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Review article

Resistome in a changing environment: Hotspots and vectors of spreading with a focus on the Russian-Ukrainian War

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A B S T R A C T

This work aims to shed light on the key factors contributing to the development of environmental resistance and the urgent need to address the growing problem of antibiotic resistance (AR) under the Russian-Ukrainian conflict. The article provides an overview of the main mechanisms involved in AR development and dissemination globally and the challenges posed by the ongoing war in Ukraine. The work outlines various international initiatives to reduce AR, including the concept of "One Health" and the strategies established, which are the key to reducing the effects on public health. Addressing AR globally and in conflict areas requires a comprehensive approach. This involves implementing monitoring of the microorganism's resistance levels to antibiotics, controlling the use of antimicrobial drugs, increasing public awareness of the AR, introducing educational programs to prevent the improper use of antibiotics, and adopting environmentally safe methods for the disposal of waste from medical, food, and other industries that produce or use antibiotics. Such initiatives are essential for promoting the responsible use of antibiotics, preventing the spread of AR infections, and preserving the effectiveness of existing antimicrobial drugs.

1. Background

Human activities have been identified as a major contributor to the environmental resistome, encompassing the soil, water, and air resistome. The environmental resistome consists of antibiotic-resistant microorganisms that rapidly proliferate and facilitate horizontal or vertical transfer of resistance genes. This poses an important threat to human and animal health and the environment [1,2]. These environmental changes due to resistance are attributed to human actions (e.g., healthcare, agriculture) that led to the emergence and spread of antibiotic-resistant microorganisms (ARM). Antibiotic resistance (AR) is a growing global challenge for humanity [3,4]. AR is defined as the ability of microorganisms to resist the action of an antibiotic to which they were previously sensitive. This enables the microorganisms to survive and multiply. Microorganisms can develop AR through various mechanisms such as mutation, horizontal gene transfer, or efflux pumps. This poses a serious threat to public health, as it can lead to treatment failure and increase the spread of infections. This increases morbidity and mortality rates [5–7]. AR organisms' formation is determined genetically due to the acquisition of new genetic information or a change in the expression level of their genes. Therefore, AR is inevitable because microorganisms develop genetic mutations to mitigate the effects of antibiotics [6,8].

However, the AR speed is breakneck for bacteria. Medicinal products, effective a few years ago, now have limited success. This threatens to prevent bacterial infection treatment and increases healthcare costs [9,10]. The World Health Organization (WHO) [11]

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recognises AR as one of the 10 major threats to the population's health, causing approximately 700 000 deaths annually. One of 4 key priorities is monitoring antimicrobial resistance (AMR) burden and responses. In 2019, 1.27 million people died due to AMR, higher than the mortality associated with human immunodeficiency virus (864 000) and malaria (643 000) [12]. In Europe, 800000 persons are affected each year by AMR, and 100 persons die each day.[1] However, AMR consequences are beyond the public health problem. They also have global socioeconomic and environmental implications. AMR increase healthcare costs and negatively affects agriculture productivity, biodiversity and the economy. Therefore, addressing AR requires a One Health approach involving coordinated efforts from various sectors, including public health, veterinary, and the environment Fig. 1 [13,14]. For instance, the ongoing war in Ukraine may have increased AR complexity [15]. There are already numerous health issues regarding the spread of diseases as highlighted by the WHO.[2] The conflict has disrupted the normal functioning of society and poses a potential risk for the increased spread of AMR. The scale of the problem and its long-term consequences are yet to be fully understood. AMR spread in Ukraine is a national concern and may have implications on a global scale. It has been highlighted in recent studies that AMR [16,17] and AR [18] are a matter of concern in the Russian-Ukrainian war. There has been an increase in antibiotic-resistant pathogens since the start of the war [19]. This was also observed in previous conflicts in Iraq [20], Syria [21], Congo [22] and in the ongoing war conflict Israel-Gaza [23]. Therefore, it is key to address this issue since it can substantially affect human and animal health, the environment, and the global economy. It is a problem with no borders that must be addressed, especially in a war context. In the conditions of war, most of the resources and priorities are shifted to military needs, and the issues of human health and environmental protection become of secondary importance. Migration (e.g. loss of human capital), environmental, sanitary and hygienic conditions deterioration, and the lack of food resources and medicine [24] directly and indirectly contribute to AMR formation and spread worldwide. Several publications highlighted that the widespread use of antibiotics increases AR formation in microorganisms, posing problems to human health [25–33]. Nevertheless, limited research was conducted on the potential impacts of the Russian-Ukrainian war on AR problem. The aim of this work is to present: 1) the formation of the environmental resistome and its development within the framework of the "One Health" concept; 2) the transmission and spread of antimicrobial resistance within food chains, and 3) an assessment of the potential consequences of the Russian-Ukrainian war on the spread of AR in the environment.

2. Antibiotic resistance as a complex problem - "ONE HEALTH" concept

During the last decade, AR has been considered a complex problem affecting human and animal health and the environment [32,34]. AR is present in humans, animals, food, plants, and the environment (water, soil, and air) and can be transmitted between persons and animals. Over 60 % of human infectious diseases are zoonotic, which is transmitted between vertebrate animals and humans. Some of these diseases can trigger significant public health crises, such as the COVID-19 pandemic. Zoonotic pathogens encompass many microorganisms, including bacteria, viruses, protozoa, fungi, helminths, and arthropods. Their transmission dynamics are often influenced by intricate interactions with their hosts and environmental conditions [35]. Zoonotic diseases are of significant concern due to their potential impact on public health, as well as their economic and ecological implications. Both Gram-negative and Gram-positive bacteria have the potential to induce zoonoses. Bacteria are the predominant etiological agents of zoonotic diseases. Studies estimate that among zoonotic pathogens originating from bovine sources, approximately 42 % are bacterial, 22 % viral, 29 % parasitic, 5 % fungal, and 2 % prion-derived [36]. Understanding the dynamics of zoonotic diseases is crucial for effective disease surveillance, prevention, and control strategies. This was stated in the One Health Concept, which focuses on the consequences, responses and actions in the animal-human-ecosystem system [13]. This involves taking a coordinated, collaborative, interdisciplinary and cross-sectoral approach to address potential or existing risks that arise from the nexus between animals, humans and ecosystems [6]. The "One Health" concept highlights that people's, animals' and ecosystems' health are interconnected (Fig. 1). In 2014, the WHO noted that the AR crisis was becoming dire [37], and most health organisations assumed that the rapid emergence of AR was a problem with catastrophic consequences [38]. This threatens the United Nations' Sustainable Development Goals achievement, mainly Goal 3, "Good health and well-being." In the European Union (EU), about 33 000 AR-related deaths have been confirmed annually. This is the equivalent of almost 1.5 billion euros per year in healthcare costs. More than 2.8 million antibiotic resistance cases in the USA are recorded annually, including more than 35 000 deaths [39]. In China, AR has an estimated cost of $77 billion, equivalent to 0.37 % of the country's GDP in 2017. This increased patient health and the healthcare system problems [40].

By 2050, it is estimated that one person will die of AR every 3 s 10 million lives per year will be at risk, and 100 trillion dollars will be lost [8,41,42]. AR problem and the shortage of innovative antibiotics exacerbated AR's rapid spread through the food supply, urban population growth and international travel [43–45]. The main reasons for AR emergence are 1) the incorrect and excessive use of antibiotics; 2) loss of sensitivity of patients and self-medication; 3) lack of people and animals access to clean water, sanitation and hygiene products; 4) unsatisfactory infection prevention and infection control in medical institutions and agricultural enterprises; 5) limited access to high-quality and affordable medicines, vaccines and diagnostic tools [46,47]; 6) low level of population awareness and 7) knowledge and lack of control over compliance with legislation [48,49]. Previous works indicate an increase in AR cases due to excessive and uncontrolled use of antibiotics in medicine and animal husbandry (Fig. 1), including poultry, swine, cattle, and fish farming, where antibiotics are often used for growth promotion, disease prevention, and treatment, and other branches of agriculture, such as horticulture or hydroponics. There is a strong association between microbial infection and antimicrobial overuse [50–52].

[1] https://www.consilium.europa.eu/de/infographics/antimicrobial-resistance/.

[2] https://reliefweb.int/report/ukraine/ukraine-war-impact-disruption-infectious-and-chronic-disease-programmes-expected-be-severe-and-durable.

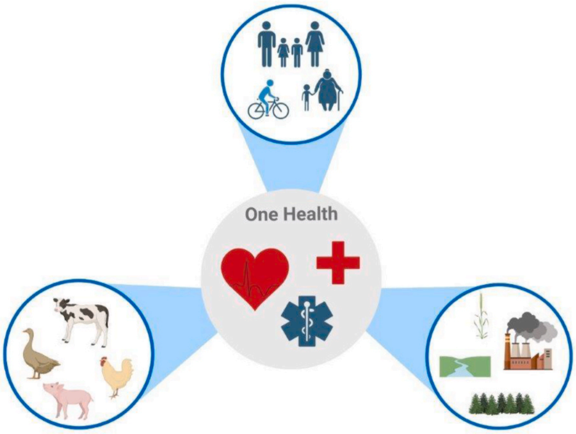

Fig. 1. The concept of "One Health" is the interconnection of human, animal and ecosystem health.

Another factor in the formation of AR is the increase in the availability of antimicrobial drugs in developing countries with imperfect control mechanisms [53]. Ukraine also recorded a 40 % increase in the total volume of antibiotics sales and purchases in 2020 compared to 2018. Pharmaceutical sales volumes of such drugs increased by 34 % [54].

A large number of wounded among the military and civilians requires the use of antibiotic therapy. The AR situation in Ukraine is deepening due to the lack of state control and the high consumption of antibiotics [55]. These drugs are classified as surveillance antibiotics (drugs used to treat bacterial infections as first- and second-line therapy) and reserve antibiotics (used to treat extremely severe bacterial infections when other antibiotics are ineffective) [54]. AR leads to infections that are difficult to treat with conventional antibiotics. They require stronger and more expensive drugs with potentially severe side effects. Pathogens resistant to all available antimicrobial drugs are called "panresistant," while those partially effective are called "polyresistant." Examples of pan-resistant strains include *Pseudomonas aeruginosa* and bacteria of the genus *Acinetobacter*. Polyresistant microorganisms include beta-lactamase and carbapenemase-producing strains of enterobacteria and methicillin- and vancomycin-resistant *Staphylococcus aureus* [56]. The "One Health" concept brings together molecular and epidemiological knowledge that contribute to understanding the AR evolution or genetic communication in pathogens/vectors and hosts (human/animal). Socioeconomic factors, such as world trade, conflicts, displacement, travel, and human and animal migration, are important factors in AR global spread [57,58]. Currently, the main attention is paid to antimicrobial substances in food product residues, which can accumulate AR due to the uncontrolled use of antibiotics in agriculture. Food products can be contaminated with AR from livestock and plant production to consumption [59,60]. To reduce the global risks associated with AMR spread, national and international organisations have begun to develop policies to control the use of antibiotics and finance research to identify the causes of resistance. This will prevent environmental problems related to contamination with antimicrobial drugs and their residues [59]. However, according to the Unated Nations only 29 out of 106 countries have national surveillance systems. Each country must involve stakeholders from different sectors, such as government, industry, academics, practitioners and international organisations, to establish strategies to reduce antibiotic consumption [41]. In Ukraine, the National Action Plan for Combating Antimicrobial Resistance [61] was developed and approved by the Decree of the Cabinet of Ministers of Ukraine dated March 6, 2019 (No. 116). It aims to ensure the rational use of antimicrobial drugs in the field of health care, veterinary medicine and food industry according to the best European and global practices, implementing an effective system of epidemiological surveillance of antibiotic resistance with its integration into the pan-European network; minimising the risks of the formation and spread of intra-hospital strains of microorganisms resistant to antimicrobial drugs, align the practices with EU requirements for infectious diseases laboratory diagnosis; determining the sensitivity of microorganisms to antimicrobial drugs, and conducting scientific research on AR problems; and implementing the latest diagnostic methods in coordination with leading European and other centres. The key aspects of the "One Health" Concept are now included in the Global and national action plans for combating AR. However, it is recognised that more attention should be paid to the AR ecological aspects, namely to understand the environmental importance of ARM spread among humans, plants and animals. Environmental monitoring can provide important information and identify evolution and resistance spread hotspots essential to improve epidemiological and human health risk assessment models [62]. Antimicrobial drugs that treat people, livestock, and crop production contaminate water resources and soils [63,64]. Therefore, microorganisms resistant to antibiotics are widely spread in the environment [14,65]. Recently, the Global Leadership Group on Antimicrobial Resistance called on all UN members to reduce the number of antimicrobials entering the environment through waste. Developing and implementing measures to properly manage the food industry, medicine, veterinary, and industry [66] is necessary. Coordinated efforts and interdisciplinary collaboration are needed to mitigate AR at the global level. Political commitment, policy formulation and implementation and education are vital to regulating antibiotic use, controlling the unethical promotion of antibiotics, implementing strategies to eliminate their over or inappropriate use, and raising awareness [67]. The spread and emergence of epizootics, zoonoses and epidemics increased the risks of pandemics in humans and animals. This situation was exacerbated by human activities such as pollution. Recent studies highlighted that pollution and other factors related to industrialisation during the last 150 years were the main drivers of AR spread [68,69].

3. Food chains - vectors of the spreading of antibiotic resistance

Food and Agriculture Organization(FAO) highlighted that AR's emergence in the food chain is related to the widespread use of antibiotics in aquaculture, livestock, and crop production [70], antibiotics have been used for decades in these sectors [71]. Treating livestock with antimicrobials improves animals' health, weight gain and high-quality products [37]. About 60 % of human infections are transmitted by animals [72]. The overuse and improper administration of antibiotics in livestock farming have spurred bacterial resistance in the animals' surroundings. This resistance, whether acquired directly or indirectly, poses a significant threat to human health through consuming contaminated food or via direct or indirect contact. Resistant bacteria not only directly induce severe health complications but can transfer antibiotic-resistant traits to other pathogens. Such diseases, often challenging to combat, heighten both morbidity and mortality rates. Furthermore, antibiotic-resistant strains can infiltrate the environment through animal waste, thereby bolstering the environmental microbiome as a reservoir for resistance [73]. AR bacteria in animals can be pathogenic to humans and spread easily through food chains and, ultimately, to humans. This can lead to complex, incurable, long-lasting infections [74,75]. AR exposure routes are indirect through food consumption and contact with infected animals or biological components: blood, urine, and faeces [76]. This is due to a sequence of 1) the use of antibiotics in animal husbandry that kill or suppress sensitive bacteria, allowing AR bacteria to develop; 2) resistant bacteria are transmitted to humans through food; and 3) these bacteria are likely responsible for infections in humans and health complications [39]. The resistant bacteria transfer from farm animals to humans was first observed more than 40 years ago when high AR rates were found in the gut microbiome of animals. Previous works found that resistant bacteria in farm animals reach consumers through meat products [9]. Antibiotics are often used prophylactically in livestock, and it is predicted to increase globally by 67 % in 2030 [77]. Antimicrobial-resistant bacteria and/or antimicrobial resistance genes (carried over in pathogenic bacteria) can contaminate food at any stage, from the field to retail and consumption. Therefore, controlling antibiotics during food production (i.e., livestock and crop production) is vital to reducing the risk of AR in humans [78]. Food from aquaculture represents a significant concern as emerging hotspots for antimicrobial resistance due to frequent genetic exchange, rendering them vulnerable to resistance acquisition. This phenomenon compromises the effectiveness of antibacterial treatments in humans and facilitates the indirect transfer of resistance genes from aquatic bacteria to pathogens associated with humans [79,80]. Previous works demonstrated that ARM and AR genes found in humans were found in animals without contact with humans. This suggests that AR transmission was through food consumption or mishandling food [81] (Fig. 2). In livestock production, this could be through contact with contaminated meat products, occupational contact (e.g., farmers, butchers, packers) and potential secondary spread to the broader community from those occupationally exposed. The spread can also be through air, water or soil near livestock farms or farms where manure is used as fertiliser [82]. For instance, previous works showed that *Staphylococcus aureus* is spread over long distances in the air through dust particles [83]. Drinking contaminated water with animal or human faeces containing AR is considered a key source of AR spread (Fig. 2), antibiotic residues, extracellular mobile genetic elements associated with AR-resistant organisms, and a source of new antibiotic resistance genes [4,84,85]. Urban wastewater, animal husbandry complexes, and effluents from enterprises producing antimicrobial drugs are also hotspots for AR bacteria and genes that spread into the environment [86–88]. Soil contamination with antibiotics or their residues increases soil resistome formation (soil microorganism communities with high AR levels), this threatens human health and has uncertain ecological consequences [88,89]. Genetically modified plants can spread AR in crop production. In genetic modification, AR marker genes are often used to identify transformed cells. These marker genes can be transferred to commensal bacteria associated with plants, soil, and animals. This will contribute to AR spread in the environment [90].

This highlights the need for the responsible use of genetic modification technologies to mitigate the potential risks of AR spread. The destruction of the Kakhovka hydroelectric power station's dam by Russian invaders on June 6, 2023 released a devastating flood onto the biodiverse habitats and farmlands of the lower Dniepr basin, with tonnes of debris and pollutants spreading the destruction to the shore waters of the Black Sea at the river's mouth. River water from flooded areas is being carried into the sea with a large amount of fuel and thousands of dead animals and birds. In addition, there is waste from destroyed sewage systems and cesspools, residues of fertilisers and other chemicals. The epidemic situation in the Ukrainian-controlled territories is predictable but not manageable; 38 monitoring points have been established in the Odesa, Mykolaiv, and Kherson regions. Since June 19, 2023, swimming and fishing have been prohibited in these regions due to the deterioration of river and seawater indicators. In the sea near Odessa, positive results for DNA of salmonella have been detected.[3] During the last 12 months of the war, more than 200 agricultural enterprises were destroyed or damaged in Ukraine (and these are only those that are currently known). Farm animals were most affected in the Donetsk, Luhansk, Kyiv, Chernihiv, Mykolaiv, Zaporizhia, Kharkiv, Kherson and Sumy regions. More than 6000 cows, about 100 000 thousand pigs, more than 4.5 million farm birds died, and 4 million chickens died in the largest poultry factory in Europe in Chornobayivka, Kherson region.[4] Disposing of deceased animal bodies on farms ravaged by war presents a complex challenge. Such sites could be seen as "hot points" for the proliferation of antimicrobial resistance. The remains of these deceased animals have the potential to serve as vectors for both opportunistic and pathogenic bacteria, compounding the issue. Furthermore, they can contribute to environmental contamination by retaining antibiotic residues, thereby fostering an escalation in the dissemination of AR. This threatens human health and has uncertain ecological consequences.

[3] https://en.zona.media/article/2023/06/26/after_kakhovka.

[4] https://life.pravda.com.ua/columns/2023/02/24/253030/.

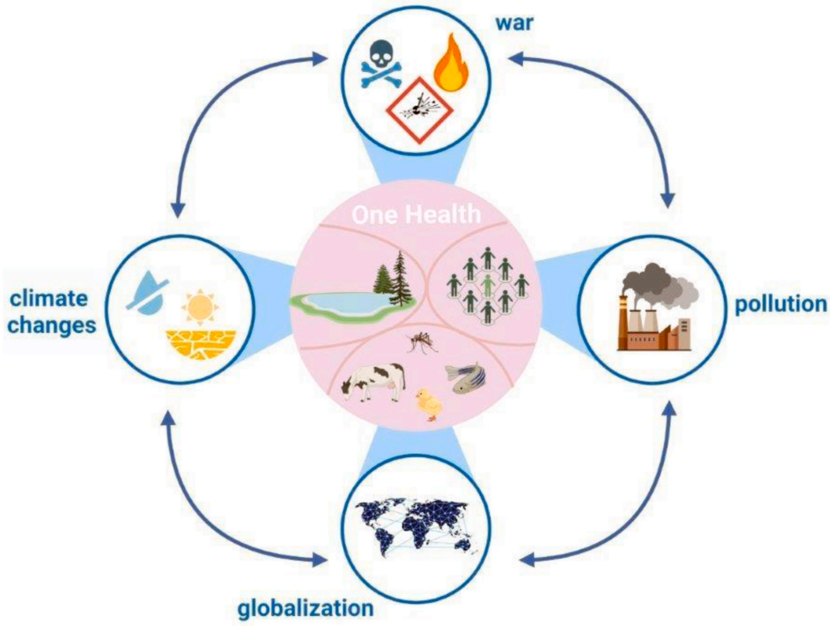

Fig. 2. Drivers of antimicrobial resistance (AMR) spread: climate change, globalization, environmental pollution, and wars in the context of the One Health approach.

4. Military conflict in Ukraine - hot spot and factor of spreading AR in the environment

Military conflicts and their consequences are among the causes of AMR spreading globally [91]. This question is relevant today because of the war launched by the Russian Federation against Ukraine in 2014 and the large-scale armed invasion on February 24, 2022. The war increased the humanitarian and refugee crisis, with geopolitical, economic and environmental implications [92]. AMR spreading in military conflicts is complex and covers several issues, such as normative and legislative regulation, state control over the use of antimicrobial drugs, the system of monitoring ARM, epidemiological surveillance and qualified personnel. Each country has different strategies for solving this problem [22,93]. Ukraine has to solve several important socioeconomic and environmental tasks, primarily ensuring life safety, health, food and energy security. These challenges impact the achievement of the Sustainable Development Goals [24] and affect AR directly and indirectly.[5] As a result of hostilities, military and civilian infrastructure, and residential areas and the number of injuries is increasing among military personnel and the civilian population.[6]

The Office of the High Commissioner for Human Rights has reported a devastating toll in the conflict: from February 24 to December 1, 2022, a total of 17 023 civilians, including 419 children, have lost their lives, with an additional 729 children sustaining injuries. The foremost priority remains providing timely and high-quality medical care, including crucial antimicrobial therapy [94]. Antibiotics have become increasingly indispensable for treating wounds, injuries, and acquired disabilities, necessitating ongoing therapy. However, the escalating resistance of microorganisms to antibacterial drugs poses significant challenges in managing combat-related injuries [95,96]. Since March 2022, the European Centres for Disease Control (ECDC) has been issuing advisories concerning the potential presence of multidrug-resistant bacteria, notably *A. baumannii and K. pneumoniae*, among others, in individuals with traumatic wounds in Ukraine.

In light of this, the ECDC has recommended the implementation of preventive measures such as isolation and screening for multidrug-resistant bacteria, particularly carbapenem-resistant, for patients who have been transferred from hospitals in Ukraine or have a history of hospital admission in Ukraine within the past 12 months. However, in the context of war, it is challenging to implement these preventive measures, mainly due to the scarcity of available healthcare professionals and resources. Instead, it will be possible to apply reactive measures once a peaceful situation is reached, as immediate actions become feasible in managing and addressing the potential spread of antimicrobial resistance in the environment.

There are also indirect impacts due to the disruption of social activities, infrastructure deterioration and the environment [97]. The war dealt a tragic blow to the healthcare system. In November 2022, WHO confirmed 630 attacks on healthcare facilities in Ukraine, 1157 healthcare facilities were damaged or destroyed [98]. To rebuild the healthcare system, Ukraine will need 14.6 to 20 billion euros [99]. The destruction of medical infrastructure, the impossibility of compliance with prevention and treatment norms, the lack of medical personnel in some regions, and the disruption of logistical connections prevent medical supplies from reaching the population.

[5] https://news.un.org/en/story/2022/12/1131607.
[6] https://news.un.org/en/story/2022/03/1114022.

The migration healthcare sector has worsened since the demand for medical services increased substantially. Health risks of Ukrainians increased due to less availability of drugs, reduced access to medical services, and chronic diseases and post-traumatic stress disorder among military and civilians. In the absence of qualified medical specialists, there is the uncontrolled use of antibiotics in the combat zone and self-medication without supervision, including for preventive purposes [100–102].

In Ukraine, there needs to be more awareness of AR potential threats, the effects of antibacterial drugs, and the principles of rational antibiotic therapy among professionals (e.g., doctors and pharmacists) and citizens. A survey conducted by the Public Health Center of the Ministry of Health of Ukraine [103] on the understanding of AR risks showed that 93 % of the citizens are not aware of the problem and 86 % consider antibiotic treatment to be effective and prefer such drugs. Also, more than 28 % of patients receive antibiotics for disease prevention. In 5 % of patients, the reason for prescribing antibiotics was unknown. Finally, about 30 % of Ukrainians treat colds with antibiotics [103] The survey also showed that military doctors have insufficient awareness of the problems related to antibiotic use. This means that they are unable to prevent AR formation and spread. In Ukraine, there is a need for the rational use of antibiotics, mainly because access to these drugs is mostly free. Only in April 2022 were restrictions on access to antibiotics adopted at the state level [104]. In May 2022, the Medical Care Standard "Rational Use of Antibacterial and Antifungal Drugs for Therapeutic and Prophylactic Purposes" was approved [54].

Since the beginning of the war, one of the most challenging issues has been the medicine logistics, especially in regions with intense combats. Due to logistics problems at checkpoints, medicine transport is delayed at the border. In addition, transporting certain medicines, raw materials for manufacture, and medical devices requires appropriate storage conditions [101]. Therefore, the Ukraine health care system has a shortage of pharmaceutical products, and people may auto-medicate themselves, contributing to AR formation. There is also a problem related to fake medicines. This problem is vital in any country [105] (Fig. 3).

Ukrainian experience highlights the urgent need for coordinated efforts to address antimicrobial resistance in conflict zones and fragile settings. It underscores the importance of integrating antimicrobial stewardship programs into humanitarian aid initiatives and promoting international collaboration to effectively combat this global health threat.

One way to spread AR is through migration and tourism [45,106] they are exposed to multiple strains of ARM. However, in the case of migrants, they are at high risk due to the inadequate conditions in refugee camps and detention centres that can increase psychological stress caused by the conditions of instability [107]. The war disrupted basic infrastructure (gas, heat, electricity and water supply), and more than 2.7 million Ukrainians are homeless. According to the United Nations High Commissioner for Refugees (UNHCR), 8.2 million refugees left Ukraine for neighbouring countries between February 24 and June 28, 2022 [92]. More than 6.9 million were internally displaced. This migration represents the largest movement of people in Europe since the Second World War, impacting various social, economic, and environmental facets [98]. Additionally, it heightens the risks of antimicrobial resistance spreading to other regions. Although AMR surveillance in the WHO European Region is one of the most advanced in the world,

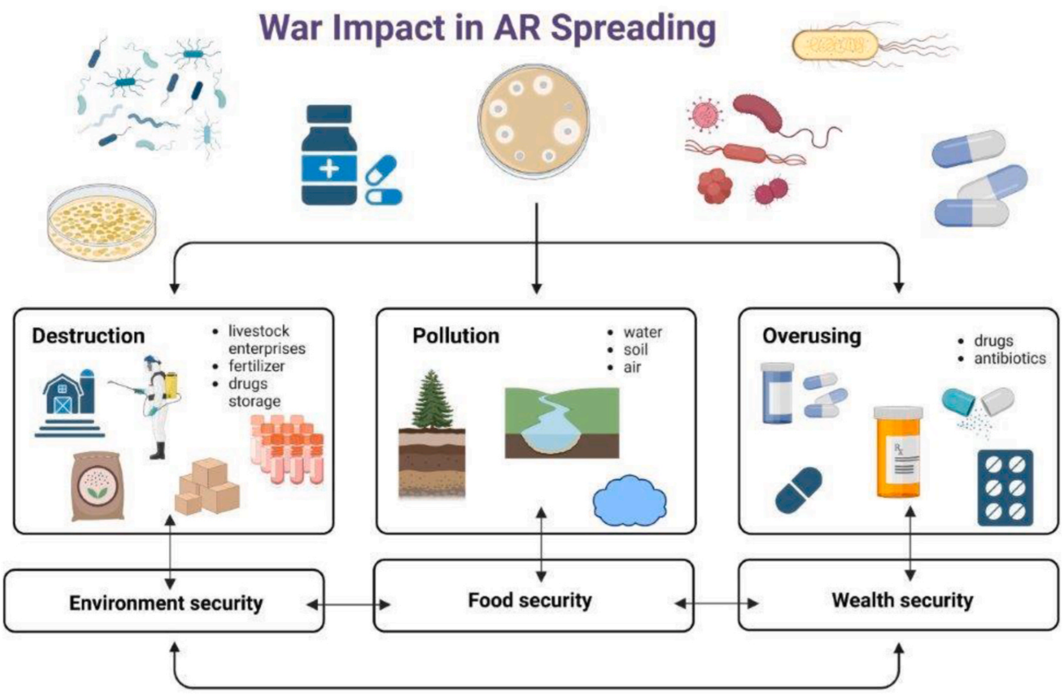

Fig. 3. The impact of war activity on the spreading of AR is multifaceted. Overuse of drugs and antibiotics in the context of war contributes to the proliferation of antibiotic-resistant bacteria. Additionally, war leads to soil, water, and air pollution, as well as the destruction of infrastructure, which further exacerbates the spread of AR. These factors collectively contribute to the decline of important interconnected socioeconomic and environmental aspects, such as health, food security, and environmental stability.

migrants are exposed to conditions that facilitate AR development [108]. As a result of buildings destruction, medical institutions and medical drugs warehouses, and industrial facilities (e.g., livestock enterprises), a large amount of waste containing hazardous substances was formed and released, affecting AR spread in the environment and resistome formation [14,109]. War creates substantial challenges in providing access to medical facilities, and often, healthcare services are inadequate or unavailable. Transportation networks and healthcare facilities may be destroyed or disrupted, making access to medical supplies, equipment, and personnel difficult (Fig. 3). The migration to war-safe zones can increase unsanitary conditions and the risk of disease transmission and infection [110]. Between March and June 2022, Schultze [111] conducted a screening study on multidrug-resistant Gram-negative bacteria among 103 Ukrainian patients admitted to the University Hospital Frankfurt, Germany. Their findings revealed the presence of 34 multidrug-resistant Gram-negative isolates in 17 out of 103 patients (17 %). Based on their results, the authors emphasised the importance of hospitals adopting infection control strategies to curtail the spread of carbapenem-resistant bacteria, particularly in cases where war-related injuries are admitted from Ukraine [111]. Statistics and health reports play a pivotal role in epidemiological studies, enabling researchers to identify correlations between risk factors and health outcomes within the general population. These insights are crucial for devising effective prevention strategies to mitigate health risks and enhance public health [112]. From March to August 2022, multiple drug-resistant bacteria in the Netherlands have emerged in persons originating from Ukraine. Most isolates were *K. pneumoniae*, *P. aeruginosa*, and *E. coli*. The high percentage of isolates containing ARG (antibiotic resistance genes) blaNDM-like in their genomes and the observation that the isolates are potentially resistant towards multiple classes of antibiotics implies that infections with these bacteria are difficult to treat [113]. Between June and December 2022, were analysed consecutive clinical cases involving infections caused by carbapenemase-producing Gram-negative bacteria in war-wounded patients from Ukraine. These patients received treatment at a university medical centre in southwest Germany. The isolated multiresistant Gram-negative bacteria underwent comprehensive microbiological characterisation and whole genome sequencing. The investigation identified five war-wounded Ukrainian patients who developed infections with *Klebsiella pneumoniae* carrying New Delhi metallo-β-lactamase 1 (NDM-1), and two of these isolates also carried OXA-48 carbapenemases. Notably, these bacteria resisted novel antibiotics such as ceftazidime and avibactam [18].

At the same time, prolonged injuries without treatment can lead to infections, which are complicated to manage in a war context. The lack of medical facilities exacerbates this problem since there are no places for people to receive medical care. Moreover, discontinuing medications can have dire consequences, especially for those with chronic illnesses who depend most on them. All these factors contribute to developing secondary infections and the emergence of drug-resistant bacteria, which can be challenging to treat [114]. Vaccinations against key pathogens with complex resistance profiles are one of the promising solutions for addressing antimicrobial resistance. While vaccines may not entirely eradicate target pathogens, reducing infection rates can lead to decreased antibiotic usage, thus helping to stem the emergence of AMR [115]. Additionally, vaccines play a crucial role in veterinary and agricultural settings, where antibiotic overuse is prevalent. To optimise the effectiveness of vaccines in curbing the emergence of AMR, it is crucial to ensure widespread vaccination coverage among populations at risk of infection, particularly in countries where antimicrobial-resistant pathogens are endemic. Regrettably, many key antimicrobial-resistant pathogens still lack available vaccines [115,116]. Therefore, it is crucial to supply medical care where the combats are intense and ensure that those in need can receive prompt and effective treatment. Vaccination, sanitation, and hygiene are also essential in preventing the spread of disease and infection. Addressing the healthcare needs of people affected by conflict is crucial to mitigating the humanitarian impact of war and promoting recovery and resilience.

5. Conclusions

The global recognition of the AR threat led to developing and implementing national strategies and action plans. These initiatives are based on the “One Health” concept, which emphasises the interconnectedness among humans, animals, and the environment. For this, the connection between sectors and disciplines is critical. However, AR is not limited by geographic boundaries and is a threat. The risks of resistance formation and spread are amplified during the war and may have catastrophic implications. Therefore, developing and implementing comprehensive strategies for combating AR that consider the risks associated with war is crucial. The situation in Ukraine highlights the urgent need to address the AR in the context of military conflict. The destruction of healthcare systems, environmental degradation, and the loss of qualified professionals can increase AR formation and spread in Ukraine, neighbouring countries, and globally. To mitigate these risks, it is crucial to implement effective measures such as AR monitoring, controlling the use of antimicrobial drugs, vaccination, implementing educational programs on the proper use of antibiotics, and adopting environmentally safe waste disposal methods from the medical and food industries. Additionally, international cooperation and support are needed to address the specific challenges related to AR in conflict-affected areas and to prevent the further escalation of the problem. It is essential to recognise that AR is a global issue that requires a comprehensive approach based on the “One Health” concept to ensure the health and well-being of people, animals, and the environment.

Key points

- Antibiotic resistance is a pressing issue affecting human, animal, and ecosystem health.
- War is a significant driver of antibiotic resistance and spread globally.
- The ongoing war in Ukraine could have devastating effects on the changing environment.

CRediT authorship contribution statement

L. Symochko: Writing – original draft, Validation, Data curation, Conceptualization. **P. Pereira:** Writing – review & editing, Supervision, Formal analysis. **O. Demyanyuk:** Writing – review & editing, Data curation. **M.N. Coelho Pinheiro:** Writing – review & editing, Visualization, Data curation. **D. Barcelo:** Writing – review & editing, Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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