Achieving Global Targets for Antimicrobial Resistance

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Over the decades neglect, antimicrobial resistance (AMR) has captured the attention and concern of the public health community and global leaders. In September 2016, a high-level meeting of the United Nations (UNGA) will discuss how countries can cooperate to preserve global access to effective antimicrobials. This will be only the third health issue (and the first One Health issue, integrating human, animal, and environmental health) to bring together heads of state at the UNGA. This is a rare opportunity to set a global agenda to combat the crisis. We believe that (i) setting targets for reducing drug-resistant infections, (ii) appropriate financing for global action, and (iii) defining the global health architecture to address AMR, should be key elements of a UN plan.

The cost of antibiotic treatment and mortality due to resistance is increasing worldwide (2). The greatest burden occurs in low- and middle-income countries (LMICs), especially among the young. An estimated 214,000 neonatal sepsis deaths are attributable to resistant pathogens each year (7). But high-income countries are not immune: an estimated 23,000 people in the United States and 25,000 in Europe die each year from resistant pathogens (2,7).

That said, access and delayed access to antibiotics kill more people than AMR. The challenge of expanding appropriate access to antimicrobials, while restricting inappropriate access, requires new approaches to financing and delivering healthcare. A One Health perspective can address connections between antimicrobial use and resistance in humans, animals, and the wider environment.

Targets and Surveillance

Use of antibiotics is the most important driver of selection for resistance and loss of effectiveness. Use is increasing globally, driven by rising incomes and increasing access. Antibiotic use varies greatly in human and animal sectors across countries, depending on prevailing medical, veterinary and regulatory practices.

We propose that no country consume more than the current median global level (P2 standard units per capita per year). We estimate that this would lower overall use by 21% globally (based on 6), see supplemental material (SM)). Reducing use is accomplished by improving public health and sanitation. In low-income countries, antibiotics are used to compensate for the lack of public health infrastructure (e.g., vaccination coverage, infection control). A target linked to UN Sustainable Development Goals (3) and 6 (on water and sanitation) that commits nations to improving public health would reduce reliance on antibiotics.

Further reductions could be achieved through public campaigns, aimed at physicians and patients, to discourage inappropriate antibiotic use (9), particularly in response to seasonal influenza (8). Though LMICs face a higher burden of infectious disease, per capita consumption of antimicrobials in most LMICs is well below our target level. Thus, meeting this target need not be compromising legitimate uses.

There is significant potential for reducing consumption in the animal sector. We propose complete global phase out of antimicrobial growth promoters: five years would be appropriate given the urgency of the problem. This could avert much of the projected 6% increase in farm animal use between 2010 and 2030 (10). Though this would incur some cost to agricultural sectors, even in China (the largest consumer of antibiotics in agriculture), that cost is likely on the order of $3 billion a year, less than a small fraction of the country’s burden of AMR (10).

Moreover, the costs of improving hygiene and biosecurity in farming operations to phase out antimicrobial growth promoters would be largely offset by lowering risks of bioterrorism and cost of antimicrobials. We envision a process similar to that in the EU where there was declared intent to phase out sub-therapeutic use followed by regulatory changes to make these transitions happen. Globally, this would happen through a multilateral process, as with global movements to phase out, e.g., asbestos or chlorofluorocarbons.

National-level restrictions on antibiotic effluents from pharmaceutical manufacturing, agricultural operations and hospital waste that end up in waterways and contribute to the buildup of resistance genes in the soil and water are an urgent priority.

While setting targets for reductions in antibiotic consumption is important, could be accomplished by antimicrobial targets are critical to our approach against the ultimate goal of reducing drug-resistant infections. We propose targets to reduce levels of a drug resistance index (e.g., the proportion of infections that are resistant), based on weighted-average of resistance of the eight World Health Organization (WHO) priority pathogens to first-line antibiotics, nationally, regionally and globally within 5 years. Reductions should be set at levels based on the eight World Health Organization (2010) priority pathogens. We do not specify the scale of reduction – the immediate priority is to prevent increases – but recommend a review of the targets to consider more stringent targets. The countries agreed to phase down use of drug-resistant strains would reflect the complex public health context and priorities of individual countries.

Existing surveillance programs for AMR can contribute to target monitoring at the national level (11), including the Global Antimicrobial Resistance Surveillance System, and ResistanceMap (12). Surveillance should include the livestock sector and the wider environment, and track access and use, and indicators such as water, sanitation, and vaccination coverage. Data on AMR must be translated into epidemiologically sound estimates of public health burden, which requires information on treatment rates and failures (7) not routinely collected at present.

Surveillance cannot be the sole responsibility of individual countries; surveillance is a global good and should be financed accordingly. Initiatives such as the Fleming Fund and the Global Health Security Agenda


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provide opportunities to strengthen surveillance in countries with poor public health architecture. Not all surveillance elements need to be replicated at a national level; integrating local activities into multi-national networks may be more efficient, with appropriate structures for data sharing, analysis and communication.

**Global financing**

Substantial funds have been committed in the U.S. and Europe to tackle AMR, but success will be limited without global scale investments. The need to incentivize development of new vaccines, diagnostics, novel therapies and stewardship methods, as well as traditional antibiotics to ensure availability of the "antibiotic umbrella" has been widely recognized (13). Vaccines, for animals and humans, face high development costs and uncertain markets; however, the GAVI Vaccine Alliance financing mechanism has been successful in bringing new vaccines into wide use.

Development and deployment of diagnostics is more difficult. Knowledge of the appropriate use of diagnostics is needed. Multiple diagnostics are needed. Diagnostics must be modified (14), but new diagnostics can interact to synergize, antagonize, or suppress each other’s effects (15), modifying the evolution of resistance.

Financial stimuli for antibiotic development must address the lack of incentives for appropriate use (16) and should enable sustainable access when clinically appropriate. "There are approaches for developing a global model where the pharmaceutical company would have no incentive to develop new antibiotics: (i) Co-funding of development and monitoring of national plans and relevant actions can (21). A new health system is more difficult. Knowledge of antibiotic resistance threats to erase decades of progress in medicine, food security, and public health. Global collective action rooted in national responses is necessary. The UNGA high level meeting on AMR could help shift world opinion, build consensus around core feasible goals, and integrate solutions into policy approaches by UN member states, international organizations, and philanthropies.

**REFERENCES AND NOTES**

16. 10.1126/science.aaf0286
17. Supplemental Materials
18. FIGURE: Caption: Based on (9). See SI for details.