Chapter 26

The Super-Wicked Problem of Antimicrobial Resistance

Jasper Littmann, A. M. Viens, and Diego S. Silva

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Antimicrobial resistance (AMR) – the progressive process by which microbes, such as bacteria, through evolutionary, environmental and social factors develop the ability to become resistant to drugs that were once effective at treating them – is a threat from which no one can escape. It is one of the largest threats to clinical and global health in the twenty-first century – inflicting monumental health, economic and social consequences.¹ All persons locally and globally, and even all future persons yet to come into existence, all suffer the shared, interdependent vulnerability to this threat that will have a substantial impact on all aspects of our lives. For example,

¹ J O'Neill, et al., *Infection Prevention, Control and Surveillance: Limiting the Development and Spread of Drug Resistance* (London: Review on Antimicrobial Resistance, 2016) https://amr-review.org/sites/default/files/Health%20infrastructure%20and%20surveillance%20final%20version_LR_NO%20CROPS.pdf (accessed September 29, 2017); President's Council of Advisors on Science and Technology, *Report To The President On Combating Antimicrobial Resistance* (Washington: PCAST, 2014); World Health Organization, *The Evolving Threat of Antimicrobial Resistance: Options for Action* (Geneva: WHO Press, 2012); World Economic Forum, *Global Risks 2013 – Insight Report, Eighth Edition* (Geneva, 2013); S.C. Davies, J. Grant and M. Catchpole, *The Drugs Don't Work: A Global Threat* (London: Penguin, 2013); O.O. Adeyi, et al., *Drug-Resistant Infections: A Threat to Our Economic Future* (Washington, DC: World Bank, 2017).

J. Littmann (✉)
Norwegian Institute of Public Health, Oslo, Norway
e-mail: jasper.littmann@fhi.no

A. M. Viens
School of Global Health, York University, Toronto, Canada
e-mail: amviens@yorku.ca

D. S. Silva
Sydney Health Ethics, School of Public Health, University of Sydney,
Sydney, NSW, Australia
e-mail: diego.silva@sydney.edu.au

while reliable data are hard to find, the European Centre for Disease Prevention and Control (ECDC) has conservatively estimated that, in Europe alone, AMR causes additional annual cost to health care systems of at least €1.5 billion, and is responsible for around 25,000 deaths per year. Furthermore, AMR significantly increases the cost of treating bacterial infections with an increase in length of hospital stays and average number of re-consultations, as well as the resultant lost productivity from increased morbidity.² With a combined cost of up to \$100 trillion to the global economy – pushing a further 28 million people into extreme poverty – this is one of the most pressing challenges facing the world.³ Most troublingly, if we do not succeed in diminishing the progression of AMR, there is the very real potential for it to threaten common procedures and treatments of modern medicine, including the safety and efficacy of surgical procedures and immunosuppressing chemotherapy.⁴ Some experts are warning that we may soon be ushering in a post-antibiotic area.⁵

26.1 Challenges in Responding to AMR

There exists a multitude of policy responses to AMR at the local, national and international levels.⁶ Unfortunately, their success to date has only been limited.⁷ This may partly be due to the fact that many microorganisms are highly adaptable and constantly evolving, thereby presenting a perpetual challenge to clinicians, researchers, public health professionals and policy-makers.⁸ However, the formulation and

²L.L. Maragakis, E.N. Perencevich and S.E. Cosgrove, 'Clinical and Economic Burden of Antimicrobial Resistance,' *Expert Review of Anti-infective Therapy* 6(2008): 751–63; F. Alam, et al. 'The additional costs of antibiotics and re-consultations for antibiotic-resistant *Escherichia coli* urinary tract infections managed in general practice,' *International Journal of Antimicrobial Agents* 33(2009): 255–57; R. Smith and J. Coast, 'The true cost of antimicrobial resistance,' *BMJ* 2013; 346: f1493; Centers of Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013* (Atlanta: Centers of Disease Control and Prevention, 2013)

³J. O'Neill et al., *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations* (London: Review on Antimicrobial Resistance, 2016), available at https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf (accessed September 29, 2017).

⁴A. Teillant, S. Gandra, D. Barter, D.J. Morgan, and R. Laxminarayan, 'Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study,' *Lancet Infectious Diseases* 15(2015): 1429–37.

⁵S.C. Davies, J. Grant and M. Catchpole, *The Drugs Don't Work: A Global Threat* (London: Penguin, 2013).

⁶World Health Organization, *Global Strategy for Containment of Antimicrobial Resistance* (Geneva: WHO, 2001); Infectious Diseases Society of America, 'The 10 × '20 Initiative: Pursuing a Global Commitment to Develop 10 New Antibacterial Drugs by 2020,' *Clinical Infectious Diseases* 8(2010): 1081–83; Bundesministerium für Gesundheit, *Deutsche Antibiotikaresistenz-Strategie* (Berlin, 2011); Department of Health, *UK Five Year Antimicrobial Resistance Strategy 2013 to 2018* (London, 2013)

⁷World Health Organization, *Antimicrobial Resistance – Global Report on Surveillance* (Geneva: WHO Press, 2014)

⁸A.S. Fauci and D.M. Morens, 'The Perpetual Challenge of Infectious Diseases,' *New England Journal of Medicine* 366(2012): 454–61.

implementation of effective policies are also compounded by the complexity of the challenge. This complexity pertains to the number of local, national and international stakeholders involved, the difficulty in establishing successful collaboration and coordination mechanisms across different policy areas, and the numerous inter-related drivers that make this a problem at the global scale.⁹

The number of stakeholders who contribute to the emergence of AMR is extraordinarily large.¹⁰ Misuse and over-prescription of antibiotics, for example, are driven not only by health care professionals but also consumers – many of whom will not use antibiotics as instructed, often without being aware of the potential consequences of their actions.¹¹ Other patient groups entirely lack access to appropriate antimicrobial treatment, especially in poorer or less developed settings.¹² Where treatment is either unaffordable for many or infrastructure is lacking, people are more likely to self-medicate or buy counterfeit drugs through unofficial channels, increasing the chance that their drugs are less effective or unsuitable for treating the infection.¹³ Beyond human usage, the pervasive use of antibiotics outside of medical settings also remains a key source of resistance. Indeed, it is estimated that more antibiotics are given to animals than consumed by humans – and, in many instances, for non-therapeutic use.¹⁴ The wide use of antibiotics within agricultural, aquaculture, horticultural and animal farming industries all provide multiple opportunities for the increase incidence and prevalence of antibiotic-resistant bacteria.¹⁵

AMR does not, therefore, squarely fall into a single policy domain and any effective policy will require collaboration among a wide range of experts, such as clinicians, veterinarians, microbiologists, pharmacologists, epidemiologists, lawyers,

⁹R. Laxminarayan, et al., 'Antibiotic resistance - the need for global solutions,' *Lancet Infectious Diseases* 13(2013): 1057–98.

¹⁰W. Albrich, D. Monnet, S. Harbarth, 'Antibiotic Selection Pressure and Resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*,' *Emerging Infectious Diseases* 10(2004): 514–17.

¹¹C.C. Butler, et al., 'Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throat,' *BMJ* 317(1998): 637–42; I. Björkman, et al., 'Infectious disease management in primary care: perceptions of GPs,' *BMC Fam Pract*, 12:1 (2011); N. Britten, 'Patients' expectations of consultations,' *BMJ*, 328 (2004):416–17

¹²M. Mendelson, et al. 'Maximising access to achieve appropriate human antimicrobial use in low-income and middle-income countries,' *Lancet* 387(2015):188–98; R. Laxminarayan, et al., 'Access to effective antimicrobials: a worldwide challenge,' *Lancet* 387(2016): 168–175.

¹³N. Gualde, *Resistance: The human struggle against infection* (New York: Dana Press, 2006); R. Laxminarayan and D.L. Heymann, 'Challenges of drug resistance in the developing world,' *BMJ* 344(2012): e1567.

¹⁴J. O'Neill, et al., *Antimicrobials in agriculture and the environment: reducing unnecessary use and waste* (London: Review on Antimicrobial Resistance, 2016) <https://amr-review.org/sites/default/files/Antimicrobials%20in%20agriculture%20and%20the%20environment%20-%20Reducing%20unnecessary%20use%20and%20waste.pdf> (accessed September 12, 2017).

¹⁵Food and Agriculture Organization of the United Nations, *Drivers, Dynamics and Epidemiology of Antimicrobial Resistance in Animal Production* (Geneva: WHO, 2016); R.W. Meek RW, H. Vyas and L.J.V. Piddock, 'Nonmedical Uses of Antibiotics: Time to Restrict Their Use?' *PLoS Biology* 13(2015): e1002266. <https://doi.org/10.1371/journal.pbio.1002266>.

philosophers, economists and public health professionals.¹⁶ This requires high degrees of multi-sectorial integration, coordination and accountability mechanisms, for which existing policy-making structures are inappropriate or insufficient.¹⁷ This is further compounded by the fact that AMR has numerous interdependent biological and social drivers that make it a problem on the global scale. Expanding international travel, tourism and trade will continue to perpetuate resistance beyond current levels.¹⁸ As such, while national and regional policies can certainly impact on the prevalence of drug-resistant infections,¹⁹ the global dissemination of resistant bacteria demonstrate why such localised efforts alone cannot be ultimately effective.²⁰

As a result of all of these considerations, AMR also raises distinctive ethical issues, which must not only be accounted for in our policy and response activities, but will play an important role in supporting the numerous difficult choices involved in balancing the benefits and burdens associated with protecting antibiotic effectiveness and reducing the spread of drug-resistant infections.²¹ Our traditional normative theories and principles, as developed in other infection prevention and control contexts, will be insufficient if mechanically applied as if it were just another problem of infectious disease ethics. It will require careful attention to the morally-relevant features of what makes AMR a distinctive problem, and due care and context-specificity in the application of moral guidance and regulation. The ethical analysis required to shape and guide our policy response to the problem of AMR

¹⁶ S.B. Levy, *The Antibiotic Paradox* (Cambridge, MA: Perseus Publishing, 2002).

¹⁷ R.D. Smith and J. Coast, 'Antimicrobial resistance: a global response,' *Bulletin of the World Health Organization* 80(2002): 126–133; R. Laxminarayan, et al., 'Antibiotic resistance-the need for global solutions,' *Lancet Infectious Diseases* 13(2013): 1057–98; C. Årdal, et al., 'International cooperation to improve access to and sustain effectiveness of antimicrobials,' *Lancet* 387(2015): 296–307; S. J. Hoffman and T. Ottersen, 'Addressing Antibiotic Resistance Requires Robust International Accountability Mechanisms,' *The Journal of Law, Medicine and Ethics* 43(2015): 53–64.

¹⁸ D.W. MacPherson, B.D. Gushulak and W.B. Baine, 'Population Mobility, Globalization, and Antimicrobial Drug Resistance,' *Emerging Infectious Diseases* 17(2009): 1727–1732; Z. S. Ahammad, et al., 'Increased Waterborne blaNDM-1 Resistance Gene Abundances Associated with Seasonal Human Pilgrimages to the Upper Ganges River,' *Environmental Science & Technology* 48(2014): 3014–3020; A.H. Holmes, L.S. Moore and A. Sundsfjord, 'Understanding the mechanisms and drivers of antimicrobial resistance,' *Lancet* 387(2016): 176–87.

¹⁹ For instance, as illustrated by the significant variation in the proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) infections across European hospitals. See, e.g., European Centre for Disease Prevention and Control, *Annual epidemiological report on communicable diseases in Europe* (Stockholm: ECDC, 2011).

²⁰ I.N. Okeke and R. Edelman, 'Dissemination of Antibiotic-Resistant Bacteria across Geographic Borders,' *Clinical Infectious Diseases* 33(2001): 364–369; S.E. Majowicz, et al., 'The Global Burden of Nontyphoidal *Salmonella* Gastroenteritis,' *Clin Infect Dis* 50(2010): 882–89; L.S. Tzouvelekis, et al., 'Carbapenemases in *Klebsiella pneumoniae* and Other Enterobacteriaceae: an Evolving Crisis of Global Dimensions,' *Clinical Microbiology Reviews*. 25(2012): 682–707; Nicola K. Petty, et al. 'Global dissemination of a multidrug resistant *Escherichia coli* clone,' *PNAS* 111(2014): 5694–5699.

²¹ J. Littmann and A.M. Viens, 'The Ethical Significance of Antimicrobial Resistance,' *Public Health Ethics* 8(2015): 209–224.

also necessitates thinking and theorizing that is able to incorporate and reflect the various biological, social, political and legal factors involved in the spread and control of drug-resistant infections.

In this paper, we will argue that the concept of super-wicked problems can provide an apt description of the current situation regarding AMR, and that it will help us better understand some of the complex ethical challenges associated with AMR. Furthermore, framing AMR as a super-wicked problem will help to explain why at first glance, AMR appears to be so similar to other large policy challenges, such as climate change. However, we will argue that the structural similarity should not lead us to conclude that attempts to mitigate one super-wicked problem can simply be transferred to another. Instead, we suggest that the crucial feature of super-wicked problems is the need to change *path dependency* – a term we will explain more fully below – and that this change will likely require unique approaches, methods and tools for each super-wicked problem. To develop this argument, we will first introduce the ideas of super-wicked problems as a way to frame AMR. Second, we will argue that conceptualizing AMR as a super-wicked problem can help inform policy making by highlighting how our efforts should be focused. Finally, in sections four and five, we provide a potential way to move forward, and highlight key ethical issues that arise in this context.

26.2 Framing AMR as a Super-Wicked Problem

The concept of wicked problems, which has its origins in Rittel and Webber's paper about planning theory, describes certain policy problems as complex challenges that do not respond to standard problem-solving mechanisms.²² Rittel and Webber suggest that the success of social policy in the 19th and early twentieth century was essentially the picking of low-hanging fruits, and that the policy challenges that societies are now facing are much more difficult to address.²³ Inherent complexity (i.e., the overlapping and varied sources of influence or causes to a social problem that resist simple linear solutions),²⁴ inter-relatedness with other policy fields, and several conflicting goals that might each be reasonably pursued, make some policy problems "wicked". According to Rittel and Webber, these problems are not solvable by traditional instruments of policy making, especially not by cost-benefit or

²² H.W.J. Rittel and M.M. Webber, 'Dilemmas in a General Theory of Planning,' *Policy Sciences* 4:2 (1973): 155–69.

²³ H.W.J. Rittel and M.M. Webber, 'Dilemmas in a General Theory of Planning,' *Policy Sciences* 4:2 (1973): 155–69.

²⁴ M.C. Jackson, *Systems Thinking: Creative Holism for Managers* (West Sussex, UK: John Wiley and Sons, Ltd., 2003).

system analysis, as these approaches cannot make sense of all dimensions of wicked problems.²⁵

Wicked problems are characterized by the fact that proposed solutions cannot be judged as ‘right’ or ‘wrong’ but merely as more or less suitable, and they do not allow for a trial-and-error approach to policy-making. Instead, Rittel and Webber argue, wicked problems only allow policy-makers a single shot at solving the problem – if this fails, the unsuccessful policy will have changed the original problem to such an extent its initial alternatives may no longer be viable contenders.²⁶

The concept of wicked problems has been applied to a number of areas as diverse as coastal governance,²⁷ liberal arts and design²⁸ and, more recently, climate change. It has been argued, however, that the latter no longer presents a wicked, but a ‘super-wicked’ problem.²⁹ Super-wicked problems provide an even greater challenge due to four additional complications that policy makers have to engage with. These criteria are:

- (i) Time for finding a solution to a policy challenge is running out;
- (ii) Those seeking to solve the problem are part of the cause;
- (iii) Central authorities to address the problem are either weak or non-existent; and
- (iv) Policy responses discount the future irrationally.³⁰

The following section illustrates how these criteria can be applied to the case of AMR, why it should be viewed as a super-wicked problem and how each aspect of the problem raises important ethical concerns that must be factored into how we will be justified in responding to AMR as a super-wicked problem.

26.2.1 *Criterion 1: Time Is Running Out*

Super-wicked problems require drastic and urgent responses if they are not to become unsolvable policy dilemmas. In the case of AMR, it is evident that increasing drug resistance will exacerbate the existing challenge, which has led to concerns

²⁵ H.W.J. Rittel and M.M. Webber, ‘Dilemmas in a General Theory of Planning,’ *Policy Sciences* 4:2 (1973): 155–69.

²⁶ H.W.J. Rittel and M.M. Webber, ‘Dilemmas in a General Theory of Planning,’ *Policy Sciences* 4:2 (1973): 155–69.

²⁷ S. Jentoft and R. Chuenpagdee, ‘Fisheries and coastal governance as a wicked problem,’ *Marine Policy* 33(2009): 553–60.

²⁸ R. Buchanan, ‘Wicked Problems in Design Thinking,’ *Design Issues* 8(1992): 5–21.

²⁹ R. Lazarus, ‘Super wicked problems and climate change: restraining the present to liberate the future,’ *Cornell Law Review* 94(2009): 1153–234; K. Levin, et al., ‘Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change,’ *Policy Sciences* 45:2 (2012): 123–52.

³⁰ K. Levin, et al., ‘Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change,’ *Policy Sciences* 45:2 (2012): 123–52.

about a “post-antibiotic era”.³¹ There is thus, in short, an observable trend towards more complex cases of AMR, which will either be very difficult to treat or no longer respond to antibiotics at all.³² Indeed, for some infections, such as tuberculosis or gonorrhea, resistance to all common treatments can already be observed.³³ As multi- and extensively drug resistant infections are being registered more and more frequently and with a lack of new antibiotics under development, the prospect of total antimicrobial resistance is no longer an abstract worst-case scenario.³⁴ This not only signals the need to make exigent decisions about a large and serious risk of harm for individuals and populations, but also factoring in the ethics of acting under conditions of necessity, urgency and uncertainty – and how this may differ from policy responses taken under conditions of normalcy.³⁵

26.2.2 Criterion 2: Those Seeking a Solution Are Part of the Problem

AMR is a multi-factorial problem and often those involved in combating it also contribute to, or exacerbate it, in some important way:

- *Health care professionals*, who in many countries act as gatekeepers for access to antibiotics, often prescribe more antibiotics than necessary, which can lead to higher prevalence of drug-resistant infections.³⁶ There is an increasing number of studies, which indicate that a high proportion of prescriptions of antibiotics do not comply with scientific guidelines.³⁷ Furthermore, appropriate infection

³¹ N. Brown, ‘Dawn of the post-antibiotic age?’ *BMJ* 309(1994): 615; A.J. Alanis, ‘Resistance to Antibiotics: Are We in the Post-Antibiotic Era?’ *Arch Med Res* 36(2005): 687–705.

³² European Centre for Disease Prevention and Control, *Antimicrobial resistance surveillance in Europe: Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net) 2011* (Stockholm, 2012).

³³ E. Alirol, et al., ‘Multidrug-resistant gonorrhea: A research and development roadmap to discover new medicines,’ *PLoS Med* 14(2017): e1002366; World Health Organization, *Treatment guidelines for drug-resistant tuberculosis, 2016 update* (Geneva: WHO, October 2016 revision) <http://apps.who.int/iris/bitstream/10665/250125/1/9789241549639-eng.pdf?ua=1&ua=1> (Accessed September 25, 2017).

³⁴ European Centre for Disease Prevention and Control, *The bacterial challenge: time to react* (Stockholm, 2009).

³⁵ See, e.g., A.M. Viens, ‘Normative Uncertainty and the Ethics of Risk Regulation in Emergency,’ in A. Alemanno (ed.), *Governing Disasters: The Challenges of Emergency Risk Regulation* (Edward Elgar Publishing, 2011), pp. 137–46; A.M. Viens, *In Extremis: Morality in Times of Emergency* (London: University of London PhD, 2012).

³⁶ R.G. Finch, ‘Antibiotic resistance: a view from the prescriber,’ *Nature Reviews Microbiology* 2(2004): 989–94; V.I. Enne, ‘Reducing antimicrobial resistance in the community by restricting prescribing: can it be done?’ *Journal of Antimicrobial Chemotherapy* 65(2010): 179–82.

³⁷ K.E. Fleming-Dutra, A.L. Hersh and D.J. Shapiro, ‘Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010–2011,’ *JAMA* 315(2016): 1864–1873. doi:<https://doi.org/10.1001/jama.2016.4151>.

prevention and control can reduce the need for antibiotics in the first place – which is an area where improvements can be made too.³⁸

- *Pharmaceutical companies* have steadily decreased research efforts into new antimicrobial drugs, despite mounting pressures on health care systems to introduce new and effective drugs. The lack of investment is, at least, partly caused by concerns over limited returns on investment due to advancing AMR.³⁹ Margaret Chan, former World Health Organization (WHO) Director-General, recently alluded to this problem, when she rhetorically asked: “[f]rom an industry perspective, why invest considerable sums of money to develop a new antimicrobial when irrational use will accelerate its ineffectiveness before the R&D investment can be recouped?”⁴⁰ Recent advances in clinical research show that it may be possible to develop entirely new classes of antibiotics.⁴¹ However, the time frame for their development remains unclear and unless novel ways of financing are introduced, their prices are likely to be prohibitive for most patients in low and middle-income countries (LMICs). The industry perspective is that the investment into new antibiotics is only financially feasible, if considerable lump sum payments, so-called market entry rewards, are paid out. These are usually estimated to have to be greater than \$ 1 billion.⁴² Moreover, the antibiotic production process and discarded antibiotic-laced waste can also have a considerably negative environmental impact that further perpetuates resistance.⁴³

³⁸ J. O’Neill et al., *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations* (London: Review on Antimicrobial Resistance, 2016), available at https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf (accessed September 29, 2017).

³⁹ C. Morel and E. Mossialos, ‘Stoking the antibiotic pipeline,’ *BMJ* 340(2010): c2115.

⁴⁰ M. Chan, *Secondary Antimicrobial Resistance in the European Union and the World* (Geneva: World Health Organization, 2012), available at: http://www.who.int/dg/speeches/2012/amr_20120314/en/ (accessed September 29, 2017).

⁴¹ L.L. Ling, et al., ‘A new antibiotic kills pathogens without detectable resistance,’ *Nature* 517(2015): 455–59.

⁴² R. Laxminarayan, P. Matsoso, S. Pant, C. Brower, J.A. Røttingen, K. Klugman and S. Davies, ‘Access to effective antimicrobials: a worldwide challenge,’ *Lancet* 387(2016): 168–175; K. Outtersson, et al., ‘Delinking Investment in Antibiotic Research and Development from Sales Revenues: The Challenges of Transforming a Promising Idea into Reality,’ *PLOS Medicine* 13(2016): e1002043. <https://doi.org/10.1371/journal.pmed.1002043>.

⁴³ K.D. Brown, et al., ‘Occurrence of antibiotics in hospital, residential, and dairy effluent, municipal wastewater, and the Rio Grande in New Mexico,’ *Science of the Total Environment* 366(2006): 772–783; J. Fick, et al., ‘Contamination of surface, ground, and drinking water from pharmaceutical production,’ *Environ Toxicol Chem* 28(2009): 2522–7; D.G.J. Larsson, ‘Pollution from drug manufacturing: review and perspectives,’ *Phil. Trans. R. Soc. B* 369(2014): 20130571; Changing Markets Foundation, *Superbugs in the Supply Chain: How Pollution from Antibiotics Factories in India and China is Fuelling the Global Rise of Drug-Resistant Infections* (Utrecht: Changing Markets Foundation, 2016); R. Laxminarayan and R.R. Chaudhury, ‘Antibiotic Resistance in India: Drivers and Opportunities for Action,’ *PLoS Medicine* 3(2016): e1001974; C. Lübbert, et al., ‘Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended-spectrum beta-lactamase and carbapenemase-producing pathogens,’ *Infection* 45(2017): 479–491.

- *Patients* who are prescribed antibiotics often fail to adhere to treatment recommendations. This problem is exacerbated in countries where antibiotics are available for purchase over the counter, and patients may be unable to afford or have access to a health care professional who can prescribe and dispense the appropriate drug.⁴⁴
- *Food Producers and Sellers* must continue to take significant steps to reduce the use of antibiotics as growth promoters and adopt practices that reduce the extent to which the food chain continues to be a key pathway for the transmission of resistant pathogens.⁴⁵ We also need to ensure AMR surveillance systems include resistance levels in animal stocks and food systems.
- *Governments and intergovernmental organizations* still lack the requisite regulation and governance structures to address the complexity associated with AMR and remain focused on multilateral and bilateral agreements that were commonly used in the middle of the twentieth century.⁴⁶

The various and complex interacting contributions to the spread of AMR make it difficult (though certainly not impossible) to attribute causal responsibility to past action, including a failure to act. This also raises important questions about how our policy response should hold individuals, groups and institutions morally responsible for their complicity or causal contribution to AMR in any accountability mechanisms developed going forward.

26.2.3 *Criterion 3: Central Authorities to Address the Problem Are either Weak or Non-existent*

There is currently a lack of institutional structures that can meet the challenge of AMR effectively and at all policy levels. While international organizations, such as WHO or ECDC, have developed guidelines for prudent use of antibiotics, as well as

⁴⁴ M.B. Planta, 'The Role of Poverty in Antimicrobial Resistance' *J Am Board Fam Med*, 20:6 (2007):533–39; I.N. Okeke, A. Lamikanra, R. Edelman, 'Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries,' *Emerging Infectious Diseases* 5(1999): 18–27; D.J. Morgan, I.N. Okeke, R. Laxminarayan, E.N. Perencevich and S. Weisenberg, 'Non-prescription antimicrobial use worldwide: a systematic review,' *The Lancet Infectious Diseases* 11(2011): 692–701.

⁴⁵ C. Verraes, et al., 'Antimicrobial Resistance in the Food Chain: A Review,' *International Journal of Environmental Research and Public Health* 10(2013): 2643–2669; T. P. Van Boeckel, et al., 'Global trends in antimicrobial use in food animals,' *Proceedings of the National Academy of Sciences of the United States of America* 112(2015): 5649–5654; T. P. Van Boeckel, et al. 'Reducing antimicrobial use in food animals,' *Science* 357(2017): 1350–1352.

⁴⁶ A. C. Singer, et al. 'Review of Antimicrobial Resistance in the Environment and Its Relevance to Environmental Regulators,' *Frontiers in Microbiology* 7(2016):1728; Gabriel Birgand, et al., 'Comparison of governance approaches for the control of antimicrobial resistance: Analysis of three European countries,' *Antimicrobial Resistance & Infection Control* 7(2018): 28. More is written regarding the role of these stakeholders below, under criterion 3.

programs for co-operation and data sharing, their implementation lies with the respective national governments and adherence cannot be enforced.⁴⁷ Failure to follow these recommendations is not necessarily a matter of ignorance or antipathy – in many instances countries may simply lack the control mechanisms, infrastructure, expertise, or resources to meet all requirements and recommendations of best-practice guidelines. It is also being increasingly recognized that poor governance and political corruption make major contributions to our inability to effectively respond to AMR.⁴⁸ However, since drug resistance cannot be confined by national borders, these discrepancies and deficiencies in national health systems and policies inevitably threatens the effectiveness of antibiotics and control of drug-resistant infections, even in countries that strictly enforce measures to reduce and control the use of antibiotics and mitigate the spread of AMR. More recently, the United Nations has sought to address AMR more comprehensively across sectors and policy areas, both by establishing a temporary interagency coordination group, and by strengthening the tripartite, a coordinating forum comprised of WHO, FAO, OIE, and UN Environment.⁴⁹ Nevertheless, coordination between international mechanisms and national institutions remains a voluntary process, for which few dedicated resources are available.

This raises important questions about, for instance, who should take ultimate responsibility for antimicrobial stewardship when there are no central authorities or where jurisdictions lack the resources or infrastructure to undertake stewardship activities in accordance with international recommendations.⁵⁰ Indeed, the effect of the absence of authorities and resources in the face of the inherent complexity of global health governance has gained greater and greater traction in the global health arena. In particular, we are starting to see more of a role for formal and informal stakeholders (e.g., Wellcome Trust, Bill and Melinda Gates Foundation, World Bank, corporations) increasingly shaping and guiding global health activity through many channels – many of which are no longer transparent nor are the varied values and interests of these stakeholders always easy to fully comprehend.⁵¹ As such, the super-wicked problem of AMR sits within a much broader complex challenge that

⁴⁷ See e.g. the World Health Organization's *Global Action Plan on Antimicrobial Resistance* (Geneva: WHO, 2015).

⁴⁸ P. Collignon, et al., 'Antimicrobial Resistance: The Major Contribution of Poor Governance and Corruption to this Growing Problem,' *PLoS One* 10(2015): e0116746; B. Rönnerstrand and V. Lapuente, 'Corruption and use of antibiotics in regions of Europe,' *Health Policy* 121(2017): 250–256.

⁴⁹ See World Health Organization, 'Interagency Coordination Group on Antimicrobial Resistance (IACG), <https://www.who.int/antimicrobial-resistance/interagency-coordination-group/en/> (accessed October 10, 2018), and World Health Organization, *FAO, OIE, WHO – Tripartite Concept Note* (Geneva: WHO, 2010) http://www.who.int/foodsafety/areas_work/zoonoise/concept-note/en/ (accessed October 10, 2018).

⁵⁰ B. Bennett and J. Iredell, "Global health governance and antimicrobial resistance" In *Ethics and Drug Resistance: Collective Responsibility for Global Public Health*. Springer, Cham.

⁵¹ C. Clinton and D. Sridhar, *Governing Global Health* (Oxford: Oxford University Press, 2017); J. Youde. *Global Health Governance* (Cambridge: Polity Press, 2012); Nora Kenworthy, Ross

is making sense of, and impacting, global health governance, thus amplifying and multiplying the complexity of addressing AMR.

26.2.4 Criterion 4: Current Policies Discount the Future Irrationally

There is a notable disparity between the enormous significance that antibiotics have in today's health care systems and the lack of a comprehensive and realistically implementable global strategy to protect them as a resource for current and future generations.⁵² Indeed, while the impact of AMR on health outcomes today and in the future is increasingly recognized, there remains a lack of coordination and sufficient funding to address the problem. When the health ministers of the G20 countries met for the first time in 2017, they declared "AMR has the potential to have a major negative impact on public health as well as on growth and global economic stability".⁵³ Other impact assessments have come to similar conclusions.⁵⁴ Since modern medicine relies so heavily on antibiotics as a prophylactic for standard surgical procedures, the further progression of AMR would be detrimental not only for infectious disease policy, it would also affect the outcome of surgical care or the survival chances of cancer patients. In short, AMR has become a wider health system issue.⁵⁵ It is therefore all the more surprising that current policies do not place greater emphasis on long-term strategies to preserve antibiotic effectiveness and best-case policy scenarios consist in the preservation of some level of antibiotic effectiveness in the short run, without a comprehensive replacement strategy for ineffective drugs.⁵⁶

Due to the complexity of the drivers of AMR, its costs are extremely difficult to assess, even if they are only measured locally or in the short run.⁵⁷ A number of recent economic models have attempted to model the long-term costs, but due to the

MacKenzie, and Kelley Lee (eds.), *Case Studies on Corporations and Global Health Governance: Impacts, Influence and Accountability* (Rowman & Littlefield, 2016).

⁵² M. Millar M, 'Can antibiotic use be both just and sustainable... or only more or less so?' *Journal of Medical Ethics* 37(2011): 153–7; L. Leibovici, M. Paul and O. Ezra, 'Ethical dilemmas in antibiotic treatment,' *Journal of Antimicrobial Chemotherapy* 67(2012): 12–16.

⁵³ Berlin Declaration of the G20 Health Ministers, Berlin 2017, p. 5 https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3_Downloads/G/G20-Gesundheitsministertreffen/G20_Health_Ministers_Declaration_engl.pdf (accessed on September 25, 2017).

⁵⁴ O. Adeyi, et al., *Drug-resistant infections: A threat to our economic future*, Volume 2 (Washington, D.C: World Bank, 2017), available at <http://documents.worldbank.org/curated/en/323311493396993758/final-report>

⁵⁵ R. Smith and J. Coast, 'The true cost of antimicrobial resistance,' *BMJ* 346(2013): f1493.

⁵⁶ A.J. Alanis, 'Resistance to Antibiotics: Are We in the Post-Antibiotic Era?' *Arch Med Res* 36(2005): 687–705.

⁵⁷ D.H. Howard, R.D. Scott, 'The Economic Burden of Drug Resistance,' *Clin Infect Dis* 41(2005): S283–S86; R. Smith and J. Coast, 'The true cost of antimicrobial resistance,' *BMJ* 346(2013): f1493.

complexity of AMR, they inevitably have to restrict their analysis to a select number of bacterial pathogens or consider a limited number of potential cost factors.⁵⁸ As a result, existing cost models likely underestimate the long-term effects of AMR. However, even these conservative cost models, which – by their own admission – systematically underestimate some of the costs associated with drug resistance, come to the conclusion that the cost of AMR (including resistance to antiviral drugs) may exceed \$100 trillion in total GDP loss by 2050.⁵⁹ What this shows quite clearly is that current efforts to address AMR are simply not proportionate to the magnitude of the challenge at hand.

This also raises questions about the proportionality of our policy responses – in a moral and legal sense – in light of how it will be legitimate for us to act given the seriousness of the challenge faced. If the spread and magnitude of harm of AMR will be as predicted, what could be currently seen as a disproportionate response – for instance, what might be seen as overly paternalistic or coercive measures – may be seen to be justified as the problem worsens. Nevertheless, if the long game here is about keeping AMR at bay for as long as possible, should we actually have to wait until the problem gets much worse before we are justified in utilizing more paternalistic or coercive measures to achieve the same goal? The moral and legal calculus involved – and the extent to which the legitimacy of our responses should be determined in proportion to the risk of harm – could signal, for example, the development of new or more stringent stewardship obligations, the imposition of more risk on individuals (even without consent) and potential limitations on once established and uncontroversial entitlements and rights.⁶⁰ The nature of super-wicked problems are such that we must consider not only what norms and values should advance particular social, medical and public health goals, but also how such norms and values can set constraints or limits on these goals.

⁵⁸ J. Taylor, et al., *Estimating the economic costs of antimicrobial resistance: models and results* (Cambridge, UK: RAND Europe, 2014); KPMG, *The global economic impact of antimicrobial resistance* (London: KPMG: 2014).

⁵⁹ J. O'Neill et al., *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. (London: Review on Antimicrobial Resistance, 2016), available at https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf (accessed September 29, 2017).

⁶⁰ Gro Harlem Brundtland, who served three terms as Prime Minister of Norway and as Director-General of the World Health Organization from 1998 to 2003, maintained that “AMR is just as much about human rights and justice as it is about health” [<http://blogs.bmj.com/bmj/2017/12/06/gro-harlem-brundtland-new-who-guidelines-are-crucial-step-to-fighting-antimicrobial-resistance/>]

26.3 How Conceptualizing AMR as a Super-Wicked Problem Can Inform Policy Making

The account of AMR as a super-wicked problem is not merely descriptive, but offers a framework for assessing the expected impact of policy making. Understanding AMR as a super-wicked problem underlines three important facts. First, it highlights the tendency of current policies to focus on preserving antibiotic effectiveness, while failing to reduce the future need for antibiotics. Second, it explains why traditional instruments, such as cost-benefit analysis (CBA), are unsuited to determining an appropriate policy response. Third, it helps bring to light how the complex interaction of ethical considerations will contribute to shaping which policy options will be viewed as acceptable.

Many of the existing policies that address AMR (and a considerable portion of the academic literature) emphasize the need for new antibiotics, as well as the cost-effective and prudent use of available resources.⁶¹ The policy focus is thus on addressing problems on the supply side, and the creation of new resources, where a broad number of policy campaigns already exist.⁶² However, if AMR is understood as a super-wicked problem, it becomes apparent that such approaches – while a necessary contribution – will ultimately and inevitably fall short of the goal of effectively controlling AMR in the long run. Consideration must take place of the relative value of focusing on upstream versus downstream determinants of drug-resistant infections, and the extent to which values other than efficiency or innovation (e.g., health equity) should guide both which drivers of resistance we focus on as well as which preventive and therapeutic responses we should pursue.

Framing AMR as a super-wicked problem should lead policy makers to place a much stronger emphasis on those policies, which – to paraphrase Levin et al. – generate a shift in path dependencies.⁶³ The concept of path dependencies explains current policies in light of their development of time, and as a result of earlier decision.⁶⁴ A given policy may therefore be more influenced by legacy decisions than by

⁶¹ E. Mossialos, *et al*, *Policies and incentives for promoting innovation in antibiotic research* (Copenhagen: European Observatory on Health Systems and Policies, 2008); T. Groves, 'Back to basics with the three Rs,' *BMJ* 344(2012); R. Laxminarayan and G.M. Brown, *Economics of Antibiotic Resistance: A Theory of Optimal Use* (Washington D.C. Resources for the Future, 2001); C. Morel and E. Mossialos, 'Stoking the antibiotic pipeline,' *BMJ* 340(2010): c2115.

⁶² L.D. Högberg, A. Heddini, and O. Cars, 'The global need for effective antibiotics: challenges and recent advances' *Trends Pharmacol Sci* 31(2010): 509–15.

⁶³ K. Levin, et al., 'Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change,' *Policy Sciences* 45(2012): 123–52.

⁶⁴ A more complete definition of path dependence is as follows: 'Path dependence is the idea that decisions we are faced with depend on past knowledge trajectory and decisions made, and are thus limited by the current competence base. In other words, history matters for current decision-making situations and has a strong influence on strategic planning... A well-known example is the QWERTY layout for typewriters. Despite the fact that different keyboard layouts in modern computer keyboards would allow faster typing, the QWERTY layout prevails.' *Financial Times Lexicon* <http://lexicon.ft.com/Term?term=path-dependence> (accessed September 30, 2017).

the current state of affairs and the latest available evidence. A shift in path dependencies is necessary once it has become apparent that the trajectory of earlier policy decisions is leading to an unsustainable outcome in the long run. In the case of climate change, for example, such path dependency is exemplified by the widespread and continued reliance on fossil fuels.⁶⁵ In the case of AMR, this path dependency is reflected by the reliance on antibiotics as not only a treatment against acute infection, but also as a tool for infection prevention in both clinical and veterinary settings. This dependency is replicated in most current policies that focus on pulling on the same levers, which aim at either increasing the availability of antibiotics or decreasing the use of antibiotics. What is crucially missing is sufficient emphasis on infection prevention and control measures that reduce the need for antibiotics in the first place.

Consequently, current policies do not offer a long-term fix to the problem of AMR and create, at best, a “faux paradigmatic change”, in which the implementation of policy only makes small corrections to a previous policy failure temporarily.⁶⁶ The most obvious example for a faux paradigmatic shift is the reliance on future developments of new antibiotics, which are effective against resistant bacteria. While such a development will provide significant short-term improvements, past experience suggests that bacteria will ultimately develop resistance to new classes of antibiotics, as well. Consequently, as Spellberg has observed, “we will never truly defeat microbial resistance; we can only keep pace with it.”⁶⁷ In the absence of a realistic option for true paradigmatic change (i.e., a technological method to avoid the further emergence and spread of AMR altogether), it appears advisable to abandon ambitions to outpace the adaptation of microbes to new antibiotics, and instead focus on the creation of incremental but transformative changes, which no longer follow the same policy trajectory and instead reduce the dependence on antibiotics. In particular, this new trajectory must have as a chief focus policy options that can be effectively implemented in LMICs.

One analogy that summarizes this situation, and which has been used repeatedly to describe the problem at hand, is that of a “leaky bucket”.⁶⁸ If we think of antibiotic effectiveness as a resource contained in a bucket, the emergence of resistance is

⁶⁵ G. Unruh, ‘Understanding Carbon Lock-In,’ *Energy Policy* 28(2000): 817–30; P. Aghion, C. Hepburn, A. Teytelboym, and D. Zenghelis, *Path dependence, innovation and the economics of climate change* (London: Centre for Climate Change Economics and Policy Grantham Research Institute on Climate Change and the Environment, 2014) http://www.lse.ac.uk/GranthamInstitute/wp-content/uploads/2014/11/Aghion_et_al_policy_paper_Nov20141.pdf (accessed September 29, 2017).

⁶⁶ B. Cashore and M. Howlett, ‘Punctuating Which Equilibrium? Understanding Thermostatic Policy Dynamics in Pacific Northwest Forestry,’ *Am J Pol Sci* 51(2007): 532–51; K. Levin, et al. ‘Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change,’ *Policy Sciences* 45(2012): 123–52.

⁶⁷ H.W. Boucher, et al. ‘Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America,’ *Clin Infect Dis* 48(2009): 1–2.

⁶⁸ This analogy was originally proposed by Prof. Otto Cars, ReAct-Action on Antimicrobial Resistance, Uppsala University Sweden.

akin to holes in this bucket, slowly draining the effectiveness of available drugs. The development of a new drug would effectively add water to the leaking bucket. But, in the absence of a realistic option to develop antibiotics that avoid the subsequent emergence of resistance, this will only have a temporary effect and not address the underlying problem; namely, the holes in the bucket. Thus, not only are the antibiotics currently in clinical development not adequate to counter the increasing prevalence of AMR, it is unlikely they ever could be.⁶⁹

A second argument for framing AMR as a super-wicked problem is that this approach discourages a reliance on CBA in policy making. Super-wicked problems – by their nature – are not easily solvable with standard CBA tools because they describe scenarios in which the cost of inaction will be very high, yet occur at some point in the distant future. Consequently, CBA will usually recommend an insufficiently large commitment of resources to address super-wicked problems because costs incurred today are pitted against benefits at a later stage for which neither magnitude nor time frame are known.⁷⁰ As outlined earlier, existing cost-models for the assessment of the economic burden of AMR systematically underestimate the true cost of AMR because, as Smith and Coast argue, “[none] considered the bigger picture – a world in which there are no effective antibiotics for situations where they are currently used routinely”.⁷¹ And where it has been attempted to take these wider costs into consideration, the complexity of AMR has usually forced analysts to restrict their models to pathogens and geographical regions for which reliable data exists.⁷² One response to this criticism of CBA in policy-making is to suggest that a bad estimate of cost is still better than no estimate at all. However, as Jamieson rightly points out, this response overlooks that whenever uncertainties about future developments are great, relying on the supposedly neutral judgment of a bad cost-estimate is a leap of faith – and it may prompt us to reach policy decisions that, in the long run, are far worse than the ones we might have considered had we not aimed for cost-efficiency based on unreliable or incomplete information.⁷³

A final argument for framing AMR as a super-wicked problem is that this approach provides a greater prominence on the importance of the values and norms that should inform what would make particular policy options more or less

⁶⁹ World Health Organization, *Antibacterial Agents in Clinical Development: An Analysis of the Antibacterial Clinical Development Pipeline, including Tuberculosis* (Geneva: World Health Organization, 2017).

⁷⁰ R. Lazarus, ‘Super wicked problems and climate change: restraining the present to liberate the future,’ *Cornell Law Review* 94(2009): 1153–234.

⁷¹ R.D. Smith and J. Coast, ‘The true cost of antimicrobial resistance’. *BMJ* 2013; 346: f1493. Also cf. J. Coast and R.D. Smith, ‘Distributional Considerations in Economic Responses to Antimicrobial Resistance,’ *Public Health Ethics* 8(2015): 225–237.

⁷² See e.g. the RAND corporations cost model for O’Neill’s AMR review: https://www.rand.org/pubs/research_reports/RR911.html (accessed September 29, 2017).

⁷³ D. Jamieson, ‘Ethics, Public Policy and Global Warming,’ in S.M. Gardiner, et al. (eds.) *Climate Ethics* (Oxford: Oxford University Press, 2010), pp. 77–86. Also cf. A. Williams, ‘Cost-effectiveness analysis: is it ethical?’ *Journal of Medical Ethics* 18(1992): 7–11.

acceptable.⁷⁴ Through diminishing an analysis of the cost of AMR in primarily economic terms, it helps bring to light the non-economic costs and values involved in shaping which policy options will be viewed as acceptable. By emphasizing the need for shifts in path dependencies, and the resultant changes in our approaches and responses, it also emphasizes the need to re-evaluate the values and norms which underpinned our previous policies and activities. To put it another way, through framing AMR as a super-wicked problem, we not only acknowledge that previous approaches are unlikely to be sustainable in the long run, but we are also forced to ask what sort of values and norms could justify new policy options that would not only be effective but also ethical. This is all the more relevant because understanding AMR as more than a scientific or technical issue is a relatively new perspective. For most of the existence of antibiotics, their use has been primarily viewed as a medical or microbiological issue, and was governed accordingly. This means that value judgments were commonly only implicit and often incoherent. We have seen that these technical or medical matters do not exhaust all of the relevant considerations, and much of the decision-making and policy-making around AMR concerned matters that were inherently and inescapably ethical. Acting as an anti-microbial steward, for instance, often involves making moral judgments, promoting particular values and prioritising different aims – which are normative, and not merely technical, activities. In viewing AMR as a societal challenge, we can see the failings of earlier approaches that had not considered the normative significance this shift implies.

26.4 Incrementally Creating Transformative Shifts in Path Dependency: Alternative Strategies

Creating transformative changes in path dependency will require adjustments on all types and levels of antibiotic use, and is unlikely to come in the shape of a single intervention. While there are no formulaic strategies to address wicked and super-wicked problems, different kinds of policy response will be suited to different time frames and address different aspects of the challenge that AMR presents. Nancy Roberts distinguishes between three possible approaches to super-wicked problems: authoritative, competitive and collaborative strategies.⁷⁵

⁷⁴ For different ways in which framing the problem of AMR can have ethical and political implications, see, for instance, A.M. Viens and Jasper Littmann, 'Is Antimicrobial Resistance a Slowly Emerging Disaster?' *Public Health Ethics* 8(2015): 255–265.

⁷⁵ N. Roberts, 'Wicked Problems and Network Approaches to Resolution,' *Int Public Manag Rev* 1(2000): 1–19.

26.4.1 *Authoritative Strategies*

These strategies involve a small number of decision-makers who develop policy solutions, which are then implemented by others. Such approaches require that decision-makers have the ability to enforce the implementation of their chosen strategy. The advantage of such a policy is that decision-making complexity is reduced, and policies can be implemented and adjusted relatively quickly. On the other hand, such approaches to solving super-wicked problems are likely to alienate a large proportion of stakeholders and they depend on the existence of power structures where they can be enforced.⁷⁶ To this end, recent proposals for international legal frameworks and an intergovernmental panel have been put forward.⁷⁷ However, the question how adherence at the local level could be controlled and, where necessary, enforced – let alone sufficiently resourced – make such centralized and costly proposals very difficult to implement. Authoritative strategies may therefore be of greater use at the national or regional level. At the global level, however, the current lack of adequate resource, governance and accountability structures, which could help to effectively implement them, is likely to limit their usefulness in addressing the challenge of AMR.

26.4.2 *Competitive Strategies*

These strategies let different stakeholders or corporations compete for the creation of (market-based) solutions and often lead to creative approaches to problem solving.⁷⁸ However, the commitment of stakeholders will largely depend on the strength of incentives to focus on a given policy area. In the case of AMR, the absence of sufficient market incentives has led to minimal investments into R&D for new antibiotics, which lies well below a socially optimal level.⁷⁹ Recent initiatives such as

⁷⁶L. Briggs, 'Tackling Wicked Problems – A Public Policy Perspective,' in *Contemporary Government Challenges* (Australian Public Service Commission, 2007).

⁷⁷J. Anomaly, 'Combating Resistance: The Case for a Global Antibiotics Treaty,' *Public Health Ethics* 3(2010): 13–22; M. Woolhouse and J. Farrar, 'Policy: An intergovernmental panel on antimicrobial resistance,' *Nature* 509(2014): 555–557; Steven J. Hoffman, 'An international legal framework to address antimicrobial resistance,' *Bulletin of the World Health Organization* 93(2015): 66; S.J. Hoffman, J.-A. Røttingen and J. Frenk, 'International Law Has a Role to Play in Addressing Antibiotic Resistance,' *Journal of Law, Medicine & Ethics* 43(2015): 65–67; A.D. So, et al., 'An integrated systems approach is needed to ensure the sustainability of antibiotic effectiveness for both humans and animals,' *J Law Med Ethics*. 2015;43(Suppl 3):38–45; N. Gulati, et al., *Using International Instruments to Address Antimicrobial Resistance* (Ottawa: University of Ottawa Global Strategy Lab, 2016).

⁷⁸N. Roberts, 'Wicked Problems and Network Approaches to Resolution,' *Int Public Manag Rev* 1(2000): 1–19.

⁷⁹E. Mossialos, et al., *Policies and incentives for promoting innovation in antibiotic research* (Copenhagen: European Observatory on Health Systems and Policies, 2008).

the US Generating New Antibiotic Incentives Now (GAIN) Act or the European Innovative Medicines Initiative (IMI) are trying to address this, but even if successful, their overall budget does not permit any kind of paradigmatic shift to current antibiotic use policy.⁸⁰ Other strategies which have been offered, such as antibiotic de-linkage schemes,⁸¹ health impact funds,⁸² public-private partnerships,⁸³ innovation prizes⁸⁴ and other mechanisms⁸⁵ have mostly sought to replicate the old approach of developing new antibiotics in the hopes of outpacing resistance. While some AMR funding streams now include calls for projects in behavioral science, communication and education, their funding remains a miniscule fraction of what is currently being invested into drug development. From an ethical perspective, this creates additional problems. New drugs are likely to disproportionately benefit high-income countries (HICs), despite LMICs having the greatest burden of drug-resistant infections. Behavioural science research is also predominantly focused on HICs. We currently lack sufficient behaviour change research into what can be effectively achieved in regions with high levels of resistance and limited resources, e.g. some African countries, India, or countries in South East Asia. Competitive strategies are unlikely to change this as they are currently structured and incentivized.

26.4.3 Collaborative Strategies

These strategies involve a large number of stakeholders, especially in cases where responsibility and decision-making power are widely dispersed. While more difficult to establish than top-down authoritative approaches, collaborative strategies are widely considered to be the most suitable approach to dealing with wicked and

⁸⁰ J.P. Roberts, 'Incentives aim to boost antibiotic development,' *Nature Biotechnology* 30:8 (2012):735.

⁸¹ C. Clift, et al. (eds.), *Towards a New Global Business Model for Antibiotics: Delinking Revenues from Sales* (London: Chatham House, 2015).

⁸² K. Outterson, T. Pogge and A. Hollis, 'Combating Antibiotic Resistance Through the Health Impact Fund,' in I. Glenn Cohen (ed.), *The Globalization of Health Care: Legal and Ethical Issues* (Oxford: Oxford University Press 2013), pp. 318–338.

⁸³ For example, DRIVE-AB (Driving reinvestment in research and development and responsible antibiotic use), available from: <http://drive-ab.eu>; CARB-X (Combating antibiotic resistant bacteria biopharmaceutical accelerator), available from: <http://www.carb-x.org>

⁸⁴ For example, the Longitude Prize, available at: <https://longitudeprize.org>; Antimicrobial Resistance Diagnostic Challenge, available at: <https://dpcpsi.nih.gov/AMRChallenge>. Also see J. Love and T. Hubbard, 'The Big Idea: Prizes to Stimulate R&D for New Medicines,' *Chicago-Kent Law Review* 82(2007): 1519–1554.

⁸⁵ K. Outterson, J.H. Powers, G.W. Daniel, and M.B. McClellan, 'Repairing the Broken Market for Antibiotic Innovation,' *Health Affairs* 34(2015): 277–285; M.J. Renwick, D.M. Brogan and E. Mossialos, 'A Systematic Review and Critical Assessment of Incentive Strategies for Discovery and Development of Novel Antibiotics,' *The Journal of Antibiotics* 69(2016): 73–88; R.D. Smith, and J. Coast, 'The economics of resistance through and ethical lens,' In *Ethics and Drug Resistance: Collective Responsibility for Global Public Health*. Springer, Cham.

super-wicked problems, especially in the absence of a strong global planning authority to address the challenge.⁸⁶ Collaborative strategies can and are already being used at different levels, from UN initiatives to regional local campaigns that focus on raising awareness or improve prescribing.⁸⁷

These three strategies are not mutually exclusive and different approaches can and should be combined, where viable and appropriate. Viewing AMR as a super-wicked problem suggests that sustainable change is most likely to result from collaborative strategies focusing on multiple drivers, yet the urgency with which a response to AMR must be found may necessitate, for example, the inclusion of competitive strategies to develop new drugs and authoritative strategies at the national level to enforce strict prescribing guidelines or prohibitions on using antibiotics in farm animals as growth promoters. However, the critical reader will also notice that, for the most part, present efforts to address AMR can already be categorized as authoritative, competitive or collaborative strategies respectively. This begs a question as to whether framing AMR as a super-wicked problem can be of any further help in developing novel and effective strategies to combat drug resistance. In the paper's penultimate section, we canvass a few potential ways in which the super-wicked problem frame can impact on current AMR policy going forward.

26.5 Shifting Path Dependencies – The Way Forward

Understanding AMR as a super-wicked problem itself does not, unfortunately, generate a set of novel, easily implementable policy solutions. Yet, as outlined before, the complexity of AMR, as well as the countless factors that contribute to it, make one-stop solutions highly unlikely in the first place.

While it does not offer any immediate solution to the problem, the understanding of AMR as a super-wicked problem may, however, achieve another goal – namely, to prompt a reconsideration of the relative importance of different responses to drug resistance. One of the most important insights of framing AMR as a super-wicked problem is that there is no technological fix we can engineer, nor any simple market-based solution that will avoid the impending scarcity of effective antibiotics in the future. Any responses that will help us keep AMR at bay in a significant way will involve a delicate balancing of benefits and burdens that will require difficult choices and restrictions to be imposed on individuals and populations. This insight is at odds with current research funding in the area of AMR, which is heavily skewed towards drug development.⁸⁸ Moreover, given the global scale of the problem, success in one

⁸⁶L. Briggs, 'Tackling Wicked Problems - A Public Policy Perspectiv,' in *Contemporary Government Challenges* (series) (Australian Public Service Commission, 2007).

⁸⁷For a selection of local initiatives see for example the ReAct Toolbox, <https://www.reactgroup.org/toolbox/>

⁸⁸R. Kelly, et al., 'Public funding for research on antibacterial resistance in the JPIAMR countries, the European Commission, and related European Union agencies: a systematic observational analysis,' *The Lancet Infectious Diseases* 16(2016): 431–440.

part of the world will likely only be temporary, given the drivers brought and accelerated by globalization. Framing AMR as such a fundamentally unsolvable policy challenge may appear to be defeatist. However, the point is not to admit defeat, but to focus on those interventions that may be of greatest use in the long run – even if we can never overcome the vicious cycle of bacterial resistance and antibiotic obsolescence.⁸⁹ It may come as good news at this stage that many potential candidates for such a strategy already exist, but have simply not have been implemented properly.

The most obvious example in this context is infection control and prevention and water, sanitation and hygiene (WASH). While ultimately decisive for the control of nosocomial infections, hospital and healthcare hygiene and infection prevention have often appeared to be more of an afterthought in recent policy discussion. However, they remain of crucial importance for the prevention of infections, in both high- and low-income settings.⁹⁰ Similarly, many of the ongoing efforts for the creation of broader public awareness for the problem and causes of AMR have not yet achieved their desired goals.⁹¹ Education and hygiene measures are no silver bullets – and have their own issues with compliance and recalcitrance – but if AMR is understood as a super-wicked problem, these policies should receive much greater recognition as a crucial part of an effective AMR strategy. Indeed, these are just some of the many different behaviour change interventions – aimed at both professionals and the public – that should comprise a multipronged and diversified response to AMR.⁹² Of course, the success of such behavior change interventions will itself be dependent upon fixing even more fundamental problems plaguing global health, including poverty and extreme income inequality, since many

⁸⁹ A.E. Aiello, N.B. King and B. Foxman, 'Ethical Conflicts in Public Health Research and Practice Antimicrobial Resistance and the Ethics of Drug Development,' *American Journal of Public Health*, 96(2006): 1910–1914; B. Spellberg, J.G. Bartlett and D.N. Gilbert, 'The Future of Antibiotics and Resistance,' *New England Journal of Medicine* 368(2013): 299–302.

⁹⁰ S. Harbarth, et al., 'Antimicrobial resistance: one world, one fight!' *Antimicrobial Resistance and Infection Control* 4(2015): 49 – <https://doi.org/10.1186/s13756-015-0091-2>; Peter Collignon, et al., 'Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis,' *The Lancet Planetary Health* 2018; 2: e398–405. Also World Health Organization, *Guidelines on Sanitation and Health* (Geneva: WHO, 2018).

⁹¹ Special Eurobarometer, *Antimicrobial Resistance Report, May – June 2013* (Brussels: EU Directorate-General Communication, 2013).

⁹² See, for example, T. Edgar, S.D. Boyd and M.J. Palamé, 'Sustainability for behaviour change in the fight against antibiotic resistance: a social marketing framework,' *Journal of Antimicrobial Chemotherapy* 63(2009): 230–237; C.S. Lundborg and A.J. Tamhankar, 'Understanding and changing human behaviour—antibiotic mainstreaming as an approach to facilitate modification of provider and consumer behaviour,' *Uppsala Journal of Medical Sciences* 119(2014):125–133; Public Health England, *Behaviour Change and Antibiotic Prescribing in Healthcare Settings: Literature Review and Behavioural Analysis* (London: Public Health England, 2015); S. Tonkin-Crine, A.S Walker and C.C Butler, 'Contribution of behavioural science to antibiotic stewardship,' *BMJ* 2015; 350:h3413; K. Chaintaril et al., 'Impact of a United Kingdom-wide campaign to tackle antimicrobial resistance on self-reported knowledge and behaviour change,' *BMC Public Health* 16(2016):393.

technical and behavioral interventions are limited by adverse social, economic, and political contexts.⁹³ Tackling AMR will require those working in global health to directly address injustices, however one conceives of justice. Here, for our purposes, any conception of justice will do since the problem of injustices in global health are theoretically overdetermined.⁹⁴ In other words, practically speaking, tackling the levers that make AMR a super-wicked problem will have to include making real efforts to address global injustices for the various ways in which they contribute to the level of drug-resistant pathogens around the world.

Finally, understanding AMR as a super-wicked problem and thereby as a global challenge that defies simple solutions by any one party suggests that a much greater part of our efforts must be directed towards increasing standards of access and quality of prescribing in those regions where resources continue to be limited. We have not yet managed to ensure the provision of adequate access to antibiotics in many regions of the world, where the price of drugs is often prohibitive for patients and where over-the-counter sales have led to an unregulated and uncontrolled use of antibiotics.⁹⁵ We are, therefore, faced with a situation in which we have to reduce the excessive use of antibiotics in some regions of the world while ensuring greater access in others.⁹⁶ As Daulaire et al. maintain, ‘meaningful access is dependent on good stewardship and vice versa.’⁹⁷ Nevertheless, this will require us to successfully confront and find answers to difficult distributive questions about when access should be increased or limited, and how to maintain sustainable fair access in a way that attempts to diminish the rate of AMR as long as possible. Stewardship to protect the effectiveness of antibiotics presupposes a functioning healthcare and legal system with sufficient oversight to regulate antibiotic usage adequately. New drugs, especially against Gram-negative bacteria, are badly needed and if resistance against drugs of last resort (e.g., carbapenems, colistin) further increases, we are officially out of options for treatment. In many of the countries that require greater access, it is difficult to guarantee even the most basic stewardship mechanisms. As a result, there is a need to explore different ways of approaching antibiotic governance in a global setting as part of responding to this super-wicked problem that genuinely

⁹³ S. Gill and I. Bakker, ‘The global crisis and global health,’ in S. Benatar and G. Brock (eds.), *Global Health and Global Health Ethics* (Cambridge: Cambridge University Press, 2011), pp. 221–238.

⁹⁴ See, for example, L. Reid “Antimicrobial resistance and social inequalities in health: considerations of justice” In *Ethics and Drug Resistance: Collective Responsibility for Global Public Health*. Springer, Cham, where the author provides an egalitarian argument toward this conclusion.

⁹⁵ R. Laxminarayan, et al. ‘Antibiotic resistance – the need for global solutions,’ *Lancet Infect Dis*, 13:12 (2013): 1057–98.

⁹⁶ G. Heyman, O. Cars, M.T. Bejarano, and S. Peterson, ‘Access, Excess, and Ethics—Towards a Sustainable Distribution Model for Antibiotics,’ *Uppsala Journal of Medical Sciences* 119(2014): 134–141.

⁹⁷ Nils Daulaire, et al., ‘Universal Access to Effective Antibiotics is Essential for Tackling Antibiotic Resistance,’ *The Journal of Law, Medicine and Ethics* 43(2015): 17–21 at 18.

empowers local and regional stakeholders to shape the path dependencies that guide our response.

26.6 Conclusion

While AMR is a complex and arduous challenge, understanding it as a super-wicked problem does not mean it is intractable or that the multitude of drivers and stakeholders defy making substantial progress. The discussion of potential initiators of path dependency in this paper serves as an illustration of possible scenarios rather than as a comprehensive list of recommendations, but it highlights that recognizing AMR as a super-wicked problem would indeed have policy implications and should lead us to reconsider our values and priorities in responding to AMR.

This will also include a discussion of ethical norms and standards that should be met in addressing the problem of drug resistance. Given that AMR has only recently moved from being a purely clinical (or veterinary) problem into the realm of global challenges that require a broader societal response, there exists currently little research, and even less agreement on what the most important ethical issues in AMR are, and what we should do about them.⁹⁸ Ethicists should weigh in on such complex and wicked problems,⁹⁹ but they must also be aware of the fact that this is not an abstract problem, but already a health challenge on a global scale.

Understanding AMR as a super-wicked problem is not merely a matter of categorization. Instead, it should lead us to reconsider current policy approaches in light of their expected usefulness and likely success of implementation. New approaches to tackling AMR should seek to avoid replicating earlier patterns and problems of jumping between ‘one-best-way’ approaches or ‘one-size-fits-all’ interventions – both empirically and ethically. If AMR does indeed present a super-wicked problem, policy efforts should be primarily directed at shifting path dependencies. As such, the aim is not ‘solving’ AMR but to make progress towards better mitigation and management through these shifts. Current policies, for instance, which promote infection prevention and control, antimicrobial stewardship and the development of new drugs, are a crucial contribution to curbing AMR because they prolong antibiotic effectiveness and prevent infections in the first place. However, they are clearly insufficient as answers in the medium to long run, and should therefore only constitute a first step in initiating more fundamental changes to public health policy to reduce future dependence on antibiotics and more general social policy affecting the drivers of drug resistance.

⁹⁸J. Littmann J and A.M. Viens, ‘The Ethical Significance of Antimicrobial Resistance,’ *Public Health Ethics* 8(2015): 209–224.

⁹⁹D.S. Silva, M.J. Smith MJ, and C.D. Norman, ‘Systems thinking and ethics in public health: a necessary and mutually beneficial partnership,’ *Monash Bioethics Review* 2018 Jun 13. doi: <https://doi.org/10.1007/s40592-018-0082-1>. [Epub ahead of print].

Framing AMR as a super-wicked problem also emphasizes the importance of ongoing trends towards more integrated collaborations across sectors and research disciplines. It should help in creating greater awareness for the true scope of the problem we are faced with and the urgency with which we must address it.

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