

Mini Review

Global Burden and Future Outlook of Antimicrobial Resistance

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Abstract

Antimicrobial resistance (AMR) is a serious global health crisis. It is getting worse every year. Low- and middle-income countries (LMICs) are the most affected. This is mainly because infectious diseases are very common there. Poor water, sanitation, and hygiene (WASH) systems make things worse. On top of that, vaccination rates in these countries remain very low. All these factors together make AMR a much bigger threat in LMICs than anywhere else.

The recent data showed that bacterial AMR was linked to about 4.95 million deaths worldwide, and 1.27 million of the deaths were directly attributable in 2019. Using information from the Global Burden of Diseases, Injuries and Risk Factors Study 2021. The GBD Antimicrobial Resistance Collaborators employed statistical modelling to evaluate AMR trends from 1990 to 2021 and to forecast the burden through 2050 across 204 nations and territories.

The results are concerning. AMR-related deaths have increased significantly. Older adults aged 70 and above are the most affected group. However, there is some good news too. Deaths among children under five have dropped by nearly 50%. This is a big achievement. Better infection prevention has played a major role in this. Vaccination programs have also made a real difference. Improved water and sanitation (WASH) initiatives have helped as well. These combined efforts have clearly saved many young lives.

Key pathogens contributing to AMR mortality include *Klebsiella pneumoniae*, *Escherichia coli*, *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* (MRSA). In the absence of improved interventions, deaths attributable to AMR are anticipated to rise to 1.91 million annually by 2050. It is important to strengthen infection prevention, surveillance, vaccination, and WASH with integrated One Health approaches to ease the future impact of AMR.

Introduction

Global burden of AMR

The rising issue of antimicrobial resistance (AMR) is now acknowledged as a worldwide public health crisis [1]. This situation demands action from everyone. No single group can tackle AMR alone. Governments, healthcare workers, and communities must all work together. The evidence is very clear. AMR is directly linked to higher death rates. Patients with AMR infections also stay in hospitals much longer. This puts enormous pressure on healthcare systems. Urgent and

collective action is the only way forward. Impacting the economies of both communities and nations, particularly in low- and middle-income countries (LMICs) where the prevalence of infectious diseases is significantly greater [2]. The situation is aggravated with insufficient water, sanitation and hygiene (WASH) infrastructure and practices, alongside low vaccination rates [3].

Previous estimations released in 2022 suggested [4.95 million (95% UI 3.62–6.57)] deaths were associated with bacterial AMR [4]. This includes [1.27 million (0.911–1.71)]

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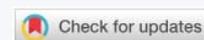
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deaths attributed to bacterial AMR in 2019 [5]. According to the data, it tracks how the burden of AMR has changed over time. It also looks ahead at what is coming. Experts have made forecasts for the next thirty years. The projections are alarming. AMR is expected to become an even greater threat. The burden on health systems will grow significantly. Understanding these trends is crucial. It helps policymakers prepare and respond in time. The present research, conducted by the GBD (2021) Antimicrobial Resistance Collaborators in The Lancet, employed a statistical modelling technique utilising various datasets to estimate the burden of AMR across different regions of the world [6].

They include seven countries' data with outputs and references derived from a thorough evaluation of the world AMR burden (1990 to 2021), the projections forecasting the AMR burden up to 2050 [4]. Calculating the AMR burden is not simple. It is based on several key factors. Deaths caused by infections are a major part of this calculation. Estimated rates of various underlying health conditions are also included. These figures are not random. They are taken from a well-known global study. It is called the Global Burden of Diseases, Injuries and Risk Factors Study 2021. This study is widely trusted by researchers and health experts. It provides reliable data from across the world. This makes the AMR burden estimates as accurate as possible.

The methodology facilitates the evaluation of AMR burden data that was not previously accessible. The diverse range of pathogens and pathogen-drug combinations provides global and regional estimates for 204 countries and territories, enabling the observation of trends from 1990 to 2021 [7]. On the other hand, the earlier studies offered just a brief overview of the year 2019.

The model has proven to be very effective. It successfully tracked how AMR mortality has changed over time. It also compared trends across different locations. This is extremely valuable. Understanding how the AMR burden is progressing is very important. It helps us see where things are getting better. It also shows where things are getting worse. But the model does more than just track trends. It provides solid evidence for decision makers. Governments and health organisations can use this data. Researchers and policymakers

can also benefit from it. It helps all stakeholders choose the right interventions. Ultimately, it supports smarter and more informed decisions in the fight against AMR.

With this model, the projected that the AMR burden is anticipated to rise to 1.91 million (1.56–2.26) attributable deaths and [8.22 million (6.85–9.65)] associated deaths by the year 2050 [8].

Despite a 50% decrease in the number of deaths among children under the age of 5 Years. The pathogens responsible for the highest number of deaths attributable to AMR in 2021 included *Klebsiella pneumoniae*, *Streptococcus pneumoniae* and *Escherichia coli* (Table 1).

Across all age demographics, the pathogen-drug combination that showed the most significant increase in attributable burden was methicillin-resistant *Staphylococcus aureus* (MRSA) [13]. It surged from [57,200 (34,100–80,300)] attributable deaths in 1990 to [130,000 (113,000–146,000)] attributable deaths in 2021 [14].

The numbers are striking. AMR-related deaths among adults over 70 years old more than doubled. This happened between 1990 and 2021. That is a massive increase over just three decades. But why are older adults so vulnerable? The answer lies in their overall health condition. Most elderly patients have multiple health problems at the same time. These are known as comorbidities. Conditions like diabetes, heart disease, and kidney problems are common among them. These existing conditions act as serious risk factors. They make older adults much more susceptible to infections caused by AMR. Their weakened immune systems also make it harder to fight back. This combination makes them the most at-risk group of all.

The burden attributable to carbapenem resistance in Gram-negative bacteria showed a notable increase (1990 to 2021). In the absence of further intervention strategies, the proposed 10% reduction in AMR mortality by 2030. The targets outlined in the WHO 10-20-30 target will not be reached. If new antimicrobials are developed for the currently antimicrobial-resistant Gram-negative bacteria. It is estimated that [11.1 million (9.08–13.2)] AMR deaths can be prevented till 2050 [14].

Table 1: Global priority pathogens, resistance mechanisms, and epidemiological trends in antimicrobial resistance.

Pathogen	Dominant Resistance Mechanism	Clinical & Public Health Impact	Epidemiological Trend (1990–2021) Projections)	References
<i>Klebsiella pneumoniae</i>	Carbapenem-resistant (CRKP), ESBL production.	A major cause of hospital-acquired infections and high mortality in ICU settings is associated with sepsis and pneumonia.	Rapidly increasing, particularly in LMICs; projected to remain a leading contributor to AMR mortality by 2050.	[9,10]
<i>Escherichia coli</i>	Extended-spectrum β -lactamase (ESBL), fluoroquinolone Resistance.	The leading cause of urinary tract infections and bloodstream infections globally; significant community and hospital burden.	Increasing globally, with a high prevalence in both community and healthcare settings.	[10]
<i>Staphylococcus aureus</i> (MRSA)	Methicillin resistance (mecA gene)	Major pathogen in the skin and soft tissue tissue, and invasive infections, High morbidity and mortality in both community and hospital settings.	Substantial increase from 1990 to 2021; it remains a persistent global threat.	[11]
<i>Streptococcus pneumoniae</i>	Multi-drug resistance (penicillin, macrolides)	Because of pneumonia, meningitis, and sepsis in children, high burden of under-five mortality.	Decreasing trend in children due to vaccination; remains significant in elderly populations.	[12]



The situation demands increased investment in the discovery of new antibacterial agents. This alone will not serve as estimated [28.03 million (23.7–32.8)] annual AMR deaths are still projected to occur till 2050. After considering the deaths averted through the Gram-negative scenario. In a situation categorised with enhanced management of severe infections and increased availability of antibiotics. It is estimated that a total of [92.0 million deaths (ranging from 82.8 to 102.0 million)] could potentially be prevented in all age demographics between the years 2025 and 2050 [15].

The decline in mortality rates among children under the age of 5 years due to sepsis exceeding 60% over the last 31 years. The extensive vaccination initiatives and enhanced access to water, sanitation and hygiene (WASH). Effective infection prevention and control strategies have significantly mitigated the burden of antimicrobial resistance (AMR). In low- and middle-income countries (LMICs), the prevalence of bacterial infections and AMR is notably high. Lewnard and colleagues project that enhancing infection prevention and control programs could avert at least [337,000 (95% CI 250,200–465,200)] deaths associated with AMR each year [16].

Improved access to WASH infrastructure and practices could prevent an additional [247,800 (160,000–337,800)] AMR-related fatalities [17]. The administration of pediatric vaccines could lead to a further reduction of [181,500 (153,400–206,800)] AMR-associated deaths, achieved through both the direct prevention of resistant infections and a decrease in antibiotic use [18]. But statistical modelling utilising comprehensive datasets is important for estimating disease burden and prompting action. It is not without its limitations. Data collection was a major challenge in this study. Many low- and middle-income countries simply lack reliable data. This made the analysis much more difficult. Even when some data was available, it was not always useful. In many cases, the data was scattered and incomplete. It was not strong enough for proper time trend analysis. Gaps in data can lead to inaccurate conclusions. This is a serious problem for researchers. It limits our understanding of the true AMR burden in these regions. Better data collection systems are urgently needed. Without good data, it is very hard to make good decisions.

The situation can be linked to inadequate laboratory capacity. The absence or scarcity of microbiological facilities, weak governance of health systems and information systems. Limited resources for systematic data collection. Therefore, there is a pressing need for renewed efforts, such as resources, political backing and enhanced capabilities in LMIC. The environments to effectively implement national action plans aimed at combating and controlling AMR.

Significant analytical inaccuracies can arise when integrating and standardising data from various providers and sources of infection. Mostly due to selection bias

in passive microbial surveillance data, discrepancies in diagnostic culture application, variations in antimicrobial usage between the private and public health-care sectors and inconsistent temporal distribution of available data from different regions and countries. These features complicate the exact picture of global, regional and national AMR dynamics. That's why it impacts the reliability and interpretation of time trend analyses. The projections and scenarios about the AMR burden till 2050 are also constrained by limitations inherent in historical estimates.

Conclusion

AMR is not a distant threat. It is a growing crisis happening right now. Deaths linked to AMR are rising steadily around the world. Low- and middle-income countries are bearing the heaviest burden. The evidence paints a mixed picture. On one hand, there is progress. AMR-related deaths among children under five have gone down. This is encouraging and worth celebrating. On the other hand, the situation among older adults is worsening. The burden in this age group keeps climbing. And the future looks even more challenging. Experts warn that things could get significantly worse by 2050. This is a wake-up call for everyone. Immediate and sustained global action is necessary. The time to act is now.

Development of new antimicrobials alone will be insufficient to control this trend. Strengthening infection prevention and control, surveillance, vaccination and WASH infrastructure offers the greatest potential to reduce avoidable deaths. Urgent, coordinated One Health action with sustained political and financial commitment is essential to mitigate the future impact of AMR.

Author contributions

M.A.D., M.A.B. and S.A.Z. were involved in conceptualisation, editing and original manuscript writing, language editing; all authors approved the final version of the manuscript.

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