The scope of the antimicrobial resistance challenge

Okeke, Iruka N.; de Kraker, Marlieke E.A.; Van Boeckel, Thomas P.; Kumar, Chirag K.; Schmitt, Heike; Gales, Ana C.; Bertagnolio, Silvia; Sharland, Mike; Laxminarayan, Ramanan

DOI
10.1016/S0140-6736(24)00876-6

Publication date
2024

Document Version
Final published version

Published in
The Lancet

Citation (APA)
Okeke, I. N., de Kraker, M. E. A., Van Boeckel, T. P., Kumar, C. K., Schmitt, H., Gales, A. C., Bertagnolio, S., Sharland, M., & Laxminarayan, R. (2024). The scope of the antimicrobial resistance challenge. *The Lancet*, *403*(10442), 2426-2438. https://doi.org/10.1016/S0140-6736(24)00876-6

Sustainable Access to Antibiotics 1

The scope of the antimicrobial resistance challenge

Iruka N Okeke, Marlieke E A de Kraker, Thomas P Van Boeckel, Chirag K Kumar, Heike Schmitt, Ana C Gales, Silvia Bertagnolio, Mike Sharland, Ramanan Laxminarayan

Lancet 2024; 403: 2426–2438

Published Online May 23, 2024 https://doi.org/10.1016/S0140-6736(24)00876-6

See Comment page 2355

See Perspectives page 2367

This is the first in a Series of four papers on sustainable access to antibiotics. All papers in the Series can be found at thelancet.com/series/antibiotic-resistance

Department of Pharmaceutical Microbiology, Faculty of Pharmacy, University of Ibadan, Ibadan, Nigeria (Prof I N Okeke PhD); **Infection Control Program, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland** (M E A de Kraker PhD); **WHO Collaborating Centre on AMR, Geneva, Switzerland** (M E A de Kraker); **Health Geography and Policy Group, Department of Environmental Systems Science, ETH Zürich, Zürich, Switzerland** (T P Van Boeckel PhD); **One Health Trust, Bengaluru, India** (T P Van Boeckel, C K Kumar BA, Prof R Laxminarayan PhD); **Centre for Zoonoses and Environmental Microbiology, Dutch National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands** (Prof H Schmitt PhD); **Environmental Biotechnology, Faculty of Applied Sciences, Delft University of Technology, Delft, Netherlands** (Prof H Schmitt); **Division of Infectious Diseases, Paulista School of Medicine, Federal University of São Paulo (EPM-UNIFESP), São Paulo, Brazil** (Prof A C Gales MD PhD); **Department of Surveillance, Control, and Prevention of Antimicrobial Resistance, WHO, Geneva, Switzerland** (S Bertagnolio MD); **Centre for Neonatal and Paediatric Infection, St George's, University London, London, UK** (Prof M Sharland MD); **High**

Each year, an estimated 7·7 million deaths are attributed to bacterial infections, of which 4.95 million are associated with drug-resistant pathogens, and 1·27 million are caused by bacterial pathogens resistant to the antibiotics available. Access to effective antibiotics when indicated prolongs life, reduces disability, reduces health-care expenses, and enables access to other life-saving medical innovations. Antimicrobial resistance undoes these benefits and is a major barrier to attainment of the Sustainable Development Goals, including targets for newborn survival, progress on healthy ageing, and alleviation of poverty. Adverse consequences from antimicrobial resistance are seen across the human life course in both health-care-associated and community-associated infections, as well as in animals and the food chain. The small set of effective antibiotics has narrowed, especially in resource-poor settings, and people who are very young, very old, and severely ill are particularly susceptible to resistant infections. This paper, the first in a Series on the challenge of antimicrobial resistance, considers the global scope of the problem and how it should be measured. Robust and actionable data are needed to drive changes and inform effective interventions to contain resistance. Surveillance must cover all geographical regions, minimise biases towards hospital-derived data, and include non-human niches.

Introduction

As many as 1·27 million of the 7·7 million estimated deaths attributable to bacterial infections could be caused by bacterial pathogens resistant to the antibiotics available to treat them.[1,2] This untenably high burden from antimicrobial resistance (AMR) keeps growing.[3–5] Yet AMR is typically presented as a discreet problem and thus is invisible to many stakeholders. AMR currently affects the health, wellbeing, and potential of most humans and other species that inhabit the world. Today, humans begin and end life with a substantial probability of contracting an antimicrobial-resistant infection and a decreasing likelihood of being able to access effective treatments. Infections from resistant bacteria are a health concern comparable to, if not potentially greater than, HIV and malaria and affect all regions of the world

Search strategy and selection criteria

38 experts in antimicrobial resistance and global health reviewed Sustainable Development Goal targets, the current state of data availability, and then elected the following focal areas for in-depth review: neonatal sepsis, health-care-associated infection, typhoid, gonorrhoea, and pneumococcal infection (tuberculosis was excluded). MEDLINE was searched via PubMed for relevant review articles from January, 2003 to June, 2023 about antimicrobial or antibiotic resistance or antimicrobial or antibiotic consumption. Papers cited in the reviews were selected from the reference lists. Supporting data for the focal areas were retrieved from the following publicly available curated resistance databases or sources: the 2019 GBD study and 2019 GRAM project, NeoOBS, CHAMPS, BARNARDS, the DeNIS study, ResistanceMap, ResistanceBank, PathogenWatch, Typhinet, and the Medicine Quality Scientific Literature Surveyor. The expert group additionally listed relevant policy documents associated with the WHO *Global Action Plan for Antimicrobial Resistance*.

Key messages

- Antimicrobial resistance, specifically antibiotic resistance, is compromising health and development targets, including the UN's Sustainable Development Goals; this puts not just vulnerable individuals, such as neonates, older people and the chronically ill, but entire health systems at risk.
- Increases in resistance among bacterial pathogens in humans, animals, the food chain, and the environment have been documented in the past two decades.
- Progress in treating non-communicable diseases, including diabetes and cancer, in people of all ages is threatened by antimicrobial resistance.
- Antibiotic use in medicine and agriculture, the selective force for resistance, is insufficiently documented, as are resistance rates, trends, and burden.
- Diagnostics that determine when and which antibiotics are needed will enhance patient care and inform the public health response.
- Resistant bacteria are disseminated by humans and non-human and inanimate intermediaries, including health-care apparatus. The resistant microbial lineages can become entrenched in health-care facilities, in the community, and across food chains. Unless detected quickly and stopped through infection prevention and control, these lineages can spread in facilities across the world, endangering millions.
- Every country needs a surveillance system to track antibiotic use and resistance and to evaluate interventions.

Panel 1: Trends in the burden of AMR

AMR in humans

AMR trend analyses point to a rise in resistant infections, notably in Gram-negative organisms, in the past decade.[6] In Europe in 2019–21, increasing rates of resistance were reported, particularly carbapenem-resistant *Acinetobacter* spp causing bloodstream infections in 2017–21.[7] The substantial estimated burden of resistant infections in Europe increased between 2007 and 2015.[8] In 2015, the 426 277 antimicrobial-resistant HCAIs accounted for an estimated 33 110 attributable deaths and 874 541 DALYs.[8] Projections from high-income countries predict a 2·1-times rise in resistance to third-line antimicrobials—the last-resort drugs—by 2035 compared with 2005.

The Global Research on Antimicrobial Resistance study estimated that 4·95 million (95% CI 3·62–6·57 million) deaths were associated with bacterial AMR in 2019 (ie, the patient died with a bacterial AMR infection that might or might not have been the cause of death), including 1·27 million (0·91–1·71 million) deaths attributable to bacterial AMR (ie, the patient likely died of a bacterial AMR infection).[1] The upper limit would place AMR in the top three causes of death, after ischaemic heart disease, stroke, and chronic obstructive pulmonary disease. In addition to absolute AMR rates, the burden from resistance is driven by the overall infectious disease burden and access to second-line and reserve antimicrobials that can be used to treat resistant infections. Thus, the estimated all-age death rate attributable to resistance was highest in west Africa (27·3 deaths per 100 000 people) and lowest in Australasia (6·5 deaths per 100 000 people). Such estimates have several limitations: the data come from a small number of countries; DALYs did not account for prolonged treatment effects, disability, or other sequelae; and burden estimates included non-hospitalised patients, but pathogen distributions and case fatality ratios were derived from hospital data. Furthermore, due to sparse data, resistance proportions and relative risks were assumed equal across subpopulations, infection sites, and locations, affecting the reliability of the rankings.

The appendix (pp 7-8) has information on the burden of AMR in domesticated animals.

AMR=antimicrobial resistance. DALY=disability-adjusted life-year. HCAI=health-care-acquired infection. LMIC=low-income and middle-income country.

Meadows Environmental Institute, Princeton University, Princeton, NJ, USA
(Prof R Laxminarayan)

Correspondence to:
Dr Iruka N Okeke, Department of Pharmaceutical Microbiology, Faculty of Pharmacy, University of Ibadan, Ibadan 200284, Nigeria
iruka.n.okeke@gmail.com

or

Prof Ramanan Laxminarayan, One Health Trust, Bengaluru 560042, India
ramanan@onehealthtrust.org

For the **GRAM project** see https://www.tropicalmedicine.ox.ac.uk/gram

For **NeoOBS** see https://penta-id.org/severe-infections-and-antimicrobial-resistance/neoobs/

For **CHAMPS** see https://champshealth.org/

(panel 1).[1] AMR threatens infectious disease management at all ages and constrains medical progress.

In children younger than 5 years, a drastic decline in deaths (as much as 50% between 2000 and 2013) was achieved through improvements in water and sanitation, vaccination, and other public health interventions.[9] However, Sustainable Development Goal 3 (ie, to ensure healthy lives and promote wellbeing at all ages and to reduce newborn mortality to less than 12 deaths per 1000 livebirths by 2030) is jeopardised when antibiotics do not work, resistant organisms are disseminated, or patients cannot access the medicines they require (figure 1). A third of newborn deaths are attributable to infection and half of those to sepsis[14] and, increasingly, the pathogens no longer respond to the most readily available antibiotics.

At the other end of life, the comorbidities and immunosenescence that can accompany ageing aggravate the propensity for infection—increasingly, antimicrobial-resistant infection (figure 2). Roughly a tenth of the world's population is older than 65 years, a proportion likely to double by 2050.[16] Additionally, progress in treating non-communicable diseases (NCDs), including diabetes and cancer, in people of all ages is constrained by AMR. For example, 26·8% of the pathogens causing infections in patients with blood cancer and undergoing chemotherapy are resistant to antimicrobials used for infection prophylaxis.[17] Drug-resistant health-care-acquired infections (HCAIs) in such patients complicate treatment and survival, lengthen hospital stays, and increase cost of care.

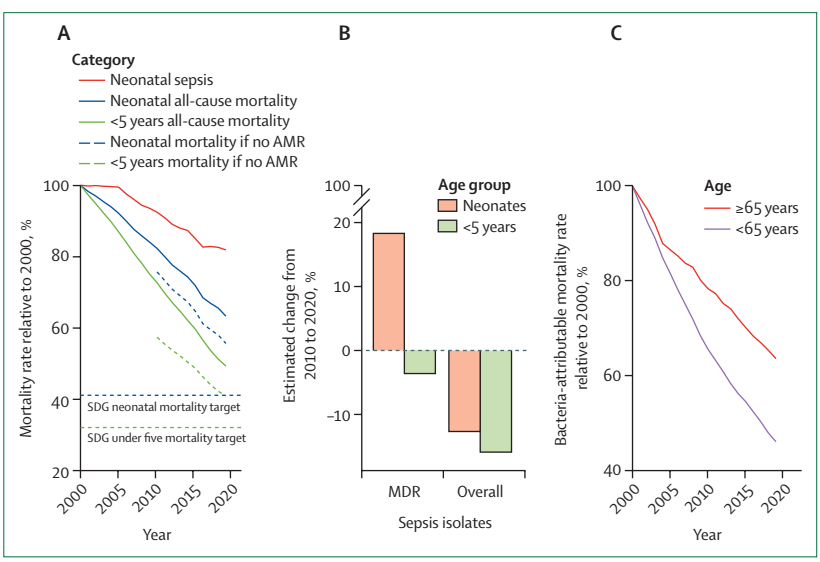

Figure 1: **AMR delays progress towards global childhood survival targets**
(A) Progress in reducing mortality in children younger than 5 years, neonatal mortality, and neonatal sepsis since 2000 in comparison with the SDG targets for mortality in neonates and children younger than 5 years. Dashed lines present a counterfactual scenario were there to be no AMR-attributable deaths (see appendix p 3 for details); the shift from the reported values is based on the Global Burden of Disease Antimicrobial Resistance study[1] and the rate of change is calculated from cohort studies on AMR.[10–12] (B) Reported percent changes in the past decade of neonatal sepsis isolates by drug resistance. Source data is the same as that for the counterfactual scenario of no AMR in the first panel. MDR is defined akin to Sievert and colleagues[13] to mean drug resistance to a majority of the currently prescribed antibiotic treatments at the time of data analysis. (C) Progress in reducing bacterial mortality since 2000 for people aged 65 years and older compared with people younger than 65 years. To obtain estimates of bacteria-attributable mortality, all Global Burden of Disease syndromic causes that have bacterial underpinnings are summed for the two age groups. AMR=antimicrobial resistance. MDR=multidrug resistance. SDG=sustainable development goal.

For **BARNARDS** see https://www.cardiff.ac.uk/research/explore/research-units/burden-of-antibiotic-resistance-in-neonates-from-developing-societies-barnards

For **ResistanceMap** see https://resistancemap.onehealthtrust.org

For **ResistanceBank** see https://resistancebank.org

For **PathogenWatch** see https://pathogen.watch

For **Typhinet** see https://www.typhi.net

For the **Medicine Quality Scientific Literature Surveyor** see https://www.iddo.org/mqsurveyor/

For the **WHO *Global Action Plan for Antimicrobial Resistance*** see https://www.who.int/publications/i/item/9789241509763

See Online for appendix

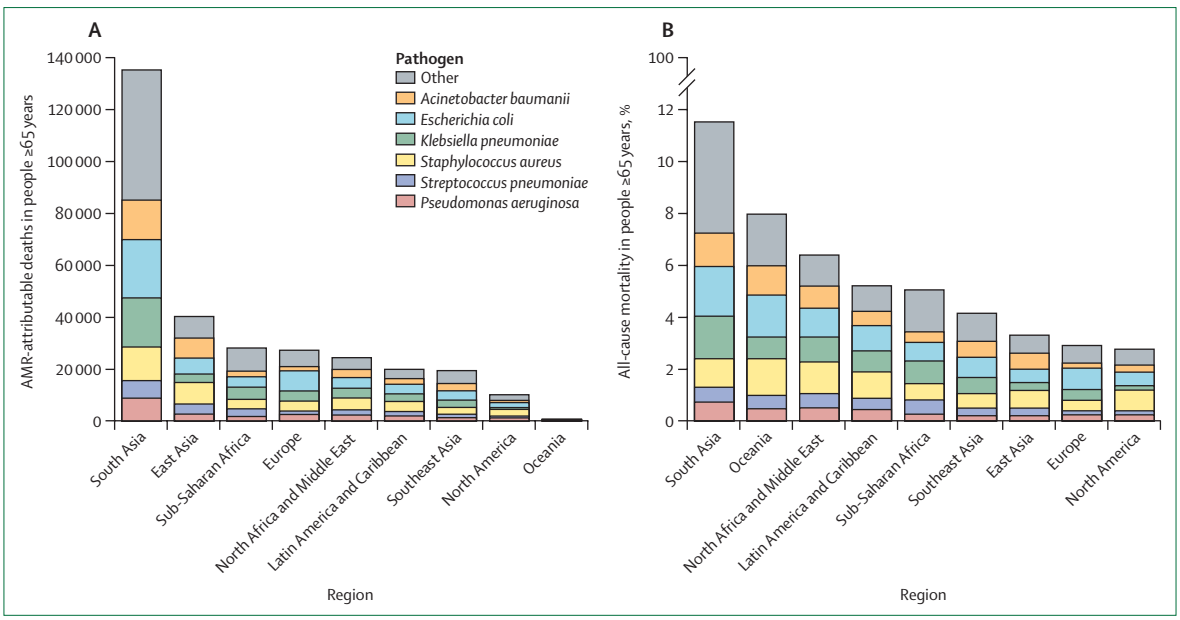

Figure 2: **Drug-resistant infections present a substantial burden on ageing populations**
(A) Estimated number of AMR-attributable deaths (ie, infection from a drug-resistant pathogen that is in the causal chain of death) stratified by the top five pathogens among individuals older than 65 years. The height of the bars represents the total number of all-cause deaths that are attributable to an AMR pathogen and the coloured section of each bar represents the contribution of each pathogen. Data are shown by geographical GBD super region. (B) Percentage of all-cause mortality in people older than 65 years that are attributable to AMR by pathogen. Source data on the burden of AMR pathogens are from the GRAM study,[1] and estimates for the total number of all-cause deaths in people older than 65 years for scaling in (B) are from the GBD study.[15] Estimates reflect the situation as of 2019.

AMR also threatens global health through food insecurity as it restricts our ability to treat sick livestock. Overuse of antibiotics on farms and discharge of active antimicrobials into the environment select for resistant bacterial lineages in those settings and place humans and animals at risk of a future pandemic from an untreatable bacterial infection.[18,19] AMR is thus a One Health challenge that requires surveillance and interventions across human, animal, and environmental domains.

Drivers of resistance in both humans and animals include antibiotic use and insufficient application of preventive measures (eg, poor access to water and sanitation, insufficient vaccination, and failure of infection prevention in health-care facilities).

In the past decade, many countries have created national action plans (NAPs) on how they plan to address antimicrobial resistance. Most of these NAPs are modelled on the WHO Global Action Plan[20] and emphasise the importance of increasing awareness of AMR among health workers and the general public, carrying out surveillance to quantify the problem, preventing infections and the dissemination of antimicrobial-resistant bacteria, researching and developing new antimicrobials, and other strategies for overcoming or avoiding resistance, as well as highlighting the economic benefits of strategies to address AMR. According to a WHO factsheet, 178 countries have developed NAPs on AMR as of November, 2023, and of those, only 25% are effectively implementing and monitoring their NAPs; LMICs in particular face substantial barriers.

This 2024 *Lancet* Series on sustainable access to effective antimicrobials presents initiatives and targets to tackle the global threat to health of AMR. This is the first paper in this Series and examines how AMR and antibiotic use have intersected with disease burden over the past decade and the need for improved surveillance. The second paper in the Series models the effectiveness of interventions to stop the rise of, or reduce, AMR in resource-limited settings.[21] The third paper in the Series examines how research and development can address AMR.[22] The fourth paper in the Series proposes achievable targets for a 10% reduction in disease burden from AMR by 2030.[23]

Here, we present evidence on the growing effect of AMR on global health and examine options for pragmatic, rapid improvements in global AMR and surveillance of antibiotic use. Our aim in this paper, and throughout the Series, is to present the problem of AMR as a horizontal or cross-cutting one that is exacerbated by inequitable access to antimicrobials. Our scope is restricted to non-tuberculosis bacterial and fungal pathogens, although drug resistance is a growing impediment to the treatment of tuberculosis, malaria, HIV infection, and other infections. We begin by outlining the challenge posed by AMR to global goals for child survival, healthy ageing, and food security. We review the state of AMR in infections caused by community-acquired pathogens that infect people across

For the **WHO factsheet on antimicrobial resistance** see https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

the courses of their lives, depending on exposure and risk. We then summarise progress and gaps in measuring and reporting of AMR and antimicrobial use, and we propose suggestions for improving surveillance.

AMR in health-care settings

Threats to newborn survival

AMR prevents the achievement of multiple health-related targets. For example, neonatal sepsis remains a global concern, as the eighth most common cause of death in neonates and children younger than 5 years, with high rates in low-resource settings.[24,25] Babies with early onset sepsis might be infected before or during birth because of premature rupture of maternal membranes; late onset (age 3–28 days) sepsis commonly represents a HCAI. Outbreaks of resistant bacteria attributable to poor infection prevention and control are increasingly detected in neonatal sepsis, often only retrospectively. Babies born at a health facility can benefit from emergency obstetric or newborn care,[13] but HCAIs could stall or reverse such child survival gains.

AMR constrains neonatal sepsis management: in a study across 11 countries, 18% of babies who had pathogen-positive blood cultures did not survive despite receiving empirical antimicrobial therapy.[26] Similar neonatal sepsis outcomes due to resistance to first-line empirical treatment regimens recommended by WHO have been reported elsewhere in the past two decades.[27,28] Overall, an estimated 214 000 neonatal deaths globally were attributed to antimicrobial-resistant neonatal sepsis each year a decade ago.[1,29] *Klebsiella* (particularly *pneumoniae*), *Staphylococcus, Acinetobacter,* and *Escherichia* spp are the most common causes of neonatal sepsis (not necessarily in that order), particularly in low-resource settings.[1,27,28,30,31] In addition, maternally acquired *Streptococcus agalactiae* is a common cause of early-onset neonatal sepsis in high-income settings.[11,26,30] Real and perceived risk of mortality due to resistant bacteria causing sepsis has prompted overuse of carbapenem antibiotics and a consequent increase in rates of carbapenem resistance. Clinicians increasingly need to use last-resort drugs like colistin,[26] which has more (and more serious) adverse effects than first-line, second-line, and third-line empirical drugs and whose long-term effects for neonates are largely uncertain.

Neonatal sepsis is most commonly secondary to a systemic bacterial infection, but fungal infections can also initiate sepsis, particularly in infants with low birthweights. Sepsis following fungal infection occurs worldwide but is best documented in high-income settings.[27,32] *Candida albicans* and *Candida parapsilosis* are common causes, but since 2009, *Candida auris* is of even greater concern.[33] *C auris* isolates are typically resistant to most or all known antifungals, infections have high mortality rates, and the organism was labelled critical on the 2022 WHO Fungal Priority Pathogens List.[34] A possibly ongoing fluconazole-resistant *C auris* outbreak in a South African neonatal unit has involved 91 cases over 4 years.[35]

Identification of causative bacteria and antimicrobial susceptibility information are crucial to managing sepsis and to identifying outbreaks. These data, generated in health-care facilities, can feed into local, national, and regional surveillance at little extra cost. For neonatal sepsis and other infections caused by blood-borne bacteria, pathogen information derives from blood cultures, which have a low yield (typically <20%) and a high contamination rate (perhaps >10% in low-resource settings).[36] Because blood culture sampling is most challenging in neonates, contamination rates can be higher than the institutional average. Deep molecular diagnostics, such as metagenomic approaches, can yield a causative agent in almost 4 times as many cases, but cost currently precludes their routine use.[27,30] Genomic enrichment methods and point-of-care aetiological tests are promising but are still under development. In high-income settings, a neonate with suspected sepsis typically undergoes more than one blood culture and supporting tests to confirm the diagnosis and guide care. The current goal for low-resource settings is that blood culture testing be available at referral centres,[37] but even there, the required infrastructure, consumables, skilled personnel, and quality management systems are often missing, and thus very few infections are cultured.[38,39] National and regional surveillance networks built around existing blood culture machines largely consist of tertiary sentinels, where resistance patterns of opportunistic pathogens differ markedly from primary-care and secondary-care isolates, limiting the actionability of the data.[27]

Surveillance is increasingly uncovering outbreaks in neonatal intensive-care units.[40,41] Applying whole-genome sequencing, which will ultimately support tools to prevent mortality (see the third paper in this Series[22]), permits fine-level tracking of the opportunistic causes of neonatal sepsis, revealing routes through which bacteria are transmitted, whether directly among patients or via intermediaries, including medical devices and parenteral medications.[35,42,43] Whole-genome sequencing has revealed that specific lineages of *Escherichia coli* (eg, sequence types 69, 73, 95, and 131) and *K pneumoniae* (eg, sequence types 11, 15, and 17)[44,45] are over-represented in neonatal sepsis and HCAIs.[11,46] A maternal vaccination strategy targeting these lineages could significantly lower neonatal sepsis rates.[47] Surveillance through whole-genome sequencing provides lineage and antigen information at no extra cost and offers more granularity than earlier genotypic methods; however, it does not yet achieve predictiveness to consistently guide empirical prescriptions or prevent HCAIs. Because turnaround times are typically long, few outbreaks have been shortened, stopped, or shrunk by sequencing. A short turnaround has been achieved in some instances;[42] the barriers to the full potential of genomic surveillance arise from its use in large flagship initiatives too far

removed from patients at risk of antimicrobial-resistant infections. Facility-based genomic surveillance of neonatal intensive-care wards can help prevent infections by identifying and segregating infants colonised with potentially resistant pathogens, monitoring them for sepsis, and administering treatment on the basis of actual susceptibility profiles.

Threats to older people and people with chronic illnesses

People of any age can contract HCAIs, but people older than 65 years face substantial risk due to immunosonesence, comorbidities, and frequent or protracted interactions with health care or assisted living, as ageing populations benefit from advancements in medical care. The UK National Health Service alone spends approximately £2 billion annually on HCAIs,[48] mostly bacterial but increasingly fungal.[34] HCAIs can be acquired at any age but are most frequent among older people. Despite some improvements in infection prevention and control, treatment costs continue to rise. Drug resistance prolongs the need for infection management, requires more expensive medicines, and threatens patients lives.[49] Resistance is also a barrier to surgical care, directly affecting surgical outcomes. Evidence suggests that some surgeries, particularly at older ages, are deemed too risky given the likelihood of contracting an untreatable infection.

AMR also undermines the treatment of chronic illnesses across the life course, putting at risk the effectiveness and value of organ transplantations, joint replacements, cancer chemotherapy, and treatment of NCDs, which account for 80% of deaths and 70% of disability-adjusted life-years globally.[50] Sub-optimally managed NCDs are poorly quantified but could be a substantial burden of AMR.[51] AMR complicates treatment for chronic kidney disease,[52] diabetes and associated urinary tract and foot infections,[53] chronic obstructive pulmonary disease,[54] and liver cirrhosis.[55] Sepsis following HCAI in patients being treated for NCDs urgently requires improved surveillance to detect bacterial resistance outbreaks and to inform vaccine development and other prevention strategies.

Cancer patients have a particularly high risk of infection. Cancer itself can lead to malnutrition and psychological stress. Cancer treatments (including invasive medical devices, surgery, chemotherapy, radiation, immunotherapy) can also increase the risk of infection.[56,57] In a retrospective study, the mortality rate due to fatal infection in US cancer patients was 260·1 per 100 000 person-years, nearly 3 times that of the general population.[58] In that cohort, patients aged 20–39 years or those older than 80 years, as well as those receiving chemotherapy, showed a higher risk of fatal infections.[58] Antibiotic use to prevent infection in cancer patients can then select for resistant infections.[17] The most resistant ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, K pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* spp) are frequent HCAIs in patients with cancer.[56,59] Among patients with cancer in Spain, Bodro and collaborators reported increased persistence of bacteraemia (25% *vs* 10%), metastatic infection (8% *vs* 4%), and early case-fatality rates (23% *vs* 11%) for infections caused by antimicrobial-resistant ESKAPE pathogens, compared with other, antimicrobial-susceptible pathogens.[60] Patients with infections caused by multidrug-resistant Gram-negative bacteria, especially non-fermentative bacteria such as *Acinetobacter* spp, have particularly early mortality rates.[61,62]

To estimate the potential effect of AMR on the efficacy of antibiotic prophylaxis across a range of surgeries and cancer treatments,[17] researchers modelled a 30% reduction in the effectiveness of antibiotic prophylaxis and projected that an additional 6367 infection-related deaths could occur annually in the USA, primarily among patients undergoing colorectal surgery (4586 additional deaths), blood cancer chemotherapy (683 additional deaths), and total hip replacement (376 additional deaths).[17] In the USA, declines in the efficacy of antibiotic prophylaxis in preventing surgical site infections following colorectal surgery have been reported.[63]

AMR in community settings

The vast majority of AMR infections are acquired in the community across most of the life course.[1] Community-acquired urinary tract infections (UTIs) affected more than 404·6 million people globally and led to nearly 236 800 deaths in 2019.[64] UTIs are the most common indication for antibiotic prescription in pregnancy,[65] when the range of antibiotics that can be safely administered narrows, and are associated with maternal pre-eclampsia, low birthweight, and preterm birth if improperly treated.[25] Although *E coli* is the most frequent urinary tract pathogen in both community and hospital settings, ESKAPE pathogens are important UTI causes as well.[66,67] Community-acquired UTIs are commonly caused by resistant *E coli, K pneumoniae, Proteus mirabilis,* and *Staphylococcus saprophyticus*.[66,67] Extended-spectrum β-lactamase producers, such as CTX-M-15-producing *E coli* ST131 strains, are globally disseminated and resistant to multiple antimicrobials.[68,69] In some regions, community-acquired UTIs caused by carbapenemase-producing *E coli* increasingly necessitate intravenous antibiotics.[70,71]

Sexually transmitted infections

Sexually transmitted bacteria cause considerable morbidity. The stigma associated with these infections, along with few diagnostic resources, limits access to care and contributes to disease spread. In 2020, an estimated 82 million people contracted gonorrhoea worldwide.[72] The incidence in middle-income settings is estimated to be 2 times as high and in sub-Saharan Africa, 5 times as

high as the global average.[73] In high-income settings, gonorrhoea infection rates have increased drastically in the past two decades, largely among men who have sex with men—the demographic for which concerns about AMR are greatest.[74–76] Resistant *Neisseria gonorrheae* clones rapidly spread rapidly because of high transmission rates and strong selection arising from empirical antibiotic use.[77–79] Patients with suspected gonorrhoea typically receive empirical treatment, often from unlicenced providers in settings with weak regulation.[80]

Rational gonorrhoea treatment consists of single doses or short courses of antibiotics known to be active against 95% or more of sentinel surveillance isolates.[81] Culture and susceptibility tests take several days, and access to testing is very scarce because *N gonorrheae* requires specialised methods. The diagnosis and susceptibility profile would ideally be confirmed in a single health-care visit so that appropriate treatment could begin immediately. Today, nucleic-acid-based tests can guide therapy, but only where technical and human capacity is available.[82] Currently, patients with gonorrhoea receive ceftriaxone alone or with azithromycin, which is effective for most patients.[74,76] If approved, zoliflodacin, which has been trialled over the past few years, could offer a reserve option for resistant infections.[83] Mathematical modelling shows that the use of rapid tests to screen for susceptibility to largely discontinued tetracycline and ciprofloxacin (seen in almost 70% of isolates in some settings) could, in addition to reducing the cost of treatment, prolong the usable lifespan of new drugs.[84] Prevention of gonorrhoea infection reduces treatment demand. Sexually transmitted infections are best prevented with behavioural interventions, and gonorrhoeal vaccines in development offer additional promise.[85,86]

Typhoid and *Streptococcus pneumoniae* infection

Typhoid fever is a life-threatening bloodstream infection caused by the Typhi serovariety of *Salmonella enterica* subspecies enterica, a faeco-orally transmitted bacterium that only infects humans. Untreated or improperly treated infections are commonly fatal: 10–20% of people infected with *S* Typhi before the antibiotic era died.[87] With little shift in incidence, antimicrobials dropped the mortality from typhoid fever to less than 1% in endemic regions.[87] That success in typhoid control has been reversed by rapidly evolving resistance to every broad-spectrum antimicrobial treatment option that has been used (appendix p 10). Typhoid is largely imported to Europe and North America by returning travellers but remains a major cause of febrile illness in parts of Africa and Asia with poor sanitation.[88] Prevention is crucial because antibiotics treat infections but do not control transmission.[88–90] After accounting for location, outbreaks attributable to multidrug-resistant strains are increasingly common and typically larger than outbreaks caused by antimicrobial-sensitive *S* Typhi.[91] Surveillance in typhoid-endemic areas would not only support treatment and sanitation priorities but also identify transmission chains and guide deployment of typhoid conjugate vaccine (see the second paper in this Series[21]). Genomic surveillance has identified major *S* Typhi clones and their routes of local and global dissemination,[92,93] including locations where drug-sensitive lineages continue to circulate. *S* Typhi genomic surveillance is based on large numbers of genomes (with disproportionately fewer from Africa) and allows non-experts to contribute and interpret genomic information.[93–95] Surveillance is inhibited by its dependence on blood cultures, which are expensive, uncommon in many endemic areas, and insufficiently sensitive to detect most typhoid cases.[96] Nevertheless, surveillance preceded adoption of the typhoid conjugative vaccines in all but one (ie, Liberia) of the countries that started immunisation by 2023 (ie, Liberia, Malawi, Nepal, Pakistan, Samoa, and Zimbabwe).[97] Neighbouring countries commonly have little or no typhoid surveillance.

In contrast to *S* Typhi, good genomic surveillance resources exist for *S pneumoniae,* a community-acquired cause of childhood illness and mortality that is also vaccine preventable. In 2009, an estimated 0·6 million deaths were associated with antimicrobial-resistant *S pneumoniae*.[1] Isolates can be retrieved from nasal-swab surveys in healthy populations and added to information from blood and cerebrospinal fluid cultures,[98] compensating for the poor access to microbiology resources. Surveying for *S pneumoniae* carriage in healthy individuals in turn makes it possible to obtain lineage-specific information that can inform vaccine deployment and empirical treatment.

For typhoid and other infections without easily accessible pathogenic or potentially pathogenic isolates, emerging surveillance approaches (including direct specimen testing and environmental surveillance) offer promise. Monitoring of drug resistance and identifying resistance mechanisms need to be built into the new approaches, even at additional cost.

Antimicrobial use: a key driver of resistance

Antimicrobials cure infections but also drive resistance by providing resistant microbes with a selective advantage over sensitive ones. Global antimicrobial use (AMU)—the key driver of resistance—surged by 46% over the past two decades.[99] Nevertheless, the 2016 *Lancet* AMR Series observed that more deaths were due to poor access to antibiotics than to resistance.[29] Although more patients now have access to antimicrobial drugs, resistance has made previously useful antimicrobials less effective and access to previously second-line drugs has thus become more important. For example, affordable and safe antimicrobials (ie, antibiotics on WHO's Access list in the AWaRe classification;[100] panel 2) were the mainstay of neonatal infection management in the mid-to-late 20th century. The close-to and actual last-resort options (ie, antiobiotics on WHO's Watch list and Reserve list) are

Panel 2: AWaRe—a traffic light approach to antibiotic use

In 2017, WHO developed the AWaRe system for categorising the more than 250 antibiotics used in humans according to their clinical efficacy, safety, selection on resistance or effect on microbiome, and cost. Antibiotics on the Access list (eg, amoxicillin) are generally older, often narrow-spectrum drugs that are still effective in treating common infections, particularly in primary care. These antibiotics have a good safety profile and are inexpensive (where widely available). Watch antibiotics (eg, third-generation cephalosporins) have a broad spectrum of activity against resistant organisms, are still widely effective against more severe infections in hospitals, generally are more likely to select for resistance, and typically have higher toxicity and higher cost. Reserve antibiotics (eg, colistin) are used as a last resort to treat multidrug-resistant infections in severely ill patients. The WHO Essential Medicines List includes about 30 antibiotics on the Access and Watch lists and 10 in the Reserve list. In 2019, WHO added a Not Recommended category of antibiotics, mainly inappropriate fixed-dose combinations.

The WHO 2022 AWaRe book guides on the optimal choice of drug, dose, and duration for about 35 common infections in adults and children in primary care and hospital settings, with a strong focus on universal health care.[100]
The recommendations now underpin the development of future policy goals. For example, antibiotics on the Access list (most commonly amoxicillin) are the first-choice recommendation for 90% of the most common infections seen in primary care. The AWaRe book also takes a risk-based approach, giving guidance on when an antibiotic is not recommended, usually for minor respiratory infections. AWaRe-based quality indicators, quality metrics, and educational and stewardship interventions have been developed. The AWaRe system's traffic light approach has simplified surveillance and monitoring of antibiotic use and will dictate in the future which Access antibiotics should be universally available to meet Sustainable Development Goal 3.8 (ie, achieving universal health coverage). Many older antibiotics on the Watch list with little usefulness are still widely produced, and further guidance on unnecessary antibiotics is needed. Developing policy goals on the basis of absolute amounts of Access, Watch, and Reserve antibiotics at a country level will require risk adjustment for burden of disease, demography, mortality, and rates of AMR.

AMR=antimicrobial resistance. AWaRe=Access, Watch, Reserve.

For the **Medicine Quality Scientific Literature Surveyor** see https://www.iddo.org/mqsurveyor/

increasingly used today. Most pathogens isolated from 19 facilities in a multicountry study[26] were resistant to antibiotics on the Access list. More than a third (37%) of neonates started on regimens from the Watch list and 25% of infants started on regimens from the Access or Watch lists had to be escalated from Access to Watch or from Watch to Reserve antimicrobials within 24 hours because their condition deteriorated or laboratory results indicated resistance. Thus, currently recommended neonatal sepsis regimens are commonly ineffective or undereffective empirical treatments because of resistance (appendix pp 5–6).

Since 2016, the World Organisation for Animal Health has collected data on antibiotic sales for livestock from more than 150 countries. Because the reporting countries are not specified and the national reports are aggregated by region (ie, Europe, Africa, Americas, Middle East, and Asia–Far East–Oceania), the effect of national policies on AMU cannot be determined. Moreover, one country's success in reducing AMU is diluted at the regional level if usage rises in neighbouring countries. Between 2016 and 2018, the World Organisation for Animal Health reported a decline in global AMU from 92 269 to 69 455 tonnes, which was largely attributable to China (where consumption fell from 44 186 to 29 774 tonnes). Modelling estimates of national-level AMU attempt to overcome such limitations. For 2020, one estimate named China, Brazil, India, and the USA as the top four countries for absolute AMU, measured in tonnes.[101] From 2017 to 2020, AMU in pigs fell slightly (from 193 to 173 mg per Population Correction Unit), but in poultry this measure fell sharply (from 68 to 35 mg per Population Correction Unit) despite continued growth of the poultry sector.

AMU estimates assume that claims on medication labels of active ingredients are accurate, but an estimated 10% of antimicrobials marketed in LMICs are substandard or falsified.[102] Medicines can contain less (or sometimes more) than the labelled amount. Antibiotics can be incorrectly transported and stored, leading (particularly in the tropics) to physical and chemical degradation that affects shelf life and therefore effectiveness. Falsified antimicrobials are particularly common when regulation and supply chains are weak and infection burdens (and therefore demand) are high. The Medicine Quality Scientific Literature Surveyor finds that substandard antibiotics are commonly reported from west and east Africa, south and east Asia, and central America. Besides confounding consumption estimates, substandard medicines could exacerbate selection for AMR even when used according to prescription through various mechanisms.[102,103] Substandard or falsified antimicrobials also undermine the resistance-thwarting goals of combination regimens, and formulations containing no active ingredient or the wrong active ingredient can generate false impressions of resistance. Overall, because of inertia and the difficulties of documentation (appendix p 9), AMU in human clinical medicine, veterinary medicine, and agriculture is grossly under-reported.

The need for antimicrobial resistance surveillance

The fourth paper in this Series proposes ambitious but achievable targets for containing AMR.[23] These targets

cannot be met, nor can progress towards them be measured, without robust surveillance of both resistance and its burden. However, in many parts of the world surveillance is insufficient for this purpose. Surveillance strategies might be non-representative of the target population or might bias the responses, including prompting antibiotic overuse.[104,105] Traditional laboratory-based resistance surveillance, which aggregates data from routine testing of patients in health-care facilities, has obvious drawbacks: the data typically reflect the conditions of a selected sample of patients accessing health services and diagnostics (often from tertiary-care facilities where resistance rates can be high) and resistance patterns are often reported out of epidemiological and clinical context, thus limiting their ability to inform empirical treatment guidelines (panel 3).[116]

The 2014 WHO *Antimicrobial Resistance: Global Report on Surveillance*[117] observed that data on antimicrobial resistance were scarce for pathogens of major public health importance and absent for more than half of the world's countries. The WHO *Global Action Plan on Antimicrobial Resistance*, adopted in 2015,[20] emphasised improving the evidence base of AMR and prompted the 68th World Health Assembly to recommend NAPs to tackle resistance.[118] The WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) now enables harmonised reporting of AMR data by country and sharing of aggregated data on AMR prevalence. GLASS has incorporated data from existing AMR surveillance networks, such as the European Antimicrobial Resistance Surveillance Network,[119] the Central Asian and European Surveillance of AMR,[120] the Latin American Network for Antimicrobial Resistance Surveillance (Rede Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos),[121] and the Western Pacific Regional Antimicrobial Consumption Surveillance System. After the 2015–19 early implementation phase, GLASS introduced indicators to assess countries' AMR surveillance, including the number of reporting sites, participation in quality-assurance programmes, representativeness of the population and health system levels, and laboratory diagnostics standards. In 2020, GLASS began monitoring of antimicrobial use and consumption (appendix p 9). In addition, WHO has developed survey methods to generate reliable, representative data on the prevalence and attributable mortality of drug-resistant bloodstream infections, particularly where surveillance systems are suboptimum.[122,123] These surveys will be initially rolled out in Kyrgyzstan, Indonesia, Malawi, and Rwanda, with plans for further scaling up in LMICs.

Surveillance has multiple purposes: supporting treatment guidelines, tracking the prevalence of AMR, identifying practices that exacerbate resistance, evaluating temporal trends, detecting outbreaks, enabling emergency preparedness, and informing risk assessment. Surveillance enables benchmarking of AMR across regions.[124–128] Surveillance can follow the evolution of novel resistance mechanisms and dangerous resistant clones. For example, in 2016 a new family of mobile colistin resistance genes, *mcr*, were observed following an increase in colistin resistance identified through routine surveillance.[129] Surveillance data can inform policies for infection prevention and control and for antibiotic stewardship. Once interventions are implemented,

Panel 3: Pathways to more actionable AMR surveillance

The first step in designing an actionable AMR surveillance is to define the objectives and target population. Complementary data sources that do not rely on the availability of microbiology capacity could allow rapid and affordable geographical characterisation and tracking of AMR, help strengthen surveillance of AMR, and expedite the scientific basis to identifying regions or subpopulations requiring more access to (*vs* justification of) antibiotics.

This approach could include active sampling of healthy populations across a diversity of hosts (ie, human and animal) and environmental sampling. One exemplary and low-resource approach for community sampling is included in the WHO TriCycle protocol on integrated AMR surveillance through analysis of the prevalence of ESBL-producing *Escherichia coli* in healthy pregnant women.[106] Wastewater analysis, currently in international validation, can complement human surveillance: resistance rates in isolates retrieved from wastewater have been shown to be highly correlated with those of the associated human community.[107,108]

Available surveillance information needs to be collated and conveyed to policy makers in easily interpretable forms for decision making. Several COVID-19 platforms that distilled information about the epidemiological distribution and trajectory of genetic variants were used by pandemic policy makers.[109] Similar tools are emerging for AMR. These tools include pathogen-specific platforms, such as Typhinet and Klebnet, as well as the ResistanceMap database and amr.watch and amr.net dashboards in development.[94]

Data on human exposure to AMR from different domains are one output of the Integrated One Health surveillance. Other purposes are evaluating trends in AMR or AMU in several domains, monitoring new forms of AMR, and analysing the effectiveness of interventions. These goals require different sample sources, analysis endpoints, and guidance support. Among the efforts to develop guidance on integrated surveillance are Joint Actions within the EU and the Quadripartite Technical Group on Integrated Surveillance.[110] A blueprint for a harmonised sampling effort with ESBL-producing *E coli* as one common indicator has been suggested by WHO.[111] This integrated TriCycle protocol includes resistance in bloodstream infections and in the community, poultry and poultry wet market or slaughterhouse wastewater, human wastewater, and river water.[111] First TriCycle iterations have been completed in Indonesia,[112] Madagascar,[113] Ghana,[114] and Pakistan,[115] and the protocol is being applied in other countries.[115]

Modelling to fill data gaps can help synthesise evidence to estimate a burden for comparison across regions or diseases and can thus help set priorities. Filling data gaps can also motivate surveillance by presenting people who doubt the model to try to challenge it with data. Extrapolation has greater uncertainty than gap filling because it assumes that a relationship between AMR and risk factors will remain valid beyond the temporal or geographical domains used for training the model. Extrapolations can nevertheless serve a purpose for what-if scenarios. For example, what happens if the animal sector continues to grow and antibiotics are used with the same intensity as currently? It is crucial to differentiate scenarios (ie, what could happen) from projections (ie, what will happen).

AMR=antimicrobial resistance. AMU=antimicrobial use. ESBL=extended-spectrum β-lactamase.

For **amr.watch** see https://amr.watch/

For **amr.net** see https://amr.net/

Panel 4: **Updating AMR surveillance for the 21st century—recommendations**

- Every country should have a national surveillance system that tracks AMR and antibiotic use, with in-country granularity, and that can be used to evaluate programmes against goals for addressing resistance.
- Diagnostic testing for patients suspected of having a bacterial or fungal infection should be supported at all levels of care, to promote rational antimicrobial use and enhance surveillance.
- Data from routine clinical bacteriology laboratories can and should contribute to antimicrobial resistance surveillance system. However, alternative data sources are also needed to remedy the scarcity of data globally. Countries should complement routine clinical surveillance with other surveillance modules, such as those recommended by WHO. The TriCycle protocol generates information on resistance in the clinic, the community, the food chain, and the environment at low cost. Nationally representative surveys should complement laboratory surveillance in settings where coverage of laboratory-based surveillance is poor or quality is unreliable. Surveys will generate reliable, direct measurements of AMR prevalence, health, and economic burden to inform national policies and model estimates.
- WHO's methods to estimate attributable mortality of AMR have been piloted by ACORN[104,130] in some LMICs and can provide data linking AMR with mortality and morbidity outcomes.
- Regulations on antimicrobial distribution must be strengthened to reduce selection for resistance. Surveillance should be used to inform regulation of antimicrobial distribution, to justify their use of or increase access to medicines when most needed.
- Electronic data capture is essential for collating and sharing surveillance information, as is making this information available, in a timely manner and in easily used formats, to clinical, antimicrobial stewardship, and public health decision makers.
- The value of existing surveillance systems should be evaluated, and the methods honed to increase cost-effectiveness and the quality and actionability of the information obtained.

AMR=antimicrobial resistance.

surveillance can help evaluate their effectiveness prospectively (see the second paper in this Series[21]). Surveillance aids in assessing the risk and burden of disease and helps evaluate transmission between One Health reservoirs of antibiotic resistance, and it can be used to heighten awareness among health professionals, policy makers, and the general public. Modalities for surveillance can and should use existing systems and programmes where possible to provide information at low cost (panel 4).

Some parts of the world do not undertake enough susceptibility testing. The Mapping Antimicrobial Resistance and Antimicrobial Use Partnership reports that only 1·3% of diagnostic laboratories in sub-Saharan Africa are capable of bacteriological testing, and only a subset of those can do susceptibility tests.[39] Mycology expertise is truly scarce: fungal surveillance lags bacterial infection surveillance and is insufficient to support interventions to tackle the growing prevalence of resistant fungi responsible for both community-associated infections and HCAIs. For example, *Cryptococcus neoformans*, a difficult-to-treat, community-acquired opportunistic infection in people living with HIV (with a high incidence in Africa) and other immunocompromised people, is typically diagnosed late and susceptibility patterns are uncertain. *C neoformans* isolates are reported as showing resistance to one or more of the accessible antifungals; backup options are few.[131,132]

Electronic data capture systems are absent from the majority of African hospitals.[39] WHONET offers laboratory data management that is the mainstay of strong surveillance systems in the Philippines and much of South America; it is compatible with the ACORN platform.[133,134] Development of other open-access platforms tailored to microbiology data, such as SEDRI-LIMS, is expected to further mobilise laboratory data on antimicrobial susceptibility for surveillance applications. Data intended to inform empirical prescribing guidelines must include details of the clinical presentation, underlying disease, empirical and subsequent switching of therapy, all relevant microbiology results, and in-hospital and 28-day mortality.[102] ACORN enables clinical caregivers to collect such information electronically so that it can be merged with laboratory data and shared via easily interpretable dashboard displays.[130]

The ultimate value of a surveillance system depends on how the information is used. The use of surveillance data depends on the epidemiological context from which the data are derived, on the reliability of the data, and the operational considerations; for example, if surveillance suggests a change in treatment but the recommended drugs are unavailable, then it has little value. Finally, the value of surveillance data depends on estimates of the benefit of interventions informed by it—these estimates can then help justify the costs of surveillance.

Conclusion

Antibiotics have saved millions of lives but have also driven the accompanying resistance pandemic and its considerable attributable mortality. The burden of resistance is enormous, growing, and unevenly distributed; it is preventing infectious disease control. Everyone is at risk from AMR, including those that have never taken an antibiotic, such as neonates, as they face the consequences of antimicrobial selective pressure created by previous generations. In parts of Asia and sub-Saharan Africa, the burden is aggravated by the scarcity of access to effective antibiotics and infrastructural

shortfalls that promote the spread of resistant pathogens. In these cases, AMR is inadequately documented because laboratory testing is insufficient and its burden of disease is poorly measured. Strengthening surveillance is a prerequisite for halting antimicrobial resistance and measuring successes in its containment.

Contributors

INO: conceptualisation, project administration, formal analysis, methodology, visualisation, original draft writing, and reviewing and editing. MEAdK: conceptualisation, original draft writing, and reviewing and editing. TPVB: conceptualisation, data curation, methodology, visualisation, original draft writing, and reviewing and editing. CKK: data curation and visualisation. HS: conceptualisation, original draft writing, and reviewing and editing. ACG: conceptualisation, original draft writing, and reviewing and editing. SB: original draft writing, reviewing, and editing. MS: original draft writing and reviewing and editing. RL: conceptualisation, data curation, formal analysis, funding acquisition, methodology, project administration, resource acquisition, supervision, visualisation, and reviewing and editing.

Declaration of interests

A meeting held to coordinate this paper was supported by the Bill & Melinda Gates Foundation (BMGF; INV-055356 to RL) and the Africa Centres for Disease Control and Prevention (to all authors). Neither funder had any role in the design, writing, or decision to submit this paper for publication. RL has received grant funding from the US National Science Foundation (CCF1918628). INO is a Calestous Juma Science Leadership fellow supported by BMGF (INV-036234, as well as INV-067684, INV-048135, and OPP1210746); receives grant funding from the UK National Institute for Health and Care Research (project number NIHR133307), Wellcome Trust, Public Health Alliance for Genomic Epidemiology, SEQAFRICA, Grand Challenges Africa Award (GCA/DD/rnd3/021), and International Vaccine Institute Award; receives royalties from Oxford University Press, Cornell University Press, and Springer; receives consulting fees from the Wellcome Trust; has received payment for lectures from the UK Microbiology Society; received travel support from BMGF, the European Society for Clinical Microbiology and Infectious Disease, and the American Society for Microbiology; has or had paid leadership roles in BMGF's surveillance advisory group (2019–21), the Thomas Bassir Biomedical Foundation Nigeria (2019 to present), and The International Centre for Antimicrobial Resistance Solutions Technical Advisory Forum (2021 to present); and has other unpaid positions in the *African Journal of Laboratory Medicine*, *Microbial Genomics*, *The Lancet Infectious Diseases*, Nigeria Center for Disease Control, and the *Lancet* Commission for Nigeria. SB is a member of staff at WHO; the views presented in this Series paper are those of the authors and do not reflect those of WHO. ACG receives consulting fees from Aché, Eurofarma, and União Química; receives payment for lectures from bioMérieux, Eurofarma, MSD, Pfizer, and Sandoz; received travel support from MSD and Pfizer; participates on the data monitoring board of Aché, Eurofarma, Hypera Pharma, MSD, Pfizer, Roche, Sandoz, United Medical, União, and Química; is a member of the Scientific Advisory Committee of the Global Antibiotic Research and Development Partnership (GARDP), the Health 1 Area Coordination board, and Fundação de Amparo à Pesquisa do Estado de São Paulo; and is a researcher for the Brazilian National Council for Scientific and Technological Development. MS receives funding from the Wellcome Trust (222051/Z/20/Z), GARDP, and EDCTP (NeoSep1); has unpaid leadership positions on the WHO Essential Medicine List Antibiotics Working Group and GARDP; and has been the Chief Investigator of clinical trials in children, where generic antibiotics have been donated by Sandoz, InfectoPharm, and Shionogi. All other authors report no competing interests.

Acknowledgments

We thank John Stelling and Christiane Dolecek for helpful comments and are grateful to Ambika Lall, Isabella Impalli, and Sally Atwater for figure and editorial assistance.

References

1 Murray CJ, Ikuta KS, Sharara F, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* 2022; **399:** 629–55.

2 Ikuta KS, Swetschinski LR, Aguilar GR, et al. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2022; **400:** 2221–48.

3 Gladstone RA, McNally A, Pöntinen AK, et al. Emergence and dissemination of antimicrobial resistance in *Escherichia coli* causing bloodstream infections in Norway in 2002–17: a nationwide, longitudinal, microbial population genomic study. *Lancet Microbe* 2021; **2:** e331–41.

4 Iroh Tam PY, Musicha P, Kawaza K, et al. Emerging resistance to empiric antimicrobial regimens for pediatric bloodstream infections in Malawi (1998–2017). *Clin Infect Dis* 2019; **69:** 61–68.

5 Carey ME, Dyson ZA, Ingle DJ, et al. Global diversity and antimicrobial resistance of typhoid fever pathogens: insights from a meta-analysis of 13 000 *Salmonella* Typhi genomes. *Elife* 2023; **12:** e85867.

6 Langford BJ, So M, Simeonova M, et al. Antimicrobial resistance in patients with COVID-19: a systematic review and meta-analysis. *Lancet Microbe* 2023; **4:** e179–91.

7 Kinross P, Gagliotti C, Merk H, Plachouras D, Monnet DL, Högberg LD. Large increase in bloodstream infections with carbapenem-resistant *Acinetobacter* species during the first 2 years of the COVID-19 pandemic, EU/EEA, 2020 and 2021. *Euro Surveill* 2022; **27:** 2200845.

8 Cassini A, Högberg LD, Plachouras D, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *Lancet Infect Dis* 2019; **19:** 56–66.

9 Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *Lancet* 2015; **385:** 430–40.

14 Mahtab S, Madhi SA, Baillie VL, et al. Causes of death identified in neonates enrolled through Child Health and Mortality Prevention Surveillance (CHAMPS), December 2016–December 2021. *PLOS Glob Public Health* 2023; **3:** e0001612.

10 Chaurasia S, Jeeva Sankar M, Agarwal R, et al. Characterisation and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centres in Delhi, India: a cohort study. *Lancet Glob Health* 2016; **4:** e752–60.

11 Sands K, Carvalho MJ, Portal E, et al. Characterization of antimicrobial-resistant Gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries. *Nat Microbiol* 2021; **6:** 512–23.

12 Ingle DJ, Levine MM, Kotloff KL, Holt KE, Robins-Browne RM. Dynamics of antimicrobial resistance in intestinal *Escherichia coli* from children in community settings in south Asia and sub-Saharan Africa. *Nat Microbiol* 2018; **3:** 1063–73.

13 Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Control Hosp Epidemiol* 2013; **34:** 1–14.

15 Murray CJ, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396:** 1223–49.

16 Statista Research Department. Proportion of selected age groups of world population and in regions in 2022. 2023. https://www.statista.com/statistics/265759/world-population-by-age-and-region/#:~:text=Globally%2C%20about%2025%20percent%20of,over%2065%20years%20of%20age (accessed March 19, 2024).

17 Teillant A, Gandra S, Barter D, Morgan DJ, Laxminarayan R. Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study. *Lancet Infect Dis* 2015; **15:** 1429–37.

18 Ikhimiukor OO, Odih EE, Donado-Godoy P, Okeke IN. A bottom-up view of antimicrobial resistance transmission in developing countries. *Nat Microbiol* 2022; **7:** 757–65.

19 Bouiller K, Bertrand X, Hocquet D, Chirouze C. Human infection of methicillin-susceptible *Staphylococcus aureus* CC398: a review. *Microorganisms* 2020; **8:** 1737.

20 WHO. Global action plan on antimicrobial resistance. 2016. https://www.who.int/publications/i/item/9789241509763 (accessed Feb 11, 2024).

21 Lewnard JA, Gleason A, Hsu LY, et al. Burden of bacterial antimicrobial resistance in low-income and middle-income countries avertible by existing interventions: an evidence review and modelling analysis. *Lancet* 2024; published online May 23. https://doi.org/10.1016/S0140-6736(24)00862-6.

22 Laxminarayan R, Impalli I, Rangarajan R, et al. Expanding antibiotic, vaccine, and diagnostics development and access to tackle antimicrobial resistance. *Lancet* 2024; published online May 23. https://doi.org/10.1016/S0140-6736(24)00878-X.

23 Mendelson M, Lewnard JA, Sharland M, et al. Ensuring progress on sustainable access to effective antibiotics at the 2024 UN General Assembly: a target-based approach. *Lancet* 2024; published online May 23. https://doi.org/10.1016/S0140-6736(24)01019-5.

24 Stoll BJ, Puopolo KM, Hansen NI, et al. Early-onset neonatal sepsis 2015 to 2017, the rise of *Escherichia coli*, and the need for novel prevention strategies. *JAMA Pediatr* 2020; **174:** e200593–200593.

25 UNICEF. Levels and trends in child mortality 2023. 2024 https://data.unicef.org/resources/levels-and-trends-in-child-mortality-2024/ (accessed March 19, 2024).

26 Russell NJ, Stöhr W, Plakkal N, et al. Patterns of antibiotic use, pathogens, and prediction of mortality in hospitalized neonates and young infants with sepsis: a global neonatal sepsis observational cohort study (NeoOBS). *PLoS Med* 2023; **20:** e1004179.

27 Saha SK, Schrag SJ, El Arifeen S, et al. Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): an observational cohort study. *Lancet* 2018; **392:** 145–59.

28 Breiman RF, Blau DM, Mutevedzi P, et al. Postmortem investigations and identification of multiple causes of child deaths: an analysis of findings from the Child Health and Mortality Prevention Surveillance (CHAMPS) network. *PLoS Med* 2021; **18:** e1003814.

29 Laxminarayan R, Matsoso P, Pant S, et al. Access to effective antimicrobials: a worldwide challenge. *Lancet* 2016; **387:** 168–75.

30 Mduma E, Halidou T, Kaboré B, et al. Etiology of severe invasive infections in young infants in rural settings in sub-Saharan Africa. *PLoS One* 2022; **17:** e0264322.

31 Mashau RC, Meiring ST, Dramowski A, et al. Culture-confirmed neonatal bloodstream infections and meningitis in South Africa, 2014-19: a cross-sectional study. *Lancet Glob Health* 2022; **10:** e1170–78.

32 Cook A, Ferreras-Antolin L, Adhisivam B, et al. Neonatal invasive candidiasis in low- and middle-income countries: data from the NeoOBS study. *Med Mycol* 2023; **61:** myad010.

33 Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. *Clin Infect Dis* 2017; **64:** 134–40.

34 WHO. WHO fungal priority pathogens list to guide research, development and public health action. 2022. https://www.who.int/publications/i/item/9789240060241 (accessed Sept 29, 2023).

35 Kekana D, Naicker SD, Shuping L, et al. *Candida auris* clinical isolates associated with outbreak in neonatal unit of tertiary academic hospital, South Africa. *Emerg Infect Dis* 2023; **29:** 2044–53.

36 Obeng-Nkrumah N, Labi A-K, Addison NO, Labi JEM, Awuah-Mensah G. Trends in paediatric and adult bloodstream infections at a Ghanaian referral hospital: a retrospective study. *Ann Clin Microbiol Antimicrob* 2016; **15:** 49.

37 Fleming KA, Horton S, Wilson ML, et al. The *Lancet* Commission on diagnostics: transforming access to diagnostics. *Lancet* 2021; **398:** 1997–2050.

38 Okeke IN. Divining without seeds: the case for strengthening laboratory medicine in Africa. 2011 https://doi.org/10.7591/cornell/9780801449413.001.0001 (accessed March 29, 2016).

39 Mapping AMR & AMU Partnership. Incomplete antimicrobial resistance (AMR) data in africa:the crisis within the crisis. 2022. https://aslm.org/wp-content/uploads/2022/09/ASLM_MAAP-Policy-Brief_Embargoed-until-15-Sept-6AM-GMT.pdf?x26552 (accessed May 2, 2024).

40 Köser CU, Holden MT, Ellington MJ, et al. Rapid whole-genome sequencing for investigation of a neonatal MRSA outbreak. *N Engl J Med* 2012; **366:** 2267–75.

41 Okomo U, Senghore M, Darboe S, et al. Investigation of sequential outbreaks of *Burkholderia cepacia* and multidrug-resistant extended spectrum β-lactamase producing *Klebsiella* species in a West African tertiary hospital neonatal unit: a retrospective genomic analysis. *Lancet Microbe* 2020; **1:** e119–29.

42 Harris SR, Cartwright EJ, Török ME, et al. Whole-genome sequencing for analysis of an outbreak of meticillin-resistant *Staphylococcus aureus*: a descriptive study. *Lancet Infect Dis* 2013; **13:** 130–36.

43 Jauneikaite E, Baker KS, Nunn JG, et al. Genomics for antimicrobial resistance surveillance to support infection prevention and control in health-care facilities. *Lancet Microbe* 2023; **4:** e1040–46.

44 Hu Y, Yang Y, Feng Y, et al. Prevalence and clonal diversity of carbapenem-resistant *Klebsiella pneumoniae* causing neonatal infections: a systematic review of 128 articles across 30 countries. *PLoS Med* 2023; **20:** e1004233.

45 Hetland MAK, Hawkey J, Bernhoff E, et al. Within-patient and global evolutionary dynamics of *Klebsiella pneumoniae* ST17. *Microb Genom* 2023; **9:** 001005.

46 Lipworth S, Vihta K-D, Davies T, et al. Molecular epidemiology and antimicrobial resistance phenotype of paediatric bloodstream infections caused by Gram-negative bacteria. *Commun Med* 2022; **2:** 101.

47 Kumar CK, Sands K, Walsh TR, et al. Global, regional, and national estimates of the impact of a maternal *Klebsiella pneumoniae* vaccine: a Bayesian modeling analysis. *PLoS Med* 2023; **20:** e1004239.

48 Guest JF, Keating T, Gould D, Wigglesworth N. Modelling the annual NHS costs and outcomes attributable to healthcare-associated infections in England. *BMJ Open* 2020; **10:** e033367.

49 Serra-Burriel M, Keys M, Campillo-Artero C, et al. Impact of multi-drug resistant bacteria on economic and clinical outcomes of healthcare-associated infections in adults: systematic review and meta-analysis. *PLoS One* 2020; **15:** e0227139.

50 The Institute for Health Metrics and Evaluation. GBD Compare. 2024. https://vizhub.healthdata.org/gbd-compare/ (accessed Feb 12, 2024).

51 Hocking L, Ali G-C, d'Angelo C, et al. A rapid evidence assessment exploring whether antimicrobial resistance complicates non-infectious health conditions and healthcare services, 2010-20. *JAC Antimicrob Resist* 2021; **3:** dlab171.

52 Miranda MV, González FC, Paredes-Godoy OS, Maulén MA, Vásquez CC, Díaz-Vásquez WA. Characterization of metal(loid)s and antibiotic resistance in bacteria of human gut microbiota from chronic kidney disease subjects. *Biol Res* 2022; **55:** 23.

53 Signing AT, Marbou WJT, Penlap Beng V, Kuete V. Antibiotic resistance profile of uropathogenic bacteria in diabetic patients at the Bafoussam Regional Hospital, west Cameroon region. *Cureus* 2020; **12:** e9345.

54 Ronconi G, Dondi L, Calabria S, et al. Community acquired pneumoniae and chronic obstructive pulmonary disease: the RWE analysis of events that required hospitalizations, and healthcare integrated costs. *Recenti Prog Med* 2023; **118:** 204–21 (in Italian).

55 Sonkoue Lambou JC, Noubom M, Djoumsie Gomseu BE, Takougoum Marbou WJ, Tamokou J-D-D, Gatsing D. Multidrug-resistant *Escherichia coli* causing urinary tract infections among controlled and uncontrolled type 2 diabetic patients at Laquintinie Hospital in Douala, Cameroon. *Can J Infect Dis Med Microbiol* 2022; **2022:** 1250264.

56 Nanayakkara AK, Boucher HW, Fowler VGJ Jr, Jezek A, Outterson K, Greenberg DE. Antibiotic resistance in the patient with cancer: escalating challenges and paths forward. *CA Cancer J Clin* 2021; **71:** 488–504.

57 AMR Control. AMR control supplement: the challenge for the cancer community. 2022. http://resistancecontrol.info/amr2022/ (accessed Nov 24, 2023).

58 Zheng Y, Chen Y, Yu K, et al. Fatal infections among cancer patients: a population-based study in the United States. *Infect Dis Ther* 2021; **10:** 871–95.

59 Cornejo-Juárez P, Vilar-Compte D, Pérez-Jiménez C, Ñamendys-Silva SA, Sandoval-Hernández S, Volkow-Fernández P. The impact of hospital-acquired infections with multidrug-resistant bacteria in an oncology intensive care unit. *Int J Infect Dis* 2015; **31:** 31–34.

60 Bodro M, Gudiol C, Garcia-Vidal C, et al. Epidemiology, antibiotic therapy and outcomes of bacteremia caused by drug-resistant ESKAPE pathogens in cancer patients. *Support Care Cancer* 2014; **22:** 603–10.

61 Scheich S, Weber S, Reinheimer C, et al. Bloodstream infections with Gram-negative organisms and the impact of multidrug resistance in patients with hematological malignancies. *Ann Hematol* 2018; **97:** 2225–34.

62 Tang Y, Xu C, Xiao H, Wang L, Cheng Q, Li X. Gram-negative bacteria bloodstream infections in patients with hematological malignancies—the impact of pathogen type and patterns of antibiotic resistance: a retrospective cohort study. *Infect Drug Resist* 2021; **14:** 3115–24.

63 Gandra S, Trett A, Alvarez-Uria G, Solomkin JS, Laxminarayan R. Is the efficacy of antibiotic prophylaxis for surgical procedures decreasing? Systematic review and meta-analysis of randomized control trials. *Infect Control Hosp Epidemiol* 2019; **40:** 133–41.

64 Yang X, Chen H, Zheng Y, Qu S, Wang H, Yi F. Disease burden and long-term trends of urinary tract infections: a worldwide report. *Front Public Health* 2022; **10:** 888205.

65 Ansaldi Y, Martinez de Tejada Weber B. Urinary tract infections in pregnancy. *Clin Microbiol Infect* 2023; **29**: 1249–53.

66 Foxman B, Manning SD, Tallman P, et al. Uropathogenic *Escherichia coli* are more likely than commensal *E coli* to be shared between heterosexual sex partners. *Am J Epidemiol* 2002; **156:** 1133–40.

67 Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol* 2015; **13:** 269–84.

68 Gibreel TM, Dodgson AR, Cheesbrough J, Fox AJ, Bolton FJ, Upton M. Population structure, virulence potential and antibiotic susceptibility of uropathogenic *Escherichia coli* from Northwest England. *J Antimicrob Chemother* 2012; **67:** 346–56.

69 Nicolas-Chanoine M-H, Bertrand X, Madec J-Y. *Escherichia coli* ST131, an intriguing clonal group. *Clin Microbiol Rev* 2014; **27:** 543–74.

70 Kumarasamy KK, Toleman MA, Walsh TR, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* 2010; **10:** 597–602.

71 Lee J, Sunny S, Nazarian E, et al. Carbapenem-Resistant *Klebsiella pneumoniae* in large public acute-care healthcare system, New York, New York, USA, 2016–2022. *Emerg Infect Dis* 2023; **29:** 1973–78.

72 WHO. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021. 2021. https://www.who.int/publications/i/item/9789240027077 (accessed Feb 11, 2024).

73 Rowley J, Vander Hoorn S, Korenromp E, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. *Bull World Health Organ* 2019; **97:** 548–562.

74 Mortimer TD, Pathela P, Crawley A, et al. The distribution and spread of susceptible and resistant Neisseria gonorrhoeae across demographic groups in a major metropolitan center. *Clin Infect Dis* 2021; **73:** e3146–55.

75 US Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2018. 2019. https://www.cdc.gov/std/stats18/STDSurveillance2018-full-report.pdf (accessed Feb 11, 2024).

76 Kakooza F, Golparian D, Matoga M, et al. Genomic surveillance and antimicrobial resistance determinants in *Neisseria gonorrhoeae* isolates from Uganda, Malawi and South Africa, 2015–20. *J Antimicrob Chemother* 2023; **78:** 1982–91.

77 Yahara K, Ma KC, Mortimer TD, et al. Emergence and evolution of antimicrobial resistance genes and mutations in *Neisseria gonorrhoeae*. *Genome Med* 2021; **13:** 51.

78 Fifer H, Cole M, Hughes G, et al. Sustained transmission of high-level azithromycin-resistant *Neisseria gonorrhoeae* in England: an observational study. *Lancet Infect Dis* 2018; **18:** 573–81.

79 Lahra MM, Martin I, Demczuk W, et al. Cooperative recognition of internationally disseminated ceftriaxone-resistant *Neisseria gonorrhoeae* strain. *Emerg Infect Dis* 2018; **24:** 735–40.

80 Attram N, Dela H, Behene E, et al. Antimicrobial use of patients with sexually transmitted infection symptoms prior to presentation at five health facilities in southern Ghana. *Antimicrob Resist Infect Control* 2023; **12:** 146.

81 Bolan GA, Sparling PF, Wasserheit JN. The emerging threat of untreatable gonococcal infection. *N Engl J Med* 2012; **366:** 485–87.

82 Gaydos CA, Melendez JH. Point-by-point progress: gonorrhea point of care tests. *Expert Rev Mol Diagn* 2020; **20:** 803–13.

83 Bradford PA, Miller AA, O'Donnell J, Mueller JP. Zoliflodacin: an oral spiropyrimidinetrione antibiotic for the treatment of *Neisseria gonorrheae*, including multi-drug-resistant isolates. *ACS Infect Dis* 2020; **6:** 1332–45.

84 Yaesoubi R, Xi Q, Hsu K, et al. The impact of rapid drug susceptibility tests on gonorrhea burden and the life span of antibiotic treatments: a modeling study among men who have sex with men in the United States. *Am J Epidemiol* 2024; **193:** 17–25.

85 Lyu Y, Choong A, Chow EPF, et al. Vaccine value profile for *Neisseria gonorrhoeae*. *Vaccine* 2023; published online Dec 13. https://doi.org/10.1016/j.vaccine.2023.01.053.

86 Padeniya TN, Hui BB, Wood JG, Seib KL, Regan DG. The potential impact of a vaccine on *Neisseria gonorrhoeae* prevalence among heterosexuals living in a high prevalence setting. *Vaccine* 2023; **41:** 5553–61.

87 Stuart BM, Pullen RL. Typhoid: clinical analysis of three hundred and sixty cases. *Arch Intern Med* 1946; **78:** 629–61.

88 Denyer Willis L, Chandler C. Quick fix for care, productivity, hygiene and inequality: reframing the entrenched problem of antibiotic overuse. *BMJ Glob Health* 2019; **4:** e001590.

89 Mintz ED, Guerrant RL. A lion in our village—the unconscionable tragedy of cholera in Africa. *N Engl J Med* 2009; **360:** 1060–63.

90 Andrews JR, Qamar FN, Charles RC, Ryan ET. Extensively drug-resistant typhoid—are conjugate vaccines arriving just in time? *N Engl J Med* 2018; **379:** 1493–95.

91 Kim S, Lee KS, Pak GD, et al. Spatial and temporal patterns of typhoid and paratyphoid fever outbreaks: a worldwide review, 1990–2018. *Clin Infect Dis* 2019; **69** (suppl 6)**:** S499–509.

92 Wong VK, Baker S, Pickard DJ, et al. Phylogeographical analysis of the dominant multidrug-resistant H58 clade of *Salmonella* Typhi identifies inter- and intracontinental transmission events. *Nat Genet* 2015; **47:** 632–39.

93 Carey ME, Dyson ZA, Ingle DJ, et al. Global diversity and antimicrobial resistance of typhoid fever pathogens: insights from a meta-analysis of 13,000 *Salmonella* Typhi genomes. *eLife* 2023; **12:** e85867.

94 Carey ME, Dyson ZA, Argimón S, *et al*. Unlocking the potential of genomic data to inform typhoid fever control policy: supportive resources for genomic data generation, analysis, and visualization. *Open Forum Infect Dis* 2023; **10** (suppl 1)**:** s38–46.

95 Baker KS, Jauneikaite E, Hopkins KL, et al. Genomics for public health and international surveillance of antimicrobial resistance. *Lancet Microbe* 2023; **4:** e1047–55.

96 Mogasale V, Ramani E, Mogasale VV, Park J. What proportion of *Salmonella* Typhi cases are detected by blood culture? A systematic literature review. *Ann Clin Microbiol Antimicrob* 2016; **15:** 32.

97 Coalition Against Typhoid. Typhoid vaccines. https://www.coalitionagainsttyphoid.org/the-issues/typhoid-vaccines/ (accessed Feb 15, 2024).

98 Bentley SD, Lo SW. Global genomic pathogen surveillance to inform vaccine strategies: a decade-long expedition in pneumococcal genomics. *Genome Med* 2021; **13:** 84.

99 Browne AJ, Chipeta MG, Haines-Woodhouse G, et al. Global antibiotic consumption and usage in humans, 2000–18: a spatial modelling study. *Lancet Planet Health* 2021; **5:** e893–904.

100 WHO. The WHO AWaRe (access, watch, reserve) antibiotic book. Geneva: World Health Organization, 2022.

101 Mulchandani R, Wang Y, Gilbert M, Van Boeckel TP. Global trends in antimicrobial use in food-producing animals: 2020 to 2030. *PLOS Glob Public Health* 2023; **3:** e0001305.

102 Cavany S, Nanyonga S, Hauk C, et al. The uncertain role of substandard and falsified medicines in the emergence and spread of antimicrobial resistance. *Nat Commun* 2023; **14:** 6153.

103 Weinstein ZB, Zaman MH. Evolution of rifampin resistance in *Escherichia coli* and *Mycobacterium smegmatis* due to substandard drugs. *Antimicrob Agents Chemother* 2018; **63:** 10–1128.

104 van Doorn HR, Ashley EA, Turner P. Case-based surveillance of antimicrobial resistance in the ACORN (A Clinically Oriented Antimicrobial Resistance Surveillance Network) study. *JAC Antimicrob Resist* 2020; **2:** dlaa018.

105 Laupland KB. Defining the epidemiology of bloodstream infections: the 'gold standard' of population-based assessment. *Epidemiol Infect* 2013; **141:** 2149–57.

106 Sintondji K, Fabiyi K, Hougbenou J, et al. Prevalence and characterization of ESBL-producing *Escherichia coli* in healthy pregnant women and hospital environments in Benin: an approach based on Tricycle. *Front Public Health* 2023; **11:** 1227000.

107 Blaak H, Kemper MA, de Man H, et al. Nationwide surveillance reveals frequent detection of carbapenemase-producing Enterobacterales in Dutch municipal wastewater. *Sci Total Environ* 2021; **776:** 145925.

108 Hutinel M, Huijbers PMC, Fick J, Åhrén C, Larsson DGJ, Flach C-F. Population-level surveillance of antibiotic resistance in *Escherichia coli* through sewage analysis. *Euro Surveill* 2019; **24:** 1800497.

109 Argimón S, Abudahab K, Goater RJE, et al. Microreact: visualizing and sharing data for genomic epidemiology and phylogeography. *Microb Genom* 2016; **2:** e000093.

110 WHO. Quadripartite Technical Group on Antimicrobial Resistance and Use Integrated Surveillance (QTG-AIS). https://www.qjsamr.org/technical-work/technical-group-on-integrated-surveillance (accessed Nov 30, 2023).

111 WHO. WHO integrated global surveillance on ESBL-producing E coli using a "One Health" approach: implementation and opportunities. 2021. https://www.who.int/publications/i/item/9789240021402 (accessed March 19, 2024).

112 Puspandari N, Sunarno S, Febrianti T, et al. Extended spectrum beta-lactamase-producing *Escherichia coli* surveillance in the human, food chain, and environment sectors: Tricycle project (pilot) in Indonesia. *One Health* 2021; **13:** 100331.

113 Milenkov M, Rasoanandrasana S, Rahajamanana LV, et al. Prevalence, risk factors, and genetic characterization of extended-spectrum beta-lactamase *Escherichia coli* isolated from healthy pregnant women in Madagascar. *Front Microbiol* 2021; **12:** 786146.

114 Banu RA, Alvarez JM, Reid AJ, *et al*. Extended spectrum beta-lactamase in river waters collected from two cities in Ghana, 2018–2020. *Trop Med Infect Dis* 2021; **6:** 105.

115 Ruppé E; Network for Enhancing Tricycle ESBL Surveillance Efficiency (NETESE) group. Lessons from a global antimicrobial resistance surveillance network. *Bull World Health Organ* 2023; **101:** 672–78.

116 Hasegawa S, Livorsi DJ, Perencevich EN, Church JN, Goto M. Diagnostic accuracy of hospital antibiograms in predicting the risk of antimicrobial resistance in enterobacteriaceae isolates: a nationwide multicenter evaluation at the Veterans Health Administration. *Clin Infect Dis* 2023; **77:** 1492–500.

117 WHO. Antimicrobial resistance: global report on surveillance. 2014. https://www.who.int/publications/i/item/9789241564748 (accessed Feb 13, 2024).

118 World Health Assembly. Global action plan on antimicrobial resistance. May 26, 2015. https://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_R7-en.pdf (accessed Feb 11, 2024).

119 European Centre for Disease Prevention and Control. European Antimicrobial Resistance Surveillance Network (EARS-Net). https://www.ecdc.europa.eu/en/about-us/networks/disease-networks-and-laboratory-networks/ears-net-data (accessed Feb 14, 2024).

120 WHO. Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR). https://www.who.int/europe/groups/central-asian-and-european-surveillance-of-antimicrobial-resistance-(caesar) (accessed Feb 14, 2024).

121 Pan American Health Organization. Latin American and Caribbean Network for Antimicrobial Resistance Surveillance—ReLAVRA+. https://www.paho.org/en/topics/antimicrobial-resistance/latin-american-and-caribbean-network-antimicrobial-resistance (accessed Feb 14, 2024).

122 WHO. GLASS method for estimating attributable mortality of antimicrobial resistant bloodstream infections. 2020. https://www.who.int/publications/i/item/9789240000650 (accessed March 19, 2024).

123 WHO. Methodological principles of nationally representative surveys as a platform for global surveillance of antimicrobial resistance in human bloodstream infections. 2023. https://www.who.int/publications/i/item/9789240067004 (accessed Feb 11, 2024).

124 Grundmann H, Aanensen DM, van den Wijngaard CC, Spratt BG, Harmsen D, Friedrich AW. Geographic distribution of *Staphylococcus aureus* causing invasive infections in Europe: a molecular-epidemiological analysis. *PLoS Med* 2010; **7:** e1000215–1000215.

125 David S, Reuter S, Harris SR, et al. Epidemic of carbapenem-resistant *Klebsiella pneumoniae* in Europe is driven by nosocomial spread. *Nat Microbiol* 2019; **4:** 1919–29.

126 de Kraker ME, Wolkewitz M, Davey PG, et al. Burden of antimicrobial resistance in European hospitals: excess mortality and length of hospital stay associated with bloodstream infections due to *Escherichia coli* resistant to third-generation cephalosporins. *J Antimicrob Chemother* 2011; **66:** 398–407.

127 Esteban-Cantos A, Aracil B, Bautista V, et al. The carbapenemase-producing *Klebsiella pneumoniae* population is distinct and more clonal than the carbapenem-susceptible population. *Antimicrob Agents Chemother* 2017; **61:** 10–1128.

128 Grundmann H, Glasner C, Albiger B, et al. Occurrence of carbapenemase-producing *Klebsiella pneumoniae* and *Escherichia coli* in the European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE): a prospective, multinational study. *Lancet Infect Dis* 2017; **17:** 153–63.

129 Liu Y-Y, Wang Y, Walsh TR, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis* 2016; **16:** 161–68.

130 Turner P, Ashley EA, Celhay OJ, et al. ACORN (A Clinically-Oriented Antimicrobial Resistance Surveillance Network): a pilot protocol for case based antimicrobial resistance surveillance. *Wellcome Open Res* 2020; **5:** 13.

131 Ordaya EE, Abu Saleh OM, Vergidis P, Deml SM, Wengenack NL, Fida M. Temporal trends in antifungal susceptibility of *Cryptococcus neoformans* isolates from a reference laboratory in the United States, 2011-2021. *Mycoses* 2024; **67:** e13691.

132 Bongomin F, Oladele RO, Gago S, Moore CB, Richardson MD. A systematic review of fluconazole resistance in clinical isolates of *Cryptococcus* species. *Mycoses* 2018; **61:** 290–97.

133 Argimón S, Masim MAL, Gayeta JM, et al. Integrating whole-genome sequencing within the National Antimicrobial Resistance Surveillance Program in the Philippines. *Nat Commun* 2020; **11:** 2719.

134 O'Brien TF, Stelling JM. WHONET: an information system for monitoring antimicrobial resistance. *Emerg Infect Dis* 1995; **1:** 66.