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Toward a bioethical framework for antibiotic use, antimicrobial resistance and for empirically designing ethically robust strategies to protect human health: a research protocol

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Abstract

Introduction: Antimicrobial resistance (AMR) is a challenging global and public health issue, raising bioethical challenges, considerations and strategies.

Objectives: This research protocol presents a conceptual model leading to formulating an empirically based bioethics framework for antibiotic use, AMR and designing ethically robust strategies to protect human health.

Methods: Mixed methods research will be used and operationalized into five substudies. The bioethical framework will encompass and integrate two theoretical models: global bioethics and ethical decision-making.

Results: Being a study protocol, this article reports on planned and ongoing research.

Conclusions: Based on data collection, future findings and using a comprehensive, integrative, evidence-based approach, a step-by-step bioethical framework will be developed for (i) responsible use of antibiotics in healthcare and (ii) design of strategies to decrease AMR. This will entail the analysis and interpretation of approaches from several bioethical theories, including deontological and consequentialist approaches, and the implications of uncertainty to these approaches.

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Introduction

Antimicrobial resistance (AMR) is a challenging global and public health issue that gives rise to bioethical challenges, considerations and strategies. According to the World Health Organization (WHO), AMR threatens the very core of modern medicine and the sustainability of an effective, global public health response to the enduring threat from infectious diseases.[1] Deciding whether to use antibiotics in a responsible way and the proliferation of multi-resistant microorganisms defy current global public health approaches. Such a decision entails in-depth bioethical analysis that can and should be applied at both clinical and global public health levels.

Our research protocol, entitled "Toward a bioethical framework for antibiotic use, antimicrobial resistance and for empirically designing ethically robust strategies to protect human health: a research protocol", aims to develop a bioethical framework for antibiotic use and for designing ethically robust strategies to protect and promote human health against AMR in community and hospital settings. This research is part of a larger project of the Instituto de Bioética, Universidade Católica Portuguesa, entitled "Developing a Public Health Bioethical Framework for Antibiotic Use and for Designing Ethically Robust Strategies to Protect and Promote Health from AMR". The project objective is to address this bioethical and societal issue and investigate how decision-making processes for the use of antibiotics occur in community and hospital settings.

The project is currently in its initial stages and this article aims to present the state of the art, background and research protocol of this study. Because this is a study protocol, we only report on planned and ongoing research studies. It is our conviction that, in the future, the results will be useful for tailoring ethically framed strategies to decrease the problem of AMR and help to protect and promote health. This is of foremost relevance as the WHO has recognized that without harmonized and immediate action at global scale, the world is heading towards a post-antibiotic era in which common infections could once again be deadly.[1]

Antimicrobial resistance from a bioethical perspective: the state of the art

AMR is a challenging global and public health issue that gives rise to several concerns, challenges, considerations and strategies. Much emphasis has been placed on the implications for human health of increasing antibiotic resistance in pathogens, which is owing to imprudent antibiotic prescription and consumption as well as to widespread and common use of antibiotics in agriculture.[2–4] However, more attention is needed on the decision-making processes underlying these practices.

Humanity is facing the very real possibility of a post-antibiotic era.[5–8] Urgent action is therefore needed to maintain the effect of antibiotics[9] and ensure equity of access to this type of medication. From a global and public health perspective, while developed societies are struggling with problems related to AMR, less-developed societies still face the paucity and lack of access to antibiotics.

AMR poses particularly important challenges for human health. The development of a bioethical framework for antibiotherapy calls for careful analysis of the ethics ''behind the scenes''. Responsibility is of utmost complexity in this context as it lies with individuals, healthcare professionals, managers, policy makers and health systems; all stakeholders are simultaneously vulnerable to and responsible for AMR.

Several global and public ethical issues have been raised about the use of antibiotics and AMR with respect to human health. For instance, according to Leibovici et al.[10], a central question can be posed, namely, whether we could and should consider benefits in the distant future for unidentified patients as being more important than benefits in the near future for an identified patient. This must be discussed within a broader ethical debate by considering diverse ethical theories, principles and values. Using Kass's[11] definition, bioethics can help healthcare professionals and public policy makers to recognize the ethical dilemmas surrounding antibiotic use as well as strategies to reduce the extent of AMR.

Currently, owing to diverse reasons (e.g., AMR, economic hardship, population ageing), physicians must sometimes choose between the welfare of an individual patient and a healthcare system directive to restrict antibiotics.[12] Preventing harm, preserving the public good and protecting individual liberty can conflict with each other because infectious diseases not only threaten individual health but also the welfare of other human beings.[7] The lack of consensus on an ethical framework makes these decisions more difficult, transforming physicians' decision whether to prescribe antibiotics and/or design strategies for fighting AMR into a complex phenomenon.

The various components, values, principles and theories behind clinical and ethical decisions become manifest in different ways with respect to AMR. This depends on the degree of uncertainty surrounding the consequences of antibiotics' use for human health and has implications for the moral intensity of the ethical decisions to be undertaken. Interventions aimed at promoting the proper and prudent use of antibiotics, using an empirically based and bioethically sound framework, should encompass 'upstream' policy-relevant actions, both within and outside the healthcare system. By doing so, physicians will be able to act more objectively when deciding whether to prescribe antibiotics.

Why a bioethical framework for AMR?

AMR is a challenging global and public health issue, raising several concerns, challenges, considerations and strategies.[1,8,13–15] Compelling questions from the domains of global, population and public health ethics and the bioethics of infectious disease will therefore be posed. Responsibility, in this context, is of utmost complexity; all parties are simultaneously vulnerable to and responsible for AMR.[16,17]

The use of antibiotics leads to the increase of AMR. This has implications for consumer safety[18] and health, and constitutes a global and public health issue, challenge and concern. In 2015, the World Health Assembly passed a new global action plan on AMR, and the topic was discussed as a priority for policy actions among the G7 countries.[19]

AMR is spreading rapidly in developed societies worldwide, making it one of the most serious threats to human, public and global health. The WHO[6] has stated that a post-antibiotic era is a very real possibility. Hence, urgent actions are needed to maintain the effect of antibiotics.[9] In contrast, underdeveloped countries still do not have equity of access to antibiotics, which maintains the high risk of death owing to common infectious diseases in these countries.

Antibiotic consumption is a major driver of AMR and there is large cross-country variation in AMR.[2] This is mainly owing to different patterns of antibiotic prescription and consumption. Indeed, prescribing style is an important source of variation, not only across but also within countries.[20,21] Prescribing style involves the subjective tendency of physicians to be more or less inclined to prescribe antibiotics.[22,23] Variations in the prescription style sometimes suggest poor clinical practices and can contribute to the inadequate use of healthcare resources. Resource allocation is a key ethical issue in health organizations and systems. Interventions aimed at promoting the rational use (clinically and ethically sound) of antibiotics should encompass actions at the policy-making level. This highlights a need for common clinically and ethically sound frameworks, not only at individual but also at public, global and policy levels.

Bioethics owes its development to awareness of the seriousness and magnitude of ethical issues or problems that no society can ignore, no matter its level of technological development. Ethical principles, such as individual responsibility (autonomy), social responsibility (solidarity), vulnerability, integrity, privacy, reciprocity and equity of resource allocation must be pulled together to simultaneously ensure individual interests, societal welfare and the sustainability of future generations.[16,24]

Population and individual-level approaches have been used extensively to explain variations in prescription styles and consumption. However, little is known about any bioethical framework behind or within the decision-making processes for prescribing and using antibiotics and for preventing AMR.

The present bioethical framework will encompass and integrate two models: global bioethics and ethical decision-making. In the first model, the conceptual global bioethics problem of AMR is built in three steps. First, AMR is a global bioethics problem because of its following characteristics: (i) worldwide scale, (ii) interconnectedness, (iii) persistence, (iv) general scope and (v) need for global action.[17] Second, AMR is considered a bioethical problem because it has specific relevance for health and human life and poses normative challenges. Finally, the problem of AMR has three characteristics: ambiguity, situation and horizon.[17] The second model,[24–26] which has been concerned with ethical decision-making in organizations,[27–29] can be successfully applied to healthcare settings. The following relevant features will be addressed: (i) awareness of the ethical and moral dimensions posed by the use of antibiotics; (ii) ethical and moral judgements associated with the use of antibiotics in the provision of human healthcare; (iii) the main ethical risks associated with development of strategies to fight antibiotic resistance of bacteria; (iv) whether there is the intention to prioritize ethical and moral considerations when addressing the problems posed by AMR; and (v) whether the actual behaviour displayed in the use of antibiotics is ethically grounded and sound.

Moving from a bioethical conceptual framework towards an empirical one: the research protocol

This research protocol presents a conceptual model leading to the formulation of an empirically based bioethics framework for antibiotic use, AMR and for designing ethically robust strategies to protect human health.

Objectives

The main objective of the research project is to develop a bioethical framework for

antibiotic use and for designing ethically robust strategies to protect and promote human health against AMR in community and hospital settings. To empirically study this global and public health issue, we defined the following specific objectives: (i) To understand the ethical rationale and decision-making processes behind antibiotics' use in community and hospital care settings; (ii) to identify the main ethical issues associated with AMR in these settings; (iii) to evaluate ethically different, scientifically sound strategies to fight AMR and (iv) to comprehend micro-meso-macro linkages of the decision-making processes concerning AMR in human healthcare provision.

The following research questions will complement our bioethical analysis and framework: Can post-modern societies infringe upon individual rights to promote the common good and public health when a person is diagnosed with a multidrug-resistant infectious disease? When they are diagnosed, should individuals be allowed to self-determine whether they are too infectious to use public transport (e.g., airplanes, subways, trains, buses)? What procedures should be applied when individuals are diagnosed with new diseases of unknown or uncertain contagiousness? How should we deal with patients and next-of-kin when they decide not to take prescriptions correctly, thereby allowing dangerous pathogens to mutate and become resistant to antibiotics? What implications exist and what burdens are likely to result if health practitioners and policy makers propose targeting public health interventions only to certain groups?

To achieve the main objective of this project, diverse research methods and techniques will be used and operationalized. Because this manuscript refers to the research protocol of the abovementioned project, which is currently in its initial stages, no data and no findings will be presented here. We foresee that, based on our findings and use of a comprehensive, integrative and evidence-based approach, we will develop a step-by-step bioethical framework for antibiotic use and the design of strategies to decrease AMR. This will entail the analysis and interpretation of various approaches from several bioethical and ethical theories, including deontological and consequentialist approaches, and the implications of uncertainty in relation to these approaches.

Methods

A mixed-methods approach will be implemented to achieve the main objective of this research project. Therefore, quantitative and qualitative research methods, techniques and instruments will be combined to gather empirical data and information on the perceptions, attitudes and practices of primary and hospital care physicians concerning the following aspects: (i) antibiotics consumption; (ii) antibiotics prescription; (iii) AMR; (iv) clinical pathways associated with the diagnosis and treatment of multi-resistant infections; (v) evidence-based strategies to reduce the problem of resistance; (vi) bioethical frameworks of antibiotics use; and (vii) bioethical frameworks for designing strategies to decrease AMR.

This project will include the following substudies: (I) Systematic literature review on bioethics, ethical issues and antibiotics consumption, prescription and resistance. (II) Systematic literature review on strategies to decrease the problem of AMR. (III) Empirical studies embracing both quantitative (survey of healthcare professionals' attitudes) and qualitative (documentary analysis of existing guidelines and protocols in Portuguese hospitals) approaches, including use of the Delphi technique to build an expert consensus on empirically and bioethically framed practices for protecting and promoting human health in the face of AMR. (IV) Development of a bioethical framework for antibiotic use in the

provision of human healthcare, by integrating substudies (I) and (III). (V) Development of a bioethical framework for the design of strategies to face the problem of AMR.

Currently, abstract screening for substudies I and II (i.e., the two systematic reviews) is underway and the first results are expected to be publicly available by mid 2017. A summary of the reviewed materials will be presented in tabular form complemented by a narrative description. The results will be classified into the main conceptual categories, which will be obtained during extraction of the results. We anticipate that the results of these studies will enable the development of instruments for data collection to be used for substudy III (empirical study using a mixed-methods approach).

All substudies will follow the corresponding EQUATOR Network reporting guidelines. It is our conviction that these studies will yield relevant data and information, which will be useful to tailor the development of a bioethical framework of antibiotic use in human healthcare provision (substudy IV) and ethically framed strategies to decrease the problem of AMR and to protect and promote health (substudy V).

Concluding remarks

AMR is a challenging global and public health issue that gives rise to numerous bioethical challenges, considerations and strategies. Deciding whether to use antibiotics in a responsible way and the proliferation of multidrug-resistant microorganisms defy current public health approaches.

This article reflects the research protocol of a project aimed at developing a bioethical framework for antibiotic use and for designing ethically robust strategies to protect and promote human health against AMR in community and hospital settings. Based on our ongoing data collection and future findings and using a comprehensive, integrative and evidence-based approach, a step-by-step bioethical framework will be developed for (i) responsible use of antibiotics in healthcare contexts and (ii) design of strategies to decrease AMR. This will entail the analysis and interpretation of various approaches from several bioethical and ethical theories, including deontological and consequentialist approaches, and the implications of uncertainty with respect to these approaches.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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