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Antimicrobial Resistance: Implementing an Effective Response for a Growing Global Health Threat

Susan Ekuri

ABSTRACT

The growing threat of antimicrobial resistance (AMR) is a major public health challenge. The rising prevalence of resistant microbes increases the risk of spreading infectious diseases. Although AMR has gained global attention in recent years, public health experts are still faced with the challenge of implementing effective policies and programmes to combat the threat.

The aim of this review was to examine the global health threat and significance of AMR. The review explores the public health impact of AMR and the drivers of its spread as well as the current strategies used in combating the problem. The paper also critically analyses the existing public health response, policies and legislations and offers possible future directions for a more effective response.

Google and Google Scholar search engines as well as the PubMed database were searched to identify literature concerning the global impact of AMR as well as the public health response and the current control strategies. Websites of the World Health Organization and similar organisations were also searched. The key search terms used were ‘antimicrobial resistance’, ‘global health’, ‘impact’ and ‘response’.

The review findings highlighted the challenges and gaps in the current response ranging from inadequate implementation of national plans due to poor commitment to a lack of surveillance data. Other challenges include the multifactorial drivers of AMR, changing trends and diverse geographical patterns of some of these factors.

This article was able to emphasise the urgent need for a coordinated global plan, multi-sectoral collaboration among key stakeholders, including embracing a One Health approach to address the use of antimicrobials in agricultural practices for food production. The control of AMR requires a more uniform and guided response for more effective AMR action.

Keywords: Antimicrobial resistance, Public health policies, Antibiotic misuse, Global health threat, One health approach

Introduction

Antimicrobial resistance (AMR) is a public health issue of growing concern on a global level. Antimicrobials are medicines used to treat and prevent infections in humans, animals and plants. They include antibiotics, antifungals and antiparasitics¹ AMR occurs when antimicrobial drugs are no longer able to inhibit the activity of microorganisms¹ This results in drug resistance and, as a result, the drugs are ineffective and infections become difficult to treat.¹ AMR increases the risk of the spread of infections and diseases, leading to increased disability and death.¹

AMR is mainly caused by the misuse and overuse of antimicrobials, which leads to the development of drug-resistant pathogens.¹ Improper use of antibiotics is further exacerbated by poverty and inequality and is most prevalent in low- and middle-income countries.¹ Research shows that the highest burdens associated with AMR are in sub-Saharan Africa and South Asia.² Factors such as lack of access to clean water, poor infection control and disease prevention practices and limited access to vaccines, medicines and health facilities are all drivers of the problem.¹ These factors are more common in low-resource and vulnerable communities.¹

The global burden of AMR is quite significant. According to the World Health Organization (WHO), approximately 1.27 million deaths were directly caused by bacterial AMR worldwide in 2019^{1,2} (see Figure 1). It also contributed to 4.95 million deaths in the same year.^{1,2} It is projected that AMR could cause up to 10 million deaths by 2050³ (see Figure 2). Alongside morbidity and mortality, the economic cost of AMR is also significant. According to the World Bank, AMR could lead to an additional 1 trillion US dollars in healthcare costs by 2050.⁴ Due to drug resistance, there is a need for more treatment and care strategies that are expensive, as well as longer hospital stays.¹ AMR is also estimated to result in 1 trillion to 3.4 trillion US dollars gross domestic product losses per year by 2030.⁴

Other health challenges caused by AMR include increased difficulty with treating infections and increased risk with medical procedures, such as surgeries.¹ Drug resistance also threatens animal and plant health, agricultural productivity and food security.¹

Among the strategies developed to address AMR are improving access to quality diagnosis and treatment of infections, implementing infection prevention measures which reduce indiscriminate antimicrobial use and developing new vaccines and medicines.^{1,5} However, there is an urgent need for additional research in the area of drug resistance as well as improving efforts in achieving equitable medicine access.¹

In spite of the global attention on AMR, there is still inadequate implementation of national plans and uncertain progress in addressing the problem.⁵ Limited data availability on infections from low- and middle-income countries restricts the implementation of national policies.^{2,6} The overall response to AMR globally remains inadequate and fragmented.⁷

In light of the global threat of AMR, research is required to understand the gaps in current strategies to curb the problem. There is an urgent need to analyse the dynamics and challenges facing AMR management.

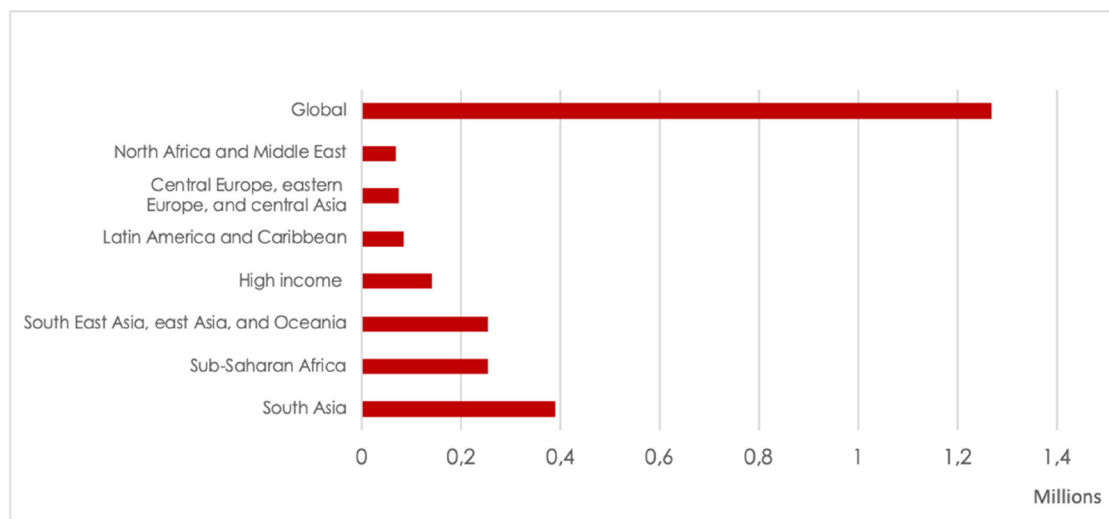


Fig 1 | Attributable deaths to antibiotic resistance 1.27 million deaths direct result of antibiotic resistance infections in 2019

Source: React. Antibiotic resistance claims more than 1.2 million lives a year. 2022. <https://www.reactgroup.org/news-and-views/news-and-opinions/year-2022/antibiotic-resistance-claims-more-than-1-2-million-lives-a-year-says-new-large-study/>



Fig 2 | Global impact of AMR

Source: Fleck A Antimicrobial Resistance. Deaths from drug-resistant infections set to skyrocket. 2023 <https://www.statista.com/chart/3095/drug-resistant-infections/>

The aim of this paper is to examine the public health significance of AMR, explore the gaps in existing strategies and offer possible suggestions for equitable and cost-effective interventions for controlling the threat.

Methods

A literature review was conducted to address the global impact of AMR, the public health response and the current control strategies. Various search terms, search engines and databases were used to ensure relevant literature was captured. The key search terms used in the search include 'antimicrobial resistance', 'global health', 'impact' and 'response'. Articles searched include research studies, reviews, opinion pieces and reports written in English. Google and Google Scholar search engines and PubMed database as well as

websites of WHO and similar organisations like the World Bank Group were searched.

Study Findings and Results

This review identified literature that examined the public health significance of AMR, including the gaps and challenges in current response strategies. The following themes were identified across the selected literature: the current situation of the AMR threat, the major drivers of AMR and the current strategies in place to curb the problem.

Current Situation

Since the discovery of antimicrobials over 70 years ago, their use has helped destroy disease-causing microbes, including bacteria, viruses, parasites and

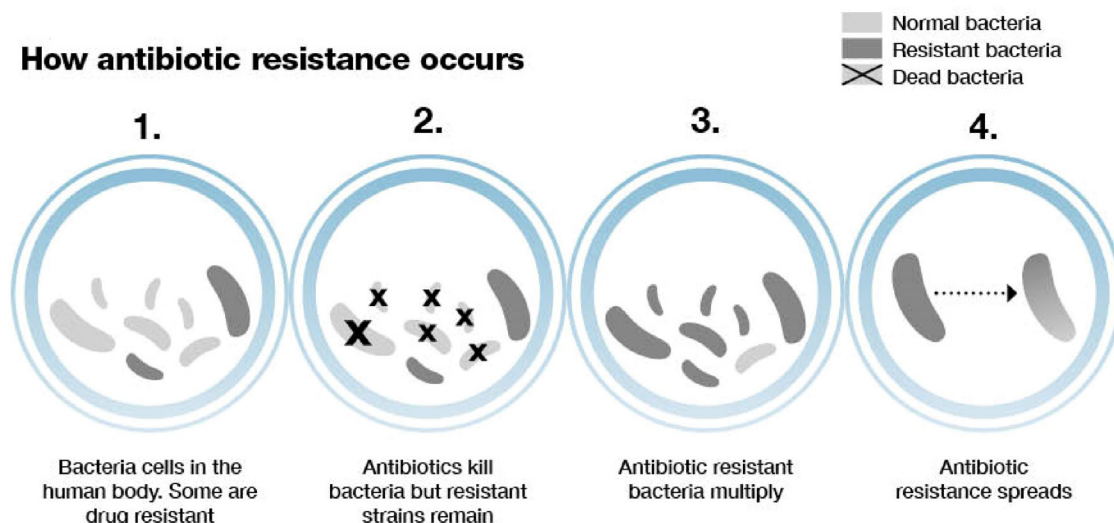


Fig 3 | How antibiotic resistance occurs

Source: PHE. Health matters: antimicrobial resistance. 2015. <https://www.gov.uk/government/publications/health-matters-antimicrobial-resistance/health-matters-antimicrobial-resistance>

fungi.⁴ In the course of eliminating pathogens, antimicrobials have helped save millions of lives.⁴ Unfortunately, evolutionary changes allow pathogens to resist the effects of antimicrobials, which brings about AMR⁴ (see Figure 3).

Drug-resistant pathogens cause infections that are difficult to treat, thus increasing the cost of medical care.⁴ The growing trend of AMR has the potential to reverse the public health progress made in the last century, including the accompanying global economic growth and development.⁴ In 2019, the WHO listed AMR among the top 10 global public health issues threatening the world's population.⁸

For several years, countries have been tasked with developing and implementing individual AMR National Action Plans.⁹ However, the burden of AMR remains significant despite their efforts, with low- and middle-income countries, particularly in sub-Saharan Africa, bearing the bulk of the impact.² For instance, children in sub-Saharan Africa are almost 60 times more likely to die from AMR than their counterparts in high-income countries.² It is estimated that the burden of AMR will increase significantly over the next two decades,⁷ with millions of people likely to be pushed into extreme poverty by 2050.⁴

So far, efforts by governments and stakeholders have resulted in commitments that do not provide sustained, consistent AMR action at the national or global level.⁷ There is a lack of cohesiveness, accountability and shared vision across various countries.⁷ In addition to this, inadequate surveillance data on infections and AMR is also a significant challenge.^{2,7} Information on the patterns of consumption and levels of resistance of antimicrobials is important.³ This is necessary to allow countries adequately understand AMR trends and prioritise next steps and areas for interventions.⁷ Surveillance data can also help countries monitor the impact of AMR-targeted interventions.¹⁰

However, surveillance is lacking in many parts of the world, leaving large gaps of the much-needed information on the trends of consumption and drug resistance.¹⁰

Drivers of AMR

Multiple factors contribute to the spread of AMR. These factors range from antibiotic overuse to poor sanitation and hygiene, sub-standard or counterfeit antibiotics, limited laboratory infrastructure and poor access to second-line and third-line antibiotics.^{2,11} Others include poverty, lack of education and misconception.¹⁵ Some of the major drivers are elaborated in the following section.

Antibiotic Overuse

Overuse and misuse of antimicrobials lead to AMR emergence and spread.⁴ According to a study by Klein et al., antibiotic use increased by 65% globally between 2000 and 2015, particularly across low- and middle-income countries.¹² This excessive use of antibiotics in low-resource settings is a result of the easy accessibility of antimicrobials, which can be purchased easily without prescription.¹⁰ In many developing countries, antibiotics are sold over the counter, which encourages self-medication.¹⁰ In Africa, antimicrobial use without prescription is as high as 100%, while in Asia, it is up to 58%.¹³ In Southern Europe, Northern Europe and Central Europe, self-medication is reported at 19%, 3% and 6%, respectively.¹³

Misuse of antibiotics also includes inappropriate use and choices, suboptimal dosing and poor adherence to treatment guidelines.¹⁰ Inappropriate prescribing of antibiotics is a contributory factor to their overuse.¹⁴ There is an overreliance on antibiotics for the purpose of patient management in many developing countries, where there is inadequate diagnostic infrastructure.¹⁵ On the other hand, in high-income countries, misuse

and overuse of antibiotics have led to the development of 'superbugs', microbes that are resistant to most antimicrobial drugs.^{14,16} These superbugs cause infections that have high morbidity and mortality as there are limited or no treatment options available.¹⁶ For example, multidrug-resistant tuberculosis (MDR-TB) is responsible for 3.5% of active tuberculosis (TB) and 18% of previously treated TB cases worldwide.¹⁷

Antimicrobial misuse and overuse is also of significant concern in agriculture, where its effects can impact human health. Consumption of animal products and vegetables that contain resistant bacteria can lead to their transmission to humans.¹⁹ The use of antimicrobials for disease treatment or prevention in food-producing animals contributes to the problem of AMR.¹⁰ The AMR Action Plan launched by the WHO in 2015 acknowledges the concerns in the agricultural sector, as it highlights the need for a One Health approach.¹⁹ With this approach, initiatives and policies developed for containing AMR will incorporate human and veterinary medicine, agriculture and the environment.¹⁹

Access to Sanitation and Healthcare Services

Poor access to water, sanitation and hygiene as well as healthcare services encourages the spread of AMR in low- and middle-income countries.¹⁴ A study by Luchen et al. shows that inadequate access to water, sanitation and hygiene facilities in low-resource settings promotes the transmission of AMR bacteria between humans, animals and the environment.¹⁸ This highlights the cyclical nature of the problem of resistant bacterial transmission.¹⁸ Failure to adhere to proper infection control measures in hospital settings also fuels AMR pathogens.^{14,19} This is because healthcare facilities are perfect breeding grounds for resistant microorganisms.¹⁴ Patients on admission in hospitals have a higher chance of developing AMR than outpatients.²⁰ Prolonged hospital stays and extensive use of antimicrobial drugs contribute to the development and spread of resistant hospital-acquired infections.¹⁰

Current Strategies

Addressing the challenge of AMR involves the implementation of five main categories of strategies. These include infection prevention and control, vaccination, reducing exposure to antibiotics, ensuring appropriate use of antibiotics and investment in the development of new antibiotics.²

Developing improved access to vaccines, water, sanitation and hygiene infrastructure and implementing infection control measures are among the current strategies being implemented to reduce AMR-related morbidity and mortality, especially in low-resource settings.⁵ Infection prevention and control is the bedrock of preventing infectious diseases and is, therefore, a critical aspect of managing AMR.²¹ Studies have shown a reduction in sepsis-related deaths between 1990 and 2017.²² This was mainly as a result of a decline in child mortality¹⁸ and the prevention of deaths from lower respiratory infections²³ and diar-

rhoea, conditions which are preventable with access to vaccines and hygiene infrastructure.^{24,25} Therefore, infection prevention programmes, particularly community-based programmes in resource-poor settings with poor sanitation infrastructure, remain vital in combating AMR.^{2,26}

Immunisation is a well-known strategy effective in the prevention of infectious diseases.¹ Vaccination programmes help prevent infections, thus reducing the need for antibiotics.¹⁹ The WHO encourages the use of vaccines which target resistant microbes, particularly *Klebsiella pneumoniae*.¹ Studies show that maternal vaccination against *K. pneumoniae* has the potential to prevent over 80,000 neonatal deaths and almost 400,000 cases of neonatal sepsis annually worldwide.²⁷ Research and development for new vaccines for pathogens that currently have none is also important.²

Reducing exposure to antibiotics and ensuring appropriate use of antibiotics are also strategies currently in place against the spread of AMR.² Clinicians are encouraged to accurately diagnose infections so that antibiotic use can be streamlined or stopped when necessary.²⁸ Strict legislation and enforcement around the sale of antimicrobials without prescription are policy measures to reduce antimicrobial overuse and misuse.⁴ Consistent investment in the development of new antibiotics is also an important strategy.²

However, future trends might necessitate a change in the approach to these interventions. An ageing population due to a demographic transition suggests an increase in chronic, non-communicable diseases and comorbidities. This results in a population more at risk of sepsis-related deaths and AMR mortality.⁵ Existing interventions such as vaccines are much less effective in this population group.⁵ In addition, there has been a reduction in the development of new antibiotics by pharmaceutical companies, with only a few new antibiotic groups in the pipeline.²⁹ There is, therefore, an urgent need to preserve the efficacy of the antimicrobials that are currently available.¹⁵

As the patterns and drivers of AMR differ geographically, tailor-made responses need to be implemented as opposed to a one-size-fits-all approach.² Ensuring the appropriate use of antibiotics, also known as antibiotic stewardship, is an important aspect of combating AMR. It involves implementing policies and regulations to restrict indiscriminate antibiotic use while promoting judicious administration of antibiotics by health professionals. However, some experts argue that reducing access to antibiotics may not be suitable in all settings.² For instance, in western sub-Saharan Africa, increasing access to antibiotics would help reduce the burden of AMR. This is because an increase in access will provide lifesaving second-line antibiotics where they are currently unavailable.² On the other hand, in South Asia, antibiotic stewardship is a more appropriate response because overuse of antibiotics is a major driver of AMR in that region.^{29,30}

In order to effectively manage AMR, it should not be managed in isolation. As drug-resistant infections are similar to all other diseases with a pandemic potential, it would be cost-effective over time to tackle the full range of infectious threats.⁴ This means establishing a common core of surveillance, diagnostic and disease control infrastructure and capabilities that addresses these threats.⁴ Robust national health systems, skilled and motivated health workforce and reliable health information systems are all necessary for effective AMR action.⁴

Discussion

The aim of this review was to examine the public health significance of AMR, with a focus on highlighting the gaps and challenges in current response strategies. The review analysed literature found in this area under three major themes: the current situation of the AMR threat, the major drivers of AMR and the current strategies in place to curb the problem.

Poor implementation of national action plans was identified as a key factor currently impeding progress in addressing the problem of AMR. This is largely due to a lack of commitment by governments, resulting in inconsistent and insufficient AMR action. In spite of the global attention on the threat of AMR over the last few years, stakeholders have yet to form a cohesive approach for sustained action.

A lack of surveillance data was also highlighted as a challenge, which contributes to insufficient AMR action. Data reports on antimicrobial consumption and resistance are inadequate in many countries, as such implementation of interventions is difficult. The changing population trends and the diverse geographical patterns of AMR emphasise a need for a shift in the current strategies for combating AMR. These include an ageing population more susceptible to infection-related deaths and less responsive to vaccines; differences in access to antibiotics and drivers of antibiotic resistance and reduction in the development of new antibiotic groups by pharmaceutical companies.

The findings of this review show that combatting AMR requires coordinated action across multiple sectors at national and international levels. International agencies, governments and non-governmental organisations need to strengthen collaboration to promote consistent effective action against AMR. Effective solutions for controlling the spread of AMR also require engagement and collaboration across human, agricultural and environmental sectors.¹² This One Health approach is critical to address the responsible use of antimicrobials in animals for food production.

There is also a need for uniform reporting of AMR infections and standardisation in the use of antibiotics.¹¹ This approach, in addition to improved diagnostics, will help highlight AMR prevalence patterns and better inform guidelines for appropriate antimicrobial use.¹² Existing strategies including improving access to water, sanitation and hygiene infrastructure, antimicrobial stewardship and investment in new medicines and vaccine research need to be strengthened.

Conclusion

AMR is a growing global health problem and a threat to public health worldwide, particularly in sub-Saharan Africa and South Asia. Its impact and implications are far-reaching from rising morbidity and mortality due to the spread of infectious diseases to increased health-care costs, economic cost and poverty. Despite the global attention and political inputs in recent years, AMR action remains inadequate. Current efforts have yet to be translated into sustained, consistent action. Surveillance data on AMR and consumption patterns are lacking in many countries, thus limiting the progress on implementation plans. The drivers of the spread of AMR are multifactorial and require coordinated action across multiple sectors to contain the problem. There is a need for a more coordinated global plan to address the issue of AMR. Tailor-made solutions that take into consideration the diverse geographical patterns of AMR and shift in population trends need to be developed and implemented. Current strategies and national action plans need to be strengthened with effective governance structures. Further research is also needed for the development of new vaccines and antibiotic groups.

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