

# Tackling antimicrobial resistance in low-income and middle-income countries

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Antimicrobial resistance (AMR) is a global threat that claims 700 000 lives every year. If no urgent actions are taken, by 2050, AMR will cause an estimated loss of 10 million lives and \$US100 trillion.<sup>1</sup> Over the years, commonly identified infectious agents have developed resistance to antimicrobials. Since the discovery of penicillin in 1928, 20 000 potential resistant genes of nearly 400 different types have been identified.<sup>2</sup> Methicillin-resistant *Staphylococcus aureus* alone causes more than 80 000 severe infections and claims more than 11 000 lives each year.<sup>3</sup> The World Bank estimates a reduction in global domestic product per annum of 1.1%–3.8% by 2050 if AMR remains unchecked, and that an investment of US\$9 billion per year will be required to counteract the problem.<sup>4</sup>

AMR affects all countries, but the burden is disproportionately higher in low-income and middle-income countries.<sup>1</sup> To halt the spread of AMR, it is important to understand what contributes to its emergence. While the overuse of antimicrobials in both humans and animals is broadly implicated and strategies are developed to counteract such an overuse, the broader factors that contribute to AMR are often overlooked. In addition, national action plans on AMR are often constrained by lack of comprehensive multisectoral and multipronged approaches (eg, too focused on the health sector), and their findings are only relevant for a limited period of time as AMR continues to evolve at a fast pace.<sup>5</sup> A recent assessment of country situational analyses against the political, economic, sociological, technological, ecological, legislative, and industry (PESTELI) framework identified important gaps in addressing AMR.<sup>6</sup>

Indeed, collaborative efforts are necessary to delineate global, regional and local contingency plans for AMR. A multitude of factors contribute to the development of AMR. Many of these factors transcend discipline and

sectors. Efforts to counteract AMR through a traditional biomedical approach alone may fail to curb the current challenges. In this editorial, we draw insight from some recent papers in *BMJ Global Health* on AMR, and we use the PESTELI framework to highlight the multifaceted challenges involved in tackling AMR in low-income and middle-income countries, and the need for a holistic and multisectoral approach.

## POLITICAL FACTORS

Weak governance often leads to lack of attention to health system functioning and, hence, to weakened regulations for the antimicrobial stewardship. Poor antimicrobial stewardship and inappropriate antimicrobial use often in substandard doses challenge the efforts to contain the emergence and spread of AMR.<sup>7</sup> In addition, budgetary constraints limit the prioritisation for surveillance of AMR.<sup>8</sup> Improved surveillance systems and surveillance data, for example, through establishing computerised data repository, are necessary to inform policies and to respond to both the emerging threats and the long-term trends in resistance.<sup>9</sup> However, existing surveillance systems to monitor antimicrobial consumption in both humans and animals and to identify the rate and trends in development of resistance are often inadequate.<sup>8</sup> Strong political commitment with multistakeholder engagement to strengthen surveillance networks and AMR reporting, and stewardship are essential.

The lack of infrastructure due to poor economy, corruption and low preparedness in many low-income and middle-income countries has led to inadequate attention to preventive measures, such as water, sanitation and hygiene, leading to high burden of infectious diseases. Often in such settings, antimicrobials function as a ‘quick-fix’ infrastructure, used in place of and to rescue the fractured infrastructures of care, water, sanitation and hygiene.<sup>10</sup>



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Universal access to water and sanitation alone is expected to lead to a 60% reduction in diarrhoeal illnesses treated with antimicrobials. Maintaining hygiene through hand washing alone by clinicians in healthcare settings can decrease the infectious diseases and the use of antimicrobials by 40%.<sup>11</sup> The political awareness and prioritisation of these simple yet highly effective preventive measures remain low; hence, they remain inadequately addressed.

### ECONOMIC FACTORS

As health systems in low-income and middle-income countries often lack resources (functional and infrastructural) to reach a large population, more so in rural areas, universal access to primary healthcare services becomes a major challenge.<sup>8</sup> Access to appropriate antimicrobials against common infections is imperative to save lives.<sup>12</sup> However, because regulatory mechanisms are weak, antimicrobials are often used inappropriately and irresponsibly. The struggle between ensuring universal health coverage and at the same time preserving the currently available antimicrobials is a major concern in low-income and middle-income countries.<sup>13</sup> In rural and under-resourced settings of many low-income and middle-income countries, where access to qualified healthcare workers is severely constrained, universal health coverage has been erroneously equated with the availability of antimicrobials.<sup>10</sup> Such a quick fix for the weak health systems further exacerbates the inappropriate antimicrobial use. Moreover, in settings where access to high-quality health services at health facilities is constrained by limited functional capacity to serve large populations,<sup>13 14</sup> inadequate health coverage and out-of-pocket (OOP) expenditure for healthcare, especially in the private sector, are often catastrophic.

In Nepal, for instance, household OOP expenditure for healthcare comprises about 55.4% of health spending, with OOP at private hospitals being up to 80% of the total expenditure at all kinds of hospitals.<sup>15</sup> Consequently, healthcare delivery largely depends on informal providers, pharmacists, drug dispensers and traditional practitioners.<sup>14</sup> Often unqualified and profit driven, these providers sell antimicrobials over the counter (OTC) for mild to moderate illnesses, a large proportion of which are self-limiting viral infections.<sup>16</sup> In addition, poor pharmacovigilance and drug regulation make populations vulnerable to counterfeit and substandard medicines. Due to weak governance entwined with the complex socioeconomic, cultural and behavioural factors that drive healthcare seeking, it is difficult to implement a stringent regulation to control the unregulated OTC dispensing of antimicrobials.

### SOCIOLOGICAL FACTORS

Poor educational status and low awareness leave populations with popular myths, cultural practices and belief systems towards the use of medicines, especially antibiotics.<sup>16</sup> These social factors and cultural practices,

combined with poverty, further leads people to self-medicate against common infections (another quick fix), buy medications from unregulated drug dispensaries, visit traditional practitioners and borrow medicines from their neighbours. Medicines obtained from traditional practitioners are often unknown chemical agents mixed with antimicrobials in substandard doses, which also foster AMR and delay timely treatment at allopathic health centres. Driven by the desire to get well soon and at minimal cost (again, a quick fix), patients often demand treatment regardless of the type of infection (bacterial or viral) and avoid necessary investigations during consultations.<sup>7</sup> For instance, in Kenya, patient expectations were often felt as pressure by healthcare practitioners to prescribe antibiotics.<sup>17</sup>

### TECHNOLOGICAL FACTORS

Technological innovations in diagnostics to rapidly detect infections and AMR are critical for both improved patient care and better surveillance.<sup>13</sup> Peripheral health facilities often lack laboratory facilities and skilled human resources. Diagnostics to inform the appropriate prescription of antimicrobials are not available at the point of care, while antimicrobials are easily accessible OTC and a wide variety of infections are treated empirically.<sup>7</sup> In addition, healthcare innovations through computerised real-time reporting of data are essential for improved surveillance and action. A robust mechanism to routinely monitor diagnostics-based use of antimicrobials through increased reporting of infectious diseases and the prescription is essential.

### INDUSTRY FACTORS

In the absence of political, social and economic changes, especially in low-income and middle-income countries, the rise of AMR may only be counteracted through investments in research and development of newer drugs. The decline in stakes of pharmaceutical industries to develop new antibiotics has dwindled in the last few decades compared with drug development in other health conditions such as cancer.<sup>1 18</sup> With the diminished production of newer antibiotics and growing AMR, remaining antibiotics have become extremely expensive and are unaffordable in many low-income and middle-income countries.<sup>7</sup> Adding on this, pharmaceutical companies' incentives to medical practitioners and drug dispensers to prescribe specific antimicrobials further escalate the use and cost of antimicrobials. Another way to curb the overuse of antimicrobials is through the use of available vaccines against common infections to reduce the burden of resistant infections. The use of existing pneumococcal vaccine, for instance, can reduce the antimicrobial-resistant infections by more than half.<sup>19</sup> However, again, such new vaccines are not easily available and affordable in many low-income and middle-income countries unless they are subsidised with wide coverage by health systems.

## ECOLOGICAL FACTORS

AMR cannot be tackled well without an ecological approach embedded in the concept of ‘One Health’.<sup>13</sup> The rising commercial farming, animal husbandry, food and agricultural products use antimicrobials in huge proportions. The use of antimicrobials have become, paradoxically, a quick-fix economic panacea in producing standard-sized animals, fish and crops, which overlooks the enormous economic losses due to overuse of antimicrobials.<sup>10</sup> Around 70% of medically important antimicrobials in the the USA are sold for use in food-producing animals.<sup>20</sup> Such widespread antimicrobial use also echoes across Europe.<sup>21</sup> Although the available information from many low-income and middle-income countries is limited, empirical estimates suggest that the antimicrobial use in animal food is very high. Use of antimicrobials in these sectors puts a huge amount of drug pressure and accelerates the rate of emergence of AMR. Legislative mechanisms are urgently required to contain the current trend of use of antimicrobials in food and agriculture sectors through greater collaboration with wider stakeholders and multidisciplinary embrace of One Health.<sup>22</sup>

## CONCLUSION

High burden of infectious diseases, poverty, weak governance and health systems, and low awareness in many low-income and middle-income countries remain major challenges in the fight against AMR. Efforts to address AMR globally must take into consideration these peculiar challenges. Low-income and middle-income countries must strengthen their health systems in ways that address these systems issues, with a focus on developing regulatory strategies against unauthorised antimicrobial use, antimicrobial stewardship and treatment guidelines for common infections, along with sustainable public awareness campaigns aimed at changing health-seeking behaviour. These efforts should be based on evidence—on each component of the PESTELI framework—tailored to the context in each setting. Increased investment in research and development of vaccines, newer drugs and improvement in water, sanitation and hygiene to prevent common infections, together with the promotion of diagnostic tests to timely detect and treat infections, are essential to curb the current trends of AMR.

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