- 2 Laxminarayan R, Matsoso P, Pant S, et al. Access to effective antimicrobials: a worldwide challenge. *Lancet* 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00474-2.
- 3 Holmes AH, Moore LSP, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet* 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00473-0.
- 4 Mendelson M, Røttingen J-A, Gopinathan U, et al. Maximising access to achieve appropriate human antimicrobial use in low-income and middle-income countries. Lancet 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00547-4.
- 5 Dar OA, Hasan R, Schlundt J, et al. Exploring the evidence base for national and regional policy interventions to combat resistance. *Lancet* 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00520-6.
- Árdal C, Outterson K, Hoffman SJ, et al. International cooperation to improve access to and sustain effectiveness of antimicrobials. *Lancet* 2015; published online Nov 18. http://dx.doi.org/10.1016/50140-6736(15)00470-5.
- 7 Van Boeckel TP, Brower C, Gilbert M, et al. Global trends in antimicrobial use in food animals. Proc Natl Acad Sci USA 2015; 112: 5649–54.
- 8 Zhang QQ, Ying GG, Pan CG, Liu YS, Zhao JL. Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance. Environ Sci Technol 2015; 49: 6772–82.
- 9 Mather AE, Matthews L, Mellor DJ, et al. An ecological approach to assessing the epidemiology of antimicrobial resistance in animal and human populations. Proc Biol Sci 2011; 279: 1630–39.
- Price LB, Stegger M, Hasman H, et al. Staphylococcus aureus CC398: host adaptation and emergence of methicillin resistance in livestock. MBio 2012; 3: e00305-11.
- 11 Larsen J, Petersen A, Sørum M, et al. Methicillin-resistant Staphylococcus aureus CC398 is an increasing cause of disease in people with no livestock contact in Denmark, 1999 to 2011. Euro Surveill 2015; 20: pii=30021.
- 12 Nordstrom L, Liu CM, Price LB. Foodborne urinary tract infections: a new paradigm for antimicrobial-resistant foodborne illness. Front Microbiol 2013; 4:30
- 13 Forslund K, Sunagawa S, Kultima JR, et al. Country-specific antibiotic use practices impact the human gut resistome. *Genome Res* 2013; 23: 1163–69.
- 14 Woolhouse M, Ward M, van Bunnik B, Farrar J. Antimicrobial resistance in humans, livestock and the wider environment. *Philos Trans R Soc Lond B Biol Sci* 2015; 370: 20140083.

- 15 Gupta A, Nelson JM, Barrett TJ, et al; NARMS Working Group. Antimicrobial resistance among Campylobacter strains, United States, 1997–2001. Emerg Infect Dis 2004; 10: 1102–09.
- 16 Dutil LR, Irwin R, Finley LK, et al. Ceftiofur resistance in Salmonella enterica serovar Heidelberg from chicken meat and humans, Canada. Emera Infect Dis 2010: 16: 48–54.
- 17 Aarestrup FM, Seyfarth AM, Emborg H-D, Pedersen K, Hendriksen RS, Bager F. Effect of abolishment of the use of antimicrobial agents for growth promotion on occurrence of antimicrobial resistance in fecal enterococci from food animals in Denmark. Antimicrob Agents Chemother 2001; 4: 2054–59.
- 18 Food and Drug Administration. Guidance for industry: the judicious use of medically important antimicrobial drugs in food-producing animals, no 209. Rockville MD: Food and Drug Administration, 2012. http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ GuidanceforIndustry/UCM216936.pdf (accessed Oct 20, 2015).
- 19 Chick-fil-A. Antibiotic-free chicken. 2014. http://www.chick-fil-a.com/ Antibiotic-Free (accessed Oct 22, 2015).
- 20 McDonald's. McDonald's USA announces new antibiotics policy and menu sourcing initiatives. March 4, 2015. http://news.mcdonalds.com/pressreleases/mcdonald-s-usa-announces-new-antibiotics-policy-and-menusourcing-initiatives-nyse-mcd-1179405 (accessed Oct 20, 2015).
- 21 Layne N. Costco working to end use of human antibiotics in chicken. Reuters March 5, 2015. http://www.reuters.com/article/2015/03/06/us-costcoantibiotics-idUSKBN0M201520150306 (accessed Oct 22, 2015).
- 22 Grace D. Review of evidence on antimicrobial resistance and animal agriculture in developing countries. Report produced by the International Livestock Research Institute (ILRI) for Evidence on Demand with the assistance of the UK Department for International Development (DFID). June, 2015. http://rdd.dfid.gov.uk/pdf/outputs/EoD/EoD\_Consultancy\_ June15\_Ag\_Related\_AMR.pdf (accessed Oct 20, 2015).
- 23 Laxminarayan R, Van Boeckel T, Teillant A. The economic costs of withdrawing antimicrobial growth promoters from the livestock sector. OECD Food, Agriculture and Fisheries Papers, no 78. Paris: Organisation for Economic Cooperation and Development Publishing, 2015. http://dx.doi. org/10.1787/5js64kst5wvl-en (accessed Oct 20, 2015).
- 24 WHO. Critically important antimicrobials for human medicine, 3rd revision 2011. Geneva: World Health Organization, 2011. http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485\_eng.pdf (accessed Oct 20, 2015).

## National action for global gains in antimicrobial resistance



Few public health problems are of greater global importance today than antimicrobial resistance. Multidrug resistant pathogens are a challenge in high-income countries, and many countries, including the USA and the UK, have created national plans as well as legislation and regulation to address antibiotic resistance issues. However, middle-income and low-income countries are likely to bear the brunt of this problem. Many of our citizens do not have access to antibiotics. In the Lancet Series on antimicrobial access, sustainability, and effectiveness, Ramanan Laxminarayan and colleagues<sup>1</sup> make the case that far more people die from lack of access to antibiotics than from antimicrobial resistance. They estimate that 75% of community-acquired pneumonia deaths in children younger than 5 years could be averted by universal access to antibiotics. Marc Mendelson and colleagues echo this finding in their Series paper, and highlight the need for improved access to diagnostics so that infectious diseases can be identified and treated correctly. Even for those with access to first-line antibiotics, more expensive second-line antibiotics are not affordable for our countries. Some new antibiotics are needed, but conserving the antibiotics we already have is the highest immediate priority.

Published Online November 18, 2015 http://dx.doi.org/10.1016/ S0140-6736(15)00668-6

See Comment page 102

See Series pages 168, 176, and 188



See Online/Series http://dx.doi.org/10.1016/ S0140-6736(15)00520-6 and http://dx.doi.org/10.1016/ S0140-6736(15)00470-5 The World Health Assembly endorsed the Global Action Plan for Antimicrobial Resistance in May, 2015, calling on member states to put in place national plans within 2 years.<sup>3</sup> The Series papers by Osman Dar<sup>4</sup> and Christine Årdal<sup>5</sup> and their colleagues review the evidence base for national and regional policies on antimicrobial resistance and call for coordinated global action to support the WHO plan. Hospital antibiotic stewardship and infection prevention and control are among the most broadly effective policies in all settings.

However, few low-income and middle-income countries have taken even preliminary steps in this direction. We are ahead of the curve because our countries—India, Mozambique, South Africa, and Kenya—along with four other countries in Africa and Asia (Nepal, Tanzania, Uganda, and Vietnam) have assessed the current status of antibiotic access and resistance and have begun to develop national action plans.<sup>6</sup>

The Government of India's first step is bringing 24 antibiotics under a new Schedule H1 drug category; sale of these drugs without a doctor's prescription could attract substantial penalties.7 Pharmacists now have to document details of patient, drug, and prescriber, subject to regular inspections by drug control officials. Through the Kayakalp and Mission Indradhanush, the Government of India is also working to reduce the burden of bacterial infections by improving access to sanitation and vaccination at an unprecedented scale.8,9 The Indian Council of Medical Research has established a National Programme on Antimicrobial Surveillance, in ten laboratories at academic centres, that covers priority pathogens identified by WHO, and the Drugs Controller General of India has started a pharmacovigilance programme for antibiotics. 10 In addition, the Department of Biotechnology and its Biotechnology Industry Research Assistance Council are investing in science and early stage startups that hold the promise of producing novel antibiotics against Gram-negative pathogens, that pose a significant global health threat.

Meanwhile, in Kenya, the Ministry of Health formed a multisectoral National Antimicrobial Resistance Advisory Committee in 2015 with representatives from human and animal health, and created a position for an antimicrobial resistance focal point. The Ministry is now designing a national plan, with support from the advisory committee. The Ministry also actively supports formal awareness-raising activities throughout the country.

In 2011, the South African Medical Journal published the Global Antibiotic Resistance Partnership-South Africa situation analysis that highlighted the emerging threat of antimicrobial resistance.11 This started a process that led to the publication of the Antimicrobial Resistance National Strategy Framework 2014–2024 by South Africa's National Health Council.12 Development of the plan and its continuing implementation has involved coordinated actions, programmes, and efforts across sectors and government departments. South Africa's Department of Health is finalising its antimicrobial resistance implementation plans, to be announced during the 2015 World Antibiotic Awareness Week. Strategic alliances with stakeholders, particularly the South African Antibiotic Stewardship Programme, and support from the Center for Disease Dynamics, Economics and Policy (CDDEP) are essential to ultimate success.

South Africa also has a sound antibiotic surveillance programme, which has facilitated addressing treatment failures and amending the standard treatment guidelines.<sup>13</sup> The current national resistance profile was included in CDDEP's report *State of the World's Antibiotics*, 2015.<sup>14</sup>

Mozambique is a recent entrant into the national antibiotic resistance policy process in Africa, and has completed a situation analysis with recommendations on addressing antibiotic resistance, including a commitment to develop a national plan over the next year. Priority activities include improving infection prevention and control in hospitals, improving surveillance, and gathering information on antibiotic use in food animals with the aim of reducing unnecessary use. To improve public health and reduce the bacterial disease burden, Mozambique is among the earliest adopters in sub-Saharan Africa of vaccination against *Haemophilus influenzae* type b and pneumococcal disease, and has scheduled introduction of rotavirus vaccine.

In our countries we face many of the same challenges as high-income countries in confronting antimicrobial resistance. But we also face additional challenges: weaker health-care systems, difficulty in enforcing regulations, an inadequate supply of trained health-care providers, poor public health infrastructure, a higher burden of infectious disease, and limited resources.

We commend the *Lancet* Series and its recommendations for providing a factual basis for developing national plans to reduce the burden of infection, to improve infection prevention and control,

to increase surveillance, and to move towards access to antibiotics for all while preserving the global effectiveness of these life-saving drugs. The strategies must address antibiotic use in hospitals, communities, and agriculture, in partnership with all relevant sectors. Extending access to all must be balanced with the conservation of our current antibiotic supply. While global cooperation is essential, action must come from the national level, with national-level ownership and regional collaboration.

Our first steps show that national-level policy action on antimicrobial resistance is possible in low-income and middle-income countries, and, as highlighted in this *Lancet* Series, attention to preserving access to effective antibiotics for all is an urgent need.

Nazira Abdula, James Macharia, Aaron Motsoaledi,
\*Soumya Swaminathan, Krishnaswamy VijayRaghavan
Ministry of Health, Government of Mozambique, Maputo,
Mozambique (NA); Ministry of Health, Government of Kenya,
Nairobi, Kenya (JM); Department of Health, Pretoria, South Africa
(AM); and Departments of Health Research (SS) and Biotechnology
(KV), Government of India, New Delhi, India
soumyas@trcchennai.in

NA is Minister of Health for the Government of Mozambique. JM is Cabinet Secretary, Ministry of Health for the Government of Kenya. AM is Minister of Health for the Government of South Africa. SS is Secretary, Department of Health Research and KV is Secretary, Department of Biotechnology for the Government of India. We declare no competing interests.

1 Laxminarayan R, Matsoso P, Pant S, et al. Access to effective antimicrobials: a worldwide challenge. Lancet 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00474-2.

- Mendelson M, Røttingen J-A, Gopinathan U, et al. Maximising access to achieve appropriate human antimicrobial use in low-income and middle-income countries. *Lancet* 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00547-4.
- 3 WHO. Draft global action plan on antimicrobial resistance. Geneva: World Health Organization, 2015.
- 4 Dar OA, Hasan R, Schlundt J, et al. Exploring the evidence base for national and regional policy interventions to combat resistance. *Lancet* 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00520-6.
- 5 Årdal C, Outterson K, Hoffman SJ, et al. International cooperation to improve access to and sustain effectiveness of antimicrobials. Lancet 2015; published online Nov 18. http://dx.doi.org/10.1016/S0140-6736(15)00470-5.
- 6 Gelband H. The Global Antibiotic Resistance Partnership. In: Carlet J, Upham G, eds. AMR control 2015: confronting antimicrobial resistance. Woodbridge: Global Health Dynamics, 2015: 98–101.
- 7 Department of Health and Family Welfare, Government of India. Gazette notification G.S.R. 588. Aug 30, 2013. http://cdsco.nic.in/ writereaddata/588E30thAug2013.pdf (accessed Oct 16, 2015).
- 8 Ministry of Health and Family Welfare, Government of India. Health Minister launches "Kayakalp"—an initiative for Award to Public Health Facilities. New Delhi: Government of India, 2015. http://pib.nic.in/newsite/PrintRelease. aspx?relid=121768 (accessed Oct 16, 2015).
- 9 Travasso C. Mission Indradhanush makes vaccination progress in India. BMJ 2015; 351: h4440.
- 10 Ministry of Health and Family Welfare, Government of India. Measures to contain deaths from antibiotic resistance. New Delhi: Government of India. 2015.
- 11 Winters C, Gelband H. Part I: the Global Antibiotic Resistance Partnership (GARP). South Afr Med J 2011; 101: 556–57.
- 12 Department of Health, Government of South Africa. Antimicrobial Resistance National Strategy Framework 2014–2024. Pretoria: Department of Health 2014
- 13 Wasserman S, Boyles T, Mendelson M, on behalf of the South African Antibiotic Stewardship Programme. A pocket guide to antibiotic prescribing for adults in South Africa, 2014. 2014. http://www.fidssa.co.za/images/ SAASP\_Antibiotic\_Guidelines\_2014.PDF (accessed Oct 20, 2015).
- 14 Gelband H, Miller-Petrie M, Pant S, et al. The state of the world's antibiotics, 2015. Washington, DC: Center for Disease Dynamics, Economics and Policy, 2015.
- 15 Sigauque B, Sevene E. Situation analysis and recommendations: antibiotic use and resistance in Mozambique. Maputo: Center for Disease Dynamics, Economics and Policy, 2015.