original peer-reviewed studies, official reports, and departmental statistics were selected for the final analysis based on eligibility criteria. Exclusion criteria included conference abstracts, editorial materials, letters, and book chapters.

ETHICS

This review is based on the analysis of publicly available scientific data from peer-reviewed publications, databases, and clinical guidelines. As the study did not involve conducting new clinical trials or the direct collection of primary patient data, there was no need for personal identification or approval from an ethics committee.

In the course of preparation, the authors adhered to the principles of the Declaration of Helsinki and international publication standards, including the recommendations of the ICMJE. The work was carried out in accordance with the principles of academic integrity. The text contains no indications of plagiarism or data manipulation in addressing the health issues of veterans with PTSD, and all primary sources related to clinical studies and statistics have been properly cited and included in the reference list.

FRAMEWORK

The study was conducted without financial support from external organisations and forms part of the "Plan of Scientific and Scientific-Technical Activities of the National Academy of Internal Affairs for 2026", approved by the decision of the Academic Council of the NAIA dated 30.12.2025 (Minutes No. 25). The content of the article directly correlates with item 26 of the said Plan: "Administrative and legal mechanism for the reintegration of veterans and combatants into the system of bodies and units of the Ministry of Internal Affairs".

REVIEW AND DISCUSSION

The consequences of modern warfare create long-term challenges for mental health, requiring adaptation of public governance systems. There is a high probability that the actual prevalence of PTSD significantly exceeds official statistics due to the latent nature of the disorder, insufficient diagnostic capacity, and a substantial number of unregistered cases. For EU countries bordering Ukraine, studying these dynamics is strategically important, as uncontrolled maladaptation within the veteran community generates shared risks – from increased cross-border crime to additional pressure on European healthcare systems due to migration processes. Therefore, the development of preventive resocialisation models in Ukraine is a necessary condition for ensuring the collective socio-economic resilience of the European region.

Studies by A. Zalihić, H. Skobić, and N. Pejanović-Skobić demonstrate a direct correlation between the mental health of veterans and their socio-economic adaptation. In particular, employment rates among veterans without signs of PTSD are significantly higher than in the group with a confirmed diagnosis. The clinical profile of veterans with PTSD is characterized by higher comorbidity, including frequent sleep disturbances, systematic use of psychoactive and anxiolytic substances, and a tendency towards addictive behaviours (including alcohol misuse). These findings confirm that undiagnosed PTSD is a key barrier to the successful reintegration of combatants into civilian life [8].

The validity of these assumptions is confirmed by reports of the United Nations Office on Drugs and Crime (UNODC), which systematise the relationship between military trauma, substance abuse, and increasing criminal risks. UNODC identifies psychological trauma as a

dominant predictive factor of drug use in post-conflict regions. For EU countries, this conclusion has strategic significance: undiagnosed PTSD, combined with addictive behaviour, creates preconditions for the formation of transnational criminal networks and illicit trafficking of substances [9]. Timely treatment of combat-related trauma, in accordance with UNODC protocols, is considered not only a humanitarian measure but also an instrument for stabilising the criminogenic situation at the international level.

Standardisation of indicators has shown that veterans are more likely to serve sentences for violent crimes – 64% (including 35% for sexual offences); property crimes account for 12%; drug-related offences for 14%; and driving under the influence for 3%. Overall, the offender profile indicates that for a significant proportion of veterans (32%), the offence represents a first episode occurring in adulthood. This directly points to a crisis of resocialisation and the impact of trauma rather than an inherent criminal predisposition.

The analysis shows that 53% of veterans are held in penitentiary institutions awaiting sentencing. This stage is critical for the involvement of probation authorities and psychological services in implementing programmes for the treatment of addictions and PTSD. Such a strategy enables the application of alternative forms of punishment, replacing isolation with specialized therapy. The effectiveness of this approach is supported by the fact that 22% of veterans receive prison sentences of up to one year; this period has a high preventive potential for intensive community reintegration, helping to prevent criminal recidivism and ensuring the rational use of budgetary resources [10].

Studies by Horesh D., Solomon Z., and Ein-Dor T. confirm the critical role of social resources as a buffering mechanism in overcoming PTSD. The authors demonstrate that a stable supportive environment at both the micro level (family) and macro level (community) is a key determinant of successful resocialisation. Clinically significant are the identified markers of early manifestation: a persistent association between initial reactions to combat stress and the risk of delayed-onset PTSD enables early intervention. An effective rehabilitation governance strategy should include multilevel interventions – from peer-to-peer support groups to systematic psychoeducation of society. From an economic perspective, investments in strengthening the social capital of veterans are highly cost-effective, as maximising internal community resources at early stages reduces the need for prolonged and costly clinical treatment in the future [11].

Hoyer J. N., Chavez M., Lind J., Hamm B., Melillo C., and Besterman-Dahan K conclude that the effectiveness of veterans' resocialisation directly depends on the inclusiveness of research approaches and the active involvement of local self-government bodies and territorial communities in the rehabilitation process. According to the authors, integrating scientific developments into local governance practice is a key factor in overcoming gaps in the provision of medical and social services and improving long-term recovery outcomes for combatants. To address existing service gaps, public governance should promote partnerships between the scientific community and local organizations that directly interact with veterans in their places of residence. Dissemination of research findings on the importance of social support among policymakers and healthcare professionals is critical for shaping an adequate understanding of the needs of the veteran community.

An important element of this process is the integration of veterans into community and religious organizations, where the principle of peer-to-peer support is implemented, contributing to the restoration of an individual's sense of social purpose. Particular attention within public policy should be paid to the diversification of samples: resocialisation programmes must include previously underrepresented groups (women veterans, minority representatives, and individuals not registered within specialised healthcare systems), while also accounting for geographical diversity (from metropolitan areas to rural settings). Analysis of existing practices has revealed a significant limitation – the short-term nature of programmes, which does not allow for the assessment of long-term reintegration dynamics. A multidisciplinary analysis of these gaps confirms the difficulty of unifying the concept of "veteran services", which requires flexible governance decisions and the development of comprehensive indicators for monitoring the process of lifelong social adaptation of veterans [12].

The effectiveness of decentralised governance models for resocialisation is directly dependent on their technological content, which creates a critical need to integrate the most promising innovative therapeutic methods into the public health system that can be tested in Ukrainian clinical practice. For example: 1. Biotechnological and neurophysiological methods: stellate ganglion block (SGB), repetitive transcranial magnetic stimulation (rTMS); 2. High-tech rehabilitation methods: virtual reality exposure therapy (VRET), neurofeedback therapy (biofeedback); 3. Psychopharmacological innovations: psychedelic-assisted therapy (MDMA-assisted therapy), ketamine therapy; 4. Complementary and somatic methods: eye movement desensitisation and reprocessing (EMDR), animal-assisted therapy (canine therapy) [13–16].

The extreme intensity of combat operations and persistent threat contribute to the formation of cumulative traumatic exposure, known as chronic operational stress. Insufficient systematisation of rotations and prolonged exposure of personnel to active combat zones without adequate recovery significantly increases the risk of delayed and chronic forms of PTSD. Although the aetiology of PTSD is directly linked to combat experience, its clinical manifestation and progression are substantially determined by extra-medical factors, including the quality of social support and the family and living environment. This makes PTSD not only a subject of military psychiatry but also a complex socio-governance issue requiring integrated management approaches.

The clinical manifestations of PTSD are traditionally grouped into four main clusters: intrusion (intrusive memories, flashbacks), avoidance (of trauma-related stimuli), negative alterations in cognition and mood, and changes in arousal and reactivity (hyperarousal). These criteria are defined both in the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

In addition to the core categories of post-stress pathology, the scientific literature, as noted by O. Chaban, O. Khaustova, and V. Omelianovych, actively employs concepts describing conditions that do not meet full diagnostic thresholds: 1. Partial (subthreshold) PTSD: this term is used for patients who exhibit clinically significant post-traumatic symptoms but whose constellation of symptoms does not reach the threshold for a full PTSD diagnosis; 2. Complex PTSD (CPTSD) (ICD-11 code 6B41): this nosological entity is used to classify conditions resulting from prolonged and repeated trauma exposure (e.g., sustained combat operations). CPTSD is characterised not only by core PTSD symptoms but also by significant disturbances in self-organisation [18].

The etiological factors of PTSD in military personnel are multiple; however, the most significant triggers that act as a direct precipitating cause of the condition are the death of fellow soldiers or the necessity to use lethal force with its corresponding psychological consequences. During a traumatic event, the individual experiences an extreme state of fear combined with a total loss of control over the situation. The clinical manifestation of PTSD develops in a delayed manner, usually approximately one month after the traumatic incident. However, the post-traumatic continuum begins much earlier: within the first 48–72 hours, pronounced symptoms of acute stress reaction are observed; in the following days, signs of acute stress disorder may be diagnosed [19].

The clinical symptomatology of PTSD in military personnel is characterised by a multidimensional spectrum of disturbances: recurrent memories of the traumatic event (intrusions, flashbacks, nightmares, strong emotional and/or physiological reactions); hyperarousal and sleep disturbances; avoidance of trauma-related reminders; increased anxiety, a need for excessive control, and heightened vigilance; nightmares often related to the traumatic situation; memory impairments; loss of interest in usual activities; emotional instability; and detachment from others, including close relatives and family members [19].

In 2019, a comprehensive medico-social study conducted by O. Lashyn identified significant deficits in the healthcare system for military personnel. It confirmed the absence of an integrated, structurally and functionally interconnected system of measures encompassing detection, assessment, treatment, rehabilitation, and prevention of PTSD. This created an urgent need for scientific substantiation and the development of new methods and comprehensive interventions for managing PTSD.

Particular attention in the study was given to the description of the "Hybrid War Syndrome". It was found that in its development, the place and timing of the crisis acquire specific characteristics, as conventional and non-conventional actions occur against the backdrop of the predominant role of informational, psychological, and cognitive influences. Unlike the Gulf War Syndrome (which involves multisystem damage affecting the central nervous system, gastrointestinal tract, heart, liver, immune, endocrine systems, bones, and skin), the pathogenesis of "Hybrid War Syndrome" revealed for the first time a pronounced ophthalmological pathology (damage to the visual analyser in more than 90% of patients).

The key aggravating factor sustaining the development of PTSD and sensory system damage is informational and cognitive trauma, reinforced by almost constant continuous overload of sensory systems. Physical and physiological manifestations were recorded in 75% of cases and included headaches, dizziness, physical weakness, somatic pain, nausea, and dysfunction of internal organs.

The clinical picture of the syndrome is also characterised by:

• Psychological and psychosocial disorders: personality and reactive anxiety, reduced emotional stability, sexual dysfunction and interpersonal problems (including family breakdown), addictive disorders (alcoholism, drug addiction, gambling, and a return to extreme activities);

• Socio-psychological manifestations: reduced self-esteem, decreased social adaptability, and reduced frustration tolerance;

• Physiological and somatoform disorders: predominance of sympathetic over parasympathetic nervous system tone, haemodynamic changes, and increased activity of the sympathoadrenal and hypothalamic-pituitary-adrenal systems. Severe somatoform disorders with predominant localisation of bodily sensations are combined with psychovegetative paroxysms in the cardiovascular (54%), gastroenterological (26%), and cerebral (20%) anatomical domains;

• Metabolic changes: increased transport forms of lipids in the blood with a shift in the lipoprotein spectrum towards atherogenic fractions [20].

The socio-economic effectiveness of the implemented differentiated approach was confirmed by the analysis of medical indicators. Among the key achievements, the following were recorded: 1. Reduction in treatment duration: the average length of hospital stay in the psychiatric clinic decreased by almost 25 bed-days, from 45.97 bed-days in 2015 to 21.08 in 2016, and remained at a low level in subsequent years (23.54 in 2017, 21.21 in 2018). This reduction in hospitalisation days and minimisation of treatment volume, particularly pharmacotherapy (due to early intervention at the pre-PTSD stage), resulted in decreased state expenditure on inpatient care; 2. Improvement in rehabilitation outcomes: the proportion of medical leave granted due to health status (ICD-10 code F43.0) decreased from 10.4% in 2015 to 5.8% in 2018. At the same time, the proportion of service members returning to military units for further service increased significantly, from 36.3% in 2015 to 64.5% in 2018; 3. Reduction in disability rates: the proportion of military personnel discharged from the Armed Forces due to mental health conditions decreased almost twofold, from 46.6% in 2015 to 21.2% in 2018 [20].

A particular scientific interest is the study by O. Venger, aimed at assessing the prevalence of depressive symptoms. The study differentiated participants into two groups based on the duration of combat experience: Group 1 (up to three months of participation) and Group 2 (more than three months). Depressive symptoms were identified in 31% and 53% of individuals, respectively.

Overall, participants in Groups 1 and 2 exhibited the following symptoms: depressed mood (55.3% and 66.7%); anhedonia (77.3% and 83.3%); fatigue (51.5% and 65.8%); pessimism (21.2% and 31.7%); feelings of guilt, worthlessness, anxiety, or fear (78.0% and 87.5%); low self-esteem (21.2% and 31.7%); impaired concentration and decision-making ability (25.8% and 43.3%); thoughts of death or suicide (25% and 35.8%); fluctuating appetite and weight changes (17.4% and 24.2%); and sleep disturbances (47% and 61.7%) [21].

The assessment of psychopathological symptomatology using the SCL-90-R (Symptom Checklist 90-Revised) conducted by O. Venger revealed a clear positive correlation between the length of military service and the intensity of psychopathological manifestations in service members. In particular, the group with longer service experience demonstrated statistically higher scores across several key syndromal scales. The dominant manifestations included increased somatisation, obsessive-compulsive symptoms, heightened interpersonal sensitivity, pronounced depressive states (often combined with phobic reactions), as well as elevated levels of hostility, anxiety, and paranoid ideation [21].

The study conducted by I. Klymenko, O. Shelestova, and N. Naumenko provided an objective analysis of the distribution of psychological trauma among former prisoners of war. The authors' conclusion that the findings are critically important for the development of individualised rehabilitation and psychological support strategies for this specific category of victims is well substantiated and should be supported.

A study of a group of 50 former military prisoners revealed an extremely high level of psychotraumatic exposure: acute stress reactions were recorded in 94% of respondents. The leading traumatic factors included physical violence (100%), social degradation/disrespect (82%), and emotional aggression (80%). The rate of sexual violence was 24%, although this figure may be underestimated due to socio-cultural barriers and gender-specific perceptions of trauma.

It was established that dissociative experiences are determined directly by the experience of captivity (physical torture and neglect), rather than by individuals' pre-traumatic history [22]. Dissociative symptomatology was diagnosed in 25% of former prisoners of war, with the leading manifestation (38%) being intense reminiscences. High levels of amnesia and cognitive immersion correlated with the use of dissociation as an adaptive defence mechanism to reduce psychological distress.

Within the diagnostic structure, depersonalization-derealisation syndrome (10%) and dissociative disorders with neurological symptoms (8%) were predominant. Less prevalent were dissociative amnesia (6%), trance states, and identity disorders (2–4%). The similarity of these symptoms to PTSD intrusion criteria confirms the complexity of differential diagnosis and the need for a multidisciplinary approach to the rehabilitation of this group.

A longitudinal analysis conducted three months after liberation showed positive dynamics: the overall prevalence of dissociative disorders decreased by

50%. The most pronounced regression was observed in depersonalization-derealisation syndrome (a 60% reduction) and dissociative neurological disorders (a 50% reduction). The statistical significance of the improvement in mental health status was confirmed using McNemar's test ($p<0.05$) [22].

These findings indicate a complex architecture of the dissociative spectrum in former prisoners of war and highlight the need to develop adaptive, individualised rehabilitation protocols.

CONCLUSIONS

Ukraine's veteran resocialisation policy represents a unique precedent of significant importance for stabilising the European security space. Timely treatment of combat-related trauma serves as an instrument for preventing cross-border risks, ranging from increased crime and drug abuse to migration-related pressure on healthcare systems in partner countries. To minimise transnational risks and ensure regional resilience, the implementation of a decentralised multidisciplinary rehabilitation model is advisable. This model is based on the synergy of clinical PTSD treatment protocols and flexible governance decisions by local self-government bodies. It envisages the creation of an inclusive environment within territorial communities, ensuring continuity of care and early detection of maladaptation.

The economic efficiency of this approach is driven by a shift from costly, isolated inpatient treatment to preventive community-based interventions. Maximizing veterans' social capital and implementing alternative sentencing programmes instead of penitentiary isolation significantly reduces public expenditure on prison maintenance and the treatment of chronic conditions. Thus, the model transforms the rehabilitation process from a budgetary cost item into an instrument of socio-economic stabilisation and strengthening of the security framework.

The experience of Ukrainian medical professionals in treating complex forms of PTSD using innovative methods is shaping new standards in military psychiatry. Given the participation of foreign volunteers in combat operations, these developments are becoming a foundation for updating rehabilitation protocols within the medical systems of NATO and the European Union.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Financing of dental care in Ukraine: Current status, comparative aspects with European union countries, and prospects for reform in the context of public health

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STATE INSTITUTION OF SCIENCE «CENTER OF INNOVATIVE HEALTHCARE TECHNOLOGIES» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Aim: To assess the state of dental care funding in Ukraine under martial law, compare aspects with the European Union (EU) countries, and identify prospects from a public health perspective.

Materials and Methods: We analyzed government regulations and scientific sources from the past 20 years regarding the state of dental care provision in Ukraine and EU countries in terms of sector financing, access to treatment and preventive care facilities, and medical personnel. We utilized time series analysis, statistical data (the Ministry of Health of Ukraine, National Health Service of Ukraine), and international sources – the World Health Organization (WHO) and the Organization for Economic Cooperation and Development (OECD). Bibliosemantic, content-analytical, and comparative methods were applied. The search for primary sources for analysis was conducted in international scientific databases (PubMed, Scopus, Web of Science, ScienceDirect) and national resources (the V.I. Vernadsky National Library of Ukraine, Google Scholar). Bibliosemantic, content-analytical, and comparative methods were applied.

Conclusions: In Ukraine, a low share (20%) of public institutions was established, along with a 60% reduction during the period 2008–2023. A directly proportional decline was observed in the availability of dentists (–49%) and in the number of patient visits (–80%) over the same period. The most critical failure was in the area of prevention (–84.8%). Increased funding in 2023–2025 is redirected to narrowly targeted groups and does not cover the system as a whole.In comparison with EU countries, Ukraine lags behind on all key indicators. Public coverage of dental costs in Europe is 30–33% and combines public and voluntary insurance, with partial co-payments — the prevention-driven "shared cost" model. In Ukraine, the state covers less than 10–15%, and the treatment-driven "pay-out-of-pocket" model, financed by patients, predominates.Dental care in Ukraine is significantly lower compared to European countries, remains underfunded, narrowly targeted, and dependent on private spending by the population, as evidenced by reductions in staffing, preventive care, and accessibility. Reform of the financial model is necessary, with an emphasis on preventive care, health insurance, and expanding the role of the National Health Service of Ukraine (NHSU).

KEY WORDS: dental care, dental sector financing, prevention

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INTRODUCTION

In the current context of martial law in Ukraine, the healthcare system faces a number of challenges stemming from the redirection of financial resources toward the country's defense capabilities, the deterioration of the economic situation, and limited public access to medical services, particularly in areas near the front lines. These issues are particularly relevant in the context of dental care, which is a vital component of the healthcare system and directly impacts the quality of life for people not only in the country but worldwide [1–4].

For a long time, the main problems in dentistry in Ukraine have been insufficient budgetary funding, limited coverage under the Medical Guarantees Program, the dominance of private expenditures on treatment — a situation exacerbated by the declining financial capacity of the population — the fragmentation of mechanisms, and the use of targeted state programs only for the most vulnerable population groups, in particular veterans, people with disabilities resulting from the Chernobyl Nuclear Power Plant accident, and Category 1 victims, specifically those suffering from radiation sickness [5, 6]. At the same time, the structure of dental care financing in Ukraine is undergoing dynamic changes due to healthcare system reforms and the introduction of new mechanisms for the procurement of medical services [7].

AIM

The aim of our study was to assess the state of dental care funding in Ukraine under martial law, compare key aspects of the sector with European Union (EU) standards, and identify the prospects for this field from a public health perspective.

MATERIALS AND METHODS

We analyzed government regulations and scientific sources from the past 20 years regarding the state of dental care provision in Ukraine and EU countries in terms of sector financing, access to treatment and preventive care facilities, and medical personnel. We utilized time series analysis, statistical data (the Ministry of Health of Ukraine, National Health Service of Ukraine), and international sources – the World Health Organization (WHO) and the Organization for Economic Cooperation and Development (OECD). Bibliosemantic, content-analytical, and comparative methods were applied. The search for primary sources for analysis was conducted in international scientific databases (PubMed, Scopus, Web of Science, ScienceDirect) and national resources (the V.I. Vernadsky National Library of Ukraine, Google Scholar).

ETHICS

This study is a review-based analytical work conducted using publicly available sources of information. No personally identifiable patient data were used, no clinical interventions were performed, and no primary collection of individual patient information was undertaken; therefore, approval by a local ethics committee was not required. In preparing this article, the authors adhered to the ethical principles of the World Medical Association Declaration of Helsinki and to international standards of publication ethics, including the recommendations of the International Committee of Medical Journal Editors (ICMJE). The authors confirm that the work contains no plagiarism, data fabrication, or falsification, and that all sources have been properly cited.

FRAMEWORK

The study was conducted as a fragment of the scientific project of the Scientific Department of Healthcare Organization of the State Scientific Institution «Center for Innovative Healthcare Technologies» State Administrative Department on the topic «Medical and social justification, development and implementation of the «Center of innovative healthcare technologies» model based on the trinity of science, education and practice in the work of a multidisciplinary healthcare institution and determining its role in the formation of a single medical space» (state registration number 0125U000318; term: 2025-2029).

REVIEW AND DISCUSSION

In Ukraine, the financing of dental care is multifaceted, relying on state funding, local budgets, private payments by the population, and charitable and international programs.

The National Health Service of Ukraine acts as the national purchaser of medical services under the Medical Guarantees Program, serving as the key institutional mechanism. However, unlike other types of medical care, the dental sector has many gaps and is only partially integrated into the public financing system [8]. Specifically, out of the National Health Service of Ukraine's budget of over 142 billion UAH in total funding for medical services, a minimal share is allocated to dentistry, estimated by experts to be less than 5%. For the provision of dental care within general hospitals, the budget allocates 134.68 UAH per case, which is far below the actual cost of the service. The limited funding under the Medical Guarantees Program is due to a number of factors: funding primarily covers specific service packages; payments are made under contracts between the National Health Service of Ukraine (NHSU) and medical facilities; and base rates remain low [8]. At the same time, according to relevant resolutions of the Cabinet of Ministers, state funding for specialized dental facilities is limited. Only certain categories of the population receive dental care at the state's expense through special programs.

In 2025, approximately 750 million UAH was allocated for dental care for veterans under a joint initiative of the Ministry of Health, the National Health Service of Ukraine, and the Ministry of Veterans Affairs, covering dental prosthetics and dental treatment up to 34966 UAH and 24952 UAH, respectively [5]. In 2025, over 59000 patients (military personnel/veterans) received dental care. In 2026, a Government Resolution provided for expanded access to free dental prosthetics and routine dental care for people with disabilities whose disabilities are related to the consequences of the Chernobyl nuclear power plant accident, as well as for people classified as Category 1 victims, specifically those suffering from radiation sickness. All of the aforementioned programs indicate that state funding for dental care is targeted and limited [6].

Due to underfunding of the sector, certain legislative initiatives are being considered for 2025–2026 to increase funding for dental services to 190000 UAH per patient and to introduce a voucher model with a "dental certificate" mechanism.

Amid discussions of legislative reforms and given the limited and fragmented nature of public coverage, dental care in Ukraine continues to be financed primarily through out-of-pocket payments, with most dental services paid for directly by patients, particularly among the adult population [9]. Budget programs cover certain pediatric dental procedures and services

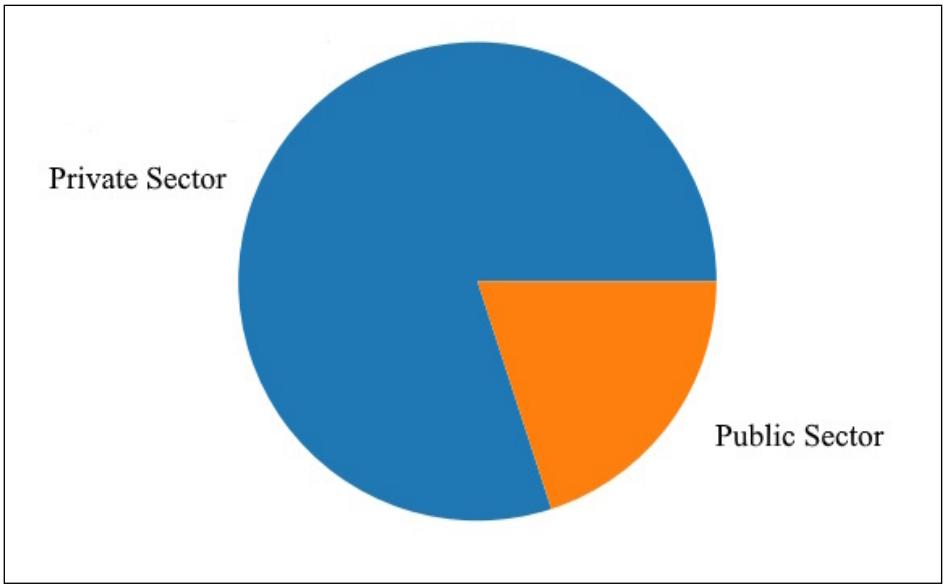


Fig. 1. Structure of the dental market
Picture taken by the authors

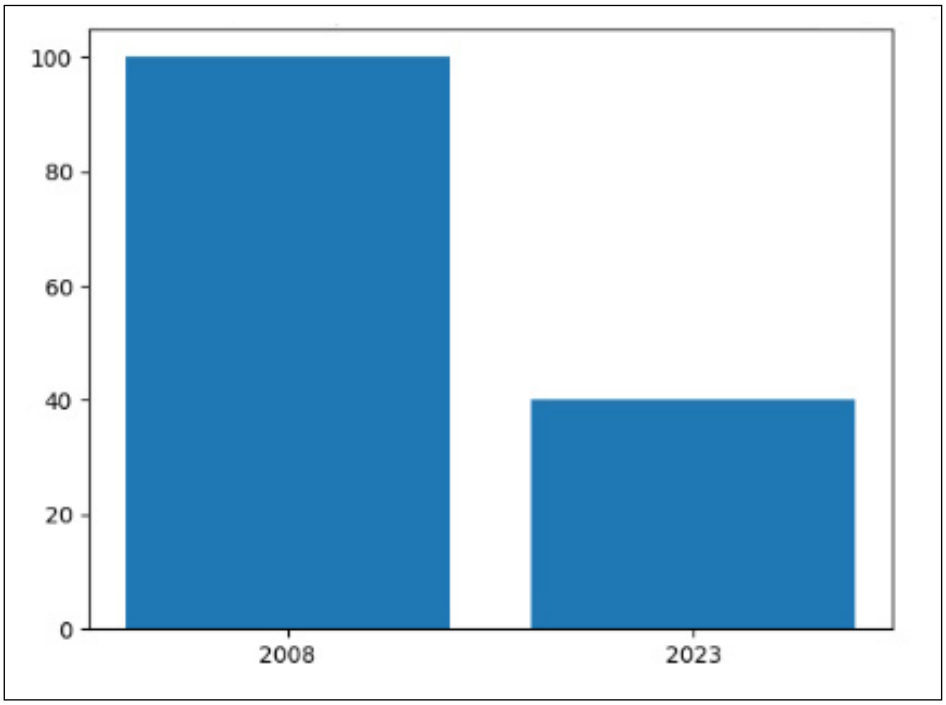


Fig. 2. Trends in the number of public dental care facilities from 2008 to 2023
Picture taken by the authors

for eligible groups. Because these programs are implemented through local budgets, there is significant variability in service provision across regions.

We conducted an analysis of dental service coverage in Ukraine. As of 2021, there were 22180 dentists working in the country, in 64443 specialized facilities, 80% of which were privately owned, indicating a marked privatization of dental care (Fig. 1).

Between 2008 and 2023, the number of public dental clinics decreased by approximately 60%, confirming the shift toward a market-based funding model. The downsizing of the public sector in the industry has led to a decrease in preventive checkups and an increase in advanced dental pathologies, indicating underfunding of preventive care (Fig. 2).

In direct proportion to the decline in the number of clinics over 15 years, the number of visits to dentists has decreased by nearly five times (–80%): from 49.9 million in 2008 to 9.5 million in 2023 (Fig. 3). The number of dentists over the same period halved from 4.48 to 2.3 per 10,000 population, indicating a 49% decline in coverage (Fig. 4). The most critical decline was observed in the area of preventive care. The percentage of preventive examinations decreased from 100% to 84.8%. An analysis of orthopedic dentistry revealed a decrease in the number of crowns placed from 150.8 per 10,000 population in 2008 to 46.3 in 2023. A negative trend of 69% was recorded for this parameter [10].

It should be noted that funding for the dental sector increased by 250 million UAH from 2023 to 2025 (Fig.

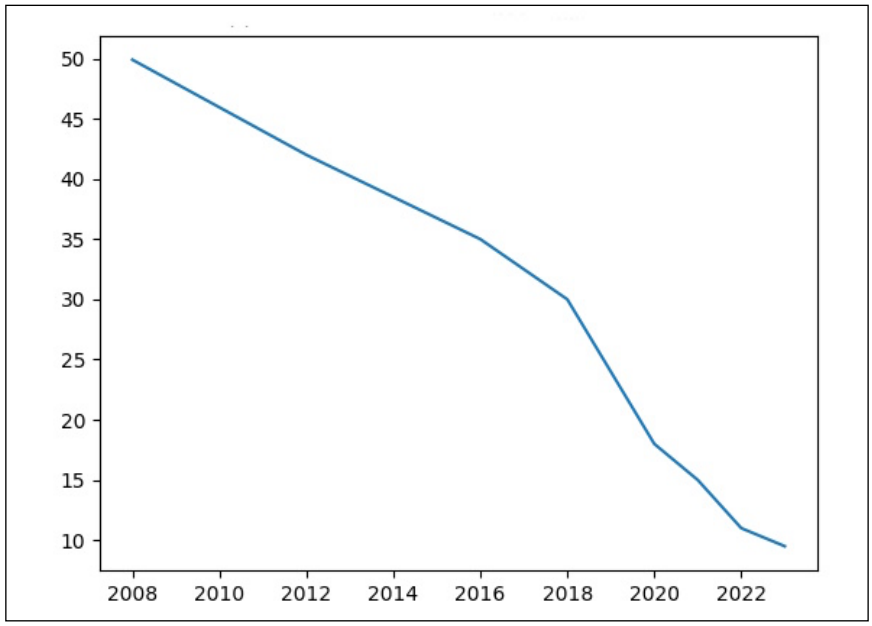


Fig. 3. Trends in visits to the dentists from 2008 to 2023
Picture taken by the authors

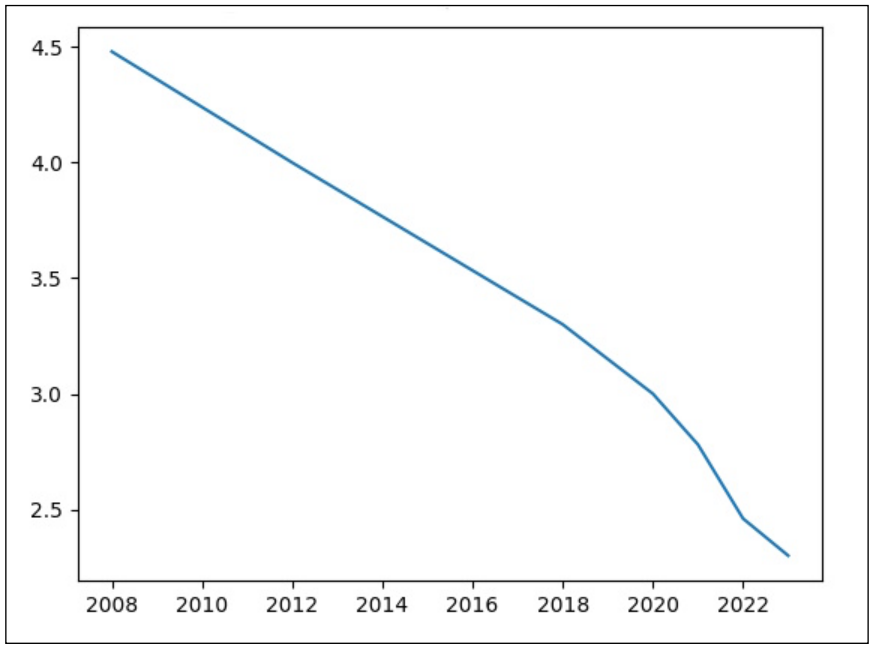


Fig. 4. Trends in the number of dentists per 10000 people from 2008 to 2023
Picture taken by the authors

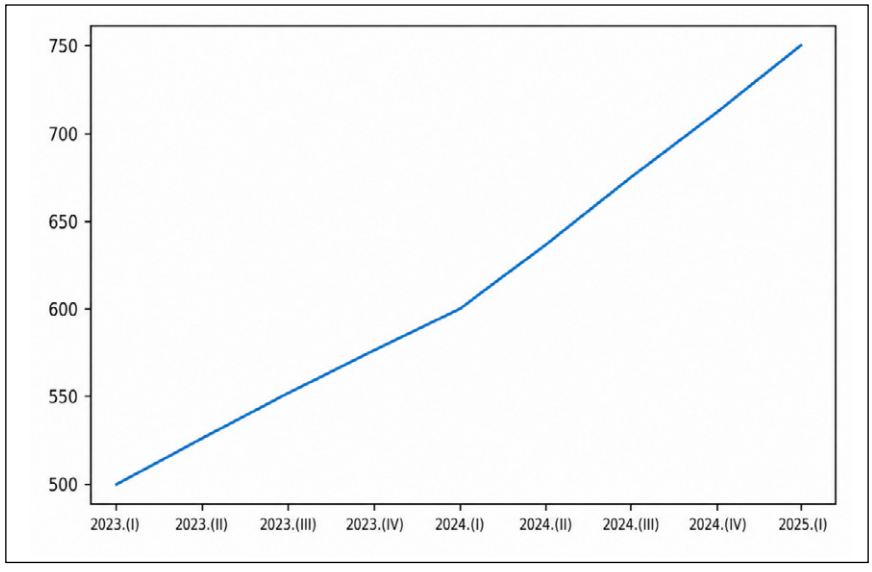


Fig. 5. Funding (National Health Service of Ukraine/Ministry of Health of Ukraine) for the dental sector for the period 2023–2025 (I-IV – quarter of the year)
Picture taken by the authors

Table 1. Systemic differences in the provision of dental care (structural analysis)

Parameter	EU	Ukraine
Model	Insurance-based / mixed	Predominantly private
Public funding	~30%	<15%
Coverage for children	High	Partial
Adult coverage	Limited, but exists	Almost nonexistent
Prevention	Well-developed	Deteriorating
Financial protection	Partial	Nonexistent
Inequality	High, but controlled	Very high

Source: compiled by the authors of this study

5). However, a more in-depth analysis reveals that this assistance is narrowly targeted and does not cover the system as a whole. Specifically, in 2025, free dental care was provided to combatants, individuals with war-related disabilities, military personnel who defended Ukraine's independence and territorial integrity, and people who survived captivity. Overall service coverage is assessed as very low, as only 25504 patients received dental care in the previous year [2].

The main challenges facing the provision of dental care in Ukraine include insufficient public funding; limited coverage under the Medical Guarantees Program; fragmented financial flows resulting from the regulation of certain areas by government regulations and varying coverage across regions; a high proportion of out-of-pocket expenses; and insufficient emphasis on preventive care.

To determine the prospects for the sector's development, the following reform directions can be considered: expanding the National Health Service of Ukraine's coverage for dentistry; introducing voucher-based financing mechanisms; developing public insurance; and integrating preventive programs into primary care. the development of state insurance

Oral diseases are a global public health problem with an unprecedented impact on the world's economy [11, 12]. Of particular interest are the comparative aspects of healthcare provision in Ukraine and EU countries (Table 1). Ukraine lags significantly behind the EU on all key indicators: level of public coverage, accessibility, prevention, and financial protection. At the same time, the EU also faces systemic issues (high out-of-pocket expenses), but these are significantly lower than in Ukraine. When analyzing the share of public coverage of dental expenses in EU countries, this figure varies significantly across nations, averaging 30–33%. Germany and France lead in funding, with coverage rates exceeding 60%. At the same time, there are countries with very low coverage, such as Spain and Romania [13–15].

In Ukraine, the main source of funding for dental care is out-of-pocket payments. The state covers less than 10–15% of the costs and only through narrowly focused programs. Therefore, Ukraine has a level of public funding that is 2–3 times lower than the EU average.

The EU's healthcare financing system features a clear combination of funding streams that integrates public insurance, voluntary insurance, and partial copayments [16]. Out-of-pocket costs are high but are offset to some extent by insurance. In Ukraine, insurance-based dental care is virtually nonexistent; direct patient payments dominate. Therefore, there are two completely different models: the European "shared cost model" and the Ukrainian "pay-out-of-pocket model" [17–19].

When assessing the accessibility of dental care, 6.3% of the EU population has unmet needs, reaching 13–27% among low-income groups [20]. In Ukraine, analysis can only be conducted using indirect indicators—an 80% drop in visits and an 85% drop in preventive care. This indicates a significantly higher actual lack of access to services in Ukraine than in the EU. There is a shortage of dentists in Ukraine, as evidenced by a staffing level that is 2–5 times lower than in European countries—2.3 per 10000 people according to 2023 data, according to 2024 data—3.7 per 10000 population, while in the EU this figure ranges from 0.5 to 1.3 dentists per 1,000 population, or 5 to 13 specialists per 10000 population. In EU countries, the frequency of dental visits is approximately 1.2 visits per person per year. Under the current conditions of martial law in Ukraine, a sharp decline in the number of visits has been recorded; specifically, only 9,482,028 million visits were recorded in 2023, and 8,786,082 million visits in 2024. There has been a decline in the number of visits, which is attributed to the inaccessibility of dental care due to patients' low purchasing power. The above confirms the stable demand for dental care in EU countries and the collapse in the use of such services in our country [21].

In EU countries, the primary focus is on a preventive model, particularly in pediatric dentistry, through screening programs and community-based preventive measures. In Ukraine, there has been an 85% decline in preventive care. In the EU, prevention is predominant, while in Ukraine the system is treatment-driven [22].

In EU countries, dental care for children is often free; mandatory health insurance is in place; and there is a significant emphasis on prevention [23]. By comparison, in Ukraine, the treatment-oriented model predominates; prevention is underfunded; and there is no comprehensive insurance model for dentistry.

It should be noted that even in the EU, dentistry is the least covered part of the healthcare system and involves high out-of-pocket costs. However, Ukraine is in an even more extreme position, where the system operates effectively under market conditions, with the state playing a minimal role. The significant impact of dental diseases on the global economy is prompting researchers to continuously reform the system to optimize the health of the population [24–27].

CONCLUSIONS

The financing of dental care in Ukraine is undergoing a transformation. Despite the existence of government programs and procurement mechanisms through the National Health Service of Ukraine, the system remains underfunded and narrowly targeted, as evidenced by the decline in preventive care, reduced accessibility, a shortage of personnel, and reliance on out-of-pocket expenses by the population.

Significant gaps in the provision of dental care in Ukraine, which distinguish it from EU countries, include: the lack of dental insurance; the absence of a guaranteed basic package that would reflect the actual costs of treatment and prevention; underfunding of preventive care; the lack of financial protection for the population; and weak integration into primary care.

Ukraine needs to reform its financial model for the provision of dental care, which would create conditions for the development of the public sector in dental care and foster a competitive environment with the private sector, with an emphasis on prevention, health insurance, and expanding the role of the National Health Service of Ukraine.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Cranberry products in the prevention of recurrent urinary tract infections in adult women: Efficacy, safety, and place in non-antibiotic prophylaxis – literature review

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ABSTRACT

Recurrent urinary tract infections are among the most frequent bacterial infections in adult women and are associated with impaired quality of life, like repeated medical consultations, and cumulative exposure to antibiotics. In the context of increasing antimicrobial resistance, non-antibiotic preventive strategies have attracted growing attention. Cranberry products remain one of the most commonly used and most extensively studied options. The aim of this review was to summarize current evidence regarding the efficacy, safety, and practical role of cranberry products in the prevention of recurrent urinary tract infections in adult women. Contemporary guidelines, systematic reviews, meta-analyses, and randomized clinical trials indicate that cranberry products may reduce recurrence risk, particularly in women with recurrent uncomplicated cystitis. However, cranberry should not be regarded as a single uniform intervention. The clinical effect appears to depend on formulation, proanthocyanidin content, and duration of administration. Preparations providing at least 36 mg of proanthocyanidins daily seem to offer the most consistent benefit, whereas non-standardized products yield heterogeneous and less reliable results. Cranberry products are generally safe and well tolerated, although adherence may be affected by palatability, pill burden, or uncertainty regarding product composition. Overall, cranberry may be considered a reasonable non-antibiotic prophylactic option for selected adult women, provided that counseling includes realistic discussion of expected benefits, limitations of the evidence, and the importance of using standardized preparations.

KEY WORDS: drug resistance, female, dietary supplements, proanthocyanidins, cystitis

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INTRODUCTION

Recurrent urinary tract infections are one of the most common infectious problems in adult women. They are usually defined as at least two symptomatic episodes within six months or at least three episodes within one year [1, 2]. Although recurrent infection is rarely life-threatening in otherwise healthy women, it causes considerable morbidity, including dysuria, urinary frequency, pain, sleep disturbance, anxiety, repeated healthcare contacts, and reduced quality of life [1, 2]. In many patients, recurrence also leads to repeated empirical antibiotic treatment, which increases the risk of adverse effects, disturbs the intestinal and vaginal microbiota, and contributes to antimicrobial resistance [2-4].

For these reasons, the modern approach to recurrent uncomplicated cystitis increasingly includes non-antibiotic prophylaxis. Among the available options, cranberry products have retained particular interest because they are widely accessible, generally well tolerated, biologically plausible, and supported by a relatively broad clinical literature [2, 4]. Nevertheless, cranberry remains a controversial topic. The literature contains both positive and neutral studies, and the interpretation of results has long been complicated by wide variation in formulation, proanthocyanidin content, treatment duration, and outcome definitions [2-4].

AIM

The aim of this review was to evaluate the role of cranberry products in the prevention of recurrent urinary tract infections in adult women, with particular emphasis on mechanisms of action, evidence from guidelines and clinical trials, product heterogeneity, safety, and practical use in non-antibiotic prophylaxis.

MATERIALS AND METHODS

SEARCH STRATEGY AND INFORMATION SOURCES

A systematic literature search was conducted in April 2026 by two independent reviewers to identify studies evaluating the efficacy and safety of cranberry products in the prevention of recurrent urinary tract infections (rUTIs). The primary source of evidence was the PubMed/ MEDLINE database. To ensure inclusion of the most recent clinical data, only articles published between January 2021 and April 2026 were considered. The search was limited to full-text articles published in English.

The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators. The following search string was applied: *"cranberry" AND ("urinary tract infection" OR "cystitis") AND "prevention"*.

Study eligibility was determined according to predefined PICO-based criteria. Eligible studies included adult women (≥18 years of age) with recurrent urinary tract infections, defined as at least two episodes within six months or at least three episodes within one year, who received prophylaxis with standardized cranberry products, including capsules, tablets, or extracts with a specified proanthocyanidin (PAC) content. Only randomized controlled trials (RCTs), systematic reviews, and meta-analyses were included.

Studies involving pregnant women, pediatric patients (<18 years of age), individuals with indwelling urinary catheters, or patients with neurogenic bladder were excluded. Case reports, editorials, conference abstracts, animal studies, and pilot studies with insufficient sample sizes were also excluded. Furthermore, studies evaluating non-standardized cranberry juice preparations or products with unspecified PAC concentrations were not considered.

Titles and abstracts were screened independently by both reviewers, followed by full-text assessment of potentially eligible articles. Any disagreements regarding study selection were resolved through discussion and consensus. A total of 19 publications met the eligibility criteria and were included in the final narrative review.

REVIEW AND DISUSSION

CLINICAL IMPORTANCE OF RECURRENT URINARY TRACT INFECTION AND THE SHIFT TOWARD ANTIBIOTIC-SPARING PREVENTION

The index patient in contemporary guidance is an otherwise healthy adult woman with recurrent localized cystitis, without structural or functional abnormalities of the urinary tract and without features suggesting upper or systemic infection [2]. This distinction is important because recurrent uncomplicated cystitis differs substantially from catheter-associated urinary tract infection, neurogenic bladder, postoperative infection, or infection related to foreign bodies. The updated American Urological Association/ Canadian Urological Association/ Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (AUA/CUA/ SUFU) guideline emphasizes that diagnosis should rely on the combination of symptoms, evidence of urinary inflammation, and bacteriuria interpreted in clinical context, rather than on microbiology alone [2].

The clinical burden of recurrent infection extends beyond the acute episodes themselves. Women with recurrent urinary tract infections often report substantial physical and psychological distress, dissatisfaction with care, and delayed access to specialist management [1,2]. Repeated antibiotic exposure is one of the main reasons why non-antibiotic prophylaxis has become a central topic. Recent reviews frame recurrent urinary tract infection as a setting in which antibiotic-sparing strategies are not only desirable but increasingly necessary from both an individual and public health perspective [3,4]. Cranberry therefore needs to be considered not in isolation, but as part of a broader movement toward prevention strategies that may reduce recurrence while limiting cumulative antimicrobial exposure.

CRANBERRY PRODUCTS AND PROPOSED MECHANISMS OF ACTION

The most widely accepted mechanism of cranberry is anti-adhesion. Cranberry contains proanthocyanidins, particularly A-type proanthocyanidins, which are thought to inhibit the adhesion of uropathogenic *Escherichia coli* to the urothelium [2, 5]. Since bacterial attachment is an early step in the pathogenesis of cystitis, interference with this process provides a biologically plausible explanation for preventive benefit. Importantly, this mechanism differs fundamentally from that of antibiotics, because cranberry does not primarily aim to kill bacteria but rather to reduce successful colonization.

More recent research suggests that cranberry may have broader biological effects. González de Llano et al. showed that cranberry-derived digestive fluid and cranberry phenolic metabolites can improve intestinal and urinary epithelial barrier-related parameters, including transepithelial resistance and expression of tight-junction-associated genes [5]. These findings support the concept that cranberry may contribute not only to anti-adhesion but also to preservation of epithelial integrity in the gut and urinary tract (Fig. 1).

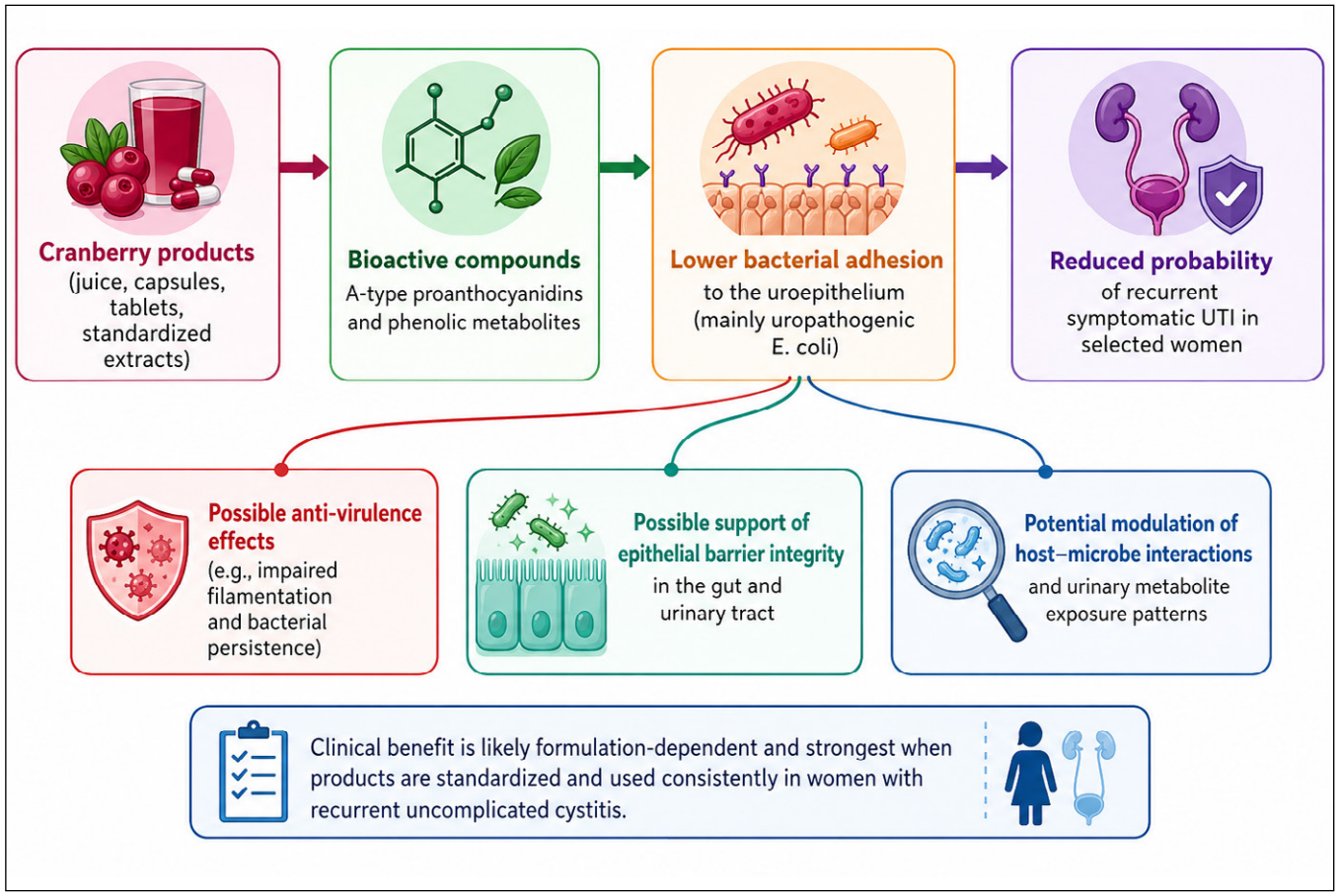


Fig. 1. Proposed mechanisms by which cranberry products may reduce the risk of recurrent urinary tract infections in adult women
Source: Own materials

Additional mechanistic support comes from the work of Zhao et al., who showed that cranberry intake produces measurable urinary metabolites that may serve as intake biomarkers, which is especially important in a field where patient adherence and actual exposure are often difficult to confirm [6]. Prinster et al. further demonstrated that cranberry constituents can prevent SOS-mediated filamentation of uropathogenic *Escherichia coli* [7]. Because bacterial filamentation may promote persistence and immune evasion, this anti-virulence effect provides a novel explanation for the possible clinical efficacy of cranberry.

At the same time, interpretation of mechanistic findings is complicated by variability in the polyphenolic composition of cranberry-derived products, as different processing methods may yield fractions with different biological activity [8].

EVIDENCE FROM GUIDELINES AND SYSTEMATIC REVIEWS

The updated AUA/CUA/SUFU guideline clearly states that clinicians should offer cranberry as an option for prophylaxis in women with recurrent urinary tract infections [2]. This is one of the most important practical messages in the current literature. The recommendation is moderate, with evidence level B, which reflects meaningful but not definitive evidence. Of particular relevance is the guideline's observation that products standardized to at least 36 mg of proanthocyanidins daily appear more effective than lower-dose preparations, while many commercial products fail to validate the amount of active compound they contain [2].

The most influential modern evidence synthesis is the 2023 Cochrane review [9]. It included 50 randomized comparisons involving 8857 participants and concluded that cranberry products reduce the risk of symptomatic, culture-verified urinary tract infections in selected susceptible populations, with a particularly relevant signal in women with recurrent infection. At the same time, the review emphasized heterogeneity among populations and interventions, and the effect was not equally convincing in all groups [9]. This dual conclusion is clinically important: cranberry is no longer unsupported, but neither is it universally effective.

Other meta-analyses broadly align with the Cochrane

Table 1. Key guidelines, systematic reviews, and meta-analyses on cranberry products for prevention of recurrent urinary tract infections

Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline (2025). [2]	Guideline update	Women with recurrent uncomplicated UTI	Cranberry should be offered as a non-antibiotic prophylactic option; products standardized to at least 36 mg PAC daily appear more effective	Recommendation based on heterogeneous underlying studies; commercial products are poorly standardized	Key guideline source for clinical positioning of cranberry
Cranberries for preventing urinary tract infections. Cochrane Database Syst Rev. 2023 [7]	Cochrane systematic review	Multiple susceptible populations, including women with recurrent UTI	Cranberry products reduced the risk of symptomatic, culture-verified UTI in selected groups, particularly women with recurrent infection	Marked heterogeneity in populations, formulations, and outcome definitions	Core evidence synthesis supporting cranberry prophylaxis
Cranberry Juice, Cranberry Tablets, or Liquid Therapies for Urinary Tract Infection: A Systematic Review and Network Meta-analysis [8]	Systematic review and network meta-analysis	Studies of cranberry juice, tablets, and liquid therapies	Cranberry juice showed the most consistent effect; lower UTI rates versus placebo liquid and no treatment; reduction in antibiotic use	Variable formulations and study quality; indirect comparisons	Essential source for comparing cranberry formulations
. Consumption of cranberry as adjuvant therapy for urinary tract infections in susceptible populations: A systematic review and meta-analysis with trial sequential analysis [9]	Systematic review and meta-analysis with trial sequential analysis	Susceptible populations, including women with recurrent UTI	Cranberry products reduced UTI incidence overall and in women with recurrent UTI; juice appeared more effective than capsules/tablets	Not limited to adult women with recurrent uncomplicated cystitis	Strong supporting evidence for efficacy
Preventive effect of cranberries with high dose of proanthocyanidins on urinary tract infections: a meta-analysis and systematic review [10]	Systematic review and meta-analysis	Cranberry products stratified by PAC dose	Preparations providing at least 36 mg PAC daily were associated with significant benefit; lower-dose products were not	Considerable inter-study heterogeneity; limited standardization across trials	Most important source on dose-response relationship
Nonantibiotic prophylaxis for urinary tract infections: a network meta-analysis of randomized controlled trials. Infection [11]	Network meta-analysis	Non-antibiotic prophylaxis for UTI	Cranberry was superior to placebo and did not significantly increase adverse events	Includes interventions beyond cranberry; not limited to one female subgroup	Useful for positioning cranberry among other non-antibiotic strategies
. Stair SL, Palmer CJ, Lee UJ. Evidence-based review of nonantibiotic urinary tract infection prevention strategies for women: a patient-centered approach [4]	Narrative evidence-based review	Women, patient-centered preventive strategies	Cranberry is a reasonable non-antibiotic option in women seeking antibiotic-sparing prevention	Narrative design; not a formal pooled analysis	Helpful for the practical discussion section

Source: Compiled by the authors of this study

Table 2. Key clinical trials of cranberry products in adult women

Study	Population	Cranberry product/ formulation	PAC dose	Duration	Main outcome	Interpretation
Randomized, placebo-controlled, double-blinded study of prophylactic cranberries use in women with recurrent uncomplicated cystitis. [12]	Adult women with recurrent uncomplicated cystitis	Standardized cranberry preparation (Cysticlean)	High-dose standardized preparation	12 months	Reduced number of UTIs, prolonged UTI-free survival, reduced vaginal and rectal E. coli colonization; no adverse events reported	Strongest recent RCT supporting cranberry prophylaxis in the target population
Cranberry Juice, Cranberry Tablets, or Liquid Therapies for Urinary Tract Infection: A Systematic Review and Network Meta-analysis [8]	Women at risk of recurrent UTI	Cranberry juice vs placebo liquid / no treatment	Variable	Variable	Juice-based interventions showed the most consistent benefit among cranberry formulations	Suggests that formulation may substantially influence efficacy
Consumption of cranberry as adjuvant therapy for urinary tract infections in susceptible populations: A systematic review and meta-analysis with trial sequential analysis [9]	Women with recurrent UTI and other susceptible groups	Cranberry juice, capsules, tablets	Variable	Variable	Overall reduction in UTI incidence; stronger signal in women with recurrent UTI	Supports benefit, but heterogeneity limits direct comparison
Preventive effect of cranberries with high dose of proanthocyanidins on urinary tract infections: a meta-analysis and systematic review [10]	Women and mixed susceptible populations	Standardized and non-standardized cranberry products	<36 mg/day vs ≥36 mg/day	Variable, benefit clearer at 12–24 weeks	Significant preventive effect mainly with ≥36 mg PAC/day	Suggests a clinically relevant threshold effect for PAC dosing
The Clinical Trial Outcomes of Cranberry, D-Mannose and NSAIDs in the Prevention or Management of Uncomplicated Urinary Tract Infections in Women: A Systematic Review [15]	Women with uncomplicated or recurrent UTI	Cranberry products in various formulations	Variable	Variable	Mixed results across clinical trials	Negative or neutral findings may reflect poor standardization, dose, or adherence rather than absence of biological effect

Source: Compiled by the authors of this study

findings. Moro et al. reported the most consistent benefit for cranberry juice, which lowered recurrence rates compared with placebo liquid and no treatment and also reduced antibiotic use [10]. Xia et al. found that cranberry-based products significantly reduced urinary tract infection incidence overall and in women with recurrent urinary tract infections, and their subgroup analysis suggested that juice-based interventions may be more effective than tablets or capsules [11]. Xiong et al. further clarified the importance of dose, showing that cranberry products providing at least 36 mg of proanthocyanidins daily were associated with a significant reduction in urinary tract infection risk, whereas lower-dose products were not [12]. Han et al., in a network meta-analysis of non-antibiotic prophylaxis, also found cranberry superior to placebo without an increase in adverse events[11] (Table 1).

EVIDENCE FROM RANDOMIZED CLINICAL TRIALS

The strongest recent primary trial in adult women with recurrent uncomplicated cystitis was published by Tsiakoulias et al. [14]. This randomized, placebo-controlled, double-blinded trial showed that a standardized cranberry preparation reduced the number of urinary tract infections, prolonged infection-free survival, and lowered vaginal and rectal *Escherichia coli* colonization. No adverse events were reported [14]. The importance of this study lies not only in its positive result, but also in the fact that it addressed the appropriate target population, used a defined preparation, and followed participants for a clinically meaningful period.

Earlier and pooled trial evidence has been more variable. Some randomized studies suggested benefit, whereas others did not reach statistical significance, especially when lower-dose or poorly characterized products were used [9-12,15]. This inconsistency has often been used as an argument against cranberry, but it may be more accurately interpreted as evidence that cranberry efficacy is not class-wide. In other words, neutral trials do not necessarily refute the concept of cranberry prophylaxis; they may instead reflect inadequate standardization, suboptimal dosing, poor adherence, or inappropriate population selection.

Population differences are also relevant. Evidence is strongest in women with recurrent uncomplicated cystitis. By contrast, benefit has been less consistent in elderly institutionalized adults, pregnant women, or procedure-related settings [9-13]. Therefore, any recommendation in favor of cranberry should remain specific to recurrent uncomplicated cystitis in adult women rather than generalized to all urinary tract infection contexts (Table 2).

PRODUCT HETEROGENEITY AND THE PROBLEM OF STANDARDIZATION

Perhaps the most important issue in the cranberry literature is product heterogeneity. "Cranberry" may refer to juice, juice cocktails, tablets, capsules, dry extracts, or mixed nutraceutical combinations, all of which may differ substantially in their content of biologically active compounds [2,8]. This is not a minor technical issue but a major source of inconsistency across the literature (Fig 2).

The meta-analysis by Xiong et al. is particularly informative here [12]. The authors found that cranberry products delivering at least 36 mg of proanthocyanidins daily were associated with a statistically significant reduction in urinary tract infection risk, whereas lower-dose products were not. They also suggested that benefit was more evident when cranberry was used for 12 to 24 weeks [12]. These findings are consistent with the AUA/CUA/SUFU guideline and strongly support the view that cranberry efficacy is dose-sensitive.

The challenge is that many products on the market do not state or verify their proanthocyanidin content. Reviews on cranberry chemistry and processing show that extraction methods, source material, and analytical methods can markedly affect the composition of final products [8]. As a result, two studies both labeled as "cranberry trials" may in reality be evaluating interventions that are chemically and biologically very different. This makes it difficult to interpret older trials and complicates translation into clinical recommendations.

Thus, one of the key messages of this review is that the main question is not simply whether cranberry works. The more useful clinical question is which cranberry product, in what formulation, at what proanthocyanidin dose, and for what duration may reduce recurrence risk.

SAFETY, TOLERABILITY, AND ADHERENCE

Cranberry products are generally safe. Modern systematic reviews and network meta-analyses have not shown a significant increase in adverse events compared with placebo [2, 13], and the best recent randomized trial also reported no adverse events [14]. This favorable safety profile makes cranberry attractive as a long-term preventive measure, particularly in women seeking to reduce antibiotic exposure.

However, safety alone does not guarantee effectiveness in practice. Adherence is a recurring issue in cranberry research. Juice-based regimens may be limited by taste, acidity, treatment fatigue, and caloric load, whereas solid formulations may be easier to maintain but only if they contain adequate amounts of active compounds [10,13]. Biomarker-based work suggests

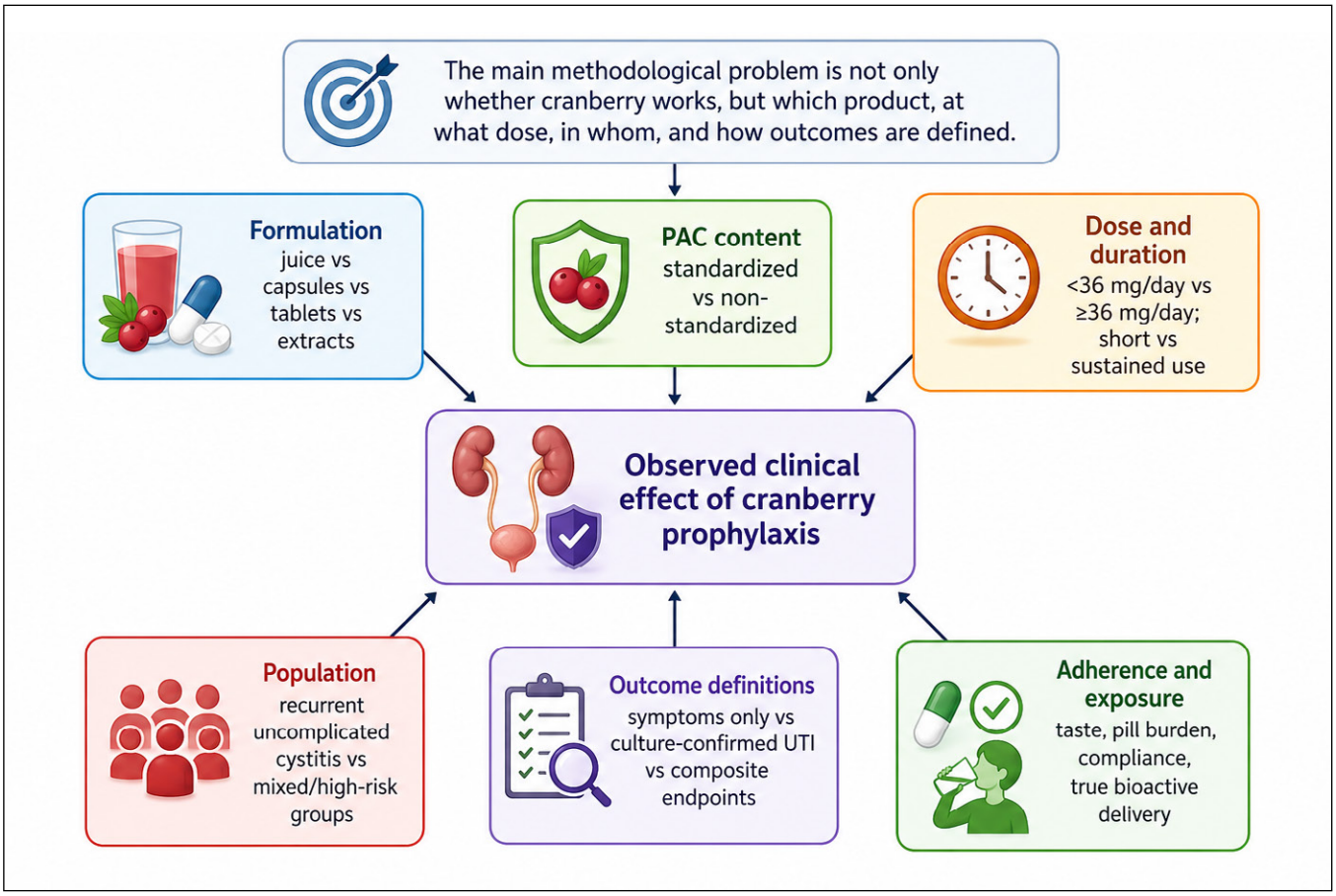


Fig. 2. Main sources of heterogenity in studies evaluating cranberry products for prevention of recurrent urinary tract infections
Source: Own materials

that poor compliance may have contributed to the inconsistent results of earlier trials [13]. Therefore, the real-world success of cranberry prophylaxis depends not only on biological efficacy but also on whether a patient is willing and able to use a standardized product consistently.

PRACTICAL PLACE OF CRANBERRY IN NON-ANTIBIOTIC PROPHYLAXIS

In everyday practice, cranberry is best positioned as a reasonable non-antibiotic prophylactic option for adult women with recurrent uncomplicated urinary tract infections who prefer an antibiotic-sparing strategy or who wish to try a low-risk intervention before long-term antimicrobial prophylaxis [2, 4]. It is especially suitable in women with a well-defined recurrence pattern, no major urinary tract abnormality, and willingness to use a standardized product regularly (Fig. 3).

Real-world studies also show that preventive behaviors are common among women with recurrent infection. Most women initially receive care from primary care physicians, and specialist input remains underused, despite the fact that preventive strategies such as cranberry extract, low-dose antibiotic prophylaxis, or other structured approaches may be implemented more often in women with recurrent disease [16]. Differences also exist across female life stages, with premenopausal women more likely to use behavioral measures and over-the-counter prevention, whereas postmenopausal women more often receive vaginal estrogen or antibiotic-based strategies [17]. These observations support the idea that cranberry has an established place in real-world prevention, although its use is not always systematic or guided by product standardization.

At the same time, counseling must remain realistic. Cranberry should not be presented as a universal solution, and patients should not be told that all cranberry products are equally effective. The expected benefit is preventive rather than curative, and the magnitude of benefit is probably modest to moderate. If cranberry is recommended, the patient should be advised to choose a standardized preparation delivering at least 36 mg of proanthocyanidins daily and to continue it for several months before efficacy is judged [2, 12].

Some supportive studies also evaluated combined nutraceutical strategies that included cranberry togeth-

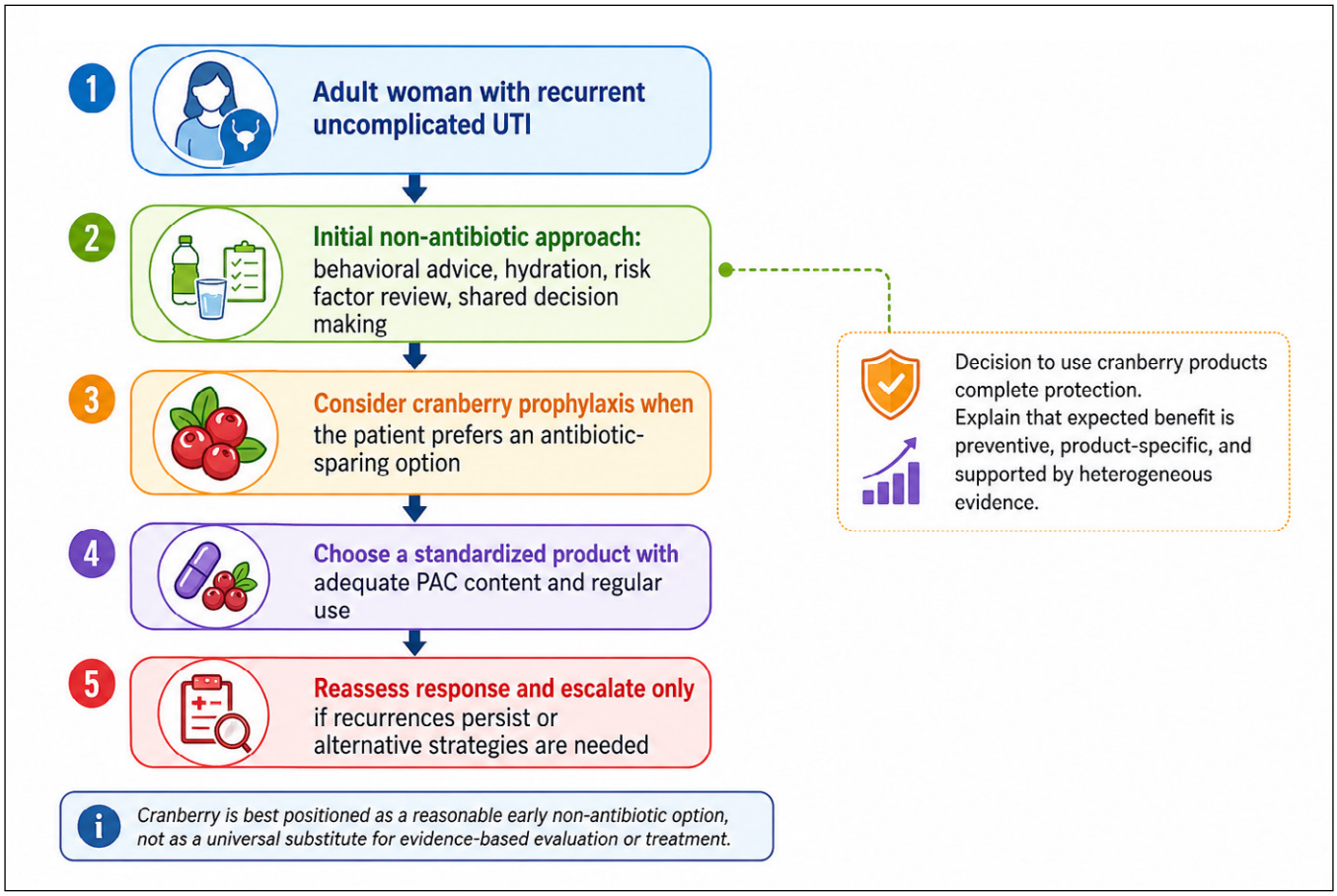


Fig. 3. Suggested practical positioning of cranberry products within non-antibiotic prophylaxis of recurrent uncomplicated urinary tract infections in adult women
Source: Own materials

er with probiotics, cinnamon, pumpkin seed extract, or vitamins [18,19]. Although such interventions may be clinically interesting, they do not provide pure evidence for cranberry alone and should be interpreted cautiously when defining cranberry's specific role in prophylaxis.

LIMITATIONS OF CURRENT EVIDENCE

The available evidence has several limitations. First, there is major heterogeneity in product composition, proanthocyanidin dose, treatment duration, population, and recurrence definition [9-13, 15]. This makes direct comparison difficult and reduces the certainty of pooled estimates. Second, some clinically relevant studies involve combined formulations rather than cranberry alone [18,19], limiting attribution of effect. Third, adherence has often been poorly measured, and true biological exposure may have varied substantially even among participants assigned to the same intervention [13].

Another limitation is the persistent variability in cranberry composition itself. Chemical composition depends on cultivar, environmental conditions, processing, extraction, and formulation, which may directly influence biological activity and partly explain inconsistent clinical outcomes [20]. Without rigorous product standardization, the comparison of trials remains methodologically challenging.

Future trials should therefore focus on clearly defined adult female populations with recurrent uncomplicated cystitis, use rigorously standardized products, verify proanthocyanidin dose, incorporate adherence assessment or urinary biomarkers, and apply consistent microbiological outcome definitions. Without such improvements, the literature will likely continue to generate partially conflicting results despite an underlying biologically real effect.

CONCLUSIONS

Cranberry products have a plausible mechanism of action and a growing evidence base as a non-antibiotic preventive strategy in adult women with recurrent uncomplicated urinary tract infections. The most reliable data suggest that benefit is most likely when standardized products containing at least 36 mg of

proanthocyanidins daily are used consistently for an adequate period [2,12].

Cranberry should not be viewed as a single homogeneous intervention class. Much of the inconsistency in the literature is likely explained by variation in formulation, dose, and product quality. Therefore, the most accurate conclusion is that cranberry may reduce recurrence risk in selected women, but its effectiveness is product-specific and context-dependent.

In practice, cranberry may be recommended as a safe and reasonable component of non-antibiotic prophylaxis, particularly in women seeking to reduce antibiotic exposure. Its use should be accompanied by careful product selection, realistic counseling, and awareness that it complements, but does not replace, appropriate diagnostic evaluation and evidence-based treatment of acute infection. We conclude that all commercially available cranberry products intended for medical prophylaxis should obligatorily state their standardized proanthocyanidin (PAC) content to guide appropriate clinical use.

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CONFLICT OF INTEREST

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REVIEW ARTICLE

CONTENTS

Surgical stage of dental implant placement with immediate loading: Indications and contraindications

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ABSTRACT

Aim: To analyze the scientific literature on indications for and contraindications to dental implant placement using immediate loading protocols.

Materials and Methods: The scientific literature reporting clinical situations corresponding to absolute and relative indications for and contraindications to dental implant placement with immediate loading was reviewed.

Conclusions: The literature reports that one-stage implant placement with immediate loading and simultaneous placement of a transmucosal healing abutment or abutment has demonstrated effectiveness in clinical practice. However, despite its advantages, this approach has certain limitations. While absolute indications are largely determined by the potential to preserve the volume of hard and soft tissues, relative indications necessitate modifications to the existing protocol, including measures for infection control, gap management, potential biotype thickening, and modulation of the immune response. In analyzing relative contraindications, particular attention should be paid to the patient's medical history, metabolic status, the presence or absence of inflammatory processes, and the potential for their correction in collaboration with a multidisciplinary team to prevent iatrogenic injury. The implementation of modern diagnostic algorithms and biotechnologies may reduce the range of absolute contraindications; however, this approach requires careful analysis.

In experimental and clinical studies aimed at improving diagnostic algorithms and strategies for modulation of homeostasis, a personalized approach can reduce the number of relative contraindications to immediate implant placement.

KEY WORDS: dental implant placement, immediate loading, absolute and relative indications and contraindications

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INTRODUCTION

Despite the successful outcomes of osseointegration achieved with modern implant systems, long-term stability depends on numerous factors. According to the literature, several key aspects of implant placement protocols can be identified (Table 1) [1-4].

Overall, the protocol of one-stage implant placement with immediate loading is a scientifically validated standard of care that ensures esthetic excellence, soft tissue stability, and patient quality of life [5]. Careful consideration of patient selection criteria, specifically indications and contraindications, is essential, as adherence helps preserve bone and gingival tissues, stabilize the arch, and promote psychological comfort. This aspect is particularly important, since, based on clinical experience, litigation related to prosthetic procedures causing pain or facial defects often requires experts to address questions regarding the quality of care, the necessity of the interventions, and the extent of injuries inflicted by the clinician [6].

AIM

To review the scientific literature on dental implant placement with immediate loading, focusing on clinical situations in which the one-stage protocol demonstrated clear advantages over the two-stage approach and the associated risks that required modifications to the surgical technique.

MATERIALS AND METHODS

To analyze the indications for and contraindications to one-stage implant placement with immediate loading,

Table 1. Key aspects of implant placement protocols

Key aspects	Two-stage implant placement	One-stage implant placement with immediate loading
Morphofunctional	- Flattening of the soft tissue architecture. - Loss of the buccal contour and interdental papillae.	One-stage implant placement with immediate loading: - acts as a scaffold - provides mechanical support to soft tissue volume - compensates for buccal bone plate resorption - helps maintain the natural geometry and contour of the gingiva.
Histostructural	- Repeated surgical exposure of the implant and manipulations with healing abutments result in hemidesmosome disruption. - Chronic trauma to the epithelial attachment induces apical migration of the epithelium and bone resorption.	- During the first weeks after surgery, a stable mucosal barrier develops and remains intact throughout the functional period of the dental implant. - Effective protection of osseointegration from bacterial invasion is ensured.
Functional	- "Functional rest" can result in local bone atrophy due to the lack of functional loading. - Wearing removable prostheses during the healing phase exerts pressure on the periosteum and reduces vascularization.	- Control of implant micromotion and splinting allow physiological loading to be transmitted to the bone matrix, promoting osteoblastic activity and accelerating trabecular mineralization around the implant threads.
Psychosomatic	- Postoperative edentulism and the need for removable prostheses cause psychological distress.	- Avoiding a postoperative period of edentulism and wearing removable prosthesis significantly improves the patient's psychological well-being and social adaptation.

thematic sources spanning the past century were reviewed, with particular focus on the period from 2000 to 2025, drawing on substantial experience gained during the development of implantology. During this review, clinical situations were identified and categorized into groups of absolute and relative indications and contraindications.

REVIEW

Drawing on implantology experience, several clinical scenarios were identified in which avoiding immediate loading would be clinically inappropriate.

ABSOLUTE INDICATIONS

Absolute indications are cases where the one-stage protocol demonstrates clear, evidence-based advantages over the two-stage protocol.

PRESERVATION OF TISSUE VOLUME AND PREVENTION OF POST-EXTRACTION TISSUE COLLAPSE

Immediate implant placement in the extraction socket, with simultaneous placement of a prosthetic restoration (temporary crown or customized healing abutment), provides significantly higher rates of preservation of hard and soft tissue volumes than any other technique [5]. The buccal bone wall is a tooth-dependent structure largely supplied by the periodontal ligament; therefore, after tooth extraction, even atraumatic, irreversible resorption of this bone occurs, leading to changes in the gingival contour. Studies have demonstrated that soft tissues require physical support in the form of a "scaffold," whereby a temporary crown placed intraoperatively acts as a scaffold that mechanically maintains the architecture of the gingival papillae and the marginal gingival contour in their natural position (the "Dynamic Compression Technique") [7]. In delayed protocols, when primary closure of the extraction socket is achieved, or a standard cylindrical healing abutment is placed, the gingival contour flattens, and reconstruction of the lost papillae at the second stage becomes a challenging plastic surgical procedure with an unpredictable prognosis. Thus, in patients with thin and medium gingival biotypes and type I extraction sockets (intact socket walls), immediate loading is the only predictable treatment approach to achieve a favorable outcome [8].

MINIMIZING THE TRAUMA TO THE PERI-IMPLANT MUCOSAL ATTACHMENT

Within 4–6 weeks, an epithelial barrier forms around the transmucosal component. Repeated disconnection of the healing abutment or impression coping disrupts newly formed hemidesmosomes and induces apical migration of the epithelium, accompanied by marginal bone resorption of approximately 0.2–0.4 mm [9]. The

immediate loading protocol implements the "One Abutment – One Time" concept, whereby the final abutment (or titanium Ti-Base) is placed under sterile conditions on the day of surgery, promoting the formation of a stable biological seal that remains undisturbed thereafter. Immediate abutment placement was associated with 0.5 mm less marginal bone loss compared to repeated abutment replacement [10].

PATIENTS WITH COMPLETE EDENTULISM OR TERMINAL PERIODONTAL TISSUE CONDITIONS

For these patients, immediate loading with full-arch restorations such as "All-on-4" or "Pro-Arch" is an absolute indication from a histological and biomechanical perspective, as the bone remodels in response to mechanical loading. Controlled immediate loading with rigid implant splinting via a full-arch framework promotes trabecular bone mineralization around the implant threads [11]. In contrast, the use of complete removable prostheses during the healing period under a two-stage protocol exerts uncontrolled pressure on the peri-implant mucosa. This compromises microcirculation, induces periosteal hypoxia, and produces implant micromotion through the soft tissues, thereby increasing the risk of implant failure. Therefore, when the total torque on the arch exceeds 120–150 Ncm, immediate prosthetic loading is indicated [12].

PRESERVATION OF ESTHETICS TO SUPPORT MENTAL HEALTH

Tooth loss often imposes a psychological burden, and the use of removable prostheses is perceived by patients as the most distressing stage of treatment, frequently resulting in reduced self-esteem and social withdrawal [12]. The Immediate Dentoalveolar Restoration (IDR) protocol helps patients avoid the functional and psychological consequences of tooth loss. Patients who achieve a positive esthetic outcome show greater adherence to oral hygiene and clinical instructions, underscoring esthetics as a key factor in supporting mental health [13].

RELATIVE INDICATIONS

Clinical scenarios in which potential risks warrant modification of the surgical strategy constitute relative indications for a one-stage protocol. In such cases, implant surgery is often performed under conditions of increased risk of early complications. The application of a one-stage protocol in these situations requires advanced surgical skills, a thorough understanding of the underlying biological processes, and the use of additional regenerative strategies [2].

INTACT, BLEEDING BONY WALLS AND THE ACHIEVEMENT OF ADEQUATE INSERTION TORQUE

Previously, periapical lesions (granuloma, cystic granuloma, or chronic periodontitis) were considered an absolute contraindication to immediate implant placement due to the risk of bacterial contamination of the implant's rough surface and the development of retrograde peri-implantitis. However, a 2010 study demonstrated that successful osseointegration in infected extraction sockets is possible, with survival rates of 92.0–96.0%, approaching those in intact sockets, provided that a meticulous debridement protocol is followed, a standardized procedure for the surgical removal of necrotic, infected tissues and contaminants from the wound [14]. If clean, bleeding bony walls are achieved after tooth extraction and curettage, and adequate insertion torque is obtained, immediate loading is considered feasible. Conversely, in the presence of an active purulent process, soft tissue swelling, or anatomical limitations that prevent complete site debridement (e.g., involvement of the maxillary sinus floor), priority is given to infection control, necessitating a delayed approach.

PROFICIENCY IN THE ONE-STAGE RECONSTRUCTION (BONE ZONE + TISSUE ZONE) FOR IMPLANT DIAMETER AND SOCKET SHAPE MISMATCH

In immediate implant placement, a mismatch between the implant diameter and the extraction socket shape creates a gap between the titanium surface and the buccal bone wall. The size and configuration of this gap are critical: a gap of less than 2 mm (jumping distance) heals spontaneously with a blood clot; however, under immediate loading, clot stability is compromised due to abutment micromotion [15]. The absence of the buccal bone wall is a high-risk scenario; therefore, immediate loading is feasible only with proficiency in the one-stage reconstruction technique (Bone Zone + Tissue Zone). This approach requires the creation of a rigid scaffold, as without it, the temporary crown would exert pressure on the soft tissues, potentially causing their recession.

INSERTION TORQUE RANGE OF 20–30 NCM

Decision-making is particularly challenging for the implantologist when primary stability falls within

threshold values. Torques above 35 Ncm are considered adequate, while those below 15 Ncm are contraindicated; the 20–30 Ncm range therefore represents a gray zone. Studies have reported that implants with low insertion torque (as low as 25 Ncm) can successfully osteointegrate, as reduced compression promotes angiogenesis by preventing necrosis. However, the risk of micromotion under the load of even a non-occluding temporary crown remains critical [16]. Within this torque range, immediate loading with a crown is not recommended; therefore, placement of a customized healing abutment without occlusal contacts is advised to maintain the emergence profile. This compromise preserves the "scaffolding effect" while minimizing the risk of implant failure.

THIN GINGIVAL PHENOTYPE (<1.5 MM)

Although immediate loading is desirable to support tissue preservation, the risk of soft tissue recession during remodeling remains high, as the thin mucosa provides insufficient blood supply to the periosteum, leading to loss of the underlying bone. In such cases, immediate loading is feasible only in combination with soft tissue thickening procedures, which are more invasive and prolong the intervention [17].

ABSOLUTE CONTRAINDICATIONS

An essential component of implant procedures performed according to the immediate loading protocol is the identification of absolute contraindications. Careful consideration of these factors helps preserve the implant–bone interface and serves as a preventive measure against severe purulent-septic complications or exacerbation of systemic diseases. The literature reports that absolute contraindications arise from the inability to achieve adequate reparative osteogenesis or from decompensated systemic disturbances of homeostasis that render surgical intervention unacceptable [18].

DECOMPENSATED CARDIOVASCULAR DISEASES

This category includes acute myocardial infarction and acute cerebrovascular events (stroke) occurring within six months prior to the planned implant placement. These conditions are considered absolute contraindications, as they pose a significant risk of emergency complications during surgery. Surgical stress associated with traumatic tooth extraction and implant bed preparation leads to a substantial release of endogenous catecholamines, which, in combination with the exogenous administration of vasoconstrictors in local anesthetics, may trigger recurrent ischemic episodes, hypertensive crises, or fatal arrhythmias [19]. During the COVID-19 pandemic and the ongoing military conflict, hospitalizations for myocardial infarction and stroke have increased; therefore, careful consideration of patients' medical history is essential [20, 21]. Similar restrictions apply to patients with unstable angina, uncontrolled grade III arterial hypertension, and congestive heart failure, as in such cases the potential risk outweighs any esthetic or functional benefits of dental treatment [22].

HEMATOLOGIC AND COAGULATION DISORDERS

One-stage implant placement is a highly invasive procedure that results in an exposed surgical site, particularly around the healing abutment. Patients with inherited coagulopathies, such as hemophilia A and B or von Willebrand disease, and acquired conditions, such as thrombocytopenia with platelet counts below the critical threshold of 50×10^9/L, are at extremely high risk of massive, uncontrolled bleeding that cannot be managed with standard local hemostatic measures. Furthermore, the inability to form a stable blood clot, which serves as a biological scaffold for osteoblast migration and angiogenesis, renders osseointegration biologically impossible. Special attention should be given to patients on chronic anticoagulant therapy with vitamin K antagonists who have an international normalized ratio value exceeding 3.0. Implant surgery under these conditions, without prior dose adjustment or conversion to low-molecular-weight heparins, is considered an absolute contraindication [23].

BISPHOSPHONATE THERAPY, MAXILLOFACIAL RADIOTHERAPY, AND OBLITERATIVE ENDARTERITIS

The use of bisphosphonates, particularly when administered intravenously (e.g., zoledronic acid or pamidronate) for oncologic treatment, represents an absolute contraindication of metabolic origin. These drugs inhibit osteoclast function and induce apoptosis. Surgical intervention in such patients may result in bisphosphonate-related osteonecrosis of the jaw, characterized by bone exposure and sequestration. Numerous clinical studies report that dental implant placement during ongoing intravenous bisphosphonate therapy carries an almost 100% risk of failure and severe patient morbidity [24, 25]. A similar clinical scenario occurs in patients who received maxillofacial radiotherapy with a cumulative focal dose exceeding 50 Gray. The resulting

obliterative endarteritis produces hypoxic, hypocellular, and hypovascular bone tissue, which loses its regenerative capacity and renders implant placement impossible due to the risk of osteoradionecrosis [26].

FAILURE TO ACHIEVE PRIMARY IMPLANT STABILITY

A critical threshold is an insertion torque below 35 Ncm or an implant stability quotient (ISQ) value below 60. Immediate placement of a healing abutment or temporary crown is strictly contraindicated in cases of severe alveolar ridge atrophy, low bone density (type D4), or active purulent inflammatory processes (e.g., acute periodontitis or osteomyelitis) that prevent achieving adequate implant stability. Implant micromotion exceeding the tolerated threshold of 150 μm disrupts fibrin network formation and mesenchymal cell differentiation into fibroblasts, resulting in the development of a connective tissue capsule around the titanium surface rather than osseous integration [27].

DISCUSSION

Although the mechanics of the "scaffolding effect" are understood, the optimal design of the subgingival portion of the temporary crown's emergence profile – concave or convex – remains unclear. Furthermore, the influence of temporary crown material on epithelialization of the inner surface of the gingival cuff has not been sufficiently studied. Therefore, the study of bioactive coatings for temporary abutments is particularly important, as it may convert the prosthetic restoration from a passive scaffold into an active promoter of soft tissue regeneration.

The implementation of the "One Abutment – One Time" concept is limited by the difficulty of predicting soft tissue positions. Determining the optimal abutment collar height on the day of surgery to anticipate a degree of gingival recession during healing remains a significant challenge. Errors in abutment collar height selection may result in esthetic failure (metal exposure) or biological complications (cementitis). Therefore, protocols for using scan markers on the day of surgery to fabricate individualized zirconia abutments are recommended, as this approach would integrate the accuracy of digital measurements with the biological benefits of immediate loading.

The study of how various framework materials affect stress distribution in peri-implant bone through finite element analysis (FEA), alongside clinical data on their osseointegration, represents an important area of future research.

Currently, there is no standardized protocol for chemical decontamination of infected extraction sockets before immediate loading (e.g., laser decontamination, photodynamic therapy, or antibacterial treatment). Investigating the local application of immunomodulators and antioxidants in the socket is important, as these agents may help normalize pH from acidic to neutral, a change critical for osteoblast activity at sites of prior inflammation.

The relationship between ISQ values (resonance frequency analysis) and the level of safe occlusal loading remains unclear. In particular, it is uncertain whether an implant with an insertion torque of 25 Ncm can be subjected to loading when its ISQ value exceeds 70. Therefore, developing methods to improve implant stability through osseodensification or the use of biological adhesives (e.g., fibrin sealants, gels, or biomembranes) is important to stabilize the implant in a soft extraction socket. Overall, the study of bioactive substances and biomembranes that can induce angiogenesis and promote gingival thickening without additional surgical incisions could expand the absolute indications for immediate loading.

Absolute contraindications include conditions that are potentially life-threatening or may prospectively prevent successful osseointegration (e.g., bisphosphonate-related osteonecrosis and the effects of high-dose radiation therapy).

Recent literature suggests that many relative contraindications are increasingly regarded as controllable clinical conditions owing to advances in laboratory and instrumental diagnostic algorithms. The key hypothesis is that a more comprehensive diagnostic assessment inversely correlates with the incidence of intra- and postoperative complications, thereby enabling immediate loading in patients previously considered unsuitable for this treatment approach [28].

METABOLIC DISORDERS

For a long time, diabetes mellitus was considered a significant obstacle to dental implantation, as hyperglycemia promotes the accumulation of advanced glycation end products, which negatively affect osteoblast differentiation. In addition, microcirculatory disorders develop, neutrophil chemotaxis and phagocytic activity decrease, and type I collagen synthesis by fibroblasts is suppressed. In a model of streptozotocin-induced diabetes mellitus combined with isoproterenol-induced heart failure, heterogeneous capillary congestion and stromal edema were observed [29]. However, the current diagnostic standard requires the mandatory assessment of glycated

hemoglobin (HbA1c) levels, which serve as an integral indicator of carbohydrate metabolism over the preceding 3 months. Scientific evidence indicates that in patients with HbA1c levels below 7.5%, osseointegration and the long-term survival of dental implants do not differ statistically from those in systemically healthy individuals. Thus, laboratory monitoring enables precise adjustment of the treatment algorithm and surgical planning. Under conditions of stable glycemic control and adequate antibiotic prophylaxis, immediate implantation with healing abutment placement is a safe procedure [30, 31].

Edematous and degenerative changes in the cardiovascular and endocrine systems under conditions of iodine deficiency and altered thyroid status underline systemic metabolic disorders [32, 33]. Such alterations may compromise healing, increase the risk of inflammation, and impair implant osseointegration; however, restoration of normal thyroid function can lead to favorable outcomes [34].

The approach to rehabilitating patients with reduced bone mineral density (systemic osteoporosis or localized osteopenia) has undergone considerable reconsideration. Low bone density (types D3 and D4) has traditionally been regarded as a high-risk factor for immediate loading protocols due to challenges in achieving the required implant insertion torque and the associated risk of micromotion [35]. However, the implementation of cone beam computed tomography with densitometric analysis in clinical practice enables objective assessment of bone architecture during virtual treatment planning. Radiographic density measurements in Hounsfield units (HU) allow the surgeon to accurately select implant placement sites in areas of highest bone density. Intraoperative resonance frequency analysis using devices such as Osstell has been shown to provide an objective numerical measure of implant stability, expressed as the implant stability quotient (ISQ). Research demonstrates that an ISQ value above 70 allows for the safe application of immediate loading protocols, even in bone with reduced mineralization [36]. Screening serum 25-hydroxyvitamin D levels represents an important adjunct, since identification and preoperative correction of vitamin D deficiency can markedly improve the reparative capacity of bone [37].

PATIENT'S PERIODONTAL STATUS

A history of generalized periodontitis is a well-established risk factor for biological complications, such as mucositis and peri-implantitis, due to the translocation of pathogenic microbiota from periodontal pockets to the implant surface. Fungal infection is a significant factor in the pathological processes that compromise the integrity of implant-supporting bone. *Candida* species can form resilient biofilms in the oral cavity and, within polymicrobial infections, promote chronic peri-implant inflammation. Inflammation at the implant site can precede the onset of peri-implantitis or worsen its course [38]. However, the polymerase chain reaction enables precise identification and quantification of periodontopathogens of the "red complex", including *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*. Antimicrobial treatment combined with comprehensive oral decontamination, aimed at achieving microbiological remission, effectively mitigates infectious risk. When a reduction in pathogen titers is confirmed, the intraoperative placement of transgingival components (healing abutments) poses no increased risk, enabling these patients to be regarded as suitable candidates for immediate implant placement [39].

CIGARETTE SMOKING

Nicotine causes sustained peripheral vasoconstriction, and carbon monoxide reduces tissue oxygenation, critically impairing the healing of peri-abutment mucosa. However, the implementation of short-term smoking cessation protocols has demonstrated high clinical effectiveness. Quitting smoking for one week before surgery and 4–6 weeks afterward restores microcirculatory function and immune response to a level sufficient for uncomplicated healing. The use of biochemical tests to measure nicotine levels allows objective monitoring of patient compliance. Thus, rather than excluding patients from treatment, the clinician can manage risk through lifestyle modification, thereby significantly expanding the indications for modern implant placement protocols [40].

CONCLUSIONS

The distinction between absolute and relative contraindications has evolved into a complex clinical decision-making system grounded in a comprehensive understanding of bone histophysiology and overall homeostasis. Scientific evidence demonstrates the potential to enhance adaptive responses to surgical trauma under loading through pharmacological interventions and lifestyle modifications. However, implementing such strategies requires clearly defined protocols for managing patients with comorbidities. Therefore, experimental and clinical studies aimed at improving diagnostic algorithms and methods for modulating an individual's dynamic equilibrium are promising.

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CONFLICT OF INTEREST

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CASE STUDY

CONTENTS

Duodenal wall hematoma imitating a pancreatic tumor as a rare cause of obstructive jaundice – a case report

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ABSTRACT

Obstructive jaundice is mostly caused by malignant lesions such as pancreatic head cancer and cholangiocarcinoma. Atypical benign conditions such as intramural duodenal hematoma (IDH), can imitate malignant processes in both clinical and radiological presentation. The diagnostic workup included computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS) with biopsy. A 65-year-old patient was referred for assessment of obstructive jaundice and endoscopic retrograde cholangiopancreatography (ERCP). Initial presentation included hematemesis, anemia, cholestasis, and coagulopathy. Imaging (MRCP, CT) showed dilation of intra- and extrahepatic bile ducts and pancreatic duct, suggesting obstruction at the pancreatic head. CT also revealed a heterogeneous mass in the duodenum. ERCP demonstrated duodenal stenosis due to external compression and distal bile duct narrowing, and a self-expandable metal stent (SEMS) was inserted. Endoscopic ultrasound with biopsy revealed an intramural duodenal hematoma without malignant features. The patient's medical history was significant for multiple comorbidities and previous anticoagulation therapy. Follow-up imaging demonstrated complete regression of the hematoma, confirming its benign nature. The observed clinical course was consistent with spontaneous resolution; consequently, there was no need for surgical intervention. Intramural duodenal hematoma is a rare but important condition that may mimic pancreatic head tumors causing obstructive jaundice. Early detection using imaging techniques is critical to accurately establish the diagnosis. Early recognition facilitates conservative treatment and helps avoid unnecessary highly invasive surgical procedures.

KEY WORDS: hematoma, duodenum, jaundice, pancreatic neoplasm, endosonography

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INTRODUCTION

Obstructive jaundice is a frequent clinical challenge with multiple possible causes ranging from benign to malignant. Typical malignant etiologies include pancreatic head adenocarcinoma and cholangiocarcinoma with primary neoplastic infiltration of the biliary tree [1]. In contrast, benign disorders frequently involve gallstone disease, chronic pancreatitis, and post-surgical strictures [2]. Among the exceptionally rare and atypical benign conditions of extrahepatic biliary obstruction is the intramural duodenal hematoma [3]. In contrast to neoplastic diseases, this pathology provokes obstruction through an entirely different pathophysiological mechanism, requiring careful consideration in diagnosis [1].

Duodenal wall hematomas are traditionally classified into traumatic and non-traumatic categories. The majority are secondary to blunt abdominal trauma, predominantly in pediatric and young adult populations [4]. Conversely, non-traumatic or spontaneous intramural duodenal hematomas typically occur in patients with specific predisposing conditions [5]. Major non-traumatic risk factors include systemic anticoagulant therapy, primary coagulopathies, and iatrogenic injuries resulting from endoscopic procedures such as biopsies [6;7]. In susceptible patients, spontaneous bleeding originates from the dense submucosal vascular plexus, and progressively accumulates within the relatively confined layers of the intestinal wall [8].

The anatomical features of the duodenum, especially its fixed retroperitoneal location, significantly influence their clinical manifestations. Rapid expansion of a hematoma within the descending part of the duodenum can lead to significant extrinsic mechanical compression of the ampulla of Vater or the distal common bile duct [1]. This external mass effect fundamentally differs

from intrinsic neoplastic duodenal obstruction but can radiologically and clinically mimic a pancreatic head tumor or a cystic neoplasm [9]. Consequently, patients may present with atypical abdominal pain, gastric outlet obstruction, and obstructive jaundice, severely complicating the initial diagnostic workup [10].

Due to the similarities in clinical presentation between this benign hemorrhagic condition and malignant neoplasms, clinicians should maintain a high index of suspicion. Appropriate differential diagnosis is critical to distinguish extrinsic compression caused by a hematoma from a duodenal neoplasm [9]. Most intramural duodenal hematomas resolve completely with conservative medical management [11]. Recognizing that this condition can mimic more serious disease is essential to avoid unnecessary, high-risk surgeries, such as a pancreaticoduodenectomy (Whipple procedure), which carry significant risks and offer no benefit for a resolving hematoma [12].

AIM

The objective of the case is to describe how an intramural hematoma can mimic a pancreatic head tumor and to highlight the importance of multimodal diagnosis in patients with obstructive jaundice.

CASE REPORT

A 65-year-old patient was transferred to the Department of Internal Medicine and Gastroenterology in February 2025 in order to carry out endoscopic retrograde cholangiopancreatography (ERCP) procedure.

Initially, the patient was admitted to a different hospital due to hematemesis, dehydration, and an episode of atrial fibrillation. Laboratory findings showed anaemia, increased inflammation markers and cholestasis.

The gastroscopy was performed. The bleeding resulting from the ruptured vessel in cardiac orifice of the stomach was treated with a hemostatic clip. The MRCP showed significant dilation of the bile ducts. The common bile duct measured 17 mm in width, and a significantly dilated pancreatic duct was noted in the pancreatic body and tail, measuring up to 9 mm. This suggested an obstruction at the level of the head of the pancreas. Due to recognized atrial fibrillation, electrical cardioversion was performed and the chronic anticoagulant therapy (rivaroxaban) was stopped.

Upon admission to the ward, the patient reported weakness, decreased exercise tolerance, insomnia, and stool discoloration. In three and a half months, he lost about 14 kg. The patient's medical history revealed chronic heart failure, persistent atrial fibrillation, type 2 diabetes, hyperlipidemia, nicotine addiction, an umbilical hernia, and colonic diverticula. The patient's treatment regimen included a PPI, metoprolol succinate, ramipril, torasemide, eplerenone, ezetimibe, atorvastatin, empagliflozin, metformin, and enoxaparin. Notably, rivaroxaban was discontinued and replaced with heparin (enoxaparin) to ensure more controlled anticoagulation.

CT scan revealed significant dilation of the intra- and extrahepatic biliary ducts - the right hepatic duct to about 10 mm, the left to about 13 mm, the common hepatic duct to about 12 mm, the common bile duct to about 17 mm. The gallbladder was enlarged to a width of approximately 56 mm. The gallbladder wall remained thin, and no occlusive deposits were visualized within the lumen. Imaging showed an atrophic pancreas. The head and uncinate process contained multiple calcifications (Fig.1), a pattern that is highly characteristic of chronic pancreatitis.

The pancreatic duct was dilated, measuring up to 14 mm. Significant widening of the distal section of the duodenum was observed, reaching a diameter of approximately 49 mm. A protruding heterogeneous solid-necrotic mass measures roughly 44 x 56 mm; this mass demonstrated slight contrast enhancement upon imaging (Fig.2). The ERCP showed a narrowing of the duodenum with external compression and stenosis of the distal part of the common bile duct. The SEMS was placed. EUS imaging and lesion biopsy findings were consistent with a duodenal wall hematoma, with no features of cancer in cytology.

During hospitalization, recurrence of the arrhythmia was observed and beta-blocker therapy was initiated. The patient was qualified for a percutaneous left atrial appendage closure. Following the procedure in March 2025, the patient was enrolled in the SAFE LAAC clinical trial, which assessed the duration and effectiveness of dual antiplatelet therapy after such interventions. In the control imaging studies, regression of the duodenal hematoma was observed. Gastroscopy confirmed inflammatory changes and signs of hemangioma in the medial wall of the duodenum. Laboratory findings revealed anaemia, cholestasis features, prolonged coagulation parameters, and the presence of a lupus anticoagulant (Table 1.) The cancer markers were negative. An increased tendency toward spontaneous haemorrhages was also observed.

Imaging tests identified chronic pancreatitis and duodenal hematoma as the causes of mechanical jaundice. Due to the presence of lupus anticoagulant, antiphospholipid syndrome (APS) was suspected; however, subsequent testing failed to confirm this diagnosis.

In September 2025, the patient was readmitted on schedule for stent revision. He reported abdominal

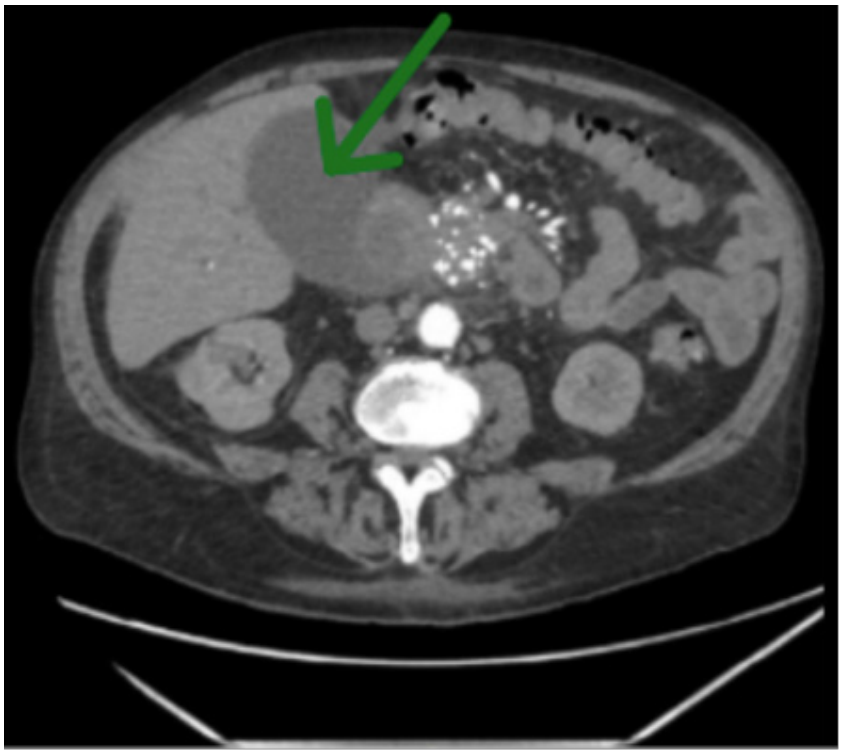


Fig. 1. Abdominal CT: pancreatic calcifications and enlarged gallbladder
Source: Own materials

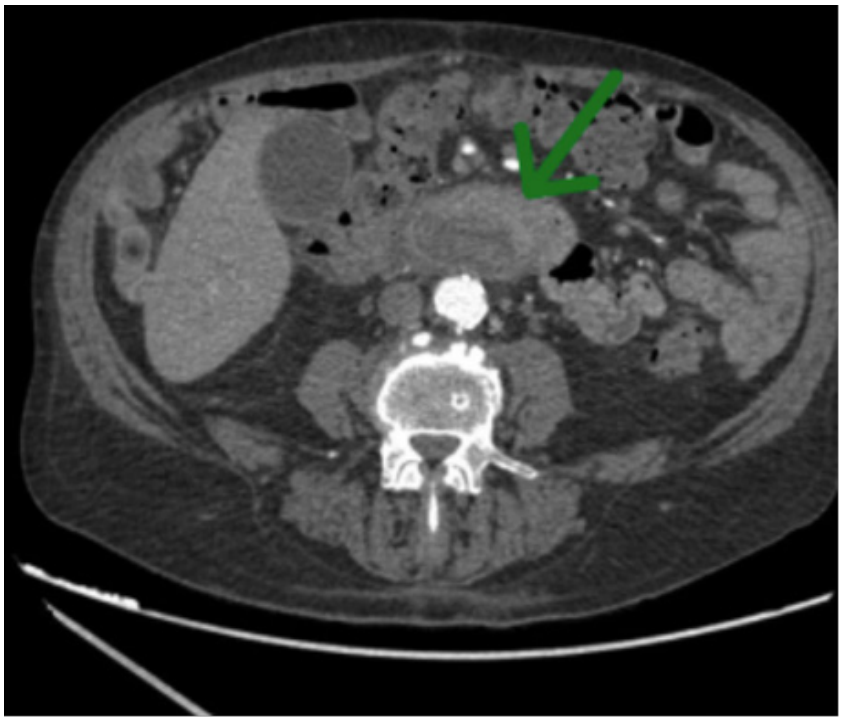


Fig. 2. Abdominal CT: solid-necrotic duodenal mass
Source: Own materials

pain, diarrhoea and further weight loss (a total of approximately 30 kg). CT showed complete regression of the hematoma. The ERCP was rescheduled as the patient had not suspended SGLT-2 inhibitor therapy as required. Gastroscopy revealed a shortening of the duodenal ampulla and deformation of the pylorus. In the prepyloric part of the stomach, the mucosa was focally congested with erosions. Colonoscopy showed intestinal diverticula and two colorectal polyps.

In October 2025, revision ERCP procedure was performed. The SEMS was removed, cholangiography revealed a 15-mm-long stricture of the intrapancreatic portion of the bile duct. Within the stenosis, the bile duct lumen was preserved. The bile ducts were inspected, with subsequent removal of some small food debris into the duodenum. They were irrigated in order to obtain a clear outflow. Due to the observed rapid, spontaneous contrast runoff, bile duct stenting was not recommended.

Table 1. Abnormalities in laboratory findings

Parameter [unit] [reference range]	Value
WBC [10^3/μl] [4,00-10,00]	11,37
HGB [g/dl] [13,00-17,50]	9,8
APTT [s] [20,00-40,00]	48,3
INR [-] [0,80-1,20]	1,43
PT [s] [9,4-13,8]	16,5
Lupus anticoagulant [-] [-]	Positive
ALP [U/l] [40-150]	225
GGTP [U/l] [12-64]	664

Note: ALP, alkaline phosphatase; APTT, activated partial thromboplastin time; GGTP, gamma-glutamyl transpeptidase; HGB, hemoglobin; INR, international normalized ratio; PT, prothrombin time; WBC, white blood cell count
Source: Compiled by the authors of this study

DISCUSSION

Among the many causes of obstructive jaundice, IDH requires careful consideration. Obstruction of the extrahepatic bile ducts is usually caused by more common conditions, such as pancreatic head cancer or choledocholithiasis. However, IDH should be recognized as a benign but potentially serious alternative [10]. In the literature, IDH is most often described as a rare cause of obstruction in the upper gastrointestinal tract. Its coexistence with biliary stricture is therefore unusual and may complicate the diagnostic process [1]. In our case, a patient receiving anticoagulant therapy developed a hematoma in the postbulbar part of the duodenum. This finding adds to the existing literature, where most non-traumatic cases are associated with anticoagulant therapy rather than antiplatelet drugs [13;6]. Similarly to a few previously reported cases, the hematoma in our patient led to secondary biliary stricture, which required appropriate and careful management [12].

The pathophysiology of IDH formation is closely related to the anatomical features of the duodenum [5]. The relatively fixed, retroperitoneal position of this organ and the rich vascular plexus located in the submucosal layer make this area highly susceptible to injury and accumulation of extravasated blood [14]. Historically, blunt abdominal trauma was considered the primary precipitating factor for this condition, especially in the pediatric population [19]. In adults, however, iatrogenic or spontaneous IDH is being recognized more frequently and may result from factors such as systemic anticoagulant or antiplatelet therapy, severe primary coagulopathies, or direct endoscopic interventions [7]. In the presented case, it was the anticoagulant drugs that predisposed the patient to massive intramural bleeding and a secondary mass effect.

The main diagnostic challenge in these cases results from the significant clinical and radiological similarities between an enlarging IDH and neoplastic tumors [9]. With progressive submucosal bleeding, the growing hematoma causes major mechanical compression of surrounding structures [1]. When this compression involves the ampulla of Vater or the distal common bile duct, as in our patient, it may closely mimic a pancreatic head tumor and lead to jaundice and biliary obstruction [10]. In clinical practice, it is important to understand that the following obstruction results strictly from the extrinsic mechanical compression of organs, and not from the actual neoplastic infiltration [12].

The accurate differentiation between a benign hematoma and malignancy depends on the proper use of advanced imaging modalities [9]. Non-contrast CT is the first-line tool, most often depicting an intramural mass that promotes bowel lumen narrowing [13;5]. MRI facilitates the identification of specific blood degradation products, occasionally presenting the pathognomonic "concentric ring" sign [16]. Furthermore, EUS is of pivotal diagnostic value. Its high spatial resolution enables precise visualization of the duodenal wall layers and facilitates the accurate differentiation of an avascular submucosal hemorrhage from a pancreatic parenchymal tumor [17].

An accurate diagnosis determines the management strategy, in which the general clinical approach strongly favors conservative treatment [18]. Management based on bowel rest strategy, correction of coagulation parameters, and temporary drainage allows for the spontaneous resorption of the hematoma [5;7]. In critical situations, the use of a temporary stent allows for the control of obstructive jaundice [3;8]. This intervention was effective in our patient, who had a SEMS successfully removed once free flow of contents was restored. High-burden surgical procedures, particularly the highly morbid pancreaticoduodenectomy (Whipple procedure), are strongly discouraged and should be reserved exclusively for severe complications such as ischemia, bowel perforation, or a persistent inability to rule out a malignant neoplasm [19].

CONCLUSIONS

Intramural duodenal hematoma (IDH) is a rare cause of obstructive jaundice. The ability of the following condition to mimic a pancreatic head tumour clinically and radiologically poses a significant diagnostic challenge. Diagnostic alertness is particularly important in patients with pre-existing coagulopathies or undergoing systemic anticoagulant therapy. These pharmacological and systemic factors can predispose patients to spontaneous submucosal bleeding, as it's clearly demonstrated by the clinical picture of our patient.

Effective differentiation of this mild, external mechanical compression from actual tumor infiltration relies heavily on advanced multi-modal imaging, which provides the necessary tissue resolution to exclude invasive growth. Initial assessment of a bile duct mass and occlusion is possible with CT and MRI, but it is EUS that plays the most decisive diagnostic role in these complex cases. EUS, in conjunction with a biopsy, allows the final identification of the layers of the duodenal wall, which effectively confirms the non-neoplastic nature of the haemorrhagic lesion and prevents serious diagnostic errors.

The main clinical implication of cases like this is that early and accurate IDH detection requires a highly effective conservative treatment strategy based on spontaneous resorption of the hematoma. By recognising the pattern of this condition, clinicians can save patients from the significant morbidity and mortality associated with unnecessary, extensive surgical interventions such as Whipple procedure. Therefore, it is strongly recommended that the priority is given to a thorough review of the patient's pharmacological history and coagulation status whenever they encounter an atypical pancreatic tumour. Ensuring that mild haemorrhagic etiologies have been definitively ruled out before considering invasive options remains the foundation of safe patient care.

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CASE STUDY

CONTENTS

Psoriasis associated with stress following a through-and-through gunshot wound in a military service member: A case report

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ABSTRACT

The paper presents a clinical case of psoriasis that developed in a 23-year-old Ukrainian service member after a combat-related through-and-through gunshot wound to the lower leg sustained in 2022. The patient had no previous dermatological diseases or family history of psoriasis. Two weeks after the injury, irregular pink plaques appeared around the damaged skin areas and gradually spread to the lower limbs, trunk, and upper extremities, becoming generalised within two months. The disease subsequently progressed to severe plaque psoriasis, complicated by nail dystrophy and psoriatic arthritis. By 2026, skin lesions involved more than 50% of the body surface area (Psoriasis Area and Severity Index (PASI) 25,9) and were associated with a significant impairment in quality of life (Dermatology Life Quality Index (DLQI) 16). Persistent psycho-emotional stress related to military service, sleep disturbances, smoking, and poor adherence to therapy contributed to recurrent exacerbations. Screening revealed clinically significant anxiety, and the patient was referred for psychological evaluation and support. After referral to a mental health centre and implementation of comprehensive management that included psychological support and improved adherence to dermatological therapy, gradual improvement in skin condition and quality of life was observed.

KEY WORDS: psoriasis, gunshot wounds, stress, military medicine

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INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder with a complex clinical presentation that is currently incurable and requires continuous dermatological management [1]. Psychological stress is recognized as a trigger factor for the development of psoriasis [2, 3]. In turn, psoriasis significantly worsens patients' quality of life and contributes to deterioration of the psycho-emotional state and the further development of alexithymia, anxiety, depression, and sleep disorders [4]. Stress may also provoke or aggravate the course of acne, vitiligo, lichen planus, and atopic dermatitis [5]. Since the beginning of the full-scale invasion, a significant proportion of the Ukrainian population has demonstrated increased levels of anxiety, depression, and stress associated with the war [6]. Previous studies on the psychological status of military personnel in Ukraine indicate a substantial burden of stress-associated disorders [7]. Military members, who have sustained traumatic injuries, including firearm wounds, are at higher risk of developing post-traumatic stress disorder, depression, and anxiety [8], which may potentially act as triggers for chronic inflammatory skin diseases.

FRAMEWORK

The article is part of the research work of the Department of General Practice (Family Medicine) at Bogomolets National Medical University: «Improvement of approaches to detecting and preventing the development of chronic non-infectious somatic diseases and psychomotional states in primary care under contemporary conditions», 2024-2026, 0123U105321.

CASE REPORT

A 23-year-old Ukrainian male consulted his family doctor in January 2026 with complaints of a widespread, generalised rash. According to the patient, prior to February 2022, he had no chronic diseases, skin changes, previous injuries, or surgical interventions. He reported a family history of hypertension in his parents and de-



Fig. 1. Left lower leg after the gunshot injury in March 2022, prior to the onset of psoriasis. No psoriatic lesions are visible
Picture taken by the authors

nied any dermatological diseases in the family history. While performing a combat mission in March 2022 in the Donetsk region, he sustained a gunshot wound. The bullet passed through the muscles of the left lower leg and superficially injured the skin of the right lower leg. The wound healed slowly over several months (Fig. 1).c

Within two weeks after the injury, the patient noticed the appearance of irregular pink plaques around the bullet-damaged skin areas. The lesions gradually enlarged and merged, initially involving both lower limbs and subsequently spreading to the trunk and upper extremities. Within approximately two months, the eruption became generalised. In November 2022, the patient was hospitalised due to severe pruritus, marked scaling of the scalp, deformation of the nail plates with purulent discharge around the nail folds, and pronounced pain in the thigh and lower leg muscles. At the time of the first hospitalisation, the eruption had a widespread symmetrical distribution. The skin of the trunk and extremities appeared cyanotic-red and was covered with multiple plaques measuring 1–10 cm in diameter (Fig. 2). Clinically, the characteristic "stearin spot" sign was observed, and in several plaques the "terminal film" and Auspitz sign ("blood dew") phenomena were detected. The nail plates were yellowish, deformed, and brittle.

During hospitalization, the patient received systemic and topical therapy combined with phototherapy, including antihistamines, topical corticosteroids, keratolytic agents, and supportive dermatological treatment. Clinical improvement was observed, and the patient was discharged with recommendations for methotrexate therapy (10 mg once weekly) with folic acid supplementation, emollients, and vitamin therapy. According to the patient, he adhered to the prescribed treatment for only two weeks after discharge, taking two doses of methotrexate before discontinuing therapy upon returning to military duties. Following the gunshot injury and diagnosis of psoriasis, he experienced severe sleep disturbances and reported a period of alcohol abuse lasting more than one month, explaining that alcohol became the only way he could fall asleep. Hypnotic medications were reportedly ineffective. During this period he did not seek medical assistance or report sleep problems to doctors. Poor adherence to therapy, together with ongoing stress and unhealthy coping strategies, contributed to further disease progression.



Fig. 2. Widespread psoriatic plaques on the trunk and extremities in November 2022, accompanied by nail dystrophy
Picture taken by the authors

The patient developed severe pain in the small joints of the hands and feet that gradually limited daily activities in early 2023. On 16 January 2023, he was hospitalised and diagnosed with widespread psoriasis in the progressive stage, complicated by psoriatic arthritis involving the small joints of the hands and feet. A similar exacerbation occurred in early February, requiring repeated hospitalisation on 9 February 2023. Despite systemic and topical treatment, clinical improvement remained limited. Methotrexate therapy (15 mg weekly) with folic acid supplementation was recommended.

On 7 March 2023, the patient was examined by a dermatologist at a municipal consultative diagnostic centre and was advised to continue methotrexate therapy together with antihistamines and topical corticosteroids. He followed these recommendations while continuing military service until 2024 but later discontinued treatment on his own initiative.

In April 2023, the disease progressed during a period of severe psycho-emotional stress. The diagnosis at that time was widespread plaque psoriasis with psoriatic onychodystrophy and psoriatic polyarthropathy grade II with functional insufficiency grade II. The patient received systemic therapy together with topical corticosteroids and psoralen plus ultraviolet A (PUVA) phototherapy.

In January 2025, the patient reported a marked increase in the number of skin lesions accompanied by intense pruritus and severe pain in the small joints of the hands and feet. Self-administered topical corticosteroids produced no significant improvement. On 23 January 2025, he was hospitalised again. By early 2025, the scalp, trunk (including the genital area), and upper and lower extremities were covered with cyanotic-red plaques measuring 1–10 cm in diameter, which were elevated above the skin surface, prone to coalescence, and covered with large seropurulent scales. Purulent discharge was observed from some lesions, and the Auspitz sign was positive. Nail plates were deformed, yellowish, brittle, and covered with hyperkeratotic deposits accompanied by purulent discharge. The total affected body surface area exceeded 70%. Treatment included topical keratolytic and corticosteroid therapy. During this period, the patient did not modify his lifestyle. Psycho-emotional stress remained high due to ongoing military service, combat missions, and shelling. He also reported increased smoking associated with stress.

By January 2026, when he was hospitalized again because of exacerbation of psoriasis and psoriatic arthritis, he smoked approximately 20 cigarettes per day. Dermatological examination revealed multiple papular eruptions measuring 3-5 cm in diameter with well-defined margins and covered with silvery-white scales on the scalp, retroauricular folds, and extensor surfaces of the extremities. In the lumbar, inguinoscrotal, axillary, intergluteal, perianal, pubic, and genital regions, as well as on the extremities, lesions merged to form large plaques up to the size of the patient's palm with pronounced infiltration, affecting more than 50% of the body surface area. Deep fissures were present, particularly on the palms and soles, accompanied by marked hyperkeratosis and hemorrhagic crusts. The psoriatic triad was positive. Hyperemia and maceration were observed in skin folds and the perineal area. Nail plates of the hands and feet



Fig. 3. Severe plaque psoriasis (PASI 25.9) with generalized symmetrical erythematous papules and plaques, silvery-white scales, confluent lesions on the trunk and extremities, grayish-brown crusts on the lower legs, and marked infiltration
Picture taken by the authors

were thickened, deformed, yellowish and demonstrated the characteristic "thimble sign".

After discharge in late January 2026, the patient consulted a family doctor for the first time to sign a primary care declaration at the University Clinic of Bogomolets National Medical University. Considering the patient's occupation in a high-stress environment and persistent sleep disturbances since 2022, screening for anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) was performed [9]. The patient reported that his psychological condition had never been previously evaluated and that consultations with mental health specialists had not been recommended, which was confirmed by discharge summaries from 2022. The HADS score was 14 on the Anxiety subscale, indicating clinically significant anxiety, and 5 on the Depression subscale, corresponding to normal levels without clinically significant depressive symptoms. Following the mhGAP algorithm "Other Significant Mental Health Complaints" [10], the doctor provided psychoeducation and recommended lifestyle modification, smoking reduction, and improved adherence to therapy. The family doctor also became the first specialist to whom the patient disclosed his previous alcohol abuse as a coping mechanism for insomnia following the gunshot injury. He reported that stress exacerbated his psoriasis, which in turn increased psychological distress related to concerns about his health. Because the patient described episodes resembling flashbacks associated with the traumatic event during sleep onset, post-traumatic stress disorder (PTSD) was suspected and he was referred to the Mental Health Center of the University Clinic and to a dermatologist for further evaluation. Despite ongoing treatment, skin lesions remained widespread (Fig. 3). The eruption was inflammatory and generalized, involving the trunk, extremities, scalp, and face, with the most prominent lesions located on the lower extremities and hands. The rash was symmetrical and monomorphic, represented by erythematous papules with a strong tendency to enlarge and merge into plaques. Many plaques were covered with silvery-white scales, while some lesions on the lower limbs were covered with grayish-brown crusts. Infiltration was most pronounced on the lower extremities. Nail changes included thickening, irregular surface, and pronounced onycholysis. The Psoriasis Area and Severity Index (PASI) score was 25.9, indicating severe psoriasis, and the Dermatology Life Quality Index (DLQI) was 16, reflecting a severe impact on quality of life [11]. The final diagnosis corresponded to widespread papulo-plaque psoriasis with psoriatic onychodystrophy.

The patient initiated treatment at the Mental Health Centre of the University Clinic and also underwent inpatient treatment for 7 days. Although psoriasis treatment remained standard, the patient reported a subjective reduction in pruritus during psychotherapy sessions. In addition, according to the patient, the rash became paler and exhibited fewer scales. Upon assessment using the DLQI by the family doctor after discharge, the patient scored 5 points, which corresponds to a small effect on the patient's quality of life. The period of the patient's treatment in Kyiv also

coincided with a relatively calm period, during which no missile attacks occurred, and only one preventive air-raid alert was recorded during the 7-day hospitalisation. The patient agreed that the improvement in his condition may be associated with the absence of stress related to military service.

The development of psoriasis in a patient without a family history of the disease and without prior dermatological complaints following a through-and-through gunshot wound is uncommon but plausible. Cases of psoriasis developing after skin trauma in individuals with previously healthy skin have been described only sporadically in the literature. Among them are reports of the Koebner phenomenon occurring after burns [12], accidental skin scratches [13], and insulin injections [14]. The formation of new psoriatic lesions within the Koebner phenomenon is driven by a complex interaction of several pathophysiological mechanisms.

A key role is played by the activation of inflammatory mediators released by mast cells, including tryptase and interleukins IL-6, IL-8, IL-17, and IL-36γ [15-18]. Skin injury also induces type I interferons from cutaneous cells, which may initiate autoimmune cascades capable of triggering psoriasis [18]. This process may be further amplified by increased production of neurotrophic and angiogenic factors such as nerve growth factor (NGF) and vascular endothelial growth factor (VEGF), which stimulate cellular proliferation and tissue remodeling [15, 17]. Cell adhesion molecules, particularly integrin α2β1, as well as proteins S100A7 (psoriasin), and S100A15 (koebnerisin), also play an important role in regulating inflammatory responses and epidermal differentiation. In parallel, an immunological imbalance develops, characterized by alterations in the CD4 / CD8 T-lymphocyte ratio, reduced expression of the mechanosensitive protein polycystin-1, and dysregulation of the atypical chemokine receptor ACKR2, which normally limits inflammatory activity [15]. Epidermal keratinocytes are a rich source of CC chemokine ligand 20 (CCL20) and recruit CCR6-expressing T cells producing interleukin-17A, which are considered pathogenic in psoriasis [19].

In the present case, the patient had no history of dermatological disease prior to sustaining the gunshot wound, suggesting a temporal association between trauma and the onset of psoriasis. However, it cannot be definitively concluded that the wound itself served as the primary trigger. The patient, who had no previous military background, was exposed to substantial psychological stress related to military service and combat deployment. Psychological stress is a well-established trigger for the onset and exacerbation of psoriasis. The patient also reported sleep disturbances and a period of alcohol abuse following the injury. Previous studies suggest that psoriasis itself does not necessarily impair sleep quality [20]. Based on the clinical interview and detailed medical history, the family doctor suspected post-traumatic stress disorder (PTSD), which had not been diagnosed in 2022 and therefore had not been appropriately managed. An additional limitation of this case is the absence of a family doctor involved in the patient's care until January 2026. The patient reported limited trust in physicians who treated him during hospitalizations in military hospitals and municipal consultative-diagnostic centers.

Previous research indicates that patients tend to have the highest level of trust in their family doctors, who often act as interpreters of medical information and long-term advisors. Patients frequently trust recommendations from their family doctor more than those from well-known specialists [21]. Earlier involvement of a family doctor, beginning in 2022, might therefore have contributed to better adherence to treatment recommendations and earlier identification of mental health disorders. Psoriatic arthritis represents another factor complicating the course of psoriasis in this patient. According to previous studies, the global prevalence of psoriatic arthritis among patients with psoriasis is approximately 17.58% [22]. Psoriatic arthritis has also been described as potentially triggered by a deep Koebner phenomenon [23]. However, in the present case there is no evidence suggesting a direct causal relationship between the gunshot wound and the development of psoriatic arthritis. Instead, the progression of the disease is more likely related to the absence of structured management of the chronic condition and the patient's discontinuation of prescribed treatment, partly associated with harmful habits and ongoing exposure to chronic stress [24].

This situation may have led to the formation of a vicious cycle in which chronic stress—peaking at the time of the gunshot injury—acted as a trigger for the onset of psoriasis, while the severe course of the disease subsequently generated additional psychological stress. This, in turn, contributed to increased anxiety regarding the patient's health status in the context of continued military service. Currently, there is limited evidence regarding the effectiveness of mhGAP protocols in populations living under martial law and prolonged exposure to war-related stressors. These protocols remain one of the few practical tools available for primary care doctors to identify mental, neurological, and substance use disorders and initiate early management or referral. However, several challenges arise when applying these recommendations in wartime conditions.

The guidelines emphasize the importance of addressing current psychosocial stressors as a priority [10]. In the context of military service, however, potential stressors, their timing, and the duration of threats are unpredictable. Furthermore, under life-threatening circumstances, stress may also serve an adaptive function by mobilizing the organism and enabling rapid physical responses that may be life-saving [25-29]. In the present case, other mhGAP recommendations-including referral for specialized mental health care and cautious use of anxiolytics or antidepressants in primary care- were followed. This case illustrates the multifactorial nature of psoriasis onset in the context of physical trauma, chronic stress, and insufficient continuity of care.

CONCLUSIONS

This clinical case illustrates the potential role of severe physical trauma and chronic psycho-emotional stress as contributing factors in the onset and progression of psoriasis. In this patient, psoriasis developed shortly after a combat-related gunshot wound and rapidly progressed to severe generalized disease complicated by psoriatic arthritis. The case highlights the importance of a multidisciplinary approach that includes dermatological treatment, psychological assessment, and continuous primary care follow-up. Early identification of mental health disorders and improved adherence to therapy may contribute to better disease control and improved quality of life in patients exposed to prolonged stress.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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