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ANALYSIS OF ANTIBIOTIC PRESCRIBING PRACTICES IN PRIMARY HEALTH CARE SETTINGS. PART II. LITERATURE REVIEW

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Abstract

Introduction: Antimicrobial resistance (AMR) poses a major global health threat that requires coordinated international strategies to limit its spread and impact. Scientific approaches, including surveillance, innovative drug development, and stewardship programs, are essential to address the biological complexity of resistance. At the same time, economic and social dimensions—such as healthcare costs, access to medicines, and public awareness—must be integrated into global efforts to achieve sustainable solutions.

Objective: To describe the global strategies, scientific approaches, socioeconomic aspects of AMR

Materials and Methods: A systematic review of the literature was carried out, drawing on peer-reviewed publications from medical and public health databases such as PubMed, Google Scholar, and EBSCO, along with WHO reports, epidemiological data, and recent studies on AMR patterns and antibiotic prescribing practices. The analysis centered on global developments, with particular attention to Central Asia, especially Kazakhstan and its neighboring states.

Results: Limited surveillance systems and inconsistent data collection hinder accurate assessment of AMR trends in Kazakhstan and neighboring countries. Socioeconomic factors, such as self-medication, over-the-counter antibiotic sales, and low public awareness, exacerbate the problem. Strengthening stewardship programs, improving diagnostics, and enhancing international collaboration are critical for reducing the spread of AMR.

Conclusion: Findings emphasize the urgent need for coordinated global strategies, evidence-based policies, and context-sensitive interventions to address inappropriate antibiotic use and strengthen resistance surveillance.

Keywords: antimicrobial resistance, global strategy, stewardship.

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Резюме

**АНАЛИЗ ПРАКТИК НАЗНАЧЕНИЯ АНТИБИОТИКОВ
В ПЕРВИЧНОМ ЗВЕНЕ ЗДРАВООХРАНЕНИЯ. ЧАСТЬ II.
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Введение: Антимикробная резистентность (AMR) представляет собой серьёзную глобальную угрозу для здоровья, требующую скоординированных международных стратегий для ограничения её распространения и последствий. Научные подходы, включая эпидемиологический надзор, разработку инновационных препаратов и программы рационального использования антибиотиков, имеют ключевое значение для решения биологической сложности резистентности. В то же время экономические и социальные аспекты — такие как расходы на здравоохранение, доступ к лекарствам и информированность населения — должны быть интегрированы в глобальные усилия для достижения устойчивых решений.

Цель: Охарактеризовать глобальные стратегии, научные подходы и социально-экономические аспекты AMR.

Материалы и методы: Был проведён систематический обзор литературы с использованием рецензируемых публикаций из медицинских и общественно-здравоохранительных баз данных (PubMed, Google Scholar, EBSCO), а также отчётов ВОЗ, эпидемиологических данных и современных исследований по динамике AMR и практике назначения антибиотиков. Анализ был сосредоточен на глобальных тенденциях с особым акцентом на Центральную Азию, включая Казахстан и сопредельные страны.

Результаты: Ограниченные системы надзора и непоследовательный сбор данных препятствуют точной оценке тенденций AMR в Казахстане и соседних государствах. Социально-экономические факторы, такие как самолечение, продажа антибиотиков без рецепта и низкая информированность населения, усугубляют проблему. Усиление программ рационального использования, совершенствование диагностики и расширение международного сотрудничества имеют решающее значение для снижения распространения AMR.

Заключение: Полученные данные подчёркивают острую необходимость в согласованных глобальных стратегиях, основанных на доказательной политике и адаптированных к региональному контексту мерах для предотвращения нерационального применения антибиотиков и укрепления системы надзора за резистентностью.

Ключевые слова: антимикробная резистентность, глобальная стратегия, рациональное использование антибиотиков.

Для цитирования:

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Түйіндеме

**БАСТАПҚЫ ДЕНСАУЛЫҚ САҚТАУ БУЫНЫНДА АНТИБИОТИК
ТАҒАЙЫНДАУ ТӘЖІРИБЕСІН ТАЛДАУ. II БӨЛІМ.
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Кіріспе: Антимикробтық резистенттілік (АМР) – оның таралуын және салдарын шектеу үшін үйлестірілген халықаралық стратегияларды талап ететін денсаулыққа төнген маңызды жаһандық қатер. Ғылыми тәсілдер, соның ішінде эпидемиологиялық қадағалау, инновациялық препараттарды әзірлеу және антибиотиктерді ұтымды пайдалану бағдарламалары резистенттіліктің биологиялық күрделілігін еңсеруде шешуші рөл атқарады. Сонымен бірге денсаулық сақтау шығындары, дәрі-дәрмекке қолжетімділік және халықтың хабардарлығы сияқты экономикалық және әлеуметтік қырлар тұрақты шешімдерге қол жеткізу үшін жаһандық күш-жігерге енгізілуі тиіс.

Мақсат: АМР-дың жаһандық стратегияларын, ғылыми тәсілдерін және әлеуметтік-экономикалық қырларын сипаттау.

Материалдар мен әдістер: Әдебиетке жүйелі шолу жүргізіліп, медициналық және қоғамдық денсаулық сақтау дерекқорларынан (PubMed, Google Scholar, EBSCO) рецензияланған жарияланымдар, сондай-ақ ДДСҰ есептері, эпидемиологиялық деректер және АМР динамикасы мен антибиотик тағайындау тәжірибесіне қатысты заманауи зерттеулер пайдаланылды. Талдау жаһандық үрдістерге бағытталып, ерекше назар Орталық Азияға, оның ішінде Қазақстан мен көршілес елдерге аударылды.

Нәтижелер: Қадағалау жүйелерінің шектеулілігі және деректерді жинаудың бірізді еместігі Қазақстан мен көрші мемлекеттердегі АМР үрдістерін дәл бағалауға кедергі келтіреді. Өзін-өзі емдеу, антибиотиктердің рецептсіз сатылуы және халықтың төмен хабардарлығы сияқты әлеуметтік-экономикалық факторлар мәселені күрделендіреді. Антибиотиктерді ұтымды пайдалану бағдарламаларын күшейту, диагностика сапасын арттыру және халықаралық ынтымақтастықты кеңейту АМР таралуын төмендетуде шешуші мәнге ие.

Қорытынды: Алынған деректер антибиотиктерді ұтымсыз қолдануды болдырмау және резистенттілікке қадағалауды күшейту үшін дәлелді саясатқа негізделген және өңірлік контекстке бейімделген үйлестірілген жаһандық стратегиялардың аса қажет екенін көрсетеді.

Түйінді сөздер: антимикробтық резистенттілік, жаһандық стратегия, антибиотиктерді ұтымды пайдалану.

Дәйексөз үшін:

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Background

Antimicrobial resistance (AMR), defined as the ability of microorganisms to adapt and survive exposure to antimicrobial agents, poses a major global public health threat. Its emergence is driven by a wide range of human, animal, and environmental factors. Human-related contributors include the excessive and inappropriate use of antimicrobials in healthcare, the application of antibiotics in cosmetics and biocides, and inadequate sanitation and hygiene in community settings. Additional drivers of AMR include agricultural practices, environmental contamination, and the use of antibiotics in animals [55]. Importantly, these elements are interconnected in complex ways. For example, *Ljungqvist et al.* (2025) emphasize the multifaceted links between socioeconomic determinants across sectors, underscoring the need for multisectoral approaches [30, 33]. Similarly, finance, governance, and disease management have been shown to be strongly associated with AMR risks [7], while Chan et al. (2022) demonstrate the role of multisectoral factors in the spread of AMR in Pacific Asia [10]. Rather than being attributable to a single cause, AMR arises from multiple, overlapping drivers, including behavioral, managerial, and institutional governance factors [59]. Moreover, several studies suggest that these multisectoral influences are insufficiently recognized by the public, even though experts increasingly acknowledge the broader and more complex determinants of resistance [20,46]. This highlights the necessity for collaboration across diverse fields, integrating knowledge and skillsets not only as translational tools but also as fundamental to understanding AMR [25]. Therefore, **the aim** of this study was to identify key factors affecting antibiotic prescription practices in clinical setting.

Search strategy. A systematic literature search was carried out using predefined key terms and their synonyms. Searches were conducted in English-language databases such as PubMed, Google Scholar, and EBSCO, along with an additional review of resources from the World Health Organization (WHO) website. To maintain relevance, only publications from the past decade were considered. Following the identification of suitable publications, the authors reviewed all bibliographic references cited within these works, as well as studies that had cited them. Abstracts were then screened to select the most pertinent research, after which the literature was organized according to established inclusion and exclusion criteria, and full-text articles were obtained for detailed evaluation. Ultimately, only validated and reliable sources were included in the final analysis.

Inclusion and Exclusion Criteria. The inclusion criteria were as follows: (a) thematic relevance to the study's scope; (b) availability English. Conversely, publications that did not satisfy these predefined standards were consequently excluded from the review.

The main part

Global Strategies and Initiatives

Global strategies and initiatives play a crucial role in addressing antimicrobial resistance (AMR). The WHO "Global Action Plan on AMR" provides a structured framework to support countries in developing surveillance systems, infection prevention strategies, and national policies (WHO, 2023) [57, 62]. In addition to the WHO,

international organizations such as the United Nations (UN), the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (WOAH), and the U.S. Centers for Disease Control and Prevention (CDC) have made significant contributions to global AMR control efforts. Evidence from national programs in the United States, Sweden, the Netherlands, and Thailand demonstrates that AMR action plans—when reinforced by effective policy enforcement, education, and investment in research—can substantially reduce resistance rates. These experiences highlight the necessity of global collaboration to address AMR as a long-term public health challenge.

AMR has emerged as a major global health crisis that threatens the foundations of modern medicine. The widespread misuse of antibiotics in human healthcare, veterinary medicine, and agriculture has accelerated the development of resistant strains [11]. Tackling AMR therefore requires coordinated international cooperation that involves governments, health organizations, and regional initiatives (Centers for Disease Control and Prevention) [8]. To address this, the WHO launched the "Global Action Plan on Antimicrobial Resistance (GAP-AMR)" in 2015, providing a comprehensive, multisectoral strategy for combating resistance through global cooperation and national-level implementation. The WHO strategy emphasizes raising public awareness through education campaigns, strengthening surveillance systems to monitor resistance patterns, and promoting responsible antimicrobial use across sectors such as healthcare and agriculture [57].

One of the WHO's key initiatives, the "Global Antimicrobial Resistance and Use Surveillance System (GLASS)", was established to standardize the collection and analysis of AMR-related data, thereby guiding evidence-based policymaking and improving treatment outcomes [16]. Addressing AMR requires a multidisciplinary perspective, often conceptualized within the "One Health framework", which integrates human, animal, and environmental health [14]. The UN has recognized AMR as a critical global health security issue, advocating for international cooperation and policy development across nations [58]. In this regard, the Interagency Coordination Group on Antimicrobial Resistance (IACG) was formed to provide best-practice recommendations to mitigate AMR's economic and healthcare burdens [62]. Similarly, the FAO has strengthened antibiotic use regulations in food production and livestock farming, promoting sustainable agricultural practices and biosecurity measures to reduce infections [4]. The WOAH has developed international guidelines to standardize antibiotic use in veterinary medicine and restrict excessive administration [63]. Together, these initiatives promote responsible antibiotic stewardship in humans, animals, and agriculture, thereby curbing the spread of resistant pathogens.

At the regional level, the European Centre for Disease Prevention and Control (ECDC) has played a central role in developing AMR surveillance systems and providing policy recommendations based on resistance trends. Its "European Surveillance of Antimicrobial Consumption Network (ESAC-Net)" monitors antibiotic consumption patterns to inform national strategies [48]. There are different strategies depending on the countries. For example, one of the strategies of UK to fight AMR is a room

improvement [1,2]. It is also suggested that raising awareness is one of the key strategies to tackle AMR [23] because one of the main drivers of antimicrobial resistance is inappropriate antibiotics use [13]. Several countries have implemented successful national action plans (NAPs). For example, the U.S. “CARB Strategy” was established to slow AMR by expanding antibiotic stewardship programs in hospitals and outpatient clinics, improving laboratory capacity for AMR detection, and supporting the development of new antibiotics. It also includes measures to limit non-therapeutic antibiotic use in agriculture and reduce the consumption of medically important antibiotics in animals [3]. Since its implementation, declines in hospital-acquired infections caused by resistant bacteria have been reported, illustrating the strategy’s effectiveness.

In the European Union (EU), strict prescription regulations and coordinated surveillance initiatives have made AMR a policy priority. Sweden’s “Strama Program” is a particularly successful national strategy, involving collaboration between healthcare professionals and policymakers to optimize antibiotic use, resulting in some of the lowest resistance rates in Europe [49]. The Netherlands has achieved similar success through stringent hospital infection control programs and national antibiotic restriction policies, significantly lowering resistance rates [4].

In Asia, Thailand has emerged as a regional leader in AMR control. According to Sumpradit (2021), the Thai NAP on AMR aimed to reduce antibiotic use in agriculture by 50% and in human medicine by 20%, while strengthening hospital infection control measures [39]. The government also introduced electronic prescription systems to monitor antibiotic consumption and launched public awareness campaigns to educate citizens on the risks of AMR and the importance of adhering to prescribed treatments [10]. These combined efforts have contributed to measurable progress, including reductions in colistin-resistant bacteria, further demonstrating the effectiveness of multisectoral interventions.

Scientific Approaches and Innovations

Antimicrobial resistance (AMR) represents one of the most critical global health challenges, threatening the effectiveness of antibiotics and the treatment of infectious diseases. The emergence of resistant microorganisms reduces therapeutic options and leads to higher morbidity and mortality. In response, modern medicine is adopting innovative scientific approaches to prevent, diagnose, and treat AMR more effectively. These approaches include artificial intelligence (AI), alternative drug delivery systems, and cross-sectoral collaboration. A notable initiative is the “Vivli Antimicrobial Resistance Register”, which compiles susceptibility data from pharmaceutical companies, governments, and researchers into an open-access platform. By providing real-time observation of resistance trends and patterns, this database fosters innovation and informs evidence-based medicine and policy. Mori et al. (2025) emphasize that open-access AMR databases enable early trend detection and enhance data-driven interventions [34, 21].

Artificial intelligence has emerged as a transformative tool in combating AMR. Machine learning algorithms can predict resistance patterns, optimize treatment strategies, and estimate the likelihood of drug effectiveness. AI-based platforms such as “DeepARG” and “ARIBA” have

demonstrated the ability to accurately identify resistance genes in metagenomic data, thereby improving diagnostic precision and guiding clinical decisions [6]. Moreover, Stokes et al. (2020) report that AI models have been used to predict novel antibiotic classes, including halicin, identified using neural networks trained on the features of bioactive compounds. Despite its promise, the clinical integration of AI remains constrained by challenges in data standardization, privacy, and regulatory approval [39].

Innovative drug delivery systems also play a critical role in addressing AMR. Nanotechnological approaches, including liposomes and metallic nanocarriers, have been designed to improve drug targeting and bioavailability, thereby minimizing adverse effects. Zhou et al. (2015) argue that nanocarriers can penetrate bacterial cell walls—one of the primary defenses of resistant pathogens—allowing for direct drug release at infection sites [65]. Smart delivery systems, which respond to environmental stimuli such as pH, temperature, or enzymes, are under development to ensure targeted release exclusively in infected tissues. This strategy reduces systemic toxicity and improves therapeutic accuracy [29]. Combination therapies that co-deliver antibiotics with efflux pump inhibitors or β -lactamase blockers have also shown promise in reversing resistance, as demonstrated by Zhang et al. (2024) [54].

Rethinking innovation ecosystems has become increasingly important in light of lessons learned from the COVID-19 pandemic. Rapid funding mechanisms, public-private partnerships, and regulatory flexibility accelerated the development of diagnostics and therapeutics during the pandemic. Piot et al. (2012) argue that similar innovation systems should be applied to AMR, with a focus on aligning research ecosystems with societal health priorities rather than purely market-driven models [32, 39]. However, while human and veterinary health sectors have been relatively active in AMR surveillance and innovation, the environmental dimension remains underfunded and underrecognized [36, 37]. The “One Health” framework, which integrates human, animal, and environmental health, is essential to address this gap. Environmental reservoirs of resistance genes, including wastewater and soil, significantly contribute to AMR transmission, yet surveillance in these areas is limited. Expanding One Health research to encompass environmental microbiology and incorporating it into national AMR strategies is vital for comprehensive mitigation [7, 28]. It is suggested that surveillance may help to identify resistance genes as well as controlling them [44].

Antibiotic discovery and development continue to face major scientific and economic challenges. The process remains slow, costly, and burdened by high rates of clinical trial failure due to toxicity or inefficacy. Furthermore, antibiotics are less profitable than drugs for chronic diseases, discouraging pharmaceutical investment. According to WHO (2021), most antibiotics currently in development share mechanisms of action with older drugs and target similar pathways, with only a few representing true innovation [5]. Llewelyn et al. (2017) suggest that bacteriocins and antimicrobial peptides could provide alternative therapeutic approaches [31]. Similarly, Vivekanandan et al. (2025) highlight research into non-

antibiotic molecules that restore the activity of existing drugs, thereby extending treatment options [53].

To effectively combat AMR, scientific and technological innovations must be integrated with cross-disciplinary collaboration. Open-access initiatives should be expanded, and equitable access to innovation must be prioritized. Public engagement is equally important to increase awareness and encourage responsible antibiotic use. Ultimately, addressing AMR requires systemic collaboration in how research, data, and innovation are harnessed for global health.

The economic impact of antimicrobial resistance (AMR) is profound and far-reaching. A study by the World Health Organization (WHO) estimates that AMR could result in additional healthcare costs of up to US\$1 trillion by 2050, with global gross domestic product (GDP) losses ranging from US\$1 trillion to US\$3.4 trillion per year by 2030 [19]. These projections highlight the severe financial burden that AMR may impose on global economies. According to Prestinaci et al. (2015), the annual cost of AMR in the United States is approximately US\$55 billion, comprising US\$20 billion in direct healthcare costs and an additional US\$35 billion due to lost productivity [40]. Similarly, the European Union incurs around EUR 1.1 billion annually in excess healthcare expenditures attributable to AMR [61].

Despite this alarming threat, funding for AMR research and development remains inadequate. Education and research are critical for both healthcare systems and the general public, yet they are often constrained by underfunded infrastructure [24]. The pharmaceutical industry remains reluctant to invest in antibiotic development due to low profitability and high risk of inefficiency. To address this challenge, various initiatives have been proposed. "Push funding" mechanisms, such as grants and public-private partnerships, have been implemented in countries like the United Kingdom and Sweden [57]. However, these initiatives require sustained and adequate investment. A report by Lord Jim O'Neill (2016) suggests that the estimated cost to effectively combat AMR would be around US\$40 billion [42].

Several global initiatives have been established to stimulate antibiotic innovation. For example, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) supports the development of novel antibacterial products and has attracted significant funding. Similarly, the Global AMR Innovation Fund (GAMRIF) focuses on early-stage research in underfunded areas of AMR, with particular emphasis on developing countries. Collaborative organizations, such as the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), adopt a One Health approach by integrating human, animal, and environmental health strategies. In parallel, the Global AMR R&D Hub coordinates international research priorities, while the Global Antibiotic Research and Development Partnership (GARDP) advances new treatments for drug-resistant infections through international cooperation [31, 10].

Beyond research and development, public awareness and stewardship programs are critical in reducing the misuse of antimicrobials. Stewardship interventions have been shown to significantly decrease inappropriate antibiotic use [7]. Educational initiatives directed at healthcare professionals and the wider public are essential

for encouraging responsible antibiotic practices and preventing the emergence of new resistance mechanisms. Addressing the economic and social challenges posed by AMR requires a multifaceted strategy, encompassing robust research investment, international collaboration, and sustained public education. Given the significant economic losses projected, greater investment in research and the development of alternative therapies is urgent. Scalable solutions, such as digital platforms, community-based programs, and curriculum integration in educational institutions, are being actively explored [26]. Through coordinated global action, it is possible to mitigate the impact of AMR and protect both public health and economic stability.

Challenges and Barriers to Implementing Global Approaches to Antimicrobial Resistance (AMR)

While international strategies such as the WHO Global Action Plan have been developed to address AMR, multiple barriers hinder their effective implementation across diverse contexts. Tiong et al. (2016) argue that the lack of efficient collaboration between sectors is a major impediment, with efforts often remaining uncoordinated and communication gaps between national priorities and global goals leading to inconsistent practices [50]. These challenges are particularly evident in low- and middle-income countries (LMICs), where implementation is further obstructed by weak governmental responses [43]. Raka et al. (2024) highlight that financial constraints frequently result in fragile healthcare systems, limited access to quality antimicrobials and diagnostic laboratories, and shortages of trained healthcare professionals, making even basic stewardship programs difficult to sustain [41]. Similarly, Ferreira et al. (2023) note that agricultural systems in regions with inadequate veterinary services and poor hygiene standards face parallel obstacles [15].

Regulatory weaknesses and market failures further exacerbate the situation. In many regions, antibiotics remain available without prescription, and weak enforcement mechanisms enable widespread misuse in both human and animal sectors. Compounding this issue, pharmaceutical industries have retreated from antibiotic development due to limited commercial incentives, leaving the global antibiotic pipeline fragile and heavily reliant on public or philanthropic funding [42]. The absence of comprehensive AMR surveillance systems poses another major barrier. Despite substantial investment, implementation remains uneven, and even among high-income countries data validity is compromised by inconsistent methodologies and reporting standards [2, 10]. This lack of standardized global surveillance makes it difficult to monitor AMR trends reliably.

Public awareness also remains insufficient. In many countries, low awareness contributes to self-medication, overprescription, and poor adherence to treatment protocols [45]. Cultural perceptions of antibiotics as "cure-all" remedies further exacerbate irrational use, while healthcare providers may resist stewardship protocols due to time constraints, lack of institutional support, or fear of patient dissatisfaction [15]. Weak water, sanitation, and hygiene (WASH) infrastructure amplifies the spread of resistant organisms, particularly in healthcare settings and food production systems [45]. In LMICs, insufficient laboratory

infrastructure limits diagnostic capacity, leading physicians to rely on empirical prescribing, thereby driving inappropriate antibiotic use. Ethiopia, for example, has identified weak laboratory systems, delays in reporting, and communication gaps as major obstacles to antimicrobial stewardship program (ASP) implementation [54, 36].

Economic and political barriers compound these technical challenges. High out-of-pocket healthcare costs reduce access to quality-assured antibiotics, while political instability and weak governance structures undermine the enforcement of AMR policies and divert resources away from health priorities. Cultural norms, patient expectations, and environmental contamination from poor pharmaceutical waste management further fuel the problem. Engaging the private healthcare sector and informal providers—who play a substantial role in service delivery in LMICs but are often excluded from AMR strategies—is also crucial [12].

Although many LMICs have developed national action plans (NAPs) for AMR, implementation is inconsistent and hindered by governance gaps. Assessments of NAPs highlight areas requiring strengthening, including accountability, sustained engagement, equity, behavioral economics, sustainability planning, transparency, international collaboration, and integration of the environmental sector [12]. This persistent gap between policy development and practical implementation underscores the need for robust governance, accountability mechanisms, and cross-sectoral collaboration to ensure the effectiveness of global AMR strategies.

Conclusion

Antimicrobial resistance (AMR) represents one of the greatest threats to global health, economics, and development, requiring urgent and coordinated action. Despite significant international strategies, such as the WHO Global Action Plan, challenges persist due to weak governance, limited resources, cultural factors, and inadequate surveillance systems, particularly in LMICs. At the same time, scientific and technological innovations - including artificial intelligence, nanotechnology, and open-access data platforms - show promising potential to strengthen prevention, diagnosis, and treatment. However, sustainable progress depends on overcoming economic disincentives, investing in research and development, and ensuring global collaboration across human, animal, and environmental health sectors. Ultimately, addressing AMR demands a unified, multidisciplinary, and equitable approach to safeguard the effectiveness of antimicrobials and protect global health security.

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