This is a ”preprint”, the authors’ mausript to an article published in the scientific journal Bioethics, vol. 33, issue 7, pp. 731-33. Citation should refer to the final, published version, available here: https://onlinelibrary.wiley.com/doi/10.1111/bioe.12655

The Ethics of Antibiotic Resistance: Towards an Agenda for Feasible and Justified Global Health Policy

Guest editorial to a special issue of *Bioethics* on the ethics of antibiotic resistance.

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Acknowledgement
This research was supported by the UGOT Challenges Initiative of the University of Gothenburg, and by Riksbankens Jubileumsfond, RJ (application F17-1078:1), for the project *Ethics and Value Challenges in Antibiotic Resistance Management, Policy and Research*.

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Antibiotic resistance (ABR) is a major threat to public health and modern healthcare worldwide, jeopardizing the treatment of bacterial infections, and limiting all types of medical procedures where efficient infection prophylaxis is key. Development of truly new antibiotics has stalled, at the same time as new forms of resistance emerge and spread quickly. The latter is a consequence of a combination of overuse of antibiotics in healthcare and food production systems, insufficient transmission control of resistant bacteria, and a vast reservoir of resistance factors in the environmental microbiota that emerges one by one in pathogens. The stakes are massive both in terms of morbidity, mortality and societal costs[1]. Some regions in the world, including northern Europe, have managed to reduce the pace of this destructive process[2], but translating their solutions to other parts of the world is a daunting, sometimes infeasible, task. While the driving forces of ABR are bacteria´s ability to evolve rapidly under the selection pressure from antibiotics, together with a flow of bacterial genes across species and environments, the global societal *challenge* of ABR is the result of human and social practices and values. Initiatives to curb these challenges therefore quickly meet with complex societal, behavioural political, economic and – underlying all of these – ethical challenges[3]. On the one hand, ethical reasons of different kinds can be mustered in support of radical and swift action in the face of ABR. But different and mutually conflicting ethical outlooks may nevertheless result in very different recommendations, and present difficult dilemmas. In addition, as action in the face of ABR is ultimately motivated by ethical reasons, it is imperative to consider potential downsides of proposed actions, in order to identify truly justified ways forward, and to reflect on how such options, despite their attractiveness from an ideal perspective, relate to differing values, stakes and practices across individuals and societies. This calls for a research approach where ethics is closely integrated across disciplines to help bring about effective, justified and implementable changes in policy and practices.

With this aim and previous initiatives to this effect[4] in mind, in 2017, the Centre for Antibiotic Resistance Research (CARe) at the University of Gothenburg[5] organized the symposium *Ethics and Value Challenges in Antibiotic Resistance Management, Policy and Research*[6]. The presentations and

1 World Health Organization, WHO (2015). *Global action plan on antimicrobial resistance*. Geneva, Switzerland: WHO. Available at: http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/

2 See: https://resistancemap.cddep.org/

3 Littmann, J. & Viens A.M. (2015). The Ethical Significance of Antimicrobial Resistance. Public Health Ethics 8(3), 209–224.

4 See, especially, Hoffmann, S., & Outterson, K. (eds.) (2015). Special Issue: Antibiotic Resistance. Journal of Law, Medicine and Ethics, 43(S3), 6-78; Littmann, J., & Viens, A.M. (eds.) (2015). Special Symposium: Antimicrobial Resistance. Public Health Ethics, 8(3), 209-265; and the forthcoming volume Jamrozik, E., & Selgelid, M. (eds.), *Ethics and antimicrobial resistance: Collective responsibility for global public health*. Cham, Switzerland: Springer, in press.

5 CARe is a multidisciplinary centre, comprising academic disciplines across six faculties and involving partnership with practitioners, decision makers, and public and private institutions. For more information, see http://care.gu.se.

6 The symposium was generously sponsored by Riksbankens Jubileumsfond, the Västra Götaland County Government, the Wallenberg Foundations, and the Royal Swedish Academy of Sciences. The symposium program and videos from the lectures are available here: https://care.gu.se/news-events/n//see-all-ethics-and-value-challenges-in-antibiotic-resistance-management--policy-and-research-talks.cid1537410

discussions at that event formed the backbone of the present special issue, to which some additional contributors were invited to make the scope appropriately wide[7]. The ethics of ABR stretches across all main areas of bioethics: research ethics, clinical ethics, public health ethics and general health policy. It also includes aspects of agricultural ethics and environmental and food ethics and policy, thereby presenting drastic needs of both comprehensive global and “one health” perspectives that challenge mainstream concentrations of bioethical research on issues mostly fitting well-functioning health systems in high income settings. We, of course, hope that the contributions to this issue serve to move the ABR ethics landscape ahead along these lines, at the same time recognizing that much, much work remains to be done.

An already rather well identified area of the ethics of ABR regards how to design justifiable policies of so-called antibiotic stewardship within healthcare systems, and how to resolve moral dilemmas occurring due to such policies. Annette Rid, Alena Buyx and Jasper Littmann argue that current public health ethical frameworks offer insufficient guidance in evaluating the trade-off between the best clinical interests of present patients and the benefit of a given program to others. By way of example, the authors examine the notion of “rational” use of antibiotics, which involves programs that aim to affect antibiotic use and prescription. Some of these programs restrict the use of potentially beneficial antibiotics, thus exposing patients to greater risk. By drawing on the analogy with clinical research, the authors propose a framework for evaluating public health programs’ risks and potential benefits.

Two contributions serve to complicate this discussion from a global health and justice standpoint, and to provide further suggestions for how an appropriate ethical theoretical framework for antibiotic stewardship should look like. First, Michael Millar observes that significant and deeply unfair inequalities exist with respect to antibiotics and ABR. He approaches this issue from a Scanlonian, contractualist framework, applied to the particularly difficult problem of the use of antibiotics in the prevention of growth stunting, which is a particular risk to underprivileged children. His analysis takes into account alternative feasible actions, as well as current and future interests and international responsibilities, thereby complicating the structure proposed by Rid and colleagues. Second, Eva Krockow and Carolyn Tarrant describe how socio-economic, organisational and cultural differences between different parts of the world may significantly influence what kind of antibiotic stewardship policies become justifiable, and how ethical dilemmas can be expected to play out and be perceived by key actors due to this. Using South Africa, Sri Lanka and the United Kingdom as cases in point, they argue in favor of a contextualized approach to the justification of ABR policies that take such differences into account.

A further important ingredient of ABR policy concerns the surveillance of resistant bacteria in healthcare institutions, as well as in the general community. At the same time, Euzebiusz Jamrozik's and Michael Selgelid's contribution presses the need for actions to ensure such surveillance to be based on adequate knowledge about the nature and actual spread of carriership of resistant bacteria of different types, effectiveness of screening programs to identify such carriers, of interventions to curb the spread of resistance based on that, and of resolving ethical conflicts due to burdens imposed on people that are identified as carriers. In this context, the ethical dilemmas are different from when stewardship programs aim to ration the use of antibiotics, and instead of conflicts

7 All contributions have been subjected to double blind peer review, with editorial decisions by the guest editors, except for the contribution by Munthe and Nijsingh, where the editorial decisions were taken by the regular editors of *Bioethics*.

between traditional clinical ethical perspectives and public health ethical values, we face dilemmas *within* public health and general health policy frameworks in need of resolve. Albeit not explicitly highlighted by Jamrozik and Selgelid, we propose that global health perspectives and differences of the sort highlighted by Krockow and Tarrant, as well as Millar, may be relevant also in this context. If nothing else, because what is perceived as acceptable in different settings may impact the pragmatic feasibility of effective programs for surveillance of antibiotic resistance in healthcare and general society.

Besides specific antibiotic stewardship policies targeting different loci of the ABR challenge within health systems, health policy in the face of ABR may also be of a more general nature. Alberto Giubilini discusses the proposal to tax antibiotics as a strategy justified in the light of describing ABR as a collective action problem. Addressing this problem requires interventions that limit consumption and charge relevant stakeholders for imposing burdens on others. Taxation, so Giubilini argues, is therefore morally justified. It could create incentives for people to refrain from taking drugs in the case of mild and self-limiting infections and has the additional benefit of providing financial resources which could be put to use for the purposes of innovation and conservation of antibiotics. Again, one may imagine that the pragmatic aspect lifted by Krockow and Tarrant could be relevant to further analyse this proposal, and that there may be some variation across the world in how feasible ABR taxation reforms may be.

The feasibility aspect is a main theme also when Christian Munthe's and Niels Nijsingh's contribution moves the focus from clinical and public health ethics to clinical research ethics and policy. One suggestion to tackle the main hurdle of weak antibiotic innovation is to provide better incentives for researchers and drug companies by relaxing the regulation of clinical research and, based on that, clinical introduction of new drugs. Such “cutting of red tape” can be given a rather strong support from a combination of ethical perspectives, but these reasons are undermined by a number of pragmatic challenges, which arise from the ways in which interventions may trigger adverse responses by stakeholders. The underlying dilemma relates to the justification of compromises between ideal ethical justification and pragmatic risks, giving policymakers reasons to tread with quite a bit of care. Continuing on the theme of antibiotic research and innovation, Jonathan Anomaly and Julian Savulescu argue provocatively that the urgency of better antibiotic innovation means that there is no principled limit to paying subjects to participate in dangerous antibiotic research trials, specifically challenge studies, which involves purposely infecting subjects with pathogens. They consider various worries concerning payment for participation in such risky trials and argue that these worries can be addressed on the condition that proper screening mechanisms are in place.

The complexity of the ethical conflicts involved in the justification of ABR policies, as of the pragmatics and feasibility perspectives pointed out, attain massive proportions when we lift ABR as a global policy challenge. This regards all areas addressed by the previous contributions. Steven Hoffman, Reema Bakshi and Susan Rogers Van Katwyk recognize this and discuss domestic and international legal mechanisms to address ABR. They argue that an international agreement that addresses the interconnected problems of access, conservation and innovation is called for. The authors propose ten provisions for such an agreement as well as an equal amount of implementation mechanisms. Now is the time to negotiate global coordinated action to institutionalise solutions to the root social causes of the problem of ABR.

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