ANTIMICROBIAL RESISTANCE AND DISTRIBUTIVE JUSTICE

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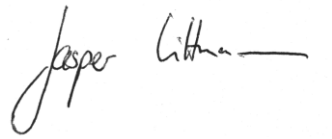
Thesis Declaration

I, Jasper Littmann, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.



Abstract

The rapid emergence of Antimicrobial Resistance (AMR) over the past decades together with a lack of research into new drugs presents health care systems with serious challenges and threatens their ability to effectively treat serious bacterial infections. As a result, it is realistic to expect that effective treatment options for some infections will run out in the future. The thesis begins by outlining the mechanisms and consequences of AMR and argues that AMR differs from other distributive problems, due to the specific characteristics of antibiotics. It is suggested that for considerations of distributive justice, antibiotic effectiveness should be treated as a resource, which can be depleted and which must be fairly distributed between people and generations.

The thesis then goes on to examine the distinctive moral challenge posed by AMR. It begins by considering a consequentialist account, which suggests that AMR is a moral problem due to the bad health outcomes it entails. However, this approach is subsequently dismissed because it struggles to account for some of the particular features of AMR. An alternative is to consider AMR as a morally wrongful harm to individuals, which requires not only that AMR has adverse effects, but also violates the victim's rights. It is shown that the harm caused by AMR is morally wrongful and that people have a right to be protected from adverse health outcomes, which AMR violates. However, it is difficult to specify correlative duties that result from such a rights claim.

As an alternative, the thesis suggests and defends a form of Scanlonian contractualism, which offers the best model to represent and address issues of distributive justice in the case of AMR. It is shown that a principle of antibiotic use, which rules out the use of antibiotics for infections that do not pose a serious risk of irreversible harm, offers a convincing contractualist argument. The thesis examines the concerns for intergenerational justice that arise as a consequence of AMR and shows that contractualism is capable of addressing them. The thesis concludes by suggesting a new way of framing AMR as a specific type of policy challenge, which better captures its complexity and advocates a reduction of future dependency on antibiotics.

FOR MY PARENTS

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Abbreviations

AMR	Antimicrobial Resistance
APUA	Alliance for the Prudent Use of Antibiotics
CBA	Cost-Benefit Analysis
CDC	Centres for Disease Control and Prevention
ECDC	European Centre for Disease Prevention and Control
ESAC	European Surveillance of Antimicrobial Consumption
FDA	U.S. Food and Drug Administration
FDASIA	FDA Safety and Innovation Act
GAIN Act	Generating Antibiotic Incentives Now Act
HCAI	Health Care Associated Infection
HPA	Health Protection Agency (now Public Health England)
IMI	Innovative Medicines Initiative
MDR-TB	Multi-Drug-Resistant Tuberculosis
MRSA	Methicillin-Resistant *Staphylococcus Aureus*
PHE	Public Health England
RKI	Robert Koch Institute
WHO	World Health Organization
XDR-TB	Extensively-Drug-Resistant Tuberculosis

Chapter 1: Introduction and overview of the thesis

1.1 Introduction

On April 7th 2011, the World Health Day, the WHO announced that urgent actions were necessary if the effectiveness of antibiotics was to be ensured in the future. Failure to confront the rising problem of antimicrobial resistance (AMR)[1] would result in the loss of the 'miracle cures' offered by antibiotics, the WHO's Director-General Margaret Chan announced.[2] These worries have been reiterated by Sally Davies, the Chief Medical Officer for England, who described AMR as an "apocalyptical threat" in a speech to MPs.[3] In a recent publication, she and her colleagues warned of the possibility that health care system might no longer be able to treat bacterial diseases effectively in as little as twenty years.[4] The World Economic Forum has voiced similar concerns and in 2013 declared that AMR constitutes one of the main risks to human health.[5]

A mere 68 years earlier, in his introductory remarks to the laureate, Professor Theorell, the director of the Department of Biochemistry at the Nobel Institute, had compared the invention of antibiotics to a Grimm fairy tale. The laureate he addressed that night was Alexander Fleming, who was awarded the Nobel Prize for the discovery of Penicillin. Theorell told Fleming that his invention "cannot kill a mouse, though it can heal a man".[6] Today we know that while penicillin has cured many, its use was not quite as unproblematic as Theorell had thought. In fact, Fleming himself was already a vocal advocate of the careful use of antibiotics at the time - during the Nobel lecture he gave he warned: *"[T]here may be a danger [...] in underdosage [of penicillin]. It is not difficult to make microbes resistant to penicillin*

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1 The terms 'antibiotic resistance' and 'antimicrobial resistance' are often used interchangeably and I shall adopt this practice throughout the thesis. While antimicrobial resistance can also refer to resistance against other substances such as antivirals and antifungals, the focus will here solely be placed on resistance against antibiotics.

2 http://www.who.int/mediacentre/news/releases/2011/whd_20110406/en/index.html

3 Sample, I. (2013). Antibiotic-resistant diseases pose 'apocalyptic' threat, top expert says. The Guardian. London.

4 Davies, S. C. (2013). The Drugs Don't Work: a global threat. London, Penguin.

5 World Economic Forum (2013). Global Risks 2013 - Insight Report Eighth Edition. Geneva.p. 28

6 http://nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-speech.html

in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body."[7]

As it turned out, this property was not unique to penicillin but applies equally to all known antibiotics. In fact, recent research has shown, that bacteria became resistant to organisms with antibiotic properties, such as fungi, long before antibiotic drugs were even discovered and used.[8] The past years have seen an increased interest in the emergence of AMR and the associated risks, yet as much as the topic appears to be timely it is by no means a new problem. Before discussing the causes and ethical implications of AMR, it will be helpful to introduce a working definition of the term. There are numerous similar explanations of the phenomenon, however a particularly well-phrased and non-technical definition has been provided by Mossialos et al. It defines AMR as:

'[t]he ability of a bacterium to survive and even replicate during a course of antibiotic treatment with a specific antibiotic. Failure to resolve an infection with the first course of antibiotic treatment may mean that the infection may spread, may become more severe and may be more difficult to treat with the next antibiotic that is tried."[9]

Since their invention, and despite Fleming's early warning, the use of antibiotics has steadily increased. As a result, AMR quickly emerged, although initially its effects were largely offset by a constant stream of new and more potent antibiotics that entered the market, routinely replacing antibiotics against which bacteria had already become resistant.[10] While not a solution to the problem, this stream of new antibiotics was sufficient to stave off the consequences of AMR. If one drug failed, others took its place.[11] However, the replacement of ineffective drugs with new ones has not been sustainable. Since the 1980s, a growing number of multi-drug resistant

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7 Fleming, A. (1945). Penicillin. Nobel Lecture. Stockholm.

8 Martinez, J. L. (2008). "Antibiotics and Antibiotic Resistance Genes in Natural Environments." Science **321**: 365-367. ; D'Costa, V. M., C. E. King, et al. (2011). "Antibiotic resistance is ancient." Nature **477**: 457-461.

9 Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies. p. xiii

10 Moellering, R. C. (2012). "MRSA: The first half century." Journal of Antimicrobial Chemotherapy **67**(1): 4-11.

11 Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP. Chapter 6

and increasingly difficult to treat bacterial strains have emerged.[12] Available therapeutic options against these infections are often less effective, more expensive and carry a greater risk of side effects.[13] Especially the case of extensively and completely drug resistant (or "pan-resistant") strains of bacteria has prompted fears that the world is entering what some commentators refer to as a 'post-antibiotic age'.[14] Today, AMR already has grave implications for health care and causes significant morbidity and mortality. According to estimates from the European Centre of Disease Prevention and Control (ECDC), 25,000 deaths per year are caused by multi-drug resistant bacteria in the EU alone.[15] Drug resistance also puts enormous costs on health care systems.[16] While the total cost is difficult to assess and calculations vary according to the number of cost factors they take into account, the available data shows that AMR puts severe strains on health care financing. In the US for example, estimates for the total annual costs of treating drug-resistant strains of bacteria range between $21 billion - $34 billion.[17] To put this into perspective, annual funding for the American National Institutes of Health, the largest state-owned research network in the US, currently stands at $32 billion.[18]

The financial and human cost of AMR has sparked research efforts in a number of academic disciplines such as economics, politics and history and AMR is no longer considered to be a mere medical issue.[19] However, despite this growing concern over AMR, very little attention has so far been paid to the ethical issues, which arise

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[12] Witte, W. and M. Mielke (2003). "ß-Laktamasen mit breitem Wirkungsspektrum." Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz **46**(10): 881-890.

[13] European Centre for Disease Prevention and Control. (2010). "Antimicrobial Resistance - Factsheet for Experts." Retrieved 21.04., 2011, from http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/basic_facts/Pages/factsheet_experts.aspx.

[14] Brown, N. (1994). "Dawn of the post-antibiotic age?" BMJ **309**(6954): 615. Alanis, A. J. (2005). "Resistance to Antibiotics: Are We in the Post-Antibiotic Era?" Archives of Medical Research **36**: 687-705.

[15] European Medicines Agency & European Centre for Disease Prevention and Control (2009) Joint technical report: the bacterial challenge—time to react, available at: http://ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf.

[16] Kaufmann, S. (2007). The New Plagues: Pandemics and Poverty in a Globalized World. Frankfurt a.M., Haus Publishing.: 165

[17] Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).: 1115 Smith, R. and J. Coast (2013). "The true cost of antimicrobial resistance." BMJ **346**.

[18] Figures available from the NIH budget office, see http://officeofbudget.od.nih.gov/pdfs/FY12/Volume%201%20-%20Overview.pdf

[19] Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP. Roberts, J. A., Ed. (2006). The Economics of Infectious Disease. Oxford, OUP. Battin, M. P., L. P. Francis, et al. (2009). The Patient as Victim and Vector: Ethics and Infectious Disease. New York, Oxford University Press.

as a consequence of antimicrobial resistance.[20] This thesis will examine some of these problems in greater detail. In particular, the thesis will consider questions of distributive justice, which arise as a consequence of AMR.

1.2 Aims of the thesis and the question it tries to answer

This thesis has two primary aims. First, it will examine how and why AMR raises questions of distributive justice. Second, it develops a framework within which these questions of distributive justice can be structured and - hopefully - answered. A rough outline of the arguments in each chapter is presented below.

1. AMR is largely the result of excessive use of antibiotics. It is already a major health problem but due to current patterns of antibiotic use, the problem will likely become worse in the future. The emergence of AMR and the lack of research into new drugs is leading to a lack of effective antibiotics. Due to the diminishing effectiveness of antibiotics, we will be unable to treat many bacterial infections in the future. This effect cannot be overcome by merely eliminating the wasteful use of antibiotics. (Chapter 2)

2. We can therefore think of antibiotic effectiveness as a resource which we are currently depleting and which – due to the time it takes to develop new antibiotics – is non-renewable in the medium run. This resource depletion is similar to some other kinds of collective action problems but, due to the characteristics of AMR, creates a set of specific problems. (Chapter 3)

3. For our discussion, it is necessary to examine the ways that AMR is not just a distinctive distributive problem, but also presents a distinctive moral challenge. The thesis will examine different ways of framing and analysing the moral challenge that AMR poses.

4. A first potential answer to the question what makes AMR a moral problem is provided by consequentialism. Since AMR exacerbates the harm caused by bacterial infections and results in high additional health care costs (which in

[20] Notable exceptions include Millar, M. (2011). "Can antibiotic use be both just and sustainable... or only more or less so?" Journal of medical ethics **37**(3): 153-157. ; Battin, M. P., L. P. Francis, et al. (2009). The Patient as Victim and Vector: Ethics and Infectious Disease. New York, Oxford University Press.

turn create opportunity costs), consequentialism can explain the moral relevance of AMR in terms of its bad consequences.

5. However, upon closer inspection, it is unclear what results from this assessment, since consequentialism's approach of maximising expected benefits across persons struggles to accommodate for some of the factors of AMR. In particular, it struggles to assess the morally right course of action, because it cannot account for the uncertainty of future effects of AMR. (Chapter 4)

6. An alternative is to consider AMR as a morally wrongful harm to individuals, which requires not only that AMR has adverse effects, but also violates the victim's rights. We can show that AMR adversely affects people, although the cause of the harm may be diffuse and the size of harm to the individual quite small. However, it will be argued that even very small harms can be morally wrongful. The account of AMR as a morally wrongful harm also considers the possibility of framing the excess risk that drug resistance creates as harm, but it will be suggested that such an account is unconvincing, because it presupposes awareness of the risk factor. (Chapter 5)

7. To substantiate the claim that AMR constitutes a morally wrongful harm, it will be considered if AMR constitutes a rights violation. Building on Raz's interest theory of rights, it will be argued that people can be said to have a right to be protected from adverse health outcomes if an effective treatment could be administered. This supports the view that AMR is a morally wrongful harm but it is difficult to specify correlative duties that result from such a rights claim. Moreover, the rights account of AMR struggles to incorporate the fact that with increasing rates of AMR, the content of the right becomes gradually harder to provide to all rights holders. This diminishes the rights practical relevance over time. It will be outlined that a better way to deal with this conflict is to consider a contractualist approach. (Chapter 6)

8. The thesis suggests that a form of Scanlonian contractualism offers the best model to represent and address the moral issues of AMR and in particular the concerns of distributive justice, which arise in this context. Scanlon proposes

that to assess the justifiability of principles that determine the moral permissibility of an action, we must measure the strength of what he calls objections to permission and objections to prohibition respectively. Building on the work of Michael Millar, the thesis will explore in detail how such a principle can be applied to the case of AMR. The thesis shows that Millar's principle of antibiotic use, which rules out the use of antibiotics for infections that do not pose a serious risk of permanent irreversible harm, offers a convincing contractualist argument. It will be argued that contractualism could in principle justify more demanding principles to restrict the use of antibiotics for the preservation of antibiotic effectiveness. However, it will also be suggested that the positive externalities of antibiotics somewhat limit the scope for restricting antibiotic use and that existing principles also face a number of problems, including the inability to decide clearly, what risk we can legitimately expose people to. (Chapter 7)

9. Since AMR will also affect the lives of future generations, we will have to consider what our obligations to future people are. The consideration of future generations is complicated, by a number of factors including the time frame under consideration, the uncertainty about outcomes in the future and the overlap of generations, which makes it difficult to treat them as separate entities. The greatest challenge of an intergenerational account of justice, however, is Parfit's non-identity problem, which suggests that our actions cannot harm future persons, if their existence is contingent upon our previous actions. It will be shown that a contractualist account can sidestep this problem and assign equal moral value to the interest of future persons. (Chapter 8)

10. To better capture the complexities of AMR, the thesis will conclude by developing an account of AMR as a specific kind of policy challenge, a so-called super-wicked problem. On this account, AMR is a problem we cannot solve with technological means. Consequently, it will be suggested that obligations for future persons may therefore not only entail the preservation of antibiotic effectiveness, but also a duty to reduce the current dependence on antibiotics in health care. (Chapter 9)

1.3 The scope of discussion and the questions I do not try to answer

While the main focus of research into AMR continues to lie in the biomedical disciplines, the emergence of wide-spread resistance has sparked a significant number of research projects in other disciplines not traditionally concerned with AMR.[21] The challenge in addressing a question pertaining to AMR is thus twofold. On the one hand, the high degree of complexity and interconnectedness of the problem makes it difficult to delineate its boundaries. On the other hand, the increasing number of academic disciplines concerned with AMR, all with their own methodologies and theories, has led to a large number of possible approaches to the problem. Not all of them can and will be considered in this dissertation.

In focussing the question and thereby reducing its scope to one that allows for a comprehensive analysis and critical evaluation, some of the ethical concerns surrounding AMR will therefore have to be left out. In the case of this thesis, the most obvious topic to be excluded is a discussion of the use of antimicrobial drugs in farming. Given that a large proportion of the overall production of antibiotics is designated for the use in animals, this may seem like a rather glaring omission, especially since many commentators consider this use of antibiotics to be one of the major driving forces in the emergence of AMR. However, the focus of this thesis is on distributive justice and as such will be concerned with parties that can be seen to have moral claims to the use of scarce resources. I do not wish to claim that animals may not have rights, nor do I wish to suggest that such rights claims do not matter in the case of distributing antibiotics. However, a full discussion of these aspects would simply go beyond the scope of this thesis. On occasion, the aspect of using antibiotics in animal farming will be mentioned but this will primarily be for the sake of completeness, rather than as a substantial part of the overall argument.

Furthermore, the focus of this thesis is on the macro-level distribution of antibiotics. While the second chapter will consider prescription practices in different health care settings, the ethical analysis will mostly focus on fair resource distribution. AMR creates a host of additional problems in addition to those discussed in this thesis.

[21] Laximinarayan, R. (2006). Economic Issues related to antimicrobial resistance. The Economics of Infectious Disease. J. A. Roberts. Oxford, OUP. Laxminarayan, R. and D. L. Heymann (2012). "Challenges of drug resistance in the developing world." BMJ **344**. Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP.

Many of these pertain to the treatment of patients with extensively resistant bacterial infections, the management and containment of infection and the enforced social distancing of contagious patients.[22] In particular, the emergence of multi- and extensively drug-resistant tuberculosis (MDR-TB and XDR-TB respectively) has exacerbated the need to formulate ethical guidelines for the treatment of patients with dangerous infectious diseases in resource-poor settings.[23] The decision to forego a systematic analysis of these problems in the thesis stems from the fact that many of these ethical problems do not pertain to AMR specifically, but are a "by-product" of infectious disease control more generally. To be sure, as the example of MDR- and XDR-tuberculosis has shown all too clearly, the difficulties in treating drug-resistant infections greatly amplify the problem and create additional urgency. However, in this thesis, the focus will be placed on moral challenges that are not applicable to infectious diseases in general but apply specifically to the case of AMR.

Finally, the thesis does not claim to offer a comprehensive refutation of normative theories and their relevance to AMR. Since there is little previous research on issues of distributive justice in the context of AMR, much of the following discussion breaks new ground. As a result, the primary aim is to establish which theory of distributive justice offers the most coherent account of the challenges posed by AMR. However, the thesis does not amount to a conclusive rejection of the alternatives it considers.

1.4 Why the questions addressed in this thesis are important

AMR has been described as one of the major challenges to health care in the 21st century and presents policy-makers with a scenario of potentially *"apocalyptic dimensions."*[24] It should therefore come as no surprise that it is an area of concern for health policy makers. However, to date very little has been written about the specific ethical questions that AMR raises. As chapters 3 and 9 will explore in greater detail, there is no straightforward solution to the problem of AMR and many of the current

[22] Selgelid, M. J., A. R. McLean, et al. (2009). "Infectious Disease Ethics: Limiting Liberty in Contexts of Contagion." Journal of Bioethical Inquiry **6**(2): 149-152.

[23] See e.g. Coker, R. (2001). "Detention and mandatory treatment for tuberculosis patients in Russia." Lancet **358**: 349 - 350. Coleman C, J. E., Reis A, Selgelid M (2010). Guidance on ethics of tuberculosis prevention, care and control. Geneva, World Health Organization.

[24] Smith, R. and J. Coast (2013). "The true cost of antimicrobial resistance." BMJ **346**.

initiatives, such as the conservation of antibiotic effectiveness by promoting the 'prudent use' of antibiotics inevitably raise ethical questions that have so far not been addressed in detail. These questions seem to apply particularly to macro-level decision-making. Adjusting current use of antibiotics to socially optimal or cost-effective levels will require a conception of what such an optimal distribution could look like and - most importantly - whose interests we must take into consideration. This requires, for instance, that we make a decision whether or not we respect future people's claims to effective antibiotics and at what level of tolerable cost to currently living persons. An answer to these questions will help us to determine the criteria we should use to assess the fairness of the policy options we adopt. Moreover, it will also outline more clearly, what interests and moral claims are at stake as a result of the rapid progression of AMR.

1.5 Research approach and interdisciplinary work

A project on ethical aspects of infectious disease control and ethics will necessarily have to take an interdisciplinary research approach - without some biomedical background information, the ethical analysis has no subject matter to explore. At the same, time, medical expertise and knowledge of infectious diseases alone will be insufficient to establish normative claims about the fair use of effective antibiotics. The thesis seeks to bridge this gap by not only drawing on medical and public health literature, but also by making extensive use of the existing literature and discourses in bioethics and public health ethics.

Ethics is certainly not an academic discipline that is commonly associated with the study of AMR and it may therefore be necessary to locate more clearly the role that ethical analysis can play in this field. To be sure, AMR itself is a biomedical problem but, as will be discussed in greater detail in the following chapters, its origins lie at least partially in human behaviour. As a result, medical researchers are increasingly becoming aware of the need to address AMR in cooperation with different academic disciplines and non-academic organisations and interest groups.[25] Such cooperations include public engagement and information campaigns, the study of financial

[25] Larson, E. L., L. Saiman, et al. (2005). "Perspectives on antimicrobial resistance: Establishing an interdisciplinary research approach." American Journal of Infection Control **33**(7): 410-418.

incentives to reduce rates of infection in hospital wards, or qualitative studies of prescription behaviour among general practitioners.[26] But, as Larson et al have pointed out, the current state of interdisciplinary research in the field of AMR suffers from a problem, namely the question, how one can even know which research areas may be beneficial, as long as the problem itself is only loosely defined.[27]

The thesis will not be able to provide a general answer to this problem but it will show that ethical analysis of AMR is an important aspect that has so far not received sufficient attention. Researching the thesis revealed that this view is not universally shared. I encountered a number of practitioners and policy makers who were kind enough to share their expertise with me. However, some of them were rather sceptical of the role that ethics could potentially play in informing health policy. This scepticism appeared to be founded in a common misunderstanding of the function of ethical discourse, which Jonathan Glover has identified precisely:

Many people think that [...] arguing about the merits of general moral principles is either superfluous of impossible. This is often because they make one of two false assumptions. One of these assumptions is that there is one set of 'true' moral beliefs, which no humane, rational and informed person could reject once he understood them. This makes moral argument redundant. The other assumption is that moral beliefs are so subjective that no useful discussion can take place between those who differ [...]. This makes moral argument impossible.[28]

Particularly the second concern mentioned by Glover is fairly pervasive. A worry that was expressed repeatedly in conversations with health care professionals was that an ethical analysis of AMR would merely amount to the expression of one person's opinion. While it will hardly come as a surprise that the thesis in its present form reflects the author's views, this fact need not pose any real limitation to the soundness of the argument. Ethical discourse, while often pluralistic, has at its disposal a number of methods which allow for an appraisal of competing normative arguments that venture beyond the 'mere expression of opinion'.

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[26] Björkman, I., M. Erntell, et al. (2011). "Infectious disease management in primary care: perceptions of GPs." BMC Family Practice **12**(1).

[27] Larson, E. L., L. Saiman, et al. (2005). "Perspectives on antimicrobial resistance: Establishing an interdisciplinary research approach." American Journal of Infection Control **33**(7): 410-418.

[28] Glover, J. (1977). Causing Death and Saving Lives. New York, Penguin. p. 21

These methods include for example:

- scrutinising arguments for inconsistencies or 'blurred concepts'
- exposing logical inadequacies, e.g. by showing that certain premises that are assumed to be generally applicable do in fact not hold
- pointing out undesired consequences that a moral theory might inevitably entail.[29]

As the thesis will hopefully show, the current discussion surrounding AMR can greatly benefit from more normative analysis, particularly with regard to the fair distribution of scarce resources.

1.6 Research methods

Given the complexity of the subject matter and the number of disciplines on which the thesis draws, the research process involved the consultation of a wide range of sources. The main components are summarised below.

Literature Review

As an indication for the availability of literature on the subject matter, a simple literature review on the medical research database *PubMed* received 95 hits for the subjects of "antibiotic resistance" and "ethics".[30] Many of the results are relevant to the project and - where publicly available - have been consulted throughout the research process. However, given the interdisciplinary nature of the problem which this thesis seeks to explore, it was important to sample a broad range of literature. To obtain it, the following methods were employed:

Library catalogues

University library catalogues at UCL, as well as at the universities of Berlin, Zurich, Hamburg and Copenhagen were consulted. Furthermore, the subject-specific library

[29] Ibid. pp. 24-25

[30] Search via http://www.ncbi.nlm.nih.gov/pubmed (accessed 12.01.2012) Search terms used: ("drug resistance, microbial"[MeSH Terms] OR ("drug"[All Fields] AND "resistance"[All Fields] AND "microbial"[All Fields]) OR "microbial drug resistance"[All Fields] OR ("antibiotic"[All Fields] AND "resistance"[All Fields]) OR "antibiotic resistance"[All Fields]) AND ("ethics"[Subheading] OR "ethics"[All Fields] OR "ethics"[MeSH Terms])

at the Wellcome Trust in London was used extensively, as well as the British Library, and other collegiate libraries within the University of London.

Snowballing

In many instances, further literature was found via references in the works that were initially consulted. This proved particularly useful for less widely known government studies that were not generally listed in library catalogues, but also became relevant for the inclusion of literature that discussed related problems, such as the ethical dilemmas created by climate change and global warming or the use of management theory in chapter 9.

Consultation of Guidelines

Many national and international health institutions have published guidelines, policy briefings or workshop summaries on the issue of AMR, often including national or international statistics of prevalence and incidence of infections that were caused by bacterial strains resistant to antibiotics. These institutions include the World Health Organisation (WHO), the European Centre for Disease Prevention and Control (ECDC), the UK's Department of Health as well as Public Health England (PHE), the German and South African Ministry of Health, the South African National Institute for Communicable Diseases (NICD), the Robert-Koch-Institute (RKI), and others.

Expert Opinion

Due to the collaboration between UCL and PHE, the writing of the thesis and the identification of key problems benefitted enormously from discussions with PHE staff, as well as policy makers in the Department of Health. These discussions ranged from basic questions about biochemical mechanisms of AMR to the participation in PHE specialist board meetings and the presentation of specific ideas to policy makers. PHE staff also made available statistics and surveillance data, and explained the mechanisms of risk assessment and calculation of economic forecasts for modelling the costs of AMR.

Furthermore, academic experts in the fields of public health, bioethics, infectious disease control and medicine contributed to this thesis, either through informal

conversations or by providing feedback on drafts or particular ideas. Lastly, many of the international institutions mentioned in the previous paragraph were contacted directly and in some instances allowed me to visit them for more in-depth conversations. The National Institute for Communicable Diseases in Johannesburg welcomed me for a three-day visit in December 2011, where I had the chance to meet with a number of tuberculosis experts, and I was able to attend a number of meetings and workshops at the WHO in Copenhagen, which helped to better understand the perspective of international organisations.

1.7 Main conclusions of the thesis and its contribution to the field

The main conclusion of this thesis is that moral duties to preserve antibiotic effectiveness will require that current consumption is reduced, even if this means that people will have to forego some health benefits. The thesis develops an account of contractualist ethics, on which the restriction of antibiotics is permissible wherever those who are adversely affected by such restrictions could not reasonably reject such restrictions. It is shown that the extent of such restrictions is partly dictated by contractualism but will equally depend on the consideration of medical and epidemiological facts, since the use of antibiotics also generates positive externalities for infection control, which reduces the future burden of contagious diseases.

The argument developed in this thesis is shown to be consistent with considerations of distributive justice within and between generations. Its conclusions build on and expand existing research and the thesis offers one of the first detailed examinations of distributive justice in the case of AMR. The thesis challenges the frequently made assumption that AMR represents a problem, which can be treated as analogous to other policy challenges and outlines the characteristics that separate AMR from comparable cases. Moreover, it outlines the normative importance of AMR and develops a novel account of framing AMR as a special policy challenge, a so-called super-wicked problem.

Chapter 2: Antibiotics, their use, and the emergence of drug resistance

Chapter 1 gave an overview of the research questions and the methodological approach of the thesis. The second chapter pursues three goals. First, it will outline the basic functioning of antibiotics and the reasons for the emergence of bacterial resistance to these drugs. Second, it will examine more closely, how and why the present use of antibiotics is unsustainable and what policy efforts have so far been undertaken to curb the spread of AMR. Third, the factors that motivate overuse of antibiotics in different settings and by different groups of stakeholders will be discussed. We shall begin, however, with a brief overview and taxonomy of bacteria.

2.1 Bacteria - a brief microbiological overview and taxonomy

Since antibiotics are drugs which are only effective against bacteria, it is useful to start with a brief discussion of their targets. Bacteria are simple but highly adaptive and resilient organisms. Unlike human tissue cells which are eukaryotic, bacteria are prokaryotes, meaning that they do not have a nucleus.[31] In bacteria, the DNA thus lies in the cytoplasm, usually in circular form.[32] Circular DNA is more prone to be replicated imprecisely, increasing the chance of random mutation. Many of these mutations will not be able to survive but some, by sheer chance, can display new biological features, which may for example render them immune to a certain type of antibiotic. We will return to these properties later on in this chapter. Generally speaking, bacteria have three defining structural features[33]:

(1) A cell membrane (and often a cell wall)
(2) Internal cytoplasm, which contains the DNA and ribosomes (the site for protein synthesis in both, prokaryotic and eukaryotic cells)
(3) External structures, which will vary according to the type of bacteria, including flagella and pilli on the bacterium's surface.

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[31] Black, J. G. (2005). Microbiology: Principles and Explorations. Arlington, VA, Wiley & Sons. p. 77
[32] ibid.
[33] ibid. p. 80

Bacteria exist in a multitude of shapes, such as spheres, spirals or curves. The name of a bacterium will usually include a reference to its shape. *Staphylococci* for example have a spherical structure, which is referred to as *coccus*.[34] In the case of *Staphylococci*, the first part of the name refers to the arrangement in which they can be found ('*staphylo*' denotes the grape-like clusters of bacteria).

Bacteria are classed in many different ways - one standard text book on microbiology lists a total of 25 common classification criteria.[35] These criteria range from simple morphology to the reaction to specific chemical tests that will lead to the partial breakdown of parts of the cell and/or staining to distinguish between different types of bacteria. The most widely used method (which will also be relevant to the following discussion) is the Gram stain test, named after the microbiologist Hans-Christian Gram.[36] Gram discovered that in a three-step staining process, where crystal violet and iodine are added to the cell, before decolourization with ethanol is performed, some bacterial cells retain the stain while others don't.[37] Based on this test, the most common taxonomy for bacteria distinguishes between Gram-positive cells (which will retain crystal violet even after decolourization), and Gram-negative cells (which will not retain the stain). A smaller group of bacteria is not reactive to the Gram-Stain test at all. Since Gram-positive and Gram-negative cells display very different properties and react differently to antibiotics, the distinction will be relevant throughout the following chapters.

While ten years ago, Gram-positive bacteria such as *S. aureus* were the primary concern of infectious disease specialists, their attention has recently shifted to newly emerging threats posed by multidrug-resistant Gram-negative bacteria such as *K. pneumoniae*. These bacteria develop resistance more readily and often exchange mobile genes via plasmids that are transferred between cells.[38] Of particular concern are those bacteria which have developed resistance to carbapenems, one of the most

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34 ibid. p. 78

35 ibid. p. 252

36 Ingraham, J. (2010). March of the Microbes: Sighting the Unseen. Cambridge, MA, The Belknap Press of Harvard University. p. 9

37 Black, J. G. (2005). Microbiology: Principles and Explorations. Arlington, VA, Wiley & Sons. p. 68-69

38 Kumarasamy, K. K., M. A. Toleman, et al. (2010). "Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study." The Lancet Infectious Diseases **10**(9): 597-602. p. 597

effective classes of intravenous antibiotics against Gram-negative bacteria that clinicians currently have at their disposal.[39] While still rare, the number of carbapenem-resistant bacterial infections registered in UK hospitals has increased significantly over the past decade - in 2004, there were a mere five registered cases, while seven years later, this figure had already risen to more than 300.[40] This development is all the more worrying because, as will be discussed in greater detail below, there is a significant lack of research into drugs that specifically target Gram-negative bacteria.[41]

2.2 Antibiotics

Antibiotics are a special group of chemotherapeutic agents. Even though in everyday language 'chemotherapy' is commonly used as synonymous with cancer treatment, the term actually describes all forms of therapy in which a chemical rids the body of malignant cells.[42] The literal translation of *antibiosis* is 'against life' and antibiotic drugs are chemical substances, which specifically attack and kill pathogenic bacteria. What makes antibiotics so special is their property of selective toxicity. This means that they are toxic enough to destroy the pathogenic prokaryotic cells but not so toxic as to attack the eukaryotic tissue cells of the patient. Unlike synthetic antibacterial agents, such as sulphonamides, antibiotics are mostly biosynthesized and are usually the metabolic product of particular types of fungi or other bacteria.[43] Different antibiotics have different mechanisms of action but crucially, antibiotics either interfere with bacterial growth processes (bacteriostatic antibiotics), or kill off bacteria (bactericidal antibiotics).[44] They commonly achieve their purpose by employing one of three mechanisms to attack their target:

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[39] Department of Health & Health Protection Agency (2011). Advice on Carbapenemase Producers: Recognition, infection control and treatment. (ARHAI). London, Department of Health.

[40] Owen, J. (2011). Antibiotics losing the fight against deadly bacteria. The Independent. London.

[41] Kumarasamy, K. K., M. A. Toleman, et al. (2010). "Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study." The Lancet Infectious Diseases **10**(9): 597-602.

[42] Black, J. G. (2005). Microbiology: Principles and Explorations. Arlington, VA, Wiley & Sons. p. 353

[43] Mascaretti, O. A. (2003). Bacteria versus antibacterial agenst: an integrated approach. Washington DC, ASM Press.

[44] ibid. p. 97

1) Inhibition of cell wall synthesis - particular antibiotics, such as β-lactams weaken the bacterial cell wall, which results in the breakdown of the cell (also known as lysis)
2) Inhibition of protein synthesis - by attacking prokaryotic ribosomes, certain antibiotics render bacterial cells incapable of synthesizing proteins that are needed for the cell's survival.
3) Disruption of the bacterial cell wall - some bactericidal antibiotics specifically target molecules in bacterial cell walls and destroy these, which causes lysis.[45]

Antibiotics are often classified in terms of the order in which they should be used for specific infections. First-line drugs are those, which initially proved to be effective, while second and third-line drugs are subsequent generations of antibiotics that are effective against resistant or multi-resistant strains of bacteria. What will be classed as a first-, second-, and third-line drug will depend on the respective pathogen.

2.3 Discovery and initial use of antibiotics

The first antibiotic was discovered in the 1920s by Alexander Fleming, who named his invention penicillin. Due to its success story it remains the best-known antibiotic to date.[46] However, it was not until the 1940s that antibiotics were used more widely as a standard therapeutic measure against infections, and dramatically changed the role and perception of infections as a disease burden in modern society. Initially reserved for use in the armed forces during WWII, penicillin was made available to the wider public after the end of the war and became widely used. This was due to at least two reasons. Not only could penicillin cure a wide range of infections and diseases that were previously untreatable, it also did so at breathtaking speed, with significant improvements in patients' health being observable in the space of hours. In one of the first cases in the United States, where penicillin was used to treat septicaemia (blood poisoning), doctors were astonished that the patient not only survived but also fully recovered from a critical condition in less than 24 hours.[47] It is therefore not surprising that in the decades following their discovery, antibiotics

[45] Bauman, R. W. (2004). Microbiology: International Edition. San Francisco, Pearson Benjamin Cummings. Chapter 10
[46] Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP.
[47] Gualde, N. (2006). Resistance: The human struggle against infection. New York, Dana Press. p. 83

were hailed as 'miracle drugs'.[48] To some extent, this belief in a medical 'miracle' went far beyond curing bacterial infections. It has been suggested that penicillin transformed the way in which we view medication and changed the expectations patients and relatives place in drugs.[49] After all, if a single pill can cure deadly infections, then why not other conditions such as cancer, coronary heart disease or stroke? As is all too clear today, modern medicine has not been able to deliver on such a promise. Miracle cures are rare and AMR shows that even where we believe that we may have found them, the medical triumph is often temporary. Nevertheless, in the early days of antibiotic use, confidence in their continued effectiveness was such that in 1967 the US surgeon general was credited with claiming that that *'[t]he time has come to close the book on infectious diseases. We have basically wiped out infection in the United States'*.[50]

In the decades following their initial discovery, a broad range of antibiotics were identified and put into production. By 1960, more than a dozen different classes of antimicrobial drugs had been commercialised.[51] Some of them were very similar to already existing drugs, yet a few of them addressed one of the shortcomings of penicillin. Despite its immense curative power, penicillin is only effective against a comparatively small number of bacteria and crucially does not work on most Gram-negative bacteria. The answer to this limitation came in the form of broad-spectrum antibiotics, which - unlike narrow-spectrum drugs like penicillin - attack a much wider range of bacteria, including both Gram-positive and Gram-negative pathogens. One enormous advantage of these drugs is that in cases where immediate treatment is needed or lab cultures cannot be taken and analysed, broad-spectrum antibiotics massively improve the chance that the patient receives effective treatment in time. However, this increased effectiveness comes at a price. For example, the higher toxicity of broad-spectrum antibiotics increases the risk of superinfections, due to a

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48 Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP.

49 Gawande, A. (2009). The Checklist Manifesto. London, Profile Books Ltd. pp. 18-19

50 Upshur, R. (2008). "Ethics and infectious disease." Bulletin of the Whorld Health Organization **86**. It is noteworthy that while this quote has become well-known and is frequently cited, it is not clear whether Surgeon General Stewart actually ever used those exact words. However, while Stewart himself does not recall saying them, he agrees that it is something he could have said given the spirit of the time and his (ultimately mistaken) belief that infectious diseases could be overcome.

51 Högberg, L. D., A. Heddini, et al. (2010). "The global need for effective antibiotics: challenges and recent advances." Trends in Pharmacological Sciences **31**(11): 509-515.

reduction in microbial antagonisms.[52] Such a reduction occurs when antibiotics diminish the overall load of microbes, but leave certain types unaffected. Because microbes are usually in competition for nutrients, their co-existence limits the extent to which they can spread. If an antibiotic drastically reduces the numbers of multiple types of microbes, the remaining ones can multiply more quickly, which can result in secondary infections.[53]

2.4 Emergence and mechanisms of AMR

Despite the fairly recent public interest in AMR, the phenomenon itself is not new.[54] In many ways, it is therefore surprising that it was only in 2011 that the WHO made AMR one of its major policy issues.[55] However, it would be untrue to claim that there was no awareness of the problem before. The U.S. Office of Technology Assessment, for example, published a report in 1995 entitled *Impacts of Antibiotic-Resistant Bacteria*, in which it discussed not only difficulties in treating infections caused by bacteria that were resistant against first-line antibiotics but also raised the problem of completely drug-resistant strains of bacteria.[56] While the report stated that untreatable infections were rare at the time of writing, it warned that the number of such infections was rapidly increasing and that there were a significant number of bacterial strains, which displayed resistances against all but one antibiotic. The report concluded that it was therefore likely that total drug-resistance for these types of bacteria was merely a matter of time.[57]

AMR can occur in different ways, but the most important distinction is between intrinsic and acquired resistance.[58] The former refers to natural defence mechanisms a bacterial cell may have. Gram-positive bacteria for example have a thicker cell wall, which makes it harder for certain antibiotics to penetrate the cell. Intrinsic

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[52] Bauman, R. W. (2004). Microbiology: International Edition. San Francisco, Pearson Benjamin Cummings. p. 297

[53] ibid.

[54] Martinez, J. L. (2008). "Antibiotics and Antibiotic Resistance Genes in Natural Environments." Science **321**: 365-367.

[55] The WHO did publish extensive guidelines for health care professionals before, but did not place a particular emphasis on engaging and informing the public about the risks of AMR

[56] Office of Technology Assessment (1995). Impacts of Antibiotic-Resistant Bacteria. Washington D.C., U.S. Government Printing Office.

[57] ibid. p. 1

[58] Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies.

resistance is usually limited to a few antibiotics and often only to a single type of action mechanism. Acquired resistance is the result of genetic mutation. As outlined before, due to their simple cell structure, their high rate of cell division and the lack of a nucleus, prokaryotic cells are more frequently subjected to naturally occurring mutation. Consequently, resistance against a particular antibiotic may simply be a matter of chance. The development of AMR as a result of mutation or gene acquisition is unavoidable.[59] However, the speed with which this will occur is greatly influenced by man-made factors, such as the overall use of antibiotics, adherence to therapy protocols and the circumstances in which antibiotics are prescribed. Low dosages of an otherwise effective antibiotic or incomplete treatment cycles for example may render bacteria resistant against the same drug in the future. In a recent joint statement, the U.S. Centres of Disease Prevention and Control (CDC) together with a number of national health organisations succinctly highlighted the dilemma that is inherent in any antimicrobial usage policy:

"*The more we use antibiotics, the more we contribute to the pool of antibiotic-resistant microbes. The development of resistance is an inevitable by-product of exposure to antibiotics. All antibiotic use, whether warranted or not, places selection pressure on bacteria, and some organisms that possess genetic mutations will survive antibiotic treatment."*[60]

Fundamentally, there are five common mechanisms of AMR, which prokaryotic cells can develop.[61] These are:

(1) **Production of enzymes that destroy antibiotics**. The most common enzymes are ß-lactamases, which destroy a molecular structure of ß-lactam antibiotics such as penicillin, thereby rendering the antibiotic inactive.
(2) **Slowing down or preventing the antibiotic from entering the cell**. This is usually the result of changes in electrical charges on the cell surface and

[59] Davies, J. (1997). Origins, acquisition and dissemination of antibiotic resistance determinants. Antibiotic resistance: origins, evolution, selection and spread. S. B. Levy. Chichester, Wiley**:** 15-35.
[60] CDDEP (2012). Joint Statement on Antibiotic Resistance with the U.S. Centers for Disease Control and Prevention (CDC) and 25 National Health Organizations. Washington, The Center for Disease Dynamics Economics and Policy.
[61] Bauman, R. W. (2004). Microbiology: International Edition. San Francisco, Pearson Benjamin Cummings. pp. 302-303

confers resistance against broad-spectrum antibiotics such as tetracycline, and narrow-spectrum antibiotics such as penicillin

(3) **Altering the receptor to which the antibiotic binds**. This mechanism occurs mainly in pathogens that become resistant to antibiotics that interfere with protein translation in prokaryotic cells.

(4) **Changing the cell metabolism**, for example by stopping to produce certain enzymes which an antibiotic would normally attack.

(5) **Developing transport mechanisms** that pump antibiotics out of the prokaryotic cell before they can act on their target site.[62]

While AMR is a long-standing phenomenon, increased use of antimicrobials in health care settings has exacerbated the problem dramatically.[63] A good example is the progressive resistance of staphylococci infections. In the case of *staphylococcus aureus*, resistance to the antibiotic methicillin was first discovered in the 1960s.[64] However, since then, the prevalence of methicillin resistance amongst *S. aureus* strains has increased dramatically. One study found that between 1975 and 1991 the prevalence of MRSA among nosocomial *staphylococcus* infections in the US increased from 2.1% to 35%.[65] Today, *S. aureus* is the most common cause of bloodstream infections in the United States, Canada and Latin America, with a significant proportion of the infections displaying drug-resistance.[66] In Europe MRSA is also one of the most prevalent drug-resistant pathogen that causes blood stream infections.[67]

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[62] This list merely provides a very rough overview of resistance mechanisms - the underlying biochemical processes are highly complex, and their discussion would venture significantly beyond the scope of this thesis.

[63] Davies, J. (1997). Origins, acquisition and dissemination of antibiotic resistance determinants. Antibiotic resistance: origins, evolution, selection and spread. S. B. Levy. Chichester, Wiley**:** 15-35.

[64] Diekema, D. J., M. A. Pfaller, et al. (2001). "Survey of Infections Due to Staphylococcus Species: Frequency of Occurrence and Antimicrobial Susceptibility of Isolates Collected in The United States, Canada, Latin America, Europe and the Western Pacific Region for the SENTRY Antimicrobial Surveillance Program, 1997-1999." Clinical Infectious Disease **32**(Supplement 2).p. S115, Moellering, R. C. (2012). "MRSA: The first half century." Journal of Antimicrobial Chemotherapy **67**(1): 4-11.

[65] Panlilio, A., D. Culver, et al. (1992). "Methicillin-resistant Staphylococcus aureus in U.S. hopsitals 1975-1991." Infection Control and Hospital Epidemiology **13**(10): 582-586.

[66] Diekema, D. J., M. A. Pfaller, et al. (2001). "Survey of Infections Due to Staphylococcus Species: Frequency of Occurrence and Antimicrobial Susceptibility of Isolates Collected in The United States, Canada, Latin America, Europe and the Western Pacific Region for the SENTRY Antimicrobial Surveillance Program, 1997-1999." Clinical Infectious Disease **32**(Supplement 2).

[67] ECDC and EMEA (2009). The bacterial challenge: time to react. Stockholm, ECDC. p. vii

2.5 Causes of AMR

AMR has been described as a prime example of Darwin's theory of evolution.[68] While antibiotics have greatly helped in reducing morbidity and mortality from bacterial infections in the last 60 years, their use has inadvertently led to the natural selection of resistant strains, which are stronger, more virulent, and in some cases almost untreatable. In addition to random genetic mutation, most studies of AMR identify at least three reasons why drug-resistance has become more pronounced as a problem in recent years. These are overprescription, a lack of research into new drugs, and the widespread use of antibiotics in agriculture and cattle farming.[69]

2.5.1 Overprescription

Overprescription and 'empirical therapy' (also known as 'calculated therapy') have been identified as one of the key problems in the rise of AMR. 'Empirical therapy' refers to the practice of prescribing antibiotics without obtaining a sample for laboratory testing and precise identification of the bacterial strain that caused the infection.[70] This is not merely a matter of cost-saving or ignorance. Sometimes, there may not be enough time for such testing, or the wait for confirmation of lab results would be painful for the patient and place him at unnecessary risk. The result of empirical therapy, however, is that antibiotics will sometimes be used on patients for whom they are ineffective or provide only very limited benefits. In the case of *otitis media* (middle ear infection) it is estimated that only thirty to fifty percent of patients will benefit from antibiotic therapy.[71] However, since most patients are children, doctors will usually refrain from puncturing the eardrum to obtain a sample of pus, which can be analysed. The immediate prescription of broad-spectrum antibiotics thus continues to be the most common therapy for middle ear infections.[72] Yet, it remains unclear, in which cases empirical therapy is in the interest of the patient. In the case of *S. aureus* bacteraemia for example, recent findings suggest that calculated

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[68] Levy, S. B. (1997). Antibiotic resistance: an ecological imbalance. Antibiotic resistance: origins, evolution, selection and spread. S. B. Levy. Chichetser, Wiley**:** 1-14.

[69] Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies.

[70] World Health Organization (2001). WHO Model Prescribing Information: Drugs used in Bacterial Infections. Geneva. See Introduction

[71] Office of Technology Assessment (1995). Impacts of Antibiotic-Resistant Bacteria. Washington D.C., U.S. Government Printing Office. p. 4

[72] ibid. Venekamp, R. P., S. Sanders, et al. (2013). Antibiotics for acute otitis media in children. Cochrane Database of Systematic Reviews 2013, The Cochrane Collaboration. Issue 1. Art. No.: CD000219

therapy is not in fact associated with lower mortality.[73] Judging whether or not non-laboratory-confirmed antibiotic therapy is in the interest of the patient is thus a difficult question to assess. While empirical therapy carries the risk of administering an ineffective antibiotic treatment, thereby also increasing the chances of creating AMR, it may also aid in alleviating painful symptoms quicker than would be possible if microbiological tests were carried out in advance. Furthermore, empirical therapy may decrease the chance of serious complications, as the therapy is provided more quickly. Physicians may thus be faced with a trade-off between short term and long-term costs and benefits of prescribing antibiotics. In this trade-off lie many of the ethical dilemmas that the following chapters will examine in detail.

To some extent, antibiotic overprescribing is measurable. Institutions such as ESAC, the *European Surveillance of Antimicrobial Consumption*, record the number of prescribed daily doses across 27 European countries.[74] These display stark differences across European countries - with regard to both volume of consumption and the types of antibiotics that are being prescribed. In light of the fact that health outcomes will often not be better in countries that prescribe particularly large amounts of antibiotics, it has been suggested that the difference in consumption can be explained by excess prescriptions. However, this is difficult to prove conclusively, as higher levels of antibiotic prescribing may also simply indicate a higher burden of infectious diseases in a country.[75] It must also be noted that the degree to which people adhere to treatment protocols may vary between countries, and that a comparison of national statistics on antibiotic *prescription* is thus not an accurate estimate of actual rates of antibiotic *consumption*. Grigoryan et al found for example that in a cross-European study on attitudes and beliefs about antibiotics, some countries (among them the UK) displayed lower levels of knowledge about antibiotics and their mechanism of action than others such as Sweden, Belgium or the Netherlands.[76]

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[73] Schweizer, M., J. Furuno, et al. (2012). "Empiric Antibiotic Therapy for Staphylococcus aureus Bacteremia May Not Reduce In-Hospital Mortality: A Retrospective Cohort Study." PLoS one **5**(7).

[74] see European Centre for Disease Prevention and Control. (2011). "European Surveillance of Antimicrobial Consumption." Retrieved 25.07., 2011, from http://app.esac.ua.ac.be/public/.

[75] Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies. pp. 39ff

[76] Grigoryan, L., J. G. M. Burgerhof, et al. (2007). "Attitudes, beliefs and knowledge concerning antibiotic use and self-medication: a comparative European study." Pharmacoepidemiology and Drug Safety **16**: 1234-1243.

At the other end of the spectrum, lack of access to antibiotics is a serious problem in many developing countries.[77] Where treatment is not affordable or access to health care resources is restricted, people are more likely to self-medicate, buy counterfeit drugs through unofficial channels or fail to complete treatment cycles. [78] In all these cases, bacteria are subjected to an insufficient dose of antibiotics, thereby increasing the chance of AMR among the surviving pathogens. In many cases, failure to conform with treatment instructions is thus not due to the patient, but results from systemic failure in the health care sector. This problem will be discussed in greater detail in chapter 9 of the thesis.

2.5.2 Lack of research into new drugs

For a period of around four decades, following the discovery of penicillin, pharmaceutical companies produced a steady flow of new antibiotics.[79] New developments did not only include drugs that were similar to already existing ones, but also products that used novel mechanisms to attack bacteria. This helped to circumvent some of the pharmacological problems that had arisen as a consequence of emerging AMR. However, since the 1970s, development of new antibiotics has slowed down considerably and the available stocks of effective antibiotics are currently being depleted, while little research effort is geared towards the development of new antibiotics.[80] Despite the significant levels of mortality and morbidity associated with AMR, in 2004 a mere 1.6% of the research budget of the world's 15 largest pharmaceuticals was spent on the development of new antibiotics.[81] In particular, there is a lack of research into new antibiotics specifically targeted at Gram-negative bacteria. A survey of the pharmaceutical industry from 2013 reported that presently no drugs with a novel action mechanism against Gram-negative bacteria are in advanced stages of clinical development.[82] This is particularly problematic, as Gram-negative bacteria account for a majority of

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77 WHO (2001). Global Strategy for Containment of Antimicrobial Resistance. Geneva, World Health Organization.

78 Gualde, N. (2006). Resistance: The human struggle against infection. New York, Dana Press. p. 86

79 ECDC and EMEA (2009). The bacterial challenge: time to react. Stockholm, ECDC. p. 2

80 Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

81 ibid.

82 Boucher, H. W., G. H. Talbot, et al. (2013). "10 × '20 Progress—Development of New Drugs Active Against Gram-Negative Bacilli: An Update From the Infectious Diseases Society of America." Clinical Infectious Diseases **56**(12): 1685-1694., p.

infections, and some strains such as *Klebsiellae* have already become a cause of concern for physicians due to their extensive drug-resistance.[83]

There are a number of causes for the decrease in research activity for the development of new antimicrobial drugs, but they mostly appear to concern the expected rate of return on investment.[84]

The initially very rapid development of new antimicrobials over the past decade was partly explicable by the relatively low level of basic research that was needed to get a new antimicrobial drug into the market.[85] However, antimicrobial drugs have been developed in what Christopher Walsh described as "a target-poor environment".[86] Many classes of drugs work on similar action mechanisms and with increasing levels of AMR, the discovery of completely new target sites is becoming more and more important. This, however, requires extensive research and investment, long before it is clear if the development costs can be recovered. It is estimated that for the development of a new compound that can act as an antibacterial agent, only one out of twenty candidates will lead to a new drug.[87] Once a new antibiotic has been developed, its profitability is limited by the short length of prescription and the relatively low volume of sales, which is further reduced, if there is pressure to preserve the drug's effectiveness.[88] Such a pressure will primarily exist for new second- and third-line drugs, which are often therapies of last resort and are consequently prescribed sparingly. Given the high cost and long time span it takes to develop a new antimicrobial drug, pharmaceutical manufacturers that seek to maximise profits currently have few incentives to conduct research into new antibiotics.[89]

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[83] Bauman, R. W. (2004). Microbiology: International Edition. San Francisco, Pearson Benjamin Cummings. p. 571ff

[84] Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

[85] Levy, S. B. (2002). The Antibiotic Paradox: How the Misuse of Antibiotics destroys their curative powers. Cambridge, MA, Perseus Publishing.

[86] Walsh, C. (2003). "Where will new antibiotics come from?" Nature Reviews Microbiology **1**(1): 65-70. p. 67

[87] Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies. p. 71-72

[88] Royal Society (2008). Innovative Mechanisms for Tackling Antibiotic Resistance. London. p. 15

[89] Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

2.5.3 Antibiotic use in agriculture

Early antibiotics like penicillin were intended to be used on humans only.[90] However, over the last five decades antibiotics have also increasingly been used on animals and even plants in order to combat bacterial infections.[91] Until a ban to use antibiotics without veterinary indication in cattle farming was passed in the European Union in 2006, around 50 percent of the annual production of antimicrobials in the EU was designated for animal use.[92] The use of antibiotics on farm animals is not primarily aimed at treating acute infections. Instead, antibiotics are used as growth enhancers, and for infection prophylaxis.[93] The widespread use of antibiotics in animals may have consequences for bacterial infections in humans. For example, there is an observable correlation between the prevalence of vancomycin-resistance in humans and the use of avoparcin as a growth promoter in farming animals. Countries in which avoparcin was routinely given to livestock also displayed significantly higher rates of resistance to vancomycin, which like avoparcin is a glycopeptide antibiotic and thus very similar in structure.[94] It is thus widely accepted that the emergence of vancomycin-resistance is at least partially attributable to the widespread use of avoparcin in farm animals.[95] Animal farming is, however, not the only area of food production that utilises antibiotics on a large scale. In the early 1990s, an estimated ten percent of the US annual production of antimicrobials were used on neither persons nor farm animals, but designated for use on organisms such as honeybees and fruit trees.[96]

The use of antibiotics in animals and on plants is problematic, as low dosages of an antibiotic consumed over prolonged periods of time facilitate an optimal selection for drug-resistant strains.[97] There are a number of reasons why this ought to be of

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90 Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP.

91 Levy, S. B. (1997). Antibiotic resistance: an ecological imbalance. Antibiotic resistance: origins, evolution, selection and spread. S. B. Levy. Chichetser, Wiley**:** 1-14.

92 World Health Organization (2002). Use of Antimicrobials Outside Human Medicine and Resultant Antimicrobial Resistance in Humans Fact Sheet 268. Geneva.

93 Kaufmann, S. (2007). The New Plagues: Pandemics and Poverty in a Globalized World. Frankfurt a.M., Haus Publishing.

94 van den Bogaard, A. and E. E. Stobberingh (2000). "Epidemiology of resistance to antibiotics. Links between animals and humans." International Journal of Antimicrobial Agents **14**: 327-335.

95 Kaufmann, S. (2007). The New Plagues: Pandemics and Poverty in a Globalized World. Frankfurt a.M., Haus Publishing. p. 207

96 Levy, S. B. (2001). "Antibiotic Resistance: Consequences of Inaction." Clinical Infectious Diseases **33**(Supplement 3): S124-S129.

97 ibid.

concern to us. First, there is a risk that antibiotic-resistant bacteria can be transferred between animals and humans, either by direct contact or through contaminated products such as eggs.[98] Second, there is evidence to suggest that even very low doses of antibiotics that remain in animal products can contribute to the selection of antibiotic-resistant bacteria.[99] Third, the fact that plants and animals become hosts to (multi-)drug resistant bacteria is an ecological problem, as greater density of resistant organisms will reduce the number of drug-susceptible microbes in the environment even further by natural selection.[100] The phenomenon is well established in hospital settings.[101] However, by increasing the use of antimicrobials outside health care settings, the spread of drug-resistant bacteria in other settings has also increased.

2.5.4 Other factors

There are a number of additional factors, which have facilitated the emergence of antimicrobial resistance over the past decades. Some of them are difficult to address with specific policies, because they concern societal change over time. A good example is the demographic change that is observable in many developed countries. Increased life expectancy, paired with improved medical technology and better treatment options for chronic conditions have led to an increase of the proportion of people who are particularly susceptible to bacterial infections.[102] Similarly, the increase of international travel, greater cross-border mobility, and large-scale immigration have had an impact on the global distribution of bacterial infections, and consequently on the spread of antimicrobial resistance. A recent example of the speed with which new infections can spread was the emergence of patients with

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98 Health Protection Agency (2004). Overview of Antimicrobial Usage and Bacterial Resistance in Selected Human and Animal Pathogens in the UK: 2004 - A Joint Report, Communicable Disease Surveillance Center Northern Ireland, Food Standards Agency, Health Protection Agency, Veterinary Laboratories Agency. p. 23 ; Leverstein-van Hall, M. A., C. M. Dierikx, et al. (2011). "Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains." Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases **17**(6): 873-880.

99 Gullberg, E., S. Cao, et al. (2011). "Selection of Resistant Bacteria at Very Low Antibiotic Concentrations." PLoS Pathogens **7**(7).

100 Levy, S. B. (2001). "Antibiotic Resistance: Consequences of Inaction." Clinical Infectious Diseases **33**(Supplement 3): S124-S129.

101 Filius, P. M. (2005). Antimicrobial Use and Resistance in Hospital Settings - PhD Thesis. PhD, University of Rotterdam.

102 Cohen, M. (1997). Epidemiological factors influencing the emergence of antimicrobial resistance. Antibiotic Resistance: origins, evaluation, selection and spread. Chichster, Wiley**:** 223-237.

carbapenem-resistant enterobacteriaceae in Pakistan in India.[103] Within a short period, similar cases were reported all around the world, for example in the UK and Germany.[104]

Beyond the epidemiological factors, individual patients' medical histories and characteristics can also play a role in the spread of AMR. Poor absorption of oral antibiotics or bad circulation, which impedes the transport of antibiotics to the target site can increase the chances that some bacteria survive antibiotic therapy and become resistant.[105] This is a particular problem for bone infections where only few blood vessels are within proximity of the infection site.[106]

While it has been stressed so far that antibiotics should be used sparingly wherever possible to avoid an increased risk of the development of AMR, it must also be noted that the prophylactic use of antibiotics may sometimes be unavoidable. This applies in particular to patients with a weakened immune system, e.g. as a result of rheumatic fever or for patients with HIV. Antibiotics are also commonly used as prophylaxis for very invasive types of surgery, such as hip replacements, where the chances of post-surgical site infection can be significantly reduced with a dose of broad-spectrum antibiotics before the first incision.[107]

2.6 Current responses to AMR

The current policy responses to address AMR vary greatly between countries, both in their extent and success. However, there are some observable trends in the kinds of policies that are being adopted. The European Centre for Disease Prevention and

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103 Rasheed, J. K., B. Kitchel, et al. (2013). "New Delhi Metallo-β-Lactamase–producing Enterobacteriaceae, United States." Emerg Infect Dis **19**(6): 870-878.

104 Deutsches Ärzteblatt (2010). NDM-1-Resistenzen: Vier Fälle in Deutschland. Cologne, Deutscher Ärzte-Verlag.

105 Greenwood, D., R. C. B. Slack, et al. (2002). Medical Microbiology. Edinburgh, Churchill Livingstone. p. 647

106 Häusler, T. (2008). Viruses vs. Superbugs - a solution to the antibiotic crisis? New York, Macmillan.

107 Greenwood, D., R. C. B. Slack, et al. (2002). Medical Microbiology. Edinburgh, Churchill Livingstone. p. 66

Control (ECDC) has suggested that policies to curb the spread of AMR must address three areas.[108] These are

i) the prudent use of available antibiotics,
ii) the undertaking of all hygienic precautions to control cross-transmission and
iii) the research and development of antibiotics with a novel mechanism of action.

Other policy guidelines make similar recommendations, and we shall therefore briefly examine these responses and their current effectiveness.[109]

2.6.1 The prudent use of antibiotics

There is widespread consensus that antibiotic prescribing should be limited to cases where their application is 'prudent'. Policy initiatives such as the *Alliance for the Prudent Use of Antibiotics* (APUA) or the EU Commissions' 'Prudent Use of Antibiotics' campaign reflect a concern for improved stewardship of antimicrobial resources.[110]

However, definitions of prudent use tend to be rather general and often merely focus on the elimination of wasteful prescribing of antibiotics. It is worth illustrating this point by giving two examples of commonly used definitions of prudent use. The first, provided by the z The second definition, from the *Alliance for the Prudent Use of Antibiotics* (APUA), adds to this that prudent use is essentially *"the right drug for the right condition for the right amount of time."*[111]

Thus, one way of understanding prudent use is that the concept merely promotes a maximally efficient use of antibiotics (i.e. that the marginal benefit of their use ought to be greater or equal to the marginal cost).[112] Yet, unless it is specified how marginal costs and benefits are to be calculated in these cases, current definitions of

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[108] European Centre for Disease Prevention and Control. (2012). "Antimicrobial Resistance in Focus." Retrieved 25.01., 2012, from http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/Pages/index.aspx.

[109] Avorne, J. L., J. F. Barrett, et al. (2001). Antibiotic resistance: synthesis of recommendations by expert policy group - Alliance for the Prudent Use of Antibiotics. Geneva, World Health Organization.

[110] ibid. see also European Commission. (2012). "Europe for patients: prudent use of antibiotics." Retrieved 07.03., 2013, from http://ec.europa.eu/health-eu/europe_for_patients/prudent_use_antibiotics/index_en.htm.

[111] Wilson, M. and M. Tan (2010). Raising Awareness for Prudent Use of Antibiotics in Animals: Position Paper of the global Alliance for the Prudent Use of Antibiotics (APUA). Rome, APUA., p. 2

[112] see e.g. Laxminarayan, R. and G. M. Brown (2001). Economics of Antibiotic Resistance: A Theory of Optimal Use. Washington D.C., Resources for the Future. **00-36**.

prudent use are largely descriptive and amount to little more, than a declaration of intent to reduce the waste of antibiotics. Moreover, the focus on cost-effectiveness may distort the concept of prudent use, since - due to the low cost of many antibiotics - even limited effectiveness will often be cost-effective.[113]

Alternatively, prudent use can include the possibility of restricting the use of antibiotics such that only those treatments for which the effectiveness (and the associated magnitude of risk that the patient avoids by being treated) is above some threshold value, which must be defined. There are, some practical examples of policies, which define an acceptable 'cost level' in order to preserve antibiotic effectiveness. In these instances, antibiotic prescribing was restricted, and second-line drugs could only be administered, after a local threshold value for AMR to first-line treatments had been reached. Daneman et al report a case in which such a restrictive use of antibiotics led to an additional risk of death of one percent.[114] What is noticeable in these instances is a general absence of discussion of normative standards that govern the definition of such thresholds for prudent use. We will consider this question in more detail in the second half of this thesis.

Another point worth noting about definitions of prudent use is that they generally suffer from a lack of precision, a characteristic they share with many other concepts of 'sustainable consumption'.[115] Effectively this greatly limits their usefulness for setting targets for the quantity of antibiotics that should be used in a given society or health care system.[116] Such target setting is further complicated by the fact that fixed targets are unlikely to be of much practical use in the first place. Setting fixed targets for prudent consumption of antibiotics would overlook the permanently changing social and demographic conditions as well as progress in health care, all of which may require adjustments to predefined consumption levels. It is therefore crucial to realise that when 'prudent consumption' is being promoted, this does not refer to clearly denoted target levels or permissible overall amounts of drugs that can be

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113 Note that this need not be the case, if the long-term effects of AMR are taken into account. We will return to this point in chapter 4.

114 Daneman, N., D. E. Low, et al. (2008). "At the Threshold: Defining Clinically Meaningful Resistance Thresholds for Antibiotic Choice in Community-Acquired Pneumonia." Clinical Infectious Disease **46**: 1131-1138. See also chapter 7.

115 Curry, P. (2011). Ecological Ethics. Cambridge, Polity Press.

116 Comim, F., R. Tsutsumi, et al. (2007). "Choosing sustainable consumption: a capability perspective on indicators." Journal of International Development **19**(4): 493-509.

consumed. Rather, given the wide range of factors that contribute to AMR, the prudent use of an antibiotic will often have to be determined on a case-by-case basis. As a result, the concept of 'prudent use' appears to be more relevant at the micro-level, where it affects the doctor-patient relationship, than as a concept for public health policy, which so far lacks a coherent account of establishing quotas for usage of antibiotics.[117]

2.6.2 Infection control to reduce transmission

The basic principles of modern infection control through hand hygiene were pioneered by Ignaz Semmelweis in 1847. Semmelweis worked as a doctor in the maternity ward of the Vienna hospital, where the mortality due to childbed fever was extraordinarily high.[118] Semmelweis introduced systematic hand disinfection in his ward, which resulted in a significant decrease in mortality. Even though he was unaware of the germ theory of disease and therefore could not explain this observation properly, his research findings addressed one of the significant problems of hospital care: the exposure of patients to pathogens, which are present in the hospital environment or on other patients. These infections are commonly referred to as Health Care Associated Infections (HCAI), or nosocomial infections, and according to international studies, they affect between 4-9 percent of patients in European hospitals.[119] Their detection and prevention has become a high priority in primary care settings. Yet, given the fact that in the US and UK between 40 and 60% of *S. aureus* strains commonly found in hospitals display some form of drug resistance, this interest should hardly come as a surprise.[120]

Hospitals constitute ideal breeding grounds not only for infections but also for AMR. They host a large number of people receiving antibiotic treatment (either therapeutic or, in the case of many surgeries, prophylactic) with weakened immune systems in the same enclosed space, looked after by health care workers who will have to attend to a large number of people in a single shift. Especially in patients who take a single

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117 I owe this point to a conversation with Prof. Anthony Kessel

118 Rotter, M. (1998). "Semmelweis' sesquicentennial: a little-noted anniversary of handwashing." Current Opinion in Infectious Diseases **11**: 457-460.

119 Mielke, M. (2010). "Prevention and control of nosocomial infections and resistance to antibiotics in Europe - Primum non-nocere: Elements of successful prevention and control of healthcare-associated infections." International Journal of Medical Microbiology **300**(6): 346-350.

120 Weinstein, R. A. (2001). "Controlling Antimicrobial Resistance in Hospitals: Infection Control and Use of Antibiotics." Emerging Infectious Diseases **7**(2).

type of antibiotic over prolonged periods of time, emerging resistance to not only the prescribed antibiotic but to other drugs can often be observed after around ten days.[121] And since the responsible genes are commonly transmitted between bacteria of different taxonomy via plasmids, an environment with numerous long-term users of antibiotics will commonly create instances of AMR.[122] This process is not entirely avoidable but a lack of appropriate hygiene standards will facilitate the spread of microbes between patients and wards. Hospital hygiene is thus commonly cited as one of the areas of paramount importance in developing a strategy to combat AMR.[123] Its effectiveness is widely accepted, as aggressive management programmes for resistant strains of MRSA in hospitals in the Netherlands and across Scandinavia have achieved prevalence of less than 1 percent, whereas many South European countries still report MRSA rates in excess of 40 percent.[124] To further promote these efforts, the WHO launched the World Alliance for Patient Safety in 2004 and two years later, the Council of Europe adopted a recommendation on management of patient safety and prevention of adverse events in healthcare.[125] However, what is also recognised in these guidelines is that reducing incidence and prevalence of HCAIs does not merely require behavioural changes of staff or greater insistence on hand hygiene. Conditions under which such policies can be properly implemented also require a work environment and a sufficiently high staff-to-patient ratio to be realistically implementable.

2.6.3 Research and development of new antibiotics

In light of the dearth of new antimicrobial drugs under development, the substantial lack of new antibiotics has so far not been addressed sufficiently. There is currently a move towards the establishment of incentive programmes to encourage research. The U.S. Food and Drug Administration's recent Safety and Innovation Act (also known as the "Generating Antibiotic Incentives Now", or GAIN act), for example, identified a list of pathogens for which the development of new drugs will be incentivised by

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121 Levy, S. B. and B. Marshall (2004). "Antibacterial resistance worldwide: causes, challenges and responses." Nature Medicine **10**(12): 122-129.

122 ibid.

123 Hansen, S., F. Schwab, et al. (2010). "Methicillin-resistant Staphylococcus aureus (MRSA) in Europe: which infection control measures are taken?" Infection **38**(3): 159-164.

124 Mielke, M. (2010). "Prevention and control of nosocomial infections and resistance to antibiotics in Europe - Primum non-nocere: Elements of successful prevention and control of healthcare-associated infections." International Journal of Medical Microbiology **300**(6): 346-350.

125 ibid.

granting five years of patent extension.[126] In Europe, the establishment of public-private partnerships such as the Innovative Medicines Initiative (IMI) have been launched.[127] In 2012, the EU-financed IMI invested around €220 million into a programme called 'newdrugs4badbugs', which aimed to develop new antibiotics, in partnership with pharmaceutical companies GlaxoSmithKline and AstraZeneca.[128] However, it is too early to predict whether or not these incentive schemes will generate the desired research output over the next years. Currently, a major research breakthrough is unlikely, due to the continued lack of basic research into new target sites for antibiotics and the fact that only a few pharmaceutical companies invest into antibiotic research.[129] Moreover, the provision of financial incentives alone is unlikely to generate sufficient research activity to protect antibiotic effectiveness in the future. This is due to a number of reasons.

To begin with, the existing incentive schemes, such as the GAIN act, work primarily through the extension of patents. Yet, such an extension does not remove the initial risk of investing into basic R&D with highly uncertain returns, but - if anything - promotes the development of drugs that have a high chance of passing market approval and are thus structurally similar to existing drugs. Existing incentive schemes are thus largely pull-mechanisms that reward marketable products, rather than push-mechanisms that support early-stage research. The advantage of pull mechanisms is that they award only successful research (push-mechanisms may end up supporting unsuccessful research projects). However, the complexity of AMR and the need for basic research suggest that a combined approach of incentives will be needed to generate a higher level of antibiotic R&D.[130]

So far, the measurable success of incentive schemes appears to be limited. In a recent assessment of the US 10x20 initiative, which seeks to bring ten new antimicrobial drugs to the market by 2020, Boucher et al found that ongoing R&D into new drugs

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126 FDA (2012). Food and Drug Administration Safety and Innovation Act., available at http://docs.house.gov/billsthisweek/20120618/BILLS-112s3187-SUS.pdf . Retrieved 04.11.2013

127 see Innovative Medicines Initiative (IMI). (2013). "Innovative Medicines Initiative (IMI)." Retrieved 17.08., 2013, from http://www.imi.europa.eu/.

128 See Innovative Medicines Initiative (2012). Uniting European Researchers in the fights against antibiotic resistance. IMI launches €223.7 million programme for combatting antibiotic resistance. Press Release. IMI. Brussels.

129 ECDC and EMEA (2009). The bacterial challenge: time to react. Stockholm, ECDC.

130 Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

was limited and mostly conducted by smaller enterprises. Moreover, few of the ongoing research projects could report significant progress and the compounds under development did not systematically address the areas of greatest clinical need, notably the creation of new antibiotics against Gram-negative infections.[131] While the progress of research remains elusive, there is certainly increasing awareness that the development of new antibiotics must be appropriately incentivised. For instance, the UK's current AMR strategy acknowledges a need *"to do more to address the commercial viability and market failure issues that are hampering investment in antibiotic development."*[132] Yet, it remains unclear, which strategy should be adopted to appropriately incentivise research. Moreover, there is so far only limited discussion about the appropriate *size* of any financial incentive.[133] In light of the enormous human and financial costs of AMR, which were presented earlier, the current incentive system does not seem to reflect the urgency, with which new drugs are required.

2.7 Antibiotic Prescribing and consumption

As was mentioned earlier in this chapter, some level of AMR is inevitable, as it occurs as part of a natural selection process, even under exact observation of treatment protocols. However, it is also known that a significant proportion of the current problem is due to human behaviour and thus, at least in principle, avoidable.[134] Greater emphasis on hygiene, observance of guidelines and avoiding overprescription can all help to substantially slow down the emergence of AMR.[135] To this end, it is important to review in greater detail what different groups or organisations can contribute in order to slow down the further spread of drug resistance. Here, the discussion shall be limited to those groups that are primarily involved in 'using' antibiotics, either by prescribing or by taking them.[136]

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131 Boucher, H. W., G. H. Talbot, et al. (2013). "10 × '20 Progress—Development of New Drugs Active Against Gram-Negative Bacilli: An Update From the Infectious Diseases Society of America." Clinical Infectious Diseases **56**(12): 1685-1694.

132 Department of Health (2013). UK Five Year Antimicrobial Resistance Strategy 2013 to 2018. London. p. 18

133 Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

134 Burke, J. P. and S. L. Pestonik (1998). "Antibiotic resistance - the combat zone." Current Opinion in Infectious Diseases **11**: 441-443.

135 Murray, B. E. (1994). "Can antibiotic resistance be controlled?" The New England Journal of Medicine **330**(17): 335-337.

136 Since the thesis is concerned with the use of antibiotics in humans, a more detailed discussion of antibiotic use in farming and agriculture is omitted at this point.

Unlike in some South American and Asian countries, across Europe antibiotics are only available on prescription. Physicians thus act as gatekeepers to access, which might also explain why much of the literature on antibiotic use focuses on prescription practices rather than consumption (and thus the role of the patient). Yet, the role of physicians in promoting and ensuring the prudent use of antibiotics is complex and requires differentiation between levels of health care provision. What constitutes prudent use will vary considerably with the severity of an infection, the overall condition of the patient and the urgency with which treatment is required. Similarly, demands placed on health care providers by patients will be context-dependent. The next two sections will distinguish between the use of antibiotics in primary and in secondary care, and it will be discussed how antibiotic prescribing varies in both settings.

2.7.1 Antibiotic prescribing in primary care and general practice

People often associate AMR with hospital settings and public knowledge and opinion on this matter has been heavily influenced by media stories about drug-resistant MRSA 'super-bugs'.[137] Nonetheless, while the most visible cases of AMR usually occur in hospital settings, most antibiotic consumption does not take place there. In the UK, it is estimated that almost 80 percent of prescriptions for antibiotics are written in primary care settings.[138] If we are interested in adjusting prescription practices and reducing overall consumption, general practice may thus be a good place to start looking.[139]

Despite a growing awareness for the threats of AMR among both, the public and health care professionals, statistics of the use of antibiotics in primary care show that since 2001 the number of antibiotic prescriptions by GPs has steadily increased.[140] It should be noted that this effect may not be entirely due to changing prescription

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137 Arias, C. A. and B. E. Murray (2009). "Antibiotic-Resistant Bugs in the 21st Century: A Clinical Super-Challenge." N Eng J Med **360**(5): 439-443.

138 Finch, R. G. (2004). "Antibiotic resistance: a view from the prescriber." Nature Reviews Microbiology **2**: 989-994. Similar figures have been reported for other European countries, see e.g. De With, K., H. Schröder, et al. (2004). "Antibiotikaanwendung in Deutschland im europäischen Vergleich." Deutsche Medizinische Wochenschrift **129**: 1987-1992.

139 Levy, S. B. (2002). The Antibiotic Paradox: How the Misuse of Antibiotics destroys their curative powers. Cambridge, MA, Perseus Publishing.

140 See statistics of the NHS Prescription Services, available at http://www.nhsbsa.nhs.uk/PrescriptionServices/Documents/PPDPrescribingAnalysisCharts/Antibiotics_Jun_11_-_National.pdf

practices, but could also simply reflect higher incidence of bacterial infections. However, there is no compelling evidence to suggest that the rise in antibiotic prescribing can entirely be explained by such a change in morbidity. There are, however, a number of reasons that surveys and studies of prescription practices have identified as contributing factors to the rise in antibiotic prescribing.

Many practitioners cite a need to maintain good relations with their patients - a task that is easier to achieve if patients feel that their doctor complies with their expressed needs and meets their expectations with regard to prescriptions.[141] There is an added financial incentive to prescribe antibiotics in health care systems where practices are not awarded a global budget but receive remuneration based on patient contacts. Since only satisfied patients are likely to return (or to recommend their physician to others), GPs have an incentive to meet patients' expectations. However, there is evidence to suggest that in at least some instances, doctors anticipate patient expectations and act upon these anticipations, even when the patient does not actually hold them.[142] Empirical studies suggest that patients rarely demand antibiotic treatment explicitly, and are often more interested in reassurance and provision of information than in a particular type of treatment.[143] Assessing how relevant the pressure exerted on physicians by patients is to the issue of overprescription of antibiotics thus requires further quantitative and qualitative research.

Another issue for antibiotic prescribing in primary care is the difficulty of testing more broadly for bacterial strains before commencing treatment. Testing for most bacterial strains requires laboratory facilities and takes between 24-48 hours. However, for most infections that are treated in community settings (i.e. by GPs), no bacterial cultures are taken, and consequently, antimicrobial therapy is based on the clinical assessment of symptoms. This increases the chance of choosing the wrong treatment, or to use antibiotics for viral infections, against which they are ineffective. It also encourages the use of broad-spectrum antibiotics as these promise a greater

141 Björkman, I., M. Erntell, et al. (2011). "Infectious disease management in primary care: perceptions of GPs." BMC Family Practice **12**(1)., Britten, N. (2004). "Patients' expectations of consultations." BMJ **328**: 416-417.

142 Britten, N. (2004). "Patients' expectations of consultations." BMJ **328**: 416-417.

143 Butler, C. C., S. Rollnick, et al. (1998). "Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throat." Ibid. **317**: 637-642.

chance of therapeutic success if the pathogen is unknown - albeit at the cost of using a stronger antibiotic than may often be necessary. These decisions are not really down to the physician's individual choice, however. Currently, there is a lack of rapid tests for many bacterial strains, which is primarily caused by the lack of research into new types of tests: it is estimated that the total sum spent on medical diagnostics for bacterial infections is equivalent to only one to two percent of the money that is spent on antibiotics annually.[144]

Prescription of antibiotics can often reduce the severity of symptoms and shorten the course of the infection, even if antimicrobial therapy was not crucial to the patients' recovery and merely accelerated it somewhat.[145] In qualitative studies, doctors have cited the obligation to do everything they can for the patient's wellbeing as one of the strongest motivators for prescription of antibiotics.[146] From a societal perspective, this may appear to be undesirable, but this in turn raises the difficult question of how much added discomfort is acceptable, if this marginally reduces the chances of further AMR in the future. We will return to this point in chapters 4 and 7.

An additional factor to influence prescribing in general practice is that antimicrobial therapy often reduces the chance of complications arising later on.[147] This has two implications. First, physicians reduce the risk of overlooking a symptom or misdiagnosing a serious condition. This may be of particular relevance for younger doctors who lack clinical experience and prefer to err on the side of caution.[148] Secondly, abstaining from the use of antibiotic therapy requires follow-up visits of the patient. These may not always be possible or physicians may have cause to believe that the patient will not show up again. In such cases, the prescription of antibiotics may not be strictly necessary, but represents an option that rules out risks for both the patient (in terms of health effects) and the physician (in terms of professional codes of conduct or risking malpractice lawsuits).
The immediate personal benefits of antimicrobial treatment compared to the potential negative impact on public health due to resulting drug resistance are likely to also

144 Finch, R. G. (2004). "Antibiotic resistance: a view from the prescriber." Nature Reviews Microbiology **2**: 989-994.
145 This can for example be the case in patients with otitis media
146 Björkman, I., M. Erntell, et al. (2011). "Infectious disease management in primary care: perceptions of GPs." BMC Family Practice **12**(1).
147 ibid.
148 ibid.

affect physicians' decisions. Many GPs will only encounter the results of AMR infrequently, while they have to deal with patients whose condition could be treated with antibiotics on a daily basis.[149] They are therefore likely to place greater value on the potential health benefits to the individual, rather than the risk of future resistance in the community.[150] An American survey that looked at the prescription of antibiotics for community-acquired pneumonia confirms this view. The study found that while most doctors were aware of and concerned about the public health implications of AMR, societal concerns ranked low in deciding whether to administer a course of antibiotic treatment to a patient.[151]

AMR is a highly complex field of research and some qualitative studies have found that GPs would welcome better information on such aspects as local resistance patterns, as well as a greater emphasis on the problems of drug resistance in medical training.[152] It is noteworthy that this does not seem to be a problem of a lack of available guidelines or recommendations. Rather there appears to be an oversupply of information. Different issuing bodies at regional, national and international levels use different evidence bases and place differing emphases and consequently arrive at varying recommendations.[153]

The complexity of the causes of AMR paired with limited public awareness has practical implications for many GPs. Explaining to the patient the reasons for not prescribing antibiotics is time-consuming and if physicians work under a very tight schedule, it may simply be quicker to prescribe them, than to convince a patient that the treatment is not necessary.[154]

Two conclusions can be drawn from this brief overview of factors, which influence antibiotic prescribing in primary care: first, it is evident that antibiotic prescribing is driven by a wide range of factors, not all of which are remediable by introducing

[149] Simpson, S. A., F. Wood, et al. (2007). "General practitioners' perceptions of antimicrobial resistance: a qualitative study." Journal of Antimicrobial Chemotherapy **59**: 292-296.
[150] Butler, C. C., S. Rollnick, et al. (1998). "Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throat." BMJ **317**: 637-642.
[151] Metley, J. P., J. A. Shea, et al. (2002). "Tensions in antibiotic prescribing: pitting societal concerns against the interests of individual patients." Journal of General Internal Medicine **17**(2): 87-94.
[152] Simpson, S. A., F. Wood, et al. (2007). "General practitioners' perceptions of antimicrobial resistance: a qualitative study." Journal of Antimicrobial Chemotherapy **59**: 292-296.
[153] Finch, R. G. (2004). "Antibiotic resistance: a view from the prescriber." Nature Reviews Microbiology **2**: 989-994.
[154] Björkman, I., M. Erntell, et al. (2011). "Infectious disease management in primary care: perceptions of GPs." BMC Family Practice **12**(1).

stricter guidelines. Second, and following on from the previous point, reducing antibiotic consumption is not merely a matter for health care professionals. It will also require input from a wide array of other disciplines, as diverse as health economics, psychology and communication theory.

2.7.2 Antibiotic Prescribing in secondary care settings

The prescribing of antibiotics in secondary care reflects many of the challenges that primary care physicians face. However, it also differs from the primary care sector in a number of ways. For one, patients in hospital often require immediate care and there may be even less time to reach decisions about which treatment offers the greatest benefit at the lowest risk of AMR. Secondly, many infections in hospital settings are much more severe than those which primary care staff deal with (and consequently carry greater risks for adverse health outcomes). Thirdly, the antibiotics that are used in secondary care may vary significantly from those that are routinely prescribed in primary care settings, both with regard to their strength and their potential side effects. Second-line and third-line drugs will also often require that the patient remain in hospital for at least the first part of the treatment. Finally, the containment of AMR along with the control of infections is particularly challenging in hospital settings, because many people with weakened or compromised immune systems stay in very close proximity to each other for prolonged periods of time - a circumstance that clearly separates them from primary care facilities. Antibiotic prescribing in secondary care thus faces the difficult task of having to find a balance between the quick and aggressive use of antibiotics to fight infections (and thereby improve patient outcomes and avoid the spread of infection within the hospital) and the prevention of AMR.[155] In practice, this means that physician will often have to make complex decisions about the type of antibiotic and the duration of therapy. This may for example involve a decision about whether to use a broad- or a narrow-spectrum antibiotic. While the use of the former may be unnecessary and risk the emergence of resistance against newer and versatile antimicrobial drugs, an inappropriate use of narrow-spectrum antibiotics severely reduces the patient's

[155] Paterson, D. L. (2006). "The Role of Antimicrobial Management Programs in Optimizing Antibiotic Prescribing within Hospitals." Clinical Infectious Diseases **42**(Supplement 2): S90-S95.

chance of a quick recovery.[156] In most European countries, hospitals often prefer to err on the side of caution. A recent Cochrane review of interventions to improve antibiotic prescribing for hospital patients reports that over the last two decades, antibiotic prescribing in many European countries has increased by between ten and twenty percent, and that there is evidence to suggest that "over a third of prescriptions are not compliant with evidence-based guidelines."[157]

In order to address this problem, hospitals have developed detailed guidelines to reduce unnecessary or excessive prescribing of antibiotics and promote antimicrobial stewardship.[158] Yet, their practical implementation is often greatly complicated by the sheer complexity of the task and by having to account not only for medical, but also for organisational, social and behavioural factors.[159] These include for example health care professional's attitudes towards disease, willingness to accept risk to the patient, or the way in which guidelines are communicated to employees.[160] Interestingly, there also seems to be a correlation between prescribing of antibiotics in hospitals and hierarchical power structures within a health care system. In a European study, Deschepper et al found that in more hierarchical societies, levels of antibiotic prescribing were also higher.[161] These factors do not constitute a comprehensive list, but they illustrate some of the reasons behind the discrepancies in antibiotic prescribing and consumption across countries. However, even within the same country or cultural environment, differences in the types of antibiotics used

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156 Leibovici, L., I. Shraga, et al. (1999). "How Do You Choose Antibiotic Treatment?" BMJ: British Medical Journal **318**(7198): 1614-1616.Note, however, that it has also been argued that the use of broad-spectrum antibiotics can help to reduce the risk of AMR due to a higher chance of successful treatment. See e.g. Kollef, M. H. (2000). "Inadequate Antimicrobial Treatment: An Important Determinant of Outcome for Hospitalized Patients." Clinical Infectious Diseases **31**(Supplement 4): S131-S138.

157 Davey P, B. E., Charani E, Fenelon L, Gould IM, Holmes A, Ramsay CR, Wiffen PJ, Wilcox M (2013). Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2013. **Issue 4**. Art. No.: CD003543 p. 5

158 Finch, R. (2012). "Current challenges in antimicrobial resistance and healthcare-associated infections: role and organization of ARHAI." Journal of Antimicrobial Chemotherapy **67**(suppl 1): i3-i10.

159 Hulscher, M. E., R. P.Grol, et al. (2010). "Antibiotic prescribing in hospitals: a social and behavioural scientific approach." The Lancet Infectious Diseases **10**(3): 167-175.

160 ibid.

161 Deschepper, R., L. Grigoryan, et al. (2008). "Are cultural dimensions relevant for explaining cross-national differences in antibiotic use in Europe?" BMC Health Services Research **8**(1): 123.

(albeit not in the total amount prescribed) are observable. These appear to be more closely linked to size and location of the hospital.[162]

2.7.3 Antibiotic Consumption - the role of the patient

Since guidelines for antimicrobial stewardship and prudent use of antibiotics are normally written for health care professionals, the role of the patient in reducing the use of antibiotics has perhaps received less attention than it should. This tendency is likely to have been strengthened by the fact that in the public perception of AMR, patients are the reported victims of drug resistance. While this is undoubtedly an accurate view in most individual cases, aggregate patient behaviour is nonetheless a significant contributing factor to the emergence of AMR.[163] Patients, through non-adherence to treatment protocols or consumption of antibiotics for non-bacterial infections, carry part of the responsibility for the emergence of AMR.

Before outlining the role of patients further, it may be useful here to quickly note that there is an ongoing discussion as to whether the non-observance of doctor's advice should be referred to as non-adherence or non-compliance. Non-adherence is often preferred, as the concept of compliance implies a strict power-relation between the doctor and the patient, in which the patients' interests are of secondary importance.[164] I believe that while this concern is legitimate, the choice of terminology is wholly context-dependant - and that especially in cases of severe and contagious infections, compliance may be a more accurate description. However, throughout this chapter, I shall refer to any acts of non-observance of doctor's advice as non-adherence. This discussion is not merely a case of semantics. What it underlines is a deep-rooted concern about patient autonomy, which could potentially be undermined by strict enforcement of 'prudent' prescription policies for antibiotics. This fear has been expressed by Leibovici et al, who argue that by not giving patients with medium to severe infections access to the full range of available antibiotics, in order to prevent

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[162] Blix, H. S. and S. Hartug (2005). "Hospital usage of antibacterial agents in relation to size and type of hospital and geographical situation." Pharmacoepidemiology and Drug Safety **14**(9): 647-649.

[163] Davies, J. (1997). Origins, acquisition and dissemination of antibiotic resistance determinants. Antibiotic resistance: origins, evolution, selection and spread. S. B. Levy. Chichester, Wiley**:** 15-35.

[164] Coker, R. J. (2000). From Chaos to Coercion: detention and the control of tuberculosis. New York, St. Martin's Press.

AMR, we do in fact infringe on to the patient's right to autonomy.[165] There are good reasons to disagree with this view - for example the fact that under such conditions, any restriction of access in the health care sector (such as the insistence on cost-effectiveness for new interventions provided by the NHS) would constitute an ethically worrying infringement of patient autonomy. However, a more moderately phrased version of the same concern, namely that it is ethically troubling if we do not fully inform patients of the reasons for restricting access is likely to meet with much wider consent. Yet, what constitutes appropriate levels of information, especially in an area as complex as antibiotic therapy is difficult to answer, and whether or not patients or their relatives can always be fully informed is questionable.

A lack of information regarding the causes and risks of AMR on the patients' side has also often been quoted as one of the main reasons behind non-adherence to treatment.[166] As outlined in the previous sections, many general practitioners report pressure from patients to prescribe antibiotics even for non-bacterial infections as one of the reasons for high numbers of prescription. This view is supported by a survey conducted by the Alliance for the Prudent Use of Antibiotics (APUA), which surveyed the view of more than 900 US-American adults on the effectiveness of antibiotics. The survey concluded that around 45 percent of participants believed antibiotics to be effective against viruses while almost ten percent would immediately use an antibiotic against a common cold.[167] What this shows is that there seems to be a continued lack of awareness of the underlying mechanisms and causes of AMR - a fact that is even more worrying in countries where antibiotics are available without a prescription. However, it is not only the initiation of treatment that is potentially problematic - incomplete treatment poses at least as great a risk to the development of AMR.[168] Reasons for the failure to complete treatment may vary and are at least partly specific to the disease and drugs in questions. While an

[165] Leibovici, L., M. Paul, et al. (2011). "Ethical Dilemmas in Antibiotic Treatment." Journal of Antimicrobial Chemotherapy.

[166] Volmink, J. and P. Garner (2000). "Interventions for promoting adherence to tuberculosis management." Cochrane Database Syst Rev **4**(CD 000010. Review).

[167] Boyd, S. and S. Foster Patient Behaviors and Beliefs Regarding Antibiotic Use: Implications for Clinical Practice - Poster 1. Boston MA, Alliance for the Prudent Use of Antibiotics.

[168] Mielke, M. (2010). "Prevention and control of nosocomial infections and resistance to antibiotics in Europe - Primum non-nocere: Elements of successful prevention and control of healthcare-associated infections." International Journal of Medical Microbiology **300**(6): 346-350.

incomplete treatment for a fairly mild urinary tract infection may be due to the fact that the patient quickly felt better and thus discontinued the course of treatment, failure to complete treatment for more severe infections (such as MDR-TB) may be motivated by the severe side-effects of second- and third-line antibiotics. As a result, there is no straightforward answer to the question why people fail to adhere to treatments. And consequently there is no straightforward solution either. However, in most cases appropriate information about risks and consequences of incomplete treatment is likely to increase adherence. At the same time, this may also require greater awareness on the health care worker's side for the patient's lack of knowledge about AMR.

2.8 Summary

In this chapter, it has been argued that AMR is an inevitable by-product of antibiotic use, but that the speed at which it progresses depends greatly on the extent and conditions under which we use antibiotics. It has been suggested that there are a number of key driving factors in the development and spread of AMR, notably the over- and misuse of antibiotics, the lack of research into new drugs and the widespread use of antibiotics in cattle farming and agriculture. However, by looking in detail at the role of different groups of stakeholders, notably doctors and patients, it also became evident that a focus on prescribing fails to appropriately reflect the responsibility of patients in using antibiotics correctly. This discussion concluded that in the near future, current policies are insufficient to halt or reverse the progress of AMR. In the following chapter, it will be examined, how current solutions are shaped by the way we have conceptualised AMR in the policy discourse and we will consider if lessons from other policy fields can be adopted to develop new solutions to the problem we face.

Chapter 3: Antimicrobial resistance and analogical reasoning

3.1 Introduction

Given that potentially life-saving treatments will become a scarce resource in the near future, we face the difficult question of how to best use the remaining stock of antibiotics, not just within a given society, but also between generations. These questions will be discussed throughout the remainder of the thesis. At this point, however, it will be useful to begin our analysis with a review of similar policy problems and the way they have been used to conceptualise AMR. In discussing the mechanisms of AMR, and exploring possible policy responses to the threat, many commentators have pointed out that the problem of AMR is analogous to other cases of collective action problems, where scare resources need to be distributed fairly. These supposedly analogous cases include the tragedy of the commons, incidences of overfishing and the use of fossil fuels. This chapter examines the usefulness of such analogies. It will suggest that while analogical reasoning is an important tool in policy-making, many of the cases, which are frequently compared to AMR differ in relevant aspects. As a result, solutions to the problem of distributing antibiotics cannot be derived from analogous scenarios, but need to be developed to match the specific characteristics that antibiotics display as a commodity. It will therefore be argued that the distribution of antibiotics raises ethical problems that are *sui generis*. More specifically, it will be shown that those analogies, which are commonly used to analyse AMR are inadequate because they each fail to reflect salient features of antibiotics.

3.2 AMR and the distribution of which commodity?

This chapter will compare distributive challenges that arise in the case of AMR with a number of related cases, in which other commodities are distributed. Before considering these other cases, a little bit more needs to be said about which commodity is to be distributed in the case of AMR. Fundamentally, we could consider (and therefore have to distinguish between) the following:

a) the distribution of the antimicrobial drugs themselves,
b) the ownership of the respective intellectual property to the manufacturing of antibiotics, and
c) the distribution of antibiotic effectiveness.[169]

All three of these options are relevant to the case of AMR. However, the following discussion will primarily focus on c) and consider, how antibiotic effectiveness can be distributed. For the purposes of the following analysis, 'antibiotic effectiveness' will therefore be treated as a measurable commodity that represents the stock of remaining doses of antibiotics that can be used to effectively target bacterial infections. This focus on antibiotic effectiveness merits some clarification and explanation.

The distribution of antibiotic drugs, and the distribution of antibiotic effectiveness are closely related, yet not identical and they will ultimately concern different aspects of distributive justice. To make the distinction more obvious, consider the following example. A manufacturer can produce a certain amount of antibiotic drugs every day and if antibiotics are scarce, who gets access to the drugs will be of tremendous importance. Dealing with these concerns will for example involve questions regarding production capacity, as well as fair price levels and coverage of health care costs for those who fall ill. However, in most countries it is not the physical access to antibiotics that constitutes the main challenge. Rather, it is the question, whether all the drugs produced remain effective, and if so for how long. In principle, a manufacturer can continue to produce and sell antibiotics even if prevailing levels of drug resistance have rendered them ineffective. Consequently, what is arguably of the greatest relevance in more developed countries is the preservation of the effectiveness of the drugs that are manufactured and used. As we saw in the previous chapter, this can be achieved either by developing new drugs or by restricting the use of antibiotics to reduce the emergence of AMR.
The remainder of the chapter will focus on the distribution and preservation of antibiotic effectiveness and examine if and how suggested policy solutions to distributive dilemmas that affect other resources can be applied to the case of AMR.

[169] For this point see in particular Wilson, J. (2013). Drug Resistance, Patents and Justice: Who Owns the Effectiveness of Antibiotics? Global Health and International Community - Ethical, Political and Regulatory Challenges. J. Coggon and S. Gola. London, Bloomsbury Publishing Plc.

Before considering these dilemmas, however, it will be useful to say more about the practice of analogical reasoning.

3.3 Analogical reasoning

Analogical reasoning is a ubiquitous practice across a wide range of academic subjects and professions. Ethical theory provides a case in point, as moral reasoning will often look for analogous cases in establishing possible solutions to a problem at hand. This happens either by creating relatively abstract case studies for which findings are hoped to be transferrable to practical decision-making, or by establishing a 'likeness' between different moral conflicts which allows for the transfer of conclusions or intuitions from one case to the other. Cass Sunstein has pointed out that the same is true for legal rulings, which rely heavily on analogical reasoning.[170] Cummings has argued that analogical reasoning is also a common practice in addressing medical and epidemiological problems, especially when a previously unknown disease or pathogen is examined.[171] Under conditions of uncertainty, important questions such as virulence or transmission paths are often tackled first by analogical reasoning. Thus, if another disease affects the same demographic, a first guess for epidemiologists will often be that transmission paths may be similar.[172] Cummings cites the case of Hepatitis B and HIV as an example, but there are numerous other cases, such as the preliminary risk assessment of a novel strain of influenza, which will often start by searching for similarities with particularly virulent strains that circulated in the past.[173] The advantage of such an approach is that it permits the adjustment of an existing theory as new facts or observations become available.[174] What makes analogical reasoning attractive in the first place, is thus its ability to not only rephrase complicated problems in more familiar terms, but also to develop solutions under conditions of epistemic uncertainty.

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170 Sunstein, C. (1993). "On Analogical Reasoning." Harvard Law Review **106**(3): 741-791.

171 Cummings, L. (2004). "Analogical Reasoning as a Tool of Epidemiological Investigation." Argumentation **18**: 427-444.

172 ibid.

173 DeGrandis, G. and J. Littmann (2011). Pandemics: Background Paper. Forward Look Seminars. London, The Nuffield Council on Bioethics.

174 Cummings, L. (2004). "Analogical Reasoning as a Tool of Epidemiological Investigation." Argumentation **18**: 427-444.

Sunstein has suggested that analogical reasoning follows a characteristic structure that can be divided into four steps.[175] These are applied to analogical thinking in law, but they can equally be applied to moral reasoning.[176] The four steps of analogical reasoning he describes are:

(1) Condition A has a certain characteristic X, or characteristics X, Y, and Z;
(2) Condition B differs from A in some respects but shares characteristics X, or X, Y, and Z
(3) It has been established that the best response to A is R
(4) Because B shares certain characteristics with A, R applies to B as well.[177]

A purely descriptive use of analogical reasoning would be restricted to the first two steps that Sunstein outlines. However, in developing a response to AMR, policy makers and researchers may wish to look beyond the purely descriptive use of analogies and instead use them to develop policy proposals.

This, however, requires that both the analogous problem and its respective solution are sufficiently similar to the case at hand, a precondition that Sunstein describes as being "similar in *all relevant aspects"*.[178] Where this similarity is not present, there is a danger of employing broadly similar analogies, which capture part of a problem, but differ enough so as to not be applicable to AMR (or indeed any other case we try to solve by analogical reasoning). In this chapter, I will consider the most frequently used analogies to AMR, and argue that in fact they differ significantly from the problem at hand and thus are not suitable for deriving a policy response.
This is not to say that the analogies discussed below do not serve a purpose - they are in fact tremendously helpful for mapping out more clearly what challenges AMR poses in the long run. Thinking through carefully which analogies are appropriate is a good way to work out, in what way AMR is different, and what aspects we need to take in to consideration.

175 Sunstein, C. (1993). "On Analogical Reasoning." Harvard Law Review **106**(3): 741-791.
176 ibid. p. 742
177 ibid. p. 745
178 ibid. my italics

3.4 Analogical reasoning and AMR

There are a number of reasons why analogical reasoning may be helpful in the context of AMR. For the economist, who is familiar with economic dilemmas but not with intricacies of infectious disease control, it may provide a useful way of conceptualizing the problem in terms of his own academic discipline. Similarly, other groups such as policy makers or the public may find it easier if the highly complex problem of AMR is explained with reference to a scenario they are already familiar with and that does not require any familiarity with the bio-medical details.

How widely analogical reasoning is employed when thinking about AMR is nicely illustrated by an interview, that microbiologist John Conly gave to the 'Bulletin of the World Health Organization' in 2010. In this interview, Conly stated that: *"[a]ntimicrobial resistance may be likened to [...] overfishing scenario[s], to cattle overgrazing the grass of the commons or to deforestation on Easter Island, which led to the population dying out."*[179] This quotation not only reflects the breadth of similar cases that economic theory is thought to provide, but also illustrates how very different scenarios (which operate on different premises and subsequently come to very different conclusions) are being used to explain the same distributive problem; namely how to address the overconsumption of antibiotics, which is understood to be the main cause of AMR.

We can also find evidence for attempts to use analogical reasoning as problem solving technique for AMR. Conly's colleague Richard James for example gave an interview to the *Guardian*, where he drew a comparison between AMR and the use of fossil fuels and remarked that *"[i]f you consider antibiotic sensitivity as a resource like oil, you want to maintain that by introducing a tax"*.[180] Similar proposals of a Pigovian tax or permit schemes analogous to carbon trading have been put forward by other authors as well, who draw similar analogies and consequently suggest an adapted version of emission trading as a method to combat the spread of AMR in the future.[181]

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[179] World Health Organization (2010). Antimicrobial resistance: revisiting the "tragedy of the commons". Bulletin of the World Health Organization. Geneva, WHO Press. **88**.

[180] Boseley, S. (2010). Are you ready for a world without antibiotics? The Guardian. London.

[181] Smith, R. D. and J. Coast (1997). The Transferable Permit Market: A Solution to Antibiotic Resistance? . Centre for Health Program Evaluation Working Papers, Centre for Health Program Evaluation. **61**. A Pigovian tax internalises the social cost of commodities with negative externalities.

The literature on AMR frequently refers to at least three scenarios: (1) the tragedy of the commons, (2) the reduction of CO_2 emissions, and (3) overfishing.[182] I will argue that all three comparisons offer valuable insights into some of the underlying mechanisms of AMR, yet they ultimately are not similar in all relevant aspects. Despite their respective shortcomings (or rather the ways in which they differ significantly from the case at hand), considering the arguments for all three comparisons will be helpful in mapping out more clearly what exactly the distributive problems are that arise in the case of antibiotics and AMR and how ethics can help us to answer them.

3.5 Antibiotic overconsumption - a tragedy of the commons?

The most commonly cited economic case to which AMR is likened is the tragedy of the commons, which is a case study originally developed by Garrett Hardin in *Science* in 1968.[183] Hardin describes a historic case of overgrazing on a shared piece of land - the commons. Individual farmers can realise a marginal benefit from adding more cattle to the commons - even if they thereby increase the overall number of animals beyond the sustainable level. Because using the commons is free and the costs are externalised while the benefits are only enjoyed by the individual farmer, it is rational for the individual to maximise his use of the resource beyond what is sustainable. Acting in this way will maximise individual utility. Hardin describes the commons scenario as a problem in which no party is compelled to change his or her behaviour and subsequently suggests that there is no easily enforceable solution. Rather, the tragedy of the commons requires the competing parties to enter into a contractual agreement, according to which they voluntarily limit the consumption of the shared good. Hardin's case study is so important to economic theory because it outlines a case of severe market failure, and has become synonymous in Economics

[182] See e.g. Ibid. Laxminarayan, R. and G. M. Brown (2001). Economics of Antibiotic Resistance: A Theory of Optimal Use. Washington D.C., Resources for the Future. **00-36**, Rudholm, N. (2002). "Economic Implications of antibiotic resistance in a globale economy." Journal of Health Economics **21**: 1071-1083.

[183] Hardin, G. (1968). "The Tragedy of the Commons." Science **162**: 1243-1248. see also Foster, K. R. and H. Grundmann (2006). "Do We Need To Put Society First? The Potential for Tragedy in Antimicrobial Resistance." PLoS Med **3**(2). Outterson, K. (2010). "The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation." Cardozo Law Review **31**(3). Andreasen, M. (2014). Arbejdspapirer om antibiotikaresistens. Copenhagen, Det Etiske Råd (Danish Ethics Council),.

textbooks with the overconsumption of common pool resources.[184] A common pool resource is a good for which consumption is i) rival, and ii) non-excludable. Such a resource is sometimes also referred to as a *common good* (as opposed to a *public good*, which is both non-rival and non-excludable). In the case of the tragedy of the commons, every farmer is entitled to add more cattle to the shared piece of land, so the good is non-excludable. However, since every added cow leaves less grass for others, adding more cattle reduces the benefit that each farmer enjoys, which makes its consumption rival.

Given that AMR is frequently linked to the tragedy of the commons, how relevant is the scenario for health policy makers? At first sight, there are obvious similarities: there appear to be no costs to the individual to consume more than is socially optimal in either scenario and personal benefits can be externalised, that is, their costs are shared by everyone. Indeed, this seems to be very similar to the case of antibiotics and may have prompted commentators in different disciplines to accept so readily that the two cases are comparable. Upon closer inspection, however, the common scenario varies significantly from many of the characteristics of AMR.

A first striking difference between the commons case and the use of antibiotics is that the latter produces two types of externality, of which only one is represented by the tragedy of the commons. Externalities are costs or benefits of a product or service, which are not appropriately reflected by the price. In the case of a positive externality, the market price will therefore not reflect the real benefit of the good, leading to its underprovision, whereas in the case of a negative externality the opposite is true and not all costs that arise as a result of consumption are reflected in the current price level.[185] How does this apply to antibiotics? As we saw in the previous chapter, antibiotics are effective against contagious bacterial infections. As a result, the cure of a contagious patient lowers the risk for future transmissions and reduces the prevalence of an infectious disease in the community, which is a positive externality.[186] The negative externality of using the same drug, however, is the fact that it may lead to the development and spread of AMR. Calculating costs and

184 see e.g. Varian, H. (1992). Microeconomic Analysis (3rd Ed.), W. Norton & Company.

185 ibid.

186 Levy, S. B. (2002). The Antibiotic Paradox: How the Misuse of Antibiotics destroys their curative powers. Cambridge, MA, Perseus Publishing.

benefits of antibiotic therapy is thus complicated, as the presence of both, positive and negative externalities will require that these be somehow quantified and traded off against each other. The analogy of the tragedy of the commons fails to reflect this problem, since the addition of more cows to the pasture will yield negative externalities (by reducing the amount of grass that the rest of the herd can consume) without creating a corresponding positive externality. Adding another cow to the commons makes the farmer who owns it better off - but not the community as a whole. In this way, the case of AMR and the tragedy of the commons as described by Hardin vary significantly.

Furthermore, it is questionable if the proponents of the similarity between the commons scenario and the case of AMR do in fact wish to argue for the close resemblance of the two cases. To do so would imply that (as Hardin argues in the case of the commons) overconsumption is entirely rational for the individual - a view, which should be called into question in the case of antibiotics. Rational consumption, as understood in the tragedy of the commons, occurs where there is a tangible benefit to the individual. It is thus entirely rational for the herdsman to put an extra cow on the commons, as there is a quantifiable, added benefit, namely the cow's ability to feed on the pasture. Conversely, for a self-interested individual, it is only rational to take an antibiotic if there is a quantifiable added benefit in doing so, especially when factoring in the potential side effects of antibiotic therapy.[187] Furthermore, since antibiotics can at best restore a previous level of utility, but not provide any additional gains for the individual, rational consumers should be even less inclined to overconsume antibiotics. As a result, the commons scenario is not suitable for conceptualizing unnecessary and ineffective overconsumption of antibiotics, which is ultimately a case of *irrational* consumption.[188] Instead, it would apply to cases, where the rational individual has good reason to take a drug - in other words, where consumption would be medically beneficial.

[187] Battin, M. P., L. P. Francis, et al. (2009). The Patient as Victim and Vector: Ethics and Infectious Disease. New York, Oxford University Press. pp. 241-242

[188] I do concede that a 'placebo effect' of taking a drug (albeit an ineffective one) may provide utility to the patient, but I hold that it is reasonable to assume that in light of potential side-effects and the dangers of antibiotic resistance this effect is comparatively insignificant.

The tragedy of the commons scenario thus only pertains to those cases in which we deliberate whether or not to withhold treatment from those who have rational reasons to seek it in the first place. This means that the scope for application of the analogy is in fact much narrower than may initially be assumed, and does not cover the general overconsumption of antibiotics for which there is no quantifiable benefit. Instead, it is only relevant to cases where people receive a medical benefit from taking an antibiotic, and thus have reasons to seek such treatment, even if it produced negative externalities in the form of higher levels of resistance. This would be a case of rationing antibiotic treatment, rather than merely reducing overconsumption. However, as outlined above, current policies of prudent use sometimes allude to the tragedy of the commons but do not seek to actively ration the use of antibiotics.[189]

3.6 Antibiotic effectiveness as a renewable resource - the analogy of overfishing

In the tragedy of the commons scenario, an implicit assumption is that the overgrazed pasture can easily recover, if a sufficiently large number of cows are removed from it. This assumption is too simplistic to appropriately reflect the reversal to drug-susceptibility in the case of AMR, because we cannot easily eliminate a large share of antibiotic use to wait for a reversal of AMR. However, more carefully managed approaches, where certain drugs are given 'recovery time' to regain effectiveness have been suggested. In this context, the comparison to overfishing and the temporary ban on catching certain species of fish for periods of time has sometimes been drawn.[190] Overfishing presents a serious problem to the sustainable use of marine resources and the ever-increasing demand for fish, which is fuelled by constant global population growth, has already led to the extinction of many species. One policy reaction to this has been the introduction of temporary bans on fishing to allow stocks to recover and grow. Following the collapse of cod stocks off the Atlantic coast of Canada in the 1990's, the Canadian government

[189] It must be acknowledged, that in the case of at least one publication, this consequence is (implicitly) accepted, and therefore I do not so much provide an argument against the analogy per se, as I wish to draw attention to the limits within which it can reasonably be applied. See Foster, K. R. and H. Grundmann (2006). "Do We Need To Put Society First? The Potential for Tragedy in Antimicrobial Resistance." PLoS Med **3**(2).

[190] See e.g. Laxminarayan, R. and G. M. Brown (2001). Economics of Antibiotic Resistance: A Theory of Optimal Use. Washington D.C., Resources for the Future. **00-36**.

declared a moratorium on fishing, with devastating effects for local industry.[191] However, cod populations have recently begun to grow again, although after almost twenty years only a third of full recovery has been achieved.[192]

Analogous to the recovery of fish populations, it has been suggested that AMR is a reversible phenomenon, where discontinuing the use of specific drugs will result in bacteria subverting to drug-susceptibility.[193] In principle, it is true that AMR is only an evolutionary benefit for bacteria as long as the drug is being used, a phenomenon that microbiologists refer to as the fitness cost of resistance.[194] A number of corresponding studies have shown that at least for some bacteria, resistance to antibiotics is an evolutionary disadvantage in antibiotic-free environments.[195] In practice, this phenomenon has also been observed in countries that banned the use of antibiotics in animal farming and reported a subsequent drop in infections caused by drug-resistant bacteria.[196]

However, numerous factors make the analogy difficult to put to a meaningful use. For one, it is fairly straightforward to introduce a ban on a particular type of fishing and any negative effects that arise as a consequence of this can be financially compensated. In the case of AMR, however, a drug ban leads to a loss of health or

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191 Ransom, M. A., J. A. Hutchings, et al. (1997). "Why do fish stocks collapse? The example of cod in Atlantic Canada." Ecological Applications **7**(1): 91-106.

192 Frank, K. T., B. Petrie, et al. (2011). "Transient dynamics of an altered large marine ecosystem." Nature **477**: 86-89.

193 Scott, R. D., S. L. Solomon, et al. (2001). "Applying Economic Principles to Health care." Emerging Infectious Diseases **7**(2): 282-285.

194 Herrman, M. and R. Laximinarayan (2010). "Antibiotic Effectiveness: New Challenges in Natural Resource Management." Annual Review of Resource Economics **4**(2). Note, however, that there is recent evidence to suggest that compensatory mutations in some strains of MDR-TB have not only conferred drug resistance but also led to increased virulence. This would suggest that in some instances, the traditional concept of fitness cost is no longer accurate. See e.g. Callaway, E. (2014). "Russia's drug-resistant TB spreading more easily." Retrieved 03.02.2014, from http://www.nature.com/news/russia-s-drug-resistant-tb-spreading-more-easily-1.14589.

195 Herrman, M. and R. Laximinarayan (2010). "Antibiotic Effectiveness: New Challenges in Natural Resource Management." Annual Review of Resource Economics **4**(2).

196 See e.g. Aarestrup, F. M., A. M. Seyfarth, et al. (2001). "Effect of Abolishment of the Use of Antimicrobial Agents for Growth Promotion on Occurrence of Antimicrobial Resistance in Fecal Enterococci from Food Animals in Denmark." Antimicrobial Agents and Chemotherapy **45**(7): 2054-2059. Note however, that it is contested if the benefits of banning the use of antibiotics as a growth promoter in animals do in fact outweigh the costs, as the sub-therapeutic use of antibiotics appeared to have prophylactic effects in many animals, the lack of which is now countered with the use of therapeutic antibiotics such as tetracyclines. See e.g. Casewell, M., C. Friis, et al. (2003). "The European ban on growth-promoting antibiotics and emerging consequences for human and animal health." Journal of Antimicrobial Chemotherapy **52**(2): 159-161.

even life, which cannot be financially compensated in the same way.[197] Thus, a temporary ban would only be useful for antibiotics for which an appropriate substitute is available, which excludes many second- and third-line antibiotics. Moreover, even where alternative drugs are available, the issue of cross-resistance would potentially undermine any recovery of effectiveness for certain antibiotics. The analogy is further complicated by the fact, that antimicrobial therapy is less likely to lead to the development of resistance, when a combination treatment of different drugs is used. As a result, the 'recovery' of the effectiveness of one drug may well come at the cost of a comparative acceleration in the build-up of resistance against the drugs which remains in use.[198] It is also important to keep in mind, how long a reversal to drug-susceptibility would take in practice. The longer this period is, the higher the associated human costs due to limited treatment options are likely to be. And it is also reasonable to assume that for many types of AMR, return to a drug-susceptible state would take much longer than the acquisition of resistance in the first place.[199] This makes it an unlikely solution to the problem of AMR in the long run.

Finally, there is an important ethical difference between the case of overfishing and AMR. We may have good non-instrumental reasons for the protection of animal species e.g. the belief of many ecocentric worldviews that a species is intrinsically valuable and deserves our protection irrespective of its direct use to us.[200] Whether or not such considerations contributed to the Canadian government's decision is another matter altogether, but in considering the ethical arguments for such a policy, the ecocentric approach to the protection of species is an argument that deserves attention. By contrast, antibiotic effectiveness is a purely instrumental commodity, as the protection of antibiotics (or disease-causing microbes for that matter) as an end in themselves that is worthy of protection is a highly implausible claim.

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197 Note that this argument is vulnerable to the response that people may not have a valid claim to antibiotics - and that they therefore need not be compensated if drugs are withheld. Chapter 7 will discuss this line of argument in greater detail.

198 Herrman, M. and R. Laximinarayan (2010). "Antibiotic Effectiveness: New Challenges in Natural Resource Management." Annual Review of Resource Economics **4**(2).

199 Laxminarayan, R. and G. M. Brown (2001). Economics of Antibiotic Resistance: A Theory of Optimal Use. Washington D.C., Resources for the Future. **00-36**.

200 Curry, P. (2011). Ecological Ethics. Cambridge, Polity Press. Chapter 1

3.7 Is AMR analogous to greenhouse gas emissions?

An alternative approach to the ones outlined above is to start not by looking at the remaining antibiotic effectiveness, but by examining the externalities that are created by using antibiotics. AMR can thus be understood as a negative externality that results from the consumption of antibiotics.[201] In this respect, AMR resembles many forms of pollution, including CO_2 emissions, which are not appropriately internalised in the cost of fossil fuels and thus result in consumption beyond a socially optimal level.[202]

To address this problem, a number of policy options have been suggested, including the legal regulation of permissible usage of any commodity with a negative externality. A typical example of this is the introduction of emission standards. Another approach is the introduction of Pigovian taxes, which level consumer charges to cover the societal costs of negative externalities. However, what these approaches will often fail to reflect is the fact that different 'polluters' have different starting points in terms of their current level of pollution, and that a fulfilment of the legal requirement may put an unfair burden on some industries. The answer is thus often seen to lie in a permits market, where polluters who use less than their allocated maximum pollution can trade permits with polluters who cannot (yet) meet the legal requirements.

How does this model relate to AMR? To begin with, levels of antibiotic use are at least partly dependent on the disease burden - higher prevalence of infectious diseases will require a wider use of antibiotics.[203] Similarly, certain hospitals that specialize in invasive surgery or the treatment of infectious diseases will experience a higher demand for antibiotics even if they are used carefully and only where clearly medically indicated. To acknowledge these differences (which a rigid cap on

[201] Smith, R. D. and J. Coast (1997). The Transferable Permit Market: A Solution to Antibiotic Resistance? . Centre for Health Program Evaluation Working Papers, Centre for Health Program Evaluation. **61**.

[202] Anomaly, J. (2010). "Combating Resistance: The Case for a Global Antibiotics Treaty." Public Health Ethics **3**(1): 13-22.

[203] Millar, M. (2011). "Can antibiotic use be both just and sustainable... or only more or less so?" Journal of medical ethics **37**(3): 153-157.

antibiotic use would not), a permit-trading system has therefore been suggested by some as an answer to the problem of AMR.[204]

On the face of it, this appears to be a reasonable approach, but whether this is the case will very much depend on the level at which such a policy is being imposed. Introducing tradable permits at the micro-level for example, yields the chance of creating perverse incentives.[205] GPs or hospitals in financial difficulties could be motivated to treat fewer patients with antibiotics than was medically indicated, in order to be able to trade the remaining 'antibiotic allowance' for money. Moreover, a strict allowance could also lead to instances of preventable illness or even death, if doctors had exhausted their allowance and there were no financial means to purchase further permits is at hand.[206] A price adjustment level for antibiotics which creates a sufficiently large disincentive will therefore not just lead to higher financial cost to the user - it may end up causing otherwise preventable deaths as well, which makes the approach much harder to argue for.

One important aspect that the analogy of greenhouse gas emissions highlights, however, is that both AMR and CO_2 emissions pose a problem on a global scale that national policy alone cannot effectively combat. Recalling the case of the resistance-conferring plasmid NDM-1 which was cause for international concern in 2010 and 2011 and briefly discussed in chapter 2 illustrates this point.[207] While originally found in India (NDM-1 stands for New Delhi Metallo Beta Lactamase-1), NDM-1 containing bacteria quickly spread across the globe, with reports of locally contained outbreaks across most of Europe.[208] However, as outlined above, due to the difficulties in implementing policies such as cap-and-trade agreements, it appears that the analogy is of limited use in developing workable solutions to the problem of AMR.

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[204] Smith, R. D. and J. Coast (1997). The Transferable Permit Market: A Solution to Antibiotic Resistance? . Centre for Health Program Evaluation Working Papers, Centre for Health Program Evaluation. **61**.

[205] Anomaly, J. (2010). "Combating Resistance: The Case for a Global Antibiotics Treaty." Public Health Ethics **3**(1): 13-22. p. 16

[206] ibid.

[207] Kumarasamy, K. K., M. A. Toleman, et al. (2010). "Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study." The Lancet Infectious Diseases **10**(9): 597-602.

[208] Deutsches Ärzteblatt (2010). NDM-1-Resistenzen: Vier Fälle in Deutschland. Cologne, Deutscher Ärzte-Verlag. 12.08.

3.8 Antibiotic effectiveness as a non-renewable resource

The analogies, which have so far been outlined in this chapter built at least in part on the assumption that AMR was reversible over time, prompting the comparison with depleting fishing stock. However, as we saw earlier, this comparison may be unsuitable, due to the time it would take for a complete reversal of current resistance patterns. As there is a very real danger that we will deplete available stocks of antibiotic effectiveness in the foreseeable future, the analogy of renewable resources thus runs the risk of underestimating the seriousness of the current situation. If this is the case, then it may be more appropriate to disregard the potential for renewed effectiveness at this point (at least at the policy level) and instead treat the current stock of antibiotic effectiveness as a finite resource that we can choose to exploit at varying rates.[209] This would be a case where the usage of antibiotics is largely analogous to that of fossil fuels. In this instance, a limited quantity remains and its use produces negative externalities. Indeed, despite ignoring the potential for renewed effectiveness, this analogy captures the problem of AMR much better than the previously discussed scenarios, while simultaneously stressing the urgency to action. At first glance, however, this approach may appear counterintuitive, and non-scientific. Surely, if AMR *is* in fact reversible, and new drugs *can* be developed, these facts should inform our decision-making. There are some pragmatic counter-arguments to this view. First, given the length of time it takes to develop new drugs and the fact that currently few new antibiotics are in the pipeline, we must assume that in the near future, there will be a shortage of drugs to combat highly resistant bacterial strains.[210] Second, given the projected demographic changes over the course of the next few generations and the ever-increasing number of people living on this planet, even a worldwide policy to restrict and control the use of antibiotics is not guaranteed to lead to a reduction in the total amount of drugs being used. While the average consumption per person may fall, the UN expects the world population to grow by 2.5 billion people until 2050, meaning that most reductions will simply be offset by population increases.[211] In sum, we may therefore have good reasons to doubt how reversible AMR will be *in practice*, which makes the use of fossil fuels as

[209] see Wilson, J. (2013). Drug Resistance, Patents and Justice: Who Owns the Effectiveness of Antibiotics? Global Health and International Community - Ethical, Political and Regulatory Challenges. J. Coggon and S. Gola. London, Bloomsbury Publishing Plc. Chapter 9

[210] Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

[211] See Zlotnik, H. (2007). Press Release (Department of Public Information): World population will increase by 2.5 billion by 2050. New York, United Nations.

an analogy to the use of antibiotics compelling. Yet, I would suggest that there are nonetheless some important differences between the two cases, which any policy for the future use of antibiotics must bear in mind.

We know that the cost of producing a barrel of crude oil will increase, as the remaining reservoirs continue to be depleted, simply because more effort is required for its production and demand outstrips supply. Yet, while the production cost of the resource increases, the effectiveness of a barrel of oil remains the same. For fossil fuels, effectiveness is commonly measured in terms of energy per unit volume.[212] Even as it becomes harder to find new oil sources in the future, we can expect the energy per barrel of oil to be consistent over time. In fact, one could argue that a barrel of oil produced in the future will yield a greater overall benefit, as combustion engines and heating systems become more efficient in their energy conversion, while producing fewer externalities in the form of pollution. For antibiotics, however, this is most certainly not the case.

If we accept that in principle, any global use of antibiotics, even under the most careful and conservative approach, will create resistance in the future, it stands to reason that the effectiveness of antibiotics cannot be sustained at the current level as long as *any* quantity of drugs is in circulation.[213] Again, it must be stressed, that via appropriate policies to control antibiotic use, the progress of AMR could be slowed down or delayed significantly. Yet, in principle antibiotic use will entail higher resistance and thus diminishing effectiveness in the long run. Lower effectiveness here means, that a Defined Daily Dose (DDD) of antibiotics that is used today will be worth less at some point in the future, where the drug is either i) no longer effective at all, ii) requires combination with other antibiotics, or iii) must be used in higher dosages, such that the DDD is no longer appropriate and must be increased by a factor >1. How quickly this effect takes place, and how much greater the factor is (or which other drugs will have to be used in combination) is likely to be different for specific pathogens. It will also depend on the overall amount of antibiotics that is being used. However, in the medium run, even under a restrictive policy for their use, antibiotics are likely to become less and less effective. This clearly separates them from other natural resources in one very important aspect, and we will have to

212 Woodruff, E. B. (2007). Energy Conversion. Encyclopedia Britannica. London, Britannica.

213 I take it to be an unrealistic assumption that antibiotic use could be reduced to zero

look at the consequences of this difference in more detail, to determine how it should be reflected in policy-making.

3.9 Economics and AMR - taking stock

So far, I have suggested that prudent use of antibiotics, while a common theme in the literature, is a poorly defined concept that provides little practical guidance in order to help us decide, what constitutes a sustainable and responsible level of consumption. I have then suggested that we must distinguish between the distribution of antibiotics, antibiotic effectiveness and the ownership of intellectual property rights to antibiotics, and that antibiotic effectiveness is a common good. While economic theory offers examples of a number of such goods, some of which are frequently compared to AMR, I have argued that these analogies fail to capture the problem in all of its relevant aspects. As a result, solutions that have been proposed for the analogous cases are unlikely to apply to AMR, because they deal with broadly comparable but not sufficiently similar problems. Instead, we should think of antibiotics as separate type of commodity, which - while bearings some resemblance to other commodities - raises a set of distinct and unique problems that policy makers will have to address. The following list attempts to capture all aspects of antibiotics and antibiotic effectiveness that will have to be considered in order to determine a fair distribution across societies and time.

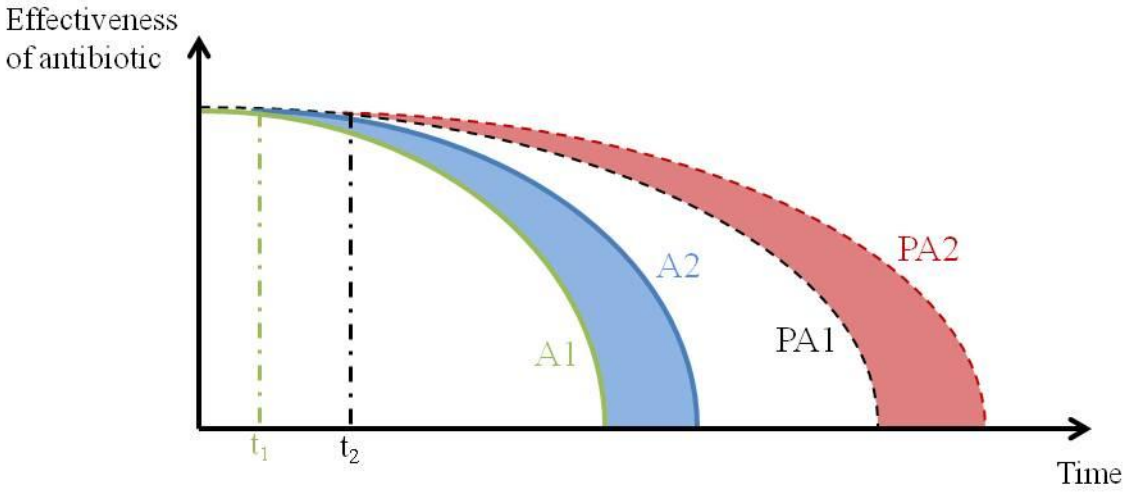
3.10 Characteristics of antibiotics as a commodity

- So far, there is no viable alternative to the use of antibiotics. No other class of drug has been able to provide the same or similar medical benefits. We can thus not simply switch to an alternative technology or intervention.
- Antibiotics are not only needed to treat acute infections, their availability also affects many other areas of medical care and is for example a precondition for many surgical interventions, where surgical site infections can be reduced by antibiotic prophylaxis.
- Antibiotics are not suited to the distribution in free markets, due to the insufficient consideration for the externalities associated with their use.

- Antibiotics can confer positive externalities, in the case of reducing the risk of infection to others when used against contagious diseases.
- The use of antibiotics results in negative externalities, when this leads to the creation of AMR.
- Antibiotics are only effective against bacterial infections, and offer no benefit at all against other types of infection.
- Using antibiotics can at best restore a previous level of utility or quality of life that the patient enjoyed before developing an infection. The consumption of antibiotics cannot yield additional utility beyond this point.
- Overconsumption of antibiotics is not rational from a cost-benefit perspective, unless it occurs under conditions of uncertainty, where the risks of side effects are pitted against potential benefits, and resistance is an externality that is not only a burden to patient taking the drug but shared across all members of a community.
- While in principle, AMR is reversible over time, if a drug is no longer being used, this may prove to be so difficult in practice that from a policy perspective, it makes sense to think of antibiotic effectiveness as a non-renewable resource. This applies in particular to the case of multi-resistant bacteria against which few drugs remain effective at this point and a switch to alternative drugs is therefore no longer an option.
- Effective antibiotics - unlike other non-renewable resources - will not merely run out at some point. With progressing resistance, there will also be a diminished effectiveness over time. Ceteris paribus, a dose of antibiotics today is likely to have a greater effect than a dose in the future. This fundamentally distinguishes antibiotics from most other resources.
- New antibiotics have so far not been a permanent solution to AMR, and have all displayed diminishing effectiveness over time.

The following diagram represents the last three points graphically:

Diagram 1



Consider the case of two antibiotics A1 and A2, which are used to treat the same condition C. A1 will be introduced first, while A2 is first introduced at a later stage (t_1). A1's long-term effectiveness decreases as bacterial resistance to A1 develops, which happens at an accelerating rate until eventually, A1 is no longer useable to treat C. To be able to continue treating C effectively, A2 is being developed and introduced. The additional antibiotic effectiveness provided by A2 is signified by the shaded light blue area under the curve of A2. Like A1, A2 becomes less effective over time, until resistance is so widespread, that A2 no longer offers a viable treatment option for C. For the purposes of the above diagram, it is assumed that antibiotics are used until they are completely ineffective and that there is no reversal of AMR between the introduction of A1 and the cessation of its use due to ineffectiveness. The slope for *f*A1 and *f*A2 in the above diagram is non-linear to illustrate the diminishing effectiveness over time.

Let us now assume further that a policy of prudent antibiotic use is introduced. This policy extends the effectiveness of A1 and A2 and shifts them to the right, which in the diagram above is represented by curves PA1 and PA2. Prudent use will thus extend effectiveness and delay the time at which a new antibiotic needs to be introduced. With prudent use, the new drug (PA2) will not be introduced at t_1 but at t_2. Yet, the overall slope of antibiotic effectiveness remains negative even with a prudent use policy and both antibiotics will ultimately become ineffective. Thus, prudent use delays the introduction of new drugs against C, but does not render their introduction superfluous. How much the time span of antibiotic effectiveness can be

extended by prudent use will depend on a number of factors, including the levels of AMR at t_1 and the frequency with which bacterial infections that cause C occur.

3.11 Summary

In this chapter, it has been argued that preservation of antibiotic effectiveness - though similar to other distributive problems - poses some unique challenges, which attempts to produce policy solutions by analogical reasoning have so far overlooked. In particular, ethical accounts of AMR need to address the question how to distribute a resource that is vital for the protection of health, but which declines in effectiveness through use. So far, accounts of the fair use of antibiotics both within and across generations have not paid sufficient attention to these specific characteristics, and as a result have often suggested policy solutions, which are unsuitable because they fail to acknowledge the distinctive features of AMR.

Chapter 4: What makes AMR a moral problem? A consequentialist approach

4.1 Consequentialism as the obvious answer?

In light of AMR's potentially catastrophic consequences in the future, it seems obvious to suggest that precisely these consequences also make AMR a moral problem. This suggestion does not yet commit us to any particular moral theory - as Rawls notes, *"[a]ll ethical doctrines worth our attention take consequences into account in judging rightness.*"[214] Yet, when considering consequences of actions as normatively relevant, it makes sense to examine more closely those ethical theories, for which the outcomes of actions matter most. This chapter will therefore discuss how a consequentialist account of AMR could be formulated. Consequentialism subsumes a number of ethical doctrines, which vary quite substantially but share the view that the normative properties of any act are solely determined by that act's consequences.[215] A number of commentators have argued that certain forms of consequentialism - in particular certain types of rule utilitarianism - are particularly well suited as guiding principles for policy-making.[216] William Shaw offers an explanation for this, which is worth quoting in full:

"In the public realm, utilitarianism is particularly compelling. Because of its consequentialist character, a utilitarian approach to public policy requires officials to base their actions, procedures and programs on the most accurate, and detailed understanding they can obtain of the circumstances in which they are operating and the likely results of the alternatives open to them. Realism and empiricism are the hallmarks of a utilitarian orientation, not customary practice, unverified

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[214] Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. p. 30

[215] This is quite a broad definition, however it is not an uncommon one, see e.g. Sinnott-Armstrong, W. (2012). Consequentialism. Stanford Encyclopedia of Philosophy. E. N. Zalta. Stanford.

[216] See e.g. Kenny, N. and M. Giacomini (2005). "Wanted: A New Ethics Field for Health Policy Analysis." Health Care Analysis **13**(4): 247-260. Goodin, R. (1995). Utilitarianism as a Public Philosophy. Cambridge ; Goodin, R. E. (1998). "Public Service Utilitarianism as a Role Responsibility." Utilitas **10**(03): 320-336.

abstractions, or wishful thinking. Promotion of the well-being of all seems to be the appropriate; indeed the only sensible, touchstone for assessing public policies[.]"[217]

Shaw's argument thus views consequentialism as the ideal moral foundation for evidence-based policy-making. Since evidence-based decision making is often considered the gold standard for deciding on public health policy, it may therefore come as little surprise that consequentialist theories have also been promoted as a particularly suitable moral framework in this field.[218] Roberts and Reich have suggested that this is because consequentialism *"captures a critical concern [for public health], namely improving individual wellbeing"* and therefore has a strong intuitive appeal for public health specialists.[219] Others agree, arguing that *"[i]t is easy for [public health] practitioners [...] to adopt utilitarian concepts almost unconsciously."*[220] On such an account, a successful public health measure will usually be one that produces better health outcomes (or prevents worse one) and therefore maximises utility. Mackenbach summarises this view succinctly, when arguing that utilitarianism is *"[a particularly attractive] theory for public health people, because it provides […] a quantitative method for determining what is a good, and what is a wrong decision.*"[221]

Crucially, however, this does not only qualify consequentialist accounts as a moral framework for policy-making. It also distinguishes them from many other moral theories, which do not consider outcomes to be of paramount importance in deciding about the moral worth of an action. As a result, consequentialism has been championed by some as the pragmatic approach to making moral decisions in the public realm. Such a view, as Onora O'Neill notices, will commonly accuse non-consequentialists of ignoring outcomes entirely and merely *"valu[ing] acts for their*

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[217] William H. Shaw, Oxford 1999 (1999). Contemporary Ethics – Taking Account of Utilitarianism. Oxford, Blackwell Publishers. p. 171

[218] For a discussion of the move towards evidence-based public health see e.g. Brownson, R. C., J. E. Fielding, et al. (2009). "Evidence-Based Public Health: A Fundamental Concept for Public Health Practice." Annual Review of Public Health **30**: 175-201. For a good overview of the criticism levelled against evidence-based policy making and its potential for success see Sanderson, I. (2002). "Evaluation, Policy Learning and Evidence-Based Policy Making." Public Administration **80**(1): 1-22.

[219] Roberts, M. J. and M. R. Reich (2002). "Ethical analysis in public health." The Lancet **359**(9311): 1055-1059. p. 1055-6

[220] Stuart Horner, J. (2000). "For debate. The virtuous public health physician." Journal of Public Health **22**(1): 48-53. p. 49

[221] JP Mackenbach, cited in Rauprich, O. (2008). "Utilitarismus oder Kommunitarismus als Grundlage einer Public-Health-Ethik?" Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz **51**(2): 137-150. p. 142

underlying motives or intentions, or for some other internal feature of agents, regardless of results."[222] Consequentialism in turn seems to provide a much more pragmatic moral foundation for policy-making.

Despite its initial plausibility, the view that consequentialism naturally lends itself to decision-making in the public realm has been met with considerable criticism. Stephen Holland has described the view that consequentialism is an obvious moral guiding principle for public health as 'naive'.[223] This 'naivety', he argues, stems from the fact that a maximisation of health (however defined) is also straightforwardly treated as a maximisation of utility and therefore seen as ethically permissible or even obligatory.[224] This rather simplistic view overlooks both practical and moral concerns, which shall next be addressed in more detail.

First, the idea that consequentialism is a suitable moral framework to inform health policy rests on the assumption that we can reliably measure alternative health outcomes and compare them between persons. In other words, any consequentialist account of public health that aims to be convincing and useful in practice must provide a measure, by which we can evaluate and compare policies that generate different kinds of health benefits for different groups of people. There are some clearly defined health outcomes that are easily comparable, for example the number of deaths that result from two different policies. However, less definitive health outcomes will be much harder to compare between different persons. We will return to this point later on in this chapter, but for now it suffices to note that measuring health benefits across persons and comparing health gains for different conditions is a methodology that comes with a number of problems and raises more questions than it answers.

A second point worth noting is that a 'naive' consequentialist account of public health, which seeks to simply maximise health outcomes, may legitimise policies that raise other ethical concerns. As Stephen Holland has observed, such a one-dimensional approach to health care would allow very Draconian health measures, purely based on the premise that the overall expected health benefits that result from

222 O'Neill, O. (2004). "Consequences for Non-consequentialists." Utilitas **16**(01): 1-11. p. 1
223 Holland, S. (2007). Public Health Ethics. Cambridge, Polity Press. p. 10
224 ibid. p. 11 & p. 37

such an approach are positive.[225] To make this point more obvious, Holland imagines a scenario in which outlawing smoking and executing a small number of smokers as a deterrent may be morally permissible, if it reduces the overall prevalence of smoking and thereby also the number of people suffering from smoking-related diseases.

4.2 A case for more sophisticated versions of consequentialism?

While the objections to the 'naive' view of a consequentialist public health ethic are substantial, they do not apply to more sophisticated versions of consequentialism, which may have quite a bit more to say about what makes AMR a moral problem.

To begin with, the majority of consequentialist models, such as the one proposed by William Shaw earlier in this chapter, are sufficiently sophisticated to avoid some of the pitfalls of the 'naive' concept that Holland criticises. They are not simple, hedonistic formulae, but are designed to develop regulations and institutions, which will maximise utility in the long run.[226] This removes some of the tensions between short-term gains and long-term effects of a policy, as it does not commit consequentialists to the maximisation of short-term benefits if these conflict with a general principle or rule that the theory promotes.[227] Such general rules are designed to be utility maximising in the long run, but do not commit consequentialists to endorsing extreme cases like Holland's smoker scenario. Thus, at least some of the criticism of the naive view of consequentialism does not extend to more sophisticated versions.[228] This, however, is not the only reason to reconsider the attractiveness of more advanced versions of consequentialism. Crucially, consequentialist accounts of public health offer a number of advantages, which are highly relevant to the discussion of AMR.

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225 See ibid. p. 12

226 Goodin, R. (1995). Utilitarianism as a Public Philosophy. Cambridge pp. 15-20

227 Sinnott-Armstrong, W. (2012). Consequentialism. Stanford Encyclopedia of Philosophy. E. N. Zalta. Stanford.

228 Note that Holland recognises this point - his critique focuses on the fact that some forms of naive consequentialism may justify questionable policy initatives, and that proponents of naive consequentialism would have to be able to defend them or alternatively amend their position.

4.2.1 Compatibility with current practice of policy-making

A first reason why consequentialism may be an attractive moral framework for considering AMR is that it fits many of the principles, which underline health policy-making. To begin with, it is not only compatible with policies that focus on cost-effective use of resources (which in most health care systems is a crucial consideration for any policy), but actively promotes their use. Cost-Effectiveness Analysis (CEA) is not in itself a moral theory but it is based on a principle of utility maximisation, which seeks to generate the greatest return on investment. More specifically, CEA is an economic tool to determine optimal rates of expenditure, which seeks to spend only up to the point where the marginal cost of a good is equal to the marginal benefit that it provides. This way, only goods for which benefits are at least as great as ensuing costs should be financed.[229] Under conditions of scarcity, CEA can help to reduce wasteful (i.e. cost-inefficient) spending and is thus a method of using public funds to greater effect. A case in point is that CEA would rule out the overuse of antibiotics, as their prescription against e.g. viral infections, which cannot be treated with antibiotics, is clearly not cost-effective. Similarly, if AMR creates high costs in the long-run then CEA may require that we dedicate more resources to fighting its effects today.[230] Of course, opponents may argue that we are not bound to accept CEA as a guiding principle - and therefore consequentialism is not a logical fit for policy-making either. Yet, the current practice of (health) policy-making nonetheless relies quite heavily on cost-effectiveness measurements for resource allocation and this would be supported by a consequentialist normative framework.

4.2.2 The ability to trade off benefits between groups of people

A second problem, which consequentialist theories can account for, is the trade-off between claims of different groups of people. Containing infections may necessitate the restriction of individual liberty to prevent harm to a greater number or the distribution of scarce resources, which can benefit different groups of people.[231] Pandemic vaccination strategies often aim explicitly at minimising any adverse

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229 Culyer, A. J. and A. Maynard (1997). Being Reasonable About The Economics of Health, Cheltenham. p. 26

230 Though, as we shall see in chapter 8 this will depend on whether future benefits are discounted, and if so, at what rate.

231 Selgelid, M. J. (2009). "Pandethics." Public Health **123**(3): 255-259.

health outcomes, while maximising improvements of the public's health.[232] Similarly, regulation to enforce social distancing of contagious patients seems to be built around the assumption that the wellbeing of the population at large outweighs the restrictions to personal freedom of the detainee.[233] In these scenarios, an approach that focuses on saving the most lives seems to be ethically sound and should even be acceptable to many non-consequentialists.[234] This method of aggregating wellbeing has been cited as one of the key advantages of consequentialist frameworks for policy-making.[235]

Opponents of consequentialism commonly cite its inability to account for what Rawls has termed 'the separateness of persons' as one of the theories major shortcomings.[236] Rawls argues that consequentialists deem what is a rational choice for an individual (namely to maximise personal utility given the choices he has) to also be a governing principle for fair distribution within a society.[237] In doing so, consequentialists treat interpersonal distributive principles in the same way as intrapersonal ones and thereby risk different personal interests being conflated into one.[238] Thus, while consequentialism can indeed aggregate individual interests, it does so not by taking account of each individual's rights or claim to a certain outcome, but merely maximises societal utility levels. As a result, consequentialist and utilitarian theories have widely been dismissed as being unable to provide a coherent account of distributive justice.[239]

However, by insisting on the separateness of individual persons and thereby ruling out any straightforward aggregation of wellbeing across persons, non-consequentialist have often struggled with situations in which decisions about saving

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232 Littmann, J. (2013). Distributing vaccine fairly during influenza pandemics - a case study from Berlin. Ethics in Public Health and Health Policy: Concepts, Methods, Case Studies. I. Hirschfeld and D. Strech. Hannover, Springer**:** 175-191. p. 178

233 Krom, A. (2011). "The Harm Principle as a mid-level principle? Three problems from the context of infectious disease control." Bioethics **25**(8): 437-444.

234 Verweij, M. (2009). "Moral Principles for Allocating Scarce Medical Resources in an Influenza Pandemic." J Bioeth Inq **6**(2): 159-169. p. 168

235 Liao, S. M. (2008). "Who Is Afraid of Numbers?" Utilitas **20**(04): 447-461. p. 447-449

236 The argument for the separateness of persons was first made by Rawls in Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. pp. 22-27

237 ibid. p. 24

238 Shoemaker, D. (2012). Personal Identity and Ethics. Stanford Encyclopedia of Philosophy. E. N. Zalta. Stanford.

239 Voorhoeve, A. and M. Fleurbaey (2012). "Egalitarianism and the Separateness of Persons." Utilitas **24**: 381-398. p. 382

one of two differently sized groups have to be made. A case in point is John Taurek's account of number-scepticism, which challenges the idea that saving a larger group of people is always preferable.[240] Taurek rejects consequentialist theories because he believes that rather than to explain *how* the harm to greater number is worse, consequentialism merely asserts it as a factual truth.[241] Few have followed Taurek's argument for the complete rejection of the moral relevance of saving the greater number, yet the difficulty in making a non-consequentialist case for saving the greater number remains. Moreover, while a number of non-consequentialist alternatives have been suggested, none is quite as simple and definitive as the consequentialist account.[242]

4.2.3 Accounting for the interests of future persons

Another argument in favour of employing consequentialist theories to examine the moral implications of AMR is related to the previous point, and while it will be explored in detail in later chapters, it shall briefly be mentioned here as well. Consequentialism's dismissal of the separateness of persons enables it to take into account the interest of future persons who do not yet exist. We shall see in chapter 8 that for ethical theories, which focus on individual rights or the concept of reciprocity, the interests of future persons are much harder to take into consideration because their present non-existence complicates the formulation of notions of mutual respect or shared interests. Since, as we have already seen, consequentialism is not concerned with any specific individual or how benefits are distributed between different persons (so long as the overall benefits are maximised), it matters less to the consequentialist, whether persons already exist or not.

4.3 The problems that remain: the case against consequentialism

While the naive view of a consequentialist approach to public health and infectious disease policy is unconvincing, approaches that are more sophisticated seem to offer distinct benefits, such as the ability to aggregate interests and thus make coherent

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240 Taurek, J. M. (1977). "Should the Numbers Count?" Philosophy & Public Affairs **6**(4): 293-316.

241 ibid. p. 304

242 Wasserman, D. and A. Strudler (2003). "Can a Nonconsequentialist Count Lives?" Ibid. **31**(1): 71-94. p.73

decisions about the protection of the greater number of persons. As we have seen, even many non-consequentialists can agree that this is a reasonable goal of infectious disease policy. However, in spite of the benefits of a consequentialist account, which were expounded in the previous section, at least three significant problems remain. These pertain to 1) the method of measuring health outcomes, 2) the uncertainty of future outcomes and 3) the fact that consequentialism does not recognise individual rights claims. We shall next consider each of them in turn.

4.3.1 The first remaining problem: measuring health outcomes

One of the most obvious problems that a consequentialist justification of public health policies will encounter is that the measurement of health outcomes across different persons is a highly complex process and fraught with difficulties. Over the past decades, the measurement of health outcomes has shifted towards the use of multi-dimensional parameters, instead of merely focussing on single-value measures such as life expectancy or five-year survival rates.[243] The most common multidimensional measuring tools are Quality or Disability adjusted Life Years (QALYs or DALYs respectively), which combine life expectancy with a measure of life quality or disease burden.[244] The advantage of these measurements over single-value parameters is their ability to better reflect the complexity of determining the health status of a patient. However, a reliance on QALYs and DALYs creates two worries. First, there are legitimate concerns about the accuracy of such measures. For example, it may not always be possible to incorporate all relevant aspects of a person's health status into a general measurement of health.[245] What weighs more heavily than these technical difficulties, however, is the second worry, namely that the use of QALYs and DALYs leads to the systematic discrimination of certain social groups, as exemplified by the problems of 'ageism' and 'double jeopardy' respectively. These problems arise in circumstances where the ability of a person to achieve a high QALY score upon recovery is reduced by old age or an already low quality of life. Both of these problems challenge the assumption of distributive neutrality on which the QALY approach builds and which is central to their use in

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243 Nord, E. (1999). Cost-Value Analysis in Health Care. Cambridge, Cambridge University Press. p. 18

244 Cubbon, J. (1991). "The principle of QALY maximisation as the basis for allocating health care resources." Journal of Medical Ethics **17**(4): 181-184.

245 For a comprehensive account of the problems of QALY measurement see Nord, E. (1999). Cost-Value Analysis in Health Care. Cambridge, Cambridge University Press.

policy-making.[246] Distributive neutrality presupposes that society is indifferent between who receives treatment, and that societal concern for health is merely the sum of individual health benefits.[247] As outlined earlier, this supposed impartiality between who receives a treatment is often cited as a strength of consequentialism in the area of policy-making; by focussing on outcomes rather than recipients, policy makers do not favour certain social groups, they merely focus on creating the greatest positive impact. Yet, as the following sections will illustrate, this argument is much less convincing if the preferred method of measurement systematically discriminates some social groups.

Ageism is a phenomenon that has been widely discussed in the literature on consequentialist allocation models of health care resources and QALYs.[248] The term describes the systematic disadvantage that old people face when receiving scarce health care resources if these are distributed according to QALY scores. Since older people have a lower remaining life expectancy, they are automatically unable to derive high QALY scores from any medical treatment or intervention.
In the context of fair resource allocation in health care, double jeopardy describes a concern, which is related to that of ageism. Specifically, the concern is that people who suffer a chronic condition will be unable to attain the same level of health as a person not afflicted by this long-standing condition. Consequently, if a scarce resource had to be distributed between the two individuals based on the expected QALY score it produces, the healthy person would be prioritized, as this would yield more QALYs. [249]

Some commentators simply accept the inherent bias of QALYs as an unfortunate side effect.[250] Others have tried to offer more sophisticated justifications for prioritising younger patients, by claiming that we should aim to create conditions where everyone's chances to reach roughly an average life expectancy should be

246 ibid., pp. 22 ff
247 ibid. Cubbon, J. (1991). "The principle of QALY maximisation as the basis for allocating health care resources." Journal of Medical Ethics **17**(4): 181-184.
248 See e.g. Daniels, N. (2009). Just Health: Meeting Health Needs Fairly. Cambridge, MA. Chapter 5 Kuhse, H. and P. Singer (1988). "Age and the Allocation of Medical Resources." Journal of Medicine and Philosophy **13**(1): 101-116.
249 Singer, P., J. McKie, et al. (1995). "Double jeopardy and the use of QALYs in health care allocation." Journal of Medical Ethics **21**: 144-150.
250 e.g. Cubbon, J. (1991). "The principle of QALY maximisation as the basis for allocating health care resources." Ibid. **17**(4): 181-184.

given priority over helping those who have already lived a long life. This position is commonly referred to as the 'fair innings' argument.[251] We need not solve this discussion here.[252] For our purposes, it suffices to note that currently we do not have an ethically neutral methodology for allocating resources based on health outcomes.

4.3.2 The second remaining problem: decision-making under uncertainty

Let us recall William Shaw's quote cited earlier, in which he suggested that "*[r]ealism and empiricism are the hallmarks of a utilitarian orientation, not customary practice, unverified abstractions, or wishful thinking."*[253] Shaw's argument in favour of consequentialism also points to one of its greatest weaknesses - the reliance on knowledge about what *will* happen. However, most policies are made under conditions of uncertainty. For obvious reasons, it is difficult to be concrete about what the world will look like in two years, let alone in twenty years, policies will therefore always have to be formulated under conditions of uncertainty. Arguably, this is a concern not only for consequentialist theories, but also for any kind of moral theory, which, in deliberating the morally right way of action, takes into account the consequences. However, if a moral theory rests exclusively on the ability to compare different outcomes and rank their moral desirability by the utility they produce, significant uncertainty about what can reasonably be expected as an outcome presents a particularly serious obstacle.

The case of AMR presents a particular challenge in this respect, as the development of drug resistance is not a linear process, which can easily be mapped out and predicted. The spread of extensively drug-resistant bacteria for example will at least in part be down to chance and depend on the place of origin, the mode of transmission, the availability of suitable vectors and the effectiveness of monitoring systems that can alert health authorities in time. In chapter 2, it was already outlined that uncertainty surrounding AMR complicates the use of cost-benefit analysis to determine appropriate expenditure on policies to slow down or reverse drug

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[251] Nord, E. (2005). "Concerns for the worse off: fair innings versus severity." Social Science & Medicine **60**(2): 257-263.
For a substantial critique of the double jeopardy argument see J. McKie et al, *The Allocation of Health Resources*, Chapters 3&5

[252] For a good and more comprehensive discussion of quality of life metrics see e.g. Phillips, D. (2006). Quality of Life: Concept, Policy and Practice. Abingdon, Routledge.

[253] William H. Shaw, Oxford 1999 (1999). Contemporary Ethics – Taking Account of Utilitarianism. Oxford, Blackwell Publishers. p. 171

resistance. This same problem also applies to the moral evaluation of future costs and benefits. While at first sight, consequentialism and its ability to trade off utility gains (or losses) between different groups seems to lend itself well to the project of establishing how antibiotics can be fairly used between persons and generations, this presupposes at least some level of knowledge about the size of future utility gains. Where such knowledge is not available, it would appear that the supposed advantage of consequentialism as an empirical normative concept, as Shaw called it, does not apply.

Consequentialists may respond to this that, ultimately, they do not need to know the exact outcome of a path of action, as long as it is reasonably likely that one will produce considerable better outcomes than another. For instance, we may be unable to calculate the utility loss to the present generation if access to antibiotics is severely restricted, or the precise utility gains that the resulting preservation of antibiotic effectiveness may yield in the future. However, if we are reasonably certain that future gains will be very substantial (or, alternatively that inaction will lead to enormous costs), we would have a good enough reason to act, since consequentialism merely proposes that utility should be maximised, even if the precise magnitude of that utility gain is not know ex ante. This argument is strongest in the case of rule utilitarianism, where merely the general principle (as opposed to an individual action) must be utility-maximising.[254]

Again, however, this kind of argument seems a long way from any claim that consequentialism provides an 'empirical' basis for policy-making, especially in light of the fact that even general principles of utility maximisation may be difficult if not impossible to formulate under sufficiently severe uncertainty. The true effects of a post-antibiotic era are impossible to calculate - but so are the odds of technological progress to replace existing drugs or the development of other medical procedures, which make the use of antimicrobials obsolete.

[254] Seee e.g. Ball, S. (1990). "Uncertainty in moral theory: An epistemic defense of rule-utilitarian liberties." Theory and Decision **29**(2): 133-160.

4.3.3 The third remaining problem: consequentialism and individual rights

A commonly raised objection to consequentialism is that it does not recognise individual rights as relevant at all, which leads to implausible normative suggestions. Philippa Foot's well-known example of the enforced organ donation nicely illustrates this problem; a healthy patient who has come to hospital for a routine check is coincidentally found to be an exact match as organ donor for five terminally ill patients in the same hospital. These patients have no alternative way of receiving an organ and will die very soon. Leaving issues of legality aside, Foot raises the question, whether or not it is morally permissible to kill the patient who came for a routine check-up to save five lives by sacrificing his.[255] As Michael Otsuka has observed, in these instances consequentialism often ends up promoting 'the wrong answer' and either has to bite the bullet by endorsing counter-intuitive actions (as illustrated for example by Foot's case of organ transplantation) or forego consistency.[256] And while more sophisticated versions of consequentialism, such as rule-utilitarianism, are capable of formulating general principles that appear very similar to rights, they are not grounded in the recognition that there are some things we simply must not do to an individual (or, conversely, have a duty to do). Instead, they are merely supposed to maximise utility in the long-run.[257] These theories are therefore incommensurable with any notion of patient rights or even a particular concern with the wellbeing of a specific individual. The last point in particular makes consequentialism an unattractive concept for health policy, as it does not show any concern with individuals. And while the approach claims impartiality, we have seen that it may overlook those that are particularly vulnerable and in need of help.

4.4 Consequentialism and AMR - not such an obvious match after all

From what we have seen so far, consequentialism's ability to aggregate utility across persons and its strong focus on outcomes make the approach a promising candidate for providing a moral account of infectious disease policy. In this field, and particularly in the control of AMR, trade-offs between the interests of different groups appear unavoidable and consequentialism offers a coherent account of how to

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[255] Foot, P. (1967). "The Problem of Abortion and the Doctrine of Double Effect." Oxford Review **5**: 5-15.

[256] Otsuka, M. (2006). "Saving Lives, Moral Theory, and the Claims of Individuals." Philosophy & Public Affairs **34**(2): 109-135. p. 109-110

[257] We will return to this argument in greater detail in Chapter 6.1

make these decisions. However, it is also important to note that citing consequentialism's congruence with current health policy as an argument in its favour risks getting the argument backwards. After all, a moral theory should be adopted because of its persuasiveness or coherence, not merely due to the extent to which it explains or justifies current policies. It may indeed be true that, as Stuart Horner argues, many public health practitioners subconsciously make decisions that follow some sort of consequentialist calculus.[258] Yet, while this may explain the partial fit between theory and current practice, it does not provide an argument, *why* we should endorse consequentialism in the first place.

Nonetheless, what this chapter has shown is that some issues which are easier to explain for consequentialist than for non-consequentialist theories will have to be accounted for in any normative examination of AMR. As we have seen, non-consequentialists who believe that saving the greater number is morally warranted, may find it more difficult to make this claim than consequentialists do.[259] However, this added difficulty seems insufficient as an argument for endorsing a consequentialist perspective, especially in light of its significant limitations.

The argument presented in this chapter does not amount to a refutation of consequentialism, nor does it rule out its application to the case of AMR. What the discussion in this chapter has shown is that despite its apparent (often self-proclaimed) suitability as normative framework for policy-making, consequentialism has to deal with a host of problems and inconsistencies. These problems need not be worse than the ones faced by the alternative theories discussed in this thesis. However, they should cast doubt on the assumption that consequentialism is an obvious candidate for the ethical analysis of AMR. In the following chapters, we will therefore examine alternative approaches to explain the moral relevance of AMR. To start with, this will require a more detailed look at the concepts of harm and risk which are employed in this context.

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[258] Stuart Horner, J. (2000). "For debate. The virtuous public health physician." Journal of Public Health **22**(1): 48-53.

[259] The term 'pro-number non-consequentialists' was introduces by Liao, S. M. (2008). "Who Is Afraid of Numbers?" Utilitas **20**(04): 447-461. p. 447

Chapter 5: AMR and Wrongful Harm

In the previous chapter, we saw that there are significant problems with using consequentialism for the purposes of guiding AMR policy, especially in light of the uncertainty surrounding the future consequences of AMR. This worry does not solely apply to consequentialism; the problem of uncertainty will also affect other normative theories, which care about the consequences of a proposed policy. However, we also saw that there is a more fundamental normative worry about consequentialism, namely its focus on reducing harm and improving consequences *in the aggregate*. This approach looks to be insufficiently attentive to the moral claims and moral standing of individuals.

The next four chapters (5-8) therefore aim to work out what a viable approach to AMR policy, which takes the claims of individuals seriously, would look like. The starting point for this analysis will be the idea that AMR policy should, in the first instance, focus on ensuring that individuals are not wronged. This view departs from the consequentialist approach, which merely looks to reduce the overall harm caused by AMR. The main point of chapter 5 is to clarify the idea of wrongful harm, in the context of AMR. The chapter examines both, the concept of harm, and the kinds of harm caused by AMR that are morally wrongful. The chapter then discusses two facets of the idea of harm that might prima facie make a difference to whether a harm is wrongful: the causation of harm, and the scale of harm. It will be argued that only harms with certain kinds of human cause can be wrongful, and that there is no minimum size of harm that can be considered wrongful. Moreover, arguments for thinking that risk imposition can be harmful in the absence of any awareness of the risk, or any other adverse consequences, are rejected.

Chapters 6 and 7 look at different attempts to explain and to justify - from the perspective of rights theory, and contractualism - how AMR could be responsible for wrongful harm to individuals. It will be argued that for various reasons, the contractualist approach seems to be a superior way of explaining and justifying both, why AMR can wrong individuals and under what circumstances it will do so.
Chapter 8 considers an additional complication posed for AMR policy, namely the question of intergenerational justice, and examines this both from the perspective of

consequentialism and contractualism respectively. Consequentialism is reconsidered, because when considering how policy should be formed for generations of individuals who have not yet been born, its weaknesses in attending to the moral claims of currently existing individuals become something closer to a strength.
We shall begin this discussion by considering in detail what harms are caused by AMR and which kinds of harm can be considered to be morally wrongful.

5.1 What is a harm in the context of AMR and why should we consider it?

The concept of harm in public health ethics has received attention from a number of commentators, primarily in relation to J.S. Mill's discussion of the restriction of individual liberty.[260] In what is perhaps the most widely cited principle of establishing limits to personal freedom, Mill writes that

"[t]he only purpose for which power can be rightfully exercised over any member of a civilised community, against his will, is to prevent harm to others. His own good, either physical or moral is not a sufficient warrant."[261]

Originally conceived as a principle to govern the limits of criminal law, the harm principle has found widespread application in public health. Its appeal is that it appears to clearly delineate the limits of right trade-offs between people.[262] While not a definitive benchmark for the moral permissibility of an action, it has often been used to justify a given course of action in public health policy.[263] It should be noted that the harm principle is by no means an uncontested approach to regulating health policy and some public health measures that are widely used clearly conflict with it. For example, regulations enforcing the use of motorcycle helmets or seatbelts are primarily designed to protect the people on whom the restriction of liberty is

[260] See e.g. Krom, A. (2011). "The Harm Principle as a mid-level principle? Three problems from the context of infectious disease control." Bioethics **25**(8): 437-444. Powers, M., R. Faden, et al. (2012). "Liberty, Mill and the Framework of Public Health Ethics." Public Health Ethics **5**(1): 6-15.
[261] Mill, J. S. (1989). On Liberty and Other Writings. Cambridge, Cambridge University Press. p. 13
[262] Holland, S. (2007). Public Health Ethics. Cambridge, Polity Press.
[263] Upshur, R. (2002). "Principles for the justification of public health intervention." Can J Public Health **93**: 101 - 103. Holland, S. (2007). Public Health Ethics. Cambridge, Polity Press. p. 54

placed.[264] The harm principle has often been applied to the case of infectious disease control, especially when deliberating how individual liberty can be curtailed to reduce the chances of transmission of communicable diseases.[265] In this chapter, however, a broader concept of harm will be explored. Instead of focussing merely on the trade-offs of liberty to prevent harm, we shall explore, what exactly constitutes a morally wrongful harm, and how this notion can be applied to the case of AMR. The chapter consists of two parts. The first will discuss the concept of morally wrongful harm in relation to AMR. The second part will then examine, if the additional risk that AMR creates can be viewed as a harm in itself.

5.2 Defining harm

The concept of harm is often only defined in very general terms, which may be partly due to the fact that the term is used widely and in very different contexts in everyday language. As Shiffrin has observed, many of these uses reduce harm to *"notions of mere loss, damage, or opportunity costs"*, which do not always describe morally problematic cases.[266] Thus, in many instances, 'harm' will simply refer to situations of *"nonwrongful setbacks to interests, or harms that are no wrongs"*, as Feinberg notes.[267] Such 'harms that are no wrongs' include for example some forms of damage to persons that are caused by natural catastrophes (although we shall see later that this does by no means have to apply to all such instances).[268] Another example of a non-wrongful harm is to lose in a fair competition, which the participant voluntarily entered. In these instances, a person will experience setbacks to their interests, but these setbacks do not generate any moral claims. This more descriptive use of 'harm' is also reflected in parts of the medical literature, where the term has frequently been

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[264] Gostin, L. O. (2008). Public Health. From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns. M. Crowley. Garrison, NY, The Hastings Center**:** 143-146.

[265] Battin, M. P., L. P. Francis, et al. (2009). The Patient as Victim and Vector: Ethics and Infectious Disease. New York, Oxford University Press. Krom, A. (2011). "The Harm Principle as a mid-level principle? Three problems from the context of infectious disease control." Bioethics **25**(8): 437-444.

[266] Shiffrin, S. V. (2012). "Harm and its moral significance." Legal Theory **18**(Special Issue 03): 357-398.
p. 359

[267] Feinberg, J. (1986). "Wrongful Life and the Counterfactual Element in Harming." Social Philosophy and Policy **4**(01): 145-178. p. 146

[268] ibid.

used interchangeably with related concepts such as 'adverse event' and 'injury'.[269] However, the resulting lack of clarity of what it means to 'harm' a person has also made it difficult to develop a common understanding of what it is that health care professionals and policy makers are trying to prevent.[270]

In this chapter, the focus will be on harms that are also *moral* wrongs or - to adapt Feinberg's terminology - wrongful setbacks to interests. More specifically, it will be considered to what extent the emergence and spread of AMR can be said to constitute a morally wrongful harm. This discussion requires two clarifications. First, we will have to distinguish between human and natural causes of harm. Secondly, we must develop an account of what exactly makes a harm morally wrongful.

5.2.1 Causes of harm: natural versus man-made

Brooks has pointed out that we tend to distinguish between harms caused by humans, and those caused by nature. As an example, he points out that a person who is hit by lightning is harmed in a physical but not a morally wrongful way, since the occurrence of lightning is neither controlled nor influenced by other persons.[271] Such a view is also supported by Feinberg's formulation of harm. According to Feinberg, morally wrongful harm has two distinct components. It must:

1) lead to some kind of adverse effect on the victim's interest (or create a risk of such an effect occurring) and
2) be inflicted wrongfully, and violate the victim's rights.[272]

While 1) could apply to natural causes of harm, 2) presupposes some greater level of human agency.[273] Yet, in practice, it may actually be difficult to distinguish between natural and man-made causes of harm. Consider an instance where a poorly

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[269] Parry, G., A. Cline, et al. (2012). "Deciphering harm measurement." JAMA **307**(20): 2155-2156.

[270] Nabhan, M., T. Elraiyah, et al. (2012). "What is preventable harm in healthcare? A systematic review of definitions." BMC Health Services Research **12**(128).

[271] Brooks, T. (2012). "Climate Change and Negative Duties." Politics **32**(1): 1-9.

[272] Feinberg, J. (1986). "Wrongful Life and the Counterfactual Element in Harming." Social Philosophy and Policy **4**(01): 145-178. We will discuss the aspect of rights violation in more detail in the following chapter.

[273] This is at least implied, unless one wishes to argue that non-human agents or natural events can 'act wrongfully' or have a duty to respect the victim's rights. I will here assume that this is not the case.

constructed building, which fails to meet basic safety regulations, collapses in an earthquake, thereby killing all its inhabitants. While the trigger of this event was a natural phenomenon, namely the movement of tectonic plates, the collapse of the building could have been averted if existing building standards had been met. Since many harmful situations could be averted or mitigated by better preparation, one therefore has to be careful in distinguishing properly between those kinds of harm, which are genuinely the result of natural causes and those, which also contain an element of human (in-)action and would meet the second component of morally wrongful harm as defined by Feinberg.

In light of this difficulty, an account of morally wrongful harm that is caused by AMR will have to be very clear about which aspects of such harm can be assigned to natural causes, and which are the result of human agency. For example, dying from an infectious disease certainly constitutes a case of being harmed by a pathogen. Yet, as will be discussed below, we may have to say a bit more about whether it also follows that the person has been wronged in the process. To make this point more obvious, consider two cases, Albert and Barry.

Albert

Albert likes to spend his holidays in remote locations - the fewer people he encounters, and the further away he is from civilization, the better. On one occasion, while out travelling in the wilderness, Albert hits his knee, the wound becomes infected and Albert develops sepsis. Because he cannot get himself to a hospital quickly, Albert dies from the bloodstream infection that could have otherwise been treated.

Barry

At the gym, Barry hits his head and starts to bleed. Using a sweaty towel to cover the little cut, Barry goes home. The wound becomes infected with a particularly virulent type of community-acquired MRSA. Barry gets worse and is sent to hospital, where he is put on antibiotics. Because of the drug resistance, he does not respond to the initial treatment and shortly after succumbs to the infection.

Both Albert and Barry die from a bacterial bloodstream infection and are thus both at the very least harmed in the descriptive sense that they are now significantly worse off. However, in one of the two cases, it is more difficult to see, how this harm could be viewed as wrongful. Albert's death is the result of a personal choice to go to a remote location, without access to medical services. He could have been helped, had he been elsewhere, but he chose to travel in a remote area and - let us assume - knew the risks involved in distancing himself so far from civilization. Consequently, the harm that Albert experienced is not morally wrongful. The existence of bacteria is not controlled by humans, so Albert could not reasonably expect to be in a bacteria-free environment (similarly, as we shall see in a bit, neither could Barry).

It should be noted that this argument only pertains to the specific case of Albert, and not all cases, in which there is insufficient infrastructure to provide help. What makes the claim that Albert was not wronged plausible is that he actively sought to distance himself from civilization for the duration of the holiday. As a result, he could not reasonably expect to be rescued. In many other instances, however, lack of access to health care should be viewed as a wrong. Think of a different scenario, where Albert (2) was living in a rural area, in which few resources had been invested into establishing emergency services. If Albert (2), who did not choose to be away from all amenities of society in the same way as Albert (1) when he fell ill, we might very well think of his condition as one in which he was wrongfully harmed. If we accept that in Albert's particular situation, the infection he acquired was harmful, but that no wrong was committed, we still need to examine whether Barry's case is different. Unlike Albert, Barry found himself in a setting where help was available, and he sought it accordingly. Yet, due to the fact that he had acquired a drug-resistant infection, and the initial treatment failed to work, Barry was unable to receive the initial help he needed.

Does this mean that Barry has been morally wronged? It has already been suggested that accidentally acquiring a bacterial infection does <u>not</u> generally amount to being wronged.[274] Thus, if we want to identify a way in which Barry has been wronged, we must look elsewhere. A more promising approach could instead start from the

[274] There may be a few exceptions to this – for example it appears reasonable to suggest that patients in an aseptic environment such as an operating theatre are wronged, if they contract a bacterial infection

premise that AMR diminishes the availability of a scare resource (namely effective antibiotics). This circumstance could be viewed as one in which Barry is morally wronged, if his expectation of benefitting from this resource could no longer be met, because it was wasted or mismanaged. Whether there is any wrongdoing in Barry's case will therefore depend on the question if the resource that Barry can no longer use has in fact been previously mismanaged or wasted. Determining if is the case will not be a simple judgement to make and depends on what kind of knowledge, resources and constraints the managers of the resource had in the past. But, as chapter 2 outlined, the causes for the emergence of AMR (and the consequences of current drug use) have been well documented for a long time. Moreover, we already saw that there is broad consensus among experts that antibiotics are being used wastefully and excessively. This would suggest that it is possible to develop an argument according to which Barry has indeed been wronged.

There are thus a number of differences between the harm caused in Albert's and Barry's case. To begin with, Barry's death was (at least to some extent) the result of human action. While AMR can occur naturally, current rates of MRSA, and its spread in the community are largely the result of past prescribing practice and use of antibiotics.[275] Albert, on the other hand, fell victim to what - for the purposes of this argument - we might call a 'natural' infection. Moreover, due to his own choices there was no help available to him. By contrast, Barry's death from MRSA was the result of previous use of antimicrobial drugs, which rendered some bacteria resistant, and made their treatment more difficult or even altogether impossible.

From what has so far been proposed, we cannot conclude, however, that all infections caused by drug-resistant bacteria necessarily constitute cases of morally wrongful harm. After all, some forms of drug resistance have occurred naturally for millions of years. [276] Yet, it will here be argued that at least in those instances, where we can reasonably assume that the prevailing level of AMR is a direct result of

[275] Navarro, M. H., B; Harbarth, S (2008). "Methicillin-resistant Staphylococcus aureus control in the 21st century: beyond the acute care hospital." Current Opinion in Infectious Diseases **21**: 372-379, Moellering, R. C. (2012). "MRSA: The first half century." Journal of Antimicrobial Chemotherapy **67**(1): 4-11.

[276] Martinez, J. L. (2008). "Antibiotics and Antibiotic Resistance Genes in Natural Environments." Science **321**: 365-367.

previous antibiotic use, the ensuing harm is also morally wrong.[277] Barry's case seems to constitute such a case.

Albert's and Barry's cases also underline the importance of distinguishing clearly what kinds of human agency we wish to consider as contributing factors to a morally wrongful harm. The mere assertion that a harm is (partially) man-made may not be enough to establish whether a harm can be legitimately seen as morally wrongful.
For instance, to say that a harm is man-made does not have to imply that responsibility-carrying acts figure among the most proximate causes.[278] This is to say that in many instances, even for a man-made harm, it will be impossible to identify the people who are directly responsible for the outcome. No one infected Barry directly with MRSA, he merely contracted it because of a small skin wound. Considering his case a 'man-made' health problem therefore presupposes that in doing so, we will not only take into account direct causal link of disease contraction (in which other persons only played a role as unknowing vectors), but also wider social, political and medical factors that contributed to the emergence of this particular type of infection.
Doing so offers a more complete picture of responsibility for the emergence of AMR, but it also raises a question about limits to responsibility. To illustrate this point, let us briefly reconsider the previous example of the structurally weak building that collapses during an earthquake. We may view the harm caused in this instance to be man-made on a number of different levels: Policy makers who allowed buildings to be erected in an area with high tectonic activity might be blamed. However, so could the building company that did not meet the required safety standards, or the council that failed to ensure that standards were met. Which of these levels to consider and what consequences to draw from it, are questions that the mere assertion of a man-made problem cannot answer. Similarly, if we call AMR a man-made problem, we may wish to say more about who did actually create it.

[277] One potential argument against this distinction is that it may be impossible to clearly establish, which kinds of AMR are actually morally wrongful, since it will be difficult to prove that a certain strain of drug-resistant bacteria is the result of previous antibiotic use. However, while this may be true for a small number of instances, the majority of multi- and extensively drug-resistant infections can quite clearly be linked to previous antibiotic use via available epidemiological and statistical data.
[278] I owe this observation to a discussion with Frej Klem Thomsen

5.2.2 Harmed by whom?

Since our definition of morally wrongful harm rests on the assumption that such harm is in some way caused by human agents, the case of AMR presents a challenge. To be sure, as chapter two illustrated already, there is overwhelming scientific evidence that despite the natural occurrence of AMR before the invention of antimicrobial drugs, current levels of AMR are largely the result of their excessive use. Yet, despite this knowledge it is difficult to ascertain who (if anyone) bears the responsibility for the harm caused by AMR today. This is primarily due to the fact that the number of people who contributed to current levels of AMR by mis- or overusing antibiotics is extraordinarily large. However, it is not only the large number of actors that complicates an assessment of who is responsible for the harm caused by AMR. Discussing the case of climate change, which - in this respect - resembles that of AMR, Sinnott-Armstrong has pointed out that establishing personal responsibility for contributing to large-scale social, or health problems is rendered almost impossible because the actions of each individual are neither sufficient nor necessary to produce the resulting harm.[279] This observation would also appear to apply to the emergence of AMR. One individual's misuse of antibiotics does not make any perceptible difference in the emergence of AMR as a large-scale health problem, nor is this individual's use of antibiotics a necessary condition for the emergence of AMR. Had one person in the past not been given antibiotics, this would most likely not have had any measurable impact on the size and characteristics of today's challenge. Thus, while in principle the contributors to the problem can be identified, this does not mean that their actions satisfy the criteria for morally wrongful harming, as outlined above, at least not on an *individual* level.

This distinction may appear somewhat artificial. After all, it could be argued, if we collectively contributed to the status quo, we are also collectively responsible for bringing it about in the first place, even if individual responsibility cannot be calculated. Yet, for the purposes of our discussion, the observation that personal contributions to AMR are so negligible that they cannot reliably be calculated amounts to more than mere semantics. At the very least, it suggests that the harm principle is unsuited to legitimise restrictive antibiotic usage polices. To see why this

[279] Sinnott-Armstrong, W. (2010). It's not my fault: Global warming and individual moral obligations. Climate Ethics. S. M. Gardiner, S. Caney, D. Jamieson and H. Shue. New York, Oxford University Press. p. 335

is the case, recall Mill's formulation of the harm principle, which states that individual liberty can only be curtailed, "*to prevent harm to others*".[280] However, if there is no clear causal link between the individual's misuse of antibiotics and some future harm caused by AMR, it stands to question, how collective responsibility can justify specific restrictions of personal liberty. This point is exacerbated by the fact that AMR can also result from antimicrobial usage, which follows best practice and takes all precautions to avoid resistance (albeit at much lower rates than currently observable). Consequently, when we consider those who are adversely affected by AMR to be harmed in a morally wrongful way, we cannot limit the discussion to instances of obvious misuse of antibiotics (which are at the centre of attention of current 'prudent use' policies). We will have to consider all cases of antibiotic usage, clinically justified or not.

5.2.3 What counts as harm? AMR and the minimal threshold problem

So far, it has been argued that the use of antibiotics will lead to an increase of drug-resistant bacteria and that the subjection to an infection, which has become resistant to antibiotics due to our previous use of them may constitute a morally wrongful harm. Yet, there is a problem of defining who has responsibility for causing this harm. If an individual's contribution to overall rates of AMR is indeed negligible, and if the (mis-)use of antibiotics by any one person is neither necessary nor sufficient to create a measurable increase in AMR, then the question arises, if the actions of anyone can properly be classed as causing harm to others. One objection to this suggestion is that even if we cannot measure the direct causal pathway, this does not mean that it does not exist. According to this argument, while such a causal link may be weak, and the overall effect of each individual's (mis-)use of antibiotics on the emergence of AMR is too small to be reliably measured, we know in principle that it exists. This, however, raises another question, namely whether we need to establish a minimum level of harm that can count as morally wrongful. Let us call this the minimal threshold problem. When invoking any argument, which relies on the measurement of wellbeing and harm, we must be clear about when an adverse effect becomes a morally wrongful harm. There are two possible answers, which will be discussed next. First, we may argue that for a harm to be morally wrongful, it has

[280] Mill, J. S. (1989). On Liberty and Other Writings. Cambridge, Cambridge University Press. p. 13

to be of a certain magnitude and lie above a threshold. I will suggest that this argument is unconvincing. Secondly, it could be argued that even if we view very small harms to be morally wrongful, this does not commit us to the view that all of them should also be prevented by state regulation. To illustrate both of these points, consider the following example.

Charles

Charles is goes to his doctor, where he is treated for a bacterial infection. The doctor prescribes penicillin. Charles, however, has acquired an infection with a low level of resistance against penicillin, so that he gets better after being given a standard course of treatment, but the infection does not fully clear. Charles is told to come back a few days after the first visit for a routine check-up. His doctor realises that some bacteria have survived, and he administers a second, larger dose of penicillin. This time, all remaining bacteria are killed, and Charles is cured.

In the above scenario, Charles is the victim of AMR. His infection can ultimately be treated, although it requires a second visit to the doctor and it takes slightly longer for Charles to get better. The harm that Charles experiences is much smaller than the one described earlier on in the case of Barry (who succumbed to his infection). In principle, however, the cases are similar - both Charles and Barry contract a bacterial infection that shows (different levels of) resistance to antibiotics, which is at least partly caused by human actions. If we accept that Barry has been wrongfully harmed, the same argument should extend to the case of Charles. Yet, intuitively, to intervene in Charles' case or compensate him for the harm caused seems excessive. After all, Charles gets better, much of the discomfort that the infection caused is reduced by the first course of treatment and he fully recovers. This difference in how Barry's and Charles' case are perceived may be explained precisely by a threshold magnitude of (morally wrongful) harm that lies above the harm caused in Charles' case, but below that caused in Barry's case.

However, there may be an alternative way of thinking about the role of a minimal threshold. Some philosophers, including Jonathan Glover and Derek Parfit, have argued that when considering harms, we should not at all be concerned about

minimal thresholds.[281] This is due to the fact that those who seek to analyse small individual contributions to large, collectively created harms make the mistake of treating them as if they had occurred in isolation, rather than in conjunction with other person's actions. It will be useful to consider this point in detail.

Glover suggests that many discussions about collective responsibility overlook what he calls the principle of divisibility. His argument is that those who reject the moral consideration of undetectably small harms overlook the contribution each individual makes.[282] To make this point more obvious, Glover provides the following example:

"Suppose a village contains 100 unarmed tribesmen eating their lunch. 100 hungry armed bandits descend on the village and each bandit at gunpoint takes one tribesman's lunch and eats it. The bandits then go off, each one having done a discriminable amount of harm to a single tribesman. Next week, the bandits are tempted to do the same thing again, but are troubled by new-found doubts about the morality of such a raid. Their doubts are put to rest by one of their number who does not believe in the principle of divisibility. They then raid the village, tie up the tribesmen, and look at their lunch. As expected, each bowl of food contains 100 baked beans. The pleasure derived from one baked bean is below the discrimination threshold. Instead of each bandit eating a single plateful as last week, each takes one bean from each plate. They leave after eating all the beans, pleased to have done no harm, as each has done no more than sub-threshold harm to each person"

The overall outcome in both cases that Glover describes is of course the same - the bandits eat all the food. Yet, to say that sub-threshold harms do not cause any moral harm, is to suggest that the actions in scenario two are morally superior. It should be obvious, how this case translates to the problem of AMR. The harm that the individual causes by taking a course of antibiotics, thereby contributing to higher levels of AMR in the future is similar to the case of taking a single bean. One may suggest that the harm caused by this action is imperceptibly small, but recall the for both cases involving the bandits, the overall outcome is the same. Insisting on the imperceptibility of the individual contribution to the problem as an argument against

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[281] Glover, J. and M. J. Scott-Taggart (1975). "It Makes no Difference Whether or Not I Do It." Proceedings of the Aristotelian Society, Supplementary Volumes **49**: 171-209. Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press.

[282] Glover, J. and M. J. Scott-Taggart (1975). "It Makes no Difference Whether or Not I Do It." Proceedings of the Aristotelian Society, Supplementary Volumes **49**: 171-209.

moral responsibility for the total outcome fails to recognise that the individual action cannot be reasonably separated from the context it occurs in. Moreover, it must also be viewed in conjunction with the actions of all other persons.
As a result, an argument for a threshold, which defines the magnitude of when a harm can be considered to be morally relevant must provide a reason why we should view each individual's action in isolation. Otherwise, it fails to be convincing.

Derek Parfit has made a similar argument in *Reasons and Persons*. In discussing "five mistakes in moral mathematics", Parfit points out two inconsistencies in moral reasoning that apply directly to the problem of sub-threshold harms.[283] In what he calls the fourth and fifth mistake, Parfit suggests that moral philosophers are mistaken if they believe

i) that bringing about a benefit to other people is not morally required, if the size of that benefit is imperceptibly small and that
ii) an act cannot be morally right or wrong if its effects are imperceptible to those who are subjected to them.[284]

According to Parfit, this belief is mistaken because it starts from the wrong premise, namely by asking if the acts of one individual will harm others. Instead, Parfit suggests, we should focus on the question what consequences the actions of the individual in conjunction with the acts of others will produce. Parfit writes:

"It is not enough to ask 'Will my act harm other people?' Even if the answer is No, my act may still be wrong, because of its effects. The effects that it will have when it is considered on its own may not be its only relevant effects. I should ask, 'Will my act be one of a set of acts that will together harm other people?' The answer may be Yes. And the harm to others may be great. If this is so, I may be acting very wrongly."[285]

While this view appears to be intuitively plausible, it comes with an obvious problem: how can the individual know, whether their act belongs to a class of acts, which together harm other people? In the case of AMR, an answer to this question may be somewhat easier to find than in other instances. We could conceive of the

283 Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press. pp. 75-78
284 ibid. p. 76
285 ibid. p. 86

following classificatory principle: Any use of antibiotics, which does not comply with a strategy that aims for a balance between satisfying current urgent needs, and preserving future effectiveness of antibiotics will lead to harm to others and is therefore morally wrong. This principle is quite broad and does not catch every conceivable case of antibiotic use, but it can classify the majority of antibiotic prescriptions.[286] Moreover, it would suggest that the current use of antibiotics (which certainly does not strike a balance between present and future needs) does cause morally wrongful harm for those who are affected by it.

Whether or not one agrees with Parfit's consequentialist view that the wrongness of the action is primarily determined by its consequences is not relevant for our discussion. Even non-consequentialists should be concerned about the isolated consideration of components of collective actions. Glover and Parfit thus do not only provide a model of analysing the moral significance of collective action problems where the effects of individual actions are small. They also provide a consistent argument as to why people have a moral obligation not to contribute to these harms, even if the size of their own contribution appears to be negligibly small.

As mentioned earlier, however, we may still require a different kind of threshold value, namely one which determines, which morally wrongful harms justify state intervention to prevent them.[287] To examine this argument more closely, let us reconsider Barry's and Charles' cases.

The two cases lie at opposing ends of a spectrum. In Barry's case, it may be quite obvious that harm has been caused and that controlling the spread of MRSA is a cause for state intervention. In Charles' case, however, it is unlikely that the harm - even if morally wrongful - is sufficiently serious to warrant similar interventions. Charles has suffered a setback in health but it was comparatively trivial and, while undesirable, the adverse effects he experienced were negligibly small. Cases at the extreme end of the spectrum, where harms are either imperceptible or enormous are fairly easy to classify. Yet, most cases about which we have to decide will be more

[286] The principle obviously raises the question how a balance could be struck – but at least at present, it would appear that cases of obvious overuse (such as the use of antibiotics against viral infections) belong to a set of actions, which wrongfully harm those who are affected by AMR

[287] I am here primarily interested in morally wrongful harms but of course states may also intervene in the types of situation where a harm would not be wrongful. For example, we may want to prevent people from swimming in shark-infested waters, or taking out sailing boats on a lake during a lightning storm.

ambiguous. We therefore face a choice in considering morally wrongful harms caused by AMR. Either, we can exclude those kinds of adverse events which are trivial (however we define this), or we include all kinds of harm into our considerations. Both of these choices come with their own problems. If we consider all harms as a cause for state intervention, this forces us to regulate extensively against every kind of conceivable harm, no matter its magnitude. On the other hand, if we define some sort of threshold value to decide at which point we respond to morally wrongful harms, this may rule out the inclusion of cases like that of Charles. At the same time, however, it creates an arbitrary cut-off point. This problem of harm definition and its impact on the usefulness of related concepts such as the harm principle has been described, especially in legal and jurisprudential writing.[288] However, there appears to be no satisfying solution thus far. One can therefore either bite the bullet, and accept the arbitrariness of a threshold value for policy-making (*not* for the recognition of morally relevant harm) or one has to endorse state legislation that seeks to regulate every potential cause of harm (which will likely be impossible in practice). I have no proposal for a solution to this conflict, but would want to note that in the case of AMR, erring on the side of caution, and regulating more rather than less may be advisable, purely because the control of infectious disease often requires very strict rules to contain the initial spread of infection.

5.2.4 Harm and AMR - taking stock

So far, it has been suggested that harm caused by AMR should be considered as morally wrongful, even if the direct causal relationship between individual agency and adverse outcome is weak. This argument rests on the premise that harms can be morally wrong even when they are imperceptibly small and therefore rejects the notion of a minimal threshold, above which has a harm has to register in order to be morally wrong. There remains, however, a related question, namely if all morally wrongful harms (irrespective of size) should also be subject to legislative or regulatory efforts that seek to curb their effect. I have proposed that in the case of infectious disease control, fairly extensive regulation may be necessary to contain the spread of infection. However, it remains possible that some kinds of small harm fall below the threshold of what will be covered by state regulation. The definition of such a threshold is borne out of practical concerns more than it is a matter of moral

[288] Holtug, N. (2002). "The Harm Principle." Ethical Theory and Moral Practice **5**(4): 357-389.

arguments for harm prevention, since I have argued that *all* harms caused by AMR, have the potential to be morally wrongful.

So far, however, our discussion of harm is not yet complete as we have only considered those instances, in which AMR causes measurable adverse health outcomes. For everyone who is not infected by a drug-resistant pathogen, AMR still leads to increased risks of either falling ill (if bacterial infections which are difficult to treat become more prevalent) or of suffering adverse health outcomes, should they become infected (due to the limited effectiveness of antimicrobial treatments). In the following section, it will therefore be discussed, whether this subjection to an elevated risk should in itself be considered to constitute a harm.

5.3 AMR and Risk

The role of risk in ethical inquiry has so far received comparatively little attention.[289] Instead, much of moral philosophy has been concerned with cases of direct causality, where one person's action will lead to any one of a set of specified outcomes, and it will do so with absolute certainty. Consider, as a case in point, the frequently cited trolley case in which the reader is given the choice to either divert a trolley (which will certainly kill one person in a tunnel), or to leave the trolley on its current course, which will result in the deaths of a greater number of people.[290] A crucial component of the trolley case is that the possible outcomes are well-known and indisputable. Either one person will die, or many will, but there is no room for any alternative outcome. Real world examples, however, have the tendency to be much more complicated, and it is rarely the case that outcomes of different paths of action will be known precisely before a decision about an appropriate response to a given moral problem is reached.[291] This also appears to be the case for many discussions in health care ethics and public health ethics, in which the outcome, and who will be affected by it is often only available as a modelled prediction of a statistical frequency.[292]

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289 Lewens, T. (2007). Risk and Philosophy: Introduction. Risk - Philosophical Perspectives. T. Lewens. Oxford, Routledge**:** 1-20.

290 e.g. Thomson, J. J. (1985). "The Trolley Problem." The Yale Law Journal **94**(6): 1395-1415.

291 Note, that this is not necessarily a shortcoming of case studies which deliberately abstract from the complexities of real world scenarios to focus on morally salient features, but this nonetheless makes it difficult to apply findings from such deliberations to cases where causal links are more difficult to establish.

292 Broadbent, A. (2009). "Causation and models of disease in epidemiology." Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences **40**(4): 302-311.

Why should we consider the role of risk in the case of AMR? To begin with, the impact that an individual's actions will have on the emergence and spread of AMR will vary, depending on a vast number of factors, including where the person lives, with whom they interact, etc. Thus, two persons behaving in the same way will likely contribute differently to the emergence of AMR. This separates it as a problem from other cases of collective (in)action such as global warming.

In the case of global warming, every person who emits CO_2 contributes to the problem. And while there is a natural absorption rate, as soon as this is exceeded, everyone's emission is of equal importance, irrespective for example of his or her respective location.[293] Emitting ten metric tons of CO_2 per year should roughly affect changes in the atmosphere the same way if this occurs in an isolated settlement on the outskirts of civilization, or in a city centre of in Europe.[294] The same, however, cannot be said for the use of antimicrobial drugs.

Let us assume that there are two persons, Dan and Erik, who are scared of catching a dangerous infection and thus frequently use antibiotics, which they have bought on the internet. Both understand the risk of AMR emerging from their behaviour, but both also believe that the personal benefits of preventing an infection will outweigh any negative side effects of drug resistance. Dan lives in his own in rural Alaska, and barely interacts with other people, while Erik works in a big city, shares a flat and has an active social life. Both Dan and Erik use the same drug irresponsibly - but they do not contribute equally to the problem of AMR. Erik interacts with other people, some of whom may have weak immune systems and be more vulnerable to opportunistic infections. Dan, on the other hand, may harbour resistant bacteria in his body but the *risk of their transmission* to other persons is much lower. The difference between Dan and Erik seems to lie in the difference in risk which these actions bring about respectively and to which they expose others. It will therefore be worth examining, if the subjection to a risk is morally relevant, even if the threat does not

293 Sinnott-Armstrong, W. (2010). It's not my fault: Global warming and individual moral obligations. Climate Ethics. S. M. Gardiner, S. Caney, D. Jamieson and H. Shue. New York, Oxford University Press.

294 This point might be open to discussion, and does not take into account the immediate effect on other persons, e.g. in the form of smog. The point I am making is merely that CO2 emissions that contribute to global warming and thus climate change will be relevant irrespective of where the polluter is located.

materialise. We will consider this question in detail in the following sections. For now, however, it will be useful to be more precise about what exactly I understand a risk to be.

5.3.1 The definition of risk

While the term is widely used, there is no single definition of what a 'risk' is and everyday usage differs greatly from scientific understandings of risk.[295] Castree et al have offered a succinct summary of this 'common' use of the term:

"In common usage, 'risk' focuses on the potential negative impacts of being exposed to harm and is therefore synonymous with loss. It extends the concept of uncertainty to decision making, where the potential for loss is known (e.g. in terms of time, money, property, environmental quality of human life), but the precise nature of the loss, whether it will occur, or even how probable it is, are unclear."[296]

There is a multitude of different understandings of what the notion of risk encompasses. Hansson for example has defined five commonly used definitions of risk, which are often used without clear distinction.[297] What complicates matters further is that often assumptions about what constitutes a risk are merely implicit in writings on the topic, and the usages of the term in associated concepts such as 'risk communication' or 'subjective and objective risk' are not always consistent with one another.[298]

For the purposes of this discussion, I shall follow a commonly used technical definition, and understand a risk to be *"the statistical expectation value of unwanted events, which may or may not occur"*.[299] In this definition, 'expectation value' describes the (weighted) average of all outcomes that are conceivable for a given event. It should be noted that this is a general definition of risk, and that it may not be the only relevant way of considering risks attached to AMR. Public health interventions for example will often not focus on absolute risks to individuals, but

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295 Haight, F. A. (1986). "Risk, especially risk of traffic accident." Accident Analysis & Prevention **18**(5): 359-366.

296 Castree, N., D. Demeritt, et al., Eds. (2009). A Companion To Environmental Geography. Blackwell Companions to Geography. Chichester, Wiley-Black. p. 83

297 Hansson, S. O. (2005). "Seven Myths of Risk." Risk Management **7**(2): 7-17.

298 ibid.

299 ibid.

instead start by calculating the relative risk to a given population by comparing the risk in an exposed group to a risk in a non-exposed group.[300] However, since we are primarily concerned with a general understanding of risk and its ethical implications, a more broadly applicable definition will suffice for our purposes.

5.3.2 Subjecting people to risks: the case of AMR

As is the case with harm, not all types of exposure to risk are morally wrongful. Arguably, many risks that people are exposed to exist independently of human actions. NASA for instance routinely calculates the risks of asteroids hitting earth.[301] If such an asteroid was large enough, it could cause serious harm, and the risk factor itself cannot currently be controlled by human action. Consequently, present and future people will have to live with this risk, yet it appears that this is not a moral problem, because there is simply no path of action available to us that might change the chances of this event occurring. There may be cases, in which a distinction between controllable and uncontrollable risks is not as clear-cut, for example in the case of volcanic activity. In this case, people could refrain from living in the vicinity of the volcano or invest into early detection mechanisms to better control for the risks. However, even in cases where human action can potentially mitigate the consequences of an adverse event, the existence of the risk itself lies outside of human control.

In the case of AMR, on the other hand, the current risk of suffering an adverse health outcome as a result of drug resistance can be traced back to human actions, which have greatly helped in exacerbating this risk since the invention of antimicrobial drugs in the mid-20th century.[302] Using antibiotics widely (and in many instances inappropriately) has created selection pressure that favours drug resistant strains of bacteria.[303] This has in turn not only made it more difficult to treat some infections, it has also increased the risk for people to be infected with a drug-resistant strain and suffer a more severe course of the disease.

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300 Gordis, L. (2009). Epidemiology. Baltimore, Saunders Elsevier. p. 202

301 see Yeomans, D. (2013). "Near Earth Object Program: Sentry Risk Table." Retrieved 12.05., 2013, from http://neo.jpl.nasa.gov/risk/.

302 Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP. Chapter 5

303 Drlica, K. and D. Perlin (2011). Antibiotic Resistance: Understanding and Responding to an Emerging Crisis. Upper Saddle River, New Jersey, Pearson for FT Press. p. 149 ff

5.3.3 Does being subjected to a risk constitute a harm in itself?

So far, we have seen that AMR does constitute an additional risk to which people are subjected. But what are the moral implications of this observation? One possible answer to this question is to suggest that subjection to a risk constitutes a harm in itself. The harm in this instance is not the materialisation of a health threat - it is merely the subjection to an elevated risk, irrespective of whether or not the adverse event occurs. There are two possible arguments for such a view, which we shall now consider. The first relates to the consequences of being subjected to a known risk.

In cases where people are aware of the additional risk posed by AMR or another hazard, this may cause severe psychological pressure. For instance, if I live in an area that is suddenly subjected to higher pollution levels and thus elevates my risk of contracting lung cancer, the grief and fear that the awareness of this risk causes me, can reasonably be considered a morally wrongful harm. Similarly, fear of contracting not only a bacterial infection, but one that is resistant to available antibiotics can reasonably be assumed to have a negative impact on my wellbeing; it raises worries about contagious diseases or of being hospitalised if nosocomial infections are no longer treatable. It may also have wider social implications in terms of how people interact with one another. Yet, much of whether subjection to risk can count as a morally wrongful harm rests on the assumption that there *is* awareness of the risk factor.[304] Stephen Perry has suggested that most arguments about risk as harm appear to be based on *"estimations of relative frequency that are made on the basis of existing knowledge rather than relative frequencies that exist whether or not anybody knows about them"*.[305]

A second argument that an exposure to risk constitutes a harm could go further and suggest that it is not merely awareness of a risk factor, but the subjection to a risk itself, which constitutes a harm. Yet, such an argument appears difficult to sustain. Suppose that researchers discover in ten years that we were in the past subjected to some form of previously unknown health risk but that no one to that date had actually suffered any adverse effects as a result. To claim that the mere subjection to a risk constitutes a harm would then imply that we are presently being harmed by a

[304] See also Perry, S. (2007). Risk, Harm, Interests and Rights. Risk: Philosophical Perspectives. T. Lewens. London, Routledge**:** 190-209.

[305] ibid. p. 196

risk we are unaware of and that has not materialised. This seems to make for a counterintuitive conception of harm.

The conceptualisation of risk exposure as harm poses an additional epistemic problem, namely how to establish, what magnitude of risk a person is actually exposed to. In epidemiological terms, this will require that we assign the correct reference class for risk exposure to an individual.[306] This, as we shall see is a particular problem for infectious diseases, which affect different cohorts in varying degrees. Consider the following example, as an illustration of the problem. If we wish to determine the risk of a patient suffering adverse health effects after a nosocomial infection with MRSA, we will have to take into account different risk factors that affect the likelihood of such an outcome. These risk factors may include age, the degree to which the patient is immunocompromised, whether or not the patient has IV lines or a catheter, etc.[307] We can now define different reference classes for establishing what risk the patient is exposed to. Say that in a given hospital, the presence of all risk factors listed above translates to a frequency of 3 in 10 people experiencing adverse health outcomes (however defined). It would in consequence appear reasonable to assume that there is a 30 percent chance for patients to experience such an adverse outcome. Yet, as Stephen Perry has pointed out, there are some variables that such an approach does not account for. For instance, the narrowest definition of a reference class may still not account for all risk factors but only those that we are aware of. However, this would mean that if exposure to risk does constitute a harm in itself, the extent of said harm would vary depending on our state of knowledge.[308]

In summary, the strategy of describing the moral wrongfulness of AMR in terms of risk of suffering a harm fails to yield a satisfying result. First, it comes with substantial epistemic and conceptual problems. Second, the approach limits the scope of morally wrongful harm to instances in which wellbeing is affected by exposure to a known risk, rather than considering all cases in which people are adversely affected

306 ibid.

307 Coello, R., J. R. Glynn, et al. (1997). "Risk factors for developing clinical infection with methicillin-resistant Staphylococcus aureus (MRSA) amongst hospital patients initially only colonized with MRSA." Journal of Hospital Infection **37**(1): 39-46.

308 Perry, S. (2007). Risk, Harm, Interests and Rights. Risk: Philosophical Perspectives. T. Lewens. London, Routledge**:** 190-209. p. 195

by AMR. Framing the moral problem of AMR in terms of increased risk of suffering harm does not appear to be a successful strategy.

However, recalling our initial definition of morally wrongful harm, its causation does not only require the occurrence of an adverse effect; it also presupposes that the victim's rights have been violated in some way.[309] In the following chapter, we will therefore consider in greater detail, if and how AMR can be viewed to constitute a violation of rights.

[309] See section 5.2.1 earlier in this chapter

Chapter 6: Does the emergence of AMR constitute a rights violation?

This chapter will examine, whether the emergence of AMR constitutes a violation of moral rights. Moral and legal rights often overlap but they are not identical and it will be important to distinguish between them throughout the discussion. However, since many legal rights also point to underlying moral right claims, a brief look at legal questions in the context of AMR may be helpful for mapping out more clearly the variety or moral rights that may be affected. There exists a significant body of work that focuses on legal implications of drug resistance. This work relates to a broad range of problems, such as the use of antibiotics (both in humans and animals)[310], the restriction of personal freedom for patients with communicable diseases that have become difficult or impossible to treat as a result of AMR[311], or the protection of intellectual property rights for antimicrobial drugs.[312] Many of these discussions also point to normative claims, which we will consider in greater detail throughout this chapter.

Why should we phrase the moral problem of AMR in terms of rights? One suggested answer to this question has recently been proposed by James Wilson, who argues that there are good reasons for justifying health policy and infectious disease policy in terms of rights. Wilson writes:

"If each citizen has a right to a particular resource, or freedom, then the duty holder of the right must secure that particular freedom or resource for each individual to whom the right applies. Rights are highly resistant to aggregation: the fact that many people have their rights fulfilled does nothing to reduce the claims of those who do not."[313]

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310 Fidler, D. P. (1998). "Legal Issues Associated With Antimicrobial Drug Resistance." Emerg Infect Dis **4**(2): 169-177.

311 London, L. (2009). "Confinement for extensively drug-resistant tuberculosis: balancing protection of health systems, individual rights and the publics health [Review article]." The International Journal of Tuberculosis and Lung Disease **13**: 1200-1209. Coker, R. (2000). "For debate. The law, human rights, and the detention of individuals with tuberculosis in England and Wales." Journal of Public Health **22**(3): 263-267.

312 Outterson, K. (2005). "The vanishing public domain: antibiotic resistance, pharmaceutical innovation and intellectual property law." University of Pittsburgh Law Review **67**: 67-123.

313 Wilson, J. (2012). On the Value of the Intellectual Commons. New Frontiers in the Philosophy of Intellectual Property. A. Lever. Cambridge, Cambridge University Press. p. 126

The quote highlights two things. First, it shows what separates rights from mere policy goals, which a regulator can be said to legitimately pursue even if ultimately not everybody benefits from these efforts.[314] Secondly, it underlines why a rights approach appears to be better than a utilitarian account at capturing the principles of a state-funded health care system like the NHS. The NHS was set up with the goal to meet the health needs of everyone, be free to users and provide services based on clinical need, not ability to pay. Moreover, in its constitution the NHS defines rights that patients and users of its services have.[315] Its stated purpose is thus not to create the greatest amount of aggregated health benefits but to provide access to free health care to everyone. A rights-based approach seems to reflect these values and principles better than the previously discussed approaches could. However, before examining in greater detail how the concept of moral rights can help to delineate the ethical challenges presented by AMR, it is important to note that the introduction of rights terminology to the field of health policy is not without problems.

First, as Jonathan Wolff has pointed out, the introduction and formulation of new rights has sparked worries among some commentators that there is a current trend of 'rights inflation', which leads to the creation of an increasing number of rights claims, thereby "devaluing the currency of rights".[316] If the concept of rights continues to be expanded and more and more specific interests are being interpreted as rights claims, the argument suggests, the relative value we assign to respecting these rights may diminish.

Second, there is, as Stephen Holland notes, *"a danger of merely restating the dilemma at the core of public health ethics, in terms of rights."*[317] In other, words, the formulation of ethical problems in terms of conflicting rights (held by individuals or communities) risks being mostly descriptive, without advancing the discussion, or getting any closer to its solution. Put differently, from a pragmatic point of view it is not enough to identify a conflict of rights if no suggestion as to how it should be resolved is proposed. Of course, to what extent this concern applies will depend on the kind of rights conflict in question. However, we should be aware of the fact that

314 ibid.
315 The Department of Health (2013). The Handbook to the NHS Constitution for England. London. p. 4
316 Wolff, J. (2012). The Human Right to Health. New York, W.W. Norton & Co., p. 14
317 Holland, S. (2007). Public Health Ethics. Cambridge, Polity Press. p. xiv

identifying a rights conflict can merely be a starting point and does not yet tell us how to reconcile competing rights claims.

Finally, there may arguably be a number of different moral rights violations that are *associated* with the use of antibiotics, but are not affected by AMR directly. Consider a patient who contracts a drug-resistant nosocomial infection like MRSA. We may wish to argue that health care providers have a moral duty not to harm their patients (and - correspondingly - the patient has a right to be protected from such harm). On such an account, the patient who is infected with MRSA (e.g. through an non-sterile catheter) might be able to claim that his rights have been violated - but this claim does not appear to relate specifically to AMR. If he had contracted a drug-sensitive infection, the right to not be harmed in the delivery of health care would still have been violated. Arguably, AMR may exacerbate the clinical effect of such a rights violation but it does not create a distinct moral challenge. Instead, AMR appears to merely worsen an existing problem. This matters to our discussion, because we are here concerned with what makes the creation of AMR a distinct moral problem. The following analysis will therefore not focus on situations where AMR exacerbates other rights violations. Instead, it will be analysed, if and when the occurrence of AMR *itself* constitutes a moral problem.

6.1 The definition of rights

While the terminology of rights claims is widely used, there exists a long-standing dispute in jurisprudence over the appropriate definition of what constitutes a right. Since we will not be able to resolve this dispute at this stage, we shall adopt a widely used concept of rights proposed by Joseph Raz, which understands rights as fundamental interest of persons. Raz states that if a person X has a right this *"is to say that X has interests which are sufficiently weighty to impose obligations on others."*[318] Thus, when considering the protection of antibiotic effectiveness, a Razian understanding of a corresponding rights claim would suggest that people have an interest in access to effective antibiotic treatment and that this interest in turn creates obligations for society to provide a sufficiently high level of antibiotic effectiveness.

[318] Raz, J. (1986). The Morality of Freedom. Oxford, Clarendon Press. Chapter 7

Raz's interest theory of rights is not universally accepted and is particularly contested by proponents of a 'will theory of rights'. Proponents of the latter believe that by having a rights claim, its holder is given control over another person's duty, which H.L.A. Hart puts as follows:

"*The idea is that of one individual being given by the law exclusive control, more or less extensive, over another person's duty so that in the area of conduct covered by that duty the individual who has the right is a small-scale sovereign to whom the duty is owed*."[319]

For will theorists, a right is therefore a way of granting exclusive control over a correlating duty.[320] We will discuss this aspect in greater detail in the following section. By contrast, the interest theory proposed by Raz holds that "*X has a right' if and only if X can have rights, and, other things being equal, an aspect of X's well-being (his interest) is a sufficient reason for holding some other person(s) to be under a duty*."[321] In other words, interest theorists ground the existence of rights claims in furthering the right holder's interest.[322]

In light of this controversy, why should we adopt an interest theory of rights? While both will theories and interest theories are subject to conceptual challenges, will theories have some intuitively implausible implications.[323] Will theories restrict rights to moral agents and claim that a right confers control over the duty to act in a particular way to that agent.[324] Yet, this understanding of rights does not seem to lend itself well to a health care setting. Patients are not independent agents who chose between different options but – more often than not – are merely recipients of treatment, which is decided by health care professionals. This seems to contradict the principle of agency, which lies at the core of will theory of rights. This principle, as McCormick has noted, also prevents young children or people with impaired

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319 Hart, H. L. A. (1982). Essays on Bentham: Jurisprudence and Political Theory. Oxford, Clarendon Press. p. 183 note that Hart originally referred to this position not as will theory but as choice theory. However, both terms are commonly used interchangeably

320 Spector, H. (2009). "Value Pluralism and the Two Concepts of Rights." San Diego Law Review **46**. p. 824ff

321 Raz, J. (1986). The Morality of Freedom. Oxford, Clarendon Press. p. 166

322 Wenar, L. (2011). Rights. Stanford Encyclopedia of Philosophy. E. N. Zalta.

323 For a detailled discussion of these challenges, see e.g. Kramer, M., N. E. S. H., et al. (1998). A Debate over Rights: Philosophical Enquiries,. Oxford, Clarendon Press.

324 Wenar, L. (2011). Rights. Stanford Encyclopedia of Philosophy. E. N. Zalta.

intellectual capabilities (e.g. comatose patients) from holding any rights.[325] I shall not conclusively defend an interest theory of rights at this stage, but will merely note that it does not share the previously discussed counterintuitive implications.

6.2 Rights and correlative duties

So far, our discussion of rights has implied that a rights claim entails a duty. This position follows Hohfeld's argument, which states that rights presuppose correlative duties and that that *"rights will be grounds of duties in others."*[326] It will be worthwhile to elaborate on this assumption and its implication. In particular, it will be useful to say more about the moral foundation of rights claims, before examining in greater detail the correlation of rights and duties, as the case of AMR presents a challenge to the formulation of obligations that are derived from rights claims.

In light of the multi-causality of drug resistance, which we have explored over the previous chapters, and the lack of a clearly established causal relationship between individual actions and subsequent emergence of AMR, a rights approach in the Hohfeldian sense seems an unsuitable approach from the outset. If rights can be identified but the rights violation is a collective action problem, then how can we determine who holds a correlative duty to respect such rights? To illustrate this point, suppose that within a community, everyone has a right to effective antibiotics (we will return to this point in greater detail later), but it cannot clearly be established who holds responsibility for the emergence of drugs resistance in the first place. Under such conditions, one can imagine an argument to the effect that we are able to state who is owed something - but in the absence of clear causal correlations, it is then impossible to determine who has an obligation to meet these rights claims. Following this line of argument, the worry would be that if we cannot clearly define who has to fulfil a duty and what exactly this duty entails, the corresponding right can never be fully met in the first place. This would render its formulation somewhat redundant.

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325 MacCormick, N. (1982). Children's Rights: A Test-Case for Theories of Right. Legal Right and Social Democracy: Essays in Legal and Political Philosophy. N. MacCormick. Oxford, Oxford University Press**:** 154 - 166.

326 Hohfeld, W. (1919). Fundamental Legal Conceptions. New Haven, Yale University Press.

However, it would be premature to dismiss a rights account based on its inability to provide unequivocal answers to these challenges. As Joseph Raz has argued convincingly, even if we cannot always identify clearly, who holds a correlative duty to a specific rights claim, we may nonetheless be in a position to develop a consistent account of rights violations.

First of all, a rights claim may entail more than one duty and the definition of the right does not entail uncompromising protection from all harm. As Raz observes, *"[m]any rights ground duties which fall short of securing their object, and they may ground many duties not one."*[327] For example, Raz notes, a right to security does not imply a correlating duty that every conceivable harm be subsequently averted.[328] Similarly, as we shall discuss in greater detail below, a right to health does not mean that every person should receive the most advanced medical treatment currently available.

On Raz's account, this is not to say that wherever the duty falls short of the objective, no rights violation has occurred. In the case of AMR, this means that even if we cannot fully protect everyone from AMR, nor define a comprehensive set of duties in order to do so, there may still be scope for a moral rights claim. For the purposes of this discussion, I will therefore follow Raz's understanding of rights and suggest that even if it is difficult to identify correlative duty holders, the emergence of AMR can still be seen to constitute a rights violation. To develop this argument further, we shall next consider, *what kind* of rights could conceivably be violated by the emergence of AMR.

6.3 AMR and rights - A right to what?

In chapter 3, it was asked, which commodity we should be trying to distribute fairly in the case of AMR - a discussion that was entitled 'Distribution of what?'. It was argued that we could focus on either the distribution of antibiotics themselves, or the distribution of their remaining stock of effectiveness and it was proposed that, for the purposes of applying principles of distributive justice to the case of AMR, a focus should be placed on the latter. Analogously, a discussion of potential rights violations in the context of AMR inevitably raises the question what *kind* of rights

327 Raz, J. (1986). The Morality of Freedom. Oxford, Clarendon Press. p. 170-171

328 ibid.

are violated, who the right holder is and - in line with Wilson's argument cited above - what corresponding duties arise to whom. A discussion of rights will thus, as Onora O'Neill succinctly summed it up have to determine "*who* has to do *what* for *whom*".[329] To examine what this means in the context of AMR, it will be useful to begin by reconsidering the cases that were discussed in the previous chapter, in particular Barry's case.

Barry

At the gym, Barry hits his head and starts to bleed. To stop the bleeding, Barry uses a sweaty towel to cover the little cut. The wound becomes infected with a particularly virulent type of community-acquired MRSA. Barry is sent to hospital, where he is put on antibiotics. Because of the drug resistance, he does not respond to the initial treatment and shortly after succumbs to the infection.

When we first considered Barry's case in the previous chapter, it was suggested that if Barry had been harmed in a morally wrongful way, this was because his legitimate expectation of benefiting from a resource (namely effective antibiotics) had been thwarted. It was argued that to show a morally wrongful harm in this instance presupposed that we could show that the resource in question had been mismanaged. So far, it was assumed for the sake of argument that Barry had been harmed in a morally wrongful way. At this point, we can examine, whether or not our earlier claim can be substantiated by framing Barry's legitimate expectation as a right, and the subsequent failure to meet this expectation as a rights violation. If this can be shown, then we have a strong case for the claim that AMR constitutes a morally wrongful harm. To this end, we should ask two questions: First, can we identify a moral right that Barry holds, which was violated by his MRSA infection, and second, which duties would this right entail, and on whom do they fall?

Answering these questions is no small challenge and there are a number of different rights we could try to appeal to; a right not to be harmed, for example, or a right to health care or perhaps a more specific and yet to be defined right to antibiotic effectiveness. An examination of what right Barry holds thus quickly runs into the

[329] O'Neill, O. (2002). "Public health or clinical ethics: thinking beyond borders." Ethics and International Affairs **16**(2): 35-45. p. 42

difficulty of distinguishing between different rights that he may reasonably have a claim to. Furthermore, depending on the right that we identify to be relevant in this context, the corresponding claims and resulting obligations are likely to change.
Finally, we may also have to decide if some of these rights have lexical priority over others or - to borrow an expression from Joseph Raz - if they are core rights rather than derivative rights.[330] Raz argues that some rights are merely derived from other rights claims. An example he provides is that people may be said to have a right to walk on their hands, but that this right is ultimately derived from a (core) right to personal liberty.[331] The relationship between these two notions of right is not that one entails the other. Instead, the distinction between core and derivative rights is useful for determining the order of justification.[332] Thus, when making a case for the protection of a moral right, the claim can be strengthened, if we can successfully distinguish between core and derivative rights, and appeal to the latter only. Note that derivative rights do not have to follow from a single core right. For example, a potential right to antibiotic effectiveness could be derived from a right to health or a right to a certain type of property. However, since there is no set of universally agreed-on core moral rights, such an argument will have to be developed systematically and carefully.

A first attempt at defining a rights violation in Barry's case may start from the (fairly uncontroversial) premise, that Barry has a moral right to not be harmed by others.[333] Given the fact that AMR is primarily caused by the over- and misuse of antibiotics, it could be argued that the subsequent inability to treat Barry's infection also constitutes a violation of his rights. But for this argument to be convincing, more must be said about what *exactly* makes the contraction of an infection a rights violation and - just as importantly – what obligations arise as a result of this.

Despite its human causes, no one has deliberately created MRSA, or tried to spread it at Barry's gym. The fact that Barry contracts the infection is the result of a large set of individual actions, none of which were individually sufficient to bring about the

330 Raz, J. (1986). The Morality of Freedom. Oxford, Clarendon Press. p. 168 ff
331 ibid. p. 169
332 ibid. p. 170
333 Recall from the discussion in chapter 5 that Barry does not have a total right, not to be harmed by others. There are circumstances, such as voluntary and fair competitions, which may harm Barry in some way but do not generate a moral claim.

final result. Consequently, it appears difficult to assign personal responsibility to any individual for bringing about Barry's death, and it is hard to see who has violated Barry's right not to be wrongfully harmed.

As was the case in discussing the causation of harm earlier, it may therefore be important to contrast Barry's circumstances of death with those of Albert (recall that Albert contracted a drug-susceptible infection but was too far away from anyone who could have provided help and died). The difference between Albert and Barry does not lie in the outcome (both die of bacterial infections). Instead, it appears to lie in the fact that Barry's death was preventable, had a previously available resource been used differently. The specifics of Albert's case make it unlikely that he could have been helped. After all, part of the appeal of his trip was to get away as far as possible from civilization.

The comparison between the two cases shows that while Barry's death could have likely been prevented if antibiotics had not been so widely misused, the same is not true for Albert's case. We have earlier provisionally assumed a right not to be harmed and suggested that Barry has been denied this right. Albert has not been wrongfully harmed and it would appear that even though he dies in the wilderness, none of his rights have been violated. Albert's case therefore suggests that there is no legitimate rights claim to be protected from all bacterial infections. This helps us to sketch out more clearly, what kind of rights violation Barry may have been subjected to. Let us therefore consider the following alternative:

Proposition 1

Barry has a moral right to the protection from adverse health outcomes, where such outcomes are preventable without undue cost.

To give this proposition more substance clearly requires that more be said about what can generally count as 'preventable'. In the context of health care delivery, it is unlikely that 'preventable' is equivalent to 'technologically feasible', since there are inevitable resource constraints within which health care practitioners have to operate. For example, it may be technologically feasible to cure a single patient with an exceptionally rare and otherwise deadly disease, if the entire research budget was allocated to this cause. However, from this it cannot be inferred that this feasibility

entails a duty to do so, as this would occur at the cost of violating the rights (or interests) of so many other people.[334]

For now, it suffices to note that proposition 1 creates a challenge of defining what will count as preventable. One could suggest economic solutions to this question. One example for this is the provision of cost-effective health care up to a predefined level of health care expenditure, as incorporated in the National Institute of Health and Care Excellence's (NICE) approach to defining a ceiling to health care cost per quality-adjusted life year.[335] However, as we saw in chapter 4, the calculation of costs and benefits in the realm of infectious disease control is fraught with methodological difficulties. The exact specification of a right based on proposition 1 will therefore likely remain controversial. Of course, this could simply be accepted as an unfortunate reality of defining complex right claims. But any appeal to proposition 1 has to accept that the rights claim can often be challenged on the technical matter of what counts as preventable (or technologically feasible). It may therefore be useful to consider alternatives to this proposition.

What is particular about Barry's case is that the lack of access to the resource is not the result of general scarcity in the health care system, but stems from the fact that the effectiveness of one antibiotic has not been *preserved* sufficiently. Consider therefore as an alternative to proposition 1 the following:

Proposition 2

Barry has a moral right to the protection from adverse health outcomes, if an effective treatment could be made available by having used appropriate resources in such a way as to avoid their over- and misuse.

As outlined in chapter 2, AMR is an inevitable by-product of antibiotic use. It can be slowed down, either by inventing new drugs or by using them more restrictively, but it cannot be entirely avoided. Disregarding for now the possibility of entirely new

334 This dilemma is also expressed in the formulation of a human right to health, which the International Covenant on Economic, Social and Cultural Rights (ICESCR) defined as: "the right of everyone to the enjoyment of the *highest attainable* standard of physical and mental health.", see Wolff, J. (2012). The Human Right to Health. New York, W.W. Norton & Co. p. 2

335 Cubbon, J. (1991). "The principle of QALY maximisation as the basis for allocating health care resources." Journal of Medical Ethics **17**(4): 181-184. See also chapter four

treatment alternatives to antibiotics, any regime of using antibiotics will thus ultimately exhaust the resource. This would suggest that fulfilling such a right has some peculiar implications, because it establishes a claim to an inevitably diminishing resource. While the interests on which a right like proposition 2 may be based remain constant, the actual possibility of meeting this rights claim will diminish over time. Assuming that at some point in the future we will run out of effective antibiotics, proposition 2 would become practically ineffective (though not normatively irrelevant, as we shall see later). In between the present situation and a presumed moment in time at which all antibiotic effectiveness has been depleted, we find ourselves in a situation, where the previously specified right will be increasingly difficult to meet. Furthermore, through the depletion of antibiotic effectiveness, every instance of fulfilling the right of one claimant will at the same time reduce the possibility of meeting the same rights claim in the future.

Let us assume for the sake of argument that every individual has an equally strong interest not to suffer from the effects of a bacterial infection, and that consequently every person has an equally strong claim to the right specified in proposition 2. In this instance, we could conclude that the normative force of the right we specified remains constant, but that its 'purchasing power', i.e. its ability to realise the good in question will diminish over time. Thus, the moral value of the right remains, but its practical value will be reduced until its disappearance.

To make this more obvious, consider a case in which Barry lived 500 years from now and to this point, the use of antibiotics had been highly restrictive with a view to preserve their effectiveness for as long as possible. If under such conditions, Barry no longer had access to an effective antibiotic, the practical value of his rights claim would have disappeared. Yet, Barry would not have become the victim of wrongdoing, because antibiotic effectiveness was managed as well as possible and past generations thus tried their utmost to also respect Barry's rights claim. Had antibiotics instead been used carelessly, the future Barry would have been wronged. What this suggests is that the normative force of the right remains, even when its realisation is no longer practically possible.

Of course, the previous argument inevitably raises the question if and how we can determine what counts as a reasonable level of commitment to preserving antibiotic effectiveness to avoid (or minimise) any rights violations to future people. There may

not be a clear-cut answer to this question and no threshold value that we can easily define. However, in light of the evidence that until now little emphasis has been placed on the preservation of antibiotic effectiveness, this problem may not be too much of a practical concern. After all, we know that past and current use of antibiotics most certainly falls short of any such a standard (however it is ultimately defined).

So far, it has been shown that if a right to antibiotic treatment can be justified, then it provides a clear case for seeing the emergence of AMR as a morally wrongful harm, and an unusual and difficult one at that. What we have so far overlooked, is the possibility of fulfilling proposition 2 not only by reducing consumption of antibiotics and avoiding waste, but also by developing new types of treatment. Chapter 3 suggested that due to the time this takes, it makes sense to treat antibiotic effectiveness as an exhaustible resource in the short and medium run. However, if we consider a longer time span, it may also be possible to argue for a right to novel treatment options.

6.4 AMR and a right to new drugs?

As outlined in chapters 2 and 3, antibiotic effectiveness differs from finite natural resources such as fossil fuels in that it can in principle be renewed through scientific progress and the invention of new drugs. When we speak of a right to an effective treatment, an obvious question that extends from this discourse is therefore whether this right also entails an obligation to develop new drugs.[336]

An answer to this question may partially depend on empirical evidence. If it were shown that antibiotic effectiveness was in fact sustainable in the long-run, for example by restricting the use of antibiotics and using drugs cyclically to allow antibiotic effectiveness to 'recover', the question of whether or not new drugs need to be developed might be redundant. In other words, there is no argument for the development of new antibiotics, if the effectiveness of existing drugs could be preserved equally well in other ways. This argument also applies to alternative types of treatment: if, for instance, new vaccines reduced the use of (and need for)

[336] Note that this obligation could be understood either as the development of drugs, or the creation of incentives for pharmaceutical R&D.

antibiotics then any rights claim to the development of new antibiotics would subsequently be weakened. However, given the speed with which AMR is currently progressing and the fact that some bacterial infections have already become essentially untreatable, it would appear safe to assume (at least in the medium run) that the protection of antibiotic effectiveness will also require the development of new drugs, in particular against Gram-negative bacterial infections.[337] Thus, if we can identify a right to effective antibiotic treatments, then this would also appear to entail some kind of obligation to attempt to develop new drugs.

One argument *against* such an obligation comes in the form of an extension of what Waldron has called the 'no hardship' argument.[338] The argument stipulates the following: If a new invention (such as a new antibiotic) is not shared with some people, who – by not having access to this resource are no worse off than they otherwise would have been, then these people cannot be said to have been harmed. Usually, the argument is applied to the distribution of (and access to) private property. However, Wilson has suggested that the argument could also apply to the regulation of access to essential drugs.[339] Wilson suggests that the no hardship argument is unconvincing, because it can justify a failure to provide essential aid, for example in a rescue situation. In such a scenario, the no hardship argument could be invoked by simply stating that the position of the person who is in need of help is independent of the actions of potential rescuers and that a failure to provide help therefore does not make the person in need worse off than he or she would otherwise have been.[340] Wilson argues, however, that a failure to provide such help amounts to a rights violation of the person who is not granted access to such help and cites the prohibitive pricing of patent-protected drugs as an example. Of course, this case differs from the failure to develop new drugs. In one instance, a resource already exists and is unfairly distributed. In the other, the failure to help stems from not having developed such a resource in the first place.

Yet, while this difference is clearly important, a variant of the 'no hardship argument' could also be extended to the case of having failed to develop new drugs.

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337 See Chapter 2.5.2

338 Waldron, J. (1993). "From authors to copiers: individual rights and social value in intellectual property." Chicago-Kent Law Review **68**: 841-887.

339 Wilson, J. (2012). On the Value of the Intellectual Commons. New Frontiers in the Philosophy of Intellectual Property. A. Lever. Cambridge, Cambridge University Press. p. 9

340 ibid.

However, we need to be specific about the stakeholder(s) whom we view to be morally responsible for the current lack of research into new drugs. In addition, we will have to specify, what criteria would have to be satisfied for such a right to be met.

As chapter 2 outlined in detail, there has been a chronic lack of investment into new antibiotics over the past decades, driven by other emphases in the research agenda and greater potential for private companies to maximise returns on investment by focussing R&D efforts on other areas. Determining who holds responsibility for the lack of new drugs is complicated by the fact that much of the necessary research has traditionally been carried out by private, for-profit organisations in developed countries. In most countries, the key government strategy in developing pharmaceuticals appears to have been the creation of incentives to promote the development of certain drugs that were needed.[341] However, as the current lack of effective drugs clearly illustrates, the strategy has been unsuccessful in securing a sufficiently high level of output. One way of framing the right to new drugs would thus be to suggest that governments have an obligation to promote a sufficiently high level of research activity into new drugs to secure scientific progress. But this is an unsatisfying strategy, as the success of research may depend on other factors than just the appropriate provision of incentives.

An alternative way of thinking about a right to new drugs is in terms of the human right to the "highest attainable standard of health", as put forward by the International Covenant on Economic, Social and Cultural Rights.[342] It seems plausible to read such a right as implying that health care systems must not only protect their citizens from infectious diseases with existing means but also advance, improve and further develop existing treatments. It may be difficult to define exactly what such a right entails but it seems rather uncontroversial to suggest that if one accepts a (human) right to health, respecting the resulting rights claims should lead governments to actively promote research designed to avert catastrophic health

[341] Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies.

[342] Wolff, J. (2012). The Human Right to Health. New York, W.W. Norton & Co. p. 2 The discourse of human rights is of course much more complex than it is presented in this section and vastly exceeds the scope of our discussion. The reference to the human right to health at this stage merely serves as an illustration that such a right can be developed and serve as the foundation for health policy.

outcomes such as complete or very extensive forms of AMR. As a result, a right to new antibiotics will probably only be a derivative right that stems from a more fundamental right to health and it remains unclear what governments need to do in order to adequately honour the right holders' claims. Nonetheless, the substantial lack of research (or effective tools to promote such research) would suggest that over the last decades, health care systems in developed countries and with sufficient resources at their disposal have failed to do enough to invigorate research efforts and that this failure can be framed as a shortcoming in honouring the human right to health.

6.5 A right to the protection from externalities caused by antibiotic consumption

So far, our discussion has centred on the question whether people who suffer from a drug-resistant bacterial infection have experienced a violation of their rights if they have no access to effective drugs. However, there is a second rights concern that needs to be mentioned at this point, namely the rights conflict that arises from antibiotic consumption. To be more specific, the concern is that antibiotic consumption itself may violate other peoples' rights, in that it harms others by creating externalities in the form of higher rates of AMR.[343] Jonathan Anomaly has made this point in relation to the pricing of antibiotics, arguing that AMR should lead us to make antibiotics more expensive to reflect the true cost of their use and to discourage overconsumption and misuse. Anomaly recognises that this may increase health inequity, by making access to antibiotics disproportionately more difficult for people in resource-limited settings but argues that *"nobody has the right—not even the poor—to inflict uncompensated harms on other people against their will"*.[344]

On Anomaly's account, the use of antibiotics and the subsequent harm caused by the emergence of AMR also generate rights claims, namely not to be subjected to this kind of harm. Note that in the case of such a rights claim, and in line with Raz's position regarding correlative duties that was outlined earlier, it does not matter whether or not we can fully meet it in practical terms, nor do we have to be able to identify exactly, who bears the corresponding duty. Furthermore, by focussing on the

[343] For a detailed discussion of externalities in antibiotic use see chapter 1 and 3

[344] Anomaly, J. (2010). "Combating Resistance: The Case for a Global Antibiotics Treaty." Public Health Ethics **3**(1): 13-22.

actual harm, rather than the potential for it, Anomaly's suggested rights claim is not subject to the critique levelled against the use of the concepts of risk and harm that were discussed in the previous chapter. While we saw that it is difficult to phrase the subjection to a small additional risk as a harm, it seems entirely plausible to define a right according to which people must not be subjected to uncompensated harm. On the other hand, by avoiding the inclusion of subjection to risk, Anomaly's definition raises the question how we can know *ex ante* whether a specific dose of antibiotic treatment will in fact produce AMR that will harm others.

While the latter question is a technical problem for Anomaly's account, it nonetheless points to an important challenge to the rights approach to AMR, namely a conflict between competing rights claims. As argued above, people can be seen to have a rights claim to effective antibiotic treatment. However, *utilising* this resource will result in negative externalities, which exacerbate the problem of AMR and in turn affect the rights of other persons. Therefore, granting universal access to antibiotics in recognition of a right to effective antibiotic treatment may ultimately undermine the availability of such treatments in the first place. As Millar has noted, *"equal access for individuals with equal need irrespective of wealth has the potential to shorten further the effective life of currently available antibiotics."*[345]

6.6 AMR and rights – some concluding remarks

This chapter has shown that a theory of moral rights can make sense of the normative challenges of AMR. Moreover, by showing that AMR does constitute a rights violation, we have strengthened the case for AMR being a morally wrongful harm, which was developed in the previous chapter. Since Feinberg's definition of harm, upon which we built our analysis stipulated that for a harm to be morally wrongful it had to violate the rights of those affected by it, the conclusions of this chapter are highly relevant. The rights approach has a number of advantages. To begin with, it allows us to consider different aspects of the moral challenge that AMR poses, since it is entirely possible for drug resistance to impact on more than one right. Secondly, the rights approach, which was developed in this chapter, was able to recognise the

[345] Millar, M. (2011). "Can antibiotic use be both just and sustainable... or only more or less so?" Journal of medical ethics **37**(3): 153-157. p. 154

moral claims of persons, even if they could not meet them appropriately. Thus, a rights based approach could make sense of a normative claim to effective antibiotics at a point, where no effective drugs were available. This seems to support the intuitively plausible view that future claims to antibiotics have equal moral worth, irrespective of how much antibiotic effectiveness remains.

There are, however also a number of drawbacks to the rights-based approach. To begin with, it remains unclear, what happens if different rights come into conflict with each other. Certainly, rights theorists can deal with this, either by rephrasing the rights, or by establishing conditions under which it is permissible to infringe upon them.[346] However, the precise process of this remains contested. Nevertheless, proponents of a rights approach would be correct to point out that the difficulty of specifying rights and dealing with their conflicts rules out neither that this is possible, nor distinguishes it from its alternatives.

Yet, there are two challenges to the rights approach and its application to AMR, which weigh more heavily. The first concerns the size of the rights violation in question. While the rights approach can show that AMR leads to the violation of individual rights, the causal remoteness of the corresponding duty makes it difficult to generate a coherent account of what rights that are affected by AMR compel anyone to do. For a problem that involves so many stakeholders, this is a significant practical concern.

The second problem, which a rights account faces in the case of AMR is that the good to which people have a moral right diminishes over time. As we saw earlier, a right to effective antibiotics will therefore progressively lose its 'purchasing power' and will be of diminishing practical relevance for the use and distribution of antibiotic effectiveness.[347]

We are therefore left with a sense that AMR seriously affects the interests of people and that something should be done about them, but – given its restrictions - a rights approach will meet this requirement only in a limited and unsatisfying way.

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[346] Sinnott-Armstrong, W. (1996). Moral Dilemmas and Rights. Moral Dilemmas and Moral Theory. H. E. Mason. New York, OUP**:** 48-65. p. 49ff

[347] Provided, as previous chapters outlined, that AMR progresses further

In the following chapter it will therefore be suggested, that a better way of framing the challenge of AMR is through a contractualist approach. In particular, it will be argued that contractualism is better equipped to deal with the kinds of collective action problems that AMR presents, and can justify schemes of cooperation among people whose interests are partially conflicting.

Chapter 7: Contractualism and AMR

Contractualism most commonly refers to a theory developed by Thomas Scanlon.[348] Scanlon's work builds on social contract theory, in particular the work of John Rawls.[349] However, while they share the view that morality is grounded in a contractual agreement between persons, Rawls' and Scanlon's theories differ in a number of important aspects.

Rawls develops a theory built on hypothetical scenarios, in which decisions are made under abstract conditions. To this end, he famously introduces a 'veil of ignorance', behind which rational individuals would chose rules for the distribution of primary goods without knowing their own social position in the hypothetical society they are constructing.[350] Scanlon, on the other hand, focuses less on the question what kind of principles people could agree to. Instead, he proposes that moral decisions should be based on principles that no one could reasonably reject.[351] We shall return to Rawls' approach in the next chapter but will begin by examining Scanlon's argument more closely.

7.1 Scanlon's account of contractualism

According to Scanlon "*thinking about right and wrong is, at the most basic level, thinking about what could be justified to others on grounds that they, if appropriately motivated, could not reasonably reject*."[352] This position, Scanlon argues, gives us reason *"to be concerned with other people's points of view: not because we might [...] actually be them, or because we might occupy their position in some other possible world, but in order to find principles that they, as well as we, have reason to accept."*[353]

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348 Scanlon, T. (1998). What We Owe to Each Other. Cambridge MA, Harvard University Press. Scanlon developed the account of contractualism earlier, however "What We Owe to Each Other" constitutes the most complete version of his argument. For earlier versions, see Scanlon, T. M. (1982). Contractualism and utilitarianism. Utilitarianism and beyond. A. Sen and B. Williams. Cambridge, Cambridge University Press**:** 103-128.

349 Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press.

350 ibid. p. 136 ff

351 Ashford, E. and T. Mulgan (2012). "Contractualism". The Stanford Encyclopedia of Philosophy (Fall 2012 Edition), . E. N. Zalta. Stanford.

352 Scanlon, T. (1998). What We Owe to Each Other. Cambridge MA, Harvard University Press. p. 5

353 ibid. p. 191

Scanlon thus locates the moral value of actions in their (reasonable) justifiability, not in whether or not they are merely in line with rational (self-)interest.

An immediate objection to this may be that this is hardly a distinctive feature of contractualism. Other moral theories (including consequentialist accounts) also seek to justify why their actions are the rights ones to pursue. For a utilitarian for example, an action is morally justified if it maximises utility. Scanlon accepts this but points out that justifiability of the action in the utilitarian's case is merely derivative. What makes the action *right*, according to the utilitarian, is not that it can be justified to others but that it maximises utility. Contractualism, by contrast, claims that it is justifiability rather than outcome, which determines the moral rightness of an action. As Scanlon puts it, his theory *"explain[s] the distinctive importance and authority of the requirements of justifiability to others by showing how other aspects of our lives and our relations with others involve this idea."*[354] Scanlon thus identifies the need to provide coherent and reasonable justification for our actions. On his account, an act is morally wrong, "*if its performance under the circumstances would be disallowed by any set of principles for the general regulation of behaviour that no one could reasonably reject as a basis for informed, unforced general agreement*."[355]

It is significant that Scanlon believes that this principle rules out the interpersonal trade-offs between serious harm to some people and aggregated small harms to a larger group.[356] A common objection to consequentialist views, namely that aggregation of small inconveniences to many individuals may ultimately outweigh serious harm to a smaller group of people, thus fails to extend to the Scanlonian principle, because such a trade-off could be reasonably rejected.[357] To illustrate this point, Scanlon envisions a scenario, in which Jones, who works in a television study during the broadcast of a world championship match, has an accident and his hand is trapped. Immediately helping Jones would lead to a disruption of the TV signal, resulting in an inconvenience to millions of sports fans watching the match. Not helping Jones until the broadcast is over would entail that he suffers very painful

354 ibid. p. 6

355 ibid. p. 153

356 ibid. p. 230f f

357 Note, however, that Scanlon does not promote a principle that assesses the reasonableness of rejecting an action based on personal circumstances of an individual. The theory he develops is not supposed to cater to the 'partial reasons' that individual cases display - rather the principles that his version of contractualism develops are supposed to be generally applicable. See ibid. p. 211-212

electrical shocks in the meantime.[358] Scanlon proposes that no sports fan who experiences the inconvenience can reasonably reject a principle, which would inconvenience him but save Jones the agony of electric shocks. The serious harm to Jones, he suggests, matters more than the inconvenience caused to sports fans. However, for this argument to be convincing, more must be said about the way in which a contractualist principle can be formulated and what constitutes a reasonable rejection of it.

7.1.1 Contractualist principles

Scanlon argues that *"[t]o justify an action to others is to offer reasons supporting it and to claim that they are sufficient to defeat any objections that others may have."*[359] This, he suggests, corresponds to the way in which we make everyday moral judgements, which tend to not simply conclude "*that an act is wrong but that it is wrong for some reason."*[360] Principles, in Scanlon's theory, are *"general conclusions about the status of various kinds of reasons for action"*.[361] Principles may thus rule out certain reasons for action as being legitimate or reasonable but they are not as clearly delineated as some kinds of rules or laws. In other words, a principle cannot simply be applied to settle a dispute. To do so will require careful deliberation of how and why a principle is not met.[362] According to Scanlon, there can be an unlimited number of principles and their formulation will depend on the way that people interact with one another.[363]

7.1.2 Reasonableness of rejections

To assess reasonableness, Scanlon's theory measures the strength of what he calls objections to permission and objections to prohibition respectively.[364] Thus, when determining if carrying out a certain act is morally right or wrong, the two questions we must ask are what burdens are imposed on those affected by *permitting* the act and what burdens are imposed (and on whom) by *prohibiting* the act.[365] Depending

358 ibid. p. 235
359 ibid. p. 197
360 ibid. p. 197 (underlining added for emphasis)
361 ibid. p. 199
362 ibid. p. 198-201
363 ibid. p. 201
364 ibid. p. 195
365 ibid.

on the answer to these two questions, we may then decide if it is reasonable to endorse or reject a principle that regulates the act in question. The question of reasonable rejection is thus a comparative one that weighs objections to either outcome against each other.[366] Unlike other moral theories that place an emphasis on rational choices, Scanlon distinguishes reasonableness from rationality by suggesting that rational choices do not always lead to morally acceptable outcomes.[367] To be reasonable, according to Scanlon, is much closer to an everyday understanding of this term, where "*what it is reasonable for a person to do presupposes a certain body of information and a certain range of reasons which are taken to be relevant, and goes on to make a claim about what these reasons, properly understood, in fact support.*"[368] The distinction between rationality and reasonableness is not merely a matter of definition. Scanlon identifies a number of instances in which it may be reasonable to make moral demands on other people under circumstances where this is not rational (for example, because doing so is unlikely to generate the desired effect, or have some negative side effect).[369] Reasonableness, according to Scanlon, therefore avoids some of the counter-intuitive moral judgements that a focus on rational choice may generate.

7.2 Can contractualism avoid interpersonal aggregation?

It was argued earlier that, among other things, contractualism differs from consequentialism because it does not consider aggregated interpersonal benefits to determine the morally right way of action. However, as we have just seen, contractualism is in principle open to some forms of interpersonal trade-offs and can demand fairly substantial sacrifices in order to generate a larger benefit elsewhere. What Scanlon rules out categorically (and where his view differs from some forms of consequentialism) is a trade-off of small benefits to a large number against substantial harm to a few.[370]

366 ibid.
367 ibid. p. 192 Here, Scanlon follows Rawls, who
368 ibid. p. 192
369 Note that Scanlon does not wish to argue that approaches built around assumptions of rational choice are untenable - they are, however, distinct from his own approach. See ibid. p. 194
370 ibid.

However, some critics doubt whether Scanlon's version of contractualism successfully avoids the need for consequentialist considerations.[371] Derek Parfit in particular has expressed scepticism regarding the ability of contractualism not to collapse into consequentialism.[372] Parfit argues that while Scanlon assumes personal responsibility to depend entirely on justifiability of the action to the *individual* (thereby ruling out aggregation), he is also bound to accept that an action can be reasonably rejected if it creates a greater burden than its available alternatives.[373]

Scanlon accepts that in situations where two unevenly sized groups of persons face harm of comparable magnitude but only one group can be aided, contractualism favours the larger group.[374] In fact, Scanlon's concession to a utilitarian calculus go even further, as he also acknowledges that in a situation, where we face a choice between either saving the lives of a few, or preventing serious, non-lethal harm (such as blindness or paralysis) to a large number of people, contractualists may have to protect the greater number.[375] Interestingly, however, Scanlon does not develop this argument fully and remains ambivalent as to whether or not such a consideration could be reflected by a contractualist principle. Rather, he seems to acknowledge that these cases merit closer inspection, but remains unsure if they can be accounted for in a contractualist theory. This is a challenging question, but ultimately we may not have to resolve it here. Scanlon's consideration of extreme trade-off scenarios, in which it may be necessary to forego a life-saving intervention in order to prevent harm to a very large group of people does not seem to reflect the kind of trade-off we are facing in the case of AMR. Scanlon seems to envision very concrete trade-offs, when he writes that *"it could be wrong to save one person's life when we could instead have prevented a million people from going blind or becoming paralyzed."*[376] In line with the argument that was developed over the past chapters, it should by now be obvious that trade-offs in the case of restricting access to AMR are much more subtle. They do not create large-scale dilemmas but present cases of risk increase of unknown magnitude, which do not resemble the kind of case that Scanlon proposes.

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371 Ashford, E. (2003). "The Demandingness of Scanlon's Contractualism." Ethics **113**(2): 273-302.

372 Parfit, D. (2011). On What Matters. Oxford, OUP. Vol. II, Part 5

373 ibid. p. 192-197

374 Scanlon, T. (1998). What We Owe to Each Other. Cambridge MA, Harvard University Press. p. 238

375 ibid. p. 239-240

376 ibid.

It may therefore make more sense to read Scanlon's discussion of interpersonal trade-offs as an acknowledgement that 'large-number cases' are difficult to solve for non-consequentialist. Nevertheless, we should note at this point that contractualism does not propose straightforward aggregation. It is sensitive to the severity of potential harm that could be mitigated and – to a lesser extent – is also concerned with the number of those affected, even though maximisation of overall utility is not its goal. We shall next consider, how such a contractualist approach can be applied to the case of AMR.

7.3 A contractualist approach to AMR

The idea of considering the problem of AMR from a contractualist perspective is relatively novel and has so far only been systematically employed in the work of Michael Millar. Millar proposes a model of Scanlonian contractualism that seeks to fairly distribute antibiotic effectiveness and links antibiotic use to the analogy of *"a leaky rescue craft which becomes less effective the more it is used."*[377] The foundation for a contractualist restriction of antibiotic availability thus lies in the fact that a scarce resource can be used in different ways, not all of which are equally acceptable. This is important, because for the application of contractualism to work, different alternatives to act must be feasible. Rejecting a principle based on entirely impossible distributive scenarios (for example by demanding a distribution that requires more goods than are actually available) misses the point of what it means to be reasonable. Millar also notes that feasibility should not be seen as equivalent to cost-effectiveness (which may be a common misreading in the context of health policy) but rather *"require[s] that the alternative arrangement is within the sphere of influence of the [acting] institution.*"[378]

Millar has developed his contractualist account of morally permissible use of antibiotics in two recent publications.[379] He suggests that the use of antibiotics

[377] Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469. p. 465

[378] Millar, M. (2013). "'Zero Tolerance' of Avoidable Infection in the English National Health Service: Avoiding the Redistribution of Burdens." Public Health Ethics **6**(1): 50-59. p. 52

[379] Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469, Millar, M. (2013). "'Zero Tolerance' of Avoidable Infection in the English National Health Service: Avoiding the Redistribution of Burdens." Public Health Ethics **6**(1): 50-59.

should be restricted according to the following principle, which he believes cannot reasonably be rejected:

"[A]ntibiotics should be used to prevent some substantial risk of irretrievable harm in patients or their contacts, where a substantial risk is a level of risk that can be reduced by the use antibiotics, and which exceeds the range of risks of irretrievable harm that we tolerate in our day-to-day lives." [380]

Millar's proposal appears to rule out two types of antibiotic usage. First, it excludes the possibility of entirely inappropriate or wasteful use of antibiotics. If antibiotics should be used to prevent some substantial risk, this implies that their use must be able to prevent a risk at all. Since the use of antibiotics against viral infections does not aid the recovery, Millar's principle would rule out this kind of use as excessive. As no benefit (neither individual nor societal) is realised through such a use, this seems an uncontroversial restriction.[381] The second type of antibiotic use, which Millar's principle rules out is for infections that bring with them an insubstantial risk of irretrievable harm. Anticipating the question, how such a substantial risk is defined, Millar proposes that it must be higher than everyday risks. We will return to this requirement shortly. The principle he proposes, Millar argues, cannot reasonably be rejected, because *"[t]he argument for reasonable rejection of the use of antibiotics for any condition other than those conditions associated with a significant risk of irretrievable adverse consequences is founded on the dire consequences of selecting antibiotic resistance for some.*"[382] As a result, Millar's principle also justifies the restriction of antibiotics in instances where their use would be beneficial for the recipient. These could be self-limiting infections, or infections where the use of antibiotic no longer affects the overall health outcome (such as in the final stages of terminal illness).[383] On a Scanlonian account, this can be justified by a rescue principle. This states that it is unreasonable to reject a principle, which demands small or moderate sacrifices, if these could alleviate some much greater pain or

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380 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469.

381 Millar notes that his principle would also rule out the non-therapeutic use of antibiotics in farming.

382 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469. p. 466

383 ibid.

suffering.[384] Scanlon concedes that this rescue principle may end up being very demanding. For instance, it may be the case that we could not reasonably reject permanent physical harm, if this saved someone else's life, though contractualism as a theory does not tell us exactly, what level of sacrifice will be required.[385] Ultimately, this principle thus appears to permit rather far-reaching restrictions of antibiotic use. We will revisit this concern in section 7.6.

7.3.1 Strengths of a contractualist approach to AMR

In light of the discussion in the preceding chapters, one of the strengths of Millar's argument appears to be that it can take into account the consequences of today's actions, without requiring a detailed cost-benefit analysis. Specifically, Millar contests that placing a monetary value on human life can generate a valid moral argument for the availability of treatment. Moreover, and similarly to the argument developed in chapter 4, he doubts whether existing cost-calculations can reliably assess the future impact of AMR.[386] The contractualist model expounded above foregoes the common attempts of defining costs and benefits for health care interventions and therefore does not have to engage in highly speculative trade-off scenarios. It is not motivated by the maximisation of some benefit (or the minimisation of cost) but focuses on the individuals affected by it. As Millar puts it:

"The contractualist approach of Scanlon requires that we take account of those who will suffer adversely from infection with antibiotic-resistant microbes, however unpredictable their numbers may be, and in so doing makes it clear why we should not use antibiotics for small gains (even when cost-effective to do so), or to treat patients with otherwise retrievable, or inevitable outcomes. There is no requirement that we cost the consequences of infection with antibiotic-resistant bacteria; it is sufficient to know that some will suffer irretrievable adverse consequences."[387]

A contractualist approach to the challenge of AMR would therefore also rule out on ethical grounds certain market-based solutions that have been suggested, such as

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384 Scanlon, T. (1998). What We Owe to Each Other. Cambridge MA, Harvard University Press. p. 224

385 ibid. see also section 7.6 below.

386 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469. p. 466

387 ibid. p. 468

tradable or transferable permits.[388] If we can identify a principle that reasonably rejects antibiotic use unless there is a substantial risk of irretrievable harm, then clearly such a position is at odds with a model that simply seeks to internalise costs by making buyers pay a premium for its use, rather than restricting use to certain conditions. A price premium does not control for which infections antibiotic will be used or how urgently they are needed. It merely reduces the number of potential consumers by making the treatment unaffordable for some. This concern is of course strongest in states without a comprehensive state-funded health care system where such a policy effectively limits the access of poor people, who tend to be most vulnerable to infectious diseases in the first place.[389]

Moreover, Millar's proposed principle seems to fit well with the argument, which has been developed over the previous chapters. It also considers AMR in terms of diminishing antibiotic effectiveness and is therefore compatible with the account that has been presented so far. However, despite this compatibility, more must be said about Millar's approach before we can judge its persuasiveness. To begin with, we have to consider in greater detail what exactly constitutes a *substantial* risk in Millar's account.

7.3.2 What is a substantial risk and when is it acceptable?

The proposition Millar puts forward is that a substantial risk must be greater than the everyday level of risk that we are faced with, yet not greater than the maximum level of a risk that someone can be exposed to without his or her consent.[390] Millar notes that the current Health and Safety Executive (HSE) legislation defines tolerable (or acceptable) levels of risk of death as 1/10,000 p.a. for an imposed risk and 1/1,000 p.a. for a consented risk.[391] It is not clear, where in between these two threshold values the maximum level of tolerable risk for AMR lies, but Millar suggests that this may be determined by *"empirical research, evidence synthesis, statistical*

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388 Smith, R. D. and J. Coast (1998). "Controlling antimicrobial resistance: a proposed transferable permit market." Health Policy **43**(3): 219-232.

389 Bates, I., C. Fenton, et al. (2004). "Vulnerability to malaria, tuberculosis, and HIV/AIDS infection and disease. Part 1: determinants operating at individual and household level." The Lancet Infectious Diseases **4**(5): 267-277. See also Michael Sandel's discussion of the limits to commodifying health services Sandel, M. (2012). What Money Can't Buy: The moral limits of markets. New York, Penguin.

390 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469.

391 Health and Safety Executive (2011). Reducing Risks, Protecting People. London. p. 44 The terms acceptable and tolerable risk are generally used interchangeably

analysis and public debate" as longs as the final figure is clearly and openly communicated to allow for transparency in policy-making.[392] However, the figures that the HSE defines are somewhat arbitrary. Since there is no external standard to which they could appeal, they are the result of expert opinion, revealed preference studies, or available statistical evidence. As a result, conceptions of acceptable risk will vary between countries or policy areas. A case in point is the US Environment Protection Agency's (EPA) level of acceptable risk for a waterborne parasite infection through drinking water. The EPA puts the level of acceptable risk of infection at 1/10,000 p.a., which translates to an acceptable annual risk of illness of approximately 1/20,000.[393] However, these infections are rarely fatal, reducing the rate of acceptable risk of death to an even smaller number than the one proposed by HSE.[394]

Not everyone sees this inconsistency as a problem. Hansson has suggested that levels of acceptable risk vary between policy areas and context, because perceptions of what is acceptable reflect social beliefs and preferences, which rank some risks higher than others. To treat risks of equal magnitude as equally relevant, he suggests, would make sense *"in complete isolation from other decisions in society."*[395] However, since this does not reflect actual practices, Hansson suggests that assessments of acceptable risks should be sensitive to public perceptions to be compatible with democratic decision-making.[396]

What does this mean for the case of AMR? Millar points out that one somewhat surprising implication of the concept of substantial risk is the conclusion that some of the existing thresholds for antibiotic prescribing may be unreasonably high. A study by Daneman et al, for example, reports that existing guidelines for the treatment of pneumonia endorse 'therapy-attributable mortality' of around 1 in 100 patients, i.e. a

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392 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469. p. 467

393 Hunter, P. R. and L. Fewtrell (2001). Acceptable Risk. World Health Organization: Water Quality - Guidelines, Standards and Health. L. Fewtrell and J. Bartram. London, IWA Publishing**:** 207-227. p. 209 Hunter and Fewtrell considered the case of an infection with the parasite *Giarda lamblia*, which only leads to an intestinal condition in about 50% of those infected. This explains the difference between the risk of infection and the risk of illness.

394 ibid.

395 Hansson, S. O. (2005). "Seven Myths of Risk." Risk Management **7**(2): 7-17.p. 12

396 ibid.

1 in 100 risk of death as a result of AMR.[397] On Millar's account, this policy produces a mortality risk, which far exceeds what is acceptable as an everyday risk. Consequently, it would appear that such a policy could be reasonably rejected by everyone who suffers an irretrievable harm as a result.[398]

7.4 The relevance of consequences for contractualism

Even if one rejects the argument that contractualism easily collapses into a consequentialist calculus, we saw in section 7.2 that the consequences of actions still matter more to the contractualist than is commonly assumed.[399] Aaron James has recently called into question to what extent reasonableness of actions can be assessed without reference to their consequences. James' view departs from that of Millar, who suggests that the exact magnitude of adverse consequences are a secondary concern for a principle of regulating access to antibiotics, as long as we can reasonably assume that a significant damage will be inflicted on an unspecified number of people. Instead, James argues that for assessing the reasonableness of a principle, we must know more about the probabilities of expected outcomes.[400] James' concern addresses the fact that when we talk about a reasonable rejection of a principle, it is not clear if the outcomes are merely projected (i.e. seen to occur with a given probability) or taken to be certain outcomes. James separates these two versions of contractualism, calling them ex ante and ex post contractualism respectively.[401] An ex post position would take an imagined retrospective, which then serves as the foundation for assessing reasonableness. But this version of contractualism seems entirely unsuitable as an action-guiding principle, since it cannot be prescriptive about how to act but merely assesses events retrospectively. Therefore, it would promote a version of contractualism that would struggle to reach normative decisions about future use of antibiotics. However, if for the sake of

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397 See Daneman, N., D. E. Low, et al. (2008). "At the Threshold: Defining Clinically Meaningful Resistance Thresholds for Antibiotic Choice in Community-Acquired Pneumonia." Clinical Infectious Disease **46**: 1131-1138. Daneman et al report that currently high threshold values for resistance to first line drugs, which must be exceeded before more potent second-line drugs can be prescribed result in complications and excess mortality.

398 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469. p. 467

399 James, A. (2012). "Contractualism's (not so) slippery slope." Legal Theory **18**(Special Issue 03): 263-292.

400 ibid. p. 267

401 ibid. p. 266

argument, we accept the possibility of an ex post reading of contractualism, the method may create some additional problems. For instance, if we knew retrospectively that some instances of antibiotic would not have contributed to AMR at all, but did generate a positive effect for the user, then an ex post reading would give rise to reasonable rejection of Millar's principle.[402] Of course, this is more of a thought experiment than an actual scenario we must consider. As Millar notes: *"It may be that there are some categories of patient or conditions that provide no contribution to the burden of antibiotic resistance, but it is hard to identify any current human treatment or condition in which this would generally apply."*[403] The burden of proof would therefore be on anyone who felt that the assumption about antibiotic use not contributing to AMR applied to cases, in which people could lead to a reasonable rejection of Millar's principle. As things stand, however, it is simply not plausible to argue for a rejection of Millar's principle on these grounds.

For our purposes, it is therefore not particularly relevant to work out if an ex post reading of Scanlon's contractualism is possible. In order to be able to deal with the problem at hand, namely the current and future distribution of health care resources, a version of contractualism must be able to assess the moral permissibility of actions that concern the future.

7.5 How far does contractualism go (and is it far enough)?

So far, we have considered the general premises of contractualism and examined Millar's proposed principle to restrict antibiotic use, as well as some of the challenges that it may face. To remind ourselves, Millar wants to restrict the use of antibiotics to situations in which they prevent a substantial risk of irretrievable harm, where the risk is greater than those we face in our day-to-day lives and could broadly correspond to categories of acceptable risk in other policy areas.

Millar's proposed principle has two implications. First, in clinical practice it may be very difficult to distinguish between some cases of substantial and insubstantial risk, if the threshold for the former is set at a low level. Put differently, if a substantial risk of irreparable harm was defined as greater than the HSE's previously cited 1/10,000

402 Recall the case of Dan in chapter 5.3 as an example of such a scenario.

403 Millar, M. (2012). "Constraining the use of antibiotics: applying Scanlon's contractualism." Journal of Medical Ethics **38**: 465-469. p. 467

chance of death per year, only very few instances of restricting antibiotic use could reliably be ruled to fall below this threshold.[404] A second, related implication is thus that a corresponding principle to govern antibiotic use might fail to restrict their use in a particularly meaningful way.

Such an objection, however, risks getting the argument backwards. After all, Millar's principle is not designed as a justification to reduce antibiotic use to an absolute minimum. Instead, it merely proposes a model of fair use that cannot be reasonably rejected. A failure to be more restrictive thus does not undermine Millar's principle. It just points to the fact that use that is more restrictive is not compatible with this theory. However, for a number of reasons it would be premature to propose that a contractualist principle of restricting AMR could not lead to effective policies to reduce the use of antibiotics.

First, the cited figure for an acceptable risk of death may simply be set too low in the case of AMR and there is indeed statistical evidence to support this view. As discussed in chapter 2, estimates for the United States put mortality from AMR at around 100,000 per year. Given the current US population size of 314 million, this means that annually, at least 0.03% of Americans (or 3/10,000)[405] die from a drug-resistant infection and the reported figures on mortality from AMR are likely an underestimate.[406] Thus, the risk of death from AMR that people face in the United States is already higher than the lower threshold defined by the HSE. Millar's principle stipulates that in order to justify antibiotic use, the risk of harm people face must be greater than their day-to-day risk. For the US case, this would imply at the very least that an acceptable level of risk of irretrievable harm from foregoing treatment could be set as equivalent to the risk of death from AMR, which people already face. However, this observation also highlights a problem of Millar's approach, namely whether or not the level of acceptable risk is sensitive to location and context. Millar suggests that antibiotic use should be limited to instances where

[404] The figure of 1/10,000 that I have picked for the threshold of a substantial risk may be uncharitable to Millar's argument, as he does not set it at this figure. However, it is the lower boundary of what counts as an acceptable risk of death in the UK, and thus represents the kind of figure Millar suggests as a benchmark.

[405] This number is calculated by dividing the estimated number of deaths p.a. (100,000) by the total population size (314,000,000) and multiplying it by 100%. The US population size is based on the most recent census, available at http://www.census.gov/popclock/

[406] See chapter 2

the risk of irretrievable harm exceeds the risks of everyday activities – but these obviously vary across countries, regions and even socioeconomic groups. The risk of dying in a road traffic accident, for example (which should fall under Millar's category of everyday risks) is highest in low and middle income countries and varies by age group (with young drivers being more likely to be killed).[407] Given that many everyday risks are higher in less developed countries, an approach that was sensitive to regional differences in risk would have the advantage that it would not create unrealistically high expectations regarding risk mitigation, which health care systems could not meet in the first place. However, in light of the fact that AMR presents a global challenge, this approach would also distribute the burden of reducing the global consumption of antibiotics very unevenly, by promoting greater restrictiveness in countries in which levels of everyday risk might generally be higher. Moreover, as we saw in previous chapters, there is a limit to the feasibility of reducing antibiotic consumption, because their use does not only aid the patient but also creates positive externalities for infection control and reduces the risk of contagion.[408] Nevertheless, the question how to deal with different levels of everyday risk still remains for self-limiting infections that are not contagious.

Another argument why we might have reason to support a higher level of acceptable risk than the lower threshold defined by the HES is that this figure relates to the *risk of death*, whereas the use of antibiotics, according to Millar's principle should be restricted to cases where there is a *risk of irretrievable harm*. This would certainly include the former (death would after all constitute the most severe form of irretrievable harm) but it is not limited to these instances. Other kinds of irretrievable harm, e.g. permanent tissue damage, scarring or chronic pain, would also be subsumed under Millar's proposal. This has two implications. First, the overall harm of AMR is obviously greater than merely the number of fatalities it causes, which we should keep in mind when calculating the level of risk that people are exposed to at present. Secondly, while highly undesirable, many forms of irretrievable harm caused by AMR are less grave than a fatal outcome of contracting an infection. Consequently, it may be reasonable to assume that the level of acceptable risk for

407 See World Health Organization (2013). Global Status Report on Road Safety. Geneva. p. 4ff

408 See chapter 3. This point is also revisited in chapter 8

irreversible, non-fatal outcomes may also be higher than in cases where we merely determine a tolerable rate of *fatal* outcomes.

7.6. AMR and contractualism – the case for more restrictive policies?

As we saw in our initial discussion of Scanlonian contractualism in this chapter, it is unreasonable for me to reject a principle that would lead to a loss if any alternative principle would require others to suffer a loss that is significantly greater than mine.[409] It was argued earlier that this might motivate much more restrictive principles, which cannot be reasonably rejected even by those who suffer a serious harm. However, if one wanted to emphasise the importance of reducing antibiotic consumption further, there might be alternative formulations to Millar's principle. Two such alternatives shall be considered at this point. The first seeks to balance the severity of harm we can prevent by using antibiotics now against their future use, while the second is based on a probabilistic model to assess future outcomes.

A first proposed alternative to Millar's principle of contractualist distribution of antibiotic use (call this A1) could be summed up as follows:

A1: Antibiotics should only be used if the severity of the harm we can prevent by using them now is the same or greater than the harm we can prevent in the future.

At first sight, A1 seems to allow for greater restriction of antibiotic use than Millar's principle by placing greater emphasis on the reduction of harm in the future and reflecting the trade-off inherent in their use. Proponents of A1 would have to be specific about whether or not they would adopt a positive discount rate, but as chapter 8 will argue later, there are no good reasons for discounting human wellbeing. A more complex challenge to proponents of A1 is the trade-off of current and future benefits itself.

In terms of outcomes it deems to be morally permissible, A1 differs rather substantially from Millar's principle. Let us assume that John cuts himself and his wound becomes infected with a multi-resistant bacterial pathogen. Without the use of antibiotics, there is a high probability (say 50 percent) that John's hand will have to

[409] See chapter 7.2 above

be amputated. However, successfully treating John's infection would require the use of a cocktail of antibiotics of last resort. Millar's principle would clearly suggest that we should use antibiotics, since John stands to suffer irretrievable physical harm, and the risk for this far exceeds a tolerable level. Yet, the above principle would not have to lead to the same conclusion. Say, for instance, that the same antibiotics could save Klaus' life at a later stage, at which their effectiveness had diminished further due to their previous use. On such a view, it might be plausible to suggest that contractualism prescribes that Klaus can reasonably reject to the use of drugs in John's case but not vice versa. Scanlon expresses uneasiness about such trade-offs and states that he "*would for example not say that we would be required to sacrifice an arm in order to save a stranger*." [410] Ultimately, however, he accepts that this is far from self-evident and requires further judgement. [411] Moreover, Scanlon maintains that such acts would not count as supererogatory. Just because a principle does not attach more weight to one's own interests is an insufficient reason for rejecting it.[412]

A contractualist principle based on A1 could thus legitimise much more restrictive antibiotic usage policies. However, there remain some issues that must be addressed before we can decide whether or not we should adopt A1 or a variation of it. First, the case of John and Klaus is problematic, because it appears to employ both ex ante and ex post considerations of contractualism. Klaus could only have a claim retrospectively if he knew that he would contract a serious bacterial infection later on. But we may be able to sidestep this by merely asking if there will be anyone who could reasonably reject to our current use of the resource in the future.[413] Second, A1 seems to require too much information to be a useful guiding tool for the use of antibiotics. By comparing outcomes between current and future uses of antibiotics and making reasonableness of claims dependent on future persons, a principle like A1 requires a degree of information about future outcomes that is unfeasible in practical terms. For Scanlon, this does not necessarily pose a challenge to his theory. Contractualism, he argues, merely provides *"a framework which allows the relevant*

410 Scanlon, T. (1998). What We Owe to Each Other. Cambridge MA, Harvard University Press. P. 225

411 ibid.

412 ibid. p. 225

413 We will return to this point in greater detail in the following chapter

factors to be considered."[414] The fact that an exact calculation of harms is tricky may be true – but contractualism simply cannot say more about the practical implication. It merely points out what the salient aspects are. Furthermore, we could adjust A1 to represent possible outcomes rather than certainties. Such a revised version, A2, could read:

A2: Antibiotics should only be used if we have reason to believe that the severity of the harm we can prevent by using them now is greater than the harm we can prevent in the future.

The revised principle A2 recognises the limitations of what we can know but still maintains that a reasonable principle should take into account future need for the resource we are using. This would address the previous concerns with A1.
There remains, however, a final problem, which applies to both A1 and A2 and should lead us to reconsider, whether or not these principles constitute an improvement over Millar's account. As we saw, Scanlon's rescue principle could invoke very far-reaching restrictions of current use of antibiotics for the realisation of some greater future benefit. However, as its name suggests, the rescue principle seems to require an immediacy of action. In other words, it is only unreasonable for John to reject a principle like A1 or A2, when the harm he would experience had directly led to the avoidance of a greater harm to Klaus. This, however, was not a part of our scenario. As things stand, John's use of antibiotics is neither necessary nor sufficient for Klaus' inability to receive treatment later on. Since Scanlon is already unclear about the permissibility of demanding a sacrifice such as the loss of an arm in the rescue case, it appears unlikely that his position could support such far-reaching restrictions to antibiotic use in a scenario like John's and Klaus', especially not in circumstances where the premises of the rescue scenario are not met.

This does not necessarily commit us to endorsing Millar's principle either. And what our discussion of alternatives to Millar's account has shown is that in principle, the contractualist account permits more restrictive policies for the protection of antibiotic effectiveness than the one proposed by Millar. However, rather than rejecting the

[414] Scanlon, T. (1998). What We Owe to Each Other. Cambridge MA, Harvard University Press. p. 238

latter, an alternative might be to propose a higher level of acceptable level of risk for irretrievable harm. In this chapter it has been suggested that in light of the already significant risk that people face, as a result of AMR (a risk which is likely to increase further in the future), a more restrictive policy of antibiotic use may be justifiable. However, such a policy would also have to take into account the positive externalities of using antibiotics, especially with regard to reducing the prevalence of infectious diseases. It will also have to deal with the problem of defining a meaningful threshold for the acceptable level of risk, to which we can subject individuals by withholding antibiotic treatment from them. This is not an easy task and despite the widespread use of such threshold values in policy-making, there appear to be few normative arguments, which point towards a specific level of acceptable risk. Nevertheless, the contractualist approach developed in this chapter arguably offers a more consistent account of what makes the use of antibiotics morally problematic. And while it takes into account the consequences of policy decisions, it does not seek to aggregate or maximise benefits in the way consequentialist theories do.

Throughout this chapter some of the problems of distributive justice that involve future persons were already alluded to. In chapter 8, we will examine these questions in more detail.

Chapter 8: AMR and intergenerational justice

In the previous chapters, the problem of AMR was categorised as a policy challenge for which no technological solution was available and it was suggested that there are good reasons to endorse a contractualist model of restricting the use of antibiotics.
This chapter will examine in greater detail what follows from these two conclusions for claims of justice between contemporary and future persons. The discussion starts from the premise that in the absence of readily available technological solutions for the problem of AMR, we must consider if (and how) the interests of future persons should be taken into account when deciding how to fairly use antibiotics whose effectiveness diminishes over time. To begin with, it will be useful to outline the concept of intergenerational justice and consider some of the associated challenges. It will then be examined how a contractualist model of distributive justice that was introduced in the previous chapter may address these challenges, and what specific questions emerge in the case of fairly distributing antibiotic effectiveness over time.

8.1 Intergenerational justice

Theories of intergenerational justice seek to apply considerations of justice (or fairness) to cases between different generations who - for the most part - will be non-contemporaries.[415] Broadly speaking, questions of intergenerational justice arise, when one generation can be seen to hold legitimate claims vis-á-vis another generation, from which corresponding duties or obligations ensue.[416] Approaches of intergenerational justice have been developed to address both, concerns of historical injustice and the prevention of future injustice.[417] Our discussion here shall largely be concerned with the latter, i.e. a discussion of future injustice that may be caused by AMR and the ways in which we can respond to the challenge. Specifically, it shall be considered how questions of distributive justice can come to apply in the intergenerational context and how the fairness of distributive patterns for antibiotic effectiveness is affected when interests or claims of future persons are taken into

[415] Gosseries, A. and L. Meyer, Eds. (2009). Intergenerational Justice. Oxford, OUP. see Introduction
[416] Meyer, L. (2010). Intergenerational Justice. The Stanford Encyclopedia of Philosophy. E. N. Zalta.
[417] Meyer, L., Ed. (2004). Justice in Time: Responding to Historical Injustice. Baden-Baden, Nomos.

account. These considerations raise a number of questions that are quite distinct from the fair distribution of goods among contemporaries. As Brian Barry has observed, while we have developed rather sophisticated methods of evaluating relations between contemporaries, these methods often translate poorly to the intergenerational context.[418]

Discussions of intergenerational justice are not new to political philosophy and ethics, nor are they exclusive to the problem of AMR. The argument that today's generation ought to act in a way that respects the interests of future persons has been made in relation to topics as varied as climate change, nuclear waste management, or the financing of social security and health care systems.[419] In contemporary political philosophy, John Rawls' and Derek Parfit's respective discussions of intergenerational equity, both of which we will discuss later in this chapter, are generally seen to constitute a starting point to this discourse.[420] However, the growing body of philosophical writing on climate change and global warming has added significantly to these discussions and will therefore be equally relevant to our analysis, especially because it highlights the importance of distinguishing between issues of distributive justice for renewable and non-renewable resources.[421]

Traditionally, theories of distributive justice were limited both in terms of time and place, since cooperation between people took place within the same generation and was largely restricted to domestic trading.[422] As a result, many of these theories work on an assumption of reciprocity, that is to say: people have duties towards others, but they also enjoy rights. The case of intergenerational justice breaks with this assumption (especially where generations do not overlap), as it constitutes a case of what Rawls refers to as "unidirectional dependence".[423] What this means is that a

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418 Barry, B. (1997). "Sustainability and Intergenerational Justice." Theoria **45**(89): 43-65. p. 43

419 See e.g. Green, R. M. (1977). "Intergenerational Distributive Justice and Environmental Responsibility." BioScience **27**(4): 260-265, Rürup, B. (2002). "Generationenvertrag und intergenerative Gerechtigkeit." Zeitschrift für Gerontologie und Geriatrie **35**(4): 275-281, Taebi, B. and J. L. Kloosterman (2008). "To Recycle or Not to Recycle? An Intergenerational Approach to Nuclear Fuel Cycles." Science and Engineering Ethics **14**(2): 177-200.

420 Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press, Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press. Part IV

421 Bickham, S. (1981). "Future Generations and Contemporary Ethical Theory." Journal of Value Inquiry **15**: 169-177.

422 Heyd, D. (2009). A Value or an Obligation? Rawls on Justice to Future Generations. Intergenerational Justice. A. Gosseries and L. Meyer. Oxford, OUP. p. 168

423 ibid. p, 169

current generation does not depend on the action of future generations (again assuming no overlap), yet the living conditions of future generations will be shaped to a large extent by the choices made today.[424]

While it would perhaps appear uncontroversial to most that present generations have *some* form responsibility for the future, it is rather difficult to map out what *particular* obligations this entails, and to what extent current actions should be influenced by considerations of the wellbeing of future people.[425] In other words, while we may feel that we owe it to future generations to preserve resources, there is no obvious answer to the questions why and to what degree we should do so, especially when the interests of current and future persons conflict. The remainder of this chapter will consider these questions in greater detail.

8.2 Intergenerational justice and some of its challenges

Discussions of intergenerational justice differ from considerations of justice among contemporaries in a number of ways. As alluded to before, the most obvious difference is arguably that the people to whom potential obligations are owed do not yet exist. And it is not clear how such non-existing persons can be recipients of *any* obligations.[426] We shall see later that this problem is of particular relevance for those kinds of moral theory that are built around theories of reciprocity.

At the same time, actions of current generations will obviously affect future people (in much the same way as that today's world has been shaped by previous generations). This happens irrespective of whether or not it is intended. Our actions will necessarily affect later generations and for example make a lifestyle comparable to our own more resource-intensive or unattainable for a greater number of persons. An obvious example of this is the process of global warming and climate change, which carries grave implications for future generations' wellbeing.[427]

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[424] The same does of course hold for historical cases of intergenerational justice, in that the present state of our environment is the direct result of choices made by previous generations.

[425] Meyer, L. (2010). Intergenerational Justice. The Stanford Encyclopedia of Philosophy. E. N. Zalta.

[426] Gosseries, A. and L. Meyer, Eds. (2009). Intergenerational Justice. Oxford, OUP. [Kindle p. 81 of 6275]

[427] Caney, S. (2008). "Human rights, climate change, and discounting." Environmental Politics **17**(4): 536-555.

A second major difference between intergenerational ethical problems and those that occur between contemporary people is the non-identity problem, posed by Derek Parfit. Parfit argues that the existence of specific future persons is the direct result of our previous actions. If, however, the existence of a specific person depends on all our actions, including the potentially harmful ones, it is difficult to see how the actual person that does come into existence can have been harmed by our actions.[428] This, Parfit claims, is true for all persons who live a life that is generally worth living.[429] The non-identity problem presents one of the major challenges to accounts of intergenerational justice and will be considered in greater detail later in this chapter.

Another problem for intergenerational justice, which shall at least be briefly mentioned is that the actions of contemporary people will not only affect the *quality* of life of future persons, but also the *size* of future populations.[430] This creates a set of related questions about the 'right' size of future populations, which our actions can actively bring about. However, this discussion extends beyond the scope of our discussion and I shall here focus on the two challenges outlined before. First, it will be important to be more specific about how we should define generations and separate between them when considering questions of distributive justice.

8.3 What is a generation?

When we talk of intergenerational justice, the first complication we encounter is that despite the widespread use of the term 'generation' it is not really clear what it represents. Furthermore, common uses of the term differ considerably. Familial generations, for example, describe kinship relations between parents and offspring. On the other hand, sociological or historical descriptions often interpret generations as communities with shared knowledge and socio-historical backgrounds, rather than as clearly distinguishable cohorts.[431] Consequently, they are more likely to focus on particular groups of people who share a set of experiences, such as the 'lost

[428] Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press. p. 351 ff

[429] ibid. p. 359

[430] Arrhenius, G. (2000). Future Generations: A Challenge for Moral Theory. PhD, University of Uppsala.

[431] see in particular Mannheim, K. (1952). The Problem of Generations. Essays on the Sociology of Knowledge. K. Mannheim. London, Routledge.

generation' that shared the trauma of WWI or 'generation X', which was defined by the experience of eroding financial and social stability in the 1980s.[432] These uses stand in stark contrast to other concepts of generations, such as an epidemiological definition. Here, the concept of generation is sometimes used in relation to birth cohorts that are examined over a time span and are used to measure population changes.[433]

It is interesting to note that despite considerable interest for questions of intergenerational justice, moral philosophers seldom take the time to explore in greater detail, what particular concept of generation they employ. Whether or not omitting a clear definition constitutes a problem for philosophical analyses of intergenerational justice will largely depend on the time frame of the discussion. Since much of the discourse on intergenerational justice focuses on obligations between non-contemporaries, the precise definition of a generation becomes less relevant, if the time span under consideration is large enough to rule out overlap (say a time span of multiple hundred years). If there is no overlap between these groups, generations will necessarily become discrete units. Adopting such a time frame does not make the discussion of intergenerational justice easier *per se* and may in fact create a distinct set of problems, which we will return to later. As we shall see next, however, a discussion of intergenerational justice that can usefully be applied in the case of AMR cannot adopt such a large time scale and will have to take into account the more immediate future.

8.4 AMR and the problem of generational overlap

It is a truism that the further some effect lies in the future, the greater the chance that it will predominantly affect future persons. However, as chapter 2 already outlined, many of the effects of widespread AMR and potential total drug resistance are likely to also affect currently living generations at a later stage in their life. This necessitates a careful consideration of instances in which there is generational overlap. These cases raise the question if actions which will largely affect a currently living generation at a later stage can qualify as challenges for justice between

[432] see e.g. the fictional account by Douglas Coupland, Coupland, D. (1991). Generation X: Tales for an accelerated culture. London, Abacus.

[433] Gordis, L. (2009). Epidemiology. Baltimore, Saunders Elsevier. Chapter 9

generations. Generational overlap occurs when considering the near future, where a significant number of new persons will have been born, but a large proportion of the current generation is still alive. In such an instance, distinguishing between generations is not straightforward, since we cannot think of them as discrete units.

A first systematic account of the problem of intergenerational overlap was developed by Thomas Jefferson. Jefferson was concerned about the legitimacy of laws that were democratically agreed upon by a majority of a generation that at a later stage would no longer be alive. This, he argued, risked that future persons would be subjected to laws that no longer reflected a majority vote, since those who made the original decision would be deceased. As a result, Jefferson suggested that laws should be periodically renewed, by his calculation once every 19 years when the majority of the previous generation's electorate had been replaced by the next.[434] In his discussion, Jefferson was obviously concerned with a problem that is distinct from the case of AMR. His focus was on political legitimacy of constitutional documents, rather than distributive justice of resources between generations.[435] However, the fundamental question that Jefferson's discussion introduced is equally relevant to the discussion of intergenerational justice in the case of AMR. If considerations of justice between generations differ from considerations of justice among contemporaries, it appears necessary to also be able to clearly distinguish between these two groups.

To make this difficulty more obvious, consider the following case. We could decide that a generation counts as the group of people that are alive at time t_0 and that anyone born at t_{0+x} belongs to one of the following generations. If we then compare the conditions of the group of persons at t_0 with those at a different subsequent moment in time (call this t_1), we could claim to make intergenerational comparisons. Yet, for this argument to be plausible, the time difference t_1-t_0 must be sufficiently large. If it is very small (for example 5 minutes), then - on a global scale - some persons will have been born and some people will have died. However, the difference clearly does not represent a time span, which is great enough to lead to the

434 Jefferson, T. (1984). Letter to James Madison, 6 Sept. 1789. Thomas Jefferson: Writings. D. Merrill. New York, Library of America: 959-964.

435 Michael Otsuka has fittingly described this as a question of 'intergenerational sovereignty', see Otsuka, M. (2003). The Problem of Intergenerational Sovereignty. Libertarianism without Inequality. Oxford, OUP: 131-149.

problems of intergenerational justice that were alluded to above. The question is therefore at which point the time span between t_0 and t_1 becomes sufficiently large to truly represent an intergenerational case. There is no straightforward answer to this - and indeed some writers have suggested that justice between neighbouring generations, i.e. instances where there is some overlap between groups at t_0 and t_1 do not properly constitute instances of intergenerational justice in the first place.[436] However, as we shall later see, for the discussion of AMR, the case of neighbouring generations is of paramount importance and we shall therefore place particular emphasis on this specific aspect.

Returning to Jefferson's example for now, his discussion is of interest to us because it seeks to systematically establish when one generation is replaced by the next. The figure of 19 years that he uses is of limited use today - it is based on the much lower average life expectancy in the outgoing 18th century and it also does not merely take into account life expectancy, but defines generations with reference to the population of voting age. In the case of AMR, such a restriction is nonsensical, since health care provision is obviously not linked to suffrage. What is interesting, however, is that the cut-off point between generations according to Jefferson should be defined by the time it takes for half of the (voting) population to be replaced. Applying such a model in the case of AMR may be difficult for at least two reasons.

First of all, if life expectancy is to be used as the foundation for defining the length of a generation, the question arises whether we define global, national or regional averages. Given the discrepancy between life expectancy in different countries, using a global average would distort the actual length of a generation in many countries.[437] If - at least for the sake of argument - we accept that a generation is replaced by the next once more than 50 percent of the population at a given time are superseded by future persons, then a global average would lead to an overestimate of the length of a generation in countries with low life expectancy and an underestimate in countries with high life expectancy. This very simplistic model of defining a generation also cannot make sense of variations in population size: rapid increases in birth rates

[436] Steiner, H. and P. Vallentyne (2009). Libertarian Theories of Intergenerational Justice. Intergenerational Justice. A. Gosseries and L. Meyer. Oxford, OUP.

[437] Jefferson's model of intergenerational sovereignty did not face this problem, because its application was restricted to a single country.

would shorten the length of one generation while low birth rates would have the opposite effect. On the other hand, a model that considers generations differently between countries appears to create a truly confusing system of intergenerational ethics, which would constantly have to be adjusted to account for population changes.

A second concern that arises from an application of a model of generational change akin to Jefferson's suggestion is that for democratic legitimacy, a population replacement of 50%+1 vote would obviously entail a significant cut-off point. However, in the case of health policy (which in most instances is not the result of direct democracy), it is at least not immediately obvious that the same principle applies.

What consequences does this have for the discussion of AMR? If we assume that in the near future, AMR will create a significant disease burden for newly born persons as well as members of the current generation at a later point in their life, two distinct sets of moral problems become apparent. Michael Millar helpfully distinguishes them as inter- and intragenerational problems of distributive justice.[438] However, Millar's own definition (whether consciously or not) more or less excludes the possibility for generational overlap. Millar writes:

"*For the purposes of this analysis, I take intragenerational distributive justice to require comparisons of individuals from the same generation (e.g., 2-year-old children in Europe with 2-year-old children in Africa) alive at the same time. Intergenerational justice requires comparison of different generations at the same chronological age (e.g., 35-year-old adults born in 1900 and 1970).*"[439]

What is interesting to note about this method is that many of the problems outlined above are sidestepped by comparing specific age groups at two different moments in time, rather than entire generations. This method by default rules out overlap (people can only be of one age once), but it also raises another question. Millar assumes that we compare people at one age, and chooses 35 as an example. However, if not

[438] Millar, M. (2011). "Can antibiotic use be both just and sustainable... or only more or less so?" Journal of medical ethics **37**(3): 153-157.
[439] ibid. p. 154

everyone out of a single generation is considered, this begs the question, which age group we ought to consider. If, for example, we chose a different, more elderly age group of all 75 year olds at two different points in time, the observable differences (depending on age-specific disease burden) may well be greater than for the groups of 35-year olds for the same dates.

There is of course another way of reading Millar's proposed method, namely to suggest that we consider all age groups at two different moments in time, not just selected ones. But this merely reintroduces the problem of intergenerational overlap, since some of the younger persons from the first date will now show up in an older age group for the second date (a five year old in 1900, for example, would then simply reappear in the 75-years group in 1970). One would therefore either have to bite the bullet and select chronological age groups in such a way as to avoid overlap, or accept that overlap will occur, in which case we return to the question, how to clearly distinguish between generations.
There does not appear to be a definitive answer on how to make this distinction. However, at the very least it is possible to state that any discussion of AMR and its implications for intergenerational justice will have to specify, whether considerations of intergenerational justice include the possibility of generational overlap. In this discussion, I will start from the premises that

a) intergenerational justice also applies to cases of neighbouring generations, but that
b) some of the demands of intergenerational justice (and with it their associated challenges) may be less relevant in cases that concern the near future.

At this point, it should be stressed that the effect of generational overlap need not be a problem for ethical discourse and may in fact help to address some of the specific challenges outlined before. Steiner and Vallentyne for example point out that in the case of generational overlap, many of the problems that intergenerational justice creates for contractualist moral theories are less poignant, due to the fact that cooperation and reciprocal acts are possible and agreements that are mutually

beneficial can be entered into.[440] We will return to this point later on in our discussion of the contractualist model of intergenerational justice. First, however, it will be worthwhile to look in more detail at the difference between considering the far and the near future and the implications this will have for distributive justice.

8.5 Considering the far future versus the near future

It appears plausible to assume that the reliability of predictions about outcomes of current policies decreases, the further these outcomes lie in the future. In some instances, however, the opposite is true. For example, we can predict with great certainty that - given current rates of exploitation - fossil fuels will no longer be available in 500 years, whereas such a prediction for the next 50 years may be more difficult. We may discover more efficient methods of extraction, or tap into previously undiscovered reservoirs, which will slightly prolong the availability of fossil fuels. If, however, we use current energy consumption as a base line for future use and calculate the time frame until complete exhaustion of resources, even such technological improvements will be insufficient to continually meet the needs of energy consumption in the long run.

On the other hand, considering the long-term future also creates some additional problems. First of all, the replacement of existing technology by entirely new and unforeseen scientific advances becomes increasingly likely and renders the prediction of future resource needs impossible. Consider as a case in point the fact that one hundred years ago the increased demand for precious metals such as platinum was not predictable, as many technologies that require these resources, such as the catalytic converter, had not yet been invented. Similarly, the discovery of nuclear energy would have severely impacted on any model of depletion of coal, oil and gas resources. Thus, the predictability of events in the future will usually rely on some *ceteris paribus* condition that may not reflect later de facto developments.

Beyond these more pragmatic concerns, the consideration of events in the far future also raises some serious ethical dilemmas, in particular from a consequentialist

[440] Steiner, H. and P. Vallentyne (2009). Libertarian Theories of Intergenerational Justice. Intergenerational Justice. A. Gosseries and L. Meyer. Oxford, OUP. [Kindle p. 909 of 6275]

perspective. Nicholas Beckstead has considered one of these dilemmas in his recent work, namely the question how demanding a theory of distributive justice can be when considering the interests of generations in the distant future. Beckstead argues that since the number of future persons will likely be very large, even small utility gains to their existence will generate a greater overall level of utility than the present use of many resources.[441] As a result, theories which seek to apply a utility-maximising principle would prescribe a preservation of most resources for future persons, that would be incompatible with our current mode of living (and resource consumption). Beckstead acknowledges that this is an uncomfortable conclusion, but suggests that if we truly care about intergenerational justice (and endorse a principle of utility maximisation), we should nonetheless restrict our consumption accordingly.[442]

There are two responses to Beckstead's argument. The first is to deny that we should act on a utility-maximising principle, as most non-consequentialists would. However, this does not solve the conundrum. As we saw in chapter 4, even if one does not take a consequentialist approach, the severe effects on the wellbeing of a large group of people should be of relevance to any credible theory of distributive justice. The second, more promising response to Beckstead's conclusion is to suggest that it cannot easily be applied to the case of AMR and antibiotic usage policies. As we shall see next, this is due to the specific consequences of antibiotic use. If we accept Beckstead's proposal, it would appear that we have a strong case for severely restricting the use of antibiotics, so as to preserve as much antibiotic effectiveness for future persons. Yet, the case of antibiotics differs from other scenarios of resource distribution, because:

1) overuse of antibiotics will (ceteris paribus) render the resource unusable in the future, but
2) underuse of antibiotics will lead to a higher disease burden, if patients with an infection are not treated, remain contagious and infect others.[443]

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441 Beckstead, N. (2013). On the overwhelming importance of shaping the far future. PhD thesis, Rutgers University.

442 ibid. p. 178

443 The point here is that antibiotics do not just have a value to the individual patient as cure to a condition but also play an important role in infectious disease control, e.g. by reducing the number of

In other words, even if we share Beckstead's view that the availability of resources in the future is far more important than it is today because of the greater number of people it affects, the case of AMR does not create overly demanding obligations for the current generation. While it would certainly propose the limitation of antibiotic use, a utility-maximising principle would also have to account for the associated positive externalities for infection control. Thus, even if the interests of generations in the far future are included into a utility calculation, the justifiable restrictions to the use of antibiotics would still have to permit infection treatment and control today. Consequently, such restrictions would likely not lead to highly restrictive antibiotic usage policies.

Beckstead's argument differs in many ways from the actual policy decisions that concern future persons. One would be hard pressed to identify any policy area in which the interests of future persons are given the same weight as those of current generations. Instead, a number of policies seem to be built around the concept of actively discounting the value of not only future commodities but also that of future persons. We shall consider this practice next and examine how it can and should be applied in the context of AMR.

8.6 Discounting the future

When considering the interest of future persons, one of the most frequently discussed questions is if (and how) future benefits ought to be discounted.[444] Broadly speaking, time discounting rests on the assumption that benefits accrued at some point in the future are worth less than benefits accrued in the present time. In economic theory, this principle stems from the assumption that marginal utility of a good decreases over time as its production cost falls and that present value should therefore exceed future value. The discounting of the value of physical commodities is widely

contagious patients. In the absence of alternatives to treatment (for example, more vaccinations) the underuse of antibiotics would likely result in a higher disease burden.

[444] see e.g. Broome, J. (1994). "Discounting the Future." Philosophy & Public Affairs **23**(2): 128-156. Caney, S. (2008). "Human rights, climate change, and discounting." Environmental Politics **17**(4): 536-555.

accepted in economics. On the other hand, discounting immaterial goods such as wellbeing of future persons poses significant philosophical challenges.[445]

In particular the concept of pure time discounting, which views future benefits to be worth less just because they are in the future has been viewed critically by many philosophers and economists. John Broome and Derek Parfit for example, have argued extensively against the underlying logic of pure time discounting when applied to future persons and their wellbeing.[446] In describing what he calls the social discount rate, Parfit explains why the interests of future persons should not count for less, just because they will not be realised immediately. Parfit defines this discount rate as *"the view [that] we can discount the more remote effects of our acts and policies, at some rate of n percent per year."*[447] In criticising this common approach in welfare economics, Parfit writes that even though remoteness in time increases the chance of unpredictability of events, it does not follow that such remoteness should lead us to discount future wellbeing as such and that on this view with a discount rate of five percent (which is commonly assumed in economics) "one death next year counts for more than a billion deaths in 500 years."[448] This outcome is strongly counterintuitive and Parfit rejects it because it stands against a utility-maximising principle that is insensitive to *when* a benefit is realised.[449] John Broome has developed a similar version of this argument by applying it retrospectively. He envisions a case, in which people are faced with a calculation of pure time discounting. In this case, a small event in the distant past is seen to be worse than a large scale catastrophe in the present (an example that follows fundamentally the same logic of time discounting as Parfit's example). Broome argues that most people will reject this approach, because *"the value of one event compared with another depends on the time when the valuation is made"*.[450] Broome thinks that because we tend to only employ time discounting arguments to cases in the future, we have a relativist bias, which leads us to view our own situation as comparably more

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445 Broome, J. (1994). "Discounting the Future." Philosophy & Public Affairs **23**(2): 128-156. p. 128

446 Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press. see Part Four (p. 351 ff)

447 ibid. p. 357

448 ibid. p. 357

449 although note that we shall later see that some utilitarian commentators such as Narveson do not share this view.

450 Broome, J. (2005). "Should we value population?" The Journal of Political Philosophy **13**(4): 399-413. p. 412

important. The fallacy of this argument, he suggests becomes more obvious when the perspective is reversed and current wellbeing counts for less than past wellbeing.

So far, we have considered consequentialist reasons against pure time discounting. However, the concept is equally unconvincing on non-consequentialist accounts of intergenerational justice. Rawls for example dismisses pure time discounting, writing that *"[t]he mere difference of location in time, of something's being earlier or later, is not in itself a rational ground for having more or less regard for it."*[451] Simon Caney has made a similar argument, in which he distinguishes between what he calls different 'subjects of discounting'.[452] While we may discount the value of a commodity based on falling production cost, the irrationality of pure time discounting becomes apparent, when we talk about 'goods' to which the intuition of falling production costs does not apply. Caney suggests that discounting moral rights constitutes such an irrationality. Consequently, he rejects the idea that a positive discount rate should be applied to the wellbeing of future persons whose moral rights count just as much as those of present persons.

However, despite reasonable scepticism about pure time discounting we should not be too quick to dismiss the concept of valuing present and future benefits differently. First of all, as already noted, the discounting of the value of most physical commodities (based on falling production costs) is a far less problematic concept. It is however doubtful, to which extent this is relevant in the example of antibiotics. As noted in chapters 2 and 3, the true value of antibiotics is not the production cost of the individual dose but its effectiveness in combating bacterial infections. Discounting antibiotic effectiveness, however, would only appear to be a sensible strategy if its value could reasonably be expected to decrease. It would appear that the most obvious way in which this could be justified is to treat antibiotic effectiveness as a renewable resource, as some commentators have done.[453] If drugs can either be recycled or replaced, so that the available 'stock' of antibiotic effectiveness can be regularly replenished, then the effectiveness of a *specific* drug

[451] Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. Chapter V, p. 293

[452] Caney, S. (2008). "Human rights, climate change, and discounting." Environmental Politics **17**(4): 536-555. p. 540

[453] Laximinarayan, R. (2006). Economic Issues related to antimicrobial resistance. The Economics of Infectious Disease. J. A. Roberts. Oxford, OUP. p. 50

could be discounted. Note, however, that this is not the same as discounting the value of antibiotic effectiveness *per se*, as the assumption is merely that a specific drug can be easily replaced. The value of antibiotic effectiveness in general would remain unchanged. In addition, as outlined in chapter 3, we should be careful in attempting to frame antibiotic effectiveness as a renewable resource.

While pure time discounting does not appropriately value antibiotic effectiveness over time, we may nonetheless have good reasons to treat present and future benefits derived from this resource differently. As Cowen has observed:

"*Many of the reasons for treating future benefits differently from current benefits do not have to do with time discounting per se. For instance, we should discount future benefits that are uncertain, but this is discounting for risk rather than for time. Similarly, we may discount benefits for future generations because they accrue to wealthier persons, but then we are discounting for wealth. Or altruism may affect how we weight the future, but again this factor is distinct from time discounting as traditionally construed."*[454]

How broadly such considerations of uncertainty can be applied has been illustrated by Tonn.[455] His argument for discounting the future starts from the premise that human extinction may be inevitable and could be caused by external factors that we cannot control (e.g. a meteorite collision with Earth). This element of uncertainty, he argues, should be taken into account when deliberating how to value benefits in the future and might lead us to discount the value of all future investments because there is a chance that they will be left for a time when human life no longer exists. However, since most scenarios for human extinction are actually based on human actions (e.g. nuclear or biological warfare, or climate change), this line of argument is actually more likely to support greater investment into safeguarding the future by limiting the use of certain technologies and resources (including antimicrobial drugs) than to serve as a justification for discounting it.[456]

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454 Cowen, T. (2001). What is the Correct Intergenerational Discount Rate? Fairfax, George Mason University. p. 3

455 Tonn, B. E. (2009). "Obligations to future generations and acceptable risks of human extinction." Futures **41**: 427-435.

456 ibid. p. 434-435

Nevertheless, Cowen's observations about discounting also appear to apply to the case of AMR. While the absence of clearly identifiable medical innovation to combat AMR in the new future should lead us to restrict the use of antibiotics wherever this can be fairly and reasonably achieved, it is true that such innovation may be technically possible. Consequently, the usefulness (or 'utility') of a given dose of antibiotics in the future is variable. It is greater if there are fewer alternative antimicrobial drugs and higher levels of drug resistance, which restrict the number of alternative therapy options. And it is smaller if technological progress and innovation have temporarily or permanently reduced the effect of AMR. Either way, this position is entirely compatible with Parfit's, Caney's and Broome's respective arguments, because it does not suggest that the value of *individual wellbeing or health* should be discounted. Instead, it merely points out that in light of *potential* technological progress we should not assume the utility of a given resource to be static over time. Whether or not one takes this to mean that a positive discount rate should be applied, will largely depend on how optimistic one is with regard to medical and technological innovation. However, given the current dearth of research into new antimicrobial drugs, there does not appear to be a sound argument for the discounting of antibiotic effectiveness over time.

In the previous sections it was outlined why AMR presents a special case for considerations of intergenerational justice, both with regard to the definition of separate generations and the possibility for discounting future benefits. We shall now consider how - in light of these caveats - we can come to develop a model of intergenerational distributive justice for antibiotic effectiveness. To this end, we will examine in greater detail, how consequentialists and contractualists account for the interests of future persons. We will begin by considering a consequentialist approach to intergenerational justice, which is a useful starting point, because it also introduces one of the main challenges to intergenerational justice, namely Derek Parfit's non-identity problem.

8.7 Consequentialist approaches to intergenerational justice

As the discussion in chapter 4 already suggested, some of the weaknesses of consequentialism in the intragenerational case can be seen as a strength when

considering justice between generations. In particular, consequentialism appears well suited to account for the interests of future persons that do not yet exist. This distinguishes the consequentialist approach from theories that are based on the concept of reciprocity, such as most contractualist doctrines, for which the consideration of non-existent persons is much more difficult. Consequentialism's principle of interpersonal aggregation of benefits and its indifference to their precise distribution among people were shown to be problematic for the distribution of goods among contemporaries. However, in the intergenerational case both of these characteristics are an advantage. As long as utility will be maximised in the long run, it should not matter to consequentialist whether the persons to realise these utility gains exist at the present time or not.[457] It is therefore not surprising that consequentialist accounts of intergenerational justice have become influential. In particular, this is due to Derek Parfit's work, which has not only developed a detailed account of intergenerational justice but has also pointed out some fundamental moral problems for the fair distribution of resources between generations.[458] It will therefore be useful to consider his arguments in detail.

With 'Reasons and Persons', Derek Parfit has developed one of the most influential accounts of intergenerational justice to date - and many of the problems he outlines remain central to current discussions of intergenerational justice. The extent of his influence is illustrated by the fact that the authors of a recent volume on the topic wrote in the introduction that their aim was to broaden the discourse *"beyond the mere non-identity problem"* that Parfit defined.[459] It is not the purpose of this discussion, to summarise Parfit's work on intergenerational justice in its entirety. However, the aforementioned non-identity problem and some of its associated concerns are highly relevant for the development of a distributive model of antibiotic effectiveness that is sensitive to intergenerational justice.

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457 Gosseries, A. and L. Meyer, Eds. (2009). Intergenerational Justice. Oxford, OUP. See in particular the introduction. Although this is a common position for consequentialists, it should be noted that it is not universally accepted. Narveson for example has argued that "the sole ground of duty is the effects of our action on other people, and from this it follows that whenever one has a duty, it *must* be possible to say on whose account the duty arises - i.e. *whose* happiness is in question", see Narveson, J. (1967). "Utilitarianism and New Generations." Mind 76(301): 62-72. p. 63.

458 See in particular Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press. Part Four

459 Gosseries, A. and L. Meyer, Eds. (2009). Intergenerational Justice. Oxford, OUP. Kindle edition, p. 69 of 6275

8.7.1 AMR and the non-identity problem

Parfit's consequentialist account of distributive justice proposes that if we accept a view of harm which he calls the person-affecting view, it becomes difficult to see how exactly future persons can be harmed by the actions of currently living persons. He calls this conclusion the non-identity problem.[460] Parfit rejects the idea that consequentialists can only engage with the needs of persons that already exist. In 'Reasons and Persons' he defends this rejection by suggesting that to create a life that is worth living is to realise a benefit, irrespective of whether that person will live in the present or the future.[461] While the question what makes a life worth living seems difficult to answer exhaustively, consequentialism allows for a fairly straightforward response. If the utility of being alive outweighs the associated disutility, then a consequentialist account would suggest that the standard of a 'life worth living' ought to be met.[462] Parfit suggests that if one shares his view about creating lives that are worth living, one will also have to endorse a second principle, namely that we benefit a future person (who will live a life that is worth living) even if part of the conditions that are necessary for creating this *specific* person will ultimately lead to a lower quality of life in the future.[463] Put differently, even if choices we make today lead to a lower overall level of utility in the future, those who will be affected by it cannot reasonably be said to be harmed if:

a) our actions were a necessary part of their specific person coming into existence and
b) future people lead lives that are worth living (by the previously defined standard).

Parfit explains his position in a quotation that is worth citing in full:

"Suppose that we are choosing between two social or economic policies. And suppose that, on one of the two policies, the standard of living would be slightly higher over the next century. This effect implies another. It is not true that whichever policy we choose, the same particular people will exist in the further future. Given

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460 Parfit, D. (1983). Reasons and Persons. Oxford, Oxford University Press. Part IV

461 The full extent of this argument goes beyond the scope of the argument of this chapter, however see ibid. Appendix G, p. 487-490

462 ibid. p. 357-358 Note that Parfit accepts that some people may reject the notion of a life ever not being worth living, but this does not create any serious challenge to his line of argument.

463 ibid. p. 358

the effects of two such policies on the details of our lives, it would increasingly over time be true that, on the different policies, people married different people. And, even in the same marriages, the children would increasingly over time be conceived at different times. As I have argued, children conceived more than a month earlier or later would in fact be different children. Since the choice between our two policies would affect the timing of later conceptions, some of the people who are later born would owe their existence to our choice of one of the two policies. If we had chosen the other policy, these particular people would never have existed. And the proportion of those later born who owe their existence to our choice would, like ripples in a pool, steadily grow. We can plausibly assume that, after one or two centuries, there would be no one living in our community who would have been born whichever policy we chose."[464]

What results from this suggestion is Parfit's non-identity problem (or contingency problem): the specific persons who are born in the future owe their existence to the actions of previous generations. And if these actions are a necessary precondition for future lives that are worth creating, it seems like future persons cannot reasonably make a claim to have been harmed by previous actions. The longer the time frame we consider, the greater the contingency of general social policies will be. In other words, when looking at the far future in a couple of hundred years Parfit suggests that it is reasonable to assume that it will affect *"the details of all the lives that, in our community, are later lived"*, including the identity of all living persons.[465]

The non-identity problem poses a serious challenge to claims of intergenerational justice. It is also of particular relevance to our discussion of the case of AMR, because it implies that, due to the contingency of future peoples' existence on today's actions, theories of intergenerational justice cannot invoke a rights claim of future persons to preserve limited resources for their use.[466] Parfit explains this with reference to a policy of depletion of natural resources. If we choose to deplete a resource, rather than to conserve some or most of it for future generations, this may lead to a dramatic reduction in the quality of life in the far future. For a consequentialist this reduction of utility is problematic and should be avoided if

[464] ibid. p. 361
[465] ibid. p. 377
[466] ibid. p. 362-363

possible. But if we take the challenge of the non-identity problem seriously, we cannot claim that a policy of depletion violates the rights of any future person because it will be worse for no one, as long as the life of people in the far future is worth living. To be sure, the policy of depletion would lower peoples' living standards and life expectancy. However, since their life is the result of all previous policy choices, they themselves should not regret that these choices were made, since they were the precondition for their existence.

With regard to antibiotic usage policies, the non-identity problem would appear to create a significant limitation to any claims that future generations may have - especially in the more distant future. Not even the potentially catastrophic scale of the consequences of a post-antibiotic era would alter this. And while we could choose to preserve antibiotic effectiveness, we could certainly not demand the restriction of their use beyond what is medically indicated, as the supposed rights clash between current and future persons simply would not exist. The non-identity problem leads to the conclusion that future persons, and especially those in the far future have no moral right to effective antibiotics.

8.8 Does the non-identity problem really apply to the case of AMR?

As we have seen, the non-identity problem creates serious challenges for accounts of intergenerational justice. However, in the case of AMR it may be less of an obstacle to developing a fair distributive model. Primarily, this is due to the speed with which AMR has been progressing and the relatively short time period we can expect to pass before the remaining antimicrobial resources are depleted. Put more drastically, the intergenerational dimension would be much more relevant for the case of AMR, were it not for the very fast progression of drug resistance that we witnessed over the past decades. As a result, the full consequences of widespread and perhaps even complete AMR will likely already affect current generations.

This observation does of course not resolve Parfit's challenge to intergenerational justice. However, the immediacy with which total AMR can be expected shifts the focus of the discussion to some extent to a question of *intragenerational* justice. Parfit's discussion of the fair depletion of natural resources is based on the assumption that benefits and costs of the policy will be enjoyed in different centuries,

thereby not allowing for an overlap between those who (don't) act on the policy and those who enjoy its benefits.[467] Given that it has taken less than seventy years to go from the introduction of penicillin to extensive drug resistance that often only leaves a single class of effective antibiotics, an argument built on a time frame of multiple centuries appears unsuitable for the question at hand.[468] Nevertheless, even if the effects of AMR will already be experienced by current generations, the non-identity problem suggests that all future people whose existence is a result of current AMR policies, do not have a subsequent moral claim to effective antibiotics. Thus, if we take the non-identity problem seriously it therefore weakens the case for rationing antibiotics to preserve their effectiveness for the future.

8.9 Social contract theory and intergenerational justice

In the previous chapter, a contractualist model of distributing antibiotic effectiveness was proposed. It was suggested that this model offered the most convincing moral account of the challenge presented by AMR and could justify the restriction of antibiotic use for the preservation of antibiotic effectiveness.

Nevertheless, as we have already discussed, the intergenerational sphere appears to create some problems for the use of social contract theories because it limits the scope for reciprocity. Social contract theories (of which contractualism is one variation) usually rely on the assumption that the concerned parties enter *mutually* into agreements. In the case of future persons, this condition cannot be met for obvious reasons. In deliberations about intergenerational justice, we must therefore deal with the challenge of 'unidirectional dependence'.[469] Today's generation does not depend on the action of future generations (assuming no overlap between generations), yet the living conditions of future generations will be shaped to a large extent by the choices made today.[470] Rawls thus observes that "*we can do something for posterity, but it can do nothing for us.*"[471] However, as we have seen, many concerns of distributive justice in the context of AMR arise in the case of neighbouring generations. This leaves much greater scope for reciprocal actions and

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467 ibid. p. 362 ff

468 Bud, R. (2008). Penicillin: Triumph and Tragedy. Oxford, OUP. Chapter 1

469 Heyd, D. (2009). A Value or an Obligation? Rawls on Justice to Future Generations. Intergenerational Justice. A. Gosseries and L. Meyer. Oxford, OUP. p, 169

470 The same does of course hold for historical cases of intergenerational justice, in that our environment is the result of the choices made by previous generations.

471 Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. p. 291

further strengthens the appeal of social contract theories for the formulation of fair distributive principles for the use of antibiotics. We shall here consider two theories. First, the Rawlsian principle of just saving between generations shall be discussed and it will be explained, why it offers an unsatisfying account for our purposes. Secondly, we will examine, whether a Scanlonian model of contractualism can provide a more coherent principle of intergenerational justice.

8.9.1 The just savings principle and AMR

As mentioned at the outset of this chapter, the discussion of intergenerational justice in contemporary political philosophy is often seen to have its origins in John Rawls' work and it will therefore make sense to consider how a Rawlsian perspective on intergenerational justice may inform our discussion.[472] In sections 44 and 45 of 'A Theory of Justice', Rawls examines how his account of justice as fairness relates to intergenerational concerns.[473] Rawls starts from the premise that a utilitarian approach fails to create fairness between generations. As we saw earlier, Rawls is sceptical of the practice of discounting. Interestingly, however, his critique is not so much directed at an insufficient consideration of future interest. Instead, Rawls argues that *"the conclusion is all the more likely that the greater advantages of future generations will be sufficiently large to compensate for present sacrifices."*[474] Thus - from Rawls' point of view - a utilitarian account of intergenerational justice is more likely to overemphasise the interest of future generations at the cost of present or near-future generations. Of course, a utilitarian response to this might simply be that the sacrifices to present generations are unfortunate but morally required. Rawls does not engage with this kind of argument and does not provide any additional arguments for his view. As a result, it is important to note that Rawls' observation that the utilitarian calculus demands excessive sacrifices from present generations does not provide much in the form of an argument *why* it is too excessive.

While he rejects a particularly high rate of savings for future generations, Rawls nonetheless recognises a duty to preserve some resources for future generations,

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472 Heyd, D. (2009). A Value or an Obligation? Rawls on Justice to Future Generations. Intergenerational Justice. A. Gosseries and L. Meyer. Oxford, OUP.

473 Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. pp. 284-298

474 ibid. p. 287

which he calls the just savings principle. Rawls describes this principle as *"an understanding between generations to carry their fair share of the burden of realizing and preserving a just society."*[475] The principle seeks to secure *"the conditions needed to establish and to preserve a just basic structure over time".*[476] Rawls does not specify what precisely this share ought to be, nor does he believe that this question has an obvious answer.[477] The only clear restriction that Rawls provides is that certain 'extremes', such as an intergenerational distribution of goods based on a utilitarian calculus are to be avoided.[478]

The application of the just savings principle to the case of AMR is complicated for a number of reasons. To begin with, the principle is not designed to govern the preservation of specific resources. Its purpose is to preserve institutional structures, by saving sufficient capital for their continued existence.[479] As Meyer has pointed out, this principle thus only really requires a weak form of sufficientarianism. Once basic structures are established, no further saving beyond what is necessary to preserve them is required.[480] These basic structural requirements would most likely not include the preservation of a specific medical resource like antibiotics. In addition, Rawls' principle does not get around the unilateral dependence of generations, which in turn is likely to affect peoples' actions, at least in non-ideal theory.[481] In order to agree on what constitutes a just rate of saving, Rawls has to adjust the original position to apply to an intergenerational case. He suggests that this can essentially be done in one of two ways. Either a) by envisioning an intergenerational 'assembly', in which people know that all those present are from different generations, but no one knows, which generation they belong to, or b) by assuming that those behind the veil of ignorance all belong to the same generation, but have no conception of which generation exactly they are part of. Rawls refers to this as 'the present time of entry' model.[482] He rejects a) because *"to conceive of the*

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475 ibid. p. 289
476 Rawls, J. (2001). Justice as Fairness. Cambridge M.A., Harvard University Press. p. 159
477 Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. p. 286
478 ibid. p. 287
479 ibid. p. 284-285
480 Meyer, L. (2010). Intergenerational Justice. The Stanford Encyclopedia of Philosophy. E. N. Zalta.
481 ibid.
482 Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. § 44

original position in [this way] is to stretch fantasy too far"[483] and instead he favours the second scenario b). However, this original position ought to compel us not to save at all for future generations. This is because irrespective of which point on the generational continuum the people in the original position end up at, their decision about a fair savings rate will merely affect the *next* generation, and for self-interested individuals behind a veil of ignorance the wellbeing of future people is of no concern.[484] Rawls anticipates this objection and adds that people are motivated to care for their family and children, and thus will not discount the future as heavily as pure self-interest might otherwise dictate. He therefore sees *"no inconsistency in supposing that once the veil of ignorance is removed, the parties find that they have ties of sentiment and affection, and want to advance the interest of other and to see their ends attained."*[485] But this is of course not necessarily the case for everyone and we have no reason to believe that even for people with such family ties, the obligations felt towards family members would motivate everyone to adopt a similar rate of saving.

However, it may still be too soon to dismiss the rationale of the just savings principle, especially in the case of AMR. After all, the importance of neighbouring generations in this context strengthens Rawls' argument, and there is even some statistical evidence to support his claim that people would feel compelled to protect resources for future persons: a recent large-scale health survey from Sweden reported that once people were informed of the long term effects of AMR, 80 percent of the more than 40.000 survey participants declared that in principle, they were willing to forego small benefits from antibiotic therapy in order to reduce the burden of AMR in the future.[486]

Nevertheless, since there will also be instances of distributive justice in which there is no generational overlap and because the Rawlsian savings principle fails to

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[483] ibid. §24 p. 139 Note that Rawls does not provide an argument for why exactly this is the case.

[484] Heyd, D. (2009). A Value or an Obligation? Rawls on Justice to Future Generations. Intergenerational Justice. A. Gosseries and L. Meyer. Oxford, OUP. p. 174

[485] Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. p. 129

[486] see Tullberg, S. (2012). "Många beredda att avstå från antibiotika." Retrieved 19.03.2012, 2012, from http://www.skl.se/press/nyheter_2/nyheter-2012/manga-beredda-att-avsta-fran-antibiotika. The survey in question was the *2002-2010 Vårdbarometern* commissioned by the Swedish municipalities. Kjellström, A., M. Kjerfve, et al. (2011). Vårdbarometern: Befolkningens syn på vården år 2002-2010, Västra Götlandsregion.

provide any guidance on *what* and *how much* should be saved for future persons, it is unlikely to be useful in practice when developing a workable principle of fair antibiotic use. We shall therefore move on to examine, if Scanlon's model of contractualism that was developed in the previous chapter offers a more robust approach to governing distributive justice between generations.

8.9.2 Contractualism and future generations

Chapter 7 presented Thomas Scanlon's model of contractualism as a feasible theory for engaging with many of the ethical dilemmas that arise in the fair distribution of antibiotic effectiveness. However, in the intergenerational context contractualism faces some serious challenges. Most obviously, contractualist theories are vulnerable to the implications of the non-identity problem. To remind ourselves, the contractualist argument is based on principles that could not reasonably be rejected. As Page has pointed out, *"for a person to reasonably reject (or raise a decisive objection to) an act or social policy on the contractualist view, this person must (1) be disadvantaged or harmed by it in some way and (2) they must have a complaint grounded in this disadvantage which is unanswerable."*[487] As a result, contractualism will struggle to accommodate the conclusions of the non-identity problem, because i) it states that future persons cannot be harmed by current acts, and ii) we do not know the particular identity of future persons who would try to make such a claim in the first place.

For Scanlon's theory, the second problem can be resolved within the theoretical framework of his approach. Unlike the Rawlsian account that was discussed earlier, Scanlon is not concerned with establishing an explicit bargain between people. As a result, it is not relevant whether all people affected by an action already exist.[488] By merely asking if a rational agent can reasonably reject a proposed policy, Scanlon's thought experiment can also apply to yet unborn persons, especially where such fundamental interests as a healthy life expectancy are concerned. However, this does not resolve the first challenge of the non-identity problem - if future persons cannot be harmed by our actions, then on what grounds could they hypothetically reject any

[487] Page, E. (1999). "Intergenerational Justice and Climate Change." Political Studies **47**(1): 53-66. p. 57

[488] Rawls, J. (1971). A Theory of Justice. Cambridge, MA, Harvard University Press. p. 284-293

policy that they disagree with? An answer to this question can appeal to three arguments.

First, we could insist that the non-identity problem fails to apply to contractualism, because it does not capture the deliberative process of assessing the reasonableness of a principle.[489] Rahul Kumar has proposed that the non-identity problem can be restated in contractualist terms, by asking the following question: "*If the existence of the wronged is not independent of the wrongdoing, whose standing as a person was it exactly that the wrongdoer failed to appropriately take account of in her deliberations?*"[490] Here, Kumar points to the difficulty of conceiving of the interests of future persons when they do not yet exist at the time of deliberation and their interests will depend in part on the decisions we make. Kumar suggests that rather than thinking of future persons as actual persons, we should instead appeal to types of persons. Instead of referring to actual persons, these 'types' represent sets of characteristics and preferences which we could expect to find in future persons. Kumar thus suggests that in deliberating what we owe to future persons, contractualism does not have to take into account specific identities but merely consider the set of characteristics we could expect them to display. On this view, contractualism can sidestep the non-identity problem. It should be noted that this view seems to be compatible only with the ex ante view of contractualism, which we discussed in the previous chapter. An ex post consideration, which would evaluate the moral value of actions after the fact clearly would have to account for the actual identity of persons. However, as we already suggested that the ex ante view constitutes a more plausible interpretation, this does not undermine the argument developed here.

A second argument that contractualists can refer to is that in the case of AMR the relevant time span is too short for the non-identity problem to fully apply. In his examples, Parfit considers a much greater time frame, before he is satisfied, that everyone's existence is dependent on earlier policy choices. Kumar calls such acts identity-fixing acts, where the act in question is a necessary condition for the

489 For an excellent summary of this discussion, see Finneron-Burns, E. (2011). A contractualist response to the non-identity problem (Msc Thesis). MSc Political Theory Research, The University of Oxford.

490 Kumar, R. (2009). Wronging Future People: A Contractualist Proposal. Intergenerational Justice. L. Meyer and A. Gosseries. Oxford, OUP. [Kindle p. 3209 of 6275]

existence of a particular individual.[491] In the case of AMR, because we are primarily concerned with relations between neighbouring generations, the number of identity-fixing acts will be limited, which is to say that some people will come into existence, irrespective of what policies we adopt. If these people suffered the adverse consequences of a given policy (for example the failure to preserve antibiotic effectiveness) their moral claim to having been harmed could not be countered with reference to the non-identity problem. Since the policy which has led to the harm was not an identity-fixing act the non-identity problem does not apply. As a consequence, the specific time frame under which we consider the case of AMR allows contractualist theories to largely ignore the effect of the non-identity problem. Considerations of the far future, on the other hand, would still have to take into account the non-identity problem because here our policy choices would likely be identity-fixing for the majority of people. What has thus been suggested so far is that we can come to have moral obligations to persons in the near future, whereas we do not owe anything to persons in the far future where all particular identities depend on previous choices we made and consequently no one with a life worth living can claim to have been harmed.

A third reason why we may want to endorse a contractualist model of intergenerational justice, despite of the challenge posed by the non-identity problem, is that future persons may have moral claims, even if they have not been harmed by our actions. In chapter 5 it was argued that persons can be seen to have been harmed, even if the harm is imperceptibly small. However, on a Scanlonian account of intergenerational justice, this claim can be extended to justify moral claims, even where no harm has been done.

The claim that someone who has not been harmed can nonetheless be wronged should be uncontroversial to many non-consequentialists. If, for example, I trespass on someone else's property, without that person noticing, I have still wronged the owner of the property, as I have acted against his rights and/or express wish. A consequentialist theory cannot justify the intuition that such an act constitutes a wrongdoing - unless it can explain who has been made worse off as a result of it. But suppose the owner of the property never finds out about my trespassing. In this case, consequentialist theories would endorse the position that no one has been

[491] ibid. [Kindle p. 3241 of 6275]

wronged, since no measurable harm was done. Kumar has suggested that this difference between consequentialist and non-consequentialist theories can explain why the non-identity problem fails to properly apply to a contractualist account of intergenerational justice.[492] Since Parfit's argument rests on the assumption that we do not owe any duties to future persons (as long as their lives are worth living) because they cannot be harmed by our actions, a theory, which does not presuppose that a moral claim necessitates the presence of some form of harm is immune to this kind of criticism.

Kumar's observation is not a knock-down argument for the non-identity problem, since consequentialists can simply dispute that people can be wronged without having been harmed. However, what his argument goes to show is that non-consequentialists do not simply have to acknowledge the non-identity problem either.

8.9.3 Contractualist obligations to future persons - how far can we go?

The discussion of Scanlonian contractualism in chapter 7 examined proposed a principle for antibiotic use, which could not reasonably be rejected. While it concluded that more extreme types of restriction of antibiotic use could be reasonably rejected, it was also shown that contractualism may still be able to justify fairly far-reaching adjustments of antibiotic use policy by invoking a rescue principle. However, Scanlon's rescue principle, which permitted extensive future savings even at great costs to present generations required a direct link between the sacrifice of present people and the harm that future persons incurred. As we have seen throughout the previous chapters, the harm that AMR causes is not attributable to individual actions in a way which would justify such a principle. Moreover, as was already highlighted in chapter 7, the relevance that antibiotics use has not only for the treatment of infections, but also for the prevention of infection makes very severe restrictions to their use counterproductive because it would likely result in an increased infectious disease burden.

It may therefore appear as if contractualism would ultimately only be able to justify limited restrictions of antibiotic use. To this, two objections can be raised. First, the extent to which the use of antibiotics can be restricted is clearly not an indicator for

[492] ibid. [Kindle p. 3306 of 6275]

the strength of the normative argument. If the most convincing account of distributive justice merely permits limited restrictions of antibiotic use, we may simply have to consider alternative strategies to preserve antibiotic effectiveness. Secondly, the restrictions of antibiotics use, which a contractualist principle could reasonably justify still far exceed current practice. As a result, any discussion of whether the principle is sufficiently restrictive seems premature, as long as significant reductions of antibiotic use can still be realised.

8.10 Contractualism or consequentialism? Some concluding remarks

This chapter has shown that some of the weaknesses, which the consequentialist argument displayed in the intragenerational case work in its favour for the consideration of intergenerational justice. In particular, its ability to aggregate interpersonal benefits allow for the trade-off of interests over time. It has been argued in this chapter that the discounting of future benefits cannot be justified, where this concerns the wellbeing of individuals. As a result, consequentialism may place very substantial demands on our current use of resources. This is due to the fact that any utility-maximising principle would likely dictate that most resources are preserved for the large number of future persons who can be expected to attain a higher level of aggregate utility. This problem is of particular relevance when we consider not just the immediate but also the far future. In the case of AMR, however, we have seen that the positive externalities, which the careful use of antibiotics create for infection control may also extend into the future by creating a world with a lower overall disease burden. As a result, the restrictions that a utility maximising principle could suggest for the use of antibiotics may be lower than for other scarce resources. This should in principle lead to a pattern of antibiotic use that is not too dissimilar from that which a contractualist account proposes, albeit for very different reasons. The contractualist account of intergenerational justice permitted a level of restrictions, which eliminated the use of antibiotics in cases where there is no substantial risk of irretrievable harm. Such a principle, it was argued, could not reasonably be rejected. As we saw in the previous chapter, this still leaves us with the question how exactly an acceptable level of risk could be defined. However, in spite of this incompleteness, the contractualist argument seems to be able to offer a coherent account of intergenerational justice. It's ability to sidestep some of the

challenges to intergenerational justice, in particular the non-identity problem, underline its capacity to take into account both the intra- and intergenerational dimension. This separates it from the consequentialist account, which – as was argued in chapter 4 – is less convincing in the intragenerational sphere.

What this leaves us with at this stage is an account of distributive justice in the context of AMR, which can help us to resolve some of the key moral problems of drug resistance. However, its principles do not appear to be reflected in current AMR policies. Furthermore, we have seen that that a morally defensible restrictions of antibiotic use will have to operate within certain boundaries and will by itself be insufficient to preserve antibiotic effectiveness. The following chapter therefore proposes a way in which AMR can be reframed as a particular type of policy challenge, which requires a much broader response than merely a restriction of current use.

Chapter 9: Policy implications: AMR as a super-wicked problem

So far, we have focused on the ethical implications of current policies that seek to deal with AMR and it has been argued that the trade-offs between persons and generations, which necessarily occur as part of these policies, are not sufficiently defined and explicitly taken into consideration. The analysis to this point has shown that for the coherence and fairness of a policy, it matters a great deal that we get its underlying moral justifications right. In the case of AMR, both ensuring and restricting access to antibiotics is an essential part of developing a workable sustainable policies. However, developing such a policy will inevitably require that we go beyond the simplified examples of our discussion of AMR, which were designed to test fundamental arguments about the fair distribution of resources. This chapter therefore combines the lessons of the ethical analysis with a broader understanding of the policy landscape for AMR, in order to make a suggestion about what the future of AMR policy should look like.

It will be suggested that a pragmatic first step towards a better incorporation of the moral concerns raised by AMR will be to frame it as a specific kind of policy challenge, namely as a so-called super-wicked problem. Super-wicked problems display a number of characteristics that prevent the implementation of a single policy solution, and highlight the need for long-term policy responses under conditions of uncertainty. The strength of the super-wicked problem approach is that it offers an explanation why many of the current policies have fallen short of their intended goal and how they could be improved in the future. Moreover, it will be suggested that framing AMR as a super-wicked problem can help to explain why some suggested solutions to the challenge will inevitably fail. The chapter will begin by outlining the concept of super-wicked problems, before applying this theory to the case of AMR.

9.1 Wicked problems

In their article ‘Dilemmas in a General Theory of Planning’, Horst Rittel and Melvin Webber, who first introduced the term in 1973, describe wicked problems as complex challenges to policy makers, which display ten characteristic features, that make them unsuitable to a mode of problem solving akin to methods commonly used

in natural sciences.[493] These include the suggestion that solutions to wicked problems are neither right nor wrong but will at best be 'better' or 'good enough'[494], and the proposition that wicked problems do not allow for a trial-and-error approach to policy-making.[495] 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 that originally suggested policy solutions are no longer viable contenders and new answers need to be found.[496]

Rittel and Webber suggest that the success of social policy in the 19th and early 20th 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. Part of the reason for this, they argue, is *"[t]he seeming consensus, that might once have allowed distributional problems to be dealt with, is being eroded by the growing awareness of the nation's pluralism and of the differentiation of values that accompanies differentiation of publics."*[497] Because of their inherent complexity, their interrelatedness with other policy fields, and the fact that in many policy areas there are several conflicting goals that might each be reasonably pursued, Rittel and Webber argue that policy makers are today faced with problems that are "wicked". On their account, these problems are not solvable by traditional instruments of policy-making, specifically cost-benefit analysis and system analysis, as these approaches fail to capture the characteristics of modern policy challenges. What Rittel and Webber suggest is that in the absence of a singular public welfare model, which meets all needs and interests equally, the definition of policy goals or targets has in itself become a major problem.[498]

The concept of wicked problems, has been applied to a number of areas as diverse as coastal governance, liberal arts and design and climate change.[499] Especially in the

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493 Rittel, H. W. J. and M. M. Webber (1973). "Dilemmas in a General Theory of Planning." Policy Sciences **4**(2): 155-169. p. 160

494 ibid.

495 ibid.

496 ibid.

497 ibid. p. 156

498 ibid.

499 See Jentoft, S. and R. Chuenpagdee (2009). "Fisheries and coastal governance as a wicked problem." Marine Policy **33**(4): 553-560.; Buchanan, R. (1992). "Wicked Problems in Design Thinking." Design Issues **8**(2): 5-21. ; Lazarus, R. (2009). "Super wicked problems and climate

latter case, however, the concept has undergone some adaption to better reflect the global scale of climate change. Levin et al have suggested that in addition to the ten criteria put forward by Rittel and Webber, some policy problems are characterized by four additional distinguishing features, making them even harder to solve, or 'super-wicked'.[500] In addition to Rittel's and Webber's list, these 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
iv) Policy responses discount the future irrationally.

While the concept of super-wicked problems was initially conceived to address concerns over environmental sustainability policies, it also lends itself to the analysis of AMR, as both problems share the characteristic that current policies focus on the generation of short-term improvements, which grossly underestimate the long-term consequences of our current actions.[501]

9.2 Does AMR constitute a super-wicked problem?

As instructive as it may appear to be for the discussion of complex policy challenges, Rittel's and Webber's list of criteria that define wicked problems invites at least two types of criticism. First, their account remains fundamentally descriptive - while they clearly identify and outline the problem, the authors concede that they *"have neither a theory that can locate societal goodness, nor one that might dispel wickedness"*[502] and as a consequence, it remains unclear what follows from identifying a policy problem as a 'wicked' one. The second kind of criticism levelled against the theory of wicked problems is the fact that the conditions of wickedness which Rittel and Webber define can in practice be extended to virtually all policy areas and thus may simply describe the difficulty of political decision-making rather than distinguish a

change: restraining the present to liberate the future." Cornell Law Review **94**: 1153-1234, Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Policy Sciences **45**(2): 123-152.

[500] Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Policy Sciences **45**(2): 123-152.

[501] ibid. p. 124

[502] Rittel, H. W. J. and M. M. Webber (1973). "Dilemmas in a General Theory of Planning." Ibid. **4**: 155-169. p. 169

specific subset of policy problems.[503] This is problematic because the criteria that Rittel and Webber suggest are so broad that to show their applicability to a given policy problem is only of limited help in figuring out how to address it. By contrast, Levin et al's account of super-wicked problem specifies a set of characteristics, which allow for a much more specific classification and thus constitutes a more helpful tool to assess the challenge which AMR presents.

As a result, and due to the aforementioned limitations of Rittel's and Webber's account of wicked problems, the following discussion will therefore focus on the question, whether AMR qualifies as a super-wicked problem. Implicit in this discussion is the assumption that AMR does in fact meet the relevant criteria for a wicked problem, even though an exact match with all ten of Rittel's and Webber's criteria is not required for our purposes. Instead, I wish to focus on the super-wicked problem account, and show that while AMR meets *most* of Rittel's and Webber's broad criteria, it certainly meets *all* of the criteria Levin et al defined for super-wicked problems.[504] To be clear, the reason for choosing to focus on the super-wicked problem criteria is by no means an attempt to side-step any inconsistencies in aligning AMR with the original wicked problem formulation. The more recent account of super-wicked problems is chosen here because it perfectly captures the challenges which policy-makers face in the case of AMR. We will therefore look at each of the four criteria defined by Levin et al in turn, to see how they can inform our understanding of AMR as a policy problem.

9.2.1 Criterion 1: Time is running out

The account of super-wicked problems points to one of the key characteristics of AMR, namely the growing urgency with which an effective policy solution must be sought. Chapter 2 already discussed this aspect in detail, however the need for action is also neatly illustrated by the evolution of the academic discourse on AMR. While some papers published in the 90s, which discussed the policy response to extensive AMR were warning of "the dawn of a post-antibiotic age", by 2005 the discussion

503 Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Ibid. **45**: 123-152.
504 ibid.

had moved to the question, if we had already entered this era.[505] As we saw in earlier chapters, this change in perception is supported by statistical evidence, with multi- and extensively drug-resistant infections becoming more common. And while in some developed countries the overall number of antibiotic prescriptions is actually decreasing, the proportion of second- and third-line antibiotics - drugs of last resort - is steadily on the rise.[506] In a recent point prevalence study for England, Public Health England reported that Meropenem, an ultra-broad spectrum antibiotic that is only administered intravenously, is by now one of the ten most prescribed antibiotics in the country.[507] There is thus an observable trend towards more complex cases of AMR, which make treatment more difficult, more expensive, and - crucially - less likely to succeed.[508] And as we saw in chapter 2, there is by now a serious risk of the emergence of completely drug resistant bacterial strains, of which a number of cases have already been reported.[509]

9.2.2 Criterion 2: Those seeking a solution are part of the problem

The paramount reason for AMR, the misuse of antibiotics not only by patients but also by healthcare providers, is accelerating the depletion of the current arsenal of effective antibiotics. This, in turn, does not only make the research into new drugs more urgent. It also acts as a disincentive for future research. Margaret Chan, Director-General of the World Health Organization alluded to this problem in a recent speech, when she 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?"*

Arguably, irrational use is not merely a problem of prescribers. As chapter 2 discussed, patients have frequently been found not to act in accordance with doctor's

505 Brown, N. (1994). "Dawn of the post-antibiotic age?" BMJ **309**(6954): 615. Alanis, A. J. (2005). "Resistance to Antibiotics: Are We in the Post-Antibiotic Era?" Archives of Medical Research **36**: 687-705.

506 Roehr, B. (2012). "Renewed efforts are needed to curb antibiotic resistance." BMJ **345**.

507 Health Protection Agency (2012). English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011. London.. p. 44

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

509 WHO (2012). Totally Drug-Resistant TB": a WHO consultation on the diagnostic definition and treatment options. WHO Consultation, Geneva, Switzerland, WHO Press.

recommendations in taking prescribed medication.[510] However, the super-wicked problem account may lead us to view current prescribing behaviour outside of a simple assignment of individual responsibility. Super-wicked problems require a shift of policy trajectories, rather than incremental changes to existing policies.[511] As was argued in chapter 3, current policies for the use of antibiotics are unsustainable. This means that the lack of new antibiotics, combined with their systematic and widespread use cannot be addressed effectively, unless fundamental changes to both use and procurement are being made. It is important, not to overlook the aspect of procurement. The reasons for a dearth of new antibiotics under development has been described cogently in the literature, but the discussion has often focussed on the lack of incentives for pharmaceutical companies.[512] Given the scale of the problem that AMR presents to modern societies, the maximisation of short-term returns on investment as sought by major pharmaceutical companies does not only undermine attempts to prolong the effectiveness of antibiotics by developing new ones, it also runs counter to all conceivable social interests. As a result, the question if drug development ought to be dictated by the projected earning potential of private companies ought to receive a much more prominent position in societal discourse.

9.2.3 Criterion 3: Central authorities to address the problem are weak

The third criterion for the existence of a super-wicked problem is the lack of an institutional structure that can meet the challenge effectively and at all policy levels. While the development of international co-operations and sharing of information on AMR between countries has been greatly improved over the past decades, health policy remains fundamentally a national matter.[513] Moreover, while international organisations can - and do - publish guidelines on good practice and prudent use of antibiotics, their implementation lies with the respective national governments, and their observance cannot be enforced. Non-observance is by no means only a matter

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[510] Butler, C. C., S. Rollnick, et al. (1998). "Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throat." BMJ **317**: 637-642. Simpson, S. A., F. Wood, et al. (2007). "General practitioners' perceptions of antimicrobial resistance: a qualitative study." Journal of Antimicrobial Chemotherapy **59**: 292-296.

[511] Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Policy Sciences **45**(2): 123-152.

[512] See e.g. Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies.

[513] Notable organisations which have contributed to international cooperation in combating AMR include for example the WHO, the European Centre for Disease Prevention and Control (ECDC), or the Alliance for the Prudent Use of Antibiotics (APUA)

of ignorance. In many circumstances, countries may simply lack the control mechanisms and infrastructure to meet all requirements and recommendations of best-practice guidelines. Since bacteria do not respect national borders, this discrepancy in national health policies inevitably threatens the effectiveness of antibiotics even in those countries, which enforce the strictest measures to reduce and control the use of antibiotics.

9.2.4 Criterion 4: Current policies discount the future irrationally

As the previous chapter outlined, the appropriate consideration of future risks constitutes a tremendous challenge for policy-making and certainly does not only apply to the problem of AMR. Yet, the discrepancy between the enormous significance that antibiotics have in today's health care systems and the lack of a promising long-term plan to protect this valuable resource for future people is startling. Moreover, as was argued in chapter 8, the discounting of future benefits fails to take into account the interests and claims of persons that have not yet been born. Programmes that promote the prudent use of antibiotics may help to slow down the further spread of AMR but they are fundamentally flawed as an instrument to reverse the current trend. This is because they fail to produce meaningful alternatives to the use of antibiotics or to restrict their availability beyond what is (cost)effective. Ceteris paribus, a best-case scenario would thus currently consist in the preservation of some level of antibiotic effectiveness for the next decade or so, without a replacement strategy once AMR progresses further and makes currently effective drugs obsolete.

While the lack of a long-term strategy for dealing with AMR perhaps reflects a general problem of incorporating the interests of future generations into today's decision making, a more comprehensive approach to dealing with AMR is still urgently needed. The previous chapter discussed the challenges that an intergenerational account of AMR faces but also concluded that the obligations we have towards current generations apply equally to future persons. Current policies on AMR do not sufficiently recognise these obligations.

9.3 How conceptualizing AMR as a super-wicked problem can inform policies

In the previous section, it was outlined why AMR is a super-wicked problem. Next, I will provide two arguments for why this account is relevant from a policy perspective. Briefly summarised, these are that first, current policies do not sufficiently recognise the scope of the problem that AMR poses and second, that policy makers might benefit from looking more closely at suggested solutions to super-wicked problems, which differ from current policy strategies.

Currently, many of the policy responses to AMR (and a fair share of the academic literature) focus on the procurement of new, effective antibiotics and the cost-effective use and 'prudent' use of currently available resources (where costs also include social costs incurred by higher resistance in the future).[514] These efforts are primarily geared towards addressing problems on the supply side and the creation of new resources. In a recent article, Högberg et al illustrated this point by providing an overview of current policy responses to AMR, all of which either focussed on resource management or the promotion of research into new drugs.[515] However, if AMR is understood as a super-wicked problem, it becomes apparent that these responses ultimately have to fall short of the goal of effectively controlling drug resistance in the long run. There are at least two reasons for this.

First, and most importantly, 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.[516] Path dependencies exist along a trajectory of policy decisions where current options are shaped (and limited) by previous policy decisions and reflect the thinking and inherent logic of planners who made decisions at an earlier point in time. A shift in path dependencies

514 See e.g. Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115). Mossialos, E., C. Morel, et al. (2008). Policies and incentives for promoting innovation in antibiotic research. London, European Observatory on Health Systems and Policies, Groves, T. (2012). "Back to basics with the three Rs." BMJ **344**. Laxminarayan, R. and G. M. Brown (2001). Economics of Antibiotic Resistance: A Theory of Optimal Use. Washington D.C., Resources for the Future. **00-36**.

515 Högberg, L. D., A. Heddini, et al. (2010). "The global need for effective antibiotics: challenges and recent advances." Trends in Pharmacological Sciences **31**(11): 509-515.

516 Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Policy Sciences **45**(2): 123-152.

becomes necessary if the trajectory of earlier policy decisions leads to unsustainable outcomes. In the case of climate change, for example such path-dependency is exemplified by the wide-spread reliance on fossil fuels that is difficult to reverse.[517] Because societies are built around a specific method of using a resource, any policy to counteract the effects of such a legacy will either only achieve marginal improvements by remaining within the same path dependency (e.g. by improving efficiency of resource exploitation) or shift the path dependency by making fundamental changes to the use and management of resources. In the case of global warming a generation of sustainable and effective changes will thus not only require the replacement of fossil fuels with an appropriate substitute but also require that we re-think the social structures in which such dependencies exist in the first place.

In the case of AMR, the reliance on antibiotics for both, the treatment and prevention of bacterial infections reflects a similar level of path-dependency. Yet, current policies which aim at either the development of new antibiotics or the prudent use of available resources continue to operate along the same path and do not create alternatives to the use of (and need for) antimicrobial drugs. Consequently, current policies do not offer long-term solution to the problem of AMR, and generate at best what Cashore and Howlett have described as "faux paradigmatic change".[518] Such "faux paradigms" occur, where large scale shifts are implemented but will only correct a previous policy failure temporarily.[519] In the case of AMR, the most obvious example for a faux paradigmatic shift is the reliance on a future development of a new antibiotic, which is effective against resistant bacteria that are otherwise hard to treat. While such a development will provide a significant short-term improvement, past experience has shown that in all likeliness, bacteria will ultimately adapt to the new drug, and again become resistant. Describing this phenomenon, Spellberg recently remarked that - given current policies - *"we will never truly defeat microbial resistance; we can only keep pace with it."*[520] Thus, in the absence of a realistic option for true paradigmatic change (for example the

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517 Unruh, G. (2000). "Understanding Carbon Lock.In." Energy Policy **28**(12): 817-830.

518 Cashore, B. and M. Howlett (2007). "Punctuating Which Equilibrium? Understanding Thermostatic Policy Dynamics in Pacific Northwest Forestry." American Journal of Political Science **51**(3): 532-551.

519 Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Policy Sciences **45**(2): 123-152.

520 B. Spellberg cited in Choffnes, E. R., D. A. Relman, et al. (2010). Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies: Workshop Summary. Forum on Microbial Threats. Washington D.C., NIH. p. 55

development of a new 'super-antibiotic' that offers lasting effectiveness against all bacterial infections), policy makers should abandon the ambition to outpace the adaptation of microbes to new antibiotics, and instead may have greater chances of devising successful policies, if they focus on the creation of incremental but sustainable changes, which no longer follow the same policy trajectory that has been prevalent over the past decades.[521] We will return to the question how such a shift in path dependencies could be generated in the next section.

The second argument for understanding AMR as a super-wicked problem is that this allows us to make sense of why the use of cost-benefit analysis (CBA) is not an appropriate policy response. Chapters 4 and 8 already discussed the limitations of cost-based approaches to AMR. AMR shares this characteristic with other super-wicked problems which - by their nature - are not solvable with standard tools of CBA. This is because for most super-wicked problems the cost of inaction now will be very high at some point in the distant future. On the other hand, responding to the challenge now will often only create benefits at a much later stage, yet impose heavy costs on present societies. Citing again the case of climate change, Lazarus observes that *"the time lag [between the reduction in greenhouse gas emissions and any mitigating effects on climate change] is at the very least longer than the lifetime of any adult. The upshot is that no one who is asked to curtail activities to reduce greenhouse gas concentrations will be likely to live long enough to enjoy the benefits of that curtailment."*[522] As we already saw in chapter 4, the challenge for CBA in the case of AMR is twofold. For one, predicting expected costs and benefits significantly into the future is made difficult by increasing degrees of uncertainty about what will actually happen at a later stage.[523] This problem is illustrated by the fact that incentive schemes to boost R&D into new antimicrobials have found it hard to decide on the size of the incentive, because the calculation of its future benefit was

[521] See e.g. Durant, R. F. and P. F. Diehl (1989). "Agendas, Alternatives, and Public Policy: Lessons from the U.S. Foreign Policy Arena." Journal of Public Policy **9**(2): 179-205. Levin, K., B. Cashore, et al. (2012). "Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change." Policy Sciences **45**(2): 123-152. Cashore, B. and M. Howlett (2007). "Punctuating Which Equilibrium? Understanding Thermostatic Policy Dynamics in Pacific Northwest Forestry." American Journal of Political Science **51**(3): 532-551.

[522] Lazarus, R. (2009). "Super wicked problems and climate change: restraining the present to liberate the future." Cornell Law Review **94**: 1153-1234. p. 1167

[523] McGowan, J. E. (2001). "Economic Impact of Antimicrobial Resistance." Emerging Infectious Diseases **7**(2): 286-292.

unknown and difficult to calculate.[524] Furthermore, even if costs and benefits could theoretically be assessed accurately in the long run, this still leaves policy makers with unanswered questions regarding the appropriate time span to consider as well as the rate, at which benefits that are enjoyed by present people ought to be traded off against the benefits that future people may enjoy.[525]

Since super-wicked problems do not allow for a simple calculation of costs and benefits of different policy responses, recognising AMR as belonging to this category of problems would rule out any policy that relies heavily on CBA. This should help to move the current discussion forward and focus it on the policy solutions that have the potential to appropriately address super-wicked problems. We shall consider next, what such policy solutions may look like.

9.4 Incrementally shifting the path dependency on antibiotics

So far, it has been argued that current strategies to combat AMR replicate existing path dependencies and thereby fail to create sustainable policy solutions. The following discussion provides a brief sketch of how a shift in path dependencies may be generated, primarily by placing greater emphasis on some aspects of currently existing antibiotic usage policies. The suggestions made in this chapter do not amount to a comprehensive policy proposal but may help in categorising policies according to their expected effectiveness in the long run.

Arguably, any effective response to the threat of AMR will first and foremost require a reduction in the dependency on antibiotics. Since there are no feasible alternative drugs or treatment options, which could be made widely available in the near future, a shift in path dependency is unlikely to be achieved by replacing antibiotics with an entirely different mode of treatment.[526]

Instead, it requires health policy makers to place much greater emphasis on the containment of infection, effective infection control, and prophylactic measures such as vaccinations that offer protection against infection in the first place. None of these

524 Morel, C. and E. Mossialos (2010). "Stoking the antibiotic pipeline." BMJ **340**(c:2115).

525 Mulgan, T. (2011). Ethics for a Broken World: Imagining Philosophy After Catastrophe. Durham, Acumen.

526 There have been suggestions that microphage therapy may offer a viable alternative to the treatment with antibiotics, however so far there is insufficient evidence to support this view. See Häusler, T. (2008). Viruses vs. Superbugs - a solution to the antibiotic crisis? New York, Macmillan.

mechanisms are silver bullets, and they may appear less heroic (and are certainly less profitable) than the scientific discovery of a (temporary) cure with the help of new drugs. However, there are already a number of examples for how a shift towards lower dependency on antibiotics could be achieved.

A good example for the successful implementation of such a policy can be found in the Netherlands, where a strict screening process for newly admitted hospital patients has been introduced to identify individuals who are colonised with MRSA.[527] By isolating these patients early on the Netherlands have managed to achieve one of the lowest rates of methicillin-resistance in the world.[528] This campaign is additionally supported by a policy of limiting the access to antibiotics and insisting on the widespread use of laboratory-confirmed testing for pathogens prior to a course of treatment with antimicrobial drugs.[529]

A second approach that has been discussed is to focus research on the development of prophylactic measures, rather than treatments of acute infections. One example is the development of vaccines against bacterial infections, which has shown promising results in some areas.[530] These measures are only examples of how a shift in path dependency may be achieved and they have already been discussed in the literature.[531] However, if AMR is understood as a super-wicked problem, this should lead us to put much more emphasis on those kinds of policy solutions that can generate a shift in path dependency.

It should be stressed that an incremental shift in path dependency will not make antibiotics superfluous. Arguably, even in scenarios where prophylactic measures such as vaccines are more widely available, opportunistic infections would still

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527 Dekker, T. J. and P. v. d. Broek (2010). "Successful Control of MRSA in Dutch Hospitals." International Journal of Infection Control **6**(1).

528 Wertheim, H. F. L., M. C. Vos, et al. (2004). "Low prevalence of methicillin-resistant Staphylococcus aureus (MRSA) at hospital admission in the Netherlands: the value of search and destroy and restrictive antibiotic use." Journal of Hospital Infection **56**(4): 321-325.

529 ibid.

530 Fattom, A., G. Horwith, et al. (2004). "Development of StaphVAX, a polysaccharide conjugate vaccine against S. aureus infection: from the lab bench to phase III clinical trials." Vaccine **22**(7): 880-887.

531 See e.g. . Wertheim, H. F. L., M. C. Vos, et al. (2004). "Low prevalence of methicillin-resistant Staphylococcus aureus (MRSA) at hospital admission in the Netherlands: the value of search and destroy and restrictive antibiotic use." Journal of Hospital Infection **56**(4): 321-325. Miller, L. S. and J. S. Cho (2011). "Immunity against Staphylococcus aureus cutaneous infections." Nature reviews. Immunology **11**(8): 505-518.

require the use of antibiotics.[532] Consequently, a shift in path dependency does not constitute a one-stop remedy for all types of AMR. However, it is reasonable to assume that the required quantities would be much lower than those, which are currently being used. Moreover, by focussing on incremental changes that counteract current path dependencies, the super-wicked problem account of AMR promotes a pragmatic policy-making approach that should respect the financial limitations of health care systems.

9.5 Summary

Understanding AMR as a super-wicked problem is not merely a matter of categorisation. Instead, it should lead us to reconsider the usefulness of current policy approaches. If AMR does indeed present a super-wicked problem, any policy approach that relies primarily on large-scale medical and/or technological solutions fundamentally misunderstands the nature of the challenge, as well as the level at which it needs to be addressed.

The super-wicked problem account does not provide a simple solution to the problem of AMR but it explains why most policy initiatives to date have been unable to address the challenge. In this chapter, I have argued that understanding AMR as a super-wicked problem ought to lead us to pursue a shift in path dependency, instead of fine-tuning existing measures. What is therefore urgently needed is a more integrated and internationally coordinated approach to combating AMR, for which the available means truly reflect the scope of the problem.

Of equal importance is the fact that understanding AMR as a super-wicked problem highlights the immense importance of considering more fully the effects that a lack of effective antibiotics will have on future people. Incorporating the interests of future people into policy-making would acknowledge the shared burden, which is created by current generations, but (partially) borne by their successors. Understanding AMR as a super-wicked problem therefore offers additional reasons to consider distributive principles such as the contractualist account developed in chapters 8 and 9, which can resolve both intra- and intergenerational problems. Furthermore, given the inherent complexity of super-wicked problems, framing

[532] Choffnes, E. R., D. A. Relman, et al. (2010). Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies: Workshop Summary. Forum on Microbial Threats. Washington D.C., NIH. p. 47

AMR as one provides further arguments for the rejection of normative approaches, which rely heavily on the exact calculation of costs and benefits.

Chapter 10:Discussion and Conclusion

In her recent book 'The Drugs Don't Work' Sally Davies, the Chief Medical Officer for England, envisioned a future in which bacterial infections had become entirely untreatable. In such a world, she and her co-authors speculated, families might have to isolate members that had acquired bacterial infections and effectively leave them to die.[533] The disturbing image was an attempt to shock us into action and realise the seriousness of the threat. However, despite increasing awareness of the size of the problem, we are still lacking appropriate responses to AMR. This thesis has highlighted the moral significance of AMR and explained what implications it has for distributive justice.

As the previous chapter outlined, we may be unable to solve the problem of AMR once and for all due to its nature and complexity. However, this should not lead us to think that we cannot do more (and in fact have an obligation to do so). Current levels of antibiotic consumption are likely to produce complete AMR in the near future, which makes it necessary to establish how we can reduce our consumption enough to at least slow this process down. To date, few policy initiatives have proposed to reduce antibiotic use, even if this means that patients will have to forego some benefits. The ethical challenges and in particular concerns over distributive justice that a more restrictive use of antibiotics presents us with may partly help to explain this reluctance. By mapping more clearly, what these challenges are and how they could be addressed, this thesis has aimed to contribute to the development of a strategy to successfully address AMR.

10.1 Summary of the main argument

We started our discussion with an exploration of the origins and causes of AMR and examined possible solutions. It was concluded that AMR is an inevitable by-product of antibiotic use but that the speed at which AMR progresses depends greatly on the extent and conditions under which we use antibiotics. Over- and misuse of antibiotics were identified as the main sources of AMR, while the lack of research into new drugs exacerbated the problem of dwindling antibiotic effectiveness further. This

[533] Davies, S. C. (2013). The Drugs Don't Work: a global threat. London, Penguin.

discussion concluded that in the near future, current policies are insufficient to halt or reverse the progress of AMR.

In chapter 3, it was proposed that the distributive problem of AMR should be phrased in terms of the fair distribution of antibiotic effectiveness. The thesis then considered a number of distributive problems, which the existing literature described as being analogous. The discussion showed that while some distributive problems such as the 'tragedy of the commons' or greenhouse gas emission bear a certain resemblance to the case of AMR, drug resistance is a policy challenge sui generis. This conclusion challenged the existing academic view of AMR as being analogous to other policy problems. It was suggested that because of the distinctive features of AMR, analogical reasoning would not produce workable solutions for the problem at hand. These features include the positive externalities that result from antibiotic use, the fact that overconsumption of antibiotics is irrational and the possibility of recovering antibiotic effectiveness in the long run by either reducing their use or developing new drugs. Chapter 3 concluded that accounts of distributive justice, which consider the case of AMR need to answer the question how to distribute a resource that is vital for the protection of health but declines in effectiveness through use.

Chapter 4 constituted a first attempt of formulating a coherent account of the specific normative challenges of AMR by considering a consequentialist approach to distributive justice. While consequentialist concepts have found widespread use to govern the distribution of scare health care resources, our discussion showed that its application to the case of AMR was complicated and had to deal with a number of inconsistencies. Chief among them was the concern that consequentialism aggregates benefits across persons and cannot account for the specific claims or rights or the individual. The argument presented in this chapter did not amount to a refutation of consequentialism, nor did it entirely rule out its application to the case of AMR. However, it challenged the assumption that consequentialism lends itself particularly well to decision-making in health policy.

Chapter 5 picked up on an aspect of the discussion in the previous chapter, namely the concept of harm. By examining if the moral relevance of AMR could be described in terms of either harm or risk, the thesis expanded the existing discourse

on the moral challenges of AMR. To this end, Feinberg's definition of morally wrongful harm was adopted and applied to the case of AMR. It emerged that – on the assumption that it constitutes a rights violation (which was shown in chapter 6) - AMR can be considered morally wrongful due to the harm it causes, even when these harms are very small. This concept did face two problems. First, the direct causal relationship between individual agency and the emergence of AMR was shown to be weak. Secondly, it did not account for the fact that in many instances, the emergence of AMR does not only create harm, but also increases the risk of harm to others. Consequently, it was examined whether the moral wrongfulness of AMR would be better captured by the describing it in terms of the risk of suffering a harm. It was shown that such an account did not yield a satisfying result either. Two reasons for the rejection were provided. First, the concept of framing subjection to risk as harm created a number of epistemic and conceptual problems. Second, the approach ultimately limited the scope of morally wrongful harm to instances, in which wellbeing was affected by exposure to a known risk. This was rejected as too narrow a focus for the moral considerations of AMR. Thus, an account of AMR being morally wrongful because of the harm it produces seemed like a possible, albeit fairly limited explanation. Moreover, this view still required that we could show that AMR constituted a rights violation, which was examined in the following chapter.

In chapter 6, it was shown that a theory of moral rights could explain the normative challenges of AMR. The thesis adopted Raz's interest theory of rights and showed that on this account, a right to protection from adverse health outcomes was defensible and that a misuse of the necessary resources constituted a violation of such a right. This violation would then in turn produce a corresponding duty on others. The rights approach was shown to have a number of advantages. In particular, it could show that people may have moral claims, even if these claims could not be met appropriately. A rights based approach could therefore make sense of a normative claim to effective antibiotics even at a stage where no effective drugs were available anymore and could therefore plausibly explain why future claims to antibiotics have equal moral worth. At the same time, the rights-based approach displayed a number of drawbacks. To begin with, while the rights approach can show that AMR leads to the violation of individual rights, it was argued that the causal remoteness of the corresponding duty made it difficult to see what such a rights

violation could actually compel anyone to do. Another problem, which the right-based account faced was the difficulty in formulating a right to a resource that would naturally diminish over time and could therefore only be provided for a decreasing number of the claimants. It was argued that while this did not affect the strength of the moral claim, it would reduce the practical relevance of such a right.

Chapter 7 suggested a contractualist approach as a better way of framing the challenge of AMR and examined Michael Millar's work, which has sought to apply a Scanlonian principle to the distribution of antibiotic effectiveness. It was argued that contractualism can capture and reconcile conflicting interests in the case of AMR and that Millar's proposed principle for the use of antibiotics cannot be reasonably rejected by contractualists. However, the discussion also showed that in some instances contractualist accounts would permit more restrictive policies for the protection of antibiotic effectiveness than the one proposed by Millar. It was suggested that this should not lead us to reject Millar's principle, but that the latter may require more specification. In particular, the thesis showed that the conception of acceptable risk in Millar's account is insufficiently specified and raises a number of normative challenges regarding its measurement. It was concluded that in the intragenerational context, a contractualist approach seems to offer the most comprehensive account of the distributive challenge presented by AMR.

Since AMR does not only affect current generations, but also limits the availability of effective antibiotics in the future, chapter 8 considered intergenerational concerns of drug resistance. Intergenerational distributive justice raises a number of specific problems. The thesis discussed four of these challenges in detail, namely the problem of distinguishing between generations (especially if they overlap), the difficulty of defining obligations towards people in the far future, the practice of discounting future events and the non-identity problem. It was proposed that the last of these presented the greatest challenge to any account of intergenerational justice The thesis then considered how both consequentialism and contractualism could deal with this challenge. It was argued that due to the fast progression of AMR, Parfit's non-identity problem does not fully apply, since complete drug resistance may already occur within the life span of the present generation. However, it was also outlined that a contractualist account of AMR could deal with the non-identity problem, as its

assessment for the reasonableness of actions was possible without knowing the exact identity of future persons. The contractualist account of intergenerational justice permitted a level of restrictions, which eliminated the use of antibiotics in cases where there is no substantial risk of irretrievable harm. Such a principle, it was argued, could not reasonably be rejected. As we saw in the previous chapter, this still leaves us with the question, how exactly an acceptable level of risk could be defined. However, in spite of its incompleteness the contractualist argument seems to be able to offer a coherent account of intergenerational justice. Its ability to sidestep some of the challenges to intergenerational justice, in particular the non-identity problem, underlines its capacity to take into account both the intra- and intergenerational dimension. This separates it from the consequentialist account, which – as was argued in chapter 4 – is less convincing in the intragenerational sphere.

After having developed an account of both intra- and intergenerational justice in the case of AMR, we were left with the question what this account implied for practical decision-making, especially since the principles that were suggested for a fair restriction of antibiotic use are not reflected by current policies. Chapter 9 proposed that a possible first step was to start by reframing AMR as a particular kind of policy challenge, a so-called super-wicked problem. These problems are characterised among other things by their degree of complexity and their lack of an easy technological solution. In addition, they displayed four key components, namely a lack of time to respond, the entanglement of those seeking a solution in the causes of the problem, a lack of central authorities and a tendency to discount the future irrationally. This approach, it was suggested, highlighted two crucial aspects of AMR. First, it underlined the urgency, with which a solution must be sought, and the lack of any technological fixes. Secondly, the concept of AMR as a super-wicked problem showed that to control AMR, we will have to do more than merely restrict the use of antibiotics, although this is clearly a highly important first step. What the approach suggested was that policies would have to create a shift in path dependency and that a comprehensive strategy to address AMR must also seek to reduce the reliance on antibiotics in the future, in order to mitigate the effects of AMR.

10.2 What can we conclude?

In chapter 1, it was outlined that this thesis has had two primary aims. First it sought to examine how and why AMR is a moral problem and raises questions of distributive justice. Second, it aimed to develop a framework within which these questions of distributive justice could be answered.

Reflecting on the overall argument, how can we answer these questions now? The argument that was developed in this thesis suggested that AMR constitutes a very specific normative challenge, which is unlike other collective action problem. AMR creates a scarcity of antibiotic effectiveness, which is a resource that we would ideally like to make available to everyone who needs it. However, the rate at which we use it will also determine how quickly the remaining stock is depleted.
Given that antibiotics play such a crucial role in health care, this presents us with a serious dilemma, namely how to preserve a resource which is of such great use to many but for which we have not found a sustainable way of consumption. It was argued that the need to find a solution to the problem of how to fairly distribute antibiotic effectiveness was exacerbated by the fact that suffering from a drug-resistant infection could be legitimately described as a morally wrongful harm, which adversely affects the health of many and thereby violates their individual rights.

The second question we initially asked was how the concerns of distributive justice, which are raised by AMR could be adequately addressed. We have seen that different moral theories prescribe different answers to this question but that a particularly convincing account has been put forward by contractualists. The contractualist argument led to the proposition and defence of a principle of antibiotic use, which restricted their application to instances where they could prevent a serious risk of irreversible harm. This principle, it was suggested, could not be reasonably rejected by anyone, not even by those with whose individual interests it conflicted. Moreover, the principle was shown to be sensitive to the interests of future persons, who may be the ones to bare most of the burden of AMR. It was also suggested that contractualism could in principle require greater sacrifices but that this seems to conflict with the use of antibiotics, which do not only create negative externalities in terms of AMR but also positive externalities in the shape of a lower disease burden for infectious diseases. As a result, there are limits to the restriction of antibiotic use

beyond which a further reduction may become counterproductive. This applies in particular to highly contagious diseases.

While the contractualist argument offers a coherent account of distributive justice in the case of AMR, it was also shown not to be without flaws and it some leaves important questions unanswered. For instance, we did not establish a convincing account of what constitutes an acceptable level of risk, and whether this figure should be the same in all countries and for all people. These are important questions, which may be addressed in future research projects but will hopefully also become part of a public discourse about the principles that should govern the fair distribution of antibiotic effectiveness in the future.

It was already emphasised in the first chapter that the proposed contractualist principle did not amount to a complete refutation of alternative theories. Indeed, we saw that consequentialist arguments and rights-based approaches have specific strengths but failed to account for the question at the heart of contractualism, namely what we owe to each other. This, I believe, is the crucial question, we should try to answer, when deciding about the allocation of scare resources like antibiotic effectiveness. The restriction of antibiotic use will be a difficult process and it will require that we forego small or moderate personal benefits for the sake of other people's wellbeing. Similarly, our own life may at a later stage depend on the preservation of antibiotic effectiveness. The contractualist approach captures this element of reciprocity, and may also help to communicate the need for a policy that is unlikely to be popular.

A recent example nicely exemplifies the difficulty of explaining the need for more restrictive antibiotic policies. In January 2014, the Danish Ethics Council released a statement on the normative problems of AMR.[534] It also mentioned the possibility of rationing of antibiotics as one potential option to preserve antibiotic effectiveness – a suggestion that was immediately met with a hostile reaction from the press. On the following day, one of Denmark's largest newspapers, *Politiken*, ran a story entitled 'Ethics Council: Doctors should no longer care about the individual patient'.[535] Part

[534] Andreasen, M. (2014). Arbejdspapirer om antibiotikaresistens. Copenhagen, Det Etiske Råd (Danish Ethics Council),. p. 2

[535] Reenberg, S. and S. Thomsen (2014). Etisk Råd: Lægerne bør ikke tage hensyn til den enkelte patient længere. Politiken. Copenhagen.

of our task, it appears, will therefore be the formulation of arguments that are not only philosophically plausible, but also accessible and convincing to a broader audience. Philosophical enquiries into AMR may therefore end up being more concerned with the relevance of conclusions for policy formulation and public communication than is common even in the field of applied ethics. However, this merely reflects how much is at stake for both, future generations and us.

10.3 Should we base ethical decisions on worst-case scenarios?

At this point in our discussion, the conclusion looks rather bleak and the restrictive principles for antibiotic use that were proposed in this thesis were all based on the assumption that the problem of AMR will continue to grow. Chapter 2 showed that these assumptions are firmly grounded in scientific research and reflect the opinions and concerns of health protection agencies. However, this perspective also raises a question that pertains to bioethics and public health ethics more generally, namely how to balance the consideration of (realistic) scenarios with very bad consequences against a tendency to base policies on worst-case assumptions. Worst-case scenarios, it has been noted by numerous commentators before, rarely make for good policies. They overreach on the intended goal, create legal exemptions that may ultimately be unnecessary or assign financial and human resources to preparedness initiatives that could be put to better use elsewhere.[536] Most importantly, however, they risk that individual rights are curtailed without proper grounds.[537] As the discussion in previous chapters has shown, erring on the side of caution in the case of AMR may not simply be a matter of over-investing into new drugs. It may also involve that medication is withheld from patients or that individual liberties are curtailed. The opportunity cost of basing policy decisions on an overly pessimistic scenario is thus not only a financial one - it will affect the health and lives of a large number of people.

However, if we take this kind of argument seriously we also must not overlook the fact that AMR already adversely affects the lives of thousands of people every year.

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[536] Annas, G. J. (2010). "Standard of Care — In Sickness and in Health and in Emergencies." New England Journal of Medicine **362**(22): 2126-2131. Coker, R. J. (2000). From Chaos to Coercion: detention and the control of tuberculosis. New York, St. Martin's Press.

[537] Enemark, C. (2013). "Drug-Resistant Tuberculosis: Security, Ethics and Global Health." Global Society **27**(2): 159-177.

Thus, the formulation of policies to meet this problem should differ notably from any scenario in which we are merely considering the possibility of a future adverse event, say an act of bioterrorism or a particularly virulent and lethal strain of pandemic influenza. The occurrence of these events is a mere probability (albeit of varying magnitude); they may or may not come about. Policy-making in the case of AMR does not have to operate under this assumption. The catastrophe is already unfolding and the most recent reports on the development of AMR are similar in their tone and message. The problem has been variously described as an 'apocalyptic scenario' and 'catastrophic'.[538] What we may, however, have to reconsider is the communication strategy for AMR. In particular the language of large-scale catastrophes can produce counterproductive results. Brigitte Nehrlich, for example, has observed that references to disasters and an impending apocalypse bring with them as sense of inevitability that does not reflect the true range of responses still at our disposal.[539] In closing, we shall return to these possible responses, and discuss what the next steps in a response to AMR could be.

10.4 Where do we go from here?

In this thesis, it has been shown that the restriction of antibiotic use can be justified on grounds of distributive justice and in order to preserve higher levels of antibiotic effectiveness for the future. However, as things stand, this measure alone – though important – is unlikely to halt or even reverse the current trend of increasing AMR. A successful strategy to address the problem of AMR will have to go further. As we have seen, there are limits to the restrictions we can reasonably place on antibiotic use, but there are other options we can and pursue.

These options include the strategies that were outlined in chapter 2, for example the investment into R&D for new antibiotics, especially against Gram-negative bacteria. However, some measures may be easier and quicker to implement. These include the development of better communication strategies that explain not only why AMR is a threat to health, but also what makes antibiotic effectiveness a special and important commodity and what everyone can do to protect it. In the past, such strategies appear

538 Smith, R. and J. Coast (2013). "The true cost of antimicrobial resistance." BMJ **346**. Godlee, F. (2013). "Antimicrobial resistance—an unfolding catastrophe." BMJ **346**.

539 Nerlich, B. and R. James (2009). "'The post-antibiotic apocalypse' and the 'war on superbugs': catastrophe discourse in microbiology, its rhetorical form and political function." Public Understanding of Science **18**(5): 574-590. p. 582

to have failed to create a general awareness for the mechanisms and consequences of AMR. We may also have to think about ways in which we can communicate the difficult decision of restricting the availability of antibiotics. As we saw earlier in this chapter, the rationing of antibiotics is unlikely to be met with widespread public approval.

Most importantly, however, our discussion of super-wicked problems highlighted the importance of looking for ways in which we can reduce the path dependency of AMR. To reduce the future dependence on AMR will likely require extensive research into alternative strategies to reduce the rate of bacterial infections, for example by developing vaccines or improving infection control in hospitals. As a result, the introduction of such measures will come at a significant cost. However, a shift towards strategies that reduce the burden of bacterial infections, rather than produce more antibiotics would also mark a paradigm shift in the way we view infections. Michael Specter has recently made the case for a reconsideration of our views towards bacteria, fittingly entitled 'Germs are us'. In it, Specter proposes that our traditional approach of viewing bacteria as germs to be eradicated does not only misunderstand their importance for our environment, but also creates a narrative which focuses on the complete eradication of pathogens.[540] This war rhetoric of eradication is unhelpful and obscures the fact that a 'victory' over bacterial infections is unlikely to be achieved by any new drug.[541]

Reducing our initial dependence on antibiotics and recognising that we will not win a pharmaceutical war against microbes, no matter how far we escalate it, may therefore be a step towards a more balanced view of bacteria. And it could help to move the policy discourse forward by offering possible alternatives to the vicious circle of new drug developments and increasing AMR.

In summary, it therefore seems that despite the fast progression of AMR we still have a number of options to meet our obligations to preserve antibiotic effectiveness for the future. It is time that we started taking these obligations seriously.

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[540] Specter, M. (2012). Germs are us. The New Yorker. New York, Condé Nast. 22.10.2012

[541] Note, however, that DeGrandis has suggested that in some limited instances, the use of war rhetoric may in fact accurately describe some of the challenges of AMR. DeGrandis, G. (2011). "On the Analogy Between Infectious Diseases and War: How to Use it and not to Use it." Public Health Ethics **4**(1): 70-83.

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