Comment

Lives lost and disease burden related to antimicrobial resistance in the Americas can no longer be ignored

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The emergence and spread of antimicrobial resistance (AMR) poses a substantial risk to modern medicine and is widely recognised as one of the most daunting challenges of our time.¹ Development of resistance is an inherent characteristic of bacterial evolution and, as such, cannot be stopped. Indeed, resistant bacterial infections carry higher morbidity, mortality, and increased healthcare costs, resulting in a large economic and disease burden to healthcare systems and societies globally.^{2,3} Access to reliable and comparable models of AMR over time and across regions is essential to inform public health decisions, define research and funding priorities, and evaluate the impact of disease prevention and mitigation initiatives, such as antimicrobial stewardship programs.^{1,4} However, the sparsity and quality of such information have repeatedly undermined efforts to estimate the real burden of AMR, especially in low- and middle-income countries, where data are particularly limited and the impact of antimicrobial-resistant infections on healthcare systems is substantial.5

In this issue of *The Lancet Regional Health—Americas*, a Global Burden of Disease study⁶ led by the Antimicrobial Resistance Collaborators, provides the most comprehensive country-specific estimates of morbidity, mortality, and disability-adjusted life years (DALYs) attributable to and associated with AMR in the Americas to date.⁶ The authors estimate the burden of AMR in 35 American countries building on recent global approximations by Murray et al.² Two scenarios are presented: a lower-bound counterfactual, where resistant infections are replaced by susceptible infections (attributable to AMR), and an upper-bound

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scenario, where resistant infections would not occur (associated with AMR).

The results offer a staggering insight into the alarming magnitude of the problem in the region. According to the authors' estimates, during 2019, ~141,000 and 569,000 deaths were directly attributed to, and associated with AMR, respectively. Altogether, these numbers account for ~11% of the global deaths related to AMR.2 To put these estimates in perspective, AMRattributable deaths in the region surpass those caused by tuberculosis (~20,300), HIV/AIDS (~51,100), and all neglected tropical diseases (~15,160) combined.7 Moreover, the study revealed an impressive 3.48 million DALYs (2.42-4.90) attributable to AMR, comparable to the joint disease burden of HIV/AIDS (2.76 million) and tuberculosis (0.77 million), and more than double the disease burden of all neglected tropical diseases combined (1.34 million).7 In terms of microorganisms, >50% of all deaths attributable to AMR during 2019 corresponded to infections with Staphylococcus aureus, Escherichia coli, and Klebsiella pneumoniae. Notably, among all 88 pathogen-drug combinations assessed, methicillin-resistant S. aureus was responsible for the largest number of attributable deaths and DALYs in all countries in the Americas, except for Haiti, where third-generation cephalosporin-resistant K. pneumoniae predominated.

Apart from providing long-awaited estimates of the burden of AMR in the Americas, the authors also illuminate the striking differences of the problem across countries in the region. Of note, estimates of agestandardised mortality rates associated with and attributable to AMR sharply contrast with the status of national AMR action plans within countries in the WHO Region of the Americas. Indeed, none of the top six countries exhibiting the highest age-standardised mortality rates had a government-published, approved, or funded national action plan to tackle AMR.⁶ Conversely, all but one of the six countries with the lowest age-standardised mortality rates already had a fully developed and approved national action plan.





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Additionally, the authors rightfully highlight that the large differences in baseline rates of infection-related mortality observed throughout the region should guide policy makers in prioritizing public health interventions. In nations grappling with high rates of infection, focussing on the development of strong infection prevention and control measures, alongside large-scale vaccination campaigns could potentially yield substantial reductions in the burden of AMR. In contrast, focussing on robust antibiotic stewardship programs and integrated surveillance systems should probably be prioritised by higher-income countries.⁸

An important caveat is these estimates were performed with data collected before the COVID-19 pandemic. Evidence suggests that the pandemic worsened the AMR scenario, leading to a sharp increase in the number of hospitalizations, invasive procedures, and days of hospital stay, all of which resulted in higher antimicrobial use.9 Recent research proposes that AMR could have increased from the massive use of antibiotics during the pandemic.9 Moreover, the pandemic highlighted critical challenges in healthcare systems, inequalities, and vulnerabilities, particularly in Latin America. These challenges include underfunded and fragmented healthcare systems, significant disparities in accessing effective healthcare, limited surveillance capabilities, vulnerability to external shocks, and pervasive inequalities.¹⁰ Of utmost concern, the pandemic's trajectory was heavily influenced by intersecting social and economic inequalities, disproportionately affecting marginalised populations and putting them at the highest risk.^{11,12} Addressing wealth disparities is crucial in our efforts to tackle AMR, especially in low- and middle-income countries, and in Latin America, a region with persistent inequalities.13

The authors recognise that data limitations pose a significant concern in their results. Indeed, the sparse availability of reliable information contributes to the wide uncertainty intervals in their estimates. Despite notable efforts to enhance AMR surveillance, such as the establishment of the Latin American Antimicrobial Resistance Surveillance Network (ReLAVRA) under the leadership of the Pan American Health Organization (PAHO), data remain far from optimal, particularly in low- and middle-income countries within the region. In spite of these limitations, the estimates of the disease burden of AMR provided in this manuscript paint a sobering picture. We hope these data will serve as a compelling wake-up call to address the threat of AMR

promptly and decisively in the region. The lives lost and disease burden related to AMR in the Americas can no longer be ignored.

Contributors

All authors contributed equally to the conceptualization, writing, reviewing and editing of the manuscript.

Declaration of interests

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References

- Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance—the need for global solutions. *Lancet Infect Dis.* 2013;13(12):1057–1098.
- 2 Murray CJL, Ikuta KS, Sharara F, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629–655.
- 3 Roope LSJ, Smith RD, Pouwels KB, et al. The challenge of antimicrobial resistance: what economics can contribute. *Science*. 2019;364(6435):eaau4679.
- 4 Chan M, Kazatchkine M, Lob-Levyt J, et al. Meeting the demand for results and accountability: a call for action on health data from eight global health agencies. *PLoS Med.* 2010;7(1):e1000223.
- 5 Allel K, Stone J, Undurraga EA, et al. The impact of inpatient bloodstream infections caused by antibiotic-resistant bacteria in low- and middle-income countries: a systematic review and metaanalysis. *PLoS Med.* 2023;20(6):e1004199.
- 6 Antimicrobial Resistance Collaborators. The burden of antimicrobial resistance in the Americas in 2019: a cross-country systematic analysis. *Lancet Reg Health Am.* 2023. https://doi.org/10.1016/j.lana.2023. 100561.
- 7 Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet*. 2020;396(10258):1204–1222.
- 8 Sadeq AA, Hasan SS, AbouKhater N, et al. Exploring antimicrobial stewardship influential interventions on improving antibiotic utilization in outpatient and inpatient settings: a systematic review and meta-analysis. *Antibiotics*. 2022;11(10):1306.
- 9 Allel K, Peters A, Conejeros J, et al. Antibiotic consumption during the coronavirus disease 2019 pandemic and emergence of carbapenemase-producing *Klebsiella pneumoniae* lineages among inpatients in a Chilean Hospital: a time-series study and phylogenomic analysis. *Clin Infect Dis.* 2023;77(Supplement_1):S20–S28.
- 10 The Lancet. COVID-19 in Latin America: a humanitarian crisis. Lancet. 2020;396(10261):1463.
- 11 Garcia PJ, Alarcón A, Bayer A, et al. COVID-19 response in Latin America. Am J Trop Med Hyg. 2020;103(5):1765–1772.
- 12 Mena GE, Martinez PP, Mahmud AS, Marquet PA, Buckee CO, Santillana M. Socioeconomic status determines COVID-19 incidence and related mortality in Santiago, Chile. *Science*. 2021;372(6545): eabg5298.
- 13 Pierce J, Apisarnthanarak A, Schellack N, et al. Global Antimicrobial Stewardship with a focus on low-and middle-income countries: a position statement for the international society for infectious diseases. *Int J Infect Dis.* 2020;96:621–629.