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Citation for published version:

Woolhouse, M, Laxminarayan, R, Blaser, M & Wang, M 2016, 'Achieving Global Targets for Antimicrobial Resistance' *Science*, vol. 353, no. 6302, pp. 874-875. DOI: 10.1126/science.aaf9286

Digital Object Identifier (DOI):

[10.1126/science.aaf9286](https://doi.org/10.1126/science.aaf9286)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Science

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OVERLINE

Achieving Global Targets for Antimicrobial Resistance

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By Ramanan Laxminarayan¹, Devi Sridhar², Martin Blaser³, Mingui Wang⁴, Mark Woolhouse⁵, Woolhouse^{2*}

After decades of 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 General Assembly (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) adequate 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, lack of 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 ac-

cess. 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 (22 standard units per capita per year). We estimate that this would lower overall use by 21% globally (based on (8); 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 (on health) 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 compromise legitimate uses.

There is significant potential for reducing consumption in the animal sector. We propose complete global phase out of use of antimicrobial growth promoters; five years would be appropriate given the urgency of the problem. This could avert much of the projected 67% increase in farm animal use between 2010 and 2030 (8). 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, to be a small fraction of the country's burden of AMR (10). Moreover, the costs of improving biosafety and biosecurity in farming operations to phase out antimicrobial growth promoters would be largely offset by lowering risk of infection 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 the transition it

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.

Targets for reductions in antibiotic consumption should be accompanied by, outcome-based targets are critical to assess progress 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 (10a). Reductions should be relative to 2016 levels, based on the eight World Health Organization (WHO) priority pathogens. We do not specify the scale of reduction – the immediate priority is to prevent increases – but recommend a review after 5 years in 2021 to consider more stringent targets. The weighting given to each drug, and strategies chosen, would reflect usage health system 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 involve 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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¹Center for Disease Dynamics, Economics & Policy, Washington, DC USA. ²University of Edinburgh, Edinburgh, UK. ³New York University School of Medicine, New York, NY USA. ⁴Fudan University, Shanghai, China.

*Correspondence to: Mark.Woolhouse@ed.ac.uk

