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ANALYSIS OF ANTIBIOTIC PRESCRIBING PRACTICES IN PRIMARY HEALTH CARE SETTINGS. PART I

Nyssan Ye. Zarpullayev¹, <https://orcid.org/0009-0000-2276-6937>

Oxana A. Yurkovskaya², <https://orcid.org/0000-0002-6251-5574>

Dinara A. Mukanova², <https://orcid.org/0000-0001-5186-2346>

Dana K. Kozhakhmetova², <https://orcid.org/0000-0002-8367-1461>

Ainur S. Botabayeva², <https://orcid.org/0009-0008-9228-7788>

Yerbol M. Smail², <https://orcid.org/0000-0003-3881-3747>

Timur M. Shamshudinov³, <https://orcid.org/0000-0001-5015-871>

Assiya A. Kussainova¹, <https://orcid.org/0000-0002-5738-0804>

Gulmira A. Derbissalina¹, <https://orcid.org/0000-0003-3704-5061>

Nailya M. Urazalina², <https://orcid.org/0000-0003-0200-1763>

Laura T. Kassym^{1*} <https://orcid.org/0000-0003-4448-6455>

¹ NJSC "Astana Medical University", Astana, Republic of Kazakhstan;

² NJSC "Semey Medical University", Semey, Republic of Kazakhstan;

³ «Medical and diagnostic Center of otorhinolaryngology» PRO-LOR, Almaty, Republic of Kazakhstan.

Summary

Introduction: Antimicrobial resistance (AMR) poses a significant threat to global health, undermining the effectiveness of antibiotics in treating infectious diseases. The increasing prevalence of AMR is driven by various factors, including environmental, drug-related, patient-related, and physician-related causes. Misuse and overuse of antibiotics contribute to the development of resistant bacterial strains, leading to higher morbidity and mortality rates.

Objective: This review aims to analyze antibiotic prescribing practices in primary healthcare settings, identify key contributors to AMR, and propose strategies for improving antibiotic stewardship to mitigate resistance.

Search Strategy: A systematic literature review was conducted using peer-reviewed sources from medical and public health databases, including PubMed, Google Scholar, and EBSCO, WHO reports, epidemiological studies, and recent research on AMR trends and antibiotic prescription behaviors. The focus was on global trends with a specific emphasis on Central Asia, including Kazakhstan and neighboring countries.

Results: The review identified multiple factors contributing to AMR, including inappropriate prescriptions, weak regulatory frameworks, and socioeconomic conditions. Studies indicate that developing countries, particularly in Asia and Africa, experience higher rates of AMR due to poor healthcare policies and excessive antibiotic use in agriculture. In Kazakhstan, AMR was associated with approximately 2,400 deaths in 2019, ranking the country 95th in AMR-related mortality worldwide. The review also highlighted disparities in antibiotic stewardship practices across different regions, with European countries demonstrating lower resistance rates due to stricter regulations.

Conclusion: AMR remains a critical global health issue, exacerbated by inadequate prescription practices and weak enforcement of antibiotic regulations. Addressing this challenge requires coordinated international efforts, including improved antibiotic stewardship, enhanced surveillance systems, and stricter policies on antibiotic use. Raising awareness among healthcare professionals and the general population is essential to combat the growing threat of antibiotic resistance.

Keywords: antimicrobial resistance, epidemiology, risk factors, Kazakhstan.

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Резюме

**АНАЛИЗ ПРАКТИК НАЗНАЧЕНИЯ АНТИБИОТИКОВ
В ПЕРВИЧНОМ ЗВЕНЕ ЗДРАВООХРАНЕНИЯ. ЧАСТЬ I****Нысан Е. Зарпуллаев¹**, <https://orcid.org/0009-0000-2276-6937>**Оксана А. Юрковская²**, <https://orcid.org/0000-0002-6251-5574>**Динара А. Муканова²**, <https://orcid.org/0000-0001-5186-2346>**Дана К. Кожакметова²**, <https://orcid.org/0000-0002-8367-1461>**Айнур С. Ботабаева²**, <https://orcid.org/0009-0008-9228-7788>**Ербол М. Смаил²**, <https://orcid.org/0000-0003-3881-3747>**Тимур М. Шамшудинов³**, <https://orcid.org/0000-0001-5015-871>**Асия А. Кусаинова¹**, <https://orcid.org/0000-0002-5738-0804>**Гульмира А. Дербисалина¹**, <https://orcid.org/0000-0003-3704-5061>**Найля М. Уразалина²**, <https://orcid.org/0000-0003-0200-1763>**Лаура Т. Касым^{1*}**, <https://orcid.org/0000-0003-4448-6455>¹ НАО «Медицинский университет Астана», г. Астана, Казахстан;² НАО «Медицинский университет Семей», г. Семей, Казахстан;³ «Лечебно-диагностический центр оториноларингологии» PRO-ЛОР, г. Алматы, Республика Казахстан.

Введение: Антимикробная резистентность (АМР) представляет серьезную угрозу глобальному здравоохранению, снижая эффективность антибиотиков при лечении инфекционных заболеваний. Рост распространенности АМР обусловлен различными факторами, включая экологические, лекарственные, связанные с пациентами и медицинскими работниками. Неправильное и чрезмерное использование антибиотиков способствует развитию устойчивых бактериальных штаммов, что приводит к повышению заболеваемости и смертности.

Цель: Данное исследование направлено на анализ практик назначения антибиотиков в учреждениях первичной медико-санитарной помощи, выявление ключевых факторов, способствующих развитию АМР, а также разработку стратегий по улучшению антимикробного надзора для снижения резистентности.

Стратегия поиска: Был проведен систематический обзор литературы с использованием рецензируемых источников из медицинских и общественно-санитарных баз данных, включая PubMed, Google Scholar, EBSCO, отчеты ВОЗ, эпидемиологические исследования и последние научные работы по тенденциям АМР и практике назначения антибиотиков. Основное внимание уделялось глобальным тенденциям, с особым акцентом на Центральную Азию, включая Казахстан и соседние страны.

Результаты: Обзор выявил несколько факторов, способствующих развитию АМР, включая нерациональное назначение антибиотиков, слабые регуляторные механизмы и социально-экономические условия. Исследования показывают, что в развивающихся странах, особенно в Азии и Африке, наблюдаются более высокие показатели АМР из-за недостаточной политики здравоохранения и чрезмерного использования антибиотиков в сельском хозяйстве. В Казахстане в 2019 году АМР было связано примерно с 2 400 смертельными случаями, что поставило страну на 95-е место в мире по смертности, обусловленной АМР. Кроме того, обзор показал различия в практике назначения антибиотиков в разных странах: в Европе более строгие регуляторные меры способствуют снижению уровня резистентности.

Заключение: АМР остается серьезной глобальной проблемой здравоохранения, усугубляемой ненадлежащей практикой назначения антибиотиков и слабым контролем их использования. Решение этой проблемы требует скоординированных международных усилий, включая улучшение антимикробного надзора, усиление систем мониторинга и ужесточение политики регулирования антибиотиков. Повышение осведомленности медицинских работников и населения играет ключевую роль в борьбе с растущей угрозой антимикробной резистентности.

Ключевые слова: антимикробная резистентность, эпидемиология, факторы риска, Казахстан.

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Түйіндеме

**БАСТАПҚЫ ДЕНСАУЛЫҚ САҚТАУ БУЫНЫНДА АНТИБИОТИК
ТАҒАЙЫНДАУ ТӘЖІРИБЕСІН ТАЛДАУ. I БӨЛІМ****Нысан Е. Зарпуллаев**¹, <https://orcid.org/0009-0000-2276-6937>**Оксана А. Юрковская**², <https://orcid.org/0000-0002-6251-5574>**Динара А. Муканова**², <https://orcid.org/0000-0001-5186-2346>**Дана К. Кожамметова**², <https://orcid.org/0000-0002-8367-1461>**Айнур С. Ботабаева**², <https://orcid.org/0009-0008-9228-7788>**Ербол М. Смаил**², <https://orcid.org/0000-0003-3881-3747>**Тимур М. Шамшудинов**³, <https://orcid.org/0000-0001-5015-871>**Асия А. Кусаинова**¹, <https://orcid.org/0000-0002-5738-0804>**Гульмира А. Дербисалина**¹, <https://orcid.org/0000-0003-3704-5061>**Найля М. Уразалина**², <https://orcid.org/0000-0003-0200-1763>**Лаура Т. Касым**^{1*}, <https://orcid.org/0000-0003-4448-6455>¹ «Астана медицина университеті» КеАҚ, Астана қ., Қазақстан Республикасы;² «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;³ «Оториноларингологияның емдеу-диагностикалық орталығы» ПРО-ЛОР, Алматы қ., Қазақстан Республикасы.

Кіріспе: Антимикробтық резистенттік (АМР) жаһандық денсаулық сақтау үшін елеулі қауіп төндіреді, антибиотиктердің жұқпалы ауруларды емдеудегі тиімділігін төмендетеді. АМР таралуының артуы әртүрлі факторларға байланысты, соның ішінде экологиялық, дәрілік, науқасқа және медицина қызметкерлеріне байланысты себептер. Антибиотиктерді дұрыс қолданбау және шамадан тыс пайдалану төзімді бактериялық штамдардың дамуына ықпал етіп, сырқаттанушылық пен өлім-жітім көрсеткіштерінің жоғарылауына әкеледі.

Шолудың мақсаты: Бұл шолу алғашқы медициналық-санитарлық көмек көрсету ұйымдарында антибиотиктерді тағайындау тәжірибесін талдауға, АМР дамуына ықпал ететін негізгі факторларды анықтауға және төзімділікті төмендету үшін антимикробтық қадағалау жүйесін жақсарту стратегияларын ұсынуға бағытталған.

Іздеу стратегиясы: Рецензияланған дереккөздерді қамтитын жүйелі әдеби шолу жүргізілді. Дереккөздерге PubMed, Google Scholar, EBSCO сияқты медициналық және қоғамдық денсаулық сақтау дерекқорлары, Дүниежүзілік денсаулық сақтау ұйымының (ДДҰ) есептері, эпидемиологиялық зерттеулер және АМР тенденциялары мен антибиотиктерді тағайындау тәжірибесі туралы соңғы зерттеулер кірді. Шолу барысында жаһандық үрдістерге, әсіресе Қазақстан мен көршілес елдерді қоса алғанда, Орталық Азия аймағына ерекше назар аударылды.

Нәтижелер: Шолу барысында АМР-дың дамуына ықпал ететін бірнеше факторлар анықталды, оның ішінде антибиотиктерді орынсыз тағайындау, әлсіз реттеу тетіктері және әлеуметтік-экономикалық жағдайлар. Зерттеулер көрсеткендей, дамушы елдерде, әсіресе Азия мен Африкада, денсаулық сақтау саясатының әлсіздігі және ауыл шаруашылығында антибиотиктерді шамадан тыс пайдалану салдарынан АМР деңгейі жоғары. Қазақстанда 2019 жылы АМР-мен байланысты өлім саны шамамен 2 400-ді құрады, бұл елді АМР-дан болатын өлім-жітім бойынша әлемде 95-орынға қойды. Сонымен қатар, шолу әртүрлі елдердегі антибиотиктерді тағайындау тәжірибесіндегі айырмашылықтарды анықтады: Еуропадағы қатаң реттеу шаралары резистенттілік деңгейінің төмендеуіне ықпал етеді.

Қорытынды: АМР антибиотиктерді тағайындаудың тиімсіз тәжірибесі мен әлсіз реттеу саясаты салдарынан маңызды жаһандық денсаулық сақтау мәселесі болып қала береді. Бұл мәселені шешу үшін антимикробтық бақылауды күшейту, мониторинг жүйелерін жетілдіру және антибиотиктерді реттеу саясатын қатаңдату бойынша халықаралық күш-жігерді үйлестіру қажет. Медицина қызметкерлері мен халықтың хабардарлығын арттыру антимикробтық резистенттіктің артуына қарсы күресте шешуші рөл атқарады.

Түйінді сөздер: антимикробтық резистенттік, эпидемиология, қауіп факторлары, Қазақстан.

Дәйексөз үшін:

Зарпуллаев Н.Е., Юрковская О.А., Муканова Д.А., Кожамметова Д.К., Ботабаева А.С., Смаил Е.М., Шамшудинов Т.М., Кусаинова А.А., Дербисалина Г.А., Уразалина Н.М., Касым Л.Т. Бастапқы денсаулық сақтау буынында антибиотик тағайындау тәжірибесін талдау. I бөлім // Ғылым және Денсаулық сақтау. 2025. Vol.27 (2), Б. 157-167. doi 10.34689/SH.2024.27.2.016

Background

Effective antibiotic prescription plays a crucial role in managing infectious diseases, preventing postoperative complications, and controlling antimicrobial resistance (AMR). However, the growing prevalence of AMR raises significant concerns regarding the effectiveness of modern medicine. AMR occurs when microorganisms, such as bacteria, fungi, viruses, or parasites, adapt to the effects of previously effective medications, rendering them ineffective [38, 50]. This process is driven by genetic mutations and natural selection, enabling microorganisms to develop resistance-enhancing genes that improve their survival against antibiotics [62].

AMR remains one of the greatest challenges to global health, contributing to rising mortality rates worldwide. A global data analysis revealed that in 2019, bacterial AMR was associated with approximately 4.95 million deaths, of which 1.27 million were directly attributed to bacterial resistance [58]. Projections indicate that by 2050, AMR could cause up to 10 million deaths annually [46, 49], making it one of the leading contributors to morbidity and mortality globally.

It is essential for physicians to adhere to national and international protocols to prevent the exacerbation of medical issues, as noncompliance not only jeopardizes patient safety but also has broader implications for healthcare systems worldwide, including increased treatment costs, limited therapeutic alternatives, and challenges in managing complications [25]. Therefore, this review aims to provide a comprehensive analysis of prescription practices, the underlying factors influencing these practices, and contributors to antimicrobial resistance, with the goal of developing strategies to promote the effective use of antibiotics.

Search Strategy

A systematic literature search was conducted following the identification of key terms and their synonyms. The search was performed in English-language databases, including PubMed, Google Scholar, and EBSCO, with an additional search conducted on the World Health Organization (WHO) website. To ensure the inclusion of the most relevant data, the search was restricted to publications from the past ten years.

After identifying relevant publications, the authors examined all bibliographic references cited within these articles, as well as studies that cited the selected publications. In the subsequent stage, article abstracts were screened to identify the most relevant studies. The collected literature was then categorized based on predefined inclusion and exclusion criteria, and full-text articles were retrieved for an in-depth review. In the final stage, only validated sources were incorporated into the study. A summary of the search strategy is presented in Figure 1. *Inclusion Criteria:* (a) Studies directly relevant to the review topic; (b) Publications in English; (c) Studies published from 2015 onward; (d) Primary and secondary research, including systematic reviews, meta-analyses, clinical guidelines, monographs, and conference abstracts. *Exclusion Criteria:* Studies that did not meet the inclusion criteria were excluded from the review.

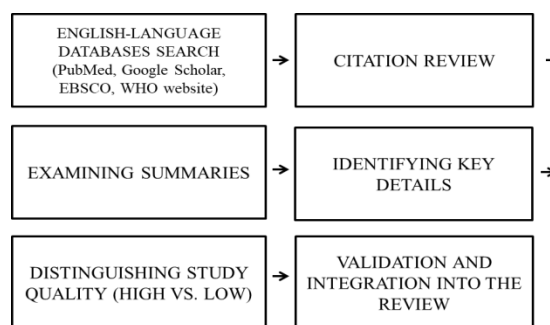


Figure. 1 Search strategy.

The main part Epidemiology

Antimicrobial Resistance: A Global Health Threat

The World Health Organization (WHO) has classified antimicrobial resistance (AMR) as one of the most pressing global health threats, with significant implications for healthcare systems worldwide. To address this challenge, the Global Action Plan was developed to assist nations in implementing effective strategies for monitoring and controlling AMR [20]. One such initiative is the Global Antimicrobial Resistance and Use Surveillance System (GLASS), which provides a standardized framework for collecting and analyzing AMR data across different regions [63]. This system enables nations and healthcare professionals to assess AMR trends, identify emerging risks, and implement targeted interventions to mitigate its spread. The prevalence of AMR varies globally, influenced by factors such as prescription practices, healthcare policies, and geographical location. WHO has warned that, without effective policies and interventions, the world may enter a post-antibiotic era, in which common infections become untreatable, leading to significantly higher mortality rates [63].

North America

In the Americas, the United States and Canada report lower AMR rates compared to South America. This disparity is likely due to weaker regulatory frameworks in many South American countries, contributing to high rates of pneumonia and other resistant infections. Antimicrobial resistance remains a critical public health problem in the United States, driven by factors like agricultural antibiotic use and inappropriate prescribing practices [56]. The study of Amin et al. (2023) found a significant burden of bacterial antimicrobial resistance (AMR) in the United States in 2019, with over 60,000 deaths associated with AMR and nearly 15,000 deaths directly attributable to AMR [4]. The COVID-19 pandemic has reversed the progress made in reducing antimicrobial resistance in the US, with a 15% increase in drug-resistant hospital-acquired infections in 2020 compared to the previous year [40]. Furthermore, the COVID-19 pandemic has undone much of the nation's progress in slowing the spread of antimicrobial resistance, especially in hospitals (CDC, 2022). Overuse of antimicrobials in agriculture, food processing, and medicine is contributing to the growing problem of antimicrobial resistance in the USA [22]. However, despite stricter regulations in North America, antibiotic-resistant pneumonia remains a significant public health concern [19].

Europe

European Food Safety Authority report demonstrated that resistance to commonly used antimicrobials was frequently found in *Salmonella* and *Campylobacter* isolates

from humans and animals. While combined resistance to critically important antimicrobials was generally low, there were some exceptions with higher levels of resistance in certain *Salmonella* and *Campylobacter* strains. The study found some concerning carbapenemase-producing *E. coli* isolates in animals and meat, which requires further investigation [17].

The European Antimicrobial Resistance Surveillance Network (EARS-Net) coordinated by the European Centre for Disease Prevention and Control (ECDC), reports concerning resistance patterns, particularly among gram-negative bacteria such as *Escherichia coli* and *Klebsiella pneumoniae*. Notably, resistance to third-generation cephalosporins in *E. coli* was recorded at 10.35 cases per 100,000 population, reflecting a 3.6% decline from 2019. However, *K. pneumoniae* has demonstrated an alarming 57.5% increase in carbapenem-resistant bloodstream infections compared to 2019, underscoring the growing challenge of treating multidrug-resistant infections [63]. Northern Europe reports relatively lower AMR rates, likely due to strict antibiotic prescription regulations. In contrast, Southern and Eastern Europe experience higher resistance rates, often attributed to frequent antibiotic misuse [11].

Africa

Antimicrobial resistance (AMR) is a growing concern in Africa, with high levels of resistance reported for commonly used antibiotics. Studies from East and West Africa show significant resistance to ampicillin, cotrimoxazole, and emerging resistance to gentamicin and ceftriaxone in Gram-negative infections [5, 13]. In West Africa, moderate to high rates of AMR were found in urinary tract and bloodstream infections, particularly among hospitalized patients [10]. Sub-Saharan Africa has the highest mortality rate attributable to antimicrobial resistance, requiring a One Health approach to implement action plans and tackle the challenge. The region is disproportionately affected by AMR due to factors like poverty, high infectious disease burden, poor antimicrobial regulation, and lack of effective alternatives [30].

However, AMR data is lacking for over 40% of African countries, and the quality of available microbiological data is concerning [57]. The World Health Organization predicts severe consequences of AMR in Africa by 2050, emphasizing the need for improved surveillance, standardized reporting, and optimized treatment guidelines to address this public health threat [21].

Asia

Several Asian countries, including India, China, and those in Southern Asia, report some of the highest AMR rates globally, primarily due to inadequate hygiene practices, insufficient infection control measures, and the widespread use of antibiotics in agriculture [36]. Additionally, certain strains of drug-resistant bacteria have become increasingly prevalent in the region. High rates of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae have been documented across Southeast Asia, complicating the treatment of common bacterial infections [28]. Furthermore, over 50% of *Acinetobacter baumannii* isolates in China and India exhibit carbapenem resistance, posing significant challenges for managing hospital-acquired infections [33].

Antimicrobial resistance in aquaculture and fisheries in Asia remains a concerning issue, with high levels of

resistance to medically important antimicrobials. In aquaculture, the percentage of antimicrobial compounds with over 50% resistance remained around 33% from 2000-2018. In fisheries, the percentage of antimicrobial compounds with over 50% resistance decreased from 52% to 22% from 2000-2018 [48]. Also drivers of AMR in Southeast Asia include rapid intensification of food production systems, widespread and unregulated access to antimicrobials, poor awareness about antimicrobial use among the public, healthcare providers and farmers, and an abundance of low-quality or counterfeit drugs [64].

Kazakhstan

In Kazakhstan, AMR presents a growing public health concern. In 2019, the country reported approximately 2,400 deaths directly attributable to AMR and 9,500 deaths associated with AMR-related complications. This placed Kazakhstan 95th in terms of age-standardized mortality rates related to AMR among 204 countries [27]. These statistics highlight the urgent need for enhanced antimicrobial stewardship programs and stricter regulatory measures to curb the spread of resistant infections. A study in a tertiary hospital's ICU revealed high resistance rates among bacterial isolates causing hospital-acquired infections, particularly in Gram-negative bacteria [60]. Factors contributing to AMR include non-judicial antibiotic use, unrestricted use in livestock, and the release of antibiotic residues into the environment. Urgent interventions are needed, including surveillance, monitoring, minimizing over-the-counter antibiotic use, improving access to quality medicines and diagnostics, and enforcing legislation [45].

The prevalence of the resistant microbial agents

The increasing prevalence of AMR underscores the urgent need for targeted interventions to combat resistant pathogens. According to the WHO Priority Pathogen List, one of the most critical resistant bacteria is carbapenem-resistant *Acinetobacter baumannii*, commonly acquired in hospital settings. This pathogen is responsible for severe complications such as wound infections and pneumonia, posing a substantial challenge for intensive care units [62]. Another widespread resistant microorganism is methicillin-resistant *Staphylococcus aureus* (MRSA), which exhibits resistance not only to methicillin but also to oxacillin and cephalosporins. MRSA is associated with soft tissue infections, bloodstream infections, pneumonia, and postoperative complications [61]. WHO classifies MRSA into two categories: (a) hospital-acquired MRSA (HA-MRSA): primarily linked to severe infections in healthcare settings; (b) community-acquired MRSA (CA-MRSA): transmitted outside hospitals, often causing skin infections and pneumonia. Although vancomycin was previously an effective treatment for MRSA, vancomycin-resistant *Staphylococcus aureus* (VRSA) has now emerged, further complicating treatment options. *Klebsiella pneumoniae*, a gram-negative bacterium, is another notable multidrug-resistant (MDR) pathogen, responsible for pneumonia, bloodstream infections, and urinary tract infections. It employs various mechanisms to evade antibiotics, including increased efflux pump activity and reduced antibiotic penetration. Alarmingly, *K. pneumoniae* has developed resistance to nearly all available antibiotics. A study by Salah et al. (2019) found that ESBL-producing *E. coli* and *Klebsiella* strains in Lomé, Togo, frequently carried plasmid-

mediated quinolone resistance (PMQR) genes, such as *qnrA*, *qnrB*, and *qnrS*. The co-occurrence of fluoroquinolone and beta-lactam resistance highlights the urgent need for alternative treatment strategies, particularly in resource-limited settings [45]. Another critical resistant pathogen is fluoroquinolone-resistant *Escherichia coli*, which is commonly associated with urinary tract infections (UTIs), gastrointestinal infections, and sepsis. Understanding the epidemiology of AMR is crucial for tracking resistance trends, developing strategies to reduce mortality and morbidity rates, and identifying key drivers of resistance to mitigate the risk of future epidemics. Strengthening AMR surveillance systems and regulatory policies remains essential for controlling antimicrobial resistance and ensuring the continued efficacy of infection treatment.

Factors Contributing to AMR

Despite various measures implemented to combat antimicrobial resistance (AMR), it continues to pose a significant burden on global healthcare systems. The development and spread of AMR are driven by multiple factors, including inappropriate antibiotic use, weak regulatory frameworks, socioeconomic disparities, environmental contamination, globalization, and inadequate healthcare policies [1, 16].

A study by *Salam et al.* (2023) identifies four primary drivers of AMR: environment-related, drug-related, patient-related, and physician-related factors [45].

Environmental factors

The natural environment plays a critical role in the dissemination of antibiotic-resistant pathogens. *Samreen et al.* (2021) reported that agricultural and hospital wastewater often contains residual antibiotics, creating conditions conducive to the selection and proliferation of resistant bacterial communities in water and soil [47]. Additionally, *Kaviani Rad et al.* (2022) noted that heavy metals, hydrocarbons, and other agricultural waste products further contribute to the emergence and persistence of resistance genes in the environment [32].

Environmental contributors to AMR include agricultural antibiotic use, mass travel, inadequate sanitation, and weak pharmaceutical policies. Antibiotics are extensively used not only in human medicine but also in agriculture to prevent infections in plants and animals. According to *Salam et al.* (2023), over 70% of antibiotics are used to treat animals, as farms frequently administer these drugs to reduce costs and increase production [45]. However, this widespread usage contributes significantly to AMR by fostering the emergence of drug-resistant pathogens. Additionally, globalization and increased international travel have accelerated the transmission of AMR. A systematic review by *Arcilla et al.* (2017) found that international travelers frequently acquire resistant bacteria during their trips, which can persist in their microbiota long after returning home, increasing the risk of spreading resistant pathogens across borders. Furthermore, inadequate medication policies at both hospital and national levels exacerbate the problem [6]. The unrestricted availability of antibiotics, coupled with the absence of stringent regulations, facilitates inappropriate antibiotic consumption, thereby promoting resistance. A study by *Masud et al.* (2024) found that one in four pharmacy purchases involves antibiotics, with over half of these transactions occurring without a prescription. This

lack of oversight significantly contributes to the uncontrolled use of antimicrobial agents, further driving the emergence of resistant bacterial strains [35]. The persistence of AMR despite intervention efforts highlights the complex interplay of environmental, economic, and healthcare-related factors. Addressing this issue requires a multifaceted approach, including stricter regulations on antibiotic use in agriculture and medicine, enhanced surveillance of international travelers, and the implementation of robust pharmaceutical policies to prevent over-the-counter antibiotic sales.

Other key factors contributing to the global spread of antibiotic resistance include overuse of antibiotics in livestock, reduced drug efficacy, lack of new vaccine development, environmental toxicity, transmission through travel, and insufficient funding for healthcare research and development. Social and economic factors like poor infrastructure, governance, and sanitation are more strongly associated with higher antimicrobial resistance levels than just antibiotic usage volumes. Interventions need to focus on addressing the social and economic factors that enable the spread or "contagion" of resistant microorganisms, rather than just limiting antibiotic usage [12].

Drug-Related and Prescription Factors Contributing to Antimicrobial Resistance.

In addition to environmental and regulatory factors, drug-related issues play a significant role in the emergence and spread of antimicrobial resistance (AMR). One major concern is the poor quality and overproduction of antibiotics. Due to the high redundancy in drug development, only 15% of newly created antibiotics are found to be effective, as many are structurally and mechanistically similar to previous generations. Notably, only 8 out of 51 recently developed antibiotics are considered innovative treatments for infections caused by antibiotic-resistant bacteria, while the vast majority are merely modifications of existing drugs [45]. A separate study highlights that the overproduction of antibiotics contributes to multidrug resistance, where pathogens develop resistance to multiple medications simultaneously. Since the introduction of antibiotics, over 150 new antimicrobial agents have been developed, yet their widespread and excessive use has inadvertently led to the evolution of highly resistant bacterial strains, commonly referred to as "superbugs" [58].

Patient - and Physician-Related Factors in AMR Development

Beyond drug-related concerns, prescription practices and patient behaviors significantly contribute to AMR. Unnecessary antibiotic use, inappropriate prescriptions, and overdosing are among the key drivers. Physicians must adhere to national and international guidelines to prevent the worsening of resistance, as inappropriate prescribing not only compromises patient safety but also has widespread economic and therapeutic consequences for healthcare systems, affecting treatment costs, available therapeutic alternatives, and the management of complications.

The study of *Hafeez et al.* (2023) demonstrated that factors contributing to antimicrobial resistance in dental practices include lack of patient awareness, over-the-counter availability, self-medication, improper guidelines, and lack of knowledge. The top factors contributing to antimicrobial drug resistance in dental practice were lack of

patient awareness, over-the-counter availability, and self-medication. Dentists were overprescribing antibiotics due to improper guidelines, a desire to satisfy patients, and a lack of knowledge. A significant proportion of the dentists' patients were self-medicating with antibiotics and lacked awareness about appropriate antibiotic use [22].

One contributing factor is patient demand for antibiotics, which can pressure physicians into prescribing unnecessary treatments. Some healthcare providers may prescribe antibiotics simply to meet patient expectations or align with pharmacy demands. A common misconception among patients is that antibiotics are universally effective against all infections - including viral and fungal diseases, which is scientifically inaccurate. A survey by *Semenova et al.* (2024) in Kazakhstan revealed that while more than 50% of respondents were aware of AMR, the majority incorrectly believed that antibiotics kill viruses and are effective treatments for colds [49].

Physician Awareness and Attitudes Toward AMR

Several studies have examined physician awareness and prescribing attitudes regarding AMR. One of the study reported that 75% of physicians identified patient demand as a primary factor influencing unnecessary antibiotic prescriptions. Despite high levels of awareness about AMR, many physicians underestimate its relevance to their own practice, viewing it primarily as a global issue rather than a local concern [29]. *Al Rahbi et al.* (2023) found that while 95% of clinicians recognized AMR as a national problem, only 77% acknowledged it as an issue within their own institution, and just 65% considered it a concern in their personal practice. Additionally, inappropriate prescribing may be unintentional, driven by time constraints, clinical uncertainty, and pressure from nursing staff [2]. A study by *Christensen et al.* (2022) suggests that some physicians, particularly younger and less experienced doctors, may prescribe antibiotics without thoroughly assessing their necessity due to limited time for decision-making. In many cases, antibiotics are prescribed as a precautionary measure, even when their necessity is uncertain, to mitigate potential complications [14].

Addressing drug-related, patient-related, and physician-related factors in AMR requires a multifaceted approach, including enhanced drug development strategies, stricter antibiotic regulation, improved patient education, and reinforced physician training. Increasing awareness among both healthcare professionals and the general public is essential to mitigating inappropriate antibiotic use and slowing the global spread of antimicrobial resistance [44].

Drivers of Antimicrobial Resistance and the Urgent Need for Global Action

Antimicrobial resistance poses a significant global public health threat, necessitating urgent international intervention. The complex issue is influenced by factors such as poverty, self-medication, misdiagnosis, and overuse in both humans and animals [51]. Globalization has exacerbated the problem, as resistant bacteria do not respect borders. AMR leads to increased morbidity, mortality, and healthcare costs, with limited therapeutic options for resistant infections [45]. Addressing AMR requires a coordinated global strategy, including surveillance, restricted antibiotic use in livestock, access to quality medicines and diagnostics, and enforcement of legislation [37, 52]. International collective action is essential, as

no country can adequately protect its population acting alone [62]. Without immediate intervention, a post-antibiotic era may become a reality [42].

Research conducted by *Ardillon et al.* (2023) on inappropriate antibiotic prescriptions in outpatient pediatric departments highlights significant disparities in prescribing practices across different regions. Their findings indicate that 75% of prescribed antibiotics in Madagascar, Senegal, and Cambodia were unnecessary, with approximately three-quarters of consultations resulting in unjustified antibiotic prescriptions. Similarly, two-thirds of all antibiotics prescribed to young children in these countries were deemed unnecessary [7]. In contrast, inappropriate prescriptions in China accounted for 25% of cases, while Kenya reported a rate of 50%. A separate study by *Hagedoorn et al.* (2020) focusing on antibiotic prescriptions in Europe found that only 12% of prescriptions were considered inappropriate, with incorrect treatment duration being the most frequent prescribing issue [23]. These findings suggest that developing countries are more prone to inappropriate prescribing patterns, with Africa exhibiting the highest prescription rates and Asia showing the highest levels of inappropriate prescriptions [31]. Antibiotics were most commonly prescribed for acute inflammatory organ diseases and common colds, despite their inefficacy against viral infections.

Ayukekbong et al. (2017) identified several factors contributing to AMR in developing nations, including limited patient awareness, inadequate diagnostic facilities, and inappropriate prescription practices. Additionally, the unauthorized sale and non-human use of antibiotics significantly exacerbate resistance. One of the primary drivers of AMR is the misuse and overuse of antibiotics in both human and veterinary medicine [8]. *Sokolović et al.* (2023) found that higher antibiotic consumption in outpatient settings, combined with lower healthcare expenditure, significantly contributes to AMR. These findings underscore the urgent need for improved prescribing practices and enhanced patient education to combat the growing threat of AMR [54].

Insufficient regulatory frameworks, particularly in developing nations, significantly facilitate the spread of AMR. The unauthorized sale and widespread distribution of antibiotics occur frequently in regions with weak or poorly enforced regulations [43]. *Pokharel et al.* (2019) argue that weak governance negatively impacts the overall functioning of healthcare systems, resulting in ineffective antimicrobial stewardship policies. Without stringent healthcare policies, the inappropriate use of antimicrobials becomes more prevalent, further driving antimicrobial resistance [41].

Laxminarayan et al. (2016) highlighted global inconsistencies in antibiotic stewardship, particularly within the Gulf Cooperation Council, where variations in regulatory policies contribute to uneven resistance patterns. These disparities make it challenging to develop a unified international strategy to combat AMR [33]. *Huttner et al.* (2013) emphasized that non-therapeutic antibiotic use and a general lack of public understanding of proper usage further aggravate the problem [26]. Similarly, *Van Boeckel et al.* (2014) analyzed national pharmaceutical sales data and found that antibiotic consumption was highest in countries with weak regulatory enforcement. These findings underscore the urgent need for strict regulatory policies and robust enforcement mechanisms to limit unauthorized

antibiotic access and reduce inappropriate prescribing practices [59].

Socioeconomic conditions are closely linked to the prevalence of AMR. Regions with high levels of poverty, unemployment, and limited healthcare access tend to exhibit significantly higher rates of antibiotic misuse [3, 34]. WHO demonstrated that socioeconomic disparities - such as inadequate sanitation and overcrowded living conditions - are strongly associated with AMR emergence and transmission. The study further highlighted that regions with a high Area Deprivation Index (ADI) face greater challenges in combating AMR [62]. Similarly, *Holmes et al.* (2016) found that low public health investment and underfunded healthcare systems exacerbate antibiotic overuse and resistance, particularly in resource-limited settings. Addressing these socioeconomic factors is essential for implementing effective interventions that will help mitigate the growing burden of AMR [24].

Globalization and increased international travel have significantly accelerated the worldwide dissemination of antimicrobial-resistant pathogens. *Sridhar et al.* (2021) emphasize that global travel plays a crucial role in the spread of AMR by facilitating the acquisition, carriage, and transmission of resistant bacteria across borders. They identified three key factors influencing this process: (a) the travel destination, where individuals may be exposed to highly resistant bacterial strains; (b) the use of antimicrobials during travel, which can encourage the development of resistance; (c) traveler's diarrhea, which increases susceptibility to resistant pathogens [55]. Furthermore, *Murray et al.* (2022) reported that global mobility and high population densities have played a pivotal role in the rapid spread of resistant pathogens worldwide [39].

Inadequate diagnostic capabilities often force clinicians to rely on empirical treatments rather than targeted therapies, which can inadvertently promote antibiotic misuse [9]. *Dyar et al.* (2017) argue that education plays a crucial role in reducing antimicrobial resistance by increasing awareness among healthcare professionals and the general public about the risks associated with antibiotic misuse [15]. The emergence and spread of AMR result from a complex interplay of multiple factors, including inappropriate antibiotic use, insufficient regulation, socioeconomic disparities, environmental contamination, globalization, and suboptimal healthcare practices. Addressing these challenges requires coordinated global action through enhanced antimicrobial stewardship, stricter regulatory policies, improved diagnostic capacity, and increased public education. Only through comprehensive, evidence-based strategies can the global community effectively combat the growing threat of antimicrobial resistance.

Conclusion

Antimicrobial resistance (AMR) remains a pressing global health crisis, driven by a complex interplay of factors, including inappropriate antibiotic use, weak regulatory frameworks, socioeconomic disparities, environmental contamination, and globalization. Despite numerous interventions, AMR continues to undermine the efficacy of modern medicine, posing a significant threat to public health and healthcare systems worldwide. The evidence presented highlights that developing countries, in particular, face higher rates of inappropriate antibiotic prescriptions due to limited healthcare infrastructure, weak governance, and insufficient public awareness [41]. Moreover, the overuse of

antibiotics in agriculture and non-human settings exacerbates the problem, facilitating the selection and spread of resistant bacterial strains.

To combat AMR effectively, a multifaceted approach is required, incorporating strengthened regulatory policies, improved antimicrobial stewardship, enhanced diagnostic capabilities, and global collaboration. Encouraging rational antibiotic use through comprehensive public education campaigns and training for healthcare professionals is crucial in reducing unnecessary prescriptions [18]. Additionally, restricting unauthorized antibiotic sales and implementing strict policies on antibiotic use in agriculture can help mitigate the emergence of resistance. Given the increasing role of international travel in spreading resistant pathogens, global surveillance systems such as WHO's GLASS must be further expanded to monitor resistance trends and facilitate coordinated responses [53].

Addressing AMR necessitates collective efforts at national and international levels. Without immediate and sustained action, the world risks entering a post-antibiotic era, where once-treatable infections become deadly. By reinforcing stewardship programs, advancing research on novel antibiotics, and prioritizing regulatory reforms, healthcare systems can work towards preserving the effectiveness of existing antimicrobial treatments and safeguarding future generations from the devastating consequences of antimicrobial resistance.

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Information about the authors:

Zarpullayev Nyssan Eldosovich – Bachelor of Nursing Science, Master's Student of Medicine, Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 771 796 00 69, e-mail: nyssan.zarpullayev@alumni.nu.edu.kz, <https://orcid.org/0009-0000-2276-6937>, Astana, Republic of Kazakhstan

Yurkovskaya Oxana Alexandrovna - Candidate of Medical Sciences, Acting Professor of the Department of General medical practice, NJSC "Semey Medical University", phone: 8 702 750 65 21, e-mail: Oksanayrk@mail.ru, <https://orcid.org/0000-0002-6251-5574>, Semey, Kazakhstan;

Mukanova Dinara Adletovna - Candidate of Medical Sciences, Associate Professor Department of simulation and educational technologies, NJSC "Semey Medical University", phone: 8 701 491 98 29, e-mail: mukanova.dinara@smu.edu.kz, <https://orcid.org/0000-0001-5186-2346>, Semey, Republic of Kazakhstan;

Kozhakhmetova Dana Kenzhibayevna - assistant of the Department of Internal Medicine and Rheumatology, NJSC "Semey Medical University", phone: 8 702 705 14 03, e-mail: dana.kozhakhmetova@smu.edu.kz, <https://orcid.org/0000-0002-8367-1461>, Semey, Republic of Kazakhstan;

Botabayeva Ainur Serikzhanovna - assistant of the Department of Internal Medicine and Rheumatology, NJSC "Semey Medical University", phone: 8 701 100 20 98, e-mail: ainur.botabayeva@smu.edu.kz, Semey, Republic of Kazakhstan;

Smail Yerbol Muslimovich - Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenereology and Immunology, NJSC "Semey Medical University", phone: 8 705 528 84 09, e-mail: erbis@mail.ru, <https://orcid.org/0000-0003-3881-3747>, Semey, Kazakhstan;

Shamshudinov Timur Maratovich – PhD, «Medical and diagnostic Center of otorhinolaryngology» PRO-LOR, phone: 8 701 204 10 70, e-mail: dr.shamshudinov@mail.ru, <https://orcid.org/0000-0001-5015-871X>, Almaty, Kazakhstan;

Kussainova Assiya Abikhasovna - PhD, Acting Associate Professor Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 707 498 73 48, e-mail: kuzilas@mail.ru, <https://orcid.org/0000-0002-5738-0804>, Astana, Republic of Kazakhstan;

Derbissalina Gulmira Azhmadievna - Candidate of Medical Sciences, Head of the Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 701 346 93 31, e-mail: derbissalina@gmail.com, <https://orcid.org/0000-0003-3704-5061>, Astana, Republic of Kazakhstan.

Urazalina Nailiya Murathanovna - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, <https://orcid.org/0000-0003-0200-1763>,

*Correspondence author:

Kassym Laura Talgatkyzy – PhD, Associate Professor Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University",

Address: Astana Medical University, 49 Abay Street, Astana city, 010000, Republic of Kazakhstan

E-mail: laura.kassym@gmail.com

Phone: 8 777 735 10 62