PUBLIC HEALTH CENTER
OF THE MOH OF UKRAINE

STUDY PROTOCOL

«Investigation of antibiotic prescribing practices among hospital healthcare workers in Ukraine»

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Contents

ACRONYMS

AMR – antimicrobial resistance

AMS – Antimicrobial Stewardship

AWaRe – Access, Watch, Reserve

BCI – behavioural and cultural insights

COM-B – Capability, Opportunity, Motivation-Behavior

ESCD – European Centre for Disease Prevention and Control

HCF – health care facility

IPC – infection prevention and control

LTCF – long-term care facilities

MDR – multi-drug resistant

MOH – Ministry of Health

PHC – Public Health Center of the Ministry of Health of Ukraine

RAP – rapid assessment procedures

WHO – World Health Organization

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ABSTRACT

Antibiotics are an important element in the treatment of infectious diseases, but their inappropriate use can lead to an increase in antibiotic resistance. This Protocol is dedicated to the study of antibiotic prescribing practices among healthcare facilities (HCFs) physicians in Ukraine.

The overall aim of the study is to identify key factors preventing and facilitating adherence to the national guidelines of rational use of antibacterial drugs, among secondary health care physicians in Ukraine, using Behavioural and Cultural Insights (BCI) approach, and to develop recommendations for improving antibiotic prescribing practices.

This goal will be achieved using qualitative methods, namely in-depth interviews with HCFs physicians who prescribe antibiotics.

The results of the study can serve as a basis for improving recommendations and standards for the use of antibiotics in medical institutions in Ukraine.

This study aims to make a significant contribution to improving antibiotic prescribing practices in Ukrainian hospitals by contributing to the understanding and optimization of antibiotic use in medical practice to ensure the effective and responsible use of these medicines.

INTRODUCTION

Antimicrobial resistance (AMR) and the emergence of multidrug-resistant bacterial strains is a global threat to the health care system of all countries and a potential problem for all mankind. The World Health Organization (WHO) has developed a global action plan on AMR and set a high priority to address it[1]. According to the WHO, medications are used rationally when patients receive the proper medicines, for the relevant indications, in dosages that fit their own specific requirements, for an acceptable amount of time, at the lowest cost to them and society, and with appropriate information. When one or more of these factors are not achieved, irrational or needless use of drugs occurs[2].

The full-scale war in Ukraine has led to an overload of HCFs with patients injured in the fighting. Such patients often require surgical interventions, adequate perioperative antibiotic prophylaxis and antibiotic therapy. In addition, even without direct impact, the war has led to the destruction of HCFs, large-scale violations of sanitation and hygiene, mental disorders and exacerbation of chronic diseases. Critical burdens on the medical system have exacerbated the existing problem of irrational consumption of antimicrobial drugs[3].

European HCFs are already accepting civilians and military personnel from Ukraine who were injured in the fighting and have colonization or infection with multi-drug resistant organisms. Such patients are complicated to treat and it is challenging, and resource intensive, to and perform proper infection prevention and control (IPC) measures for these patients in HCFs. As russia's aggression in Ukraine continues, the situation with AMR will most likely get worse. AMR knows no borders, so given the above, this problem is a threat to the medical system not only in Ukraine but also in Europe. Displaced persons may also be exposed to multidrug-resistant organisms through recent contact with health services in countries with a high prevalence of multidrug-resistant organisms in health facilities, either in their own country or in a country through which they may have traveled in transit.

Healthcare providers should be aware of these risks so they can diagnose and successfully treat infections with multidrug-resistant organisms in displaced and wounded people in a timely manner, thus preventing transmission of such organisms in hospitals and other healthcare settings.

Gaps in services such as infection control caused by limited resources and staffing are exacerbating the transmission of microbial resistance in Ukraine. As a result, healthcare networks in Europe now consider prior hospitalization in Ukraine to be a critical risk factor for colonization of microbial resistance. Healthcare practitioners treating Ukrainian nationals should be aware of the increased risk of transmission of MDRs and infection caused by the war in Ukraine and take appropriate infection control measures to mitigate their spread[4].

According to the general consensus, irrational and excessive consumption of antibiotics accelerates the spread of AMR. The principles of rational antibiotic therapy include treatment with effective antibiotics (determination of pathogen sensitivity by microbiological testing), taking into account the

[1] https://www.who.int/publications/i/item/9789241509763
[2] WHO. The world medicines situation report 2011. Published online 2011
[3] https://doi.org/10.24959/sphhcj.19.157
[4] Melwani M (2022) How war is spreading drug resistant superbugs across Ukraine and beyond. BMJ 379:o2731. 10.1136/bmj.o2731

assignment of antibiotics to WHO AWaRe groups[5], the optimal time period, in the optimal dosage and timely de-escalation (according to microbiological tests) or discontinuation of therapy.

It is also worth mentioning the methods of administering antibiotics. Antimicrobial therapy for patients with serious infections requiring hospitalization is generally initiated with parenteral therapy. Enhanced oral bioavailability among certain antimicrobials allows conversion to oral therapy once a patient meets defined clinical criteria. This can result in reduced length of hospital stay, health care costs, and potential complications due to intravenous access. Randomized studies evaluating early transition from parenteral to oral therapy in the management of adults with community-acquired pneumonia have demonstrated significant reductions in length of hospital stay and cost of care with no adverse effect on clinical outcomes. So, a systematic plan for parenteral to oral conversion of antimicrobials with excellent bioavailability, when the patient's condition allows, can decrease length of hospital stay and health care costs. Development of clinical criteria and guidelines allowing conversion to use of oral agents can facilitate implementation at the institutional level[6].

To combat the inappropriate use of antibiotics, medical standards have been approved, such as the Rational Use of Antibacterial and Antifungal Drugs for Therapeutic and Prophylactic Purposes, approved by Order of the Ministry of Health of Ukraine (MOH) No. 1513 of 23.08.2023[7].

This medical standard takes into account the above principles. Indirect signs (volumes of consumption of antibiotics, frequency of selection of certain antibiotics, etc.) indicate a low level of compliance with this medical standard. Multiple studies have identified cross-sectional relationships between antibiotic use and resistance, especially across European countries and the US. Therefore, there is a need to systematically explore and understand all the individual (e.g. knowledge, beliefs, perceptions) and contextual (e.g. social, structural and environmental) factors that influence the rational use of antibiotics by doctors. This information is central to a data-driven and evidence-based approach for developing more effective health policies, services and communications. Behavioural and Cultural Insights (BCI) is an area within public health that explores the factors that affect health behaviours. Using behavioural and cultural research and insights, BCI aims to improve the outcomes of health policies, services, and communication. BCI is identified by the WHO as a key area for further advancing public health goals in Europe.

[5] The selection and use of essential medicines 2023: Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines, 24 – 28 April 2023
Web Annex C. WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2023

[6] Timothy H. Dellit, Robert C. Owens, John E. McGowan, Dale N. Gerding, Robert A. Weinstein, John P. Burke, W. Charles Huskins, David L. Paterson, Neil O. Fishman, Christopher F. Carpenter, P. J. Brennan, Marianne Billeter, Thomas M. Hooton, Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship, Clinical Infectious Diseases, Volume 44, Issue 2, 15 January 2007, Pages 159–177, https://doi.org/10.1086/510393

[7] On Approval of the Standard of Medical Care "Rational Use of Antibacterial and Antifungal Drugs for Therapeutic and Prophylactic Purposes": Order of the Ministry of Health of Ukraine No. 1513 dated 08/23/2023 URL: https://moz.gov.ua/article/ministry-mandates/nakaz-moz-ukraini-vid-23082023--1513-pro-zatverdzhennja-standartu-medichnoi-dopomogi-racionalne-zastosuvannja-antibakterialnih-i-antifungalnih-preparativ-z-likuvalnoju-ta-profilaktichnoju-metoju

Identifying the behavioural and cultural factors that influence healthcare workers prescribing of antibiotics will allow the MOH and other Ukrainian and foreign stakeholders to adjust their approaches to working with healthcare workers to improve antibiotics use practices in the future.

STUDY OBJECTIVES

The overall aim of the study is to systematically identify key factors influencing adherence to the national guidelines of rational use of antibacterial drugs, among secondary health care physicians in Ukraine, and to develop recommendations for improving antibiotic prescribing practices and decision-making in hospital settings across Ukraine.

STUDY METHODOLOGY AND DESIGN

Study design

This is a qualitative study. The primary data sources informing the analysis will be a document review and in-depth interviews. The literature review will focus on Ukraine's neighboring countries, as well as the broader European context, which may help to identify and assess what factors may influence antibiotic selection and prescribing, as well as point to patterns of antibiotic prescribing from other studies. It will also examine Ukrainian legislation on antibiotic use, antibiotic availability, and published data on antibiotic resistance/prescribing in Ukraine. The literature review will explore research questions such as barriers that prevent healthcare providers from prescribing antibiotics appropriately, as well as practices that aim to further improve antibiotic prescribing.

The study will be based on in-depth interviews with physicians in secondary HCFs who prescribe antibiotics and will be conducted to identify key factors that influence the rational and appropriate use of antibiotics. In preparing the guide for in-depth interviews with healthcare workers, the standard of medical care, "Rational use of antibacterial and antifungal drugs for therapeutic and prophylactic purposes" No. 1513 of 23.08.2023, approved by the MOH, was be used. A guide for in-depth interviews is developed in accordance with the approved principles of rational prescribing of antibacterial drugs in HCFs and measures aimed at reducing the irrational use of antibacterial drugs. It is planned to involve physicians working within various specializations and care levels in the following departments: anesthesiology, infectious diseases, surgery, pulmonology, gynecology, with a breakdown into junior and senior level representatives, which will allow to understand the situation both at the level of the whole country and at the level of individual regions. A semi-structured interview format will allow for a conversation to be conducted in accordance with the key topics identified in accordance with the medical standard №1513, as well as those identified during the desk review while leaving room for respondents to raise topics. In turn, this will ensure the completeness of the information obtained.

STUDY SETTING

The setting

The study will be conducted in Ukrainian secondary HCFs during martial law in the country.

Characterizing the current socio-economic situation in the country of study, it should be noted that it is a country with a lower-middle income, significantly damaged infrastructure, including HCFs, which limits the development and provision of healthcare services. The country is also facing the problem of

rising AMR due to limited access to healthcare services, antibiotics, and hygienic conditions in general. In turn, this can lead to the spread of infections that are difficult to treat with antibiotics.

The overall state of the healthcare system in Ukraine during the war became extremely difficult. In particular, the medical situation in Ukraine during the war with russia posed serious challenges for the country's healthcare system and the fight against AMR. Given the difficult conditions of the war, sanitary and hygienic standards may be compromised, increasing the likelihood of an increase in infectious diseases. The war has resulted in significant restrictions on access to medical resources, including medicines, medical equipment, and qualified medical personnel.

In this regard, the increased number of wounded and internally displaced persons may increase the spread of infectious diseases. In addition, war conditions can contribute to the heavy and uncontrolled use of antibiotics, which can lead to an increase in the level of antibiotic resistance.

Theoretical perspective

AMR poses a serious threat to global health system, arising from the improper use of antibiotics in medical practice and other sectors. To develop effective strategies that promote the rational use of antibiotics and prevent the spread of AMR, it is necessary to understand and influence the behavior of patients, healthcare workers, and the public. BCI approach and the COM-B model (Capability, Opportunity, Motivation, and Behavior)[8] can be utilized for this purpose.

BCI[9] considers a wide range of sociocultural and behavioural aspects that influence medical practice. These factors include concepts that explain how people interact with the health care system and why certain standards of care may be accepted or rejected in certain sociocultural contexts[10].

In AMR research, BCI plays a crucial role in comprehending how hospital healthcare workers respond to and prescribe antibiotics, as demonstrated in prior studies analyzing the impact of sociocultural and behavioral factors on antibiotic prescribing practices[12,13].

Previous research conducted in various contexts, such as medical practices in India[11] and antibiotic use in acute pharyngitis in Iran[12], has confirmed the effectiveness of BCI approach in gathering insights. These insights not only uncover the fundamental reasons influencing antibiotic choices but also highlight specific opportunities for interventions and improvements.

The application of BCI in this study builds upon past successes and tailors this method to specific AMR context, considering the unique challenges and opportunities in medical environment in Ukraine. The

[8] Michie, S., Van Stralen, M. M., & West, R. (2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implementation science*, *6*(1), 1-12. World Health Organization. (2023). A guide to tailoring health programmes: using behavioural and cultural insights to tailor health policies, services and communications to the needs and circumstances of people and communities.

[9] https://bci-hub.org/about

[10] Smith, J. A., Jones, R. K., Brown, S. L., … Green, T. J. (2019). A qualitative interview study applying the COM-B model to explore how hospital-based trainers implement antimicrobial stewardship education and training in UK hospital-based care. Journal of Hospital Infection, 103(1), 12–21

[11] Haenssgen MJ, Charoenboon N, Zanello G, et al Antibiotic knowledge, attitudes and practices: new insights from cross-sectional rural health behaviour surveys in low-income and middle-income South-East Asia BMJ Open 2019;9:e028224. doi: 10.1136/bmjopen-2018-028224

[12] Sami, R., Sadegh, R., Fani, F. et al. Assessing the knowledge, attitudes and practices of physicians on antibiotic use and antimicrobial resistance in Iran: a cross-sectional survey. J of Pharm Policy and Pract 15, 82 (2022). https://doi.org/10.1186/s40545-022-00484-2

success of using BCI in similar studies emphasizes its necessity and appropriateness for this study, enabling a profound understanding of the AMR issue and the development of effective combat strategies.

Implementation of the BCI approach in the antibiotic resistance context contributes to understanding how contextual and individual factors influence this global societal and health challenge. This understanding aids in devising effective strategies and interventions to curb antibiotic resistance spread and preserve antibiotic effectiveness. Consequently, the obtained result will inform the development of an action plan, directed efforts toward addressing the main obstacles.

Within the BCI approach the COM-B model is the organizing theoretical framework, facilitating a thorough exploration of the factors influencing healthcare professionals' behavior in antibiotic prescription contexts. This model, covering Capability, Opportunity, Motivation, and Behavior, acts as a structure to systematically analyse the complex dynamics involved in prescribing antibiotics.

Below is a more detailed description of the methodology and the rationale for choosing these tools.

The COM-B model[13] is a theoretical model used to analyze behavior based on three main components:

- Capability: This refers to the proficiency of healthcare professionals in effectively and responsibly selecting, dosing, and monitoring antibiotics. Capability factors blend knowledge, skills, professional judgement, continuous learning, and communication to ensure optimal patient outcomes and antibiotic stewardship.
- Opportunity: This refers to the opportunities and constraints that healthcare workers have to prescribe antibiotics, including the availability of protocols and access to the necessary resources. This also includes social opportunity: primarily related to interpersonal and group dynamics, and the broader healthcare system and includes interprofessional collaboration, peer influence and norms, feedback mechanisms, organizational culture, leadership engagement, recognition and incentives in relation to prescription of antibiotics.
- Motivation: This integrates healthcare workers confidence in their capabilities, awareness of the consequences of their decisions, intention to adopt responsible practices, setting of antibiotic prescription-related goals, and alignment of their professional identity with responsible antibiotic prescribing. It also encompasses emotional responses like fear, immediate reactions to situational pressures, and deeply established habits. Also refers to motivation of healthcare workers, their values and beliefs that influence their decisions to prescribe antibiotics.
- Behaviours: This category encompasses specific behaviors related to the prescription of antibiotics, including the decision-making process, prescription patterns, and adherence to guidelines, contributing to a comprehensive understanding of healthcare workers' actions in the context of antibiotic prescribing.

Therefore, the COM-B model was chosen because it provides a comprehensive approach to behavioural analysis, considering various factors that may influence antibiotic prescribing. It will help to identify and understand the root causes of healthcare workers' antibiotic prescribing behavior.

[13] Michie, S., van Stralen, M.M. & West, R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. Implementation Sci 6, 42 (2011). https://doi.org/10.1186/1748-5908-6-42

The COM-B model has proven to be practically useful in various studies on AMR. For example, a recent study identified that various factors related to the capability, opportunity, and motivation of trainers and healthcare professionals influence the implementation of Antimicrobial Stewardship (AMS) in hospitals. The study's findings led to recommendations for enhancing AMS in hospitals through behavioral interventions that consider these factors[14].

The study titled «Antibiotic prescribing in long-term care facilities: a qualitative, multidisciplinary investigation» demonstrates the use of the COM-B model to AMR study in long-term care facilities (LTCFs). Findings include challenges in LTCF infections, nurses' role in antibiotic prescribing, pharmacist's limited involvement, surveillance and feedback gaps[15].

These instances highlight the model's effectiveness in systematically analyzing and intervening in behavior, contributing to the efficient management of AMR.

Therefore, the use of BCI approach and the COM-B model itself in this study has the following reasons:

- BCI approach will allow to take into account the different factors (e.g. barriers and facilitators) that may influence antibiotic prescribing and develop future intervention based on the context-specific insights;
- The COM-B model will provide a structured approach to analyzing the factors that influence the behavior of healthcare workers. It will help identify specific constraints and opportunities that affect antibiotic prescribing.

Using BCI approach and COM-B model will provide a deeper and comprehensive understanding of healthcare workers' capabilities, opportunities, motivations and behaviours in the context of antibiotic prescribing, which will form the basis for developing effective recommendations and programmatic solutions to improve medical practice. The chosen methodology for the qualitative study aligns with BCI approach and uses COM-B model to gain a deeper understanding of the factors that influence antibiotic prescribing by healthcare workers in inpatient settings.

Study target group

As part of the qualitative component of the study, it is planned to involve physicians working within various specializations and levels in the following six departments: anesthesiology, therapy, surgery, pulmonology, gynecology (Table 1).

Table 1

Inclusion and exclusion criteria for the study

Component	Target group	Inclusion criteria	Exclusion criteria
Qualitative study component	Physicians of secondary HCFs	• Prescribing antibiotics; • Working within various specializations in anesthesiology,	• Currently not prescribing antibiotics; • Refusal to provide verbal informed consent to

[14] Turner, R., Hart, J., Ashiru-Oredope, D. et al. A qualitative interview study applying the COM-B model to explore how hospital-based trainers implement antimicrobial stewardship education and training in UK hospital-based care. BMC Health Serv Res 23, 770 (2023). https://doi.org/10.1186/s12913-023-09559-5

[15] Fleming A, Bradley C, Cullinan S, Byrne S. Antibiotic prescribing in long-term care facilities: a qualitative, multidisciplinary investigation. BMJ Open. 2014 Nov 5;4(11):e006442. doi: 10.1136/bmjopen-2014-006442. PMID: 25377014; PMCID: PMC4225237

		infectious diseases, surgery, pulmonology, gynecology; • Physicians of different levels (junior and senior staff); • Providing verbal informed consent to participate in the in-depth interview of the study.	participate in an in-depth interview.

STUDY GEOGRAPHY

The qualitative survey of the target groups will be conducted in accordance with the selected regions. The sample will be formed using an approach where each region is considered as a separate cluster and represents different macro-regions of the country.

The geography of the study will cover pre-selected 6 regions of Ukraine and the city of Kyiv, namely:

1. Dnipropetrovs'k region;
2. Kirovograd region;
3. Lviv region;
4. Odesa region;
5. Chernihiv region;
6. Kyiv region;
7. City of Kyiv.

PREPARATORY STUDY STAGE

Prior to data collection, the main activities necessary to ensure the successful and efficient conduct of the study of the proper quality will be implemented:

1. Formation of a working study team to address organizational issues of the study;
2. Conducting a literature review in accordance with the specifics of the topic to develop the scientific context of the study;
3. Preparation and approval of the study package, namely the study Protocol, study tools and supporting documents;
4. Preparation and sending of support emails from the PHC to the heads of secondary HCFs to provide information about the study, it's main goal and objectives, and the timeline for implementation;
5. Prepare a full package of documents for submitting an application for ethical review to the Ethics Commission of the PHC of the MOH of Ukraine and WHO EURO Ethics Commission;
6. Obtaining a positive conclusion from the Ethics Commission of the PHC of the MOH of Ukraine and WHO EURO Ethics Commission;
7. Organizing and conducting online training for responsible persons involved in data collection to prepare for the field stage of the study.

Study tools

At the preparatory stage, the study will be developed and approved:

- Guide for in-depth interviews with healthcare workers (Annex 1);
- Reporting form for the implementation of the sample task of in-depth interviews with healthcare workers (Annex 2);
- Informed consent form for the participants (Annex 3);
- Confidentiality consent form for the researchers (Annex 4).

The guide for in-depth interviews with healthcare workers will be based on the standard of medical care "Rational use of antibacterial and antifungal drugs for therapeutic and prophylactic purposes" No. 1513 of 23.08.2023, approved by the MOH of Ukraine. In addition, the in-depth interview guide will be covered include questions covering all components of the COM-B model.

Preparation of interviewers

As part of the qualitative component of the study, interviewers will be responsible for conducting in-depth interview will have prior training and experience in conducting qualitative interviews, all the necessary skills in conducting this type of study, which will allow for free and unmonitored conversation. Interviewers will require proficiency in a number of skills, such as active listening, empathy, ability to ask open-ended questions, neutrality, analytical skills, communication skills, etc. Interviewers should also be able to provide a comfortable atmosphere for participants. Interviewers should understand the research objectives to cover all the topics and have the skills to ask clarifying questions to obtain more complete data. The study team will monitor the quality of work of the responsible persons.

Prior to the in-depth interviews, the interviewers will get acquainted with:

- Purpose and objectives of the study;
- Study design;
- Sample and geography of the study;
- Study tools;
- Ethical principles of the study;
- Organizational conditions of the study.

FIELD STUDY STAGE

To implement the data collection, healthcare workers from HCFs that provide specialized care to patients from six regions of Ukraine (Kyiv, Dnipro, Kirovohrad, Lviv, Odesa, Chernihiv regions) and the city of Kyiv will be invited to participate in the study, according to the geography of the study.

Sampling strategy

As part of the qualitative component of the study, in-depth interviews will be conducted with healthcare professionals who practice antibiotic prescribing.

The procedure for recruitment and the collecting data for the qualitative component of the study will be implemented in accordance with the following algorithm:

1. Selection and approval of secondary care HCFs, according to the geographical distribution of the study;
2. Identifying potential participants for the in-depth interview through outreach to healthcare workers to inform them about the study's purpose, explaining the procedures for

participation, and seeking their consent to take part in the qualitative component of the research.

3. Obtaining consent from potential participants to share their contact information with the responsible interviewers who will conduct the in-depth interviews;
4. Transferring contact information of potential participants to the responsible interviewers preserving confidentiality (only contact number, e-mail and name of the participant through protected channels);
5. Establishing contacts with potential participants by the responsible interviewers and agreement with them on the date and time of the in-depth interview;
6. Conducting in-depth interviews with healthcare workers using audio-recording, which will be done with the prior consent of the respondent;
7. Conducting a quick analysis of audio recordings of in-depth interviews with medical professionals.

Due to the ongoing military operations in Ukraine, the selection of the study sites will take into account the level of security of the territory and the availability of relevant departments. Accordingly, the regions of Ukraine where military operations are underway will not be involved. The study will involve regional clinical HCFs that have the appropriate departments and physicians of the required specializations. Letters of support from the PHC on assistance in the study will be sent to the administration of the selected HCF.

The management of the HCF will be expected to assist in the study through promotion of the study and dissemination of invitation to participate. The heads of the selected HCFs will provide a list of physicians of the required specialties according to the distribution. After this PHC will randomly select the required number of potential participants for in-depth interviews. Just before the in-depth interview, the voluntary participation of the healthcare worker will be re-checked. If a potential participant refuses, the study team will recruit another respondent with the appropriate criteria.

In addition to the main interviewer, an AMR expert will be involved in conducting in-depth interviews. An AMR expert will be competent in antibiotic prescribing in a hospital setting. Accordingly, an experienced interviewer will ensure that the interview is based on the prepared guide, but it is important that an additional person-expert is present to ask follow-up technical questions based on the participant's answers, if necessary. Both of data collection will maintain the confidentiality of the data obtained and, in turn, will help to analyze the information in more depth. Interviews with healthcare workers will be conducted in accordance with the key principles for conducting in-depth interviews, in accordance with the developed and approved guide, ensuring appropriate conditions and adherence to the ethics of conducting sociological research. Due to the danger associated with military operations in Ukraine, in-depth interviews will be conducted online using the Zoom platform to minimize time costs. Based on previous experience conducting similar research such approach will not affect the quality of the information received. In this regard, prior to the initial data collection, each participant of the in-depth interview will be instructed on the optimal conditions for participation in the interview, namely:

1. Check the stability and speed of the Internet connection;
2. Check the sound to avoid technical problems;
3. Provide a quiet and private place to express thoughts in peace;

4. Schedule a convenient time to participate in the in-depth interview so that do not feel rushed and can provide complete answers.

Healthcare workers will be informed that participation in the study is confidential and anonymous. The information provided by the participant will be used without identification and in a generalized form. All research data will be stored in compliance with the principles of confidentiality at a secured cloud locations to which only study team will have access. The study team and responsible interviewers will not record names or other identifying information on the research instruments. Audio recordings of the in-depth interviews will be conducted, followed by a rapid data analysis procedure. The materials of rapid data analysis will be analyzed by the study team in accordance with the research objectives.

During the implementation of the field stage of the qualitative component of the study, in order to keep records and progress on the implementation of the sampling task, the responsible interviewers fill out a reporting form on the implementation of the sample with healthcare workers and upload audio-recordings of interviews to the cloud storage. Each audio-recording will be coded according to the participant's number and oblast. The responsible interviewer will transmit the rapid analysis materials, which will be stored on a cloud storage with limited access.

The qualitative component of the study will involve in-depth interviews with healthcare workers in accordance with the distribution shown in Table 2. The sample is a variation sample in which participants will be selected in such a way that within each region, 3 health care workers in the regional center and 3 health care workers in district hospitals of the region from the following departments will be interviewed: anesthesiology, therapy, surgery, pulmonology, and gynecology. At the same time, junior and senior staff (1 or 2 juniors and 2 or 1 senior, respectively) will be provided in each region.

Table 2.

Distribution of healthcare workers by regions within the qualitative component of the study

№	Region	Number of respondents
1	Dnipropetrovs'k region	6
2	Kirovograd region	6
3	Lviv region	6
4	Odesa region	6
5	Chernihiv region	6
6	Kyiv region	3
7	City of Kyiv	3
	Total	**36**

ETHICAL PRINCIPLES OF STUDY

This section summarizes the ethical principles of the study. In order to implement the study within the ethical principles of the organization, after the final version of the study tools and Protocol is approved

by the PHC, the PHC will receive a positive conclusion of the Ethics Committee of the PHC and WHO Committee on the Protocol and supporting materials of the study. The collection, storage, and analysis of study data are based on compliance with ethical standards and protection of the rights of study participants to voluntariness, anonymity, and confidentiality.

Those who will be involved in data collection sign an agreement to comply with the rules of recruiting and interviewing respondents, as well as non-disclosure of respondent information. Respondents over the age of 18 will be invited to participate in the study. The recordings and data documents will not contain the names, addresses or other contact details of the respondents.

Voluntary participation

Potential participants will be informed that their participation in the study is purely voluntary and that they have the right to refuse to participate in the study at any time. In case of refusal to participate in the interview, the recording with the respondent's answers will be destroyed and will not be used for further analysis.

Researchers have the right to refuse to participate in the study if:

1. The participant does not meet the study inclusion criteria;
2. The participant's behavior is aggressive or he/she violates the rules of the interview;
3. The participant skips most of the questions or, for other reasons, the answers are general and cannot be interpreted as expert.

Ensuring confidentiality

All study data will be stored in compliance with the necessary principles of confidentiality. Only members of the study team will have access to the study materials. The members of the study team and interviewers who will participate in the implementation of the study, will sign a data use and confidentiality agreement before the study begins.

The questionnaires will not contain any information that can be used to identify the participant of the qualitative component. The interview will be conducted online. The study team will receive audio recordings of interviews coded accordingly with numbers, which will be formed from the code of the serial number of the respondent and the study region (Table 4).

Table 4.

Distribution of interview codes within the qualitative component of the study

№	Region	Respondent coding
1	Dnipropetrovs'k region	1ДНІ – 3ДНІ; 19ДНІ – 21ДНІ
2	Kirovograd region	4КІР – 6КІР; 22КІР – 24КІР
3	Lviv region	7ЛЬВ – 9ЛЬВ; 25ЛЬВ – 27ЛЬВ
4	Odesa region	10ОДЕ – 12ОДЕ; 28ОДЕ – 30ОДЕ
5	Chernihiv region	13ЧЕР – 15ЧЕР; 31ЧЕР – 33ЧЕР
6	Kyiv region	34КИЇ – 36КИЇ
7	City of Kyiv	16КИЇ – 18КИЇ

The results of study will be presented in the analytical report in a summarized form, without specifying the names of the respondents and their places of work.

Informed consent

Before participating in the study, all respondents will provide verbal informed consent to participate in the study.

Interviewers will read the informed consent out loud to the participant. Prior to obtaining informed consent, the interviewer should ensure that the potential participant meets the inclusion criteria, as well as ascertain and confirm that the participant understands the terms of the study and discuss with the participant any questions that may arise after hearing the informed consent. Participants should be provided with all answers and clarifications to any questions they may have. If an eligible participant agrees to participate in the study, the interviewer will obtain verbal informed consent, which will be confirmed by the interviewer's signature.

Risks and benefits

Participation in the study involves minimal risks associated with possible loss of confidential information. All risks will be minimized through appropriate procedures for protecting confidential information described below.

The benefits of participating in this study outweigh the risks. To avoid the risk of violating the confidentiality of the respondents' personal information, only interviewers of the study team will have access to names and contacts. The data set will contain only respondents' code numbers.

All study participants will be provided with the contact information of the research manager so that they can contact if they have any questions regarding the study methodology. In addition, the respondents will be provided with the contact details of the Ethics Commission of the PHC for possible recourse if they believe that their rights as research participants have been violated.

Participation in the study will not provide direct benefits to participants. The results of the study will be of high social importance for identifying the reasons and obstacles that prevent secondary care health workers in Ukraine from adhering to the principles of rational use of antibacterial drugs. Therefore, the results of the study will be used to develop recommendations for improving antibiotic prescribing practices and decision-making. At all stages of the study and for all participants, all principles of confidentiality will be observed.

Reimbursement

Participation in the study will not involve monetary compensation for the time spent by the participants. The study team has created such conditions that there are no additional costs for the respondents. Given that the respondents will be healthcare professionals, the study team will ensure that they are able to participate in the study in a way that is appropriate for their employment and work schedule. During the recruitment of participants, it will be ensured that arrangements are made for a day and time that will be convenient for participants.

Saving information

Paper materials and documentation will be stored in the PHC office in specially designed locked cabinets. Data and materials in electronic form will be stored in designated folders on a secure cloud storage facility PHC. Only authorized specialists involved in the study will have access to the relevant rooms and cloud storage folders. The audio-recordings of the in-depth interviews with the materials of the rapid analysis will be handed over to the PHC study team. Three years after the end of the study, paper documentation and audio-recordings will be destroyed.

Minimizing the effects of unforeseen circumstances

In the event of unforeseen circumstances that may arise during the study, interviewers should contact the study manager to provide all details of the situation and receive further instructions. All unanticipated problems/adverse events will be documented and reported immediately to the PHC Ethics Committee. These unanticipated problems/adverse events will be discussed and a verbal or written plan to resolve the problem will be developed.

To protect personal data and prevent the risk of its loss, the following algorithm of actions is provided:

- Interviewers will receive additional training, including on procedures for protecting the confidentiality of participants;
- Members of the study team who will work with information about study participants will sign a data use and confidentiality agreement;
- To protect confidentiality, no paper or electronic forms will contain names or other identifying information and will be linked only by an identification code;
- The study data will be stored in compliance with all principles of confidentiality;
- The results of this study will be presented in an analytical report in a generalized form without specifying the names of respondents and their places of work;
- The research toolkit and Protocol will receive a positive conclusion from the Ethics Commission of the PHC, which will mean that this study will be conducted within the framework of ethical principles and in compliance with human rights.

Given that the study will be conducted under martial law, it is worth noting how the safety of the study team will be ensured during data collection. In case an air raid alarm sounds during the qualitative component of the study, study team members should move to a shelter and stay in a safe place until the air raid alarm is cancelled.

STAGES OF STUDY IMPLEMENTATION

Stage 1. Preparatory study stage
✓ Preparation of a study Protocol
✓ Preparing a guide for conducting in-depth interviews with medical professionals as part of the qualitative study component
✓ Obtaining an approval from the Ethics Committee of the PHC and WHO Ethics Committee
✓ Brief training for interviewers involved in data collection
Stage 2. Field study stage
✓ Organizing (including recruiting) and conducting in-depth interviews with 36 medical professionals
✓ Preparation of 18 documents of rapid analysis of 18 in-depth interviews
✓ Preparation of 36 documents of full transcripts of in-depth interviews
✓ Preparation of a technical report based on the results of the qualitative stage
Stage 3. Data analysis, write-up and presentation of results
✓ Primary data analysis of the qualitative component
✓ Preparing a description of the main results of the qualitative stage
✓ Preparation of a presentation of the study results
✓ Presentation of the study results
✓ Translation of the report and information materials into English

✓ Submission of a manuscript to a scientific journal

CONTROL OF INFORMATION COLLECTION AND PROCESSING

In order to ensure the quality of the study, the quality control of the field stage will be carried out. The functions of such control are as follows:

- Preventive - all persons directly involved in data collection are aware in advance that their work is being monitored;
- Identification - detection of possible errors and the possibility of their early correction.

Quality stage control

The in-depth interviews will be recorded using audio-recording equipment, and then a quick analysis of the data will be conducted. In order to monitor the quality of the in-depth interviews and provide prompt feedback to the interviewers, the first interviews will be scheduled to be listened to in order to identify any problems during the qualitative data collection.

In order to quickly identify key findings from the in-depth interviews, the data will be analyzed using a rapid analysis process[16]. This approach will allow for quick identification of key barriers and behaviors of target groups, and will allow for the development of tailored interventions. In this process, the Rapid Interview Data Assessment Procedure sheets will be used to organize the in-depth interviews for analysis instead of the more traditional and time-consuming method of converting the notes into verbatim text format for analysis. To expedite the process, a member of the study team can be present during the interview and begin filling out the sheet as the discussion progresses. Alternatively, the audio recording may need to be listened to later to check and clarify notes.

The interviewers will report to the PHC study team on the progress of the fieldwork, successes or challenges of the fieldwork.

The process of monitoring the collected data to ensure the safety of participants will be implemented through the possibility for respondents to contact the PHC study team or the Ethics Commission of PHC in case of possible questions about the study methodology and/or fear of violation of the rights and opportunities of respondents during participation in the study.

Based on the results of the field stage, a technical report will be prepared, which will record the following information:

- Passport of the study;
- Description of the preparatory stage;
- Description of the field stage (target groups, inclusion and exclusion criteria, number of respondents, number of refusals and main reasons);
- Main difficulties during the study;
- Comments on the field stage of the study;
- Quality control of the results;
- The stage of processing the results.

[16] Vindrola-Padros C, Chisnall G, Cooper S, et al. Carrying Out Rapid Qualitative Research During a Pandemic: Emerging Lessons From COVID-19. Qualitative Health Research. 2020;30(14):2192-2204. doi:10.1177/1049732320951526 (https://journals.sagepub.com/doi/full/10.1177/1049732320951526, accessed 11 January 2022)

DATA ANALYSIS

During literature review the included reports and studies will be reviewed by one investigator who will extract relevant information using a data extraction form that included basic bibliographic data, country setting, objectives of the study, main factors influencing prescribing behavior, as well as recommended interventions, if any.

The interviews will be analyzed using a thematic approach using the predefined themes of the COM-B model. According to Europe WHO recommendations[17], instead of a full transcription of each in-depth interview, a rapid assessment procedure (RAP) will be used, followed by the use of a response matrix. This matrix will be organized in the form of COM-B subcategories. This will allow for the insertion of interview data directly under the appropriate COM-B theme in parallel with the interview.

DISSEMINATION AND COMMUNICATION

Based on the results of the data analysis, an analytical report will be prepared with a brief description of the study, results and recommendations. The analytical report will be an independent document designed to be comprehended without the use of the study Protocol or the technical report on the field stage.

The introductory part of the report will contain a cover page, list of authors, table of contents, abbreviations and symbols. The main part of the report will contain an introduction with a brief description of the problem, a brief description of the methodology and study design, study results, conclusions, recommendations and a list of references. The total volume of the report will be at least 50 pages.

The design of the analytical report will be in line with the PHC brand book, will include its logo and will be coordinated with the PHC communications department.

Based on the analytical report, after its approval, a study summary will be prepared, which will include: a brief description of the methodology and design, results and conclusions and recommendations. The executive summary is intended to communicate the results of the study and disseminate them to stakeholders and decision makers. It will be shared withing the MOH of Ukraine, regional PHCs and key healthcare partners. The length of the study summary will not exceed 10 pages. The design of the study summary will be in line with the PHC brand book, contain its logo and will be agreed with the PHC Communications Department.

Finally, a manuscript for a peer-reviewed journal will be drafted and submitted for publication.

SCIENTIFIC REVIEW

The protocol and data collection instruments were originally prepared by a Mariia Moshura, Scientific Research Specialist of the Scientific Research Department, State Institution "Public Health Center of the Ministry of Health of Ukraine", who has extensive expertise in qualitative and subsequently reviewed by study team members from partner institutions - Norwegian Institute of Public Health and the WHO Regional Office for Europe Regional BCI Unit and revised accordingly.

[17] WHO Europe - Rapid qualitative research to increase COVID-19 vaccination uptake, 2022

LIMITATIONS OF THE STUDY

Insight research with qualitative methods aims to understand the target audience's perspective. Qualitative research provides valuable insights into the audience's knowledge, fears, worries, hopes, and desires. Furthermore, qualitative data can help explain the reasons behind people's behaviour and thought processes and identify potential motivations for change. These insights are crucial in informing policy decisions, interventions, and communication strategies.

However, qualitative data is not statistically representative, and therefore results cannot be generalized to the entire population of health workers or key stakeholders. It is not useful for measuring a baseline or evaluating the effectiveness of a policy or activity. It cannot provide any information about what percentage of health workers, for example, adhere to the national guidelines on antibiotic prescription. In analyzing the data, referring to statistical significance or generalizability will not be possible. Rather, a discussion of the strength of the evidence will be included.

Given the situation's urgency and the narrow timeframe to complete this research, sample results might not reach saturation at the oblast or specialization level. However, altogether, the sample will most likely reach saturation.

This research is aimed at health workers and is not designed to apply to specific vulnerable, disadvantaged, or marginalized populations. The study cannot be claimed to represent those views, and the social benefit of the study may consequently be reduced. The findings of the study need to be interpreted in this context. It may be considered to conduct supplementary, more tailored, and targeted studies with specific population groups.

Conducting interviews online incurs some limitations as opposed to other more direct recruitment measures and face-to-face interviews. However, in the wake of the COVID-19 pandemic, many studies have been conducted, according to which the research team estimates that people across Ukraine have become more familiar and comfortable with communicating with others through online channels.

Despite limitations, the benefits of gaining insights into health workers' views on antibiotic prescription within a hospital setting will greatly increase the likelihood of successful interventions for increasing adherence to guidelines.

SUPPORT FOR THE PROJECT

The project is designed and implemented by the State Institution "Public Health Center of the Ministry of Health of Ukraine". Norwegian Institute of Public Health provides funding for data collection and analysis. WHO EURO provides technical support in applying BCI approach to study design.