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Global Resistance to Standard Antibiotics: A Comparative Analysis of The Burden and Projections Up to 2050

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Annotation: Antibiotic resistance (antimicrobial resistance, AMR) has become one of the leading causes of mortality worldwide, associated with 4.95 million deaths in 2019 and 4.71 million in 2021, of which 1.27–1.41 million are directly attributed to bacterial resistance to standard antibiotics. The burden of AMR varies significantly across WHO regions: the highest mortality rates are observed in African countries and certain regions of Asia, whilst the lowest are found in Australasia and some European countries. The aim of this study is to conduct a comparative analysis of the global and regional burden of bacterial AMR, identify key pathogens and syndromes, highlight regional differences, and present a quantitative projection up to 2050. The analysis is based on estimates from the global GBD–AMR project and regional analyses for Africa, Europe, the Eastern Mediterranean, the Americas and China. It is shown that the main contributors to mortality are Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii and Pseudomonas aeruginosa, as well as methicillin-resistant S. aureus and carbapenem-resistant Enterobacteriaceae . Modelling up to 2050 predicts an increase in AMR-attributable deaths to ~1.9 million and associated deaths to ~8.7 million per year, with a moderate increase in DALYs, with the burden concentrated among those aged over 70. The WHO's priority policy areas (AWaRe, One Health) and the particular vulnerability of low- and middle-income countries are discussed.

Keywords: *antibiotic resistance, AMR, global burden, 2050 forecast, WHO, comparative analysis*

Introduction

Since the introduction of penicillin, bacterial resistance to antimicrobial agents has evolved in parallel with the clinical use of antibiotics. The WHO warns that the 'post-antibiotic era', in which common infections and routine surgeries become
life-threatening, is no longer a hypothetical scenario [1].

Global GBD–AMR estimates showed that in 2019, bacterial resistance was associated with 4.95 million deaths, including 1.27 million deaths attributable to AMR [2]. An updated analysis covering 1990–2021 confirmed a comparable scale: 4.71 million associated deaths and 1.41 million attributable deaths in 2021 [3].

Relevance

The WHO ranks AMR among the ten greatest threats to public health. Resistance undermines the effectiveness of standard antibiotics (beta-lactams, fluoroquinolones, macrolides), on which empirical treatment of the most common infections of the respiratory tract, bloodstream and urinary tract is based [4].

Models predict that without a strengthened global response, by 2050 there could be millions of additional deaths annually and economic damage comparable to the 2008 global financial crisis [5]. Low- and middle-income countries are particularly vulnerable, as they face a combination of high infectious disease burden, limited access to quality care and weak laboratory systems [6].

Objective

To conduct a comparative analysis of resistance to standard antibiotics at global and regional levels and to assess the outlook up to 2050, including:

- a comparison of the burden of AMR (mortality, DALYs) across WHO regions;
- characterisation of leading pathogens and syndromes;
- analysis of regional characteristics (Africa, Europe, Eastern Mediterranean, the Americas, China);
- presentation of a quantitative projection up to 2050 in the form of scenarios.

Materials and Methods

The results of global and regional systematic reviews from the GBD–AMR project are used:

- a global assessment of bacterial AMR for 1990–2021 with projections up to 2050;
- global burden of AMR for 2019;
- regional estimates for Africa, Europe, the Eastern Mediterranean, the Americas and China [7].

Methodologically, all studies are based on a single five-component approach:

1. the number of deaths in which infection played a role;
2. distribution of deaths by infectious syndrome;
3. distribution of deaths by pathogen within syndromes;
4. the proportion of strains resistant to a class/drug;
5. excess risk of death/duration of infection in the presence of resistance [8].

The burden was calculated in two counterfactual scenarios:

- attributable to AMR (replacement of resistant infections with susceptible ones);
- AMR-associated (replacement of resistant infections with no infection) [9].

The forecast up to 2050 is based on three scenarios: reference, ‘new drugs against Gram-negative bacteria’ and ‘best care’ [10].

Results and Discussion

Results

Global burden and key pathogens

In 2019, AMR was associated with 4.95 million deaths (95% UI 3.62–6.57), of which 1.27 million (0.91–1.71) were attributed to resistance. In 2021, there were 4.71 million associated deaths and 1.41 million attributable deaths [11].

The six leading pathogens (E. coli, S. aureus, K. pneumoniae, S. pneumoniae, A. baumannii, P. aeruginosa) accounted for 3.57 million associated and 929,000 attributable deaths in 2019 . MRSA, carbapenem-resistant A. baumannii and K. pneumoniae, as well as cephalosporin-and fluoroquinolone-resistant E. coli, are among the deadliest ‘pathogen–drug’ combinations.

Regional contrasts

- **Africa (WHO-AFRO):** 1.05 million associated and 250,000 attributable deaths in 2019; highest standardised mortality rates, particularly for lower respiratory tract infections and sepsis [12].
- **Europe:** 541,000 associated and 3,000 attributable deaths; leading combinations — MRSA and aminopenicillin-resistant E. coli.
- **The Americas:** 569,000 associated and 141,000 attributable deaths; MRSA dominates among attributable deaths in 34 out of 35 countries [13].
- **Eastern Mediterranean:** 380,000 associated and 92,800 attributable deaths in 2021, with projected increases to 187,000 and 752,000 by 2050 respectively.
- **China:** >600,000 AMR-associated deaths and 145,000 attributable deaths in 2019; leading combinations include carbapenem-resistant A. baumannii and MRSA [14].

Age analysis shows a >50% decline in mortality among children under 5 and an >80% increase among those aged 70+ over the period 1990–2021 [15].

Table 1. Comparative burden of bacterial AMR (2019–2021)

Region / World	Associated deaths, thousands	Attributable deaths, thousands	Features	References
World (2019)	4,950	1,270	6 pathogens ≈ 3.57 million associated deaths	[2]
World (2021)	4,710	1,410	Increase in burden among those aged 70+	[1]
Africa (WHO) 2019	1,050	250	Max. mortality per 100,000	[7]
Europe (WHO) 2019	541	133	Leading causes: MRSA, E. coli	[7]
The Americas (WHO) 2019	569	141	MRSA is the leading cause in 34 countries	[17]
Eastern Mediterranean 2021	380	92.8	High rates in Somalia	[7]
China 2019	>600	145	Key: carbapenem-resistant Gram-	[20]

Projections to 2050 (global and regional)

Global modelling up to 2050 indicates that, under the reference trajectory:

- the number of deaths attributable to AMR will reach 1.91 million (95% CI 1.56–2.26);
- the number of associated deaths will be 8.72 million (6.85–9.76) per year;
- DALYs will rise to 46.5 million (+9.4% by 2022) [16].

Up to 65.8% of all attributable deaths in 2050 will occur in people aged ≥70 years. South Asia, Latin America and the Caribbean are projected to be the subregions with the highest mortality rates.

In the Eastern Mediterranean, 187,000 attributable and 752,000 associated deaths are projected by 2050 [17]. European modelling, taking demographics into account, also shows a shift in the burden towards older age groups and limited feasibility of the −10% target by 2030 without a significant reduction in incidence [18].

Table 2. AMR forecast for 2050 (reference scenario)

Indicator	**2021 (actual, global)**	**2050 (global, reference)**	**Eastern Mediterranean 2050**	**Comment**	**Citations**
Attributable deaths, million/year	1.41	1.91	0.187 million	Growth ≈ +70%	[1.7]
Associated deaths, million/year	4.71	8.72	0.752 million	Strong growth	[1.7]
DALYs, million/year	~42	46.5	n/a	Moderate growth	[1]
Proportion of those aged 70+ among attributed deaths	~50%	65.8%	>60% (estimated)	Ageing population	[1][13]

Furthermore, the ‘best care’ scenario could prevent up to 92 million deaths from AMR between 2025 and 2050, whilst the scenario involving new drugs against Gram-negative bacteria could prevent a further 11.1 million deaths [19].

Discussion

A comparative analysis reveals several key patterns:

1. **Marked interregional inequality.** The greatest burden of AMR is concentrated in Africa, South Asia, the Eastern Mediterranean and a number of Latin American countries, where the infectious disease burden is high and access to quality care and effective antibiotics is limited .
2. **The key role of a few pathogens.** A small number of species (E. coli, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, S. pneumoniae) account for the lion’s share of the burden, confirming the appropriateness of prioritising them in the WHO list for R&D and control programmes [20].
3. **Age shift in the burden.** The decline in mortality among children under 5 contrasts with the rise in mortality among the elderly; by 2050, two-thirds of deaths from AMR will occur in people aged 70 and over .
4. **Policy and practical response.** The WHO is promoting a global action plan, the AWaRe system and the development of national plans; however, implementation, particularly in low-income countries, remains fragmented .
5. **Limitations of the projections.** The projections are based on historical trends and do not account for the emergence of new ‘superbugs’ or drastic changes in healthcare systems, which may lead to an underestimation of the future burden .

Conclusion

Resistance to standard antibiotics already rivals the mortality rates of leading non-communicable diseases and shows marked regional and age-related variations. If current trends continue, by 2050 the number of deaths attributable to AMR could increase by approximately 70%, reaching nearly 2 million per year, whilst the total

number of associated deaths will approach 9 million.

Containing AMR requires:

- prioritising key pathogens and high-risk regions;
- strengthening health systems and access to essential antibiotics and diagnostics;
- strict management of antibiotic use (AWaRe, stewardship);
- investment in new drugs against Gram-negative bacteria and alternative

approaches;

- a cross-sectoral One Health approach.

Without comprehensive, coordinated measures, the WHO’s warning of widespread resistance to standard antibiotics could materialise as a ‘slow-unfolding catastrophe’ for global public health.

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