

## ANIMAL AND HUMAN HEALTH AND ANTIMICROBIAL RESISTANCE

Krassimira Zaykova<sup>1</sup>, Hristo Zaykov<sup>2</sup>, Asena Serbezova<sup>3</sup>

<sup>1</sup>Medical University-Varna, Faculty of Medicine, 55 Marin Drinov St., Varna 9002, Bulgaria

<sup>2</sup>Medical University-Varna, Faculty of Pharmacy, 84 Tzar Osvoboditel St., Varna 9000, Bulgaria

<sup>3</sup>Medical University-Sofia, Faculty of Public Health, 8 Bialo more St., Sofia 1527, Bulgaria

### Abstract

Antimicrobial resistance (AMR) represents a formidable global health crisis, compelling the adoption of the One Health approach which integrates human, animal, and environmental health sectors. This publication examines the challenges and strategies in combating AMR, emphasizing the application of One Health principles, especially in resource-constrained settings. The paper outlines significant lessons learned from successful AMR interventions worldwide. Materials and methods: The methodology involves a literature review and analysis of scientific articles available in global databases dedicated to the issue of AMR, as well as materials related to the implementation of various strategies to combat AMR at the national and governmental levels. Results: Challenges identified relate to gaps in surveillance, education, international cooperation, and resource allocation in low-resource settings. The analysis further delves into future research implications, advocating for a deeper understanding of resistance mechanisms, the impact of interventions, the development of rapid diagnostics, vaccine research, and the exploration of alternative therapies. Examples from the European Union, Bangladesh, Canada, China, India, and the USA have been examined. Conclusions: The paper concludes by calling for intensified collaborative efforts to mitigate AMR and tailored strategies that recognize the diverse contexts of countries grappling with resource limitations. Suggesting that addressing AMR requires concerted global efforts, the publication outlines actionable strategies within the One Health framework to maintain the effectiveness of antimicrobials. The future direction emphasizes the significance of comprehensive surveillance, the impact evaluation of interventions, policy development, and community engagement in ensuring sustainable solutions to AMR.

**Key words:** animal health, human health, antimicrobial resistance (AMR), One Health approach

### Introduction

Antimicrobial resistance is one of the most pressing global health challenges of our time, posing a significant threat to both human and animal health. This silent pandemic has the potential to undo decades of medical progress, pushing us closer to a post-antibiotic era where simple infections could once again become deadly. The widespread use of antimicrobial agents in animal populations, particularly for growth promotion and prophylaxis, has contributed to the selective pressure on microorganisms, leading to the emergence and spread of resistant strains [1, 2]. How does AMR impacts human and animal health? AMR reduces the effectiveness of antibiotics, making it difficult or even impossible to treat bacterial infections [3]. This leads to longer illnesses, increased risk of complications, and higher mortality rates. Treating resistant infections requires longer hospital stays, more expensive medications, and specialized care, placing a significant burden on healthcare systems worldwide. AMR impacts animal health and welfare, leading to prolonged illnesses, increased mortality, and reduced productivity in livestock [1, 2]. AMR can lead to significant economic losses for farmers due to reduced production, increased veterinary costs, and trade restrictions. The widespread use of antimicrobials in agriculture contributes to the emergence and spread of AMR, threatening the sustainability of food production and global food security [4]. The interconnectedness of human, animal, and environmental health means that AMR in one area can quickly spread to others [5]. For instance, resistant bacteria originating in livestock can spread to humans through the food chain or direct contact, and vice versa. Addressing AMR requires a global, collaborative effort. We need to adopt a One Health approach that recognizes the interconnectedness of human, animal, and environmental health to effectively combat this growing threat. This perspective is crucial in addressing the complex issue of antimicrobial resistance, as it requires a comprehensive understanding of the factors contributing to the problem and the implementation of coordinated

strategies across different sectors [6]. Humans and animals share many of the same microbes [7]. The overuse or misuse of antimicrobials in any sector (human health, animal health, or agriculture) can lead to the development and spread of resistant bacteria that can affect both populations. The environment plays a crucial role in the transmission of AMR. Improper disposal of pharmaceutical waste, agricultural runoff, and inadequate sanitation can contaminate water and soil, creating reservoirs for resistant bacteria to thrive and spread to humans and animals [6]. Addressing AMR requires a coordinated effort from various sectors, including human and veterinary medicine, agriculture, environmental health, and policymakers [7]. One Health provides a framework for these stakeholders to work together, share information, and implement comprehensive strategies to mitigate the emergence and spread of AMR. By acknowledging the interconnectedness of human, animal, and environmental health, One Health encourages a holistic approach to AMR. This collaborative framework is essential for developing effective strategies to prevent, control, and mitigate the threat of AMR. Antimicrobials, including antibiotics, have revolutionized medicine and dramatically improved human and animal health since their discovery. However, the widespread use of these drugs has also fueled the rise of antimicrobial resistance, presenting a significant threat to global health. Despite their benefits, antimicrobials are often overprescribed or used inappropriately, such as for viral infections, which they cannot treat. This practice contributes significantly to the development and spread of AMR [8]. Hospitals are a significant source of AMR due to the high concentration of patients with weakened immune systems and the frequent use of broad-spectrum antibiotics. In livestock production, antimicrobials are sometimes used prophylactically to prevent disease outbreaks, especially in intensive farming systems. However, this practice can contribute to AMR [9]. For decades, subtherapeutic doses of antimicrobials have been used in animal feed to promote growth and improve feed efficiency in livestock. This practice is a major driver of AMR and has been banned or restricted in many countries [10]. Like veterinary medicine, antimicrobials are used in agriculture to prevent disease outbreaks in livestock, but this practice can also contribute to AMR if not carefully managed [11]. The widespread use of antimicrobials across these sectors has created selective pressure that favors the survival and spread of resistant bacteria [9]. This highlights the urgent need for responsible antimicrobial stewardship in all sectors to preserve the effectiveness of these life-saving drugs for future generations.

### Objective

This paper aims to provide a comprehensive literature review on the complex issue of antimicrobial resistance at the animal-human interface examining the challenges and strategies in combating AMR, emphasizing the application of One Health principles. The paper outlines significant lessons learned from successful AMR interventions worldwide.

### Materials and methods

The methodology involves a literature review and analysis of scientific articles available in global databases dedicated to the issue of AMR, as well as materials related to the implementation of various strategies to combat AMR at the national and governmental levels.

### Results

#### 1. Key strategies to combat AMR

Combating the global threat of AMR requires a multifaceted approach involving individuals, healthcare professionals, veterinarians, agricultural practices and policymakers. The key strategies to combat AMR are summarized in Table 1. Addressing AMR requires a sustained and coordinated effort from all stakeholders. By implementing these strategies, we can mitigate the impact of AMR, preserve the effectiveness of existing antimicrobials, and protect human and animal health for future generations.

**Table 1. Key strategies to combat AMR**

**2. One Health in action: success stories to combat AMR**

**2.1. AMR Strategies in European Union: the multifaceted approach**

The European Union recognizes antimicrobial resistance as a significant threat to public health and has implemented a comprehensive strategy to combat it. This strategy, based on the One Health approach, involves coordinated action across various sectors and levels, presented in Table 2.

**Table 2. Tackling Antimicrobial Resistance: The European Union's Multifaceted Approach**

**2.2. US National Antimicrobial Resistance Monitoring System (NARMS)**

A collaborative effort between the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and U.S. Department of Agriculture (USDA). NARMS monitors antimicrobial resistance in bacteria from humans, retail meats, and food animals in the United States. NARMS provides crucial data on emerging resistance trends, helping to identify potential foodborne threats and guide interventions in both human and animal health [13,19].

**2.3. Canadian Antimicrobial Resistance Surveillance System (CARSS)**

Established in 2017, CARSS is a national system that monitors trends in antimicrobial use and resistance in humans, animals, and the environment [20,21]. Canadian Nosocomial Infection Surveillance Program tracks healthcare-associated infections, including those caused by resistant organisms [22]. Pan-Canadian Framework for Action outlines a collaborative approach to address AMR, involving federal, provincial, and territorial governments, as well as stakeholders in human and animal health, and the environment.

**2.4. China's Growing Role in the One Health Approach to Antimicrobial Resistance**

China has developed and implemented a National Action Plan on Antimicrobial Resistance, outlining strategies for surveillance, prevention, control, and research across human, animal, and environmental sectors. The country has been enhancing its AMR surveillance systems, including the establishment of the China Antimicrobial Resistance Surveillance System to monitor resistance trends in humans and animals [23]. The Chinese government has introduced regulations to restrict the use of antimicrobials in livestock feed and promote responsible antimicrobial use in both human and veterinary medicine.

**2.5. National Strategic Plan for Antimicrobial Resistance Containment in Bangladesh**

Bangladesh developed a National Strategic Plan for Antimicrobial Resistance Containment to guide national efforts in AMR surveillance, prevention, control, and research. Training programs are being organized for healthcare professionals, pharmacists, and veterinarians on AMR, antimicrobial stewardship, and infection control. National Guidelines for Antimicrobial Susceptibility Testing were developed to standardize laboratory practices and improve the accuracy of AMR surveillance data. Several research institutions and universities in Bangladesh are conducting studies on AMR prevalence, mechanisms of resistance, and interventions [24]. Some hospitals in Bangladesh are implementing antimicrobial stewardship programs to optimize antibiotic use and reduce resistance [25]. Public awareness campaigns are being conducted to educate the population about AMR and the importance of responsible antimicrobial use [26].

**2.6. India's Action Plan**

The National Action Plan for AMR was launched in 2017 [27]. The plan provides a comprehensive framework for tackling AMR across various sectors, including human health, animal health, and the environment. The government has taken steps to regulate the sale of antibiotics, making

it mandatory for pharmacies to dispense antibiotics only on prescription [28]. Efforts are underway to implement antimicrobial stewardship programs in hospitals and other healthcare settings to promote appropriate antibiotic use [29].

### Discussion

Antimicrobial resistance (AMR) is a challenge that all countries are facing. Every nation, regardless of its level of development, encounters difficulties in this struggle. It is essential that AMR strategies are successful; therefore, they must be based on the One Health approach and foster international collaboration in this field. A review of the literature in this field has indicated that, particularly in recent years, countries have been making more comprehensive and standardized efforts to combat AMR. However, it is evident that there are numerous challenges that countries from various regions face, which we identified during the review. For the European Union, these challenges are implementation gaps (the implementation varies across member-states); data sharing and behavioral change (addressing inappropriate antimicrobial use requires sustained efforts to change prescribing behaviors among healthcare professionals and antimicrobial use practices in agriculture). Key challenges for Canada are rising resistance rates for several important pathogens, including methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci [22]; inappropriate use and overuse of antibiotics [30], agricultural use of antimicrobials and knowledge gaps about AMR transmission pathways. For Bangladesh and India, the challenges identified are resource constraints in implementing comprehensive AMR control programs; lack of awareness about AMR among the general public, healthcare providers, and policymakers and weak enforcement of regulations related to antimicrobial use [24-29].

### Conclusion

Addressing the issue of antimicrobial resistance requires a multifaceted approach that encompasses various strategies across different sectors. Preserving the continued effectiveness of existing antimicrobials is crucial, which can be achieved by eliminating their inappropriate use and limiting the spread of resistant microorganisms. Collaboration between human and veterinary health professionals, as well as environmental scientists, is necessary to develop and implement comprehensive solutions to this complex challenge. Despite the challenges, countries from different regions across the globe are making progress in addressing AMR. Continued efforts and collaboration with international partners will be essential to effectively combat AMR.

### Statement for Potential Conflicts of Interest

The authors declare that they have no potential conflicts of interest related to this research.

### References

1. Bava R, Castagna F, Lupia C, Poerio G, Liguori G, Lombardi R, Naturale MD, Mercuri C, Bulotta RM, Britti D, Palma E. Antimicrobial Resistance in Livestock: A Serious Threat to Public Health. *Antibiotics*. 2024 Jun 13;13(6):551.
2. Marco-Fuertes A, Marin C, Lorenzo-Rebenaque L, Vega S, Montoro-Dasi L. Antimicrobial resistance in companion animals: a new challenge for the One Health approach in the European Union. *Veterinary Sciences*. 2022 Apr 24;9(5):208.
3. Jasovský D, Littmann J, Zorzet A, Cars O. Antimicrobial resistance—a threat to the world's sustainable development. *Upsala journal of medical sciences*. 2016 Jul 2;121(3):159-64.
4. Zhao C, Wang Y, Mulchandani R, Van Boeckel TP. Global surveillance of antimicrobial resistance in food animals using priority drugs maps. *Nature communications*. 2024 Jan 26;15(1):763.
5. Iriti M, Vitalini S, Varoni EM. Humans, animals, food and environment: One health approach against global antimicrobial resistance. *Antibiotics*. 2020 Jun 19;9(6):346.

## Science & Research

6. McEwen SA, Collignon PJ. Antimicrobial resistance: a one health perspective. *Antimicrobial resistance in bacteria from livestock and companion animals*. 2018 Oct 1:521-47.
7. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: one health approach. *Veterinary world*. 2022 Mar;15(3):743.
8. Meek RW, Vyas H, Piddock LJ. Nonmedical uses of antibiotics: time to restrict their use?. *PLoS biology*. 2015 Oct 7;13(10):e1002266.
9. Schwarz S, Kehrenberg C, Walsh TR. Use of antimicrobial agents in veterinary medicine and food animal production. *International journal of antimicrobial agents*. 2001 Jun 1;17(6):431-7.
10. Burroughs T, Najafi M, Lemon SM, Knobler SL (Eds.) *Institute of Medicine (US) Forum on Emerging Infections*, Washington (DC): National Academies Press (US), 2003.
11. McEwen SA, Fedorka-Cray PJ. Antimicrobial use and resistance in animals. *Clinical infectious diseases*. 2002 Jun 1;34(Supplement\_3):S93-106.
12. Murthy R. Implementation of strategies to control antimicrobial resistance. *Chest*. 2001 Feb 1;119(2):405S-11S.
13. CDC. About One Health [Internet]. One Health. 2024. Available from: <https://www.cdc.gov/one-health/about/index.html>
14. Sirota M, Habersaat KB, Betsch C, Bonga DL, Borek A, Buckel A, Butler R, Byrne-Davis L, Caudell M, Charani E, Geiger M. We must harness the power of social and behavioural science against the growing pandemic of antimicrobial resistance. *Nature Human Behaviour*. 2024 Jan;8(1):11-3.
15. Miteu GD, Achinebiri P, Raghunathan N, Sankaran S. Closing potential drivers of antimicrobial resistance: last-resort antimicrobials with the potential of being misused, the way forward—a short communication. *Annals of Medicine and Surgery*. 2023 Jun 1;85(6):3226-31.
16. Special Report Addressing antimicrobial resistance: progress in the animal sector, but this health threat remains a challenge for the EU [Internet]. [cited 2024 Aug 20]. Available from: [https://www.eca.europa.eu/Lists/ECADocuments/SR19\\_21/SR\\_Antimicrobial\\_resistance\\_EN.pdf](https://www.eca.europa.eu/Lists/ECADocuments/SR19_21/SR_Antimicrobial_resistance_EN.pdf)
17. Simonsen GS. Antimicrobial resistance surveillance in Europe and beyond. *Eurosurveillance*. 2018 Oct 18;23(42).
18. Antimicrobial resistance in the EU/EEA -AER 2019 SURVEILLANCE REPORT Antimicrobial resistance in the EU/EEA (EARS-Net). Available from: [https://www.ecdc.europa.eu/sites/default/files/documents/TQ-AC-20-001-EN-N\\_0.pdf](https://www.ecdc.europa.eu/sites/default/files/documents/TQ-AC-20-001-EN-N_0.pdf)
19. Csis.org. 2024 [cited 2024 Aug 20]. Available from: <https://www.csis.org/analysis/us-government-and-antimicrobial-resistance>.
20. Canadian Antimicrobial Resistance Surveillance System (CARSS) Report 2022 [Internet]. www.canada.ca. 2022. Available from: <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-report-2022.html>
21. Canadian Antimicrobial Resistance Surveillance System Report [Internet]. Available from: <https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-report-2021/canadian-antimicrobial-resistance-surveillance-system-report-2021.pdf>
22. Conly J. Antimicrobial resistance in Canada. *Cmaj*. 2002 Oct 15;167(8):885-91.
23. Zhou N, Cheng Z, Zhang X, Lv C, Guo C, Liu H, Dong K, Zhang Y, Liu C, Chang YF, Chen S. Global antimicrobial resistance: a system-wide comprehensive investigation using the Global One Health Index. *Infectious diseases of poverty*. 2022 Aug 23;11(1):92.
24. Ahmed I, Rabbi MB, Sultana S. Antibiotic resistance in Bangladesh: A systematic review. *International Journal of Infectious Diseases*. 2019 Mar 1;80:54-61.
25. Yusuf MA. Antimicrobial Stewardship: Bangladesh Perspective. *Bangladesh Journal of Infectious Diseases*. 2018 Aug 4;5(1):1-2.

## Science & Research

26. Yusuf MA. Prevention of Antimicrobial Resistance: Bangladesh Perspective. *Journal of Current and Advance Medical Research*. 2018 May 3;5(1):1-2.
27. Chandra P, Mk U, Ke V, Mukhopadhyay C, U DA, V R. Antimicrobial resistance and the post antibiotic era: better late than never effort. *Expert opinion on drug safety*. 2021 Nov 2;20(11):1375-90.
28. Ranjalkar J, Chandy SJ. India's National Action Plan for antimicrobial resistance—An overview of the context, status, and way ahead. *Journal of family medicine and primary care*. 2019 Jun 1;8(6):1828-34.
29. Walia K, Madhumathi J, Veeraraghavan B, Chakrabarti A, Kapil A, Ray P, Singh H, Sistla S, Ohri VC. Establishing antimicrobial resistance surveillance & research network in India: journey so far. *Indian Journal of Medical Research*. 2019 Feb 1;149(2):164-79.
30. Tan C, Graves E, Lu H, Chen A, Li S, Schwartz KL, Daneman N. A decade of outpatient antimicrobial use in older adults in Ontario: a descriptive study. *Canadian Medical Association Open Access Journal*. 2017 Dec 21;5(4):E878-85.

**Table 1. Key strategies to combat AMR**

Strategy	Elements
<b>Reducing Antimicrobial Use and Misuse</b>  Implementing robust stewardship programs in healthcare settings and agricultural practices is crucial	<b>Optimizing Prescribing Practices:</b> Encouraging healthcare professionals to prescribe antibiotics only when necessary, selecting the appropriate medicines and dosage, and limiting treatment duration [12]. <b>Restricting Over-the-Counter Access:</b> In certain countries, limiting over-the-counter access to antibiotics without a prescription can help curb unnecessary use. <b>Promoting Alternatives in Agriculture:</b> Phasing out the use of antimicrobials for growth promotion in livestock and exploring alternative strategies like improved hygiene, vaccination, and disease surveillance [8].
<b>Prevention the Spread of Infection</b>  Implementing rigorous infection control measures in healthcare facilities, communities, and agricultural settings is essential.	<b>Hand Hygiene:</b> Promoting frequent and thorough handwashing with soap and water or alcohol-based sanitizers. <b>Vaccination:</b> Encouraging vaccination against common infectious diseases to reduce the need for antimicrobial treatments. <b>Improved Sanitation and Hygiene:</b> Ensuring access to clean water, sanitation facilities, and promoting good hygiene practices in communities and livestock operations [6].
<b>Promoting Research and Innovation</b>	<b>New Antimicrobials:</b> Investing in research and development of new antibiotics, alternative therapies (like phage therapy), and novel approaches to combat resistant infections is crucial [Innovations to Slow Antibiotic Resistance, 2023]. <b>Diagnostics:</b> Developing rapid and accurate diagnostic tools to identify the causative agent of an infection and determine its susceptibility to specific antimicrobials can help guide appropriate treatment and reduce unnecessary antibiotic use [13]. <b>Vaccines:</b> Supporting the development of new vaccines for both humans and animals to prevent bacterial infections and reduce the reliance on antimicrobials.

<b>Raising Awareness and Education</b>	<p><b>Public Awareness Campaigns:</b> Educating the public about AMR, its consequences, and the importance of responsible antimicrobial use through various channels [14].</p> <p><b>Training Healthcare Professionals:</b> Providing ongoing education and training to healthcare professionals on antimicrobial stewardship, infection control, and the latest developments in AMR.</p> <p><b>Engaging the Agricultural Sector:</b> Raising awareness among farmers and veterinarians about responsible antimicrobial use in livestock and promoting best practices.</p>
<b>Global Collaboration and Surveillance</b>	<p><b>International Cooperation:</b> Strengthening global surveillance networks to track the emergence and spread of resistant organisms and share information on effective interventions [15].</p> <p><b>Policy and Regulations:</b> Implementing and enforcing policies to regulate antimicrobial use in human and veterinary medicine, as well as in agriculture [15].</p>

**Table 2. Tackling Antimicrobial Resistance: The European Union's Multifaceted Approach**

Strategy	Actions
<b>Policy &amp; Legislation</b>	<p><b>EU One Health Action Plan against AMR</b> [16].</p> <p><b>EU legislation on veterinary medicines and medicated feed:</b> These regulations aim to restrict the use of antimicrobials in animals, particularly those critically important for human health [16].</p> <p><b>European Antimicrobial Awareness Day:</b> Held annually, this initiative aims to raise awareness about AMR and promote prudent antimicrobial use.</p>
<b>Surveillance and Monitoring</b>	<p><b>European Antimicrobial Resistance Surveillance Network:</b> This network collects and analyzes data on antimicrobial resistance in bacteria from humans across EU/EEA countries [17,18].</p> <p><b>European Surveillance of Veterinary Antimicrobial Consumption:</b> This program monitors antimicrobial consumption in animals across the EU.</p>
<b>Antimicrobial Stewardship</b>	<p><b>EU Guidelines on Prudent Use of Antimicrobials:</b> These guidelines provide recommendations for healthcare professionals on appropriate antimicrobial prescribing.</p> <p><b>National Action Plans:</b> EU member states have developed national action plans on AMR, outlining strategies for antimicrobial stewardship in human and veterinary medicine.</p>
<b>Infection Prevention and Control</b>	<p><b>EU Standards for Infection Control:</b> The EU has established standards for infection prevention and control in healthcare settings.</p> <p><b>Vaccination Programs:</b> The EU promotes vaccination programs to prevent infectious diseases and reduce the need for antimicrobials.</p>

## Science & Research

<b>Research and Innovation</b>	<b>EU Funding for AMR Research:</b> The EU provides significant funding for research on new antimicrobials, diagnostics, and alternative therapies. <b>Innovative Partnerships:</b> The EU supports public-private partnerships to accelerate the development of new solutions for AMR.
<b>International Collaboration</b>	<b>Global Health Security Agenda:</b> The EU actively participates in the Global Health Security Agenda, working with international partners to combat AMR. <b>Joint Programming Initiative on Antimicrobial Resistance:</b> This initiative brings together EU member states and associated countries to coordinate research efforts on AMR.