ANTIBIOTICS AND ANTIBIOTIC RESISTANCE: WHAT DO WE OWE TO EACH OTHER?

By

MICHAEL MILLAR

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School of Health & Population Sciences
University of Birmingham
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ABSTRACT

There is a tension between the need to use antibiotics to prevent adverse outcomes from infection, and a consequence of their use, which is antibiotic (treatment) resistant infection. Actions taken to control the spread of antibiotic resistant microbes, and constraints on the use of antibiotics both give rise to ethical tensions.

I consider the evaluative framework and the principles that might be used to decide a just distribution of burdens and benefits associated with the use of antibiotics.

Nussbaum specifies a list of capabilities. A minimum sufficiency of each capability is required for a life of human dignity. Nussbaum's approach provides a richer framework for the evaluation of the distribution of burdens and benefits associated with the use of antibiotics than prevailing health economic, or prevalence of disease measures.

There are contexts in which we cannot assure a sufficiency of capabilities. I consider the potential for Scanlon's contractualism to provide principles for deciding the distribution of burdens and benefits associated with the use of antibiotics under differing levels of resource constraint.

Finally I consider the influence of metaphor and analogy in the context of the human relationship with microbes.

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ANTIBIOTICS AND ANTIBIOTIC RESISTANCE: WHAT DO WE OWE TO EACH OTHER?

What do we owe to each other when it comes to the use of antibiotics and the control of antibiotic resistance? There are tensions between the need to use antibiotics to prevent adverse outcomes from infection, and an adverse consequence of their use, which is (antibiotic) treatment resistant infection. How should these tensions be balanced?

Antibiotic resistance is a form of microbial adaptation, which allows microbes to persist in the presence of antibiotic(s). In order to sustain the effectiveness of antibiotics that are currently available there are a number of strategies that we might use.

The two strategies that are considered in this thesis are –

1. The control of the spread of antibiotic resistant microbes
2. Constraints on the use of antibiotics

Both of these strategies raise ethical questions with respect to the distribution of burdens and benefits.

Chapter One outlines the background to questions to be addressed in subsequent chapters. The ethical questions identified include the sort of information that should be used to evaluate the justice of the distribution of benefits and burdens associated with antibiotics and antibiotic resistance; the extent to which we should prioritise the control of antibiotic resistant microbes when there are alternative resource demands (for example for treatment of diseases such as

cancer); principles governing the use of antibiotics; acceptable levels of risk (associated with using or not using antibiotics); and the way in which we conceptualise and communicate the issues and concerns involved in our relationship with microbes.

In **Chapter 2** I consider the information that we should use to evaluate the justice of the distribution of burdens and benefits associated with infection (including treatment resistant forms) in healthcare contexts such as hospitals. It is important that we use the right kind of information. Antibiotics can and do have substantive effects on health (by improving the prevention and treatment of infection), but use of antibiotics potentiates the spread of antibiotic resistant forms of infection. Infection and human responses to infection can impact on a wide range of human freedoms such as freedom of movement. Infection with treatment (antibiotic) resistant microbes can have substantial social consequences, including stigmatisation, blaming and shaming. I argue that direct health consequences such as duration of illness or death are an insufficient measure (on their own) when we consider the consequences of infection for individuals, groups or institutions. I consider the strengths and weaknesses of economic frameworks such as cost-benefit analysis applied to the evaluation of the distribution of burdens and benefits in healthcare, and specifically to the risks and benefits of use of antibiotics in hospitalised patients (where the tensions between burdens and benefits are particularly acute). I conclude that measures of economic cost are insufficient to capture the range of considerations associated with the use of antibiotics and the spread of treatment resistant agents of infection.

I compare and contrast prevalent health economic approaches (such as cost-benefit analysis) with an alternative, which is capability theory, using the approach as outlined by Martha

Nussbaum. Nussbaum's theory offers potential advantages over current economic methods of evaluation. The capability theory of Martha Nussbaum extends the evaluative space to include a number of dimensions that are not included within prevalent health economic methods of evaluation. The capability theory of Martha Nussbaum has commonalities with human rights approaches but provides an additional and necessary level of specification and theoretical clarity. Perhaps most importantly the list of capabilities reminds us of the requirements for a life with human dignity, some of which might otherwise be overlooked.

In **Chapter 3** I consider how a capabilities approach based on the work of Martha Nussbaum might be applied to the evaluation of the distribution of burdens and benefits of the use of antibiotics in hospitalised patients. A life with human dignity requires a sufficiency within each of the capability dimensions. The list of capabilities can be used to evaluate the burdens that antibiotics and the control of infectious diseases (including antibiotic-resistant forms) impose on patients and the wider community, both at the individual and healthcare institutional level. I propose an antibiotic-associated infectious diseases capabilities index to evaluate the justice of institutional arrangements. This type of index would enhance the evaluative data set and broaden the range of considerations beyond bald measures of prevalence of infection or economic costs.

If capabilities are to be used in deciding the distribution of burdens and benefits associated with the use of antibiotics then we need to understand the principles that can be used to arbitrate choices. Currently there are many contexts in which there is not a high level of healthcare provision, even within developed countries and more so from a global perspective. There are inevitable trade-offs when the risks and benefits to capabilities are or will be

unevenly distributed between individuals or groups of individuals, or when some capabilities must be compromised if others are to be achieved. Nussbaum argues that for basic healthcare there should be a high level of healthcare provision. Even with a high level of provision there remains a question of the extent to which capability theory as espoused by Nussbaum has the resources to deal with trade-offs of benefits and burdens either inter-personally or intra-personally. Many patients with established infection or at risk of infection are at very low levels of capability at the time that healthcare decisions are taken. In resource limited settings it may not be possible to address all of the capability deficits even if technically feasible. In addition there are situations in which addressing threats to the capabilities of one person threatens the capabilities of others. For example using antibiotics to reduce one person's risk of an adverse outcome from infection adds some risk to the capabilities of others (of untreatable infection). The additional risk to others can be very small (almost immeasurable) or substantial depending on the context.

Effective antibiotics can be considered as public goods, and are an increasingly scarce resource. 'The Tragedy of the Commons' allegory used by Hardin suggests that we need a form of social contract to agree how common public goods such as grazing land (Hardin's example) or effective antibiotics (the subject of this thesis) should be distributed. I consider the potential for the contractualist approach of Thomas Scanlon to provide a procedure for deciding the distribution of risks, burdens and benefits (to capabilities) associated with the use of antibiotics, and to the control of antibiotic resistant microbes. The context in which antibiotics are used and antibiotic resistance spreads often involves individuals who are not and may never be in a position to argue for contracts based on mutual self-interest. Scanlon's

contractualism is sensitive to the individual perspective allowing reasonable rejection of principles by individuals fully empowered, or dependent. I return to capabilities in chapter 6.

In **Chapter 4** I consider the priority that should be given to the control of antibiotic resistant microbes when resources are limited and can be expended on many different things. We could give priority to the control of antibiotic resistant microbes over use of equivalent resources for the prevention or treatment of common and serious diseases such as cancer, diabetes, or heart disease, but should we? Current English Department of Health policy emphasises the prevention of avoidable infection in healthcare contexts using the phrase 'zero tolerance' to avoidable infection. I consider how we should understand a policy of 'zero tolerance' to avoidable infection and the implications of that understanding for the priority given to expending resources on the control of the spread of antibiotic resistant microbes and associated disease, when there are competing priorities.

Reasons to take the prevention of 'avoidable infection' acquired in healthcare contexts (such as hospitals) seriously include the irretrievable nature of the consequences of some avoidable infections; the insufficiency of compensation; social consequences (blame and mistrust); the breach of a negative right not be harmed by hospitalisation; and the reasonable rejection of 'avoidable harm' when the patient could not rationally consent to exposure to the risk of harm. However I argue that 'zero tolerance' is excessively demanding and can give rise to excessive opportunity costs, unreasonable expectations, and unacceptable constraints on feasible alternative options.

I argue from a contractualist perspective that the mitigation of risks of irretrievable avoidable harm should be given at least the same level of priority as might be given to an equivalent benefit derived from investment in treatment enhancement, and a higher priority than is given to conditions associated with more trivial burdens. We can reasonably reject any principle that allows hospitalisation to add additional, foreseeable and avoidable harms to patients when there are alternative and feasible arrangements, which would prevent those harms without the redistribution of comparable burdens to others.

In **Chapter 5** I consider another strategy for sustaining the effectiveness of existing antibiotics, which is to constrain the use of existing antibiotics. Antibiotic treatment decisions require that antibiotic prescribers take an ex-ante perspective on risks. Health strategy documents outlining 'good practice' with respect to antibiotic prescribing use terms such as inappropriate use, overuse, and antibiotic abuse, but these terms are rarely defined, and generally come from an ex-post perspective. I consider criteria that could be used to reject the use of antibiotics. A dominant reason for the rejection of the use of antibiotics in particular contexts comes from the perspective of those who will need antibiotics to prevent an irretrievable adverse consequence. We know that some individuals now (and probably more in the future) will carry a burden of irretrievable harm as a consequence of antibiotic (treatment) resistant infection. If we accept that the dominant justification for use of antibiotics is to prevent irretrievable harm to an individual or contact, then the use of antibiotics for self-limiting conditions, or for the treatment of individuals with conditions for which antibiotics do not substantially impact on outcomes (for example in the latter stages of terminal illness), or access based on preference or willingness to pay (internet or over-the-counter access), or the use of antibiotics as animal growth promoters can be reasonably

rejected. The ex-ante perspective of the person who prescribes an antibiotic requires that an acceptable level of risk of an irretrievable adverse consequence be specified. I consider how we might decide this level of risk.

In **Chapter 6** I consider the use of antibiotics in resource poor settings, and in settings where there is competition between the use of resources to control the spread of infectious diseases (including treatment resistant forms) and the use of antibiotics. Increasing access to antibiotics, without account taken of the conditions in which they are used, threatens the sustainability of the primary function of antibiotics, which is the prevention of adverse outcomes from infection. Poor socio-economic conditions such as over-crowding and poor sanitation facilitate both the spread of infection but also the spread of antibiotic (treatment) resistant forms of infection. Principles governing the use of antibiotics are insufficient by themselves (even if fully complied with) to assure the sustainability of antibiotics when there is increasing access to antibiotics alongside conditions, which facilitate the spread of antibiotic resistant microbes. The capabilities approach by emphasising sufficiency across a range of dimensions required for a life with human dignity captures the essential message that focusing on one determinant of wellbeing such as access to antibiotics is insufficient for justice. Focusing on access to antibiotics without taking account of the determinants of the spread of infectious diseases is an inadequate response when account is taken of sustainability. The capabilities approach by drawing attention to a range of requirements for a life of human dignity would seem to offer a model for public health, which resonates with the concerns of all who have an interest in the control of infectious diseases (and treatment resistant forms). Adequate shelter, clean water, nutrition and education are required for a life with human dignity but also all contribute to the control of the spread of infection and the

requirement for the treatment of infection with antibiotics. A just state of affairs extends beyond access to antibiotics.

Scanlon's approach (1998) suggests that with few new antibiotics in the pipeline and an increasing burden of disease attributable to resistant microbes, control of the spread of antibiotic resistant microbes should be given increasing priority. Scanlon's contractualism (1998) also reasonably rejects a principle of use of antibiotics when more individuals could be protected from equivalent burdens by feasible alternative (public health) interventions (such as the provision of clean water). In contexts where consideration is given to increasing access to antibiotics then we need to also consider the feasible alternative courses of action that may be more sustainable. The use of antibiotics to prevent irretrievable harm cannot be reasonably rejected as a principle for use of antibiotics in resource-replete contexts in which antibiotics are a relatively inexpensive option, but fails when it comes to resource poor contexts where we must take account of the relative burdens and benefits associated with feasible alternative uses of resources.

In **Chapter 7** I summarise some of the findings of this thesis. Principles governing the use of antibiotics may not be sufficient (on their own) to control the emergence of antibiotic resistant forms of infection. Even so, principles challenge practice, draw attention to considerations beyond the self-interest of individuals, and provide a standard against which we can judge the fairness of the allocation of the increasingly scarce resource, which is effective antibiotics. When we have identified principles of action then we must also be able to communicate those principles. Metaphors (such as that of Hardin) are commonly used to communicate concepts, and to justify actions. I consider a number of metaphors that are used to describe and

communicate perspectives on the human relationship with microbes (such as the 'war' metaphor). Analogical reasoning (often based on 'over-use' metaphors) has also been used to try to identify, and also to justify strategies to sustain the effectiveness of antibiotics.

The use of metaphor to communicate concepts, and the use of analogical reasoning to identify strategies, has both benefits and limitations. Microbes can be good *and* bad for our health. The 'War' metaphor has encouraged an adversarial relationship with microbes, and implies virtue in microbial destruction. I argue that the values that are implicit in the metaphors used to describe the human relationship with microbes, and the ethical implications of specific analogies should be made explicit. There is increasing evidence that the microbes that colonise our human bodies determine our health in many different ways (obesity, bowel disorders, immune development, and even our emotional states). Recognition of the constructive part that microbes play in the human condition can only encourage more caution in the use of antibiotics. If we aspire to constructive problem solving (and to sustaining the effectiveness of treatments for infectious diseases) then we need new metaphors to communicate and explain our relationship with microbes that emphasise the mutual dependencies. Microbes 'R' us is one such metaphor.

CHAPTER 1

ANTIBIOTICS AND ANTIBIOTIC RESISTANCE: WHAT DO WE OWE TO EACH OTHER?

Summary

Antibiotic resistance is a burgeoning problem. There are few new antibiotics under development. Antibiotic resistance is a microbial adaptation, which allows microbes to persist despite the presence of antibiotic(s). In order to sustain the effectiveness of antibiotics we can constrain the use of antibiotics and we can try to control the spread of antibiotic resistant microbes. Both of these strategies entail ethical tensions, particularly between individual burdens and benefits, and the public good associated with the control of antibiotic (treatment) resistant microbes.

This chapter provides a background to questions, which will be addressed in subsequent chapters. Substantive ethical questions include the sort of information that should be used to evaluate the justice of the distribution of benefits and burdens associated with antibiotics and antibiotic resistance, the extent to which we should prioritise the control of antibiotic resistant microbes when there are alternative resource demands (for example for treatment of diseases), principles governing the use of antibiotics and acceptable levels of risk (associated with using

or not using antibiotics), and the way in which we conceptualise and communicate the issues and concerns involved in our relationship with the microbes.

1.1 Introduction

Ethics surrounding infectious diseases (with the exception of AIDS) has received relatively little attention in the bioethical literature until recent years (for an overview see Francis *et al*. 2005). There remain many ethical challenges for example individual obligations to avoid infecting others, the acceptability or otherwise of coercive social distancing measures and third-party notification, and the obligations of health workers to treat contagious patients (Selgelid 2008).

In addition to the general issues common to the ethics of infectious disease management, there are the particular ethical issues surrounding the distribution of risks and benefits associated with the use of antibiotics, which are the subject of this thesis. I use the term antibiotic to refer to a class of drugs predominantly used to treat or to prevent bacterial infection, and antibiotic resistance to describe a relative reduction in the effectiveness of antibiotic(s) when used for the treatment or prevention of human infection(s).

At the time of marketing of an antibiotic by a company there is evidence that microbial agents of diseases are susceptible to inhibition (of growth) or killing by the antibiotic. Antibiotic resistance is a microbial adaptation which allows microbes to persist despite the presence of the antibiotic, and which reduce the potential human health benefit derived from antibiotics. The effectiveness of an antibiotic tends to diminish with the use of the antibiotic, because

microbes, which are antibiotic resistant, have a competitive advantage over their sensitive cousins, and become more common amongst the microbial population in the presence of the antibiotic.

Concerns have been raised for over 40 years that increasing use of antibiotics is leading to increasing pollution of the world with antibiotic resistant bacteria (Gleckman & Madoff 1969). Over time antibiotic resistant strains have contributed an increasing proportional burden to infectious disease with an associated increase in economic and health costs (So *et al*. 2010). If we cannot rely on antibiotics to effectively prevent and treat infection then we are faced with the prospect of untreatable infections. We are also faced with increasing constraints on those many medical procedures, which depend on antibiotics to keep patients safe by preventing or treating infection(s) associated with those procedures. Hip replacements, organ and tissue transplants, treatments for cancer, and innumerable other medical treatments require the availability of effective antibiotics to control the risks of adverse outcome from infection.

The focus of this thesis is primarily anthropocentric and concerned with the distribution of burdens and benefits of antibiotics for humans, but it is important to acknowledge the broader implications of widespread use of antibiotics (for example in farming) even if not directly within the scope of this thesis. Bacteria (and other microbes) are involved not only as determinants of human (and animal health) but also have essential roles in many natural processes. Cockell (2008) suggests that small creatures have not received the priority (in human concerns) that is given to large animals for reasons, which may not be rational. Despite their importance for human wellbeing microbes have not featured much as an area of concern

in the ethical or environmental literature. Antibiotics regulate microbial activities on many levels so have the potential to perturb naturally occurring microbial populations for example in soil ecosystems. Microbes "are ubiquitous, possess enormous metabolic and physiological versatility and are essential to virtually all biogeochemical cycling processes – microbial carbon and nitrogen are calculated to be, respectively, equivalent to and tenfold as great as the carbon and nitrogen stored in plants" (Prosser *et al*. 2007). These broader implications give further reason to question the use of antibiotics and consider the rationale for the use of antibiotics, even if not the primary focus of this thesis.

1.2 Sustaining the effectiveness of antibiotics

One solution to the loss of effectiveness of existing antibiotics is to develop 'new' antibiotics. Antibiotic resistance was not such a substantial concern when there was a steady supply of 'new' and effective alternatives, however there is no longer such a supply. The cost of developing new antibiotics is considerable. Pharmaceutical companies are focusing on more profitable areas and few new antibiotics are currently under development (Morel & Mossialos 2010). Up to the year 2000 and since the introduction of penicillin in to clinical trials in the 1940s, there had been a steady supply of new antibiotics. More recently the supply of new antibiotics has diminished. A recent article in the British Medical Journal expressed the view that "Existing antibiotics may be the best that we will ever have. We are wary of creating an expectation that economic incentives can generate a pipeline to compensate for our squandering of this non-renewable resource" (Cormican & Vellinga 2012).

A recent report from the Center for Global Development (Nugent *et al*. 2010) emphasises four critical steps if we are to retain antibiotic effectiveness. These are surveillance and laboratory capacity, drug supply chain integrity, regulatory capacity, and the technology pipeline. The first of these is required to fill the information gap so that antibiotic resistance can be identified and tracked. The remaining recommendations focus on assuring the supply, regulating the use, and feeding the pipeline for new antibiotics. The main focus of this thesis is the urgent question - how we should distribute the benefits of the effective antibiotics that we currently have, while the pipeline for new antibiotics is dry. This question has received little attention in the bioethics literature.

We can sustain the effectiveness of currently available antibiotics by –

1. Constraining the spread of antibiotic resistant microbes
2. Constraining the use of antibiotics (reducing the exposure and the pressure on microbes to become antibiotic resistant, and reducing the advantage that antibiotics give to resistant microbes)

It is the ethical implications of these two approaches to sustaining the functional utility of existing antibiotics, which I will consider in this thesis. Both approaches require the distribution of burdens and benefits across individual and groups and as such raise substantial ethical questions.

1.3 Antibiotics continue to be 'over-prescribed'

At the same time as there are increasing concerns with antibiotic resistance there is evidence that antibiotics are being prescribed in situations for which there is little evidence of benefit

for patients and in some cases contrary to national guidance (Smith *et al*. 2004). There are also striking variations in patterns of use of antibiotics in different countries without apparent justification by empirical evidence of differences in patient outcome (ESAC 2009).

Antibiotic prescribing decisions can never be entirely evidence based. Moral values and principles make an important contribution to supporting decision-making. The treatment of the common condition 'sore throat' provides an example. The decision to prescribe penicillin to a patient with a sore throat can be defended as an evidence-based decision because penicillin is very cheap, clinical studies have shown that treatment of patients presenting with sore throat with penicillin reduces the duration of illness, and treatment prevents serious (life-threatening) consequences such as rheumatic fever. The counter argument to treatment with antibiotics is that sore throat is usually self-limiting, does not usually leave any long-term adverse consequence (rheumatic fever is very uncommon), and that use of antibiotics adds to the burden of antibiotic resistant bacteria. In this case there is a balance between a small benefit to an individual and the public good derived from limiting the selection of antibiotic resistant bacteria. The patient might argue that the small contribution to the risk to others associated with a single prescription of antibiotics does not warrant the withholding of benefits of a shorter duration of illness to her, and the reduction of risk of a rare but serious adverse consequence (rheumatic fever). An individual prescription is only tenuously linked with treatment (antibiotic) resistant infection at another time and place. Is the primary responsibility of the GP to take account of individual patient preferences or a wider societal perspective? The argument is further complicated when we consider that future generations will be major beneficiaries from curtailment of present use of antibiotics, and we consider the uncertainties with respect to the extent to which technological developments may result in

new treatments as effective as current antibiotics. If we are to constrain the use of antibiotics then we must decide when it is or is not appropriate to use antibiotics.

1.4 What is appropriate use of antibiotics?

Much of the emphasis in the developed world has been on antibiotic 'overuse' and on optimising the use of antibiotics both in hospitals and in the community, with emphasis on antibiotic stewardship (see for example US Centre for Disease Control 2012). Antibiotics are extensively used in hospitals both to prevent infection and to treat established infection. At any one time about 40% of hospital patients are being actively administered antibiotics, so perhaps not surprisingly, antibiotic-resistant microbes are frequent causes of infections that arise in hospital. Concerns about the control of Healthcare Associated Infection (HCAI) frequently focus on the control of antibiotic resistant microbes such as Meticillin-Resistant *Staphylococcus aureus* (MRSA). Various descriptors are used to describe the problem with respect to antibiotic use and the relationship with antibiotic resistance in developed countries. These include words such as misuse, overuse, abuse, and inappropriate use. The English Department of Health has published guidelines on antibiotic stewardship (Advisory Committee on Antibiotic Resistance and Healthcare Associated Infection (ARHCAI) 2011). This guideline illustrates many of the problems with the current conceptualisation of antibiotic stewardship. Words such as appropriate and prudent prescribing are not defined. "Start smart" requires that antibiotics should not be started in the absence of clinical evidence of an infection that will respond to antibiotics. Viral infections (generally speaking) do not respond to antibiotics. Yet there is no statement as to what an absence of evidence of an infection that will respond to antibiotics might mean. At the time the patient presents to a

potential prescriber the evidence is limited to the patient history and examination. The results of other tests take time to accumulate. There is strong evidence that prompt initiation of antibiotics (when appropriate) improves outcomes and at the same time it is almost impossible to exclude the possibility of bacterial infection when a patient has a viral infection. What degree of certainty of bacterial infection is required to justify use of an antibiotic? The prescriber has to take an ex-ante perspective. It is much easier ex-post than it is ex-ante to say that antibiotics were 'inappropriate'.

In the same set of five "start smart" recommendations that insist that antibiotics are not started in the absence of clinical evidence of bacterial infection there is also a recommendation that antibiotics should be used when there is evidence that such use can prevent infection associated with surgery – a situation in which there is *usually* no evidence of bacterial infection. The majority of antibiotic recipients in this type of scenario (surgical prophylaxis) do not benefit from the use of antibiotics other than the 'benefit' associated with mitigating in the degree of risk associated with the procedure. In practice a high proportion of antibiotic prescriptions are given to prevent (rather than treat) infection predominantly but not exclusively in surgery. Antibiotics are being used to mitigate risks rather than to treat an established infection.

Arguably almost all use of antibiotics is an attempt at risk mitigation – antibiotics are being used to prevent an adverse outcome from what might be, or what might lead to, a bacterial infection. If guidance is to guide (and not just provide a platform for criticism) then it should take account of the perspective of prescribers, which is ex-ante and under conditions of uncertainty.

1.5 Risk mitigation

When policy makers evaluate the justice of states of affairs it is usually possible to take an ex-post perspective. When individual antibiotic prescribers make decisions about the management plan for a patient then they (generally) take an ex-ante perspective. They have to estimate the probability that one strategy will lead to better consequences than another. Whether for treatment of an established infection, or to prevent infection, the use of antibiotics can be seen as an attempt to mitigate risks of adverse outcomes for the recipient or for others. Antibiotics can mitigate risks and in so doing provide benefits, but there are also substantial risks associated with the use of antibiotics. Most of the risks of use of antibiotics are directly or indirectly linked with antibiotic resistance and the control of the spread of antibiotic resistance. Some benefits and risks are listed in Table 1.1.

Table 1.1 Benefits and Risks of antibiotics

Benefits
Treatment of infection
Prevention of infection
(Non-antimicrobial benefits)
Risks
Allergy
*2^{o} infection with an antibiotic-resistant agent of infection
*Adverse consequences from actions taken to control antibiotic-resistant microbes
*Social consequences associated with carriage of antibiotic resistant microbes
*Antibiotic (treatment) resistant infection
* *Indicates risks associated with antibiotic resistance*

1.6 Risk perception

Whether for prevention or treatment we should be able to say something about the degrees of risk, and the forms of risk that justify use of antibiotics. Risk perception is an important determinant of human behaviour (Slovic 2006). We tend to avoid forests when we believe that there are man-eating tigers in the forests, and equally it is plausible to suggest that differences in perceptions of risk (from infection) amongst individuals and across cultures make an important contribution to antibiotic prescribing decisions. The importance of risk perception in antibiotic prescribing decision-making has not been subject to detailed description. The belief that there is overuse of antibiotics comes from the observation that there may be widely differing patterns of use of antibiotics without evidence that differences impact on patient

outcomes. These differences can be found at individual and national prescriber levels (see for example the European Surveillance of Antibiotic Consumption Centre report of 2009). Retrospectively (ex-post) a decision to use an antibiotic may be seen to be excessively risk-averse. Doctors caring for patients consider the risks to the individual patient and have to act ex-ante (before knowing the outcome). Significant information available to a prescriber such as that relating to outcome and the results of diagnostic tests is limited ex-ante by comparison with the ex-post perspective. Retrospectively there is no risk – either the patient has got better or not. Ideally we should be able to justify treatment decisions both ex-ante *and* ex-post. This requires that we specify what we mean by risk (perceived risk, statistical risk or other) and also acceptable levels of risk in different contexts.

In practice we have to decide if we should take account of risk perceptions, as well as statistical risks, and we also have to be able to take account of the extent to which the individual prescriber is prepared to impose and patients are prepared to accept (or otherwise) a certain level of risk. There is reference in the English Department of Health guideline (above) to the need to take account of 'local antibiotic resistance patterns'. This means that when a certain level of antibiotic (treatment) resistance (or potential ineffectiveness) is present amongst the causative agents of a particular illness such as pneumonia, then alternative, more effective, antibiotics should be used. There is no agreed acceptable level of antibiotic resistance at which this change should be made, so again there are widely differing levels of antibiotic resistance accepted in different policies and amongst practitioners. Most patients are unaware of local antibiotic resistance patterns and do not have an opportunity to contribute to the decision making processes. When we have agreement about acceptable levels of risk then we still have to decide about the valuations of different types of outcome

and whose valuations are to be given priority. What part does the patient have in determining the valuation of outcomes associated with antibiotic treatment decisions? In the sore throat example (given above) patient perceptions and valuations of the benefits of antibiotics may be very different from the perceptions and valuations of others with a more distant perspective.

There are both empirical and ethical questions surrounding the 'appropriate' use of antibiotics. Guidelines are often based on an assumption of clear-cut diagnosis, whereas in clinical practice antibiotics are often required to be used before a clear-cut diagnosis is established. Uncertainty characterises the ex-ante perspective of the prescriber. There is no agreed (expert or public) acceptable level of risk or severity of risk (perceived or statistical) at which antibiotics should or should not be prescribed. In addition to the empirical difficulties there are a number of ethical challenges with the concept of 'appropriate' use of antibiotics. How do we justify constraints on the use of antibiotics for the treatment of individuals when each use is immeasurably small compared with the overall use of antibiotics? How much risk should we (as individuals) be prepared to carry, and should doctors be prepared to impose on their patients? How do we balance patient autonomy and choice against the benefits of constraining antibiotic prescribing for the wider community? One place that we might look for help with these questions is within existing frameworks for public health ethics.

1.7 Public Health Ethics

The control of infectious diseases has always been a key activity for public health professionals. In 1920, C.E.A. Winslow defined public health as "the science and art of preventing disease, prolonging life and promoting health through the organized efforts and

informed choices of society, organizations, public and private, communities and individuals" (Winslow 1920). The UK Faculty of public health defines public health as "the science and art of preventing disease, prolonging life and promoting health through the organised efforts of society". There are other definitions used but the focus remains on health at a population level.

The main focus for concern in this thesis is the distribution of burdens and benefits associated with the use of antibiotics. Hospitals provide a context in which tension between individual and public good becomes sharply exposed. Many consider the control of infection (including antibiotic resistant forms) in hospitals to be a natural extension of control strategies applied in the wider community for the control of spread of infectious diseases. For example the role of the English Health Protection Agency (HPA) is to provide an integrated approach to protecting UK public health. The HPA has taken a substantial role in overseeing the surveillance and strategic direction of the control strategies for antibiotic resistant microbes such as MRSA in NHS Trust hospitals. The functions of the Agency are described as "to protect the community (or any part of the community) against infectious diseases and other dangers to health" (see www.hpa.org.uk). The HPA acknowledges that "decision makers must balance individual freedom against the common good, fear for personal safety against the duty to treat the sick, and short term economic losses against the wider implications of the potential spread of serious diseases" but say little about the principles to be used in balancing these requirements. More detailed guidelines are included in the 'The Principles of the Ethical Practice of Public Health' produced by the US Public Health Leadership Society (2002); and in recent reports from the European Public Health Ethics Network (Europhen)(Munthe 2008),

and the Nuffield Council on Bioethics (2007), and a number of recent books, for example Powers & Faden (2006).

The emphasis of Public Health has been on the prevention of disease whereas the emphasis of those involved in patient care is on the treatment of disease, so there is a potential conflict arising from the different perspectives of professionals involved in Public Health and those involved in patient care. The focus of Public Health is on population health and not on the health of particular identifiable individuals. Hospital Infection Control Professionals have to take account of the health (and arguably other) needs of individuals and groups (in wards, theatres, those with infection and those at risk of infection), and of future patients (many of whom cannot be identified at the time). This difference is well illustrated by key features of 'Public Health' – "First it should aim at protecting and promoting the health of a large group or population (*this excludes individual clinical encounters between doctors and patients*). Second, public health actions will involve collective activities by, for example, governments, health care systems, or even society as a whole (*this excludes action to improve the health of a particular individual* unless it is within the context of a campaign targeted at a group or population)" (Dawson & Verweij 2008). Healthcare professionals dominate hospitals politically, and numerically. Professional codes of ethics emphasise responsibilities to individual patients, so potential and actual conflicts arise between those responsible for individual patient care and 'public' good. Hospital Infection Control professionals work in the interface between individually focused care, and the health of the present and future hospital population. "Taking infectious diseases in to account requires understanding of the patient as victim as well as vector'" (Francis LP *et al*. 2005). Patients who acquire HCAI (often

antibiotic resistant) are both victims of failure(s) to control HCAI and are also potential reservoirs and vectors for ongoing transmission.

Public Health is about protecting and improving the health of populations in which the majority are relatively 'healthy' - having a capability to function within the 'normal' range for their age group, whereas control of antibiotic resistant microbes in hospitals is about reducing the burden of disease associated with preventable infection in a population of individuals many of whom already have reduced capabilities. Some are already at the margins of a minimum capability to function and these individuals are particularly vulnerable to falling below a minimum threshold following a Health Care Associated Infection (HCAI). Some individuals (such as infants undergoing intensive care) in early stages of growth and development may never achieve a full range of capacities to function, and HCAI adds significantly to this burden of reduced capabilities. Low virulence agents of infections may become endemic, and outcomes for patients are more likely to be compromised for those who are infected.

Despite the differences in the perspectives and aims of public health and those involved with the care of individuals it has to be acknowledged that infectious disease, and the use of antibiotics and antibiotic resistance, is not confined to a particular institutional or patient treatment context. Antibiotic resistance threatens the public health and so it seems reasonable to consider recent public health ethics proposals in more detail.

1.7.1 Public Health ethics and antibiotic resistance

Many of the ethical issues associated with the use of antibiotics and the control of antibiotic resistant microbes (consequent on the use of antibiotics) can be illustrated if we consider recently proposed frameworks for Public Health Ethics. Recent proposals highlight some of the specific issues and tensions related to the use of antibiotics and the control of antibiotic resistance.

Munthe (2008) developed a model for the goals of public health within a European Public Health Network (EuroPHEN) project that was funded by the European Commission. Munthe acknowledges that there is tension between the population perspective of Public Health and the individualistic perspective of traditional medical ethical notions of autonomy. Munthe proposes an integration of the goals of the promotion of population health (traditional public health goal) and of "the promotion of equal (and real) opportunities of everyone to be more healthy." In discussing how this model might work in guiding decision making in practice he argues that the relative importance of the traditional goal increases when population health is poorer. As population health rises further gains in population health could be traded for gains in autonomy and equality.

I am not sure that the approach proposed by Munthe would help to address concerns about the overuse of antibiotics in developed countries with high levels of population health. This approach would seem to allow the use of antibiotics for trivial benefits in developed countries when mandated by individual preference and autonomous choice. Use of antibiotics when benefits are small or non-existent threatens the sustainability of the effectiveness of antibiotics

and our capacity to control outbreaks of infection and to treat infectious diseases in the future. While antibiotics are overused in developed countries, antibiotics are underused in many parts of the developing world (Selgelid 2007). The World Health Organisation (WHO) has given priority to making antibiotics available for the treatment of children less than 5 years of age with pneumonia because the use of antibiotics is highly effective in improving outcomes. At the time of a WHO report in 2010 only 20% of children less than five years of age with pneumonia received antibiotics (World Health Organization 2010). Increasing access to antibiotics potentially threatens the sustainability of the primary function of antibiotics, which is the treatment of infection. Adverse socio-economic conditions facilitate both the spread of infection and also the spread of antibiotic (treatment) resistant forms of infection. We can focus on the present injustice in the distribution of antibiotics, or alternatively we might argue for a requirement that minimal socio-economic standards come before the use of antibiotics. Antibiotics will not be effective for long when the spread of agents of infection is poorly controlled. This proposal raises the question - should we apply different principles for the use of antibiotics depending on the socio-economic conditions under which they will be used? I will return to this question in Chapter 6.

The Nuffield Council on Bioethics (2007) have recently published an ethical framework for Public Health. This framework is based on a Stewardship model. The concept of stewardship is intended to convey that liberal states have a duty to look after important needs of people individually and collectively. It emphasises the obligation of states to provide conditions that allow people to be healthy and, in particular, to take measures to reduce health inequalities (p xvi). The aims of this (stewardship) model include the reduction in the risks that people might impose on each other, and the minimisation of interventions that are introduced without the

individual consent of those affected, or without procedural justice arrangements (such as democratic decision making procedures) which provide adequate mandate, and minimisation of interventions that are perceived as unduly intrusive and in conflict with important personal values (see Box 1, p xvii).

The Nuffield Working Party describes key principles of the stewardship approach. These are shown in Table 1.2.

Table 1.2 Stewardship model: some key principles

- Harm principle
- Precautionary Approach
- Minimisation of impositions on individuals
- Openness and explicit policies
- Search for a mandate when there is tension between individual and group, or between different groups
- Prioritarian (priority is given to the most vulnerable)

I will consider the first three of these six principles (Harm, Precautionary Approach, and Minimisation of impositions on individuals).

1.7.2 The Harm principle

The Harm principle is a key principle within the Nuffield framework. The Nuffield Working Party (NWP) provides an intervention ladder, which ranks liberty-infringing measures from

the least at the bottom of the ladder to the greatest at the top of the ladder. The NWP gives a guideline (p73 section 4.62) -

> "Liberty-infringing measures to control disease, such as compulsory quarantine and *isolation*, rank towards the top of the intervention ladder. The ethical justification for such measures involves weighing the classical harm principle on the one hand, and individual consent and the importance of avoiding intrusive interventions on the other. Where risk of harm to others can be significantly reduced, these considerations can be outweighed"

The NWP consider the imposition of contact precautions to be towards the top of the intervention ladder and are suggesting that the Harm principle of John Stuart Mill be weighed against potential harms to individuals and infringements of individual liberties. The Harm principle states that (Mill 1859, p13) -

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

The Harm principle implies that only when individuals are putting others at risk of harm can we justify constraints on those individuals such as infringements of their liberties. The Harm principle requires specification. For example specification of the extent to which the harm principle can be used to justify impositions on individuals when large numbers of people are threatened, perhaps by the uncontrollable spread of a treatment (antibiotic) resistant cause of

infection? What decision rules should we follow? Should we withhold treatment or constrain treatment options for individuals in order to protect others from harm? This principle of action requires that we can specify the degree of risk and potential severity of harm at which constraints and actions can be justified. When we consider the degree of risk then should we use statistical or perceived levels of risk? The Nuffield Working Party guideline (xxii & p73) is under-specified in that it is not clear what 'significantly reduced' really means in terms of risk reduction, and there is no decision rule that specifies the degrees of harm that justifies actions.

1.7.3 Antibiotic resistance and a precautionary approach

Antibiotic stewardship programmes focus on when antibiotics should and should not be used. The Nuffield Working Party states that "Any policy, including a policy of 'do nothing', implies value judgements about what is or is not good for people, and requires justification". A substantial ethical concern is that patterns of antibiotic use today may not be sustainable because of the dissemination of antibiotic resistant microbes. Antibiotics may not be effective in the future either for the treatment of individuals or for the control of the spread of infection. These concerns would seem to justify precautionary constraints on prescribing antibiotics today and also considerable efforts to control the spread of antibiotic resistant (untreatable) strains.

The Nuffield Working Party specifies a precautionary approach derived from the precautionary principle which states that – "Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-

effective measures to prevent environmental degradation" (Principle 15, Rio Declaration made at the United Nations Conference on Environment and Development in 1992). The NWP draw on European Commission advice and propose a precautionary approach, which requires integration of at least five dimensions. These include risk assessment (including acknowledgement of uncertainties), attention to fairness and consistency, costs and benefits of different courses of action, transparency, and proportionality (actions taken should be in proportion to the risks).

Antibiotic resistance is a serious threat, individuals today benefit from the use of antibiotics while others carry the consequences of treatment resistant infection. There are also considerable uncertainties. Antibiotics and their associated risks have many of the properties referred to by Ulrich Beck – "In contrast to early industrial risks, nuclear, chemical, ecological and genetic engineering risks (a) can be limited in terms of neither time or place, (b) are not accountable according to the established rules of causality, blame and liability, and (c) cannot be compensated for or insured against" (Beck 1999, p77).

Risks may be more or less quantifiable. For the purposes of this thesis I have taken unquantifiable risks to be uncertainties. Uncertainty has been a substantial consideration in the recent history of transmissible agents of disease for example vCJD, SARS, and swine 'flu. The World Health Organisation reported 1100 epidemic events (worldwide) between 2002 and 2007. "The incidence of EID events has increased since 1940, reaching a maximum in the 1980s … controlling for reporting effect the number of EID events still shows a highly significant relationship with time" (Jones *et al*. 2008). Increasing overcrowding, international travel, transport of foodstuffs and livestock, continuing inequalities in wealth and health,

political strife, and military conflict all contribute to the emergence of new forms of infectious diseases. The emergence of new forms of antibiotic resistance and the implications for human health are also fraught with uncertainty. We don't know when, where and or even if new forms of antibiotic resistance will emerge, or the impact that emergence of new forms of resistance will have on outcomes. We cannot be compensated or insured against many of the more serious forms of adverse consequence of treatment resistant infection. Every year new forms of antibiotic resistance and associated clinical problems with antibiotic resistant bacterial infections are described. Pollution of the natural world with antibiotics, antibiotic resistant bacteria and the genes that code for antibiotic resistance has far reaching potential consequences for human health. Much of current medical practice relies on the availability of effective antibiotics. Antibiotics are used to treat infections that arise as part of everyday life and also to prevent infections during periods when patients are particularly vulnerable (for example during major surgery, or treatment for cancer). Patients benefit from the use of antibiotics but pollution of the environment with antibiotics, antibiotic resistant bacteria and the genes that determine antibiotic resistance have the potential to cause longer-term adverse consequences for human health (see Martinez 2009), albeit in ways that are yet to become clear. We do not yet know the extent of adverse patient outcomes that will be consequent on antibiotic resistance or who will be affected.

Concerns about antibiotic resistance have a direct impact on clinical decision-making. There are situations in which potential benefits associated with the use of antibiotics are withheld because of concerns that antibiotic resistance might lead to adverse future consequences. For example there is strong evidence that selective decontamination of the digestive tract (SDD) with antibiotics reduces the risk of ventilator-associated pneumonia and death in adults

admitted to intensive care units (ICUs) (Liberati *et al*. 2009) yet routine use of this intervention is limited to a minority of centres in the United Kingdom and few within the United States. Much of the reluctance to implement SDD relates to concerns about the selection of antibiotic resistant strains. Despite the clear benefits of this intervention it is still considered that there is a state of "clinical equipoise regarding this issue" (Shiloh *et al*. 2010, p1387), because the benefits are balanced by concerns about the uncertain implications of selecting antibiotic resistant strains both in individuals and within ICUs. In this example benefits to those admitted to intensive care are being denied because of an unquantifiable risk to future patients. It would seem that this approach to managing patients in ICUs could be justified as a precautionary approach. This scenario illustrates the extent to which precaution can have real opportunity costs - antibiotics are withheld despite clear evidence of substantial benefits associated with use of antibiotics. What are the limits of a precautionary approach?

Although the precautionary approach has been applied to many areas of human activity, it is not clear how this principle can or should be applied to infectious diseases, or as an approach to the control of antibiotic resistance. The principle is potentially self-contradictory (Peterson 2007) and there is so much uncertainty with respect to the emergence and development of infectious diseases that attempts to apply the principle could be paralysing. Risk assessment (including acknowledgement of uncertainties) does not help much when the risks are uncertain, attention to fairness and consistency requires that we balance the interests of those who need antibiotics today against those who will need them tomorrow, measures of costs and benefits of different courses of action require that we know both the consequences and the likely developments in treatment(s), and proportionality (actions taken should be in proportion to the risks) requires that we know enough about the future to balance the risks of

using (or not) antibiotics today. None of these aspects of the precautionary approach are clear. Much work needs to be done to clarify and specify a precautionary approach if we are going to use such an approach to control antibiotic resistance.

1.7.4 Minimisation of impositions on individuals

Codes describing ethical practice for healthcare professionals (for example General Medical Council 2006; American Medical Association 2012) emphasise responsibilities to individual patients but say little about the appropriate balance between the care of individual patients and prevention of harm to others.

The Nuffield working party acknowledges that 'in theory' there may be conflict between some of the characteristics of the proposed stewardship model. For example an aim is "to reduce the risks of ill health that people might impose on each other", while at the same time programmes should "minimise interventions that are introduced with the individual consent of those affected". The NWP imply in the note for Box 1 that conflict between aims is a theoretical rather than substantive issue. At the same time Box 2 shows the intervention ladder. The most intrusive step in the ladder is to "Regulate in such a way as to entirely eliminate choice, for example through compulsory isolation of patients with infectious diseases". In hospitals, patients are frequently isolated to prevent the spread of infectious diseases such as MRSA and often either not given a choice or are unable to express a choice about isolation. Such conflicts are not just theoretical and in my view there is a requirement that these types of conflict are acknowledged and that we seek some framework for resolution. Unfortunately the NWP proposals skate over these difficult issues.

1.8 The opportunity costs of controlling antibiotic resistance

Antibiotics can be conceptualised as a limited resource. The benefits of antibiotics can only be achieved if effective antibiotics are available and antibiotic resistance puts these benefits at risk when alternative and equally effective treatments are unavailable. Failure to control the spread of antibiotic resistant microbes such as MRSA can also be seen as a resourcing issue. The more resources that hospitals invest in cleaning, staff training, surveillance, and improvement programmes, then the better will be the control of antibiotic resistant microbes such as MRSA.

Patients admitted to hospital may have limited information and/or choice with respect to the potential infection risks to their own health associated with hospitalisation. Patients have to trust that institutional actors will respect that vulnerability. The implications of this dependency are that hospital managers (arguably) have a heightened responsibility to reduce the burden of adverse consequences attributable to preventable infection, and that healthcare institutions have a high level of obligation to protect the health of patients, visitors and staff from preventable infection. There are now 'zero tolerance' policies (to avoidable infections) in many developed countries including the English National Health Service (see Chapter 4).

Resources can be expended on many different things but are rarely unlimited, so inevitably there is competition for resources. Expenditure by pharmaceutical companies on the development of new antibiotics, or by healthcare providers on the control of the spread of antibiotic resistant microbes or on the treatment of cancer gives rise to opportunity costs.

Opportunities are foregone when a choice is made to expend resources in one area and not in another. Increasing the resources available for the control of antibiotic resistance to support a policy of zero tolerance would substantially under-cut many of the risks associated the use of antibiotics (2^o infection, risks attributable to antibiotic resistant microbes, the need for new antibiotics), but would reduce the availability of resources for other things. How do we decide the distribution of resources when resources are limited? Should the control of antibiotic resistant microbes take precedence over other competing priorities?

1.9 Dimensions beyond health

Health is but one dimension of human wellbeing. Actions available to control antibiotic resistant microbes include surveillance, education, isolation of individuals, cohorting of patients with shared causative agents of infection, treatment of infectious individuals, vaccination, and actions to contain risks associated with food, water, and airborne transmission of agents of infection. Frequently methods for the control of the spread of antibiotic resistant microbes lead to constraints on other dimensions of human wellbeing, for example through restricting contact with others (isolation), restricting access to education (children in the US cannot attend school without vaccinations), and restrictions on travel (as happened during the SARS outbreak). *The Public Health (Scotland) Act (*2008) gives statutory powers forcing quarantine in their own home on individuals with some types of serious infection and expanded requirements for compulsory notification. Both of these powers potentially bring the principles of respect for the individual (autonomy and privacy) into conflict with the greater good (preventing the spread of infection). Isolation of patients is frequently used to prevent the spread of infection but is not always in the best interests of the

isolated individual. Most of the emphasis has been on the adverse health implications of the isolated patient (Stelfox *et al*. 2003) but social implications are also important even if difficult to quantify. The prevention of ill health is one of many things, which people may value. Patients, staff, and visitors value freedom of movement, privacy, companionship and many other goods. These other dimensions of wellbeing may also be compromised by control measures. "The goal to minimize (infectious) disease burden should not be the sole aim of public health policy, because human rights and liberties matter too" (Selgelid 2008).

Infectious diseases have psychological and social impacts, which extend the range of considerations well beyond immediate threats to health. Any analysis of the use of antibiotics and the control of antibiotic resistance has to take account of these broader considerations. Fear of infection with meticillin-resistant *Staphylococcus aureus* (MRSA) by healthcare practitioners, patients, and public leads to changes in patient management including changes in antibiotic treatment decisions, imposition of contact precautions (reduced social contact), and stigmatisation of individuals, groups and institutions. Guidelines from advisory bodies such as the National Institute for Health and Clinical Excellence (NICE) of the Infectious Diseases Society of America (IDSA) on the use of antibiotics and the control of antibiotic resistant microbes often make reference to cost-effectiveness or cost-benefit analyses to justify advisory statements. There are substantial difficulties with the use of health economic methods to make decisions about antibiotics and the control of antibiotic resistance. Antibiotic resistance encompasses many uncertainties, which make costing the consequences of use of antibiotics almost impossible. Public responses such as the loss of confidence in healthcare institutions consequent upon perceptions surrounding patient safety, for example associated with fear of MRSA, are also very hard to cost.

If we are to compare the justice of arrangements and health outcomes (and associated costs) are an insufficient metric then what sort of information do we need to help with the assessment of the justice of arrangements? I will consider the capabilities approach as an evaluative framework, using the example of that approach as advocated by Martha Nussbaum.

1.10 Conceptualising antibiotic resistance and the use of metaphor

How should we conceptualise our relationship with infectious disease and the place of antibiotics in that relationship? Metaphors facilitate the communication of complex concepts. The 'War' metaphor has been extensively used to describe our relationship with microbes. In 2005 the Institute of Medicine of the US National Academy of Science held a workshop entitled 'Ending the War Metaphor'. The consensus of the workshop was that the War metaphor had led to a damaging public and professional attitude to microbes. Mitigating the development of antibiotic resistance was a substantial concern of the workshop. There was broad consensus that we need to find new metaphors that encourage a better understanding of our relationship with the microbial kingdom, and discouraged the overuse of antibiotics.

A number of other metaphors have been used to describe antibiotic resistance and several of these metaphors have emphasised the dangers of overuse of a limited resource. One example of this sort of metaphor is the 'Tragedy of the Commons'. Hardin (1968) uses this extended metaphor (allegory) to illustrate the conflict between individual benefit and public good. Hardin refers back to a pamphlet produced by William Lloyd in 1833, which describes the overgrazing of common pastureland. Each individual is motivated to use the land for their

own benefit and will continue to add animals to the pastures even beyond the capacity of the land to support grazing. This example illustrates the failure of 'raw' market forces to manage a common good sustainably. "As a rational being, each herdsman seeks to maximise his gain" (Hardin 1968, p1244). Hardin recommends coercion of individuals to abide by an agreement, whereby each individual is limited in the use of the resource. This agreement would be "mutually agreed upon by the majority of the people affected" (Hardin 1968, p1247). "Individuals locked into the logic of the commons are free only to bring on universal ruin; once they see the necessity of mutual coercion, they become free to pursue other goals" (Hardin 1968, p1248). This metaphor suggests that an agreement might be required if we are to conserve the effective antibiotics that we currently have, for example we can agree how we might limit use of effective antibiotics. There is broad agreement that we should not use antibiotics inappropriately or excessively. Unfortunately inappropriately and excessively are not clearly defined, and so the conditions under which we should use antibiotics (or not) are also unclear. Individual preference (patient and or prescriber) still dominates antibiotic prescribing decisions. A substantial strand of this thesis will be an exploration of the potential to use the contractualism of Thomas Scanlon to develop principles for the use (or not) of antibiotics. Before considering the application of Scanlon's contractualism I will consider the kind of information that should be used to capture the burdens and benefits of use of antibiotics and the significant consequence of use, which is antibiotic resistance.

1.11 Research questions

There are a number of potential benefits derived from clarifying the ethical dilemmas and potential approaches to balancing the burdens and benefits of antibiotics, and the control of antibiotic (treatment) resistant forms of infection. These include the underpinning of support for national and local strategic decisions such as those related to control of antibiotic resistant microbes such as MRSA, to identify explicit arguments (facilitating a wider debate), and most importantly to underpin and rationalise antibiotic prescribing, control, policy and practice.

Antibiotics can and do have substantive effects on health. In addition infection, and particularly infection with antibiotic resistant microbes, can impact on a wide range of human freedoms such as freedom of movement, and can also have substantial social consequences. When we evaluate the justice of states of affairs it is important that we have the right kind of information. I argue that health consequences (on their own) are an insufficient measure of the justice of states of affairs when we consider the consequences of infection for individuals. Capabilities provide an alternative framework for establishing the justice of states of affairs. I will explore the potential for Martha Nussbaum's account of capabilities to be used to capture relevant information and compare the justice of states of affairs associated with the use of antibiotics and the control of antibiotic resistance.

Question: *Can we use Nussbaum's capabilities framework to evaluate the justice of current patterns of distribution of burden and benefits associated with the use of antibiotics and the control of antibiotic resistance (Chapters 2 and 3)?*

What should be the approach to deciding trade-offs? If we do not specify a procedural approach then there will remain substantial difficulties with trade-offs when the risks and benefits of antibiotics are or will be unevenly distributed between individuals or groups of individuals, or when some capabilities must be compromised if others are to be achieved. Scanlon's contractualism offers a procedural approach to the distribution of burdens and benefits associated with antibiotics and antibiotic resistance.

Question: *How should we decide the balance of burdens and benefits consequent on the use of antibiotics for individuals against those of others (Chapter 3)? Can we use a capabilities approach such as that proposed by Nussbaum? Does the contractualist approach of Scanlon offer a decision procedure?*

Recent UK and international strategy documents have given emphasis to the prevention of avoidable infection in healthcare contexts using the phrase 'zero tolerance' to avoidable infection. Does the causal relationship between healthcare institutions and infection with antibiotic resistant agents of infection impose a moral responsibility on hospitals to prioritise the control of antibiotic resistant infection? We can give priority to the control of antibiotic resistant microbes over use of equivalent resources for the treatment of diseases such as cancer, but should we?

Question: *How do we decide the distribution of resources and the priority given to the control of antibiotic resistant microbes when resources are constrained (Chapter 4)? I apply Scanlon's contractualism to the question - should we control antibiotic resistant microbes at any cost?*

Decisions to use antibiotics require that the individual patient interest be balanced against the public good that is control of antibiotic resistance. Patients carry the risks of suboptimal antibiotic treatment and many physicians are reluctant to impose even small avoidable risks on patients. At the same time antibiotics are overused and antibiotic resistant microbes are contributing an increasing burden of adverse patient outcomes.

Question: *What criteria can we use to reject the use of antibiotics in developed countries (Chapter 5) and in countries or contexts with lower levels of public health (Chapter 6)? Can we justify different policies and practices depending on the levels of public health?*

Finally –

Metaphors are used to communicate complex concepts but almost always entrain implicit values.

Question: *Which metaphors are appropriate or inappropriate to communicate the relationship that we have (as humans) with the microbial world (Chapter 7)?*

CHAPTER 2

THE EVALUATION OF BURDENS AND BENEFITS

Summary

The main emphasis of this chapter is on the evaluation of the justice of distribution of burdens and benefits associated with the use of antibiotics.

Antibiotics are used to prevent adverse consequences from infectious disease but their use has a consequence, which is an increasing burden of antibiotic resistance. Tensions between benefits and burdens of antibiotics are particularly evident in the context of healthcare institutions (such as hospitals). I consider the strengths and weaknesses of dominant economic frameworks applied to the evaluation of the distribution of burdens and benefits associated with antibiotics and antibiotic resistance. I argue that many of the burdens consequent on the use of antibiotics are not readily captured by prevalent health economic methods.

Respect for human rights, and more recently patient rights, has become an established principle in many countries, advocated (by some) as a substantive principle in Public Health Ethics, and utilised as an important element in public health strategies to control infectious diseases such as HIV and tuberculosis. I compare and contrast capability theory using the example of the approach as outlined by Martha Nussbaum with economic methods of evaluation (such as cost-benefit analysis), and with human rights approaches. Nussbaum

considers her own interpretation of a capabilities theory as a species of human rights approach.

Nussbaum's theory extends the evaluative space to include a number of dimensions that have not been included within prevalent health economic methods of evaluation. The capability theory of Nussbaum has commonalities with human rights approaches but provides an additional and necessary level of specification and theoretical clarity. The list of capabilities reminds us of requirements for a life with human dignity that might otherwise be overlooked.

2.1 Introduction

In the introductory chapter I discussed some of the risks, burdens and benefits associated with the use of antibiotics. Benefits to an individual consequent upon an antibiotic prescription can present risks of burdens to others by facilitating the spread of antibiotic resistant microbes. There are many theoretical frameworks used for the evaluation of the justice of distributive arrangements. These include methods based on consequentialist, Kantian, contractarian/contractualist, and combined approaches. An evaluative framework for human development based on capabilities and functionings was proposed by Sen and has been further developed by others particularly Martha Nussbaum as a normative framework. A capabilities approach can and has been applied at the level of individuals, groups, institutions and nations.

In this chapter I want to consider the strengths and weaknesses of dominant health economic frameworks applied to the evaluation of the distribution of burdens and benefits in healthcare,

and specifically to the burdens and benefits of use of antibiotics in hospitalised patients, and the potential use of a capability approach to evaluation.

The main emphasis of this chapter will be on how we conceptualise and evaluate *what* we are trying to distribute rather than how we decide the distribution. The potential interface of capabilities with the contractualist theory of Thomas Scanlon will be considered in the next and subsequent chapters.

2.2 Strengths and weaknesses of current health economic frameworks

The outputs from health economic methods such as cost-effectiveness or cost-benefit analysis dominate evaluation of health care practice in the UK (and overseas) and have a substantial role in determining healthcare policy decisions. The National Institute for Clinical Excellence (NICE) which advises health policy in England gives considerable weight to cost effectiveness as a criterion for prioritising potential healthcare interventions. NICE guidance states that "most people accept that no publicly funded healthcare system, including the NHS, can possibly pay for every new medical treatment which becomes available. The enormous costs involved mean that choices have to be made. It makes sense to focus on treatments that improve the quality and/or length of someone's life and, at the same time, are an effective use of NHS resources" (National Institute for Health and Clinical Excellence 2012). For NICE if a treatment costs more than £20,000-30,000 per Quality Adjusted Life Year (QALY), it is not cost effective (National Institute for Health and Clinical Excellence 2009).

Not all of the problems identified in the following discussion apply to all forms of economic analysis, but do apply to the health economic methods that are predominantly used in the evaluation of healthcare including cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), and cost-utility analysis (CUA). For the purposes of this chapter risk cost-benefit analysis (rCBA) will be considered as a sub-category of CBA. Policies are evaluated in cost benefit analysis by comparing the relative value of benefits and the costs of the policy (including in rCBA the estimated costs of risks taking account of probability and severity). Costs and benefits are valued using a common unit of measurement (such as dollars). Cost and benefits can be aggregated at various levels from the level of the individual (over varying time periods) through to the level of large populations. Subjective valuations of goods can be included, for example by determining the average amount that individuals would be willing to pay for (or to avoid) a particular outcome. In cost-effectiveness analysis the cost of achieving health-related outcome indicators such as deaths avoided or days off work following different treatment strategies or other types of policy are compared. The objective is to maximise the effectiveness of a health process such as the treatment of arthritis. When health policies with differing types of outcome (for example in vitro fertilisation, hernia repair, treatment for pneumonia) are to be compared then the differing outcomes can be described using a common measure of utility (health benefit) such as a Quality Adjusted Life Year (QALY) which is used by NICE or Disability Adjusted Life Year (DALY). Methods of determining the relative value of different outcomes in CUA (time off work, years of life gained, degree of disability) usually involve aggregation of the valuations provided individuals for different health states. Cost benefit analysis weighs costs and benefits of different course of actions potentially across a disparate range of activities. Cost-utility analysis weighs costs and benefits within a

sphere of activity (such as healthcare) where there is a common measure of utility (such as QALYs).

Advantages of economic methods are that they link resources with outcomes (consequences of actions), benefits and costs are placed on a common scale, methods are explicit and transparent, and different policies can be ranked by relative cost-benefit or utility ratio. Despite these advantages economic methods of evaluating (and prioritising) health policies have been criticised (Brock 2006; Anand *et al*. 2006; Gardoni & Murphy 2009; Hansson 2007; Coast 2004; Wolff 2006; Hartzell-Nicols 2012.). Some relevant criticisms are discussed below.

2.2.1 Valuation of health states (QALYs or other utility measures)

Valuations (preferences) may not be stable

Objective measures such as life expectancy may not be a sufficient measure of health in that the quality of a health state may also be important for a comparison of health gains or losses. Health gains and losses associated with policies, which may have very different consequences for health, require qualitative as well as quantitative measures. There are various methods of estimating the quality of a health state but one method commonly used in health economics is based on the elicitation of preferences for example by asking individuals to compare health states or place a monetary value on a health gain or loss (willingness to pay). However the estimation of individual valuations is problematic because these may vary both from individual to individual but also from the same individual at different times. A common

approach is to determine valuations before and after a health intervention. In effect this means that large variations in individual experience through the period of intervention may not be captured in the output of analyses. Individuals adapt to long-term changes in health state and learn to cope with illness and disability, so that the selection of the timing of measurements determines valuations (see Raymont *et al*. 2004). If we are to value health states then whose valuations (preferences) should be considered and at what time point if the health state is dynamic as it can be for hospitalised patients?

The levels of acceptable risk of burden and benefit and associated preferences for different courses of action depend on perspective. In the UK there was (and to some extent persists) a perception that 'superbug' infections are common in NHS hospitals. Public perception of these risks is subject to influence by politicians and the media, so that valuations of states of affairs or outcomes may be unstable. If many lose confidence in the NHS following the reporting of an individual experience (with a 'superbug') such that patients with serious illnesses refuse admission to hospital, then aggregate good may be best served by costly measures taken to re-assure the public even when these measures go far beyond the economic consequences of the disease that the measures are designed to prevent. Valuations influenced by misinformation or political or media interest may be an unstable foundation as determinants of public policy.

Valuations require imagining of states for which we may have no experience

One way of seeing the difficulties of valuing health states for which we have no experience is through a discussion of the consent process. In order to give consent to a procedure an

individual has to be able to give consent to a propositional state or intervention (O'Neill 2004, p1133). The person who is asking for consent (or for preferences) has to be able to describe alternatives and the individual asked for consent (or for preferences) has to be able to imagine those experiences. When states are very distinct such as life or death, or use/loss of a limb then it is possible to conceive of consent as informed choice, but often there are complex trade-offs associated with choices between health states. It is hard to conceive of how the person asking for consent (or asking for a valuation of a health state) could give a true description of the experience of another even after that individual has had that experience, or for the individual asked for consent to imagine that experience other than in the most black and white cases. It seems less problematic to accept that the purpose of consent is to ensure that the individual has not been coerced or deceived, rather than as an informed choice between various options (see Manson & O'Neill 2007). Informed consent in a healthcare context usually involves individuals who are suffering from an illness (with some experience of that illness) and a limited range of choices. When preferences are obtained from individuals outside of the context of discrete healthcare choices then it is hard to see how those preferences can do more than reflect their own individual experience. Eliciting public preferences for different health states can be seen to validate policy decisions, particularly those related to resource allocation. Patients and public have been given a choice and the act of choosing gives a sense that there is consensus. Resource allocation decisions have been 'justified' by explicit dialogue and public acquiescence. It is possible to see this as a political expediency, but much harder to see these preferences as informed or as a meaningful reflection of the experience of those in different health states.

Some cannot express valuations

Many groups of hospitalised individuals are not able to express preferences or valuations – for example patients requiring intensive care. Premature infants nursed in an intensive care unit are an extreme example of a group who cannot express a preference. Most adults who have survived intensive care as an infant would probably prefer to be alive rather than dead but beyond that giving weight to preferences for different degrees and forms of disability requires that individuals can compare their own experience with another alternative. Even if an adult can imagine accurately and compare states of health it is unlikely that they could imagine their own experience of states of health as infants and young children with other states. Preference satisfaction and valuations assumes that the individual preference is based on a stable, informed and accurate imagining of the consequences of an individual choice. How can we elicit valuations about degrees of disability, pain, or effects on development from an infant who has survived a preterm birth? This may be an extreme example but it does illustrate the difficulties and implausibility of valuations of health states when those health states occur in individuals who cannot give voice to valuations.

2.2.2 Valuing 'Public Goods'

An individual may prefer to be treated with an antibiotic for a self-limiting condition. If there is widespread use of antibiotics for self-limiting conditions then that practice will ultimately undermine the sustainability of antibiotics as effective treatments. Public goods are those that impact on all of us for example the (quality of) air that we breathe and the water that we drink. Control of infectious disease is an oft-cited example of a public good. Public goods,

such as the control of the spread of agents of infection and even more so control of their treatment (antibiotic) resistant forms, raise an additional problem for advocates of individual preference satisfaction, because individual preferences may have far-reaching implications for others, just as the aggregated preferences of large numbers will have implications for the individual. O'Neill (2004) argues from a Kantian perspective that individuals (or it could be argued their preferences) cannot determine actions which may have a substantial impact on others by undermining the sustainability of public goods. I would suggest that neither individual nor aggregated preferences should determine the sustainability of public goods.

Preferences change and are biased towards the perspectives of those who are available, able and selected to give preferences. Individual preferences may run contrary to the interests of others with respect to antibiotics, vaccines, probiotics, and infectious disease control policy. On the other hand if we take account of the aggregated preferences of others then which others do we include, and is preference satisfaction an acceptable guide to decision making when we cannot ask those not yet born (who may bear the major burden of infectious disease (mis-) management), or those in other countries who may suffer adverse consequences as a result of the spread of infectious diseases? Antibiotic resistant bacteria may not be perceived as a problem at a particular time or place, but widespread use of antibiotics ultimately leads to compromise of outcomes for distant (temporal or geographical) people as antibiotic resistant bacteria become more common. The question arises of whose preferences should be considered in decision-making. If we are to sustain the effectiveness of antibiotics for distant people including future generations then the over-consumption of antibiotics today (and the consequent undermining of their utility as effective treatments) will need to be constrained.

2.2.3 Valuing Choices, which include uncertainties

Uncertainties are those risks and benefits, which I have taken to be those with probabilities that cannot be quantified with any degree of accuracy. Many ecological risks are unquantifiable because the interactions are extremely complex and poorly understood. An additional problem for the use of preference satisfaction arises when choices include uncertainties. We cannot assume that the present context represents the distant context. Expressing a preference for a temporally or geographical distant event requires an estimate of probability (likelihood) and severity (of potential consequences) and valuations of particular consequences. The evolution of antibiotic resistant bacteria involves complex and incompletely understood ecological interactions. For example at the moment we do not know whether or when we might have new treatments for infection to replace antibiotics. If we cannot accurately estimate either the probability or the significance of the consequence of an event then how can we express a preference for that event? There would seem to be substantial technical and philosophical difficulties with expressing preferences concerning uncertainties. When we estimate that the cost of infection with treatment (antibiotic) resistant bacteria is x or y then that estimate is based on a selection of historical examples (for example MRSA infection) for which we have accumulated information. We cannot assume that historical experience will or does represent future experience.

Many of the choices that are made today set precedents for future choices. If we accept a cost utility or cost benefit argument for a course of action today because the impact on levels of antibiotic resistance within a population will be small then that sets a precedent which may

lead to widespread use of antibiotics in other areas with a similar cost to benefit ratio. The consequence of more and increasing antibiotic prescribing may well be a change in the cost-benefit relationship – a change that may not have been considered in the original cost-benefit calculation.

2.2.4 Can we cost all of the dimensions of patient experience?

The allocation of resources to control infections caused by antibiotic resistant bacteria is frequently justified by a comparison of the costs of infection with antibiotic resistant bacteria with something else (for example infections with antibiotic sensitive bacteria). While discussing healthcare associated infections (HCAI) (many of which are antibiotic resistant forms of infection) Graves *et al*. (2010) state that "Complete evaluations that include changes to all costs and health benefit should be performed". They then go on to say that "the number of bed-days lost to a case of HAI is an appropriate outcome to describe a large proportion of the cost" (Graves *et al*. 2010). Graves *et al*. (2010) acknowledge the considerable technical difficulties particularly related to feedback between length of stay in hospital and the development of infections amongst hospital patients. Fukuda *et al.* (2011) also emphasise the methodological difficulties of costing healthcare associated infections. Even if we are able to disentangle the interactions between hospital stay and hospital infection and calculate potential savings in bed days, it is doubtful that economic cost will be a sufficient measure of all that is valued and potentially or actually lost through preventable infection.

I would argue that patients with HCAI experience more than a prolonged hospital stay, that the costs of aggregated bed days lost obscures the experience of individuals, and that many

significant costs should not be ignored. For example the experience of the elderly patient who suffers the indignity of *Clostridium difficile* diarrhoea at the end of their life, or the child with restricted contact with others either to protect the child from infection or to protect others from infection, or the removal of children's toys to prevent the spread of infection, or the experience of stigmatisation associated with an infectious status, or the emotional experience of fear associated with a diagnosis of MRSA infection, or the loss of control of freedom of movement are all part of patient experience of HCAI which cannot be captured by the costs of bed-days lost. These experiences are important to individuals and those that know them, but it hard to see how all of these consequences of HCAI can be given a cost.

If we imagine the case of a 32-year-old diabetic women recovering from a healthcare-associated Meticillin-resistant *Staphylococcus aureus* (MRSA) Caesarean wound infection. The infant was delivered at 30 weeks gestational age because of foetal distress and is currently being nursed on a Neonatal Intensive Care Unit (NICU). This scenario illustrates a number of potential costs that go well beyond bed days. These costs include the potential for restrictions on maternal contact with the baby to interfere with the establishment of breast-feeding (and associated health benefits) and mother-infant bonding, on the confidence that the mother and other mothers have in the service, in addition to the potential spread of MRSA to other vulnerable infants. This type of scenario illustrates the importance of attachment(s) and of taking account of the importance of attachment in patient management decisions.

If we accept that harm is something that makes a person worse off, then many of the experiences described above (for example loss of dignity at the end of life, stigmatisation, fear, failures of attachment) could be considered as harms. These harms are rarely included in

economic analyses of the costs of antibiotic resistant infections. It is not just that these costs are overlooked it is also hard to see how any monetary value can or could replace or compensate for these consequences of infection with antibiotic resistant bacteria.

2.2.5 Should we include societal costs/benefits?

Some of the consequences of infections with antibiotic resistant bacteria such as MRSA are not confined to the experience of individuals and may have far-reaching social consequences through their effects on others. The risks associated with acquisition of Meticillin resistant *Staphylococcus aureus* (MRSA) had become a substantial public concern in the United Kingdom throughout the 1990s threatening to undermine public confidence in the English National Health Service. The Labour government responded to this loss of confidence by implementing increasingly stringent targets aimed at the control of MRSA in NHS hospitals. Public concern with MRSA was fomented by press reports of individual patient experience. These societal consequences threatened to undermine the functioning of the English NHS. "Security is valuable – insecurity is problematic if the individual is vulnerable to the risk (in probabilistic terms); if they cannot control the risk; depending on the degree of resilience; and if there is anxiety about the risk" (Wolff & De-Shalit 2007, p217). There is a considerable value in assuring individual patient experience such that public confidence in healthcare institutions such as NHS hospitals is maintained. Loss of public confidence in healthcare providers is a societal cost.

Valuing societal costs

CEA focuses on costs and benefits in a healthcare context, CBA can take a more inclusive approach. Even so deciding which costs to include, how to capture these costs and their ethical implications raises substantial difficulties. We have to question the possibility that the societal costs associated with a loss of public confidence in the healthcare system can be accurately quantified (See Burnett *et al*. 2010; Easton *et al*. 2009; Gould *et al*. 2009). The 'Rule of Rescue' (RR) refers to the imperative that most people feel that they (or someone else) should try to rescue individuals seen to be at risk of a serious adverse outcome. McKie & Richardson (2003, p2410) in discussing RR suggest that this imperative seems to apply to non-life saving and life saving conditions. Relatives, friends and bystanders (including other patients) may all feel distress when a patient is seen to be suffering from a potentially avoidable infection. The reporting of patient experience in the media by individual patients and by others can have a profound effect on public confidence in healthcare institutions so from a consequentialist perspective an individual patient experience may become important (see the reference list for articles from 'The Sun'). The argument that prevention has received a lower priority because the costs of the HCAI measured in added bed days is insufficient to justify spending money on preventive actions may be seen as callous, so in effect RR may undermine the maximisation of utility when utility is measured in aggregated measurable health costs and benefits. McKie & Richardson (2003, p2413-4) suggest that a value can be placed on RR because there is a social utility associated with the public knowledge that an attempt to help (or in the context of this thesis to prevent) has been made. "It is almost certainly true that people obtain benefit from the *belief* that they are living in a caring and

humane society, and that the observation of attempts to save life, whether heroic or more mundane, reinforces this." McKie & Richardson (2003, p2413) point out that the psychological response of individuals and groups to a person's health state depends on the context and information available, so in effect the utility gained or lost "depends upon circumstances extraneous to the immediate health state." McKie & Richardson (2003) acknowledge the difficulties of placing a cost on these types of effect and discuss potential approaches to costing.

Wolff (2006) points out that the avoidance of fear (public anxiety), blame and shame are important motivations for those involved in risk management whether at the level of individual interactions or institutions (including commercial companies) or governments. In the UK the public response to concerns about MRSA led to actions at a political level to increase the priority given to the control of MRSA. The approach focused on the control of one type of MRSA infection and can be judged successful in that media and public concerns have diminished, even though some of the actions taken to control MRSA were not cost-effective in a traditional sense (based on objective measures of risks) and were potentially harmful (see for example Millar 2009). In this case perceptions have been managed successfully in that public fears have been allayed despite strong evidence up to 2009 that the overall burden of healthcare associated infection has not reduced (Public Accounts Committee 2009).

Should we include societal benefits?

There are circumstances in which there may be benefits to distant others when in a local context there are adverse effects on individuals or groups. Wars often lead to technological developments some of which may greatly benefit society in the future despite the adverse outcomes for many individuals alive at the time of the war. Should these benefits be included in a justification of war? Many see the battle against antibiotic resistant bacteria as a war. Infection with treatment resistant microbes may not benefit the individual sufferer but the public concerns consequent on publicised case reports have led to the development and commercial sale of a wide range of products leading to employment opportunities, improved treatments, and improved preventive strategies. Technological developments such as the development of new treatments (for example antibiotics) or new preventive measures (such as vaccines) arising from the urgent need to resolve the threat may have longer term social and economic benefits. While drug development and manufacturing companies have new antimicrobial products coming to the market they may benefit from antibiotic resistance because it creates redundancy in existing products.

Another example of a benefit that has arisen in response to the threat of infectious disease is the capacity to use computer models to predict the course of epidemics and to optimise preventive strategies (by predicting the impact of different control strategies). These models have been validated by comparison of the computer outputs with real epidemic curves. Data on how long patients transmit infections and the proportion that die is derived from observation of real events and is essential data in models of epidemic disease and its

consequence(s). The human capacity to control of infectious diseases improves with the information garnered from each outbreak of infection.

There are considerable technical and philosophical difficulties with including these benefits in evaluations for example the time frame over which these benefits should be measured, and the weight that we should give to future benefits.

2.2.6 Are all relevant 'goods' commensurable?

There may be many different kinds of 'goods' (see foregoing). Economic methods of evaluation such as CBA, CEA and CUA generally describe outputs using common units of measurement. Can all 'goods' be reduced to a common measure and placed on the same scale? One way of investigating this question is to ask if increasing one 'good' can compensate for lack of another. Wolff & De-Shalit (2007) suggest that a plausible monism (a single scale of measurement used for comparison) must adopt a 'compensation paradigm' (p25) and go on to provide a formal argument against substitution monism (p26). Wolff & De-Shalit argue that no amount of money can compensate for a high risk of death. It is hard to see how a loss of dignity at the end of their lives, or long-term effects on significant attachments could be compensated for. Loss of public confidence in a health system could be compensated for by providing access to another health system, but fear of hospitalisation consequent on a poor hospital experience would remain uncompensated (even if provision of an alternative health system was feasible).

2.2.7 Level of aggregation of costs, risks and benefits

The aggregation of costs and benefits is a familiar focus of critiques of utilitarianism as a moral theory. Use of antibiotics in an individual can have important benefits for others through the control of the secondary spread of disease, by contrast the selection and spread of antibiotic resistant bacteria following the use of antibiotics can give rise to harm to others. In both cases the numbers of others benefited or harmed is potentially very large. CEA, CUA and CBA tend to use aggregated cost benefit data. Aggregated risks of benefits and harms to a large number of individuals would (in many instances) dominate the benefit and/or harm to an individual even in circumstances where the individual stands to gain or lose significantly by the decision that is made. Current systems of patient care take account of the individual circumstances. Decisions based on overall (aggregated) societal costs and benefits would make individual circumstances of limited relevance to antibiotic prescribing decisions with the potential to prejudice healthcare provider - patient relationships and public confidence in the healthcare system. Benefits to the many may outweigh larger benefits to the few. Extreme forms of antibiotic resistant bacteria are common in patients with cystic fibrosis reflecting the enormous burden of antibiotics prescribed to this population. If it is the case that patients with cystic fibrosis are substantial reservoirs of antibiotic resistant bacteria then conclusions drawn from aggregated public good could lead to curtailment of use of antibiotics in this group of patients.

If we (as individuals) are responsible for supporting policies, which maximise health then where does that leave the individual? “The sense that there is really anything that is really them or their own is difficult to maintain. This worry is really a set of closely related worries:

about personal integrity, about agency, about friendship and family, about the sources of the meaning of life, and about the nature of political agency" (Nussbaum 2004, p14). Utilitarianism (Nussbaum 2006, p282) "treats the individual as an input into a social calculus, and thus is insufficiently sensitive to the distinctness of each individual life". Hansson (2007) suggests the "individualist weighing principle", for which an option is acceptable to the extent that the costs affecting each individual are outweighed by benefits for that same individual. We all benefit from the control of treatment resistant forms of infectious diseases, so to an extent we may be prepared to accept some limitations to the use of antibiotics over our lives. However the degree of benefit will depend on the context (including perceptions of risks and their acceptability) and also be a function of life expectancy. In effect an older person could have less interest (in cost benefit terms) in the control of antibiotic resistant infections than a younger person if our basis for decision-making is the individual, because the older person is less likely to be alive when treatment resistance becomes an important determinant of patient outcome. This is a public goods problem (see above) and a life expectancy problem (see below)

2.2.8 Achievable benefits depend on life expectancy

How do we take account of medical advances?

In order to calculate the number of years of benefit arising from a medical intervention (for example treatment of pneumonia) we need an estimate of life expectancy. The maximum potential benefit derived from CEA or CBA declines with age or when individuals have a shortened life expectancy. Technological advances may lead to dramatic changes in life

expectancy both for older people and for those who for other reasons at the moment have a shortened life expectancy. New cures and preventive strategies for disease are discovered. The relatively common genetic disease cystic fibrosis provides an example. Now that many of the genes for cystic fibrosis have been discovered a new genetic cure for cystic fibrosis may come very soon. Life expectancy may increase dramatically. It is difficult to see how we should take account of medical advances in economic analyses.

Whose life expectancies should we use?

Class averages may not represent a general life expectancy or the life expectancy of individuals. Policy decisions based on estimates of benefit may turn out to be inaccurate both for individuals and groups so deciding whose life expectancy is to be used in evaluations is not a straightforward decision.

Priority to life years gained?

If we use life expectancy as a substantial element in evaluation then should we be giving a lower priority to those with shorter predicted life expectancy? CBA and CEA both give priority to policies with the maximum aggregate benefit to cost ratio. There are other bases for the allocation of priorities. We could choose to allocate resources to give priority on the basis of need, reducing differences (equality), or achieving sufficiency. Priority can be relative, absolute or weighted. We could emphasis fair chances or best outcomes. Do we give individuals a chance even when the outlook is poor (some respond but the majority do not) or only give a chance to patients in whom there is a proven benefit? Antibiotics may be used to

ameliorate suffering in a patient terminally ill or to produce a small but important benefit to someone in the last years of their life for example to control infection associated with a failed and infected hip replacement - allowing the restoration of some mobility and dignity at the end of a life. There are many good reasons for use of antibiotics many of which would not stand easily beside the principle of maximisation of utility.

In the next section I consider an alternative strategy for the evaluation of the justice of the distribution of antibiotic burdens and benefits based on capability theory.

2.3 Capability theory

As discussed in the previous section (2.2) there are considerable technical and philosophical difficulties with ascribing common units of value to all costs (losses of valued goods) and benefits (gains of valued goods). The public and subsequent political response to MRSA in the English NHS illustrates the range of dimensions that may be impacted by antibiotic resistance including the social consequences (See Wolff 2006; Murphy & Gardoni 2007; Gardoni & Murphy 2009). The elicitation of preferences and life expectancy to rank outcomes is problematic when applied to dependent groups of individuals such as hospital patients. I will consider an alternative framework for the evaluation of the distribution of (health) burdens and benefits based on capabilities, using the example of the approach advocated by Martha Nussbaum (Nussbaum 2006).

Sen (1993) proposed capabilities and functionings as an evaluative framework for human development. The capability approach proposed by Sen has been interpreted and also applied

in many different ways. The extent of achievement of capabilities has been used to compare development in different countries (Sen 1999), in theoretical frameworks for Public Health (Powers & Faden 2006; Venkatapuran 2011), as the basis for an economic model to be used in poverty reduction (Alkire 2005), and proposed as a way of determining policy and resource allocation priorities for mitigating risk (Gardoni & Murphy 2009). There is also increasing interest in the use of capabilities to help with the specification of health, illness and disease (Law & Widdows 2008), and with characterising what it means to treat patients as persons (Entwistle & Watt 2013). Wolff & De-Shalit (2006) have emphasised how in the real world the interactions between capabilities may lead to clustering of disadvantage. In the next section I provide a brief overview of some of the similarities and differences between different capabilities approaches.

2.3.1 Capabilities approaches

Martha Nussbaum's approach differs from that of Sen in a number of respects (see Robeyns 2005). Nussbaum (2006) offers a normative framework for a 'partial' theory of justice. For Nussbaum and Sen a capability is a "substantial freedom he or she enjoys to lead the kind of life he or she has reason to value" (Sen 1999), resources and preferences only give a partial conception of how well off someone is. Sen uses the achievement of capabilities and functionings as an indicator of the justice of social arrangements. Freedom has two aspects. One is a process aspect – "ability to be agents" – to affect the processes at work in their own lives or as general rules in the working of society, and second an opportunity aspect – "ability to achieve" valued functionings. Sen distinguishes agency and wellbeing, freedom and achievement. Functionings represent well-being achievement and capabilities represent well-

being freedom. Sen (2005) refers to important process freedoms, which cannot be adequately analysed within the capability framework. These include the extent to which the person is free to choose or whether others intruded or obstructed. He argues that capabilities allow comparisons of systems, institutions, and the situation of different groups and individuals. Sen is interested in agency and individual freedoms and the achievement of real and effective opportunity. He does not endorse a specific list of capabilities or functionings, and does not consider capabilities to be entitlements. Sen suggests that "the capability approach points to an informational focus in judging and comparing overall individual advantages, and does not, on its own, propose any specific formula about how that information may be used" (Sen 2005, p232). "The capability perspective does point to the central relevance of the inequality of capabilities in the assessment of social disparities, but it does not, on its own, propose any specific formula for policy decisions" (p232). Sen refers to capabilities as "the right kind of information" (p233).

By contrast Nussbaum argues for a specific list of capabilities as (normative) entitlements that are required for a life of human dignity. Nussbaum (2006, p36) suggests that human beings are characterized both by dignity or moral worth (as ends in themselves) and by sociability. Nussbaum (2006, p36) quotes Grotius – "But among the traits characteristic of the human being is an impelling desire for fellowship, that is for common life, not of just any kind, but a peaceful life, and organized according to the measure of his intelligence, with those who are of his kind… Stated as a universal truth, therefore the assertion that every animal is impelled by nature to seek only its own good cannot be conceded". Entitlements flow from these ideas – "human sociability indicates that advantage is not the only reason for which human beings act justly" (p37). The capabilities describe necessary conditions for a decently just society, in

the form of a set of fundamental entitlements for all citizens (p154). The approach (unlike that of Rawls) does not employ a hypothetical initial situation (p156), and envisages cooperation out a wide range of motives including love of justice and compassion for those who have less than they need to lead decent and dignified lives. There is an assumption human beings are held together by many different ties including altruism (p158). There is an underlying conception of the person out of which basic political principles grow. This is a conception of human beings as needy temporal animal beings who begin as babies and end, often, in other forms of dependency. Rationality and sociability are temporal and relations may be more or less asymmetrical. Dignity and capabilities are intertwined. The right and the good are also intertwined. For Nussbaum capabilities should be the primary focus of concern, except in certain areas for example "self-respect and dignity itself" (p172), and compulsory education for children (p172).

Nussbaum proposes that the list of capabilities (and entitlements) is provisional, and can evolve through a form of reflective equilibrium, akin to the process suggested by John Rawls (1971). We start with a rough list, which is intuitively acceptable and then proceed to reflect on this list, and consider the implications of the choices that we have made. There may be capabilities that should be included but have been left out of the initial choices. Wolff & De Shalit (2007) proposed additional capabilities that might be added to Nussbaum's list. Once agreed the list applies to all so cannot be described as paternalistic at least in the sense that one or more individuals is making decisions about the interests of others. Interests (and their specification) are pre-defined.

For Nussbaum a sufficiency of capability in all the ten dimensions describes the necessary minimum conditions for individuals to be considered to be living in a decently just society. Health is one of the ten capabilities but the other nine capabilities are considered by Nussbaum to be of equal importance for a life of human dignity. The list is normative and not just a source of the right kind of information to be used in comparative evaluations. Nussbaum grounds the list of capabilities in an Aristotelian conception of the requirements of a life of human dignity. Critiques of the approach proposed by Sen do not all apply to Nussbaum and vice verse. Sen suggests that any selected list requires account to be taken of local context and valuations (preferences) whereas Nussbaum considers that impartial and universal application of a capability approach to evaluation requires a predefined list. The capabilities selected by Nussbaum are not fixed but could be the object for an overlapping consensus amongst citizens – justified by acceptability to all. Nussbaum emphasises skills and traits whereas Sen is criticised for over-emphasising freedoms (as opposed to for example justice) (Gasper & van Staveren 2003). Neither Nussbaum nor Sen are very specific about fair process rather it is the outcomes from different social realizations, which are important in evaluating the underlying institutions and processes. Both emphasise the plural and incommensurable nature of capability sets, and argue that social states should be evaluated and defined in the space of human capabilities. Valuable states expand human capabilities. Utility maximization is an insufficient objective (for Nussbaum) when it comes to defining just social arrangements.

In discussing the position of a capabilities approach with respect to abortion Dixon & Nussbaum (2011) consider that a focus on dignity is clearly different from a focus on utility, or resources, or preferences. They emphasise a positive obligation to foster capabilities. Each

life is of equal worth and each person is considered as an end. For the foetus survival is contingent on the mother and a life with human dignity is only a potential life, so "The asymmetry between a potential and an actual being suggests that pre-viability, the woman's claim should in general prevail" (Dixon & Nussbaum 2011, p9). Capabilities require a minimum of agency, sentience, and potential capacity for independent survival. Once the decision has been made to admit an infant to an intensive care unit then the objective to try to foster potential capabilities would seem straightforward, equally if there a sufficient certainty that an acceptable threshold for a given capability cannot (reasonably) be reached then treatment should be withdrawn. Nussbaum describes Basic, Internal and Combined capabilities. Basic capabilities are those held by a healthy infant and are required for the development of internal and combined capabilities, internal capabilities are the conditions required for certain functions such as speech, and combined capabilities are those that exist when the internal and external conditions/institutional arrangements are right. From the perspective of capabilities the key thing for infants would be the securing of thresholds of 'basic' capabilities such as seeing, hearing, or reasoning. Other aspects of capabilities are less relevant at this stage of development because without basic capabilities other capabilities cannot develop (such as the necessary conditions for free preference formation, and equal opportunity). Capabilities draw attention to the importance of a range of capabilities such as emotional development in addition to health.

The ten capabilities selected by Nussbaum are shown in Table 2.1 below.

Table 2.1 Ten Capabilities required for a life of human dignity

Capability	Functions
Life	a full life (not dying prematurely)
Bodily Health	good health and shelter
Bodily integrity	freedom of movement and security
Senses, Imagination, Thought	intellectual and religious freedoms
Emotions	emotional development un-blighted by fear
Practical Reason	one's own life plan
Affiliation	engagement in social interactions
Other species	concern for other creatures
Play	(and enjoy) recreational activities
Control over One's environment	free speech and freedom of association

For Nussbaum the choice is intuitive, can be subject to debate, and can be changed as a result of a form of reflective equilibrium, but once agreed the list applies universally.

Many others have produced similar lists and justified components in different ways (see overview in Alkire 2005, Chapter 2). For example, Alkire bases her list and the justification

of choices on the work of Finnis (1994). Alkire describes the Finnis approach as one that "(i) enables and requires participatory dialogue in application, but also (ii) has objective foundations and (iii) can coherently engage with and be refined by the large and growing literatures on happiness, subjective well-being, quality of life indicators …." (p27). Finnis grounds his list of basic human goods (non-moral) through what he describes as a process of practical reasoning on the determinants of human fulfilment. He repeatedly asks why do I do what I do and why do others do what they do? He uses this line of reasoning to develop a discrete and heterogeneous set of the most basic and simple reasons for acting which reflects the complete range of kinds of valuable (moral and non-moral) human states and actions.

Moral 'goods' are specified by Finnis by using two principles (1) The principle of non-contradiction, and (2) The principle that good is to be done and pursued. Persons or institutions should undertake to act only so that each action furthers human ends or the dimensions of development. Ethical actions and practices make their way towards human flourishing coherently – in such a way that is consonant with the desire for all people across time to enjoy sustainable human development in any or all dimensions – "in voluntarily acting for human goods and avoiding what is opposed to them, one ought to choose and otherwise will those and only those possibilities whose willing is compatible with a will toward integral human fulfilment" (Finnis 1994, p136). Finnis suggests that these reasons for action require specification and agreement by communities taking account of context (including empirical data) before they can be used to formulate political obligations or individual entitlements.

It is hard to see how the methods that Finnis applies could add to the approach taken by Nussbaum, even if we accept his methodology there remain considerable difficulties when we

try to engage patients for example newborn infants or hospital patients in any process of agreement or specification. Also it is not clear (just as with aggregated preferences) how we would select the community with which to dialogue (see the foregoing discussion of valuation of health states). Alkire (2005) describes the 'Achilles heel' of her selected approach to reducing poverty (in part by engaging poor people in the process) "is the assumption that poor people can articulate and analyse their poverty and their valued freedoms in multiple dimensions, and further that if they do so the resulting analysis will be different from a sophisticated but narrower analysis that uses income as a proxy for poverty and freedom" (p199). For me this is more than an Achilles heel when it comes to the interests of substantial numbers of hospital patients such as those who lack competence, and I have chosen not to use this example of a capabilities approach.

For the purposes of this thesis I have accepted the list that Nussbaum proposes as illustrative rather than definitive, in that there is still much debate about the elements that should be included in a capabilities list even when we accept a justification based on requirements for a life with human dignity (see for example Wolff & De-Shalit 2006).

2.3.2 Capabilities or human rights

Nussbaum states that the capabilities approach is a "species of human rights" (Nussbaum 2007, p21) so do we need the capability approach? What distinguishes the capability approach as described by Nussbaum from a human or patient rights approach?

The human rights movement has gathered momentum since the Universal Declaration of Human Rights was adopted by the United Nations in 1948. Over 140 countries have ratified the International Covenant on Economic, Social and Cultural Rights (ICESCR) since it was agreed in 1966 (*UN Document A/6316*, 1966). ICESCR recognizes the interdependency of the right to the highest attainable standard of health (in Article 12) with the achievement of other rights such as adequate housing and nutrition, freedoms of association, access to information, and of particular relevance to infection control access to safe supplies of food and water, adequate sanitation, healthy occupational and environmental conditions, and the control of epidemic diseases. The European Convention on Human Rights (ECHR) was given effect in UK law by the Human Rights Act 1998. It is unlawful for a public body to act incompatibly with those ECHR rights (section 6 of the Human Rights Act). Patient rights are increasingly recognised and officially endorsed by regulatory authorities, governments and international bodies such as the World Health Organisation. A World Health Organisation European consultation meeting held in 1994 endorsed principles for the promotion and implementation of patients' rights in European member states. The American Medical Association (2012) includes a number of patient rights within the AMA Code of Medical Ethics. The Australian Commission on Safety and Quality in Healthcare publishes a Charter of Healthcare Rights. In January 2009 the English National Health Service Constitution was launched. Providers and commissioners of NHS care are now under a legal obligation to have regard to the NHS Constitution in all their decisions and actions.

Jonathan Mann and others (see Mann 1997; Rodriguex-Garcia & Akhter 2000) have advocated human rights as a conceptual framework for Public Health, as a tool that allows comparison of the experiences of different populations and as a framework to define the

direction(s) of societal change (Mann 1997, p197). Mann argues that human rights can provide a "framework for identifying and analysing the essential societal factors that represent the 'conditions in which people can be healthy'" (p198). For others "human rights and public health ethics are distinct yet complementary tools for evaluating and analyzing public health interventions" (Cohen *et al*. 2007, p342). Cohen *et al.* (2007) also argue that "the legal integrity of human rights analysis, as much as its moral appeal, is what gives the human rights movement its authority and force" (Cohen *et al.* 2007, p344). Rights can be used to "set some threshold limits to trade-offs such that the pursuit of other aims, including greater social utility, are constrained" (Powers & Faden 2006, p47).

2.3.3 Human rights and infectious diseases

There is an existing public health literature derived from the experience of those trying to control the spread of infectious diseases such as Human Immunodeficiency Virus that emphasises that in order to achieve the goal of disease control we must also respect a range of human rights (including rights not directly linked with health). Respect for human rights has been incorporated in the design of strategies for the control of HIV/AIDS, (Cohen *et al*. 2007) and in strategies used for the control of other infectious diseases such as tuberculosis (Hurtig *et al*. 1999). Respect for human rights has been used as the basis for justification for action to control neglected tropical diseases (WHO 2007). A human rights approach requires that the right to the highest attainable standard of health is recognized and this requires both treatment and preventive measures for neglected tropical diseases are available in affected areas of the world.

It might be that human rights by emphasising the importance of the rights of individuals could be used to subvert or to obstruct the progress of policies aimed at improving public 'good'. This tension was particularly apparent in the immediate period after the recognition of HIV (Fluss1992, p3-33; Mann *et al*. 1994, p15-17). Laws were introduced in many countries which included mandatory screening of risk groups such as men having sex with men, sex workers, and injecting drug users. Individuals were subject to isolation and compulsory treatment. There were also limitations for some on international travel (Gostin & Lazarinni 1997). Some commentators deny that there is a tension between public good and individual rights. Cameron & Swanson state that - "The central point is that the protection of individual rights and the preservation of the common good, far from being antithetical, are in fact complementary" (Cameron & Swanson 1992, p202). They suggest in the context of control of the spread of HIV that "every measure that involves limitation of rights must be tested against criteria of rationality and ethical values: whether a particular measure does actually achieve its object in combating the spread of HIV; if it does, whether the measure invades a more crucial and fundamental human right; and, if so, whether it is the least restrictive way of attaining its objective" (Cameron & Swanson 1992, p202-203). Criteria for allowing breaches of human rights have been agreed under international human rights law (United Nations Economic and Social Council 1984). These Siracusa principles require that any limitation must be carried out in accordance with law; serve a legitimate purpose and be strictly necessary to achieve that aim; be the least restrictive and intrusive means available; and not be arbitrary or discriminatory in the way it is imposed or applied. The purported success of rights-based approaches when it comes to control of diseases associated with strong social correlates such as AIDS suggest a role for rights based approaches for other diseases associated with strong social correlates such as hospital infection with MRSA (Millar 2011).

2.3.4 Why capabilities when we have rights?

We have to ask if "we have the language of capabilities, do we also need the language of rights" (Nussbaum 2006, p50)? "Capabilities, I would argue, are very closely linked to rights, but the language of capabilities gives important precision and supplementation to the language of rights" (Nussbaum 2006, p48). Mann has suggested that a language of rights can act "as a tool that allows comparison of the experiences of different populations and as a framework to define the direction(s) of societal change" (Mann 1997, p197). I am suggesting that capabilities can do this more directly than can be achieved with the language of rights. Perhaps most importantly it is the specification of the capabilities framework at both theoretical and practical levels that provide much of this advantage. Nussbaum argues (Nussbaum 2005, p48) that rights claims may be based on different conceptions and premises, they may be seen as pre-political or seen as dependent on political institutions, as applying to individuals only or also groups, as constraints or as goal-promoting, as linked with specified duties or not, and to what they apply also may differ (resources, opportunities, achievement).

Despite the widespread acceptance of respect for human rights as an important aspect of public health policy there are continuing real-life tensions between respect for human rights and actions taken to protect public health (Bayer 2007). Some key difficulties for 'rights' approaches to public health include the difficulty in grounding rights claims, the extent to which rights have meaning beyond specific institutional and political contexts, the relevant status of positive (entitling) and negative (constraining) rights, and if there are positive

entitlements stemming from rights then are those entitlements to resources, outcomes, opportunities, or human behaviour?

Rights can be conceptualised in many different ways. Hessler (2010) argues that those who have advocated a human rights approach to public health ethics have failed to engage in a consideration of the philosophical foundations of human rights, so leaving the approach vulnerable to the criticisms arising from the lack of a conceptual foundation. Rights can be grounded in fundamental interests or from a conception of agency. Raz (1986) has suggested an interest based justification for rights such 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 person(s) to be under a duty" (Raz 1986, p166). An alternative conception sees rights as protecting agency or choice – allowing space for personal choices (see Powers & Faden 2006, p46). Powers and Faden see rights as foundational for an ethics of public health (taking an account of rights as secured functionings), but argue for an interest based conception of rights defined as needs – "the core notion of rights is neither individual choice nor individual benefit but basic or fundamental needs" (Powers &Faden 2006, p47).

It is hard to see how rights can be based on choices for many hospital patients who are dependent and frequently not empowered or able to make choices in a meaningful way (although it is possible to see that it may be about choice at some later time). It is also important to be clear concerning the limits to rights. For example it is hard to see how a 'right to health' in an unlimited sense can be justified when health is not a commodity (and therefore cannot be provided), and total health is not achievable (O'Neill 2005). Rights may be considered as freedoms (for example a right to use a public thorough-fare) – negative

rights, and as positive rights (a right to employment). A right can entail access to something of value and a genuine opportunity. Rights can apply universally and to specific individuals in specific contexts. Rights may be normative without being legally enforceable, or legally enforced without a clear moral mandate. Identifiable individuals, groups or institutions can be the bearers of duties. Rights may be dependent on particular relationships (for example parents and children) or independent of the nature of relationships. There are a number of substantial questions with respect to rights that require answers. So for example we might ask what is the relationship between one's own behaviour and rights – can we forfeit rights through our own behaviour? What is the function of rights? Do rights have to fit a purpose? Do we have to agree the actions/responses to an infringement of rights? If outside of a legal framework then how are these actions/responses to be enforced? When there is a lack of clarity with respect to any of these details then the scope of rights can impose unrealistic obligations on rights holders (see O'Neill 2005), equally a lack of specification can make rights unenforceable. Nussbaum's capability approach moves some way towards clarifying some of the answers to these questions.

A right may be breached but this breach may have more or less implications and significance for an individual rights holder. If we consider that a patient has a right "to be protected from epidemic diseases", then we should be able to specify the meaning of this right. If a patient catches a common cold from a visitor then does that indicate a breach of the right to be protected from epidemic diseases? Respect for human rights is included as a principle in the WHO International Health Regulations (2005) for the control of the spread of diseases such as Systemic Acute Respiratory Syndrome (SARS). "The implementation of these Regulations shall be with full respect for the dignity, human rights and fundamental freedoms of persons"

(WHO 2005, Article 3: Principles). The purpose and scope of the WHO IHR are "to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade". The WHO IHR (2005) are designed to control "illness or medical condition, irrespective of origin or source that presents or could present significant harm to humans", while also assuring "protection of the human rights of persons and travellers". Appendix 2 of the WHO IHR (2005) specifies that the "United States understands that the provisions of the Regulations do not create judicially enforceable private rights". In other words individuals may have rights but those rights do not have judicial standing.

In January 2009 the English National Health Service Constitution was launched. This constitution includes a number of patient rights (Department of Health 2010). Providers and commissioners of English NHS care are now under a legal obligation to have regard to the NHS Constitution in all their decisions and actions. By contrast the Patient Rights (Scotland) Bill specifically states that "the rights it contains are not enforceable by legal action" or give patients any new rights to "seek compensation if the rights in the bill are not met in practice" (Scottish Parliament 2010). If rights have no legal status then what do these 'rights' really mean for individuals who suffer a breach of rights? If rights are normative, then on what grounds should rights become legally enforceable? What are the limits of the obligations imposed by a respect for human or patient rights?

Pogge has proposed a human rights framework, which emphasises negative rights, selected on the basis of requirements for human flourishing (Pogge 2008). "Human rights require that we

do not harm others in certain ways – not that we protect, rescue, feed, clothe and house them" (Pogge 2008, p73). In my view negative rights are important but not sufficient for hospital patients. For example providing a space and facilities for a hospitalised child to play is not the same as supporting that child to play. A patient may be free (in principle) to discharge herself from hospital, but not in a position to do so. Assuring access to food is not the same as ensuring that a patient is adequately nourished. Another concern that I have with the approach that Pogge advocates is that much healthcare is provided beyond and across institutional boundaries. Support for individuals who are disabled or unwell may be provided from an extensive network of individuals, institutions, and social groups with or without a direct role in healthcare. Even if rights are considered to be universal, rights deficits may not be easily attributable to institutional failings. Pogge suggests that institutions have a duty to compensate those harmed by 'reasonably' avoidable causes. The force of Pogge's argument seems to focus on a requirement that at some point in time (past, present or future) someone can claim compensation as a driver for institutional change. The sufficiency of compensation is determined by the capacity of the compensated to turn that compensation into something of value. Is compensation a sufficient response, and in the context of hospital patient can we even be sure that there will be a claimant? Pogge emphasises the role of institutions but infectious diseases are a threat to us all at all times and in all places. A framework for evaluation (or that is to be used to inform policy or practice) must cross, institutional, spatial and temporal boundaries. Neither the Patient Rights as specified in the NHS Constitution nor Pogge's focus on negative rights and coercive institutions seem sufficient to adequately address the context under discussion in this thesis, although there is much to be said for the taxonomy of institutional responsibility proposed by Pogge which I will return to in Chapter 4.

The focus of Nussbaum's capability approach is on what we need to do to help people live a fully human life (a life with human dignity). All (institutions, individuals, governments) have a role in assuring a sufficiency of capabilities for all of the world's citizens. A breach of rights may have no impact on the functional or health status of an individual. The capabilities approach gives emphasis to those conditions, which might significantly impact on beings and doings. Those illnesses, which impact on capabilities or functionings are those that are most important. It would seem plausible to argue that a breach of the right to be protected from epidemic disease only becomes a significant breach when it impacts on the capabilities of individuals. In which case why do we need rights when we could have capabilities? Capabilities actually have meaning in themselves, whereas rights are something abstract and can be seen to stand alone from the seriousness of the consequences of actions. A breach of rights might have more or less significance for those impacted. Should we be trying to protect rights at any cost or irrespective of the consequences for others? The rights approach emphasises pragmatic reasons for respect for a range of human rights, but the capabilities approach goes further in also emphasising the role of respect for a diversity of human capabilities for a life with human dignity. When there a lack of clarity with respect to any of these details then the scope of rights can impose unrealistic obligations on rights holders (see O'Neill 2005), equally a lack of specification can make rights unenforceable.

2.3.5 Positive attributes of a capabilities approach

I have chosen to consider Nussbaum's approach as an evaluative framework because it is specified at a number of levels, the specification seems to align with the reality of the context

under consideration in this thesis (treatment and prevention of illness), takes account of disability, and acknowledges that under conditions of dependency negative rights (or entitlements) are insufficient. The entitlements are universal and there is consistency of approach across spatial and temporal boundaries (doesn't stop at the gates of healthcare institutions). Several of the entitlements listed have implications for directly evaluating the risks and benefits of antibiotics and antibiotic resistance both in the context of hospitals and more widely. For example if we are to respect the entitlement to affiliation, this entitlement requires that an individual is able to live for and in relation to others, to recognize and show concern for other human beings, and *to engage in various forms of social interaction*. Bodily integrity requires that an individual *can move freely from place to place*. These two entitlements could both be breached by restrictions taken to control the spread of antibiotic resistant bacteria.

The capabilities approach has a number of apparent advantages over the health economic approaches discussed in section 2.2. Nussbaum emphasises the non-utility information captured by capability such as physical needs due to handicap, and social and moral issues such as equal pay for equal work. Shame, blame and stigmatisation are recognised social associations with infectious disease and these social consequences are poorly captured within economic evaluations, which require that consequences have discrete and measurable outcomes. The capabilities approach (as proposed by Nussbaum) does not require the expression of health preferences or valuations of health states. The capability approach draws attention to a broad range of important and incommensurable dimensions and as such provides a much richer evaluative space for comparisons (including individual experience) than aggregated costs and benefits. Evaluations are also not dependent on life expectancy.

Nussbaum considers that for the capabilities on her list "it is always rational to want them whatever else one wants" (Nussbaum 2000, p88-89). For Nussbaum these capabilities lead directly to entitlements. For Nussbaum entitlements can be relational or non-relational (needed by everyone at all times). It is increasingly apparent that health involves complex social and environmental interactions. If we take the example of the spread of antibiotic resistant bacteria and associated diseases there is considerable empirical evidence that susceptibility to infection is a function of many interactions including nutritional status, education, empowerment, housing conditions and social position. The interactions between health and the determinants of health are complex and not unidirectional, so for example health both determines and is determined by nutrition, education, and social status (extensively discussed in Venkatapuran 2011). In practice it is unlikely that an individual could be healthy without a sufficiency of many if not all of Nussbaum's 10 dimensions of capability. Capabilities may be incommensurable but capabilities still interact with each other in contributing to a state of wellbeing. In the real world these interactions may lead to clustering of disadvantage (Wolff & De-Shalit 2007). By acknowledging real opportunities rather than aggregation of outcomes there is the potential to protect individuals from the worst consequences of decisions based on maximisation. Capability cannot be re-distributed. A sufficiency of capability is a universal requirement that applies to all including those who cannot advocate for themselves.

I have argued that there is an accepted 'rights-based' approach to Public Health ethics to which capabilities can add an additional level of specification and clarity. The assurance of capabilities required for a life of human dignity resonates with the insights of recent reports

such as the Mid Staffordshire NHS Foundation Trust Inquiry report (2013), in placing respect for human dignity at the heart of considerations. There is a directness associated with the use capabilities that is missing from some other forms of evaluation. Contact precautions that are taken to control the spread of agents of infection (including those that are antibiotic resistant) are identified directly as a potential injustice, rather than indirectly through the impact on health, economic costs, longevity or other consequences. Assurance of capabilities requires positive opportunities to fulfil life plans and to maintain relationships. Providing facilities or resources to those who are dependent is an insufficient response to the recognition of a capability deficit. The capabilities approach would seem to have relevance both at the level of individual experience and for the evaluation of the justice of institutional arrangements.

2.4 Conclusion

At the end of Chapter One I asked if we can we use Nussbaum's capabilities framework to evaluate the justice of current patterns of distribution of burden and benefits associated with the use of antibiotics and the control of antibiotic resistance. I conclude that Nussbaum's approach has advantages when compared to current economic and rights based approaches to the evaluation of the justice of current patterns of distribution of burden and benefits associated with the use of antibiotics. It extends the evaluative space to include a number of dimensions that have not been included within prevalent health economic methods of evaluation. The capability theory of Martha Nussbaum has commonalities with human rights approaches but provides an additional and necessary level of specification and theoretical clarity. Perhaps most importantly the list of capabilities reminds us of the requirements for a life with human dignity, some of which might otherwise be overlooked.

In the next chapter I will consider the application of a capability approach to evaluating the distribution of burdens and benefits associated with the use of antibiotics and the consequences of their use; the feasibility of Nussbaum's approach as a decision tool when there are unavoidable capability trade-offs; and the potential to use an alternative approach based on the contractualism of Thomas Scanlon to arbitrate when all capabilities cannot be assured.

CHAPTER 3

APPLYING CAPABILITY THEORY

Summary

In this chapter I consider the use of capabilities to evaluate the burdens and benefits of antibiotics, antibiotic-associated infections, and antibiotic resistance. Healthcare institutions carry a substantial burden of healthcare associated infection (HCAI) much of which is antibiotic associated.

I consider how capabilities can be used to evaluate the experience of individuals and institutional arrangements. At an institutional level I propose a burden of antibiotic-associated infection capabilities index based on (attributable) mortality data (reflecting the impact on life/health), and patient exposure to contact precautions (the impact on affiliations, freedom of movement, emotional development), and additional bed days attributable to antibiotic-associated infectious diseases (the opportunity costs to the wider community and therefore the threat to future health capabilities). This capabilities based index would be more sensitive to the burdens on individuals of antibiotic-associated infectious diseases, and the risks and benefits of control strategies, than bald measures of prevalence of infection, impact on healthcare resource utilisation, or economic costs.

Finally I consider in this chapter whether the type of capabilities approach advocated by Nussbaum can be used to decide the distribution of burdens and benefits associated with

different courses of action. Sometimes it is not possible to assure the capabilities of everyone (particularly in a healthcare context). How should priorities be decided? Nussbaum argues that for basic healthcare there should be a high level of healthcare provision. Even with a high level of provision there remains a question of the extent to which capability theory as espoused by Nussbaum has the resources to deal with trade-offs of risks, burdens and benefits either inter-personally or intra-personally. Finally I consider the potential for the contractualist approach of Thomas Scanlon to provide a procedure for deciding the distribution of (capabilities) burdens and benefits associated with the use of antibiotics, and the control of the spread of antibiotic resistant forms of infection.

3.1 Introduction

This thesis specifically focuses on the use of antibiotics and one of the most important adverse consequences of use, which is treatment (antibiotic) resistant infection. In the context of healthcare institutions it is hard to separate antibiotics and antibiotic resistant microbes from the broader range of issues encompassed by the term Healthcare Associated Infections (HCAI). Much of the following discussion is relevant to both antibiotic use, and the control of antibiotic resistant microbes, and to the broader context of the control of HCAI. Point prevalence studies of HCAI frequently include measures of the concurrent use of antibiotics (see for example Health Protection Agency 2012[b]).

3.2 Capabilities as an evaluative framework

Sen has proposed that capabilities can provide the "right kind of information" (Sen 2010, p233) to evaluate the justice of institutional arrangements. The capability approach proposed by Sen has been interpreted and applied in many different ways. The question that I am asking in this chapter is - can capabilities be used to evaluate the justice of arrangements determining the burdens and benefits of antibiotics? resistant microbes in an institutional context? The capabilities list that I will consider in this chapter is that of Martha Nussbaum specifically as described in 'Frontiers of Justice' (FJ) (2006). I do not intend to try to develop a justification for the particular elements that Nussbaum includes in her list. Many others have developed similar lists (see overview in Alkire 2005, Chapter 2). I start from the position that we have a list and that it is broadly agreed and accepted.

The context under consideration in this chapter is a healthcare institution, where (on any day) 40% of patients are receiving antibiotics and an additional 5-10% undergoing treatment for Healthcare Associated Infection (HCAI) (Health Protection Agency 2012[b]). Many of the HCAI are directly or indirectly associated with the use of antibiotics. In the healthcare context choices can impact on individual (patient) capabilities and can also (and often do) lead to an uneven distribution of burdens and benefits. Patients may not be able to advocate for themselves. Nussbaum's theory is designed to take account of disability and provides an account of the 'goods' wanted by all at all times, including those times during which individuals cannot advocate for themselves. Nussbaum's capabilities entail positive entitlements, which are required by all (patients) even under conditions of dependency. Negative rights (or entitlements) are insufficient. Capabilities entitlements are universal and

cross over spatial and temporal boundaries (so entitlements don't stop at the gates of healthcare institutions), and we all are share responsibility for assuring these entitlements (Nussbaum 2004, p13). It is increasingly apparent that health involves complex social and environmental interactions (Venkatapuran 2011; Wolff & De-Shalit 2007). There is considerable empirical evidence that the spread of antibiotic resistant bacteria and associated diseases is a function of many interactions including nutritional status, education, empowerment, housing conditions and social position. In many cases these interactions are two-way for example between health and nutrition, or health and education, or health and social position. In practice it is unlikely that an individual could be healthy without a sufficiency of many if not all of the ten dimensions of capability. Capabilities may be incommensurable but capabilities still interact with each other in contributing to a state of wellbeing.

3.2.1 The burden of antibiotic resistance

For Nussbaum and Sen a capability is a "substantial freedom he or she enjoys to lead the kind of life he or she has reason to value" (Sen 1999), resources and preferences only give a partial conception of how well off someone is. Resources and preferences are a substantial component of health economic evaluations. Graves *et al.* (2010) overview the use of economic measures to determine the cost of infections acquired in hospital and emphasise the large proportion of costs attributable to bed days lost. Graves *et al.* acknowledge the technical difficulties with accurately measuring bed days lost. There are also difficulties with valuing 'public goods' such as the control of the spread of antibiotic (treatment) resistant agents of infection (Coast *et al*. 2002) and valuations involving uncertainties, for example those

associated with an emerging problem such as new forms of antibiotic resistance. Even if we can measure these costs there remain substantial difficulties with health economic evaluations related to infection, for example the valuation of societal consequences such as loss of confidence in healthcare institutions, or the fear, blame and shame which characterise the public response to treatment resistant infection such as might be caused by Meticillin-resistant *Staphylococcus aureus* (MRSA).

3.2.2 The prevalence of infection

Currently in many countries the point prevalence of infections with antibiotic resistant microbes is measured and reported (see for example recent UK reports by Smythe *et al*. 2006 & Health Protection Agency 2012[b]). The Society for Healthcare Epidemiology of America & Healthcare Infection Control Practices Advisory Committee (HICPAC) have proposed metrics for monitoring multidrug (antibiotic) resistant organisms in healthcare settings. These metrics are designed "to monitor Multi-Drug Resistant Organisms (MDROs) and the infections they cause" (Cohen *et al*. 2008). These metrics measure the number of patients with infections, the proportions of particular types of microbe that are antibiotic resistant, the rates of specific types of infection, and the rates of colonisation with specific groups of agents of infection.

Measures of prevalence may identify two different hospitals to have similar rates of infection with antibiotic resistant microbes but we should recognise that the impact on patients in each hospital may be very different. Restrictions on individual capabilities, the distribution of burdens and benefits, the impact on other aspects of healthcare, and the social consequences

of infection are not well-captured by rates or prevalence, unless those measures can be translated into the experience of individual patients. The proportion of a population with a particular problem (in this case infection with antibiotic resistant microbes) does not tell us the impact of that problem on an individual. Infectious disease and the actions taken to control antibiotic resistance may or may not impact on the functional status of sufferers, may have shorter or longer term effects, may be treatable or untreatable, may be more or less associated with social stigmatisation, and can vary in the consequent economic consequences. None of these aspects of infection with antibiotic resistant bacteria are accurately captured by measures of prevalence, numbers, proportions, or rates of colonisation or infection.

3.3 An evaluative framework

The capabilities approach as advocated by Nussbaum (abbreviated to FJ) has a number of apparent advantages over the health economic approaches discussed in the previous chapter (section 2.3.5), and measures of prevalence of infection. It is to consider the potential advantages of capabilities as an evaluative framework for infection compared with measures of costs and benefits, or measures of prevalence that is the focus of this chapter.

3.3.1 Antibiotics, antibiotic resistance, and assuring capabilities

The use of antibiotics can be conceptualised as an attempt to try to prevent a loss of capabilities either by preventing infection in someone at risk of infection (for example when antibiotics are administered around the time of a surgical procedure to reduce the risk of post-surgical infection), or to reduce the risks of a loss of capabilities associated with an

established infection. One consequence of the use of antibiotics is antibiotic resistance. Antibiotic resistance increases the risk of an adverse outcome from infection, and can also lead to the imposition of burdens on individuals such as restrictions to social contacts and movement associated with the introduction of contact precautions. A hospital which takes draconian measures to control the spread of antibiotic resistant microbes might have a low prevalence of hospital acquired antibiotic resistant infectious diseases such as infections with Meticillin-Resistant *Staphylococcus aureus* (MRSA), yet have a poor level of patient experience.

Several of the entitlements listed in Nussbaum's list of ten capabilities (Nussbaum 2006) have implications for evaluating the risks and benefits of antibiotics and the consequences of the use of antibiotics both in the context of hospitals and more widely. For example antibiotics can be used to prevent loss of the capability of health arising from the uncontrolled effects of infection. As mentioned in the previous chapter if we take contact precautions to prevent the spread of infection from one individual to others then other capabilities become relevant, such as the entitlement to affiliation. This entitlement requires that an individual is able to live for and in relation to others, to recognize and show concern for other human beings, and to engage in various forms of social interaction. Another relevant capability is that of bodily integrity, which requires that an individual can move freely from place to place. These last two entitlements could both be breached by restrictions taken to control the spread of antibiotic resistant bacteria. The capabilities listed by Nussbaum can help us to capture important dimensions of the patient experience, such as freedom of movement and engagement in social interactions.

3.3.2 Evaluating individual experience

In the following I try to envisage how we might use a capabilities approach to evaluate the impact of a HealthCare Associated Infection (HCAI) on the experience of an individual undergoing treatment in hospital.

The majority of patients who experience hospitalisation are electively admitted to hospital for investigation or treatment of disease. In the context of healthcare it is conceivable that we could use a pre-healthcare capabilities (or health) trajectory as a threshold when the capabilities status of an individual is stable. In the less common situation in which the capability status is highly dynamic (for example following a near fatal event such as a car crash) then we could use a stabilised trajectory. Usually when the burden of HCAI is estimated the infections that arise more than 48 hours post-admission are those that are considered. The stabilised trajectory could be taken as the 48 hours post-admission trajectory. In other words the objective of healthcare is to improve the capability status of an individual by comparison with the pre-contact trajectory, or a post 48 hours stabilised trajectory.

Adequacy of capability may require equality as for political and civil liberties, or may not – for example adequate housing does not require that we all have the same housing. The touchstone is equal dignity and respect. Each individual has a pre-contact trajectory, or stabilised trajectory. The objective is not to give every individual the same capability trajectory but rather to improve the trajectory which each individual follows. There has to be

some reason for hospitalisation which links with the objective of improving the situation of the individual hospitalised, so that admission of a patient to hospital is predicated on the belief that post hospitalisation (and convalescence) the patient will be better off than they would have been without hospitalisation. So a threshold can be set by the pre-hospitalisation trajectory (or stabilised trajectory) and success is judged by the outcome relative to the expectations of what would have happened had the individual not received treatment in hospital.

Gardoni & Murphy (2009; 2010) suggest that acceptable (absolute minimum) and tolerable (short-term) thresholds be defined in the context of disaster mitigation. The situation in hospitals is dynamic. Breaches of rights (or capabilities) are frequent (for example freedom of movement) but transitory. The identification of tolerable and acceptable thresholds is relevant to healthcare. The acceptable threshold can be defined by the pre-contact (or stabilised) trajectory. The tolerable threshold can be set to take account of short term effects on capability associated with healthcare such as would follow major surgery and the period of post-operative recuperation. An acceptable (absolute minimum) threshold could reasonably be the expected outcome without hospitalisation. The tolerable minimum could include short-term impositions associated with contact precautions taken as part of the control of infection risks in hospital, but these would become unacceptable if maintained in the longer term.

For an individual with a developing capability set such as an infant a trajectory could be set by comparison with developmental norms. The capability approach points to the importance of the diversity of important developmental outcomes, and not just health outcomes as the dominant metric for success. There is acknowledgement of the importance of social and

emotional requirements for a life of dignity and human flourishing. The aspiration is not only basic capabilities such as health but also the capacity to reason and make choices, and equal opportunity (Kaufman 2006, p75). There is a real risk of clustering of disadvantage for vulnerable groups such as hospitalised children. "A society of equals is a society in which disadvantages do not cluster, where there is no clear answer to the question of who is the worst off" (Wolff & De-Shalit 2007, p10).

The evaluative data set is broadened when the focus is on the impact of hospitalisation and associated events on the individual capability trajectory. Certain sorts of events (for example the imposition of contact precautions) are directly recognised as undesirable breaches of the requirements for a life with human dignity.

3.3.3 Evaluating the justice of institutional arrangements

In the previous section I have suggested that (in the context of a healthcare institution) individual capability thresholds can be defined using the pre-hospitalisation trajectory, stabilised trajectory (48 hours post admission) or a developmental trajectory (in the case of children). Gardoni & Murphy (2009) suggest that in order to minimise the complexity of analyses at an institutional level we should limit the capabilities that we select to a minimum number relevant to the context under consideration (capabilities parsimony), and that each capability should provide information that cannot be ascertained from other capabilities (capabilities orthogonality). The United Nations (2011) calculate a UN Development Programme and Human Development Index (HDI) for each country in the world based on measures of capabilities assurance. This index is calculated from a selected number of indices

including life expectancy at birth, years of schooling, and gross national income per capita. The scores for these dimension indices are then aggregated into a composite index and reported as a geometric mean. The HDI indices can be aggregated at different geographic or population levels. Gardoni & Murphy (2009) and the UN both limit the range of measures in order to reduce the conceptual and practical complexity of the analyses and results. The ten capabilities listed by Nussbaum are shown in Table 3.1 below with potential measures relevant to hospital infection shown in italics.

Table 3.1 Capability measures relevant to hospital infection

Capability	**Functions**
Life	A full life (not dying prematurely)
	Mortality
Bodily Health	Good health and shelter
	Excess bed days
Bodily integrity	Freedom of movement and security
	Days of contact precautions
Senses, Imagination, Thought	Intellectual and religious freedoms
Emotions	Emotional development un-blighted by fear
	Days of contact precautions
Practical Reason	Follow one's own life plan
Affiliation	Engagement in social interactions
	Days of contact precautions
Other species	Express concern for other creatures
	Facility to care for pets
Play	Play (and enjoy) recreational activities
	Days of contact precautions
Control over One's environment	Free speech and freedom of association
	Days of contact precautions

Which capabilities indices would we choose to use for the evaluation of the justice of institutional arrangements for the control of antibiotic resistant microbes in healthcare institutions? If we are to use capabilities to evaluate the justice of arrangements then we need to be able to assess the distribution of benefits and burdens defined through impact on capability. Bodily health, bodily integrity, life and affiliation seem to be particularly pertinent. Possible indices might include the use of contact precautions to control the spread of antibiotic resistant microbes, the excess bed-days attributable to avoidable infection, and the numbers of deaths attributable to antibiotic resistant infection. The use of contact precautions (to control the spread of antibiotic resistant microbes) gives an indication of the degree to which capability constraints are being imposed on individuals such as constraints on affiliations, freedom of movement, and for children particularly - emotional development. Excess bed-days attributable to avoidable infection indicate the burden of opportunity cost to the health capabilities of others either directly though a reduction in the availability of beds or through an impact on the costs of healthcare. The numbers of deaths attributable to antibiotic resistant infection gives a measure of the impact on the capability of life.

The effectiveness of interventions can be compared by effects on capability levels including the distribution of adverse effects on capabilities. A capabilities index based on attributable mortality data (reflecting the impact on life/health), and patient exposure to contact precautions (the impact on affiliations, freedom of movement, emotional development), and additional bed days attributable to antibiotic-associated infectious diseases (the opportunity costs to the wider community and therefore the threat to future health capabilities) would be more sensitive to the burdens on individuals of antibiotic-associated infectious diseases, and the risks and benefits of control strategies, than bald measures of prevalence or economic

costs. The distribution of capability burdens is also important. Murphy & Gardoni (2012) recognise the importance of capturing the distribution of risks, and the impact of risk mitigation strategies on the distribution. In more recent work they have tried to develop measures of capability of individuals (rather than using population averages) in order to try to measure the effects of hazards and mitigation strategies on the distribution of capabilities (Murphy & Gardoni 2012, p988). Deciding the distribution of benefits and burdens is the subject of the following sections of this chapter.

I have tried to illustrate how capabilities can add depth to the evaluation of the justice of institutional arrangements by comparison with measures of prevalence or economic costs. Developing and validating such an index is the work of another thesis. So for the moment I will place the use of capabilities as an evaluative framework to one side and consider the application of capabilities to decide between different trade-offs, when we cannot assure the capabilities of all.

3.4 Can we assure the capabilities of all?

A substantial difficulty yet to be addressed by a capabilities approach is how to balance the competing interests of individuals at or below a given level of capability when resources are insufficient to address all of the shortfalls. Nussbaum's capabilities allow us to see what is important when it comes to respect and dignity and can be seen to provide the right kind of information for evaluations of institutional arrangements. Problems arise when we have to make decisions about the priority given to addressing the capability needs of individuals when priorities conflict. Sometimes we cannot improve the capabilities of one without threatening

the capabilities of others – for example when antibiotics are prescribed, or when there are insufficient resources available to address the needs of all individuals (such as deciding between prevention and treatment). There is also the question of the priority that we should give to future capabilities by comparison with current capabilities?

The capability approach does appear to have some theoretical advantages as an evaluative framework over current health economic methods of balancing risks and benefits. However Nussbaum is not specific as to how to use her approach to rank priorities in resource-limited settings, or as to how to balance the entitlements of individuals against the entitlements of others. There are a number of substantive difficulties with the priority of sufficiency of capability in priority setting, for example how would the approach deal with balancing the use of a limited resource in a situation where a small number far below a level of sufficiency could be helped above the sufficiency level or alternatively the same resource could be used to help a much larger number already better off but still just below a level of sufficiency (Arneson 2006)? If all else is equal aside from the numbers then should we take account of the numbers and if so then how should aggregative information be used in practice? Nussbaum says little about how we balance harm, risks and uncertainties for individuals at different starting points relative to levels of sufficiency other than a tentative proposal for a 'Rawlsian difference principle' – inequalities in capabilities can be tolerated as long as these differences lead to more people attaining the minimum threshold (Nussbaum 1995). Does this mean that if a 100 people in one scenario and 10,000 people in another scenario will be helped across a sufficiency threshold that we will go with the 10,000? Capability says little about the priority that should be given to individuals well above threshold levels of capability so would a small gain that raises one individual above a threshold be given priority over a

substantial gain to many already above a threshold? Would an individual with multiple capability insufficiencies (Wolff & De-Shalit 2006) be given priority over another with a single capability deficiency? More often in a healthcare context many are either below or at risk of falling below a number of capability thresholds, and resources are insufficient to protect the capabilities of all. In hospital practice it is also not uncommon for patients with a very poor chance of reaching capability thresholds to be given a chance even though in effect there is a consequent reduction in the availability of resources for others with a high probability of a full recovery.

The capability approach is outcome and realization orientated but to what extent should a capability approach take account of probabilities? For capabilities to be used in risk management what should be the procedural approach? Sen argues against the use of capabilities as a normative framework stating that capabilities provide an evaluative space and so do not amount to a theory of justice (Sen 2004, p337) - for Sen a theory of justice must include aggregative as well as distributive considerations. Even if we are only to use capabilities as the 'right kind of information' in allowing evaluation and comparison of social realizations there has to be some way of ranking priorities when resources are limited and sufficiency across all capabilities for all people is not achievable.

The control of infectious diseases frequently involves constraints (or in some cases harm) to the capabilities of one or more individuals in order to protect the capabilities of others (often a much larger number). Beauchamp & Faden (1979) argue that rights can be inalienable yet contingent. It is hard (if not impossible) to see how the capabilities (entitlements) of individuals can always be completely protected while at the same the capabilities of others are

also protected. Some of the questions in the subsequent chapters that will need to be addressed include our degree of commitment to help those below a capability threshold even when the necessary actions would not maximise aggregate utility, and whether we would always help those retrievably below the threshold in preference to those irretrievably below or well above the threshold. Quoting Sen (1982) "It is not unusual to think of rights as a relation between two parties i and j, for example, person i having a claim on j that he will do some particular thing for i. There is, however, some advantage in characterizing goal rights as a relation not primarily between two parties but between one person and some 'capability' to which he has a right, for example, the capability of person I to move about without harm". Most would probably agree that hospitalised patients should be entitled to expect that they will be able to go to a hospital without being harmed by reasonably preventable infection or by what we do to control preventable infection, but to protect all patients from harm may not be feasible or achievable. What we do to control the spread of infection may also cause harm. Patients placed in isolation show higher scores for depression, anxiety and anger, than non-isolated patients. Patients are also less safe (higher incidence of adverse events such as falls) (Stelfox *et al*. 2003; Abad *et al*. 2010). If we wish to use capability thresholds in the real world then we will need to decide whether these questions can be and how they should be addressed by a capability approach. How does capability theory deal with situations in which all capability entitlements cannot be achieved?

3.4.1 Inevitability of capability trade-offs

Capabilities can help with the specification of a life with human dignity. A Dutch perspective on decisions to provide treatment for infants is that treatment in intensive care should only be

offered when there is “reasonable hope of survival with a chance of an acceptable form of life” (Versluys & Leeuw 1995, p14). “Decisions have to be made even though complete certainty cannot be attained. If one waits for absolute certainty it means that, in practice, treatment is never stopped but continued indefinitely”. What is an acceptable form of life? The Dutch specialists must ask what communicative abilities the child will have later, the potential for the child be able to lead an independent life, the extent to which the child will be able to live independently of medical support, the extent of childhood suffering (mentally or physically), and the life expectancy (Versluys & Leeuw 1995). This approach seems to be consistent with the capability approach advocated by Nussbaum in that neonatal intensive care is not offered when capability thresholds are unlikely to be achieved. Capabilities draw attention to important requirements for a life with human dignity and, as such, can provide a degree of specification and potentially can help to provide a minimum requirement for a life with human dignity even for groups unable to advocate for themselves.

Often decisions require more than establishing minimum thresholds. There may be a requirement for the balancing of conflicting interests and needs. Nussbaum makes the point that we should not just be trading off health costs against health costs – but also consider trade-offs in other capability dimensions – giving the example of trading-off the driving of Sports Utility Vehicles (SUVs) against health (Nussbaum 2006, p402). When a capability threshold has already been greatly exceeded then there is scope for re-balancing, and it is possible to conceive of prioritising substantial capability gains for some over relatively trivial gains for others who are already well endowed. If there were constraints on antibiotic prescribing then priority can be given to serious infection with the potential for irretrievable losses of capability over the treatment of self-limiting infections. When there is no excess of

capability in any dimension as is often the case within a healthcare context then accepting that we will be trimming capabilities for some patients (who are sufficiently unwell to require hospitalisation) in order to help others does not seem to be an appropriate starting place. For the purposes of this chapter I will assume that all hospitalised patients are already below an acceptable threshold or trajectory for the capability of health.

Even with unlimited resources for healthcare there will still be a requirement for trade-offs both intra-and inter-personally. Individuals may have capabilities put at risk in order to protect others. For example we might take the case of a woman who gives birth to an infant by caesarean section as a result of evidence that the baby is distressed (foetal distress). The infant is admitted to the Neonatal Intensive Care Unit (NICU). The mother develops a post-operative wound infection with Meticillin-resistant *Staphylococcus aureus* (MRSA). Should the mother be allowed to visit the infant in the NICU when in so doing there is a risk of transmission of MRSA to her own baby and to other vulnerable infants? There are a number of potential risks associated with this scenario. The acquisition of MRSA may have far-reaching consequences for the infant and for contacts in the future. Considerations include the distress of the mother, concerns and fears of other mothers, implications for mother-infant bonding, the confidence of mothers and the wider community in the service, risks to the establishment of breast feeding, risk of infection of the infant and of spread of infection to another infant on the NICU, an outbreak of MRSA infection in the NICU, and consequent closure of the NICU. Nussbaum uses capabilities as a touchstone (point of reference) for the justice of states of affairs – capability deficiencies draw attention to unjust states of affairs. Nussbaum uses examples of the experience of those caring for the disabled, of women with limited opportunities in developing countries and of animals used in research. Nussbaum

might argue that the NICU facilities should be organised in such a way that all of the serious risks to capabilities can be mitigated. Indeed some of the trade-offs could be avoided if every NICU was specifically designed and with a sufficiency of staff to manage infants with potentially transmissible infections such as MRSA. Resources could be taken from areas of capability sufficiency (for example SUVs and given to NICU care). Even if there was an optimum allocation of resources to NICU care there would still be a requirement for capabilities trade-offs for example between risks to the mother and the infant, and trade-offs between risks to different capabilities for the infant, so there are risks to life, emotional development, and to health, with the potential both for interpersonal and intrapersonal trade-offs. Protecting the infant from the potential risk of infection contracted from the mother may require that mother-infant contact is limited. Either or both parties may carry the social consequences of MRSA colonisation or infection.

In the scenario presented we cannot protect all of the capabilities of all of the interested parties within current resource limitations, and even with unlimited resources the emotional needs of the mother and infant (and associated capabilities) may need to be compromised in order to protect the capability of health. In the previous chapter I referred to tolerable and acceptable levels of capability. Short-term losses of capability (without long-term impacts) may be tolerable and it would seem reasonable to accept these types of capability deficit in exchange for long-term damage to capabilities or (in the case of infants) capability potential. It is not uncommon in hospital practice for capability choices to include tragic choices between capabilities. If we use an antibiotic today to prevent death from infection then others may suffer adverse consequences such as might follow the spread of MRSA or *Clostridium difficile*. Distinguishing short-term tolerable capability deficiencies from unacceptable long-

term deficiencies, and prioritising the long-term deficiencies (over short-term effects on capability status) for prevention or remediation would seem to be a plausible approach. However often in healthcare the trade-offs involve arbitrating between substantial capability losses, for example treatment with antibiotics today threatens the effective treatment of infections in the future. Infectious diseases threaten the irretrievable loss of multiple capabilities, with differential effects on different capabilities within the same individual and the capabilities of different individuals. When we consider the use of antibiotics and the consequence that is antibiotic resistance then we also have to be able to arbitrate between the interests of individuals today and those who will be alive tomorrow.

Arneson (2006) draws attention both to the requirement to decide and to the difficulties in deciding trade-offs using the capability approach. Wasserman (2006) argues in considering disability that there is a moral necessity for trade-offs both between different capabilities within an individual and between the capabilities of different individuals – "If justice requires that we eventually halt the asymptotic progress we can make with some severely impaired children so as to enable thousands of other children to enjoy vast increases in education, or to preserve vast tracts of endangered wilderness, or to slow disfiguring and alienating sprawl, we will have to make both kinds of trade-offs" (p230). The capabilities approach identifies morally salient dimensions which are pertinent to infectious disease treatment and control so for example by highlighting the importance of social affiliation attention is drawn to the social consequences for individual patients of MRSA colonisation, and in the example given in the preceding paragraph attention is drawn to the interactions between emotional development and the trade-offs with a direct threat to health. However it is not clear how trade-offs can be balanced when there are a number of capabilities at substantial risk.

Nussbaum does not consider her approach as a complete theory of justice so perhaps it is inevitable that additional theoretical resources are required to address the prioritisation of risks to capability, and the questions that arise with the use of antibiotics.

3.5 A contractualist approach to capability trade-offs

Martha Nussbaum provides an extensive critique of contractarian approaches to distributive justice in her book *Frontiers of Justice: Disability, Nationality, Species membership* (abbreviated to FJ). Nussbaum (Nussbaum 2006, p264→) argues that a fundamental problem with the contractarian focus of Rawls (1971) is the idea of mutual advantage (p267) particularly when applied to groups or individuals who are disadvantaged. This argument is pertinent to hospitalised patients. Some of whom have extended periods of dependency, and communication and comprehension difficulties (in some cases life-long). Nussbaum suggests that capability theory (on her conception) builds in a quasi-contractarian component by incorporating the idea of equal dignity (equal respect for all). The ten capabilities that Nussbaum selects are based on a conception of the requirements for a life worthy of human dignity. She accepts that the list can be revised, that interpretation and specification may vary between different cultural contexts. The emphasis on capability (rather than functioning) reflects the importance of individual freedom(s) to choose. Nussbaum is particularly concerned that contractarian approaches to justice struggle with how best to include the needs of those who are dependent (such as children) in the design and formulation of the contract, so for example for Rawls the requirement for reciprocity amongst contractors (Rawls 1971, p504-5) excludes those who are highly dependent. I agree with Nussbaum that "society is a

care-giving and care-receiving society, and must therefore discover ways of coping with these facts of human neediness and dependency that are compatible with the self-respect of the recipients and do not exploit the caregivers" (Nussbaum 2006, p62). For Nussbaum the dignity of the dependent is important and this requires that we re-design our political conception of the person – acknowledging that there are many types of dignity in the world for example "the dignity of babies at the breast" (Nussbaum 2006, p65).

Scanlon has proposed a theory (Scanlon 1998), which does not start from a position of negotiating for mutual advantage, and in this way avoids some of the criticism that Nussbaum makes of the contractarian approach of Rawls (1971). The account is contractarian in that principles require mutual agreement but starting from principles that can be reasonably rejected rather than from principles agreed because of mutual advantage. Scanlon terms this a contractualist approach. Fitzpatrick (2008) has suggested that the contractualist approach of Scanlon and the capabilities approach of Nussbaum have much in common. He states that - "at the centre of contemporary moral and political philosophy lies the question of how to balance reason and care when theorising about justice" (Fitzpatrick 2008, p92). He goes on to ask – "Can we preserve the best parts of Nussbaum's critique (her rejection of extra-social bargaining and instrumentalist advantage, of excessive rationalism, her promotion of dignity and benevolence) within a reformed contractarian framework?" He characterises Nussbaum's critique of Rawlsian contractarianism as anthropomorphic, economistic, atomistic, and misrepresenting the human condition as bargainers motivated by mutual advantage. Nussbaum (he suggests) believes that "what we do for and with others cannot be reduced to what we gain from them", that reciprocity is not reducible to contractual advantage, that reasons are conceived as abstract and disembodied, that the veil of ignorance denies

connections to others, and that Rawlsian contractarianism confuses contracts with justice. Fitzpatrick argues that Scanlon's approach avoids some of the criticisms that Nussbaum makes of Rawls, and that Nussbaum and Scanlon have common ground in that they are both committed to individual freedom, a recognition that the right and good are intertwined, an emphasis on respect for persons, both approaches are contextually universal, impartial and objective but not impersonal.

3.5.1 Contractualism

Nussbaum argues that a Scanlon type account based on individuals as moral equals "is a powerful intuitive way of capturing the idea that human beings are moral equals despite their widely differing circumstances in an unequal world" (Nussbaum 2006, p272). Justification to others is the substantial focus of Scanlon's approach. Many of the transactions that characterise the use of antibiotics and the consequences of use involve individuals in dialogue for examples healthcare workers (such as doctors) agreeing treatment plans with patients. Justification is a key element to these transactions and it seems intuitively attractive to start from an acknowledgement of the importance of justification in assuring the quality of the interaction. Scanlon does not provide a theory of justice in that he does not specify how justification can ground justice at the level of institutions or governments.

For Scanlon principles that could reasonably be rejected are those that would cause the person serious hardship and where there are feasible alternatives that would not impose burdens on others (Scanlon 1998, p196) – this rejection comes *before* bargaining for mutual advantage.

> "We commonly take it that people have strong reasons to want to avoid bodily injury, to be able to rely on assurances they are given, and to have control over what happens to their bodies. We therefore think it reasonable to reject principles that would leave other agents free to act against these important interests...the question is whether the fact that a principle would help or hurt specific individuals can be a grounds for preferring it, and for reasonably rejecting alternatives that would not have this effect" (Scanlon 1998, p211)

The emphasis on reasons allows the inclusion of morally salient considerations such as responsibility and fairness (Scanlon 1998, p243-4). Scanlon's contractualism also allows for relational considerations such as promises to be taken into account. In Scanlon's words (Scanlon 2011, p139) –

> "Recognising the contractualist idea of justification to others as morally basic allows us at least to raise the possibility that although what is owed to others in some situations is to follow the principles that would produce best consequences, impartially understood, this need not always be the case. In other cases our responsibilities and obligations may be different"

It is also important to recognise that these are generalisable principles (Scanlon 1998, p204) –

> "An assessment of the rejectability of a principle must take into account the consequences of its acceptance in general, not merely in a particular case that we may be concerned with" – "our assessment cannot be based on the particular aims,

preferences, and other characteristics of specific individuals. We must rely instead on commonly available information about what people have reason to want"

The theory of capability proposed by Nussbaum is a theory of social justice. Nussbaum argues that Scanlon's theory is inadequate without a theory of the good, but otherwise avoids direct criticism of Scanlon's approach (Nussbaum 2006, p67). Scanlon focuses on what we owe to each other and not political principles. Both start with parties "whose deliberations focus on the related ideas of impartiality, respect and agreement" (Nussbaum 2006, p149). Nussbaum argues that a theory of social justice requires a "political theory of the good" (p153) and that justifiability is insufficient when it comes to capturing all that is valuable about human beings (p150). For Nussbaum some goods have a value that is independent of justifiability to others. Nussbaum accepts that we "cannot value persons as persons, see their distinctive value, without appeal to ideas of justifiability, which …give us a good way of capturing all-important ideas of respect and of the person as end", but believes that this in not all that is of value. "Freedom from pain and illness, bodily integrity, love and comfort – these would appear to have a value that does not derive entirely from the idea of justifiability" (Nussbaum 2006, p150). Scanlon (1998) argues that objective lists provide criteria against which the success or otherwise of basic social institutions can be assessed (Scanlon 1998, p110), but that these goods derive their significance from the moral structures in which they figure.

Scanlon acknowledges that "when we are assessing the justifiability of moral principles we must have reason to appeal to things that individuals have reason to want, and that many of these are things that contribute to well-being intuitively understood." However, "we cannot

delimit the range of considerations that figure in justification by defining the boundaries of well-being" (Scanlon 1998, p140). "Justification can appeal to more specific forms of opportunity, assistance and forbearance that we all have reason to want, rather than to the idea of well-being abstractly conceived". Nussbaum does not herself see the capabilities as more than a partial theory of justice. Kaufman (2006, p74) puts it this way –

> "Rather, far from assuming that the egalitarian obligation to assist is exhausted by necessary conditions derivable from capabilities analysis, the capabilities approach encourages evaluation of equality in terms of the capabilities metric as a basis for judgements implementing the requirements of broader accounts of justice. Among the necessary conditions that the capabilities approach does generate independent of such broader accounts of justice, the obligation to secure an environment in which persons may develop their abilities and the capacity for choice free from distortive influences upon preference formation is both substantial and independent of the obligation to secure threshold levels of capability"

Capabilities can "provide the information about what people have reason to want" even when those people are unable to participate as equal moral deliberators. Scanlon's contractualism allows for a wider range of considerations, but does not seem to preclude the use of capabilities as measures of the requirements for a life of human dignity. Capabilities can be used to evaluate the institutional arrangements and associated burdens and benefits of alternative strategies for the prevention or treatment of infection. Capability metrics are insufficient on their own as a justification for rejecting principles because as a partial theory of justice it does not tell us how to balance conflicting needs, or how to balance capabilities

when everyone is above or below a threshold against 'softer' outcomes such as consent, trust and promises. Scanlon (2011, p125) sees reasons as derivative from facts about the world. Capabilities describe states of affairs, facts about the world, and as such provide reasons. Minimum levels of capability are (for Nussbaum) universal entitlements (irrespective of circumstances). The actions, or attitudes that should result from recognition of capability deficits, when all capabilities cannot be achieved, requires that we can compare the capability status of one with another in particular contexts.

How then does Scanlon's contractualism fit with capability theories? Assurance of minimal levels of capabilities is a substantial objective within capability theory and in this way capability theory is outcome orientated. For Scanlon assurance of capabilities may provide reason to prioritise one course of action over another but this is not because achievement of capabilities provides justification in a generic and impersonal sense. For Scanlon reasons might come from avoidance of harm (damage to capabilities), but in addition from other considerations, for example from respect for interests or choices, or fairness, or expectations based on promises, or special relationships (Frei 2009, p56; Scanlon 1998, p216). For Scanlon it is the relationship between a reason, a set of circumstances and an action or attitude, rather than reasons (or capabilities) in isolation, which determines what we owe to each other. It would be a mistake to focus on assurance of capabilities as the only source of justificatory reasons.

In the particular context of healthcare assurance of capabilities will be a dominant consideration whether from the generic personal perspective (of Scanlon) or from the capabilities perspective (of Nussbaum). For the purposes of this thesis I have broadly

accepted the position that we have to be able to say something about what the 'good' should look like. I am not sure (and neither is Nussbaum 2006, p150) that Scanlon denies the importance of the 'good'. The recognition of capabilities required for a life of human dignity challenges us all to look for alternative courses of action, and alternative institutional arrangements when the assurance of capabilities is under threat. Effective treatment of infection can and does make a substantial contribution to assuring capabilities. Using antibiotics to treat one person threatens to undermine the effective treatment of others. I am proposing to use Scanlon's contractualism to arbitrate when capability trade-offs that threaten a life of human dignity are inevitable. This does not mean that avoidable subversion of a life with human dignity can in itself be justified, only that in a specific context under consideration capability trade-offs are unavoidable. Justice may require the assurance of individual capabilities but we still have to be able to decide what to do when all capabilities cannot be assured.

3.5.2 The redundancy objection

Scanlon starts from the position that we have to be able to justify our actions to others. A number of authors have raised an objection to Scanlon's contractualism based on the idea that justification to others requires the acceptance of generic principles or values to support justification (Frei 2009). If that is true then we don't need justification to others to explain why something is wrong, the generic principle or value does the work. If the assurance of capability thresholds is the primary objective in a healthcare context then what do we gain by applying Scanlon's contractualism?

Frei (2009) discusses this objection and clarifies that (for Scanlon) actions should comply with principles that cannot be reasonably rejected from a *generic personal* perspective. Reasons must be generic in that *any* person in the particular situation under consideration would accept those reasons as substantial reasons for rejecting a principle. The perspectives that matter are those of the people impacted by the acceptance (or rejection) of a particular principle. "It is reasonable to reject a principle when the actions it allows are more detrimental to what one person cares about than any alternative principle is detrimental to what anyone else cares about" (Frei 2009, p59). The judgement must take account of the general costs and benefits of accepting or rejecting the principle. This judgement is a judgement based on the intuitions that we hold about the relative weight of generic personal reasons, and not on a pre-existing set of justificatory principles.

To quote Scanlon (Scanlon 2009[a], p16) –

> "It specifies that in order to determine whether an action is morally permissible we should consider a general principle that would permit it. We then consider what objections individuals might offer to this principle based on the way in which they would be affected by it: by living with the consequences of the actions it would permit and with the possibility that agents may perform such actions, since they would be permitted to do so. We then compare these reasons with the reasons that individuals would have to object to a principle that would forbid actions of the kind in question, based, again on how they would be affected by such as principle. We then compare these reasons, and consider whether it would be reasonable for those who have reason to object the principle permitting the action to reject it, given the reasons that others

have for objecting the contrary principle. If it would be reasonable to reject that principle, then the action in question would be morally wrong."

Scanlon refers to the use of a method of reflective equilibrium (Scanlon 2009[b], p10) through which principles can be rejected. "The distinctive content of the method is negative: in its refusal to give privileged status either to particular judgements or to any class of more general truths, axioms, or a priori principles." Ultimately reasons for rejection can come from many different forms of consideration. These reasons can be based for example on quantitative differences, causal consequences, or particular forms of relationship. In this way Scanlon's contractualism extends the reach of moral consideration beyond the assurance of capabilities.

3.6 Conclusion

At the end of Chapter One I asked if we can we use Nussbaum's capabilities framework to evaluate the justice of current patterns of distribution of burden and benefits associated with the use of antibiotics and the control of antibiotic resistance. In this chapter I have considered the use of capabilities to evaluate individual experience and to evaluate institutional arrangements focusing on the burdens and benefits of antibiotics in a healthcare context. I proposed a burden of antibiotic-associated infection capabilities index based on (attributable) mortality data (reflecting the impact on life/health), and patient exposure to contact precautions (the impact on affiliations, freedom of movement, emotional development), and additional bed days attributable to antibiotic-associated infectious diseases (the opportunity costs to the wider community and therefore the threat to future health capabilities). I have suggested that a capabilities index would be more sensitive to the burdens on individuals of

antibiotic-associated infectious diseases, and the risks and benefits of control strategies, than bald measures of prevalence of infection, impact on healthcare resource utilisation, or economic costs.

Sometimes it is not possible to assure the capabilities of everyone (particularly in a healthcare context), even with a high level of resource provision. The contractualist approach of Thomas Scanlon provides a framework for deciding what we owe to each other, and potentially a procedure for deciding the distribution of (capabilities) burdens and benefits when we cannot assure all of the capabilities required for a life with human dignity.

In the next chapter I will consider the limits on institutional obligations to control the spread of antibiotic resistant microbes when control potentially leads to constraints on treatment enhancements.

CHAPTER 4

'ZERO TOLERANCE' OF AVOIDABLE HOSPITAL INFECTIONS?

Summary

'Zero tolerance' of avoidable infection events is explicit in UK and international policy documents describing strategies for the control of healthcare associated infection. Much of the focus of concern has been the control of antibiotic (treatment) resistant agents of infection such as Meticillin-resistant *Staphylococcus aureus* (MRSA). I consider what principles governing the control of avoidable infections, including those caused by antibiotic resistant microbes, might be reasonably rejected from the contractualist perspective of Thomas Scanlon.

Many hospital infections can be cost-effectively avoided. There would seem to be additional reasons to take the prevention of avoidable infection acquired in hospitals seriously in addition to optimising the cost-effectiveness of healthcare. These include the irretrievable nature of the harm of some such infections (particularly when caused by antibiotic resistant agents of infection); the reasonable rejection of avoidable harm when the patient could not rationally consent to the risk of harm; and the social consequences such as loss of trust in healthcare providers.

Despite these reasons a principle of 'zero tolerance' has implausible implications, promotes unrealistic patient expectations, and can be reasonably rejected from the perspective of those who will suffer unacceptable opportunity costs. However the contractualist perspective would

also seem to reject a principle of tolerance of harm when there is a feasible reconfiguration of institutional arrangements that reduces the risk of harm without a redistribution of a proportionate or greater burden to others.

4.1 Introduction

"It may seem a strange principle to enunciate as the very first requirement in a hospital that it should do the sick no harm" Florence Nightingale *Notes on Hospitals* 3rd Edition (1863), Preface

The quote given above captures a widely held attitude of intolerance to avoidable (preventable) harm arising in the context of healthcare. Infections that patients develop while in hospital are termed HealthCare-Associated Infections (HCAI). Antibiotic use is implicated in the causal pathway of many of these HCAIs. Antibiotics facilitate the dissemination of antibiotic (treatment) resistant microbes such as Meticillin-resistant *Staphylococcus aureus* (MRSA) and infection with antibiotic resistant microbes such as *Clostridium difficile* and fungi.

The most recent prevalence survey (2011) shows that 6.4% of hospitalised patients in England were undergoing treatment for an infection acquired in hospital on one day in 2011 (Health Protection Agency 2012[b]). This proportion is within the 5-10% range reported from previous prevalence studies in the UK and overseas. A World Health Organisation (WHO) Report suggests that HCAIs cause 37,000 additional deaths each year in Europe, and a substantially higher burden of disease in developing countries (Allegranzi *et al*. 2011). There is much

public concern about avoidable infection arising in the context of healthcare institutions, particularly MRSA (Gould *et al*. 2009). The political response to public concerns is reflected in the commitment of the English Department of Health to 'zero tolerance' to avoidable infection. "HCAIs are everyone's responsibility and reducing them remains a duty of every NHS organization". "HCAIs cause unnecessary pain and suffering to patients and cost the NHS approximately £1billion per year. The resources available here will help strengthen the NHS' commitment to a culture of zero tolerance to avoidable infection" (Department of Health 2005).

I have taken 'zero' tolerance to mean zero tolerance of episodes of avoidable infection rather than to failures of compliance of individuals or institutions with 'best practice', although the latter may contribute to the former. Dennis Murphy, President of the North American Association for Professionals in Infection Control and Epidemiology (APIC), states that "keeping people safe is the reason we do what we do – not rates. But rates and numbers measure our success so the goal must be elimination of Hospital-acquired Infections, the metric or target must be zero." "Zero tolerance means treating every infection as if it should never happen" (Murphy 2007 & APIC Position Statement 2008). This sentiment is repeated in strategic documents across the United Kingdom so for example in Northern Ireland the strategic regional action plan for the prevention and control of HCAI (2010) states that "Zero tolerance is a mindset that regards every preventable case of infection as unacceptable" (Department of Health, Social Security, and Public Safety 2010). NHS London talks of the aspiration to 'no avoidable infections' (NHS London 2013). The emphasis of many documents discussing HCAI prevention is on zero tolerance to event(s) ('never events') rather

than intolerance to an attitude (see for example WHO 2012; Clancy 2010;Warye & Murphy 2008; US Department of Health and Human Services 2012).

'Zero tolerance' sometimes requires that costs (and cost-effectiveness) become secondary considerations when actions are required to prevent infection. Mandatory universal MRSA screening for patients admitted to National Health Service hospitals was introduced in England from April 2009.This policy was introduced contrary to prevalent expert advice (at the time) that a hospital policy of screening all patients admitted (or due to be admitted to hospital) was not sufficiently evidence based and would not be the most cost-effective strategy for the control of MRSA (in hospitals) (for an overview from the Editor of the *Journal of Hospital Infection* in 2008 – the year before mandatory screening was introduced - see Dancer 2008). More recent studies have confirmed this expert advice in terms of either cases of MRSA infection avoided per unit cost (Murthy *et al*. 2010) or Quality-adjusted Life Years (QALYs) gained per unit cost (Stewart *et al*. 2011). The 'care bundle' approach for the prevention of avoidable infection has been widely promoted for over 5 years yet has only recently been subject to economic analysis (Halton *et al*. 2010). Advocacy of the intervention has been based on effectiveness rather than cost-effectiveness.

In the English NHS healthcare providers can be and are subject to blaming, shaming, and more recently substantial financial penalties when infection targets are exceeded. Penalties for excess cases of *Clostridium difficile* can be up to 2% of the Total Acute Services Contract Year Revenue (NHS Standard Contract, Section E, 2012/3). In a large Trust hospital these penalties could exceed £10 million in one year (Cordery 2012). The penalties for exceeding the threshold for MRSA blood stream infections are generally less onerous but still

substantial. For example in the 2010/11 financial year Leeds Teaching Hospitals NHS Trust was reported to have been fined £100,000 for every month in which the number of MRSA cases exceeded a target number and by the end of the financial year had been fined £500,000 (Yorkshire Evening Post 2011).

'Zero' tolerance implies that priority should be given to the prevention of avoidable harm and that high levels of opportunity costs can be foregone to achieve or even aim towards achieving 'zero'. These opportunity costs potentially include failing to fund life-saving interventions. O'Neill seems to imply (from a Kantian perspective) that we should reject any principle that says that avoidable injury (harm) is permissible, because injury undermines any principle of action (O'Neill 1996, p163). Injury arising from avoidable infection can (ONeill 1996, p168) -

> "..destroy or damage bodies (including minds), bodily (including mental) functioning and so capacities and capabilities to (inter)act and to respond. It can do so directly by affecting agents and their capacities for action. It can also do so indirectly by two routes. It may damage the social connections between agents, and so conventions, trust, traditions and relationships by which pluralities of agents maintain a social fabric and complex capabilities. It may also damage the natural and man-made environments, which provide the material basis for life and lives and for the social fabric, so once again damaging capacities and capabilities for actions and increasing vulnerabilities"

In this chapter I will consider the proposition that *any* principle that tolerates avoidable infection can be rejected from the contractualist perspective of Scanlon. Does 'zero' tolerance to avoidable infection trump alternative or more cost-effective options for improving patient outcomes? To what extent should the benefits of using antibiotics for the treatment of individuals be constrained by a requirement to control infection with antibiotic resistant microbes?

Scanlon's emphasis on individual reasons resonates with a substantial public concern in the UK about HCAI, which have been focused on the reports of the plights of individuals suffering the adverse consequences of 'avoidable' infection (see examples from a popular UK newspaper 'The Sun'). Scanlon's contractualism gives primary emphasis to the concerns of individuals and in this regard differs from consequentialist theories, which allow aggregation of risks, costs and benefits across groups of individuals. Maximization of aggregate wellbeing is not the primary determinant of 'right' action within Scanlon's contractualism. This perspective is well summarised by Robert Francis QC in a press release announcing the publication of the Final Report of the Independent Inquiry into Care Provided by Mid Staffordshire NHS Foundation Trust (Mid Staffordshire NHS Foundation Trust Inquiry Final report 2013).

> "People must always come before numbers. Individual patients and their treatment are what really matters. Statistics, benchmarks and action plans are tools not ends in themselves. They should not come before patients and their experiences. This is what must be remembered by all those who design and implement policy for the NHS."

Another way in which Scanlon's approach differs from a consequentialist approach is that it allows consideration to be given to non-consequentialist justificatory reasons such as promises, expectations and other aspects derived from human relationships. Scanlon's account emphasises the reasons that one individual has by comparison with another and so potentially can allow a veto on principles that lead to great harms to individuals when there is an alternative (less burdensome) arrangement. All will probably benefit from better control of infectious diseases in hospitals, but in a hospital context risk, harm and benefit may be unevenly distributed. It is important to be clear that the individual perspective has (for Scanlon) to be over their life course. The perspective of an individual can change dramatically through the course of an illness and over the course of a life. Circumstances change and also the information available. Individual perspectives seem to provide an unstable perspective on which to base policy decisions. Scanlon argues (1998, p207-9) that we do not need to go as far as a 'veil of ignorance', because "the requirement of justifiability (or of non-rejectability) requires that we take (these) others in to account" – emphasis should be on generic costs and benefits. "If even someone who was burdened to this (maximum) degree could not reasonably reject the principle, then that settles the matter", ".. in considering whether a principle could reasonably be rejected we should consider the weightiness of the burdens it involves, for those on whom they fall, and the importance of the benefits it offers, for those who enjoy them, leaving aside the likelihood of one's actually falling in either of these two classes." .. "it is always reasonable to reject principles that are supported only by such "particular" reasons" (p211).

Ashford (2003) suggests that - "Scanlon's theory, unlike utilitarianism, might draw a sharp distinction between the obligation to save another person's vital interests and the obligation

not to harm another's vital interests and hold that the former is considerably less stringent" (Ashford 2003, p282). I will explore the possibility that Scanlon's contractualism draws this distinction. Does an obligation on the part of healthcare providers not to harm a vital interest (for example harm consequent upon tolerance of avoidable infection) take precedence over the saving of lives (consequent upon the treatment of disease)?

Infection with treatment resistant bacteria arises as a consequence of the use of antibiotics. When antibiotics are given to a patient there is the potential for that action to lead through a causal chain to harm by facilitating colonisation and subsequent infection (both of the recipient and others) with treatment resistant microbes such as MRSA. Should we impose rigorous constraints on treatment options in order to control MRSA? It is important to understand what 'zero tolerance to avoidable infection' might mean. Avoiding any risk of infection with antibiotic resistant microbes such as MRSA leads to unacceptable limitations on medical practice, and these limitations include limits to the use of antibiotics to treat or to prevent infection. Many forms of harm are avoidable but we might have good reasons not to try to avoid them. It is important to decide which avoidable harms should reasonably be avoided.

In this chapter I consider what principles governing avoidable infections acquired in healthcare institutions might be reasonably rejected from the contractualist perspective of Thomas Scanlon (1998; 2008). I will argue that a policy of 'zero tolerance' to *any* avoidable infection has implausible implications, but that we can justify priority to prevention when irretrievable burdens to individuals can be prevented without the re-distribution of comparable burdens to others.

4.2 What is an avoidable harm?

In this section I clarify what I mean by the term 'avoidable harm'.

Health is not the only capability that may be impacted by healthcare, but stands as a dominant consideration for healthcare institutions, which exist to stabilise or improve health. I use the term 'capabilities trajectory' because capabilities in a healthcare context are dynamic and not static. An individual will have a certain trajectory before entering a healthcare institution (or a stabilised trajectory soon after admission). To be harmed by hospitalisation requires that the capability (health) trajectory of the patient is worse than it would have been had they not been exposed to the institution, and that there was a causal relationship between the deterioration in the trajectory (harm) and hospitalisation. The harm was 'avoidable' if there was a feasible alternative institutional arrangement that reduced the risk of harm. Feasible does not include a requirement for cost-effectiveness, but does require that the alternative arrangement be within the sphere of influence of the institution. The hospital has a causal role when it is possible for the hospital to intervene to make a difference (Pearl 2009, p414). Harm consequent on sub-optimal cleaning would be 'avoidable' if an alternative arrangement (improvements in cleaning) were feasible. Infections are not (generally) directly caused by institutional actions. Microbes are the causative agents and responsible in this sense. Hospitals can be said to have responsibility in the sense that they had adequate opportunity to avoid and hold the 'substantive responsibility' for mitigating infection risks (Scanlon 2008, p198-204). Infection acquired in hospital (HCAI) can and does harm patients and is to an extent

'avoidable' harm in that the hospital is involved directly or indirectly in many elements of the causal chain and there are frequently feasible alternative courses of action.

4.3 Institutional obligations for the prevention of 'avoidable infection'?

A healthcare worker may not show due care when attending to a patient and this lack of care may lead to a causal chain culminating in 'avoidable' infection. Harm is (generally) unintended by the individual healthcare worker and other actors may also have intervening roles. There are considerable practical difficulties with identifying individual responsibility for episodes of avoidable infection and consequent upon poor treatment, because the recognition of an infection is usually temporally and/or geographically distant from the causative event(s). Molecular typing methods can tell us something about the degree to which different microbial isolates share characteristics such as a DNA sequence. If we know something about the stability of such a characteristic then we can estimate the degree of relatedness between different isolates. However we need to take care in the inferences that we draw. Individuals may carry closely related strains even without the direct transmission from one to the other. For example there may be a dominant strain circulating through the population at the time of infection with many potential unrecognised individual carriers or vectors. Identifying probable transmission pathways usually requires additional information, for example the timing and context of contacts. Even so, without being able to directly observe transmission from one person to another, the most probable is rarely the only possible transmission pathway. Following transmission of infection, signs and symptoms may take some time to develop, so that the causal pathways leading to the transmission event are separated in time and place. These uncertainties raise questions about the degree of

probability required to attribute responsibility to individuals, particularly if they are to be penalised for their contribution to an outbreak of infection.

If we confine ourselves to consideration of scenarios where we can with a high level of probability (if not certainty) exclude or implicate individuals in a causal pathway then how should we consider moral permissibility, and individual (personal) responsibility for the spread of infectious diseases (Scanlon 2008)? We rarely have complete information on the knowledge, beliefs, or intentions of the actors involved in the spread of infection in hospital. There is no reason to believe that the various actors either intend or expect to act as vectors for the spread of disease, or for believing that there is indifference to the risks to others (Scanlon 2008, p88). The healthcare worker may become a victim as well as a vector (Tomlinson 2008). We may be able to judge that an individual has contributed to a causal pathway but even then the direct cause of an adverse outcome (to a contact) is the infectious agent and not the individual. "The fact that a person acted in a way that caused harm to someone else may seem to indicate a blameworthy lack of concern for the other's interests. But a requirement of psychological accuracy bars us from drawing this conclusion if the agent reasonably believed (albeit mistakenly) that this action would not be harmful" (Scanlon 2008, p180). As Scanlon puts it – "It depends also on what it is reasonable for the agent to believe in the situation, what it is reasonable for the agent to do to check those beliefs, and whether the agent has done those things" (Scanlon 2008, p52). There is a knowledge requirement, which must be fulfilled before we can hold individuals responsible.

There is another important consideration. We cannot fault an agent for contributing to a causal pathway if there was no feasible alternative course of action that would have prevented

transmission. To expect individuals to control even the known risks of any potential transmission event is unrealistic, and even if it were possible would be excessively constraining, and may generate substantial opportunity costs. Transmission of infectious agents is an inevitable aspect of the life of a social species, which shares space, contacts and vectors on a day-to-day basis. It is hard to imagine any adult living in a social context that has not been part of a causal chain of infectious disease transmission, which at some point has resulted in serious adverse consequences to someone further down the pathway. Expecting individuals to take responsibility for the transmission of infectious diseases in a general sense is unreasonable. Even in the context of healthcare the recognition and appropriate response to infection relies on expert judgements and control requires more than individual action(s).

We can, by contrast, reasonably ask and expect institutions and governments to take action to control transmissible infectious diseases. Decisions about which infectious diseases we should try to control, the measures adopted, and the implementation strategy almost always require concerted collective action, and resource requirements well in excess of those available to most individuals. Public Health authorities in contrast to individuals have the resources available to educate, facilitate, screen, treat, purchase vaccines, commission research and make decisions that lead to the control of infectious diseases. Few individuals are empowered in these ways. We can only hold individuals to be responsible for the spread of infectious disease when we are confident in their role in the transmission pathway, *and* when they are both informed, *and* understand, *and* have adequate opportunity to mitigate a risk. Improved methods of microbial typing may help to identify transmission pathways but give little help with the other requirements for the attribution of responsibility. Molecular typing methods can help to exclude or incriminate individuals in a transmission pathway, but are an

insufficient basis alone on which to ascribe responsibility. In order to say that the actors involved with spread of infection in these two scenarios were responsible we also should be able to show that there were feasible alternative actions that were foregone.

What about the scenario where individuals are fully informed, understand the implication of (in) action and have access to a course of action, which might mitigate risks to themselves or others, and yet they have foregone that opportunity? Perhaps an individual healthcare worker foregoes a vaccination opportunity because of the belief that the risk of vaccination to them outweighs the benefits, while discounting the benefits to others (Van Delden *et al*. 2008). Can we consider these individuals to be blameworthy? I don't think that we can make this judgement without information on the extent to which the individual understood the need for, or had an opportunity to take preventive actions that might have prevented spread to others. If we know that there was a deliberate decision taken to forego vaccination then could we claim that the action shows something about the agent's attitude towards others that impairs the relations that others can have with that individual (Scanlon 2008, p128)? Even in this situation it would be important to understand the reasons for this decision. There may be good reasons for individuals to believe that vaccination is not in the best interests of themselves (or their contacts) such as beliefs consequent upon a previous adverse reaction to a vaccination.

Individual healthcare workers may put themselves at risk of an infection that could be avoided and in so doing also potentially put others at risk. The burdens imposed on others when individuals fail to take advantage of considerably less burdensome preventive opportunities such as vaccination may be substantial, so it does seem plausible to suggest that incentives, disincentives, forms of sanction, or constraints on personal choice may be appropriate in some

cases. If we assume that there were no mitigating reasons for foregoing preventive actions then an action may be judged to be intentional or a due to a lack of sufficient care. Both are morally impermissible but have different implications (Scanlon 2008, p55) and warrant different responses. Whatever the reasons for preventive actions being foregone, the course of events and motivations of the actors are important in a predictive sense. We might reasonably be less inclined to rely on individuals to take appropriate action (Scanlon 2008, p143). Events can and often do have a predictive significance in that similar scenarios may happen again in the future unless actions are taken to prevent them. Institutions are relatively empowered both to recognise and to take actions designed to prevent recurrence of adverse events.

In summary there are a number of reasons for emphasising institutional obligations for 'avoidable' infections and these include the requirement for collective action and the relative empowerment of the institution (Nussbaum 2006, p306). Institutions can challenge false beliefs, can record and act on information, and can remove disincentives, and facilitate courses of action in ways that are generally unavailable to individuals. Do the obligations of healthcare institutions to prevent 'avoidable' harm override obligations to provide (health) benefit(s)?

4.3.1 Prevention of avoidable harm and providing benefit: moral differences

Hospital managers can decide to expend resources in different ways. For example resources can be expended on avoiding harms or on improving capabilities (predominantly health). Healthcare institutions can give priority to the control of the spread of infectious diseases in hospitals or give priority to treatment of disease(s) manifest pre-hospitalisation. A hospital

CEO frequently has to decide between different investment priorities. She may be aiming to produce the greatest benefit overall, for example investing in a diagnostic facility (such as a new type of scanner) which improve the speed and accuracy of diagnosis of cancer or alternatively in a new drug which is twice as expensive than another drug but much more effective. Alternatively the same resources could be expended on hospital cleaning and in so doing obtain an equivalent benefit. We can construct a scenario in which hospital managers have to make a resource allocation decision between three choices. These choices are (A) a patient safety initiative (for example avoidance of prescribing errors), (B) control of MRSA infection, and (C) a new diagnostic scanner. MRSA is given as an example of a healthcare associated infection – which could be avoided with a feasible alternative configuration of services, so for example by improving the quality of environmental cleaning.

For the purposes of this thought experiment we will assume that in each case (A, B or C) the benefit to costs ratio is identical. In each case we cannot say which specific individuals will be benefited or harmed. Many 'avoidable' infections are self-limiting with little long-term impact, for example patients may develop localised stitch abscesses following surgical procedures. These infections are usually self-limiting and of minor inconvenience. In this thought experiment I am assuming comparability of burdens and benefits across the three scenarios. So we will assume that the overall number of deaths prevented for patients will be identical whatever choice is made between A, B and C. The investment in new diagnostic methods saves as many lives as the number of lives saved from investment in avoidance of avoidable infection. We will also assume that there will be no difference in the distribution of risks and benefits across individuals or groups. Every individual patient has an equal chance of risk or benefit. Taking these provisos in to account can we distinguish any morally salient

differences between A, B and C? Is there anything morally different about failing to control MRSA than from failing to provide state of the art diagnostic facilities? Both require investment to save lives. In one case a threat is not being prioritised and in the other a potential benefit is not being realised.

There are a number of morally salient differences between these three potential resource allocation priorities. These include various relational aspects of the institution with the causal pathways, the degree of patient empowerment in acceptance of the risk and/or benefit, public perceptions of the institution, and social implications. In the case of the scanner (C) adverse outcomes result from the unmitigated effects of undiagnosed disease and are independent of the institution in that adverse events do not require institutional involvement. In the patient safety (A) and MRSA (B) cases adverse effects arise as part of the relationship between the institution and the individual patient, in that the adverse effects required the presence of the patient within the institutional context. The avoidable harms (safety initiative, MRSA) when compared with a failure to benefit (scanner)) have the potential for very serious consequences such as loss of public confidence in the institution (safety and MRSA). Patients do not (generally) consent to avoidable harm arising from a patient safety failure (safety and MRSA). The transmissible aspect of MRSA infection adds additional dimensions to those involved in the patient safety choice in part because of the potential for an epidemic, but also the social burden to the patient of carrying a transmissible infection both in terms of the reactions of others but also the sense of shame associated with personal and public attitudes to transmissible disease.

There is evidence for a moral heuristic in human behaviour such that losses are disvalued more than equivalent gains are valued (see Wolff 2006, Slovic 2006, p160 & p374). Kamm

discusses this heuristic and the implications for thought experiments designed to test moral intuitions (Kamm 2008). She distinguishes intuitions concerning losses and gains from intuitions concerning failing to benefit (non-aiding) and harm. The non-aiding / harming distinction "as it is employed in moral theory is not subject to the same framing effect as the loss/no-gain distinction as it figures in the psychological experiments". "The loss/no-gain distinction focuses on what happens to a victim. The harming-non-aiding distinction focuses on what an agent does to a victim" (Kamm 2008, p431). This is an important distinction because if we are to use thought experiments to try to identify morally salient considerations and intuitions then we need to understand the biases imposed by human psychology. It is the particular relationship between a healthcare institution, which is relatively empowered, and a patient who is dependent that distinguishes the priority given to prevention of harm (loss) as opposed to treatment (gain) from a simple loss/no gain distinction.

In summary we are comparing a failure to potentially benefit (C) with reduction in the risk of harm (A & B). The scanner does not add additional risks over and above those attributable to the disease process. The potential harm is attributable to the disease process. For A & B the exposure to the risk can only be controlled (by the patient) if the patient avoids hospitalisation and exposure to the risk takes place in a specific context - when the patient is in a dependent relationship with respect to the healthcare institution. Patients do not generally consent to failures of patient safety measures. Harm from avoidable infection acquired in hospital reflects on the extent to which we have observed duties to keep patients safe (Wolff & De-Shalit 2007, p21). The failure to control MRSA has implications for all who may need to go in to hospital in the future and there is potential for disaster either through a collapse of public confidence or uncontrolled infectious disease. The potential harms of transmissible infection

could be considerable and in addition include social costs both for the individual, for the institution and for others.

For Kamm one way of seeing the relationship between harming and not aiding is through the language of rights (Kamm 2008, p430). The recognition of patient rights gives emphasis to the experience of individuals as rights holders in the context of their relationship with healthcare providers. In the next section I ask if the negative right not to suffer avoidable harm trumps the positive right to the benefits of healthcare?

4.3.2 Negative rights

Pogge proposes a relational conception of justice. Pogge is concerned with coercive institutions (Pogge 2008, p72) and negative rights and considers rights to be evaluative and normative but not necessarily legally enforceable. He also looks to autonomous individuals and groups to specify how these rights will be assured (through legal or other means as necessary). He states that "the autonomy of adult persons ought to be respected and that the measure of a person's flourishing …is then, to some extent, to be posited by this person herself" (Pogge 2008, p38). Any institution is unjust when it foreseeably produces a human rights deficit – a breach of a negative right. For Pogge (Pogge 2008, p70) "by postulating a human right to X, one is asserting that any society or other social system, insofar as this is reasonably possible, ought to be (re) organized so that all of its members have secure access to X, with "security" always understood as especially sensitive to persons' risk of being denied X or deprived of X officially". For this to be the case the institutions must be causally connected to breaches of rights. Infringements must be 'reasonably' avoidable in that there

are feasible alternative ways of doing things. In particular he considers the relationship of institutions and of those that support institutions in the promotion of disease. "An institutional order harms people when its design can be shown to be unjust by reference to a feasible alternative design" (Pogge 2008, p47). Pogge provides 6 scenarios to describe the role that institutions take in promoting disease (Table 4.1).

Table 4.1 Promotion of disease by healthcare institutions (1 is the least acceptable)

Disease Scenarios	**Examples relevant to the control of antibiotic resistant bacteria**
1. Officially mandated	
2. Legally authorised	
3. Foreseeably and avoidably engendered	Overcrowded hospitals, not enough staff, poor cleaning, poor staff training, lack of correct materials/infrastructure, lack of surveillance, substandard equipment, substandard working conditions, poor systems for monitoring use of antibiotics Overcrowded living conditions, low levels of vaccination, poor education about hygiene, tolerance of inappropriate antibiotic prescribing
4. Legally prohibited but barely deterred	Poor practice by healthcare staff (hand-washing), inadequate decontamination of surgical instruments (dentistry)
5. Avoidably left unmitigated, for example the effects of a predisposition	Poor pre-hospital admission assessment and care
6. Avoidably left unmitigated, for example the effects of a self-caused defect	Poor sex education or food handling in the community Inadequate facilities for disposal of needles in public toilets

Table 4.1 gives a list of negative rights ordering the list from 1-6. Number 1 describes the least acceptable position. I have provided examples to illustrate examples of areas of non-compliance by healthcare providers in the second column.

Pogge (2008, p73&137) prioritises respect for negative rights over positive entitlements. My own view is that there are reasons for rejecting *absolute* priority to the negative right not to be avoidably harmed. These reasons become clear when we consider avoidable harm in healthcare contexts.

We cannot always disentangle negative and positive rights. Treatment can impose avoidable harm (as a side-effect or direct effect of treatment) and benefit on the same individual, but also in the case of infectious diseases, can lead to both benefits and harms to others. Certain infections are directly linked with exposure to antibiotics (for example fungal or *Clostridium difficile* infections). These can impact upon the recipient of antibiotics and spread to others. To completely avoid harm from these secondary infections would require that we do not use antibiotics at all. Antibiotics can be used to treat infections and in so doing prevent or control the spread of infectious diseases (preventing avoidable harm). Failing to take action to control an outbreak of infection potentially threatens the freedoms (and negative rights) of many. Control of the spread of infection may require that we constrain the freedoms of some in order to protect the rights of others. Benefits and 'avoidable' burdens are entangled. The entanglement of positive and negative rights extends to the institutions responsible for public health. Inadequate respect for positive rights to shelter, nutrition, and education will all contribute to 'avoidable harm' associated with the spread of infection. Failure to treat some types of infection potentially threatens the freedoms of all by allowing the spread of infection.

In addition to the difficulty of disentangling benefits and avoidable harm there is another reason for questioning a priority to negative rights in a healthcare context. There is a special relationship between healthcare institutions, which are (relatively) empowered and individual patients who are relatively dependent. This special relationship engenders a requirement that the healthcare institution respects at least some positive rights such as the right to adequate nourishment. Failure to address positive rights to adequate nutrition in a healthcare context would lead to harm (including an increased predisposition to 'avoidable' infection) that is beyond the capacity of the individual sufferer to control. Pogge (2008, p137) argues that - "negative duties are not, and are not thought to be, weakened by special relationships as such. Rather some can be partly waived through consent under conditions of fair reciprocity … this allocation must be fair so that (at least) participation in the scheme is not irrational ex ante." Even if we were to accept a higher priority for negative relative to positive rights then we still have to explain when we can waive those rights. We cannot simply invoke a priority for respect for negative rights to justify a priority to the prevention of avoidable harm when the healthcare institution has a positive obligation to try to improve health. It seems implausible (and could be considered irrational) to suggest that healthcare institutions should not assure the nutrition of patients, or that respect for the right to be protected from all avoidable harms (however serious) should be given absolute priority over expectations and positive rights to treatment.

Capabilities could be fostered by mitigating reasonably avoidable risks or by enhancing diagnostic or treatment strategies. Nussbaum argues that institutions are required to empower and foster the development of capabilities (Nussbaum 2006, p315-324) and this role extends

to the private as well as the public sphere, and aspires to be inclusive of peoples from different cultures and traditions. Capabilities (for Nussbaum) are positive entitlements rather than entitlements of non-interference. Nussbaum does not propose a ranking of alternative capability enhancement strategies but I can see no reason for Nussbaum to give a higher priority to diagnostic or treatment enhancement than to the mitigation of reasonably avoidable causes of disease. Capability entitlements go further than liberty rights in imposing obligations on us all to assure not only the space but also a genuine ability to achieve something within that space. Nussbaum's capabilities approach recognises the complexity and entanglement of entitlements (capabilities or rights).

The taxonomy of institutional involvement in avoidable harm that Pogge offers is helpful in considering a hierarchy of institutional responsibility, but still seems to leave open the question of how far healthcare institutions should be prepared to go with respect to negative rights (when the purpose of healthcare institutions is to promote health) and how institutions should deal with conflicts between the demands of individual rights holders, particularly in those situations where some are beneficiaries and some are losers following a course of action. Pogge suggests that individuals should be compensated when negative rights have been breached. In the next section I consider the sufficiency of compensation as a response to breaches of negative rights.

4.3.3 Compensation for harm from avoidable infection

Patients can often be treated for avoidable infections with little if any effect on the capability (health) trajectory or sustained social consequences. It is irretrievable harm to the trajectory

that is a more substantial concern. Avoidable infections may have irretrievable consequences. If we cannot recover the health trajectory of patients by treatment then perhaps we can compensate patients in such a way that harms are equalised by the benefits of compensation. The NHS Constitution specifies that patients have the "right to compensation and an apology if they have been harmed by poor treatment" (Department of Health 2010). In order to compensate patients we would need to be able to place a value on individual losses. Can we value patient losses attributable to avoidable infection? Wolff & De-Shalit (2007) suggest that a plausible monism (a single scale of measurement used for comparison) must adopt a 'compensation paradigm' (p25) and go on to provide a formal argument against substitution monism (p26). Wolff & De-Shalit argue that no amount of money can compensate for death (as may be associated with some forms of infection in hospital). This argument is very pertinent to 'avoidable' hospital infections. It is hard to see how consequences such as loss of dignity at the end of a life, social stigma, or death, or additional disability could be adequately compensated. The social consequences of hospital infections such as a loss of public confidence in healthcare providers and institutions would also be difficult to compensate for. Loss of public confidence in a health system could be compensated for by providing access to another health system, but fear of hospitalisation consequent on a poor hospital experience would remain uncompensated (even if provision of an alternative health system was feasible). These consequences would seem to be both salient and significant when comparing the allocation of resources to patient safety, hospital infection control or improvement in diagnostic or treatment strategies.

That avoidable infection may give rise to irretrievable adverse consequences is an insufficient justification for 'zero' tolerance, because irretrievable adverse consequences may be a feature

of a failure to treat as well as a failure to prevent avoidable harm. Prevention and treatment interventions are often competing for resources. We have to be able to say why one cause of irretrievable outcome should be prioritised over another. The actions taken to prevent avoidable infection can themselves give rise to irretrievable harm. Contact precautions (designed to prevent the spread of infection) isolate patients from others and may themselves contribute to irretrievable harm through a number of causal pathways (Stelfox *et al*. 2003; Morgan *et al*. 2009; Day *et al*. 2011). The irretrievable nature of some harm consequent on avoidable infection and the insufficiency of compensation cannot be considered justification for 'zero' tolerance. We still need to be able to explain why some of the irretrievable adverse consequences should be given priority for prevention over others.

4.3.4 Damage to Trust

Patients have to be able to trust individual doctors and healthcare institutions if they are to make the most of healthcare opportunities (Rowe & Calnan 2006; Groenewegen 2006). O'Neill argues that we should reject *any* principle that says that avoidable injury (harm) is permissible, because injury undermines any principle of action (O'Neill 1996, p163). If avoidable harm undermines the trust that patients can have in healthcare providers then is that sufficient reason to reject any principle that allows avoidable harm? Much of the motivation for the political focus on prevention of avoidable infection in NHS hospitals in England can be seen as an attempt to restore public trust and maintain confidence in the NHS. Patients have to trust that hospitals will respect their vulnerability and dependency and if those that manage and work in those institutions are indifferent to patient safety then that trust is not being adequately respected. Hospitals can be blamed for avoidable infection when they had

adequate opportunity to avoid that outcome and when they hold the 'substantive responsibility' for mitigating infection risks (Scanlon, 2008, p198-204), but to say that we should reject *any* principle of tolerance to avoidable harm is to go too far.

To decide where it is reasonable we can use Scanlon's differentiation between two kinds of responsibility (Scanlon 2008, p198-204). The first requires that a particular person (or presumably entity) can be more or less accurately identified as responsible for an action and as such if accurately identified can be blamed for that action. The second kind of responsibility comes from whether or not the individual had adequate opportunity to avoid an action. He argues that the second kind of responsibility is not required for a sense of blame. It is one question whether a person can properly be blamed for what he does and quite a different question whether he can be "responsible for his fate" (Scanlon 2008, p200). Scanlon (2008, p235-6) argues that blame involves five elements, which are – the ground relationship, the impairment of a particular relationship by certain attitudes of one of the parties, the position of the responder (aggrieved party), the significance of the impairment for the responder, and the response that is appropriate. For Scanlon an action or attitude can be morally objectionable irrespective of the degree of choice. Scanlon refers to 'substantive responsibility' for situations in which there was adequate opportunity to avoid an action. Healthcare institutions (such as hospitals) cannot be blamed in the first sense of responsibility in that they do not have direct responsibility for infection arising in hospital. Microbes are the causative agents and responsible in the first sense. Hospitals can be blamed in the sense that they had adequate opportunity to avoid and hold the 'substantive responsibility' for mitigating infection risks.

It is the relationship between patients and the healthcare institutions that provide care, which is at risk from failures to mitigate 'avoidable' risks of infection. In practice, individual patients are prepared to consent to an explicit risk of infection that is intrinsic to gaining the benefits of a treatment. In the context of consent to a risky procedure there may be no breach of trust (as long as the risk was explicit). The risk and the actual consequences are a necessary component of a course of action that the patient is willing to follow. The (risk of) harm is accepted because of an expectation of an overall improvement in the health trajectory. It is those risks that are not explicit and cannot be subject to any form of reasonable consent, which would seem to justify a loss of patient trust. An expectation of the healthcare institution (that risks be made explicit) has not been met, but an expectation that any avoidable infection will be avoided (zero tolerance) without taking account of the seriousness or otherwise of burdens, patient consent (see below), and the resource constraints and opportunity cost is also an unreasonable expectation. 'Zero' tolerance could increase the overall burden of disease if for example trivial avoidable infections were prioritised for prevention with a consequent reduction in the availability of effective treatment for life-threatening disease. Promoting public expectations of 'zero' tolerance has the potential to undermine rather than instil public confidence in healthcare providers by imposing unrealistic and unreasonable expectations. Deciding reasonable grounds to suspend our trust in a healthcare provider (Scanlon 2008, p163) requires that we compare the burdens and benefits of alternative and feasible courses of action.

4.3.5 Autonomy and Consent

Where individual patients are prepared to consent to an explicit risk of infection that is intrinsic to gaining the benefits of a treatment, there is no breach of trust (as long as the risk was explicit). The risk and the actual consequences are a necessary component of a course of action that the patient is willing to follow and the (risk of) harm is accepted because of an expectation of an overall improvement in the capabilities (health) trajectory. Trust is at risk when the patient is not given the opportunity to consent, or could not rationally consent (to the risk of avoidable harm) even if given the opportunity.

Respect for the autonomy of individual patients is a principle that is widely accepted in healthcare and underpins many ethical requirements including the requirement for informed consent prior to any type of medical procedure or intervention that poses risks to patients. For Scanlon (2008, p118) –

> "The fact that a person's presence, or his or her action, is causally necessary for another person's plan may indicate that the plan involves this person in a way that requires his or her consent. But being a means in this sense – being causally necessary – has no intrinsic moral significance, in my view. What matters is the cost to the person of being involved, and the claim that the person has to be informed about the nature of this involvement"

We have to consider the significance of that harm to the individual, and the resource requirements and consequences of prevention. It is the relationship between the healthcare

provider and the patient that provides the standards that ground expectations (Scanlon 2008, p138).

For Scanlon an action is wrong if (2008, p110) –

1. A's action affects or involves B in a way that is impermissible unless B consents to it.
2. Under the circumstances, B lacks the opportunity to give or withhold consent.
3. Given proper opportunity, B would refuse to consent to what A does.

"What, then, has to be the case in order for B to be involved in A's action as a means? To begin with, the action must involve some cost to B and some benefit to A. The involvement of B is a requirement of the benefit for A" (2008, p112). Patients carry the potentially very significant adverse consequences of avoidable infection and it reasonable to expect that individuals be informed and have the opportunity to accept those risks.

Hospitals only exist because of the existence of patients and the requirements of patient care. It is one thing for risks and benefits to be balanced such that some risk of (otherwise) avoidable infection is acceptable and could be subject to consent but quite another when the victim has no say in what happens and could not rationally consent to the risk of harm (because the harm is consequent on institutional actions when feasible alternative actions were available). The hospital is causally implicated in the loss in that the hospital could intervene in a way that would make a difference (and reduce the possibility of harm). In practice patients carry the costs of avoidable infections but do not (generally) give consent to a risk of 'avoidable infection' unless the risk is intrinsic to the disease process and actions that

are required to manage that condition. Patients may be unable to give consent, they may not receive all of the necessary information about risks to give informed consent, they may have little choice about the hospital to which they are admitted, they frequently (usually) have almost no say in the policies that the hospital management pursue – "the victim is put in a position that precludes the possibility of his consenting, or effectively refusing to consent, to what the agent is doing" (Scanlon 2008, p108). Patients would not rationally will a principle permitting them to be exposed to a risk of avoidable infection or give consent to such a principle (Scanlon 2008, p107) unless there is no feasible alternative.

Parfit provides another perspective on consent when he considers the claim made by Kant that it is wrong to treat people in any way to which they cannot *possibly* consent (Parfit 2011, p179) and interprets this to mean "that it is wrong to treat anyone in any way to which this person *could not rationally* consent" (Parfit 2011, p181). Parfit calls this claim 'the Consent Principle' and distinguishes this principle from the Formula of Universal Law (Parfit 2011, p182-3). Parfit develops the Consent Principle to say (Parfit 2011, p185):

> "It is wrong to treat people in any way to which they could not rationally consent in the act-affecting sense, if these people knew the relevant facts, and we gave them the power to choose how we treat them"

For this principle to work in practice we would also have to accept that individual contextual preferences and desires would not dominate. This requires that we accept something like the perspective suggested by Scanlon – "What is at issue here is not the likelihood that any particular individual, given all that is known about him or her, will be burdened, or benefited,

or both by the principle, but rather the likelihood that anyone who is burdened by the principle will also benefit from it" (Scanlon 2008, p224). We all potentially benefit from the control of avoidable infections and we also benefit from effective diagnosis and treatment of disease. For Scanlon 'reasonable rejection' and for Parfit 'rational consent' is dependent on the relative benefits and burdens for the parties involved. Parfit goes on to state that for the 'Consent Principle' to be true moral objections must be decisive and this requires that there must be a feasible alternative. Pogge (2008) also gives emphasis to the requirement for a feasible alternative before we can say that an institutional harm is 'reasonably avoidable'.

Parfit agrees that "it is wrong to act in ways to which everyone could not rationally consent" (Parfit 2011, p211) but suggests that the principle may be too demanding and that exceptions arise "when to avoid such an act, we would have to bear too great a burden" (Parfit 2011, p210). Scanlon (1998, p225) makes a similar point "we do not just compare the costs to individuals in various positions ….We have to consider also the general costs (and benefits of its acceptance)". We have to consider "generic reasons that everyone in the position of an agent has for not wanting to be bound, in general, by such a strict requirement". Unlimited control of risks would impose burdens to which we could not consent such as limitations to treatment for disease. There are circumstances in which we do consent to harm and to risks of harm because the alternatives are worse. We accept that individuals can drive cars because over our lives the benefit of this type of freedom outweighs the risks.

4.3.6 When priority to prevention constrains treatment opportunities

The foregoing suggests that we have good reasons to take the prevention of 'avoidable harm' from infection seriously and these reasons include the irretrievable nature of some types of harm and the insufficiency of compensation; consequences of blame and mistrust; breaches of negative rights; and the reasonable rejection of 'avoidable harm' when the patient could not rationally consent and may in actuality have been given no opportunity to consent to exposure to the risk of harm.

We cannot avoid all risks of harm because almost any medical (or surgical) intervention carries a risk of harm. Acceptance of a principle that we should try to control a risk of any 'avoidable infection' would have unacceptable consequences. Many infections are foreseeable and arise in the context of medical intervention. Avoidance of any risk of infection would greatly limit the range of medical interventions including many that might provide an overall benefit for individual patients. To completely avoid the harm (of secondary infection) consequent on the use of antibiotics would require that we don't use antibiotics at all. This would be an implausible conclusion from any principle of zero tolerance of avoidable infection. There are also avoidable infections that can only be avoided if we don't do something else such as treat another patient who has cancer. This is termed an opportunity cost by health economists. So what is a 'reasonably avoidable' infection?

Some risks of infection are highly improbable, or trivial, or unavoidable (with current knowledge), or control would require unrealistic levels of expenditure (with excessive opportunity costs), or take place under conditions under which precautions are impractical, or

under conditions of rescue and of such urgency that life is at risk. Hand washing may not be the first priority when rescuing a patient from a train crash. Many types of infection arising in hospital are to an extent foreseeable and cost-effectively avoidable in that the cost of control measures can be recouped in the savings recovered from preventing infection. The foregoing discussion suggests that we have good deontological reasons (in addition to reasons of utility) to give priority to prevention when cost-effective to do so. Do the responsibilities and obligations of healthcare institutions to protect patients (or the rights of patients) from 'avoidable harm' extend beyond producing the best overall consequences?

A problem arises when the cost of control of infection competes with other things (such as treatment options). When this conflict arises in the context of care of individuals (intra-individual) with a particular disease process or a discrete group of patients then the overall outcome would seem to be the substantial consideration. It would be unreasonable to try to control all potentially avoidable infection, because intra-individual trade-offs become unacceptable. The key consideration is that the patient holds the balance of risks and could (and in actuality can) consent to the decisions that impact their health. In the situation where individuals carry both risks and benefits an acceptable harm is one that the patient ***could*** reasonably consent to accept. Harm may be an expected and intended consequence of an individual action accepted by those that harm and that are harmed. Patients currently accept trade-offs between harms and benefits. Patients will accept that surgery can harm but is sometimes a necessary evil. For example all of the interested parties may agree to surgery to amputate a limb or remove an eye (harm) with the intention of achieving a greater benefit (perhaps to save the life of the patient). In a medical context a decision may be made to harm

an identifiable individual with their consent and accepted as an alternative to something worse.

The situation becomes more complicated when risks and benefits are unevenly distributed in particular those situations in which decisions have the consequence that one or more individuals carry substantial burdens while others accrue benefits.

4.4 A contractualist approach to infection prevention

We might argue that institutions should try to maximise utility and expend resources or decide medical policy or practice in such a way that we do maximise utility. A new diagnostic or treatment option may provide a better return on investment (than prevention of avoidable harm) by saving more lives or by impacting on the quality of life of a patient group or by generating income that can be used for other things. If "individuals are just as responsible for things that they allow to happen or fail to prevent as for things that they bring about" (Kamm 2008, p305) then why would we give priority to an avoidable harm instead of an equivalent treatment benefit? There would seem to be a number of morally salient reasons for increasing the relative priority given to control of avoidable harm beyond cost-effectiveness and utility, so it is worth considering an alternative perspective.

Scanlon's contractualism offers an alternative to consequentialist approaches to priority setting. Scanlon (1998) grounds his approach to moral reasoning on the idea that actions are right only if there is a principle permitting them that no one could reasonably reject. Scanlon emphasises the role of reasons for rejecting principles. "An act is wrong if and only if any

principle that permitted it would be one that could reasonably be rejected by people" (Scanlon 1998, p4) motivated to find generalisable principles. Moral principles must be justifiable to each person. A general feature of a contractualist framework is the rejection of the idea that multiple aggregated smaller benefits can justify serious harm to an individual (Scanlon 1998, p238). The considerable harm to individuals has been a feature of media reports and is reported to be a substantial focus of public concern about infection with MRSA (Gould *et al*. 2009). Scanlon's contractualism emphasises individual experience.

Can we use Scanlon's approach to decide which 'avoidable' infections should be avoided? Consider a scenario in which hospital management of an acute NHS Trust tolerates inadequate cleaning standards and this deficiency in cleaning leads to the spread of the serious infectious disease *Clostridium difficile* in the care of the elderly wards. The more vulnerable patients are the most likely to acquire an avoidable infection in hospital, and in these patients the added burden of infection contributes significantly to serious and irretrievable outcomes such as death. In this case there is a significant associated death rate (approaching 30%). The cost of improving cleaning standards for a large NHS Trust can be millions of pounds. At the same time the management invests in a cancer treatment programme for another group of patients within the same institution.

In this scenario I am making the assumption that prevention of *C.difficile* disease in the elderly will not liberate resources for other things, and that the two groups are distinct in terms of the distribution of costs and benefits. In this example the elderly carry the burden of indignity and significant risk of death (which subtracts from their pre-admission trajectory), while others benefit from improved cancer treatment. There are additional reasons derived

from the special relationship between the patient and the hospital (see above), which would seem to raise the priority that we should give to prevention over and above an equivalent treatment benefit. Whether these reasons are sufficient to allow us to completely reject tolerance of any 'avoidable infection' depends on the costs of so doing. Each of us (as individuals) would want to avoid an irretrievable adverse outcome whether from disease or from infection acquired in hospital. It seems implausible to suggest that preventable infection should be given absolute priority. For Scanlon numbers count when the burdens are comparable. It would be unreasonable to reject a principle that gives priority to investment in the cancer drug as the numbers of lives saved by that investment starts to exceed the lives saved by the prevention of infection.

On the other hand the irretrievable harm to those of the elderly who die in this example is incomparably worse than the consequences of delayed or withheld treatment for individuals with many other types of condition that are managed in a healthcare facility for example day surgery for benign lumps and bumps, hernia repair, or in vitro fertilisation. If we do as Nussbaum suggests and extend our range of consideration to include the driving of Sports Utility Vehicles (Nussbaum 2006, p402) and the wide range of human activities for which constraints would impose relatively trivial burdens then the position of the elderly in this example can be even more reasonably rejected.

A contractualist theory "allows the intuitively compelling complaints of those who are severely burdened to be heard, while, on the other side, the sum of the smaller benefits to others has no justificatory weight" (Scanlon 1998, p230). If the benefits were not comparable with the burdens so that for example the hospital continued to provide treatment for self-

limiting conditions while failing to adequately fund cleaning services for elderly patient wards (who suffer irretrievable harm as a consequence) then any principle supporting that priority could reasonably be rejected – even when the overall aggregate benefit (however measured) might be greater from providing treatment for self-limiting diseases. What is 'reasonably avoidable' depends on the resources that are available and the burdens and benefits resulting from the distribution of those resources. If some carry avoidable and irretrievable burdens to which a patient could not be expected to consent, while at the same time others receive treatments for conditions that are comparatively trivial then that would be unjust from a contractualist perspective. Redistribution of resources to elderly care (in the case given above) could be challenged if the redistribution simply resulted in the transfer of comparable burdens to others.

This contractualist approach seems to provide a more plausible justification for public and media concerns than a simple utilitarian calculus. The severity of the outcome to some who are dependent and who could not consent to this scenario justifies rejection of poor cleaning standards when there are feasible alternatives that do not impose similar burdens on others. This conclusion is also consistent with a respect for the negative rights of *each* person.

We can derive principle A: We can reasonably reject any principle that allows hospitalisation to add additional, foreseeable and avoidable harms to patients when there are alternative and feasible arrangements, which would prevent those harms without the redistribution of comparable burdens (harms) to others.

4.4.1 Differentiating risk imposition and precaution

In the case of the ward caring for the elderly (above) the institution can choose not to take preventive action and in so doing to allow harm (from otherwise avoidable infection) but does not directly impose risks of harm. Healthcare institutions do directly impose risks on patients and/or staff. In these cases we can differentiate risk imposition and precaution (Hayenhjelm 2012). Institutional obligations apply to decisions to tolerate *or* impose risks *and* to the degree of precaution that is taken. The use of antibiotics imposes a heightened risk of untreatable infection on others. In these cases there is an intended benefit for an individual and some small increase in risk to others. The imposition of risks associated with the use of antibiotics will be considered in subsequent chapters. In other cases risks of substantial harm are imposed on individuals in order to protect others from harm. It is these kinds of risk that are considered in this section.

Patients with infectious diseases may be placed in a discrete (cohort) area of a hospital with other patients with suspected or proven infection. For example it has become accepted practice in some hospitals in the UK to cohort patients with *Clostridium difficile* disease (in the same ward or area of the ward). This practice reduces the exposure of others and of the general hospital environment to *C.difficile*. These patients have diarrhoea and may carry microbes that have the potential to cause hospital infections (such as MRSA). The acquisition of 'new' hospital infections in these types of facility is well recognised. Another example comes from studies, which show that when patients are placed in single rooms (often to control the risk of infection of others), there is an increased risk that they will acquire a 'new' infection that was carried by the previous room occupant. In effect precautions taken to

protect the majority lead to the exposure of patients with infections to an increased risk of acquiring other infections. Patients may also suffer other types of (non-infection related) harm such as psychological or physical harm consequent upon the imposition of isolation measures (Stelfox *et al*. 2003; Morgan *et al*. 2009; Day *et al*. 2011).

In these examples the cohort area or single room may be designed and operated in different ways. Scanlon states that - "the cost of avoiding all behaviour that involves risk of harm would be unacceptable. Our idea of "reasonable precautions" defines the level of care that we think can be demanded: a principle that demanded more than this would be too confining, and could reasonably be rejected on that ground" (Scanlon 1998, p209). Comparability and the relevance of harms are important (Scanlon 1998, p239). The particulars of the care of patients may prevent adverse consequences to a greater or lesser extent. If the preventive (precautionary) measures are sufficient then in actuality there may be no risk imposition attributable to the decision to cohort the patients or place patients in single rooms. In these kinds of 'risk imposition' cases institutional obligations to take effective precautions to prevent adverse consequences (including infection) would seem to be particularly important because the institution has imposed these risks. We all benefit through actions taken to control the spread of infection in healthcare institutions. Even so those who suffer irretrievable harm as a consequence of actions taken to control risks to others could reasonably reject a principle supporting exposure to those risk(s) if there were feasible alternative arrangements that would not impose a comparable burden on others.

Risks may also be imposed on healthcare staff. A decision may be made to admit a patient with an infectious disease to an intensive care unit with the knowledge that this will lead to

the exposure of staff and others to a potentially fatal infection such as SARS. A number of healthcare staff died of SARS in several countries including Canada (predominantly following accidental exposure) (Tomlinson 2008). Staff harmed as a result of the risk imposition could reasonably reject a policy of admitting patients with transmissible and potentially fatal infections to intensive care units, but so could anyone who might need healthcare who would be placed at risk as well. Otherwise this would be an example of redistribution of burdens - in this case from the patient to healthcare workers, and potentially to other patients as a consequence of effects on healthcare staff. Many healthcare workers could potentially be harmed, and many actual and potential patients. It is hard to see how we could reject a principle requiring a hospital to ensure that healthcare workers are protected as far as possible in this kind of scenario. If staff cannot be protected from the additional risk of acquisition of a life-threatening infection in an intensive care unit then the admission of patients with transmissible and potentially fatal infection could be reasonably rejected. Reasonable rejection would come from the perspective of those immediately burdened (healthcare staff) but also from those deprived of healthcare resources consequent upon the spread of SARS amongst hospital staff and patients.

4.5 Conclusion

At the end of Chapter One I asked how we should decide the distribution of resources and the priority given to the control of antibiotic resistant microbes when resources are constrained. 'Primum non nocere' – first, do no harm is an adage widely taught and familiar to medical students but probably incorrectly assigned to Hippocrates (see Schwarz 2004). There is general agreement that Hippocrates did say that the physician must "have two special objects

in view with regard to disease, namely, to do good **or** to do no harm" (Schwartz 2004). Sometimes we cannot do 'good' without also risking harm and it is that tension that is the subject of the foregoing discussion. I have argued that the mitigation of risks of irretrievable avoidable harm should be given at least the same level of priority that might be given to an equivalent benefit derived from investment in diagnosis or treatment enhancement, and a higher priority than is given to conditions associated with retrievable or more trivial burdens. There are reasons derived from the relationship between the hospital and patients, which add additional weight to the economic arguments for investment in preventions of 'avoidable infection'. A 'reasonably avoidable' harm is a harm for which the institution has a causal role and for which there was a feasible alternative course of action, which would have ameliorated the risk of harm. I am proposing that protecting individuals from risks of serious, avoidable and irretrievable harm to which those individuals have not consented or could not (rationally) consent is an important moral objective for healthcare institutions, and should be given at least the same priority as equivalent benefits in health improvement. An institution should intervene to prevent foreseeable harm if the intervention will save more than it costs (releasing resources for other things), or if there is a feasible reconfiguration of services that reduce that risk without a transfer of a proportionate or greater harm to others. We could also argue that it is reasonable to try to prevent potential disasters, although the extent of this requirement needs to be further specified otherwise it could become paralysing.

We can conclude that a hospital may provide more or less benefit, but we can reasonably reject any principle that allows hospitalisation to add additional, foreseeable and avoidable harms to patients when there are alternative and feasible arrangements, which would prevent those harms without the redistribution of comparable burdens to others.

CHAPTER 5

THE USE OF ANTIBIOTICS: REASONABLE REJECTION

Summary

Decisions to use antibiotics require that individual patient interest be balanced against the public good that is control of antibiotic resistance. Patients carry the risks of suboptimal antibiotic treatment and many physicians are reluctant to impose even small avoidable risks on patients. At the same time antibiotics are overused and antibiotic resistant microbes are contributing an increasing burden of adverse patient outcomes. It is the criteria that we can use to reject the use of antibiotics that is the focus of this chapter.

Scanlon's contractualism explains why antibiotics should not be used to gain small benefits even when the direct costs of antibiotics are low. We know that some individuals now (and probably more in the future will) carry a burden of irretrievable harm as a consequence of treatment (antibiotic) resistant infection. If we accept that the dominant justification for use of antibiotics is to prevent irretrievable harm to an individual or contact, then the use of antibiotics for self-limiting conditions, or for the treatment of individuals with conditions for which antibiotics do not substantially impact on outcomes (for example in the latter stages of terminal illness), or for access based on preference or willingness to pay (internet or over-the-counter access), or the use of antibiotics as animal growth promoters can be rejected.

Scanlon's approach also suggests that with few new antibiotics in the pipeline and an increasing burden of disease attributable to resistant microbes, control of the spread of antibiotic resistant microbes should be given increasing priority.

5.1 Introduction

Concerns have been raised for over 40 years that the use of antibiotics is leading to increasing pollution of the world with antibiotic-resistant bacteria (Gleckman & Madoff 1969). Currently it is estimated that in the European Union antibiotic resistant bacteria cause 25,000 deaths a year, and contribute a yearly cost in the US of $21-34 billion (Morel & Mossialos 2010). Few new antibiotics are in the development pipeline so there are good reasons to try to conserve the effectiveness of the antibiotics that we do have (Morel & Mossialos 2010). Each time an antibiotic is used there is some impact on the burden of antibiotic resistant microbes (Costelloe *et al*. 2010; Dethlefsen & Relman 2011; Jakobsson *et al*. 2010; Martinez 2009). Over time antibiotic resistant strains have contributed an increasing proportional burden to infectious disease with an associated increase in economic and health costs (So *et al*. 2010). At the same time there is evidence for continuing over-prescribing of antibiotics in contexts where there is little evidence of benefit for patients and in some contexts contrary to national guidance (Smith *et al*. 2004). There are also striking variations in patterns of use of antibiotics in different countries without apparent justification by empirical evidence (ESAC 2009). The World Health Organisation (WHO) chose combating antimicrobial resistance as the theme of a recent World Health Day (April 7, 2011) with the slogan "No action today, no cure tomorrow." "Inappropriate and irrational use of medicines" is given by the WHO as a major contributor to the burden of antibiotic resistant infections (WHO 2011), while at the same

time globally only 1 in 5 children less than five years with pneumonia receive antibiotics (WHO 2010).

"Be quick to use a remedy while it is still effective" is quoted by Podolsky (2010) in a review of the history of antibiotic regulation and attributed to Felix Marti-Ibanez from an article published in 1955 entitled "The philosophical impact of antibiotics on clinical medicine". Perspectives have changed and most would now agree that we should not be too quick to use antibiotics because inappropriate use of antibiotics speeds the path to ineffectiveness (Levy 1993). The control of 'inappropriate' use is a common theme in strategies for the control of antibiotic resistance (Standing Medical Advisory Committee (SMAC) 1998; Aiello *et al*. 2006; Enne 2010). Antibiotics are like a leaky rescue craft, which becomes less effective, the more that it is used. If the supply of new antibiotics is drying up then perhaps we should ration the use of the antibiotics that are still effective. It seems self-evident that we should not use an antibiotic if use won't substantially impact on outcomes. However therein we have a problem, because as yet there is no agreement on which outcomes or degrees of risk justify use of particular antibiotics (Millar 2010). This is not just an empirical question of evidence, ethical considerations include the 'acceptable' levels of risk, the valuations of adverse outcomes (such as death) and of (not) selecting antibiotic resistance, and the extent to which we should use aggregate data to determine the management policies for individual patients. Information on cost and effectiveness is frequently used to differentiate 'appropriate' from 'inappropriate use' (National Institute for Health and Clinical Excellence 2009). It is the criteria that we can use to reject the use of antibiotics that is the focus of this chapter.

5.2 Antibiotic treatment guidelines can be controversial

A potential antibiotic prescriber has to decide not only whether to prescribe an antibiotic (or not), but also what threshold level of antibiotic resistance (potential ineffectiveness) precludes use of a particular antibiotic for a given condition. “Few efforts have been made to rationalize such threshold recommendations” (Daneman *et al*. 2008). There are guidelines for the use of antibiotics for specific conditions that specify antibiotic resistance thresholds above which more active alternatives should be used, for example ‘10-20%’ for trimethoprim (and combinations) for uncomplicated cystitis (Warren *et al*. 1999), and 5% for quinolones for gonorrhoea (Fitzgerald & Bedford 1996; Newman *et al*. 2007) but these guidelines are not justified empirically or ethically.

Daneman *et al* (2008) estimate the consequences of following the Infectious Diseases Society of America (IDSA) recommendations for the treatment of community-acquired pneumonia (CAP) (Mandell *et al.* 2007). The IDSA guidelines advocate use of macrolide antibiotics as monotherapy in situations where up to 25% of clinical isolates of *Streptococcus pneumoniae* are resistant by laboratory tests. “We estimate that the quantitative resistance prevalence threshold of 25% in current IDSA/ATS guidelines, as a threshold for high level resistance beyond which macrolides should not be used as empirical first-line therapy for CAP, endorses therapy-attributable mortality in ~ 1 of every 100 persons treated with empirical macrolide therapy” (Daneman *et al.* 2008). In other words the experts who authored the IDSA CAP guidelines are implicitly accepting a mortality rate of up to 1%. Daneman *et al.* question the justification for accepting this rate of mortality.

A recent paper in a British paediatric journal suggested that current empirical antibiotic recommendations for the treatment of suspected early sepsis in infants are adequate despite reporting data from 2006-8 showing that 6% of the laboratory confirmed causes of early sepsis in infants were resistant to an antibiotic regime (penicillin and gentamicin) recommended by current guidelines (Muller-Pebody *et al*. 2010), and without providing any outcome data, or acknowledging the dynamic nature of antibiotic resistance or specifying empirical or ethical criteria by which this judgement might have been made (Millar 2010). The majority of infants in NICUs are babies who have been born before 37 weeks gestational age (preterm). Preterm birth is a major cause of infant mortality (Moser *et al*. 2007) and of long-term disability (Saigal & Doyle 2008). The most preterm suffer the highest risk of death and serious adverse long-term outcome. The mortality rate from early sepsis exceeds 5% overall and is higher in preterm infants, so in effect the authors are accepting a mortality rate of >0.3% (6 X 5 = 0.3%). How much risk of an irretrievable adverse consequence justifies use of an effective (rather than potentially ineffective) antibiotic? This is an important question which I will return to in a later section of this chapter.

5.3 Costs and benefits

Hansson (Hansson 2006, 2007) identifies ten problems with the use of cost-benefit analysis (CBA) to determine policy decisions. He defines three major phases in CBA, which are **F**raming, **O**ption Characterization, and **V**aluation. Many of the ten problems identified by Hansson are relevant to the use of CBA to support antibiotic treatment decisions. For example the framing of the problem depends on perspective and this perspective may give more or less emphasis to optimising the outcomes for individuals or plural individuals at different levels of

aggregation. Option characterization requires that we can predict the future consequences of (in) action and this is clearly a problem when it comes to antibiotic resistance. Valuation requires that we value present and future outcomes and again this is problematic when it comes to antibiotic resistance. Many of these issues are alluded to in Chapter 2 of this thesis.

Daneman *et al*. (2008) apply a cost benefit approach to determine an antibiotic resistance threshold at which antibiotics choices should change. They state that - "It might be argued that a more rational and reasonable threshold for use of alternate antimicrobial therapy would be the resistance prevalence at which the hidden cost of mortality exceed the cost differential between macrolide agents and other therapeutic modalities." They are suggesting in effect that the aggregated treatment costs should be used to establish acceptable levels of deaths attributable to sub-optimally treated infection. The individual outcome is being weighed against the overall costs of a particular strategy, so in effect aggregated small benefits (treatment costs) are being weighed against the cost of a human life. There are considerable empirical (Coast 2004) and philosophical problems (Wolff 2006) with the placing of a money value on a human life. Health economic methods for deciding resource allocation decisions are frequently based on comparison(s) of the expected utility of different choices, so for example the aggregated costs and benefits of one choice are compared with the aggregated costs and benefits of another. The option with the best ratio of benefits to costs is preferred. Cost Benefit Analysis (CBA) emphasises maximisation of the benefit/cost ratio and would tend to favour strategies that maximise the overall good. A potential (and often real) problem with consequentialist approaches is that the individual outcome can become lost within the search for overall benefit (or utility) - potentially leading to policy decisions which are both

hard to justify to individual patients and potentially irreconcilable with the duties of doctors engaged in the care of individuals.

For a consequentialist it is hard to see why we couldn't use a greatest benefit (maximising utility or happiness or QALY's) argument to justify withholding antibiotics from some who would suffer great harm as a consequence. Withholding effective antibiotics might be justified because there is an alternative with greater overall utility, or simply because the consequent gain in utility does not justify the overall cost of the strategy (Daneman *et al.* 2008). Expected utility arguments are frequently used to justify policy but these arguments don't work well when it comes to justifying adverse consequences to those who suffer those consequences (Hansson 2006, 2007). A patient with community-acquired pneumonia is unlikely to be convinced by the argument that we balance their risk of death against the cost of using more effective antibiotics when the benefit for that individual patient is potentially so great by comparison with the cost of the antibiotic (for that patient) (Daneman *et al*. 2008). Doctors have to be able to justify decisions to patients (and relatives) looking backwards (ex post) as well as looking forwards (ex ante).

We also have to be able to explain why doctors should not prescribe antibiotics when the potential health benefits of prescribing are very small, for example when there is substantial societal benefit associated with earlier return to work of large numbers. Most antibiotics are relatively inexpensive and small benefits can seem to be justified when compared with the antibiotic drug costs. The implications of selection of antibiotic resistant bacteria are unpredictable and almost impossible to accurately quantify and historically have rarely been included in costing models comparing treatment strategies (Coast *et al*. 1996).

5.4 Duties of a doctor

Arguments against the 'overuse' of antibiotics generally focus on the need to conserve the effectiveness of antibiotics. Doctors advocate and prescribe antibiotics and also write the majority of guideline documents specifying when and how antibiotics should be used.
In risk situations there can be conflicts of interest when one person is the decision maker and stands to benefit from a particular decision, and another is at risk of harm (Rescher 1983, p160-63). In the case of antibiotic prescribing decisions both the individual doctor and patient lose something if the patient suffers an avoidable irretrievable adverse outcome. The loss of reputation and patient trust could be catastrophic for the doctor, and patients carry the risks of suboptimal antibiotic treatment. Perhaps it is not surprising that many physicians are reluctant to impose even small avoidable risks of harm on patients (Fiscella *et al*. 2000; Metlay 2002). The real costs of doctors complying with a policy that requires that they set aside concerns about significant risks to the patient in front of them are difficult to calculate. McKie & Richardson (2003) make a similar point when considering the rule of rescue – as being defensible from a utilitarian point of view "on the ground that rescues increase well-being by reinforcing people's belief that they live in a community that places great value upon life" (p2407). This approach was broadly accepted by the NICE citizens council when considering the use of an intervention for the treatment of severe infection (Xigris) for which they chose to disinvest in other areas in order to fund this life-saving intervention and agreed (in this context) that life-saving should be prioritised (NICE 2006). Subsequently Xigris was withdrawn because further research showed that it was ineffective.

The General Medical Council (GMC) regulates doctors in the UK. The guideline document 'Good Medical Practice' (2006) states that "Good doctors make the care of their patients their first concern", but also that they should "Protect and promote the health of patients and the public". "Good practice in prescribing medicines - guidance for doctors" (September 2008) states that doctors should –

> "Reach agreement with the patient on the use of any proposed medication, and the management of the condition by exchanging information and clarifying any concerns. The amount of information you should give each patient will vary according to factors such as the nature of the patient's condition, risks and side effects of the medicine and the patient's wishes. Bearing these issues in mind, you should, where appropriate establish the patient's priorities, preferences and concerns and encourage the patient to ask questions about medicine taking and the proposed treatment. When prescribing medicines you must ensure that your prescribing is appropriate and responsible and in the patient's best interests"

The GMC prescribing document makes no mention of the interests of others. These guidelines do little to clarify the position of a doctor trying to balance the prescribing of antibiotics for the individual with the public good.

Regulatory bodies such as the UK General Medical Council emphasise the responsibility of doctors for individual patients while at the same time advocating a wider role to protect and promote the health of patients and the public. Daniels (2007) describes the role of the doctor as an advocate and argues that clinical decisions must be A. competent (complying with

professional standards of care); B. respectful of patient autonomy; C. respectful of patient rights, such as confidentiality; D. free from consideration of physicians' interests; and E. uninfluenced by judgements about patients' worth (Daniels 2007, p234). On the other hand physicians cannot be unrestricted patient advocates. If doctors only advocate for the immediate patient then inevitably there will be occasions when actions run contrary to the interests of other patients. "Our task, then, is not to articulate professional obligations that convert patient advocates into adversaries of other patients. Instead, we want professional obligations that provide fair, reasonable protections for individual patients and at the same time are compatible with what we want from our cooperative health-care schemes, namely, the protection of population health under reasonable resource constraints" (Daniels 2007, p236). "Providers inevitably find themselves in a framework that restricts the resources for treating certain conditions to provide a more equitable distribution of resources overall" (Daniels 2007, p236).

If we accept that the currently available effective antibiotics are a limited resource (as I do) then we need an account of physician responsibilities, which captures both the relationship of trust between individual doctors and patients and also the need to constrain overuse of antibiotics. If doctors are to place aggregate above individual good then the nature of the social contract with doctors would need to be written to reflect that priority.

5.5 The sufficiency of professional guidelines

Take the scenario in which each of 100 doctors treats a single patient for community-acquired pneumonia according to the IDSA guidelines (Daneman 2008). All 100 doctors

follow the IDSA community acquired pneumonia guidelines and as a result in the worst case scenario (accepting Daneman's analysis) one patient dies (of suboptimal antibiotic treatment). Should the relatives of the patient that died re-appraise their relationship with the doctor? All of the 100 doctors have followed the same guideline so should all of the surviving patients re-appraise their relationship with their doctor and with what conclusions?

Most relationships are contingent and conditional. Trust is an important element of the doctor – patient relationship. The patient has discrete expectations, and there may also be contractual and promissory aspects to the relationship For Scanlon (Scanlon 2008, p135) –

> "Impairment …occurs when one party, while standing in the relevant relation to another person, holds attitudes towards that person that are ruled out by the standards of that relationship, thus making it appropriate for the other party to have attitudes other than those that the relationship normally involves"

The doctor patient relationship involves certain attitudes and dispositions including intentions and expectations, fulfilment of which determines the quality of the relationship (Scanlon 2008, p133). Scanlon suggests that blame follows actions that impair relationships (Scanlon 2008, p131). If we accept this perspective on blame (which I broadly do accept) then have the relatives of the patient who has died got good grounds for blaming the doctor for the death?

Currently there are no agreed *ethical* criteria for deciding if and when a particular antibiotic should be used. On the other hand there are innumerable guidelines produced by expert

groups such as the IDSA describing antibiotic guidelines. Is following a guideline a sufficient defence against blame if a patient suffers an adverse consequence?

I cannot see how adherence to guidelines can ever by itself be a sufficient defence against blame. Levels of antibiotic resistance and the implications for patients may vary with time and place. Guidelines become out-dated (with new technology, changing attitudes and information). An overall or general picture provided by national guidelines may not reflect the local situation. In addition each patient has individual characteristics, so that the doctor has to appraise the relevance of the guideline for the particular patient. Even if the doctor is exemplary in his application of the guidelines, the guidelines are often designed to optimise the overall good so that for example the IDSA pneumonia guidelines accept that (under certain circumstances) one patient in 100 will die. Should the doctor be blamed for the death if he knows and accepts that level of risk for his patient(s)? If the risk was known and clearly explained to the patient who then understood the risk and was actively prepared to accept the risk then it would be difficult to blame the doctor. It may be that other costs or burdens (for the patient) associated with a more effective treatment outweigh the risk of death from the patient's perspective. In a healthcare system where the patient carries the drug and drug administration costs it is possible to envisage patients accepting some risk in an effort to reduce personal costs. It is hard to imagine circumstances in which a patient would accept a treatment with a 1% risk of death when there are effective alternatives available within a nationally funded health care system, as in the English National Health Service.

For Scanlon (2008) we are responsible when we harm a relationship that we have with others. Relationships entail certain expectations, so when those expectations are violated, someone is

blameworthy. For Scanlon it does not matter if actions were causally determined – what matters is that actions have harmed the relationship. Doctors carry a substantive responsibility for patients under their care. In order for a doctor to be blameworthy he/she has to be in the right psychological state and has to have adequate opportunity to avoid the action. Clearly a doctor who knowingly places a patient under conditions of avoidable unconsented risk is blameworthy when as a consequence of the doctor's actions the patient suffers an irretrievable adverse outcome. The death of a patient opens the way to questioning of the motivation of the doctor and identifies the full significance of the guideline for all of the other patients (who survived). Even if an avoidable adverse event does not arise patients would seem to be justified in re-appraising their relationship with the doctor. If the patient is unwilling to accept a 1% risk of death but the doctor insists that (overall) cost-benefit analysis shows that we are all better off following the guideline and will not offer an alternative then the patient would seem to be justified in altering their attitude towards the doctor, because as we have seen CBA and professional guidelines may by themselves provide an inadequate justification for action.

In the next section of this chapter I explore the potential for a contractualist approach to help to identify principles to be used to support the use of antibiotics.

5.6 Criteria for the use of antibiotics

Development of criteria for use of effective antibiotics requires both empirical data and ethical analysis. There would be considerable benefit in agreeing ethical criteria for the use of antibiotics both to support doctors making decisions about individual patients and to support policy and regulatory decisions. Agreed criteria for use of antibiotics might go some (if not

the whole) way towards assuring a more equitable and sustainable pattern of use of antibiotics.

I argue that a contractualist approach based on the work of Thomas Scanlon (1998) may provide an approach to deciding when we should use an antibiotic, which may also be compatible with the reality of the individual doctor and patient perspective. This approach is also compatible with rationing by clinical effectiveness (Buyx 2010). I start from the premise that each use of antibiotics diminishes the availability of effective antibiotics by some amount and that there are few new antibiotics likely to be available for many years - making effective antibiotics a limited resource at least in the short to medium term.

5.7 A contractualist approach to the use of antibiotics

Scanlon (1998) grounds his approach to moral reasoning on the idea that actions are right only if there is a principle permitting them that no one could reasonably reject. Scanlon emphasises the role of reasons for rejecting principles. “An act is wrong if and only if any principle that permitted it would be one that could reasonably be rejected by people” (Scanlon 1998, p4) motivated to find generalisable principles. For Scanlon principles that could reasonably be rejected are those that would cause a person serious hardship and where there are feasible alternatives that would not impose such burdens (p196) – this rejection comes *before* bargaining for mutual advantage. Moral principles must be justifiable to each person. A general feature of a contractualist framework is the rejection of the idea that multiple aggregated smaller benefits can justify serious harm to an individual (p238). When

comparable harms and benefits are distributed between different people then numbers count as tiebreakers.

It is also important to recognise that Scanlon advocates generalisable principles (Scanlon 1998, p204). Particular individual (situational) preferences provide insufficient justification for a particular principle (or antibiotic treatment policy) – "our assessment cannot be based on the particular aims, preferences, and other characteristics of specific individuals. We must rely instead on commonly available information about what people have reason to want". On the other hand "the question is whether the fact that a principle would help or hurt specific individuals can be a grounds for preferring it, and for reasonably rejecting alternatives that would not have this effect" (p211).

I propose that the dominant justification for initiating or continuing the use of antibiotics is to prevent an irretrievable adverse effect on the capabilities of individuals (usually directly related to health effects) or others (perhaps close contacts). This consideration outweighs (most) other considerations. For Scanlon (1998, p224) (*italics inserted by author of thesis*) -

> " all we need take into account in deciding whether a principle could reasonably be rejected are such things as the following: (a) the importance of being able to get aid (*effective antibiotics*) should one need it; (b) the degree of inconvenience involved in giving it, should one be called upon to do so (*diagnosis & prescription*); (c) the generic costs of having a standing policy of giving aid in the way this principle requires (*potential reduction in antibiotic effectiveness*) ; and (d) the generic benefits of having others have this policy (*control of infectious diseases*)"

I am suggesting that the principle of using antibiotics to prevent irretrievable injury in patients or their contacts cannot be reasonably rejected. This can be expressed as a principle: Antibiotics should be used to prevent some substantial risk of irretrievable harm in patients or their contacts (P1). In the case of antibiotics the same individual generally gains from the control of antibiotic resistance as from the use of antibiotics. An individual alive today may not benefit today but may well benefit in the future from a policy that restricts use of antibiotics to those at significant level of risk of irretrievable adverse consequences. "What is at issue here is not the likelihood that any particular individual, given all that is known about him or her, will be burdened, or benefited, or both by the principle, but rather the likelihood that anyone who is burdened by the principle will also benefit from it" (Scanlon 1998, 224).

On the other hand a principle that we should use a limited resource to treat short-term reductions in capability (P2), or conditions with inevitable outcomes (that will not be substantially ameliorated by antibiotics)(P3), or to satisfy preferences (without evidence that use will prevent harm)(P4), or for conditions that don't respond to antibiotics such as viral coughs and colds (P5) could be rejected. This rejection comes from the perspective of anyone who does or will need effective antibiotics to prevent irretrievable adverse consequences, and whose outcomes may be prejudiced as a consequence of antibiotic (treatment) resistant forms of infection. The burdens associated with not using antibiotics in each of these cases (P2-5) are not comparable with the harm consequent on treatment resistant infection. In health economic terms there is an opportunity cost of prescribing antibiotics for relatively trivial ailments (Foster & Grundmann 2006). It is the burden of this opportunity cost that justifies rejection of use of antibiotics for conditions that are not associated with irretrievable harm.

5.7.1 Putting to one side the role of intention

When antibiotics are prescribed to a patient the objective is (almost always) to improve the outcome for the patient and the adverse effects such as the consequent selection of antibiotic resistance or secondary effects on other people are unintended. The Principle of Double Effect (PDE) brings together consequences and motivation (intention). There are plural goods and often respect for all basic goods is not feasible when most choices will have undesired but foreseeable effects. PDE would seem to support the use of antibiotics (even for relatively small benefits) and excuse the selection of treatment resistant forms of infection, as unintended consequences. Intuitively this does not seem to be an acceptable position. When patients are placed in isolation in an attempt to control the spread of infection, the withdrawal of social interaction is intended. The control of the spread of disease requires that individuals suffer social isolation. PDE would seem to argue against this course of action. It is important that we understand the place of otherwise of intention within a contractualist perspective.

There are a number of different definitions of the Principle of Double Effect. The weight given to different concepts varies in the different versions (Marquis 1991). A definition commonly referred to in the bioethics literature is that of Mangan (1949) which states that an act is permissible if -

- the nature of the act is itself good, or at least morally neutral;
- the agent intends the good effect and not the bad
- either as a means to the good or as an end itself;

- the good effect outweighs the bad effect in circumstances sufficiently grave to justify causing the bad effect and the agent exercises due diligence to minimize the harm

In this and other attempts to conceptualise PDE a place is being sought for intention in moral evaluation and in defining the permissibility of action. By contrast Scanlon rejects the role of intention as a determinant of the permissibility of an action. He argues that the PDE is illusory (Scanlon 2008, p20-36). Intentions tell us something about the meaning (to the actors) of actions, and in so doing tell us something about the actors, they do not tell us if an action is permissible. Understanding intentions may also help in predicting how an actor will act in the future. He uses the term 'critical' to refer to the use of an understanding of intention in the assessment of the way in which an actor made a decision. Intentions don't really tell us if an action is permissible, but do help with understanding whether or not the actor took account of the proper considerations. For Scanlon permissibility requires that we deliberate using relevant principles. Intention neither seems to justify nor to clearly define when and under which circumstances we should use antibiotics. The use of an antibiotic can more often than not be justified by referral to good intentions and as such an emphasis on intention does little to motivate the control of antibiotic over-prescribing. I broadly accept Scanlon's perspective on PDE and will not consider PDE further in this thesis. Doctors may have good intentions but this is an insufficient justification for the use of antibiotics.

5.7.2 An effectiveness razor

Principle P1 suggests that the dominant justification for the use of antibiotics is to prevent an otherwise irretrievable harm. The effectiveness of antibiotics becomes the substantive

consideration. Buyx *et al*. (2011) have suggested that we ration expensive drugs on the basis of minimum thresholds of clinical effectiveness. The focus of Buyx *et al*. (2011) is on cancer drugs but certainly the evidence suggests that their observations also apply to antibiotics as does the list of reasons that are given for the prescribing of cancer drugs when there is little benefit including fear of legal liability, unwillingness to acknowledge relative impotence, and the unrealistic expectations (of patients and relatives). Buyx *et al*. (2011, d54) suggest that "medical interventions with only minimal effectiveness should be excluded from publicly funded healthcare" – suggesting that we "cut any intervention from publicly funded healthcare that does not reach a predefined threshold of direct clinical effectiveness and which is in this sense minimally effective". By effectiveness they include prolonging life or improving wellbeing. They also argue that the threshold of effectiveness should be explicit and the process of deriving thresholds transparent. Specifically they propose that medicines with a low median benefit and narrow confidence intervals (CIs) are not provided. The CI reflects the degree of uncertainty around the estimate of benefit. Wide variations in individual responses will produce a broad CI. In the most difficult cases (such as that described by Daneman 2008) the median benefit will be low when a more effective antibiotic is chosen to treat Community-Acquired Pneumonia but the CI may still be broad, because even though the number who benefit is small the size of the benefit (to the few) may be substantial. Differences between the cancer drug scenario presented by Buyx *et al*. (2011) and scenarios in which antibiotics are prescribed are that antibiotics are generally inexpensive and that unlike cancer drugs use by one patient today will reduce the efficacy for another tomorrow. Buyx *et al*. (2011) justify rationing by effectiveness as a cost-containment strategy, but also justify rationing by clinical effectiveness as a fairer strategy than rationing by cost-effectiveness, or other criteria such as age. I am advocating rationing of antibiotics because of

the need to justify their use to those that do and will need effective antibiotics to prevent serious and irretrievable outcomes and whose outcomes may be prejudiced by the selection of antibiotic resistance. In many cases it will be the same individuals who benefit from constraints on the use of antibiotics as who lose out but over their lives benefiting much more than they lose out. Cost-benefit can and has been used both to justify antibiotic treatment of self-limiting infections, and also withholding antibiotics with adverse and irretrievable outcomes for some (Daneman et al 2008) - in each case justification comes from an overall economic benefit calculation. Excluding costs allows a focus on effectiveness as a primary justification for use of antibiotics and avoids the conclusion that because some (generic) antibiotics are inexpensive we can use them without constraints. Rationing on the basis of evidence of effectiveness is already an accepted requirement for some medicines that are in short supply such as intravenous immunoglobulins (Department of Health 2011).

5.7.3 How much risk justifies the use of antibiotics?

The principle: Antibiotics should be used to prevent some substantial risk of irretrievable harm in patients or their contacts (P1) is consistent in some cases with a category to which Scanlon would apply 'the rescue principle'. "The cases in which it would most clearly be wrong not to give aid – and most clearly unreasonable to reject a principle requiring that aid be given – are cases in which those in need of aid are in dire straits; their lives are immediately threatened, for example," (Scanlon 1998, p224). Community-acquired pneumonia is an example of a condition in which the lives of individuals are immediately threatened and 1% mortality from community-acquired pneumonia is almost certainly outside of an acceptable level of risk for those who will carry the more severe adverse consequences

(death) of the IDSA policy, particularly while feasible more effective treatment strategies are available.

Medical decisions determining individual patient care usually take place under (ex-ante) conditions of uncertainty – with estimates of probable outcomes but without knowledge of actual outcomes. Knowledge comes after the event (ex-post). Ex post risk and harm can be differentiated. But ex ante everything is a risk, rather than an actuality. A treatment may not work, an operation may be cancelled, a patient may have an allergic reaction to a drug, the diagnosis might be wrong etc. In this sense all medical decisions are taken under conditions of risk and every decision requires risk trade-offs. Whether there is an ex-ante or ex-post perspective is an important consideration. Who makes the judgement, what does the decision maker knows, and what is the context of the decision? Any medical intervention is undertaken under conditions of risk. Therefore we need to decide on the level of risk of an adverse irretrievable outcome below which an antibiotic should not be prescribed.

Antibiotic treatment decisions would seem to provide a relatively straightforward case for Scanlon's contractualism (see Lenman 2008, p109) in that those who are burdened at any one time will also most likely be benefited at another, so we are not talking (generally) about redistributing risks. We all share the risks associated with antibiotic resistance. Even so Lenman (p114) suggests we still need to be able to take account of degrees of risk when those who carry benefits and burdens cannot be clearly distinguished. This seems to be a relevant consideration when it comes to the use of antibiotics. There is always some possibility (perhaps very small) that a patient will suffer a very serious consequence because they did not receive an antibiotic. This (even remote) possibility could give reason to reject almost any

principle constraining the use of antibiotics. Lenman raises the problem of the 'strains of commitment' associated with ex-ante and ex-post perspectives. Ex-ante perspectives can only work in cases where we think that we will be able to go through with the actions at the point of imposition. For Lenman (2008, p116) a policy that is not acceptable at every time is acceptable at none – "If we think of ex ante agreement and rejection as thus morally constrained and sensitive to the strains of commitment, and if we think of ex post agreement as reasonably sensitive to the earlier epistemic perspective in which principles have been applied in conditions of risk". Lenman makes the point that "We can go some way along with Scanlon in privileging the perspective of the most burdened affected person ex post provided we also require that person to make due allowance for the epistemic perspective of the agent ex ante and it is here that probability information plausibly, properly, and indeed necessarily kicks in". Many physicians are reluctant to impose even small avoidable (ex ante) risks of harm on patients (Fiscella *et al*. 2000).

Some risk(s) are intrinsic to everyday activities, such as road transport. We tolerate these risks because over our lives there is a substantial benefit or utility intrinsic to accepting the risk. I argue that the level of risk at which we consider the use of an antibiotic to be justified should be above a level, which approximates with the levels of risk, which we implicitly accept (tolerate) in these everyday activities. When risks of irretrievable harm associated with not using antibiotics are comparable with those that we tolerate and which are intrinsic to everyday activities then use of antibiotics can be reasonably rejected. By accepting some small risk of an adverse outcome from infection (by constraining the use of antibiotics) we gain the benefit of sustaining effective treatment(s) when the risks are more substantial. The risks that we should prioritise for our concern are those which exceed the levels of risk

intrinsic to everyday activities such as cooking, car driving, playing sports, unprotected sex, and other activities which entail avoidable risks to the risk-taker or to others (Lenman 2008, p109). The principle: Antibiotics should be used to prevent some substantial risk of irretrievable harm in patients, or their contacts, (P1), can be augmented by specifying 'substantial risk'. This level of risk is the additional risk to individual(s) that antibiotics can potentially ameliorate, and that falls outside of the range of risks that we tolerate during everyday activities such as motor vehicle transport.

P1 can be further developed to P6: Antibiotics 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 (P6)

This additional burden of risk also has to take in to account the potential risks of antibiotics themselves such as those arising from allergy and supra-infection, and the confidence that we have in the estimate of risk. It is intuitively plausible to suggest that the levels of risk below which use of antibiotics could be rejected falls within this range of tolerable risk. It is not the purpose of this paper to describe exactly what levels of risk these might be. We can give an approximation of the order of risk if we consider the use of motor vehicles. There is a degree of risk intrinsic to motor vehicle usage. The number of people killed or seriously injured in car accidents in the year up to September 30th 2012 in the UK was 24,860 which approximates to 4 deaths or serious injuries / 10,000 population (Department of Transport 2013). This level of risk exceeds the level of risk of serious adverse consequence associated with many upper respiratory infections (such as those caused by the common cold virus) for

which antibiotics continue to be prescribed (albeit less commonly than in the past). At the present time most risk estimates for infection outcomes (including the risk estimates associated with the common cold virus) are based on ex post rather than ex ante analyses. By acknowledging the ex ante perspective of the prescriber we must also acknowledge the importance of gathering empirical data concerning ex ante risk. Exact levels of tolerable risk can be determined by empirical research, evidence synthesis, statistical analysis, and public debate. Levels of tolerable risk can then be made explicit in antibiotic policy guidelines, and subject to debate and review.

5.7.4 When antibiotic resistance is not a consideration

The argument for reasonable rejection of the use of antibiotics for any condition other than those conditions associated with irretrievable adverse consequences is founded on the dire consequences of selecting antibiotic resistance for some. If an antibiotic is unlikely to contribute to the selection of antibiotic resistance then the grounds of reasonable rejection of use would be undercut. Antibiotics are currently used to support a wide range of practices and processes, for example antibiotics are used to support the biosynthesis of insulin, in food production, and in animal husbandry. From the foregoing I have argued that reasonable rejection of the use of antibiotics can be undercut if there is little possibility that antibiotic resistance will be further selected and disseminated. So it follows that when the use of antibiotics in food production or drug biosynthesis processes is not going to add to the burden of antibiotic resistance then use cannot be reasonably rejected because of concerns about antibiotic resistance. It may be that there are some categories of patient or situations where antibiotic use provides no contribution to the burden of antibiotic resistance. It is hard to

identify any human situation in which this would generally apply, apart from extreme examples of individuals kept in purpose built containment facilities, or perhaps newborn babies. It is important to specify this caveat to principle P6.

5.8 Practical implications

If we accept the principle: Antibiotics 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 of antibiotics, and which exceeds the range of risks of irretrievable harm that we tolerate in our day to day lives (P6) and reject P2-5 then what are the implications?

In those countries where the majority of prescriptions for antibiotics are given by health care professionals then compliance with a policy of constraining antibiotics to those situations where antibiotics can ameliorate the risk of irretrievable harm could be audited and regulated through a requirement on the prescriber to state good reasons to support a belief that an individual patient is at a substantial level of increased risk of irretrievable harm. It is important that levels of risk are made explicit, are open to review and apply without exception. The contractualist approach outlined above seems to avoid a requirement to consider aggregate good when it comes to decisions about individual patient care. Identifying a level of avoidable risk (above everyday consented risks) justifies use of antibiotics. This level of risk can be subject to public debate, and once agreed, allows some of the risk of blame associated otherwise with a requirement that the doctor imposes risks on the patient. Guidelines, such as the IDSA community-acquired pneumonia guideline given as an example

above, or NICE guidelines, do not explicitly state levels of acceptable risk that are implicit in the guidelines. An individual doctor needs to be able to interpret the relevance of the guideline for a particular patient and explain to the patient the risks associated with specific decisions and courses of action, so it would seem reasonable to expect guidelines to be explicit particularly with respect to risks.

5.8.1 An incentive for innovation

Constraints on the use of antibiotics based on cost provide a disincentive to potential antibiotic developers (and manufacturers) and inhibit the development of new antibiotics (Morel & Mossialos 2010; Laxminarayan *et al.* 2007). In some health systems (such as the National Health Service in England) antibiotic use is constrained by cost. 'New' antibiotics tend to be more expensive because the costs of drug development are increasingly significant.

There will be periods of time when the development of new products (and therefore our capacity to treat infections) will fall behind the evolution and dissemination of antibiotic resistant microbes (as seems to be the case at the moment). We need both 'new' antibiotics *and* prudent use of those that we have already. Rationing on the basis of cost can (and probably does) prejudice the use and the development of new agents, which are usually more expensive (in part reflecting development costs). By contrast emphasising effectiveness (rather than cost) as the primary determinant of treatment policy (principle P6) may encourage rather than inhibit development of new agents. Drug costs will always be a consideration but I am suggesting that at the level of individual prescription cost should not be the substantial consideration – even though costs may a subject of substantial negotiation at institutional

level(s). We need to dissociate the motivation of those involved in antibiotic development (commercial interest) from the public good that is prudent use of antibiotics. I am arguing that prudent use is that which is likely to make a real difference for patients and that effectiveness is the primary consideration. I would also like to suggest that prudent use of antibiotics should apply to all antibiotics (and not just 'new' antibiotics or expensive antibiotics, or those used for severe infection), because it is increasingly clear that antibiotic resistances are frequently linked and co-selected (Andersson & Hughes 2011).

5.8.2 Does the principle of use (P6) challenge existing guidelines?

The principle P6 runs against the tenor of the GMC guideline 'Good practice in prescribing medicines - guidance for doctors' (September 2008), in that it does not accept that antibiotic prescribing decisions (by doctors) should be based on patient preferences. What is left out of the GMC guideline is the acknowledgement that degrees of benefit matter when it comes to prescribing antibiotics. The principle P6 acknowledges that the degree of benefit is an important consideration.

I am suggesting that we should not use antibiotics *and* we should stop using antibiotics when not using or cessation is unlikely to increase the risk of some irretrievable harm. That prolonged use can itself do harm is of course another good reason to limit antibiotic treatment durations (Kuppula *et al*. 2011). There are 'rescue' situations such as septic shock when we should emphasise the use of our most effective antibiotics - when missing the boat is likely to lead to a substantial risk of irretrievable harm such as death or disability for the patient. There are also grey areas in which the benefit of doubt should be biased in the interests of the

patient. There are also many other situations when the risks of an irretrievable harm are comparable with everyday risks such as crossing the road and this would seem to be a good place to start to constrain the use of antibiotics. In the UK there have been national recommendations for over 10 years (SMAC 1998). Evidence based guidelines are available so for example the National Institute for Clinical Excellence (NICE) provide ‘not to use’ recommendations for antibiotics. These guidelines draw attention to conditions for which there is little evidence of substantial benefit associated with the use of antibiotics, and as such are consistent with the principle of use suggested earlier in this chapter. A list of some conditions for which there is inadequate evidence of benefit to justify immediate use of antibiotics is shown in table 5.1.

Table 5.1 NICE conditions for which we don't need antibiotics

Prophylaxis of recurrent infection in infants and children following first-time urinary tract infection
Prolonged antibiotic treatment for mild diabetic foot soft tissue infections
Pre-labour rupture of the membranes without signs of infection
Prophylaxis of exacerbations of COPD
Acute otitis media
Acute sore throat/pharyngitis/tonsillitis
'Common cold'
Acute rhinosinusitis
Acute cough/bronchitis
Prophylaxis against infective endocarditis for dental procedures
Prophylaxis for clean, non-prosthetic uncomplicated surgery

This is not an exhaustive list but it does provide a starting place. We do need to develop new antibiotics and pharmaceutical companies should be encouraged through an appropriate regulatory framework to see such investment as worthwhile. But equally we should try to conserve the antibiotics that we already have and rationing on the basis of evidence of effectiveness is a strategy worthy of serious consideration. The table offers a list which applies to human medicine but justification should also be required for the use of antibiotics in animals – certainly the use of antibiotics as growth-promoters or to allow over-crowding of animals is hard to justify in itself and even more so when account is taken of those humans who do and will carry the burden of treatment resistant infections.

For many conditions a contractualist position would seem to be broadly aligned with current medical practice and would accept many of the current medical indications for use of antibiotics and policy guidelines based on cost-effectiveness considerations. Most current guidelines (see for example NICE guidelines) exclude the use of antibiotics for conditions such as viral coughs and colds for which antibiotics are ineffective (P5). Conditions for which there is a significant probability that some will suffer an irretrievable harm (foreseeably) preventable by use of specific antibiotic(s) include conditions such as complicated cystitis, community-acquired pneumonia, suspected neonatal sepsis, gonorrhoea, and prophylaxis for many types of surgical procedure. There is also a category of infections that if left effectively untreated will lead to irretrievable adverse consequences but for which there is time to change the empirical treatment options if appropriate to do so for example uncomplicated cystitis. Treatment of these infections empirically with antibiotics to which there are significant associated levels of antibiotic resistance could not be reasonably rejected as long as persistent infection can be effectively treated should the patient fail to respond to antibiotics.

5.8.3 Does the principle (P6) support current patterns of use of antimicrobials?

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.

Antibiotic prescribing decisions require that we decide when antibiotics should be prescribed, for how long, and the antibiotic resistance thresholds (degrees of ineffectiveness) that we are prepared to tolerate. I am suggesting that the contractualist approach outlined provides a principle for decision-making that requires that we should use antibiotics when use will ameliorate some substantial risk of irretrievable harm and that we can reasonably reject use for many other reasons. This may seem an obvious and trivial conclusion but acceptance of this principle requires that we move some way from the patterns of antibiotic access and use that we currently tolerate. All potentially benefit from the adoption of this principle and the rejection of alternatives (P2-5) when account is taken of the interactions with infectious diseases over the course of each of our lives.

Although broadly consistent with some guidelines the contractualist position outlined above does seem to oppose the tolerance of some current antibiotic usage scenarios (P2-5 above). Many drugs including antibiotics are available over the counter and in countries where antibiotics are more heavily regulated are still accessible for self-administration through the internet (Mainous *et al*. 2009). Unregulated access to antibiotics may be an important factor in the selection and dissemination of bacterial strains resistant to our remaining effective antibiotics (carbapenems) (Kumarasamy 2010). In China (according to Hvistendahl 2012) the healthcare system encouraged doctors to churn out antibiotic prescriptions. There was intensive marketing by pharmaceutical companies, and heavy use of antibiotics in animal husbandry and fisheries. The Chinese government had linked doctors' pay to the sales of

drugs, so that doctors were financially motivated to prescribe antibiotics. Recognising the disastrous rise in antibiotic resistant forms of infection the Chinese authorities broke the link between doctor's pay and the use of antibiotics in 2010. Unregulated use of antibiotics motivated by advertising, profit, preference or ignorance can be reasonably rejected.

Patients may request an antibiotic prescription and may be willing to pay to satisfy that preference. The GMC (September 2008) specifically draw attention to the importance of eliciting patient preferences. An individual patient and/or doctor may believe that an antibiotic prescription will be of benefit and argue that individuals should have choices when it comes to antibiotic prescribing. There is tension between patient choice and public good when it comes to antibiotics. Sandel (1997) has argued that it is immoral to buy (or be entitled to buy) the right to pollute, because it allows the wealthy to evade obligations; it turns pollutants in to commodities (removing the moral stigma); and it undermines a sense of shared responsibility. These arguments can equally be applied to antibiotics. The patient may be prepared to pay extra to obtain a real or perceived short-term benefit from use of an antibiotic. A principle allowing individuals to pay a premium to allow access to antibiotics could reasonably be rejected if we take account of those who will suffer an irretrievable loss associated with the selection of antibiotic resistance. Willingness to pay should not be a criterion because those without access to the resources required to pay may still need antibiotics and it is in all of our interests that effective treatment is not withheld when there is sufficient need. Our interests include the benefit of controlling the burden of infectious disease in a world that we increasingly share (Selgelid 2007; Millar 2010). Equally over our lives we will all be exposed to the risk of treatment resistant infection and all will potentially benefit from constraints on

over-prescribing and the consequences of over-prescribing (unless we can each find our own island to live on).

Preferences (P4) of relatives and healthcare workers may also sometimes drive treatment decisions to use antibiotics (Marcus 2001) even when patient benefits are marginal or non-existent. A large proportion of patients in the terminal stages of dementia are treated with antibiotics (D'Agata & Mitchell 2008) in many cases without much evidence of patient benefit (P5) (Givens *et al*. 2010). Schwaber & Carmeli (2008) in an editorial recognised the tension between antibiotic use and resistance state that - "The solution is not to categorically deny antibiotics to the severely demented elderly, or even to impose limits on their use …Such decisions, in addition to being ethically untenable, would run counter to the expressed wishes of patients and their families". Unfortunately the ethical justification for this statement is unclear. A contractualist might insist that the interests of those who carry the consequences of infection with treatment resistant infection should also be considered. Patients dying in Intensive Care Units frequently receive antibiotics right up to the time of death even when treatment is futile (Stiel *et al.* 2011)(P3). 'Withdrawal of treatment' orders may reduce the risk that patients will harbour (and potentially provide a reservoir for) antibiotic resistant bacteria (such as MRSA) at the end of their lives (Levin *et al*. 2010). I am suggesting that a contractualist approach would reasonably reject unregulated access to antibiotics, use in response to the preferences of relatives or healthcare workers, or the 'routine' use of antibiotics for terminally ill patients – "Physicians may feel more comfortable in continuing to try to correct a theoretically reversible condition by use of antibiotics even in the face of an irreversible dying process" (Marcus *et al*. 2001, p1698). Instead a contractualist could insist

on reasons for believing that use of antibiotics would ameliorate some substantial risk of irretrievable harm to the patient as justification in each case.

5.8.4 Implications for the non-rational

Animals and many sick patients (for example infants nursed in intensive care) are non-rational in that they are not able to express judgement sensitive attitudes, so it is important to consider the status of non-rational beings in Scanlon's contractualism.

5.8.5 The moral status of animals

Scanlon offers a number of ways in which non-rational beings gain moral standing. These are indirectly through the relationships that non-rational beings have with rational beings, through a broad ranging morality that includes a rejection of the imposition of avoidable suffering on sentient creatures, and potentially through trusteeship. For Scanlon "contractualism … locates the source of reason-giving force of judgements of right and wrong in the importance of standing in a certain relation to others" (Scanlon 2008, p177-8) – this relation is not an agreement for mutual advantage. The group that Scanlon considers as falling in to the category of creatures encompassed by the narrow morality of 'what we owe each other' are those that have a good, that are conscious and capable of feeling pain, and who are capable of holding judgement-sensitive attitudes (Scanlon 2008, p179). It is important to note that Scanlon makes it clear that what we owe to others does not stop at the boundary of rationality. Justifiability to others provides one set of reasons governing actions, but is not a sole or necessarily sufficient criterion by itself. The character of something can by itself provide sufficient reason for a moral objection to harming something (Scanlon 2008, p183), for

example avoidance of experiential harms such as pain and distress may be a sufficient justification for reasonable rejection.

Scanlon refers to "the problem of the priority of right and wrong over other values" (Scanlon 2008, p148) in that he is trying to explain why right and wrong have priority over other values. Does this mean that right and wrong trump other values such that for example a promise between two rational creatures takes priority over the destruction of a natural forest, or the habitat of rare species? I believe that Scanlon would reject this implication because although a natural forest is not itself a deliberator, rational creatures live in relation to that natural forest. Reasonable rejection (for Scanlon) has priority over mutual benefit. When Scanlon refers to an indirect relationship for the non-rational I take that to mean indirect with respect to the process of deliberation but potentially the non-rational are not excluded from being the (direct) object of deliberation (as something of value). Reasonable rejection can apply to a wide range of actions including those which impact on our culture, or our environment. As individuals we may place no value on some aspects of the world in which we exist but that does not mean that others (who are rational deliberators) do not. Rowlands (1997) makes a similar point when he argues that the contractors must be rational agents but not necessarily the recipients of the contract. "If a contractualist position is consistently applied, the recipients of protection offered by the contract must include not only rational, but also non-rational agents." Nussbaum points out the danger of running together the two questions – "who makes the laws and principles" with "for whom are the laws and principles made" (Nussbaum 2006, p349)? If we put mutual advantage to one side then we can separate the two questions. The 'whom' can be extended to include the non-rational, even though the laws when applied to the non-rational are not subject to explicit consent and are effectively imposed.

For Scanlon (1998) “The class of creatures who can be wronged … is the class of creatures to whom we can stand in the relation that underlies the form of moral motivation I have been describing “ (p177). Scanlon describes this motivation as deriving from reason in that “people have reason to want to act in ways that could be justified to others, together with the fact that when a rational person recognizes something as a reason we do not need a further explanation of how he or she could be moved to act on it” (p154). Reasons and feelings are both part of the human relationship with cultural phenomena such as great art and the natural world, but may not always motivate in the same direction. Scanlon argues for the sufficiency of reasons to explain wrongness in that the wrongness of an action “has to do with the relation with others that such acts would put me in” (p155) without a requirement for motivation from social feelings. This argument contrasts with Mill who ascribes a need to be able to justify decisions to others as attributable to “the social feelings of mankind; the desire to be in unity with our fellow creatures” (Mill 2004, p303).

Damaging trees (and even inanimate objects such as art works) is often very important to someone in that there is some relation, which gives trees value. Humans are intimately connected through emotion, identity and physical being with their environment (and with their culture). The increasing insights into the intimacy of relations (biological, physical, emotional, social) between human rational deliberators and the non-rational world gives me reason to believe that the indirect role of the non-rational does carry and will continue to carry considerable weight. As an extreme example there is increasing recognition of the role that tiny microbes play both in normal human development, health and disease, and in the earth’s geochemical processes. Damaging microbes can have important consequences for individuals and populations. In the environment microbes “are ubiquitous, possess enormous metabolic

and physiological versatility and are essential to virtually all biogeochemical cycling processes – microbial carbon and nitrogen are calculated to be, respectively, equivalent to and tenfold as great as the carbon and nitrogen stored in plants" (Prosser *et al*. 2007, p384). Although respect for individuals is fundamental to Scanlon's contractarianism appeals to the value of 'non-individualisable' goods are not ruled out (Kumar 2000, p282). Despite their important roles in human and animal health and disease and the environment microbes are frequently overlooked in ethical deliberation (Cockell 2008). We cannot owe these creatures but we can respect their relationship with the human condition. Microbes are not sentient and do not form judgement sensitive attitudes in a human sense but they still have value.

Inflicting avoidable pain or gratuitous harm on sentient animals seems to fall into the category of a broad-ranging morality. We may not be able to talk of wronging (in the sense of owing) a bacterium, worm or even a sentient bear, but in addition to the demands of the broad-ranging morality identified by Scanlon we can talk of wronging (and damaging our relationship with) those who perceive value in those natural forms, or who suffer as a consequence of man-made effects on the natural world. We might go further than that and consider the implications of viewing humans as part of 'nature' rather than separate from it. "The assumption of human distinctiveness has a strong hold on bioethics that quietly but definitively shapes the philosophical dialogue about values. It is an assumption that directly hinders ecological thinking" (Pierce 2002, p6). Rational deliberators taking a biocentric rather than anthropocentric perspective can place man in nature both biologically *and* morally. Humans exist in a context that shapes who we are and our potential in a dynamic interplay. It is these complex and fragile connections (emotional, physical, social, biological), which give us great cause for being concerned for the natural world. It seems to me that to describe the natural

world as of merely instrumental value does not do justice to the potentially defining, shaping, creative and destructive relationship that we have with the natural world.

It may be that the broad perspective referred to by Scanlon that lies beyond the boundaries of rational deliberation incorporates both the avoidance of gratuitous harm *and* the sort of respect for animal dignity advocated by Nussbaum (2006). To accept this we would need a concept of dignity that captures both the dignity of rational animals as well as the sorts of dignity that is expressed by the diversity of natural forms. Respect for the dignity of some forms of sentient non-rational creatures such as whales or bears or mice is conceivable, however I am not sure that the concept of dignity can be extended to include viruses or oral bacteria or protozoa or parasitic worms or mosquitoes. Even if sentience is chosen as an important moral boundary then discriminating the sentient from the non-sentient is a challenging prospect, in that many creatures (including parasitic worms) respond to pain but are probably not sentient in the ways that higher mammals are sentient. Animals unrestricted in their natural behaviour won't necessarily reciprocate respect for human dignity, so even if we accept a form of animal dignity we still have to be able to boundary obligations to animals. It seems implausible that we will be able to identify philosophical grounds for varying obligations to different non-rational creatures or that we can identify obligations that apply universally to all natural forms. Human sympathy for some creatures but not for others would seem to be a fragile basis for discrimination.

5.8.6 The use of antibiotics in animals

It is hard to see how animals might be given an equal status with humans such that we would use antibiotics whenever it is possible to prevent an irretrievable harm (to an animal) through the use of antibiotics. Hills (2009) has pointed out the absurd demandingness of moral theories which give every animal (human and other) including wild animals equal moral status, using the examples of sewer rats and red deer. Attempting to use antibiotics to prevent irretrievable harm to any threatened animal would be both extremely (probably impossibly) demanding, and would almost certainly promote the spread and prevalence of resistant microbes and therefore be a rapidly unsustainable strategy. Application of infection control precautions to wild animals (in order to control the spread of antibiotic resistance) is implausible.

The situation in animal husbandry is more complex in part because man has a particular relationship and responsibility for these animals. It is unlikely that antibiotic resistant bacteria in farmed animals can be confined to the animals themselves. Inevitably use of antibiotics in farm animals will have implications for humans. Animals produce waste, which enters the ground and water supplies, animal products become contaminated with resistant bacteria, and humans acquire antibiotic resistant bacteria by direct contact with animals and animal products. The use of antibiotics in animal husbandry is hard to justify to those who will suffer the consequences of infection with antibiotic resistant microbes when antibiotics are being used to promote the growth rate of an animal (as a food source) or to compensate for managing animals in degrading and overcrowded conditions. Antibiotics “have enabled us to crowd animals for profit at the expense of (animal) welfare” (Rollins 2001 p34) and have

facilitated the development of morally indefensible agriculture (Rollins 2001). The use of antibiotics to prevent irretrievable harm to an animal when the animal is imminently to be slaughtered for food is also hard to justify. On the other hand if uncontrolled infection in animals will put many others at risk of irretrievable harm (perhaps animals and humans) then use of antibiotics to prevent some from dying from animal derived infectious diseases would be more difficult to reasonably reject.

Our duties to animals inevitably would seem to be more limited than they are to other humans. Even so, respecting the dignity of animals and ensuring that there is a sufficiency across capability dimensions would do much to limit the requirement for use of antibiotics in animals, and lends further support to the idea that capability theory has something significant to say about our relationship with animals (Nussbaum 2006, chapter 6) – particularly those for whom we have a special (direct) responsibility such as farm animals. Capability dimensions that are pertinent to the spread of infection amongst animals include bodily integrity (some level of minimal freedom of movement), bodily health (adequate nutrition and shelter), and perhaps affiliation (for herd animals). Minimal standards across these dimensions would do much to limit the spread of infection and the requirements for antibiotics.

5.8.7 The moral status of infants and children

Many hospital patients are not able to advocate for themselves, so it is important to understand if (Scanlon's) contractualism has the resources to deal with those who are dependent and unable to express judgement sensitive attitudes. Infants and children provide a good example of a vulnerable and dependent group. Referring to this group and to those who do not develop 'judgement sensitive attitudes' – "this tie of birth gives us reason to want to

treat them "as human" despite their limited capacities. Because of these limitations, the idea of justifiability to them must be understood counterfactually, in terms of what they could reasonably reject if they were able to understand such a question. This makes the idea of trusteeship appropriate in their case," (Scanlon 1998, p185). Scanlon is suggesting that trusteeship is a potential way forwards in deciding what we owe to those who cannot represent themselves.

Scanlon requires that we consider the general implications of adopting particular principles. Also, for Scanlon harm to you cannot be justified by benefit to me, equally risk to you cannot be traded against risk to me. The risks of harm to each person should be minimised. An important aspect of this perspective is that it can involve intra-personal aggregation so the trustee must consider the impact over the whole life of a person. Numbers count for Scanlon (1998, p230-240) because "An assessment of the rejectability of a principle must take account of the consequences of its acceptance in general, not merely in a particular case that we are concerned with" (Scanlon 1998, p204) and "In deciding whether a principle could reasonably be rejected we do not just compare the costs to individuals in various positions, of abiding by it, or not doing so, on a specific occasion. We have to consider also the general costs (and benefits) of it acceptance" (Scanlon 1998, p225). For Scanlon (and for a trustee) there is a requirement to consider the general acceptability of risk (or costs) and not merely acceptability in a particular case (Scanlon 1998, p204). It is important to note that (from Scanlon's perspective) a trustee should take account of generalisable principles (that could not be reasonably rejected) and that should apply to anyone in the particular situation under consideration.

I have suggested that non-rational animals cannot be considered to have equal moral status with humans – certainly as far as antibiotics are concerned. On the other hand the moral status of (non-rational) infants can be defended as a phase within the fluctuating degrees of rationality that are characteristic of a (rational) human life. All human beings experience times when incapable of judgement sensitive attitudes. These states may be permanent (severe brain damage), developmental (infancy) or transitory (illness). Rational contractors are motivated (in part) to take account of inevitable periods of human irrationality as aspects of the wide range of potential states that they might find themselves experiencing over their lives. Most children become rational creatures –"Infants and young children are not separate kinds of creatures…. infancy and childhood are, in normal cases, stages in the life of a being who will have the capacity for judgement-sensitive attitudes" (Scanlon 1998, p185). Reasonable rejection on the behalf of those human creatures permanently unable to form judgement sensitive attitudes can be derived from rational deliberators who have taken account of the range of states with varying rationality that they may themselves experience. Scanlon gives moral status to the disabled because of the ties of birth (Scanlon 1998, p185). Reasonable rejection taking account of the range of human conscious states would seem to be a plausible basis for determining what we owe to the disabled, infants and those with transitory illness without a requirement for their moral status to be questioned. In a sense when we act as rational deliberators we can also acting as trustees for ourselves (and others) for those times when we are not rational deliberators (for example infancy, and confusional states). Additional motivations come from the ties of human relationships and human sentiments such as empathy, and "the social feelings of mankind" (Mill 2004, p303).

5.8.8 Use of antibiotics in infancy to protect future capabilities

Infection imposes risks of harm on the newborn infants and antibiotics can be and usually are used to try to prevent the harms consequent on infection. I took preterm infants nursed in Neonatal Intensive Care Units (NICU) as an example earlier in this chapter because they are particularly vulnerable to infection and to the deficiencies of treatment consequent upon antibiotic resistance. It may be that we know at the time of an antibiotic treatment decision that an infant will not have a "reasonable hope of survival with a chance of an acceptable form of life" (Versluys & Leeuw 1995) or that the child does not have a good chance of achieving thresholds of capability sufficient for an acceptable form of life (Nussbaum 2006), or that treatment will not be in the child's best interests (Royal College of Paediatrics and Child Health 2004) such that a decision can be made to withhold antibiotic treatment. Otherwise it is hard to see why (if we accept that infants have equal moral status as the objects of deliberation) we would not aim to reduce the risks of a deficit in the potential capabilities of the potential child and adult. Capabilities require a minimum of agency, sentience, and potential capacity for independent survival (Dixon & Nussbaum 2011, p9) but assuming that we believe that these basic capabilities are potentially achievable then we should try to optimise antibiotic use. Once the decision has been made to admit an infant to an NICU the objective to try to protect potential capabilities would seem straightforward, equally if there a sufficient certainty that an acceptable threshold for a given capability cannot (reasonably) be reached then treatment should be withdrawn. From the perspective of capabilities the key thing for infants would be the securing of 'basic' capabilities such as seeing, hearing, or reasoning. Other aspects of capabilities are less relevant at this stage of development because without basic capabilities other capabilities cannot develop (such as the

necessary conditions for free preference formation, and equal opportunity). How does Scanlon's contractualism deal with the use of antibiotics in early life?

5.8.9 A contractualist approach to use of antibiotics in early life

Infants who receive antibiotics early in life are also at risk of infection with antibiotic resistant microbes over the rest of their lives, so both health benefits and disbenefits have to be balanced for the same individual infant making this is a relatively straightforward case for Scanlon's contractarianism (Lenman 2008). We are not (in this case) generally comparing benefits for some with costs or adverse consequences for others, in that few (if any) infants could be considered free of the risks of untreatable (antibiotic resistant) infection over the course of their lives. The broad nature of risks (for infants in an NICU) both for developmental capabilities today but also prospects for sustaining levels in to the future (Wolff & De-Shalit 2007, p9) suggests a particular vulnerability. "A society of equals is a society in which disadvantages do not cluster, where there is no clear answer to the question of who is the worst off" (Wolff & De-Shalit 2007, p10). I can see no reason to reject principle P6 in the context of NICU care, unless the child does not have a good chance of achieving thresholds of capability sufficient for an acceptable form of life (Nussbaum 2006), or that treatment will not be in the child's best interests (Royal College of Paediatrics and Child Health 2004) (see previous section).

5.9 Conclusions

At the end of Chapter One I asked what criteria can be used to reject the use of antibiotics in developed countries. Scanlon's contractualism explains why antibiotics should not be used to gain small benefits even when the direct costs of antibiotics are low. We know that some individuals now (and probably more in the future will) carry a burden of irretrievable harm as a consequence of treatment (antibiotic) resistant infection. If we accept that the dominant justification for use of antibiotics is to prevent irretrievable harm to an individual or contact, then the use of antibiotics for self-limiting conditions, or for the treatment of individuals with conditions for which antibiotics do not substantially impact on outcomes (for example in the latter stages of terminal illness), or for access based on preference or willingness to pay (internet or over-the-counter access), or the use of antibiotics as animal growth promoters can be rejected.

In the next chapter I will consider the use of antibiotics where there are poor conditions of public health.

CHAPTER 6

CONSTRAINING THE USE OF ANTIBIOTICS: BROADER IMPLICATIONS FOR GLOBAL JUSTICE?

Summary

Increasing access to antibiotics threatens the sustainability of the primary function of antibiotics, which is the prevention of adverse outcomes from infection. Adverse socio-economic conditions facilitate both the spread of infection but also the spread of antibiotic (treatment) resistant forms of infection.

Principles governing the use of antibiotics are insufficient by themselves (even if fully complied with) to assure the sustainability of antibiotics. The capabilities approach by emphasising sufficiency across a range of dimensions required for a life with human dignity captures the essential message that focusing on one dimension of wellbeing such as health is insufficient for justice. Focusing on access to antibiotics without taking account of the determinants of the spread of infectious diseases is an inadequate response when account is taken of sustainability. The capabilities approach would seem to offer a model for public health, which resonates with the concerns of all who have an interest in the control of infectious diseases (and treatment resistant forms). Scanlon's contractualism would also reasonably reject a principle of use of antibiotics when more individuals could be protected from equivalent burdens by feasible alternative (public health) interventions (such as the provision of clean water).

6.1 Sustainability and justice

Antibiotic resistance imposes substantial risks on patients (Morel & Mossialos 2010). Despite decades of expressions of concern at all levels (Gleckman & Madoff 1969; WHO 2010; SMAC 1998; Aiello *et al*. 2006; Enne 2010) there is still evidence for continuing over-prescribing of antibiotics (Smith *et al*. 2004) and striking variation in use of antibiotics in different countries without apparent justification by empirical evidence (ESAC 2009). Increasing and inappropriate use of antibiotics have made them less effective with the potential for irretrievable adverse consequences from suboptimal treatment of infection. I proposed in the previous chapter that we should only use antibiotics if their use can ameliorate some substantial threat to our human capabilities.

The focus of the previous chapter was on the justification of individual prescribing decisions and the identification of principles of use that cannot be reasonably rejected. Antibiotic resistance reduces the effectiveness of antibiotic treatments. Antibiotic-resistant bacteria have only recently begun to receive consideration in either the environmental or bioethics literature (Selgelid 2007; Anomaly 2010) literature. Dwyer (2009) suggests that an important ethical task is to construct institutions and modes of living that promote health in ways that recognise the claims of sustainability *and* justice.

In this chapter I argue that there is a tension between the just use of antibiotics and the sustainability of the effectiveness of antibiotics. Principle P6 specifies that: Antibiotics 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 of antibiotics, and which exceeds the range of risks of irretrievable harm that we tolerate in our day to day lives. Is this a sufficient principle for contexts in which there are conditions, which favour the spread of infectious diseases?

6.2 Sustainability

Antibiotic-resistant bacteria are rapidly selected in individuals exposed to antibiotics and may persist for extended periods (Costelloe *et al*. 2010; Dethlefsen & Relman 2011; Jakobsson *et al*. 2010). Antibiotic resistance becomes a problem when resistant strains persist in individuals, human populations and/or in the environment to the extent that the efficacy of antibiotic treatment is compromised. It is currently estimated that in the European Union antibiotic-resistant bacteria cause 25 000 deaths a year, and contribute a yearly cost in US dollars of $21-34 billion (Morel & Mossialos 2010).

Historically antibiotic functions were considered as renewable resources, in that it was believed that if we stopped using a particular antibiotic then microbes would revert (back) to susceptibility, because maintaining defences against antibiotics was considered costly to microbes. Antibiotics may be a renewable resource in that ultimately microbes will revert back to susceptibility, but the time scale required for this reversion can be so long that the functions that particular antibiotics serve will not be available again for decades (eg, resistance of *Staphylococcus aureus* to penicillin). The costs of discovering, developing, testing and marketing new antibiotics have increased to the extent that antibiotic research and development is no longer attractive for many pharmaceutical companies. Few new classes of

antibiotic have been discovered over the past 20 years, leading to various proposed strategies to promote drug company investment in the development of new antibiotics. If current patterns of high levels of antibiotic utilisation persist (while there remains a paucity of new antibiotics) then the availability of effective antibiotics will decline. It is unlikely that the problem of antibiotic resistance will be solved by new antibiotics in the near future "Today's dearth in antibacterial research and development will take decades to reverse" (So *et al*. 2010, c2071), so sustainability of the functions of antibiotics requires that we sustain the efficacy of those antibiotics that are currently available at least for the next few decades.

There are a number of ways in which the effectiveness of existing antibiotics could be sustained. These include reducing the use of antibiotics, and/or reducing the factors that determine the transmission and persistence of antibiotic-resistant variants. We could potentially reduce consumption by using market forces, for example by increasing the price of antibiotics (Anomaly 2010). We could regulate the use of antibiotics so that market forces driving the unnecessary or inappropriate use of antibiotics are curtailed. We can try to reduce the need to prescribe antibiotics by addressing remediable determinants of infection, for example by encouraging breast feeding, improving nutrition and improving access to and uptake of vaccines (Couper 1997). We can try to control the factors that determine the transmission and persistence of antibiotic resistance such as by ensuring safe water supplies.

6.3 The epidemiology of antibiotic resistance

The use of an antibiotic in an individual impacts on others and generates what economists refer to as externalities. These can be positive or negative. Antibiotic resistance as a

consequence of the use of antibiotics is a negative externality. Prevention of the secondary spread of infection (by treatment of infectious individuals) with antibiotics is a positive externality. The extent to which these externalities become problematic depends on the context. A newborn baby has few bacteria from which to select antibiotic resistant forms so the negative externality of antibiotic resistance will be quantitatively less than follows exposure of an adult to an antibiotic. The treatment of peritonitis with antibiotics in an adult (perhaps following appendicitis) does not give rise to positive externalities resulting from the treatment of infection because the causes of infection are already widespread (and part of our commensal flora), but does give rise to the negative externality of antibiotic resistance. The treatment of gonorrhoea in an individual contributes to protecting future contacts from gonorrhoea so carries both a positive externality and the negative externality of selecting for antibiotic-resistant bacteria. The significance of the negative externality of antibiotic resistance depends on the facility with which microbes can spread between individuals, and to a large extent spread is facilitated by poor social and economic conditions such as over-crowding, and limited access to clean water and food. Poverty is significantly associated with an increased risk of many bacterial infections, (World Health Organization 2009; Carapetis 2007; Greenwood 2008; Rees Jones I *et al*. 1997; Souza *et al*. 2009) and with the spread of infection both in developing (Okeke *et al*. 1999) and developed countries (Spence *et al*. 1993; Planta 2007). So the individual circumstances and context is an important consideration when considering the scale and scope of externalities arising from antibiotic treatment decisions.

6.4 Inequity in access to antibiotics

There are no existing and equally cost-effective alternatives to antibiotics for the treatment of the majority of serious bacterial infections. The WHO and UNICEF have prioritised the prevention and treatment of pneumonia in children less than 5 years of age. Antibiotic treatment of pneumonia is highly cost-effective with the potential to generate considerable returns in terms of disability-adjusted life years averted (World Health Organization 2010). Currently (globally) pneumonia is estimated to kill 1.8 million children under the age of 5 years every year mostly in developing countries. Only one in five children less than 5 years with pneumonia is given antibiotics. The use of antibiotics to treat children with pneumonia clearly seems to fall within the range of conditions for which use of antibiotics cannot be reasonably rejected (see previous chapter). However providing antibiotics to children under the age of 5 years with pneumonia, without addressing other insufficiencies such as overcrowding, poor nutrition, education and inadequate sanitation, will only expedite the establishment and spread of antibiotic- resistant bacteria. If we are to try to conserve the function of existing antibiotics then we must try to ameliorate the factors that determine the spread of bacterial infections (and resistant forms) such as poverty (World Health Organization 2009; Carapetis 2007;Greenwood 2008; Rees Jones *et al*. 1997; Souza et al. 2009).

Anomaly (2010) argues that we need global solutions if we are to control antibiotic resistance. He suggests that "The main obligation is to make antibiotics expensive enough to curb low value consumption and encourage the development of new treatments in order to protect innocent parties." Anomaly acknowledges that increased drug costs will have a

disproportionate effect on the poor, but states that – "nobody has the right not even the poor to inflict uncompensated harms on other people against their will" (Anomaly 2010, p18). Selgelid (2007) ascribes the burgeoning problem with antibiotic resistance to the failure of the market to control externalities such as antibiotic resistance. He argues that antimicrobial agents are 'public goods' that warrant special treatment and advocates governmental intervention and funding to direct the distribution of antimicrobial drugs. Selgelid (2007) points out that (globally) antibiotics are over-consumed by the wealthy and under-consumed by the poor. He argues that health is a 'special good', and that equal access to effective health care (and this would include effective treatments for infection) can be justified on egalitarian grounds, because health is required for normal species functioning (Daniels 1985) or (it can also be argued) is an essential capability (Nussbaum 2006). Selgelid (2007) also argues that the control of the transmission of infectious disease by effective treatment of individuals (irrespective of wealth) can be justified for consequentialist reasons, which include control of the secondary spread of infections citing tuberculosis as an example. I agree with much of this analysis. Studies of the epidemiology of bacterial infectious diseases have shown that these diseases do not respect geographical or temporal boundaries. In the great majority of cases contact of an uninfected individual with an individual with an untreated bacterial infection (eg, tuberculosis, methicillin-resistant *S aureus* infection, or typhoid) increases the risk of infection of the uninfected individual. Effective control of many bacterial infections requires treatment of those who are infected so there are clear pragmatic reasons for ensuring the widespread and impartial availability of effective treatments for transmissible infectious diseases. However, I do not agree with Selgelid (2007) that the under-consumption of antibiotics generally contributes to antibiotic resistance. Under-consumption may contribute to the selection of resistance in special cases such as the selection of resistant forms of

tuberculosis. For many bacterial agents of infection levels of antibiotic resistance are directly dependent on the quantity of antibiotic prescribed (see, for example, Arason *et al*. 2006). Increasing the use of antibiotics in developing countries for the treatment of childhood pneumonia may well increase levels of antibiotic resistance. Equal access for individuals with equal need irrespective of wealth has the potential to shorten further the effective life of currently available antibiotics. If we accept that there are good egalitarian and consequentialist reasons for ensuring equal access to antibiotics based on need then use of price to curtail usage would seem to threaten both the control of infection and justice. Justice requires access to antibiotics irrespective of wealth, and effective treatment of transmissible infectious diseases is of benefit to us all.

6.5 Sustainability while improving access: incompatible objectives?

Under adverse social and environmental conditions antibiotic resistant bacteria can spread rapidly to the extent that any benefit of an antibiotic will be undermined. In the early 1990's in Romania babies and young children without families to support them were placed in orphanages. The conditions of some of these orphanages were very poor. Children were kept in overcrowded and squalid conditions, so that infections spread rapidly amongst the children. Antibiotics were used to treat infections. Antibiotic resistant microbes also spread rapidly. Some of these children were adopted by families in the UK leading to the introduction of treatment resistant pathogenic microbes in to populations that had not been previously exposed (Millar *et al*. 1991). In India antibiotics are widely available, there is little surveillance of antibiotic resistance, antibiotics can be directly purchased from suppliers without a requirement for medical or other professional assessment of need, socio-economic

conditions may be very poor, and infectious diseases are common (in part because socio-economic conditions are poor). Unregulated access to antibiotics in India has been proposed as an important factor in the selection and dissemination of bacterial strains resistant to one of the few remaining highly effective classes of antibiotics (carbapenems) (Kumarasamy *et al*. 2010). Quoting from an editorial in the Journal of the Association of Physicians of India by Abdul Ghafur (2010, p143-144) -

> "Indian medical community has to be ashamed of the NDM-1 ("New Delhi Metallo-1") gene. Even though we have not contributed to carbopenem development, we have contributed a resistance gene with a glamorous name. The overuse of antibiotics is embedded in our Indian gene. It is an Indian tradition. Why should we Indians worry? We can always depend on honey, yoghurt and cow's urine. At any rate within a few years - these products may be more useful than antibiotics!"

This new form of antibiotic resistance is becoming increasingly common in the UK (see Health Protection Agency 2012[a]). These stories illustrate three aspects of antibiotic resistance. The first aspect is that when social conditions are poor then antibiotics quickly become ineffective, and the second aspect is that antibiotic resistant bacteria can be rapidly spread around the world. The third aspect is that there is a relationship between the sustaining of the functions of antibiotics and other socio-economic 'goods' such as adequate shelter, and clean water.

6.6 International standards?

I take appropriate use of an antibiotic to be for reasons that cannot be reasonably rejected. Use in human medicine requires evidence of benefit (or good reasons to believe that there will be

a benefit) to an individual or others (who may or may not be identifiable). If one country and its people constrain the use of antibiotics so that they are only used in patients for whom there will be a substantial benefit, and another country uses antibiotics for the most trivial reasons or in excessive amounts or for unnecessary durations or to support unsustainable forms of animal husbandry, then we might judge the second country less well than the first one (Rollins 2001). If we accept that all countries should share the benefits of antibiotics, then we would probably also accept that all countries should be prepared to accept constraints on overuse. Most would agree that a life-threatening bacterial infection would provide a justification for the use of antibiotics. Lack of access to effective antibiotics contributes to reductions in life expectancy (see, for example, Nugent R et al. 2010) so could we simply calculate a sustainable level of global antibiotic usage per capita and multiply by population to give a 'fair' share per country (Dwyer 2009)?

There are data on the outpatient use of antibiotics in European countries (European Surveillance of Antibiotic Consumption Centre 2009) and this can be correlated with life expectancy. Life expectancy is very similar across the majority of countries in Western Europe, yet the use of antibiotics varies widely between European countries so that Italy and France use far more antibiotics per capita than Germany, the UK or Holland. This result suggests that there may be differences in the efficiency with which antibiotics are used to improve life expectancy across the nations of Europe, but are France and Italy also using an unjust share of effective treatments for bacterial infection? We cannot judge whether the use of antibiotics in a country is unfair without information on the contribution that the use of antibiotics makes to health or the context and reasons for antibiotics being used. Countries that use more antibiotics per capita may carry a larger burden of bacterial infections.

Constraining the use of antibiotics without taking account of need might place considerable burdens on those communities with the greatest need, stifle developments and potentially have serious adverse consequences through the spread of infection. We need to compare like with like cases to see if these countries are taking an unjust share of the limited resource that is antibiotics. We need to agree criteria for the use of antibiotics. Couper (1997) makes six recommendations to support the control of antibiotic resistance, and these include improving the availability of information and guidelines on the use of antibiotics, improved surveillance of drug resistance, regulation and assurance of drug quality, improvements in the education of prescribers and public, control of (inappropriate) promotional activities (by drug companies) and the encouragement of research for new antibiotics. I would add that in addition there should be minimum criteria for the use of antibiotics. The recent Center for Global Development (2010) report 'The race against drug resistance' makes four key recommendations (Nugent *et al*. 2010). The third recommendation is that drug regulation in developing countries should be strengthened. I would argue that a requirement for equal access based on equal need requires international agreement and regulation of antibiotic prescribing across both developed and developing countries.

There are examples of self-sustaining 'common pool resources' (CPR) in different parts of the world on a local level. I am suggesting agreements on an international level. Ostrom has defined some of the conditions required for sustainable 'common pool resources' (Ostrom 1990). These conditions include clearly defined boundaries, simple agreed rules, monitoring systems, and sanctions against non-compliance. We need to decide who should prescribe

antibiotics, simple agreed rules (that cannot reasonably be rejected), monitoring and feedback systems, and sanctions against non-compliance.

6.7 Risks and burdens

I can see no reason why in a developing country the level of additional risk at which antibiotics are used should not be at a comparable level to that in a developed country, in that we are comparing the risks associated with everyday activities – activities which are common across widely differing communities. I am suggesting that a sufficiency of access to effective antibiotics is a requirement of justice, and that the minimal or sufficient level of access should assure that no one carries a substantial risk of irretrievable harm potentially ameliorated by the use of antibiotics.

However there is another substantial consideration, which should be taken in to account and that consideration is the cost of antibiotics. In many poorer countries antibiotics are a significant cost and expending money on antibiotics reduces the availability of resources for other things. It might be that expending resources on food, improved sanitation, or providing safe shelter can save more lives. If numbers count (from a Scanlonian perspective) when the burdens are comparable then if more lives can be saved by avoiding starvation or by vaccination or by improving shelter, compared with improving access to antibiotics, then antibiotics may not be the dominant priority. Nussbaum argues that we should aspire to assure a sufficiency of capabilities across all the dimensions required for a life with human dignity. When there is an insufficiency across a number of dimensions then we may still have to make trade-offs.

6.8 Intra and intergenerational justice

Retaining the functions of antibiotics is a problem for those who are alive today but even more so for those not yet born. Most of the foregoing discussion refers to intra-generational justice. If we compare children in the first five years of life (alive today) in developing countries with the developed countries of Europe or North America then there are considerable differences in access to life-saving antibiotics. For the purposes of this analysis, I take intra-generational distributive justice to require comparisons of individuals from the same generation (eg, 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 (eg, 35-year-old adults born in 1900 and 1970). The availability of effective treatments for infection (antibiotics) is important now and is very likely to be important in the future, so sustainability is important both for inter-generational and intra-generational justice.

6.8.1 Intergenerational justice

Compliance with accepted criteria for the use of antibiotics could be seen as just, but may still be unsustainable for succeeding generations. Quoting Dwyer (2009, p498) – "the good of a relatively long and healthy life expectancy may be connected to harm done to the environment and, indirectly, to other people, nations, or generations". If current patterns of antibiotic use cannot be sustained for future generations then can we describe those current patterns as just? Present generations accrue the benefits of antibiotics and future generations

carry the adverse risks associated with environmental pollution with antibiotic-resistant bacteria. Do we have obligations to future generations (Tremmel 2009)? There are likely to be far more people alive in to the future than are alive at the present time, so can future people reject the principle P6 in favour of a more stringent principle? Future people will almost certainly have comparable burdens associated with infection. If the numbers act as tie-breakers when the burdens are comparable then how can we justify the principle P6?

6.8.2 Justifying the Principle P6 to future generations

Scanlon takes the position that "Contractualism provides no reason for saying that people who do not now exist but will exist in the future have no moral claim on us...the beings whom it is possible to wrong are all those who do, have, or will actually exist" (Scanlon 1998, p187).

There is a difference between no moral claim and an equivalent claim. One way of differentiating harm to present people from harm to future people is through the distinction between harming a specific individual and harming 'people' by altering the conditions under which they are or will be living. If our actions today lead to a diminishment in the availability of effective treatments for infection (effective antibiotics) in the future then we have made future generations worse off. Casper Hare (Hare 2007) differentiates between *de re* (of the thing itself) harm which refers to the state of a specific individual(s) (thing) who/which is made worse off, from *de dicto* (of the word) harm which refers to the state of individual(s) (thing) made worse off. What we do today determines who will be alive tomorrow. So my child who is alive today can be worse off *de re* but a future child can only be worse off *de dicto* (see Hartzell-Nichols 2012, p941). We can make future generations *de dicto* worse off.

"Our actions can be harmful to the people whose existence we causally contribute to, despite the fact that we cannot de re harm them" (Hartzell-Nicol 2012, p943). The time scales over which antibiotic resistance develops incorporate both *de re* and *de dicto* harm. Poor control of antibiotic resistance today threatens *de re* harm. *De dicto* harm is not inevitable because technology may provide novel solutions to prevent adverse consequences from infection. This distinction can be taken to undermine the reasonableness of rejection of the principle P6 by future generations. It is hard (if not impossible) to be sure of the conditions under which people will be living in the future and the degree to which treatment (antibiotic) resistance will blight their lives. This uncertainty undermines the reasonableness of rejection of the principle P6 by future generations.

We can have generic personal reasons for trying to assure the opportunities for future generations, for example reasons can be derived from a sense of empathy or from our relationships and potential relationships with our children and those of others. Scanlon argues that justificatory reasons should be generalisable and apply to anyone in the same position. We are connected with other people in all sorts of direct and indirect ways and these connections have value for most and as such can be considered generalisable. We may conceptualise future people as distinct individuals disconnected from those alive today. The relationship, between mothers and infants exposes this conceptualisation as a misrepresentation. The use of antibiotics today does change which particular neonate is alive tomorrow to the extent that it is hard to see how the future infant/child/adult can complain about de re harm. It is still possible to complain of de re harm to those closely connected to the infant/child/adult when the infant is harmed (when the conditions under which the infant and future adult lives are less able to support their interests than a feasible alternative). We

can *de re* harm their mothers and others who are invested in their wellbeing. It seems to be an unhelpful dichotomy to separate intra-generational and inter-generational justice when it comes to antibiotics and antibiotic resistance because of the overlap of inter-generational interests. So I do not find the de re / de dicto reason the most compelling reason for accepting (rather than rejecting) principle P6 instead of a more stringent alternative.

There is a third and more convincing reason for future generations to accept the principle P6 as opposed to a more stringent principle. Those alive today and those alive tomorrow are both threatened by the spectre of treatment resistant infection. Perhaps the strongest reason for future generations to accept (and not reject) the principle P6 is that each generation will have future generations. Rejecting a principle of use of antibiotics such as P6 imposes substantial burdens on *every* generation until the time when there will be no more generations – at which time the problem of intergenerational justice becomes irrelevant.

6.8.3 The tension between 'just' use of antibiotics and sustainability

At the present time there is a paucity of new antibiotics and a burgeoning problem with resistance to existing antibiotics, so potentially from this point onwards each subsequent generation may be worse off than the previous one with respect to the treatment of bacterial infections. If we constrain antibiotic use to the extent that antibiotic effectiveness is sustained, then treatment of those alive today will be compromised, if we do not then in the absence of new antibiotics future generations may be blighted by untreatable infections. We all have (present and future) an interest in rejecting the use of antibiotics for the treatment of short-term reductions in capability (P2), or for conditions with inevitable outcomes (that will not be

substantially ameliorated by antibiotics) (P3), or to satisfy preferences (without evidence that use will prevent harm) (P4), or for conditions that don't respond to antibiotics such as viral coughs and colds (P5) (see previous chapter). This rejection comes from the perspective of anyone who does or will need effective antibiotics to prevent irretrievable adverse consequences, and whose outcomes may be prejudiced as a consequence of antibiotic (treatment) resistant forms of infection. Modern medicine is using antibiotics at a level that threatens their effective use by future generations. However, there is an irreducible level of the use of antibiotics. Below that level patient outcomes will suffer, and there are good reasons (both egalitarian and consequentialist as Selgelid (2007) has argued – see above) for not trading off morbidity and mortality of present generations for the sake of conserving antibiotic functions for future generations.

Our responsibilities to ensure that future generations have access to effective treatments for infection requires that we take steps to conserve the functions of antibiotics while not prejudicing outcomes for patients at present. Allowing antibiotic prescribing without the fulfilment of minimum criteria is an abrogation of our responsibilities to future generations. We do not know when new treatments (as effective as antibiotics) will be available to treat bacterial infections, and it is in large part because of this uncertainty that we have reason (at this present time) to be cautious in the use of antibiotics. On the other hand, progress continues - justice as intergenerational 'equality' is not an option because each generation starts from a different place. Each generation inherits innovations and inventions (Tremmel 2009). Succeeding generations may have less access to fossil fuel sources of energy than we have, but will probably be able to utilise a wider range of energy sources as a consequence of technological progress. We do not know if this inequality will work in favour of succeeding

generations with respect to the development of new antibiotics. Tremmel argues that "Intergenerational justice has been achieved if the opportunities of the average member of the next generation to fulfil his needs are better than those of the average member of the preceding generation". If we are to fulfil this requirement of intergenerational justice then we will need to invest in research aimed at developing new treatments and preventive strategies for bacterial diseases. The current market model of drug development and marketing encourages high levels of use of new antibiotics while within patent protection. This model may need adjustment so that pharmaceutical companies are encouraged to see antibiotic development as a long-term investment and rewards adjusted accordingly (Morel & Mossialos 2010).

6.9 The insufficiency of antibiotic prescribing principles

As I hope is clear from the foregoing discussion principles governing individual prescribing decisions are insufficient in themselves if we want to sustain the effectiveness of antibiotics. The potential for poverty, overcrowding, and malnutrition to contribute to a catastrophic spread of treatment (antibiotic) resistant infectious disease illustrates why justice requires more than fairness in the use of antibiotics (assuring the capabilities to be healthy and to live a full life) but also control of the other determinants of the spread of disease (clean water, adequate nutrition, shelter, education). There are many 'goods' in addition to antibiotics, which contribute to infection and the consequences of infection.

There are ways in which political and distributive justice at a population level interacts with decisions at a local level. I have argued that human use of antibiotics is (generally) an

intervention that is used to prevent potentially irretrievable harm. Many determinants of infectious disease susceptibility (and therefore the frequency with which infectious disease threatens harm) are the same as those that determine the spread of treatment (antibiotic-resistant) forms of infection. How should we take account of these determinants of the spread of infectious disease? If we could prevent people from getting disease in the first place then clearly that is a better option than spending the same money on antibiotics. These determinants of the epidemiology of infectious diseases are to a considerable extent determined by the justice of the distribution of many goods including some that are relatively distant determinants of health (by comparison with access to antibiotics) such as education, and housing. A list of essential capabilities that are required to assure a life with human dignity such as that provided by Nussbaum (see Nussbaum 2006, Chapter 2) describes a range of goods – many of which directly or indirectly contribute to the control of the spread of infectious diseases (and treatment resistant forms). For example the fulfilment of educational and shelter needs requires that there are social and political institutions that are responsive to the needs of a population.

The pressing problem with antibiotic resistance adds weight to those who argue for basic entitlements across a range of dimensions of wellbeing (Faden & Powers 2006; Sen 1993; Nussbaum 2006). Faden & Powers (2006) reject the idea that justice with respect to the distribution of health opportunities can be separated from other dimensions of wellbeing (Faden & Powers 2006, p3). They also argue "that empirical judgements of how various inequalities affect one another in concrete circumstances are ineliminable moral data" (Faden & Powers 2006, p5). The theory of justice based on capabilities proposed by Nussbaum (2006) bases justice on a requirement for core entitlements (capabilities). These entitlements

are plural, mutually advantageous and outcome orientated. These entitlements require sufficiency across the range of chosen capabilities - sufficient for 'a life worthy of human dignity'. "It then seeks political procedures (a constitution, various allocations of powers, a certain type of economic system) that will achieve that result as nearly as possible" (Nussbaum 2006, p82). Controlling antibiotic resistance requires more than redistribution or reduction in the overall use of antibiotics. The control of antibiotic resistance requires that we address the determinants of infectious disease transmission as well as the provision of antibiotics.

6.10 Precautions

Scanlon emphasises the importance of probabilities in determining the degree of effort that we make to control risks. "The probability that a form of conduct will cause harm can be relevant not as a factor diminishing the "complaint" of the affected parties (discounting the harm by the likelihood of their suffering it) but rather as an indicator of the care that the agent has to take to avoid causing harm". Scanlon states that ".. the cost of avoiding all behaviour that involves risk of harm would be unacceptable. Our idea of "reasonable precautions" defines the level of care that we think can be demanded: a principle that demanded more than this would be too confining, and could reasonably be rejected on that ground" (Scanlon 1998, p209 & p235-6). The emphasis on reasons allows the inclusion of morally salient considerations such as responsibility and fairness (Scanlon 1998, p243). "Responsibility of an agent for wrongful conduct, responsibility for creating a situation that gives reason to break a promise, responsibility for engaging in risky conduct that leads to harm and responsibility for misfortune that puts one in need of aid" (Scanlon 1998, p244) are all morally salient

considerations. It is hard to see how many (if not nearly all) of those with infections whose outcome can be substantially improved by the use of antibiotics can be deemed responsible for the infection or for a lack of access to antibiotics.

From Scanlon's perspective the risk of an adverse consequence determines the precautions that we should take. What happens if there is a high level of risk of infection and of the spread of treatment resistant forms of infection and we cannot take precautions to control the risk of spread of treatment resistant infection(s) at a level justified by the level of risk? Under adverse socio-economic conditions (when we believe that antibiotics will rapidly become ineffective) then what should our attitude be to the use of antibiotics? When an analogy is drawn between global warming and antibiotic resistance there is an important difference between these two phenomena. The global warming / CO_2 analogy lacks the prevention of spread dimension – the infectious nature of antibiotic resistant microbes is not captured by the global warming analogy. We can limit global pollution with antibiotic resistant microbes not just by interfering with the causal chain of production but also by interfering with transmission pathways. This is perhaps one of the most striking aspects of antibiotic resistance.

In developed countries much more emphasis has gone in to trying to control the spread of antibiotic resistance particularly in institutional contexts (see chapter 4 of this thesis). However even in institutional contexts much more could be done, for example in Neonatal Intensive Care Units (NICUs) in the UK. The broad range of risks from infection to the well being of infants and the consequences both for individuals and society of failing to constrain avoidable infection requires that we should do what we can to minimize the risk of preventable infection in this vulnerable population. Suboptimal levels of staffing and

infrastructure are risk factors for increased mortality in NICUs, according to the UK Neonatal Staffing Group Study UK (Neonatal Staffing Study Group 2002). One way in which staff shortages contribute to an increased risk of death is through the increase in risk of avoidable infection. Staffing and infrastructure in NICUs, even in affluent countries, may be below recommended standards (British Association of Perinatal Medicine 2001). It is striking that, in the United Kingdom, only 3.8% of NICUs are achieving national standards for nursing staff working in the NICU (BLISS 2010), so even in developed countries we could do more to control the risks of spread of antibiotic-resistant microbes.

6.11 Priority to antibiotics, or Public Health

If we take the case of a 3-year old child with pneumonia living in conditions, which facilitate the spread of antibiotic-resistant forms of infection – what attitude should we have towards the use of antibiotics? If we cannot control the risks of spread of treatment resistant form of infection perhaps because of overcrowding or other social factors then what should we do about the use of antibiotics? Should use of antibiotics be restricted to contexts that can achieve a certain level of control of antibiotic resistance? Should antibiotics be used without minimum controls on the dissemination of antibiotic resistant microbes? In a world where many live in overcrowded conditions with poor sanitation there would seem to be even more reason to reject many of the criteria for the use of antibiotics (P2-5) otherwise the strategy of use will become rapidly counter-productive. We would seem to have a number of choices. These choices include increasing the constraints on the use of antibiotics with declining socio-economic conditions, and increasing the priority given to assuring minimal living standards. The latter is likely to be a much more substantial contributor to improved outcomes in the

longer term than can be achieved by antibiotics alone. Do we have to choose between using antibiotics and improving socio-economic conditions?

I have not tried to argue that Scanlon's contractualism provides a theory of justice. One of the characteristics of Scanlon's contractualism is the sensitivity of reasonable rejection (and justification) to context. For Scanlon it is the difference that we can make - rather than how badly off someone is – that determines what we should do (Scanlon 1998, p228). It is hard to reject the use of antibiotics completely because the spread of infectious diseases can itself be curtailed by the use of antibiotics (see earlier discussion), so the difference that we are making by ensuring effective treatment(s) for infection has the potential to provide substantial benefits for us all. We can reasonably reject the tolerance of an insufficiency of standards of shelter, education and nutrition. It is difficult to see how we might reasonably reject a principle that there should be a sufficiency across the dimensions required for a life of human dignity. The control of the spread of infectious diseases (and treatment resistant) forms and justice would both seem to require minimum standards across the dimensions of capabilities.

6.12 Conclusion

At the end of Chapter One I asked what criteria could be used to reject the use of antibiotics in countries or contexts with low levels of public health provision. We do not have to reject the use of antibiotics when minimum standards of public health are unfulfilled, and would be unwise to do so when account is taken of the potential for spread of disease from untreated individuals. Scanlon's contractualism does seem to suggest that we can reject a principle of use of antibiotics when more individuals could be protected from equivalent burdens by

expenditure of equivalent levels of resource on feasible alternative public health interventions (such as the provision of clean water). It is conceivable that in the future low (perhaps even sustainable) levels of antibiotic usage will be seen as a marker of a healthy society - a society with few of the currently prevalent risk factors for infection. Extending the requirements of intra-generational justice to include minimum entitlements across a range of dimensions would do much to curtail the spread of infection and antibiotic resistance. Intra-generational justice understood in this way is less threatening to the sustainability of antibiotic effectiveness and inter-generational justice than justice narrowly construed as a just distribution of antibiotics.

CHAPTER 7

CONCLUDING CHAPTER

Summary

There are few new antibiotics under development. The question that has been the focus of this thesis is - how should we sustain the effectiveness of the antibiotics that we currently have? I suggested that burdens and benefits associated with the use of antibiotic are better expressed using a language of capabilities as opposed to prevalence of disease and economic costs. The need for a social contract to address concerns about antibiotic overuse was suggested by the extended metaphor of the 'Tragedy of the Commons'. I considered the application of Scanlon's contractualism to define principles to determine a) the resource allocation priority that should be given to the control of antibiotic resistance, and b) the use (or not) of antibiotics.

In this concluding chapter I consider how metaphor(s) are (and have been) used to communicate concepts, and analogical reasoning has been used to find solutions to the issues raised by the use of antibiotics (and the control of antibiotic resistance). The war metaphor has encouraged an adversarial approach to microbes, which misrepresents the relationship of humans with microbes. 'Overuse' metaphors overlook the positive message that we can do a lot to control the spread of antibiotic resistant microbes. The use of metaphor to communicate concepts, and the use of analogical reasoning to identify strategies, both have benefits and limitations. The values that are implicit in the metaphors used to describe the human relationship with microbes, and the ethical implications of specific analogies should be made

explicit. If we aspire to constructive communication and dialogue, and effective problem solving, then we need new metaphors.

7.1 Sustaining the effectiveness of antibiotics: two approaches

When there are few new antibiotics under development, how should we sustain the effectiveness of those that we currently have? In this thesis I considered two approaches. One approach considered was to place constraints on the use of antibiotics. Each instance of use makes some contribution (albeit usually small) to the burden of treatment failure(s) (that comes from selecting antibiotic resistant microbes). Another approach that was considered was the control of the spread of antibiotic resistant microbes. There is tension between these two approaches. These tensions extend beyond the narrow scope of health.

Health is not the only consideration when it comes to infectious disease(s). Infection (particularly treatment resistant forms) can also lead to the imposition of contact precautions, which can constrain a broad range of individual freedoms (and therefore capabilities). Social consequences of infection for individuals, groups and institutions include stigmatisation, fear, blame and shame. I suggested that the burdens and benefits associated with the use of antibiotics are better expressed using the language of capabilities as opposed to measures of antibiotic utilisation, prevalence or incidence of disease, or economic costs.

The achievement of a sufficiency of capability for every individual across the range of dimensions is a worthy objective, however when resources are constrained it may not be possible to assure the capability status of everyone. Preventing infection of an individual or

group reduces the availability of resources to support treatment options for others. When use of antibiotics for one or more individuals increases the risks of treatment resistant infection for others then we have to be able to decide which threats to capabilities should be prioritised. When the decisions that we make require capability trade-offs between individuals already at or below capability thresholds (as might be the case in a healthcare institutional context) then we still require a decision method to decide priorities.

Hardin (1968) used the extended metaphor of the 'Tragedy of the Commons' to illustrate how self-interest can destroy a common good such as an animal grazing pasture. He suggested that we can sustain the utility of a common good such as a grazing pasture only if we have a social agreement that is widely acceptable, and that the majority of individuals will abide by. This social agreement would constrain the use of the grazing land and prevent destruction by overuse. The 'Tragedy of the Commons' has much in common with the current situation with antibiotics. Sustaining the effectiveness of antibiotics is in all of our interests yet each is motivated to use antibiotics for short-term benefits or to mitigate risks with very low probabilities. Over time if each individual tries to maximise their own individual short-term returns derived from the effectiveness of antibiotics then there will eventually be no effective antibiotics. We can slow the process of replacement of antibiotic sensitive microbes by their antibiotic resistant cousins by constraining the use of antibiotics. I considered the contractualist approach of Thomas Scanlon to principles of agreement. I suggested that a principle that could not reasonably be rejected is the principle of use of antibiotics to prevent an irretrievable loss of capabilities. Many other contexts of use of antibiotics can be rejected. Only if we agree and abide by principles of use (or not) of antibiotics can we constrain their use and alleviate the recurring concerns that are expressed in the medical literature that much

of the use of antibiotics is ‘inappropriate, or ‘unnecessary’, ‘misuse’, or ‘overuse’, or even ‘abuse’.

A substantial issue that was considered is the level of risk (potentially preventable by the use of antibiotics) that individual antibiotic prescribers and potential recipients are prepared to carry. I suggested that individuals accept a level of risk intrinsic to everyday activities such as risks associated with cooking, and with travel. Use of antibiotics to prevent risks within the range of intrinsic to everyday activities could reasonably be rejected. In practice the levels of acceptable risk associated with use (or not) of antibiotics requires qualitative research as well as philosophical agreement. ‘Expert’ opinion can help with defining levels of risk. There is a need for public engagement to determine how risks potentially ameliorated by antibiotics are understood and which risks are acceptable. Generally risks remain implicit (rather than explicit) in antibiotic treatment guidelines such as those produced by the English National Institute for Clinical Excellence (NICE) and the Infectious Diseases Society of North America (IDSA). Also the level of risk implicit within guidelines can vary substantially for different types of infection without clear justification. I argued that levels of risk implied in antibiotic guidelines should be explicit (and different levels of risk justified).

The analogy of the ‘Tragedy of the Commons’ (TC) is useful when it comes to explaining the need to constrain the use of antibiotics. The search for new antibiotics by pharmaceutical companies can also be compared with the search for new grazing lands. The TC analogy is less useful when we consider the ethical conflicts that arise with the second strategy for sustaining the effectiveness of our current antibiotics, which is the control of the spread of antibiotic resistant microbes, particularly the extent to which we should prioritise control of

antibiotic resistance alongside alternative uses of equivalent resources. I argued that when we have sufficient information to allow comparison of the consequences of alternative courses of action then we can reasonably reject avoidable irretrievable burdens for some while we continue to utilise resources (that could be used to prevent those burdens) for substantially less burdensome conditions. Arguably in the English National Health Service we still have some way to go to assure that extremely burdensome 'avoidable' harms such as death are avoided (see for example the Mid Staffordshire NHS Foundation Trust Inquiry report 2013).

Nussbaum (2006) advocates assurance of a minimum level of capabilities for each individual rather than maximisation for individuals or groups. Scanlon emphasises the comparability of burdens and benefits. An irretrievable loss of a capability required for a life of human dignity would seem to come pretty high up Scanlon's list of burdens. The capabilities approach adds something to Scanlon's contractualism by specifying dimensions of burdens and benefits. Capabilities capture something that is fundamental to conserving the availability of effective antibiotics, and that is the importance of assuring minimum standards across a range of dimensions. Overcrowded housing, poor education, and inadequate sanitation potentiate both the spread of infection, and the spread of antibiotic resistant forms of infection. Providing antibiotics alone is clearly an insufficient response to treatment resistant infection when there are inadequacies across a range of capability dimensions.

We might also extend the range of burdens and benefits under consideration to include activities outside of the immediate healthcare environment. In a publicly funded system such as the English NHS comparisons of burdens and benefits can be extended across the whole range of publicly funded activities. Nussbaum makes this point when she suggests that we

should not just be trading off health costs against health costs – but also consider trade-offs in other capability dimensions – giving the example of trading-off the driving of Sports Utility Vehicles (SUVs) (Nussbaum 2006, p402) against health. There is no reason to limit Scanlon's emphasis on comparability of burdens and benefits to the healthcare sector. If we do extend the sphere of consideration beyond the boundaries of healthcare institutions then there does seem to be potential to justify considerable investment in preventive (precautionary) actions.

The two strategies that have been considered in this thesis (constraining antibiotic use and control of the spread of antibiotic resistant microbes) are not clearly demarcated. If we cannot control the spread of antibiotic resistant microbes then our existing antibiotics will quickly become ineffective. If we overuse antibiotics then antibiotic resistance will be almost impossible to control. The two strategies are inter-twined. Whether in developing countries where antibiotic costs provide a significant constraint on use or in developed countries where the cost of many types of antibiotic is relatively small constraints on prescribing have to be combined with precautions designed to control the spread of treatment resistant infection. The assurance of basic capabilities requires that both areas become subjects of focus for policy makers. Both aspects need attention if we are to avoid an increasing impact of treatment resistant infection across a diversity of capabilities.

7.2 Does practice we need principles?

The dominant motivation for this thesis was to consider the moral and ethical justification for the allocation of burdens and benefits associated with the use of antibiotics. The focus in the biomedical literature has been on health benefits and burdens associated with the use of

antibiotics. I hope that through this thesis I have made it clear that there are ethical considerations that may still constrain actions even in the face of individual, group or societal benefits. In chapters 4, 5 & 6 I considered some principles derived from Scanlon's contractualism. Should we see these principles as perfect or imperfect duties, or as identifying prima facie obligations that we should respect and comply with unless there are over-riding considerations, or in some other way(s)? I see the principles developed in this thesis as relevant to practice in a number of different ways. They challenge those that prescribe, prescribing practices, and the regulations that govern the use and the users of antibiotics. They provide a basis and justification for policy and practice. Principles allow individual prescribers to step outside of the narrow confines of relationships with individual patients and those close to them, and call attention to wider considerations. Principles provide 'short-hand' rules that can be used in teaching and training. Principles can provide a common standard, and benchmark, against which we can judge fairness in allocation of a scarce resource (effective antibiotics).

The use of antibiotics in those who are dying is controversial (see Chapter 5). Justification for the use of antibiotics even when death is imminent is often placed at the door of relatives – presented as desperate to see that all that can be done to delay death is done. I have argued that the principle P6 cannot be reasonably rejected. This principle states that antibiotics 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. Perhaps a daughter could insist that failure to prescribe antibiotics to a dying mother will cause her (the daughter) irretrievable (psychological) harm. In my view this kind of

response raises questions about the context and relational aspects associated with the circumstances of the dying mother. Does the daughter really understand the implications of use of antibiotics for the mother? Why does the daughter carry such a sense of personal responsibility? What information has been provided? What was the perspective of the healthcare staff? The principle P6 challenges the practice of prescribing antibiotics to dying patients. The avoidance of psychological harm to relatives could conceivably provide a justification for the use of antibiotics, but the principle at the very least demands a level of justification, which extends well beyond the satisfaction of preferences.

7.3 Precaution when the future of antibiotics is uncertain

A substantial issue that has not been considered in depth in this thesis is the uncertainty associated with antibiotics and antibiotic resistance. We don't know the extent to which we can develop new antibiotics or the scale of impact of antibiotic resistance. We don't know if or when a plague of antibiotic (treatment) resistant infection might arise, or new pathways to antimicrobial drug discovery will be found. Currently many of the antibiotic resistant forms of infection arise in hospitals amongst patients who are already debilitated, and are outside of the experience of people in the wider community. The spectre of untreatable infectious disease spreading through the healthy population is also outside of most modern day experience in developed industrialised countries, but would be likely to have catastrophic consequences for complex societies. Should we expend resources when we don't really know how much impact antibiotic resistance will have in the future? To what extent do we take precautions against uncertain risks (risks that cannot yet be quantified)? Antibiotic resistance is an example of a known unknown – we know that we have treatment resistant infection now and will have

(almost certainly) more in the future, but we can't yet estimate their effects. There is (what has been referred to as) an uncertainty paradox – science cannot provide decisive answers yet policy makers appeal to science for certainty (van Asselt & Vos 2006). Policy makers have to decide how much resource to put in to controlling antibiotic resistance when (in resource limited settings) there are always opportunity costs. If and when we ever arrive at a situation where resource utilisation is optimised according to agreed principles (Scanlonian or other) then should we be prepared to continue to invest in prevention to the extent that we forego benefits today in order to provide the resources required to take precautions against potential future and uncertain calamitous outbreaks of treatment (antibiotic) resistant infection?

Per Sandin (Sandin 2007, p108) defines an action as precautionary in the following way -

An action *a* is precautionary with respect to something undesirable U if and only if -

1. *a* is performed with the intention of preventing U
2. the agent does not believe it to be very likely that U will occur if *a* is not performed, and
3. the agent has externally good epistemic reasons (a) for believing that U might occur, (b) for believing that *a* will in fact at least contribute to the prevention of U, and (c) for not believing it to be certain or very likely that U will occur if *a* is not performed.

This definition does not apply to antibiotic resistance in a general sense because antibiotic resistance already occurs and will continue to occur in to the future (point 2 above). The uncertainty that is of concern is the degree to which new forms of treatment resistance will impact on the human condition. If treatment resistance arises in a virulent agent of infection

and at a time when we have no alternative treatment options then there is the potential for a calamity. Expending resources on surveillance, screening of individuals or the environment, decontamination (of the environment, humans or other), vaccination, or research on control methods are precautionary in the way defined by Per Sandin when applied to potentially calamitous events associated with antibiotic resistance.

I am using the term precautionary here to refer to actions taken to prevent something calamitous from happening. A pandemic of treatment resistant infection is a foreseeable risk with uncertain probabilities. Parfit (2011, p161) states that "when the rightness of our acts depends on the goodness of their effects, we ought to try to do, not what would in fact make things go best, but what on the evidence, or given our beliefs, would make things go expectably best". It might be that we can justify taking actions to control antibiotic resistant microbes because those actions will allow a better future, because we do expect that with precautions things will go better. The difficulty is that in a resource limited setting there are inevitable opportunity costs in that taking precautions reduces the availability of resources for other things. My own feeling is that we should be prepared to trade some of the luxuries and potential choices that we do or could have in exchange for the security of assuring the effectiveness of antibiotics. The principles that might determine the extent of these trade-offs, when the future is a very long time and unknown, are the work of another thesis.

7.4 The detrimental impact of the 'War' metaphor

Metaphor is often used to illustrate complex concepts by placing those concepts within the realm of everyday experience. Lakoff & Johnson (1980, p454) suggest that "our ordinary

conceptual system, in terms of which we both think and act, is fundamentally metaphorical in nature", and that whenever we consider a metaphor we ask "What does this metaphor illuminate and what does it obscure about relationships?" If metaphors do determine how we think and act then it is worth considering in more detail the appropriateness or otherwise of the metaphors that have been used in the context of use of antibiotics and antibiotic resistance.

Hardin uses an extended metaphor to illustrate concepts that are integral to understanding the human relationship with common goods. Metaphors have considerable power and utility as communicative devices but also can mislead. "Every age has its own unique view of nature, its own interpretation of what the world is all about. Knowing a civilization's concept of Nature is tantamount to knowing how a civilization thinks and acts" (Rifkin 1983). "Metaphors are important linguistic devices. They are one of our primary means of conceptualizing the world. Their power is derived from their ability to assimilate new experiences to familiar patterns of perception; to project one knowledge domain onto another so as to allow the newer or abstract domain of experience to be understood in terms of the other and more concrete one" (Verhagen 2008, p2). However "it is necessary to critically analyze metaphors in order to unmask what they hide and to discover the interests that are at stake in the use of particular metaphors" (p2).

There is a human tendency to ascribe metaphors to disease (see Sontag 1988). The metaphors that we use can be as damaging as the disease! The 'war' metaphor has been used to explain the relationship of humans with the microbial kingdom. Metaphor has utility as a communicative tool, but at the same time as explaining concepts in terms of everyday experience, metaphor entangles those concepts with all of the baggage associated with the

everyday experience used in the comparison. A metaphor of war has frequently been used to describe the human relationship with microbes.

Annas suggests that many forms of behaviour are tolerated during times of war when intolerable at other times (Annas 2006, p359). “Fear makes it difficult to distinguish fact from fiction, reality from fantasy, and truth from lies, all of which means that our initial reactions are likely to be overreactions that we will ultimately come to regret” (p359). Annas asks if we must exchange core ethical values, such as respect for autonomy, for safety in the fight against bioterrorism (p363), gives examples of the mistreatment of political prisoners, draconian emergency bioterrorism laws, and the provision of anthrax vaccine to civilians without clear evidence of safety. The war metaphor stigmatises infected (victims), and potentially justifies mistreatment of individuals. War implies a certain form of adversarial relationship. The metaphor describes a state of affairs but also tells us something about what we are allowed to do and how we should see the rightness (or wrongness) of certain courses of action. In 2005 the Institute of Medicine of the US National Academy of Science (Institute of Medicine of the US National Academy of Science 2005) held a forum entitled ‘Ending the War Metaphor’. The summary of the meeting calls for “A new paradigm …that incorporates a more detailed and realistic picture of the dynamic interactions among and between host organisms..” and the “crafting of a new metaphor” (p2). The ‘war’ metaphor has encouraged overuse of antibiotics by identifying microbes as belligerent and threatening.

“At best, the war metaphor is a limiting mental shortcut that distracts from abundant opportunities to improve human and animal health. At worst, it represents a dangerous influence on disease control practices that have accelerated the development of antimicrobial resistance among human and animal pathogens… Put simply the war metaphor must be

replaced or, as comically (yet ominously) predicted on the epigraph of this summary, the bugs will win" (Institute of Medicine of the US National Academy of Science Forum 2005, p27).

De Grandis (2011) considers the analogy between outbreaks of severe infectious diseases and war. He suggests that war is not a useful analogy when it comes to deciding how to manage carriers of serious infectious diseases in that the metaphor encourages attitudes, which are counter-productive and potentially damaging. He suggests that the metaphor may be useful in other ways and specifically through an analogy with careless talk in times of war. Misuse of antibiotics provides strategic information to microbes that can be used to their advantage and this analogy is useful both at a theoretical level and a practical level in telling doctors and patients why they should not misuse antibiotics. He suggests that there is analogy between "citizens who – without malice – fail to observe necessary precautions in handling delicate information during wartime and patients or doctors who – without any ill-intention – fail to use appropriately antimicrobial drugs or treatments" (p6). In practice it might be possible to develop this interpretation of the war metaphor, but there is not much evidence that this is the way that the war metaphor is currently understood. For example Nerlich & James list over 60 metaphors of war used by scientists and journalists between 2005 and 2007 (Nerlich & James 2009). This plethora of war metaphors persists despite the calls for a new metaphor. They suggest that the benefits of this type of metaphor are that it raises the profile and public awareness of the importance of this problem, and may spur politicians to act. They suggest that there are also disadvantages with this metaphor. Disadvantages include the widely held perception that apocalypse is something inevitable whatever we do. Also they suggest that "The results achieved by early warnings framed in terms of fear might be similar to those

achieved by early promises framed in terms of hope – if unfulfilled they can both lead to public cynicism, loss of trust and engagement" (Nerlich & James 2009, p9).

There is evidence that the war metaphor is factually inaccurate when it comes to our relationship with microbes. Most of the hundreds of types of microbe that colonise the human body contribute more to health than to disease. Damage to human microbial communities can have far-reaching consequences for our health and wellbeing (for a recent review see Nicholson *et al*. 2012). The war metaphor provides a representation of the relationship between microbes and humans that overlooks the subtlety, complexity and mutual benefit of the relationship.The war metaphor allows us to overlook actions and attitudes, which would otherwise require justification. Metaphors can be inaccurate in the way that they illustrate the empirical and ethical dimensions of the relationship between two things, they can lead to damaging perceptions and attitudes, and they can also mislead our moral compass so that we overlook the ethical aspects of the situation that we are using the metaphor to illustrate. The war metaphor encourages forms of behaviour, which might otherwise be at worst unacceptable but perhaps more frequently allows questionable behaviour to remain unquestioned.

7.5 Argument from analogy

Metaphor can be used to communicate but comparisons between different phenomena can also have utility in scientific enquiry for example through the use of analogical reasoning. Argument from analogy is a presumption – a form of informal logical fallacy. Despite the obvious flaws in analogical reasoning this form of reasoning is widely used because of certain

beneficial features (Rescher 2006). Presumptions have a utility in facilitating some human endeavour and in the achievement of some objective(s) (Rescher 2006, p55). We accept a putative fact until "concrete evidential counter-indications come in to view" (Rescher 2006, p4). The important thing about a presumption is that it is a defeasible proposition. We presume something until our experience (experiment, observation) requires that we re-evaluate the presumption. A presumption is best described as a 'truth estimate' (Rescher 2006, p65). Presumptions are essentially pragmatic so for example the analogy between antibiotic resistance and global warming allows efficient communication of concepts that might otherwise take a lot of time to get across, and also allows the identification of potential solutions. These solutions can be subject to further analysis and testing. Argument from analogy can make a difference by providing potentially fruitful lines for investigation and research, delimiting the range of actions, allowing identification of the 'right' kinds of methods of investigation, in addition to allowing complex concepts to be communicated.

The extended metaphor used by Hardin encourages a search for a solution to the overuse of antibiotics through a search for principles that we can all agree to abide by. Inferences can be developed based on the assumption that if two things share some features then they may share other features including common solutions to the problems that they represent. We use analogy to help with predicting the behaviour of a 'new' infectious disease by comparison with another similar type of disease. We also use analogy to help to find solutions – using the success of previous strategies for analogous problems as a guide to potential strategies for new problems. Argument from analogy may have an important role in decision-making under conditions of uncertainty such as during the early years of the BSE crisis (Cummings 2009). Analogies can also be used to illustrate the range of potential ethical dimensions arising in an

area of practice. Emerging infectious diseases are associated with uncertainties such as modes of transmission, persistence, reservoirs and human health implications. Examples that have received widespread attention include BSE, avian and swine influenza, Human Immunodeficiency Virus, and Systemic Adult Respiratory Syndrome. Despite the fallacy of this form of argument there are benefits from the use of analogy. These include the capacity to justify action(s) under conditions of uncertainty and to generate avenues for scientific investigation.

When a new infectious disease is recognised then it may be necessary to take actions before there is relevant information on transmission pathways, the effectiveness of treatments, or the outcomes for those who are infected. "Early action is required, but decisions about action must be made when the threat is only modest – and consequently, they involve a trade-off between the comparatively small, but nearly certain, harm that an intervention will cause … and the uncertain probability of much greater harm from a widespread outbreak. This combination of urgency, uncertainty and the costs of interventions makes the effort to control infectious diseases especially difficult" (Lipsitch *et al*. 2009). Arguments from analogy are used in many different ways by epidemiologists and infectious diseases specialists. So for example Sedgwick in 1868 talks of "the indirect aid afforded by analogy in the investigation of disease may be said to correspond with that of a reflecting mirror, in which there is presented a more or less clearly defined image of what would otherwise be obscure or hid; and, therefore, as an assistance towards lessening the difficulty which attends the investigation (of cholera).." (Sedgwick 1868, p1). More recently Plant describes recent experience with trying to investigate and control outbreaks of life-threatening disease and describes how "..people look for analogues. For example, we considered that the SARS

organism was most likely a virus and spread predominantly via the respiratory route. Hence we acted as though that was true, meaning that infection control, patient management, patient isolation and so on were all treated as though the (assumed) virus causing SARS was similar to other viruses" (Plant 2009, p49). Verghese (2004) suggests that "The handmaiden to every outbreak of infectious disease is the metaphor it carries with it – a metaphor that has much to do with the way society will view and respond to an epidemic" (p932). Even the word 'outbreak' is itself a metaphor. Something has broken out of control. 'Outbreak' suggests that something that we want controlled is out of control.

Not only is presumption used in epidemiology it may also be a substantial determinant of individual patient management so for example patients presenting to emergency departments with similar symptoms and signs to those found in a patient with a diagnosis of serious infection are treated as though they have serious infectious disease (even though a significant proportion ultimately have other diagnoses) (Heffner *et al*. 2010). This is because infection is a relatively treatable process if treated early but not so if treatment is delayed. Analogy may be useful in allowing insights in to the pathogenesis of disease. Beharroch & Osyntov imply that infections are analogous with cancer and that this analogy may be useful in furthering understanding of these two states (Beharroch & Osyntov 2012). The Department of Veterans Affairs in the US presumes a military service connection for certain infectious diseases when specific conditions of association have been met. This presumption is important in the determination of who will receive compensation for military service related injuries (US Department of Veterans Affairs 2012). In table 7.1 list some of the ways that analogical reasoning is used in the response to infectious diseases -

Table 7.1 Use of Analogy by Infectious Diseases specialists

Analogy is used to -
Communicate the importance, significance or relevance of a problem
Identify which types of problem should be taken seriously before we really know
Identify potential actions under conditions of uncertainty
Justify actions under conditions of uncertainty
Identify avenues for scientific research
Identify plausible epidemiological hypotheses
Allow plausible predictions of future consequences

Analogical reasoning allows action under conditions of uncertainty, and can help to show how we might best proceed when we don't have enough information. Presumption licences investigators to pursue courses of action even under conditions of uncertainty (Cummings 2009, p60-62). Bovine Spongiform Encephalopathy was and still is thought to share similar characteristics with the sheep disease scrapie. The analogy with scrapie allowed "many productive lines of inquiry for scientists to pursue when little was known about BSE" (Cummings 2009, p183). Unfortunately these forms of reasoning can also be used to stifle enquiry (Cummings 2009, p186). "It is one of the tragedies of the BSE affair that it did not take place in every situation in which presumptions based on ignorance and analogical arguments were shown to be inadequate" (Cummings 2009, p184). Presumptions such as that BSE would not transmit to humans because scrapie didn't transmit to humans became unassailable theses. The presumption that BSE would not transmit to humans continued against a rising tide of contrary evidence (Cummings 2009, p185-6) – leading in the longer term to public distrust of scientific pronouncements.

Global warming has been used as an analogy for antibiotic resistance. “Increasing resistance to antimicrobial resistance is health care’s version of global warming” (Smith 1998). Excessive use of fossil fuels is likened to overuse of antibiotics in both leading to potentially catastrophic consequences. However, parallels between antibiotic resistance and other forms of environmental pollution do not justify an argument for antibiotic treaties akin to those developed to control carbon dioxide or protect the ozone layer (Anomaly 2010). Sources of energy and aerosol propellants can be changed but the functions of antibiotics cannot be replaced at the present time. Limiting carbon dioxide production by individuals is unlikely to damage their health irretrievably, whereas limiting the use of antibiotics for serious bacterial infection almost certainly will have significant health consequences for those deprived of access to antibiotics and potentially for all of us through the uncontrolled spread of infection. The global warming analogy also misses something very important about antibiotic resistant microbes, which is the multiplicative element. The numbers of antibiotic resistant forms can increase in an exponential fashion as they spread from host to host, but this is not inevitable and we can take actions to control the spread of resistant microbes once we recognise their presence. This is a positive message overlooked by the adversarial nature and catastrophic discourse of the war metaphor, but also overlooked by analogical reasoning based on over-interpretation of metaphors such as that of global warming.

7.6 Microbes are us

Larson (2011) argues that sustainability requires that we “broaden the usual ethical requirements of science, which extend mainly to commitments to truth telling and avoiding

plagiarism and undue bias" (p218). "Metaphor is a key element in scientific inquiry because it enables us not only to understand one thing in terms of another but also to think of an abstraction in terms of something more concrete and everyday" (p6), but that the ethical requirements of scientists should also include responsibilities for the metaphors that are used to communicate concepts. "When I use a metaphor, I will take into account how metaphors can cause harm and thus seek ones that seem least likely to do so" (p221). Scientists frequently use metaphors when they are advocating for resources. To some extent the use of the war metaphor by scientists and by pharmaceutical companies can be seen as self-serving – designed to promote fear and anxiety and encourage investment in research, development and marketing of new (antibiotic) treatment. Larson suggests that there should be a code of practice for advocacy by metaphor. Scientists must be prepared to justify choice(s) of analogy. He argues that metaphors have to be 'fit for purpose'. We should consider how the metaphor operates in different contexts, and we should consider the relevant similarities and differences both at the empirical and ethical levels. "Every metaphor both highlights and hides, and thus, as we might expect, it has both strengths and weaknesses" (p154). Fear appeals (perhaps linked with the war metaphor) "may simply not work. They may be maladaptive if they lead to apathy and confusion rather than action" (p170). "When I use a metaphor, I will take into account how metaphors can cause harm and thus seek ones that seem least likely to do so" (p221).

Metaphors and use of analogical reasoning can provide great benefits but are also associated with considerable danger. There may be relevant empirical and ethical dissimilarities in the analogies that we use, and these can be overlooked unless we are careful. Metaphors describing over-utilisation of a common good (antibiotics) such as the Tragedy of the

Commons help to point in the direction of a social contract, but at the same time overlook important aspects of the epidemiology of antibiotic resistance such as the potential for control of the spread of antibiotic resistance. Metaphors of war hide the ethical import of the war context in which a wide range of values and principles are tolerated that would not be tolerated at other times. Even though the human body contains vastly more bacterial than human cells the microbial world is largely invisible to us. In many respects we are as much microbes in a physiological and metabolic sense as we are humans. Recent studies have linked changes in the microbial flora of the bowel of humans to the development of atherosclerosis, inflammatory bowel disease, changes in body fat, and drug metabolism (for overview see Gordon *et al.* 2003; Nicholson *et al.* 2012). There is even evidence of bowel flora effects on emotional and psychological states, and the central nervous system from animal studies (Bravo *et al.* 2011). We haven't yet got to the court plea of "I'm sorry, sir, my microbes made me do it" but maybe it will come (Judson 2009).

There have been few studies of lay perceptions of antibiotic resistance but one study suggests that patients predominantly view antibiotic resistance as a property of the human body (and not of microbes), while at the same time attributing antibiotic resistance to over-use of antibiotics (Brookes-Howell *et al*. 2012). The lay perception described in the Brookes-Howell study suggests that perhaps for many there is already recognition that treatment (antibiotic) resistant microbes arise from within. Tending a household garden requires that we encourage some plants to grow and discourage others. We fertilise some plants and weed out others. We encourage plants to grow in conditions that keep them healthy and that discourage the spread of pests and parasites. Weeds will spread from an untended garden to the next and the next. We have a relationship with a garden and an interest in having the 'right sort of garden'.

Even a garden metaphor does not bring the relationship of humans with microbes close enough together. 'Microbes 'R' Us' (Judson 2009) draws attention to the closeness of our relationship with microbes and perhaps isn't so distant from the lay perception described by Brookes-Howell. Maybe Microbes 'R' Us is a seed (of a metaphor) that just requires a bit more fertilisation?

7.7 Conclusions

At the end of Chapter One I asked which metaphors are appropriate or inappropriate to communicate the human relationship with microbes. Metaphors have considerable power in influencing the way that we understand and conceptualise the world in which we live. The use of metaphor to communicate concepts, and the use of analogical reasoning to identify strategies, both have benefits and limitations. The war metaphor has encouraged an adversarial approach to microbes, which misrepresents the relationship of humans with microbes. 'Overuse' metaphors overlook the positive message that we can do a lot to control the spread of antibiotic resistant microbes. If we aspire to constructive communication and dialogue, and effective problem solving, then we need metaphors which express our inter-dependency with the microbial world.

REFERENCES

Abad, C., Fearday, A., Safdar, N. (2010). 'Adverse effects of isolation in hospitalised patients a systematic review'. *Journal of Hospital Infection* **76**, 97-102.

Advisory Committee on Antibiotic Resistance and Healthcare Associated Infection (ARHCAI). (2012). Antibiotic Stewardship: "Start Smart – Then Focus". Available at http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131062 (accessed September 2012)

Aiello, A.E., King, N.B., Foxman, B. (2006). 'Ethical conflicts in public health research and practice: antimicrobial resistance and the ethics of drug development'. *American Journal of Public Health* **96**, 1910-1914.

Alkire, S. (2005). *Valuing Freedoms: Sen's Capability Approach and Poverty Reduction*. Oxford: Oxford University Press.

Allegranzi, B., Bagheri Nejad, S., Combescure, C., Graafmans, W., Attar, H., Donaldson, L., Pittet, D. (2011). 'Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis.' *Lancet* **377**(9761), 228-241.

American Medical Association. (2012). *Code of Medical Ethics: Current Opinions with Annotations, 2012-2013*. Chicago: American Medical Association.

Anand, S., Peter, F., Sen, A. (eds) (2006). *Public Health, Ethics and Equity*. Oxford: Oxford University Press.

Andersson, D.I., Hughes, D. (2011). 'Persistence of antibiotic resistance in bacterial populations'. *FEMS Microbiology Reviews* **35**(5), 901-911.

Annas, GJ. (2006). 'Bioethics and Bioterrorism'. In Selgelid, M.J., Battin, M.P, Smith, C.B. (eds). *Ethics and Infectious Disease*. Oxford: Blackwell.

Anomaly, J. (2010). 'Combating resistance: the case for a global antibiotics treaty'. *Public Health Ethics* **3**,13-22.

Association for Professionals in Infection Control and Epidemiology (APIC). (2008). 'Targeting zero healthcare associated infections.' APIC Position Statement. Available at www.apic.org (accessed December 2012).

Arason, V.A., Sigurdsson, J.A., Erlendsdottir, H., Gudmundsson, S., Kristinsson, K.G. (2006). 'The role of antimicrobial use in the epidemiology of resistant pneumococci: A 10-year follow up'. *Microbial Drug Resistance* **12**, 169-176.

Arneson R J. (2006). 'Distributive Justice and Basic Capabilities Equality: 'Good enough' is not good enough'. In Kaufman, A (ed). *Capabilities Equality Basic Issues and Problems.* Routledge Innovations in Political Theory (volume 18). Oxford: Routledge.

Ashford, E. (2003). 'The demandingness of Scanlon's contractualism'. *Ethics* **113**, 273-302.

Australian Commission on Safety and Quality in Healthcare. (2010). *Charter of Healthcare Rights*. Sidney: Australian Commission on Safety and Quality in Healthcare.

Baquero, F., Coque, T.M., de la Cruz, F. (2011). 'Eco-Evo drugs and strategies: the need for novel tools to fight antibiotic resistance'. *Antimicrobial Agents and Chemotherapy* **55**(8), 3649-3660.

Bayer, R. (2007). 'The continuing tensions between individual rights and public health. Talking point on public health versus civil liberties'. *European Molecular Biology Organization Report* **8**, 1099-1103.

Beauchamp, T., Faden, R.R. (1979). 'The Right to Health and the Right to Health Care'. *Journal of Medicine and Philosophy* **4**, 118-131.

Beck, U. (1999). *World Risk Society*, Malden, MA: Polity Press.

Beharroch, D., Osyntov, L (2012). 'Infectious Diseases are analogous with cancer. Hypothesis and implications'. *Journal of Cancer* **3**, 117-121.

BLISS. (2010). 'Special delivery or second class: are we failing special care babies in the UK?' Available at: http://www.bliss.org.uk/pdfs/babyreport_updateweb.pdf (accessed June 2012)

Boyle, J.M. (1980). 'Toward understanding the principle of double effect.' *Ethics* **90**, 527-538.

Bravo, J.A., Forsythe, P, Chew, M.V., Escaravage, E., Savignac, H., M., Dinan, T., G., Bienenstock, L., Cryan, J.F. (2011). 'Ingestion of *Lactobacillus* strain regulates emotional behaviour and central GABA receptor expression in a mouse via the vagus nerve.' *Proceedings of the National Academies of Science* **108**, 16050-16055

British Association of Perinatal Medicine. (2001). *Standards for hospitals providing neonatal intensive and high dependency care* (2nd edition). London: British Association of Perinatal Medicine.

Brock, D. (2006). 'Ethical Issues in the Use of Cost Effectiveness Analysis for the Prioritization of Health Care Resources'. In Anand, S., Peter, F., Sen, A. (eds). *Public Health, Ethics, and Equity*. Oxford: Oxford University Press, chapter 10.

Brookes-Howell, L., Elwyn, G., Hood, K., Wood, F., Cooper, L., Goosens, H., Leven, M., Butler, C.C. (2012). 'The body gets used to them: patients' interpretations of antibiotic resistance and the implications for containment strategies'. *Journal of General Internal Medicine* **27**,766-772. DOI: 19.1007/s11606-011-1916-1

Bryan, C.S., Call, T.J., Elliott, K.C. (2007). 'The Ethics of Infection Control: Philosophical Frameworks'. *Infection Control and Hospital Epidemiology* **28,** 1077-1084.

Burnett, E., Lee, K., Rushmer, R., Ellis, M., Noble, M., Davey, P. (2010). 'Healthcare-associated infection and the patient experience: a qualitative study using patient interviews'. *Journal of Hospital Infection* **74**, 42-47.

Buyx, F., Schone-Seifert B. (2011). 'Ethics and effectiveness: rationing healthcare by thresholds of minimum effectiveness'. *British Medical Journal 342*, 531-533.

Cameron, E., Swanson, E. (1992). 'Public health and human rights – the AIDS crisis in South Africa'. *South African Journal on Human Rights* **8**(2), 200-233.

Carapetis, J.R. (2007). 'Rheumatic heart disease in developing countries'. *New England Journal of Medicine* **357**, 439-441.

Clancy, C.M. (2010). 'Getting to zero: New resources aim to reduce health care-associated infections'. *American Journal of Medical Quality* **25**(4), 319-321.

Coast, J. (2004). 'Is economic evaluation in touch with society's health values?' *British Medical Journal* **329**, 1233-1236.

Coast, J., Smith, R., Karcher, A-M., Wilton, P, Millar, M.R. (2002). 'Superbugs II: How should economic evaluation be conducted for interventions which aim to reduce antimicrobial resistance?' *Health Economics* **11**, 637-645.

Coast, J., Smith, R.D., Millar, M.R. (1996). 'Superbugs: should antimicrobial resistance be included as a cost in economic evaluation'. *Health Economics* **5**, 217-226.

Cockell, C.S. (2008). 'Environmental Ethics and Size'. *Ethics and the Environment*' **13**, 23-39.

Cohen, A.L., Calfee, D., Fridkin, S.K., Huang, S.S., Jernigan, J.A., Lautenbach, E., Oriola, S., Ramsey, K.M., Salgado, C.D., Weinstein, R.A., Society for Healthcare Epidemiology of America and the Healthcare Infection Control Practices Advisory Committee. (2008). 'Recommendations for metrics for multrdrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper'. *Infection Control and Hospital Epidemiology* **29**, 901-913.

Cohen, J., Kass, N., Beyrer, C. (2007). 'Human Rights and Public Health Ethics: responding to the global HIV/AIDS pandemic'. In Beyere, C. & Pizer, H.F. (eds). *Public Health and Human Rights: Evidence-based Approaches*. Baltimore: John Hopkins University Press.

Cordery, S. (2012). Clunky maths and unfair fines. *Health Services Journal* http://hsj.co.uk/opinion/columnists/clunky-maths-and-unfair-fines/5049623.article (Accessed October 2012)

Cormican, M., Vellinga, A. (2012). 'Existing classes of antibiotics are probably the best we will ever have'. *British Medical Journal* **344**:e3369 doi: 10.1136/bmj.e3369 p1.

Costelloe, C., Metcalfe, C., Lovering, A., Mant, D., Hay, AD. (2010). 'Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis'. *British Medical Journal* **340**, c2096.

Couper, M.R. (1997). 'Strategies for the rational use of antimicrobials'. *Clinical Infectious Diseases*, **24** (suppl 1), S154-156.

Cummings, L. (2009). 'Emerging Infectious Diseases: coping with uncertainty'. *Argumentation* **23**(2), 171-188.

D'Agata, E., Mitchell, S.L. (2008). 'Patterns of antimicrobial use among nursing home residents with advanced dementia'. *Archives of Internal Medicine* **168**, 357-362.

Dancer , S.J. (2008). 'Considering the introduction of universal MRSA screening'. *Journal of Hospital Infection* **69**: 315-320.

Daneman, N., Low, D.E., McGeer, A., Green, K.A., Fisman, D.N. (2008). 'At the threshold: defining clinically meaningful resistance thresholds for antibiotic choice in community-acquired pneumonia'. *Clinical Infectious Dieases* ***46***, 1132.

Daniels, N. (1985). *Just Health Care*. Cambridge: Cambridge University Press.

Daniels, N. (2007). *Just Health: Meeting Health Needs Fairly*. Cambridge: Cambridge University Press.

Dawson, A., Verweij, M. (2008). 'Public Health Ethics: A Manifesto'. *Public Health Ethics* **1**, 1-2.

Day, H.R., Perencevich, E.N., Harris, A.D., Himelhoch, S.S., Brown, C.H., Gruber-Baldini, A.L., Dotter, E., Morgan, D.J. (2011). 'Do contact precautions cause depression? A two-year study at a tertiary medical centre'. *Journal of Hospital Infection* **79**, 103-107.

De Grandis, G. (2011). 'On the analogy between infectious diseases and war: how to use it and not to use it'. *Public Health Ethics,* doi:10, 1093/phe/phr008.

Department of Health. (2005). *Clean, Safe Care*. Crown Copyright. Available from http://nhschoicestraining.spinningclock.com/index.php?pid=1 (accessed March 2013)

Department of Health. (2010). *The National Health Service Constitution for England*. Crown Copyright.

Department of Health, Social Security, and Public Safety (Northern Ireland). (2010). *Changing the Culture 2010*. Available at http://www.dhsspsni.gov.uk/changing_the_culture.pdf (accessed March 2013)

Department of Health. (2011). *Clinical Guidelines for immunoglobulin use: update to second edition.* Available from http://www.ivig.nhs.uk/documents/dh_129666.pdf (accessed January 2013)

Department for Transport. (2013). 'Reported Road Casualties Great Britain.' *Department for Transport*. Available from https://www.gov.uk/government/publications/reported-road-casualties-great-britain-provisional-estimates-q3-2012

Deshpande, G., Rao, S., Patole, S., Bulsara M. (2010). 'Updated meta-analysis of probiotics for preventing necrotizing enterocolitis in preterm neonates'. *Pediatrics* **125**, 921-930.

Dethlefsen, L., Relman, D.A. (2011). 'Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation'. *Proceedings of the National Academy of Sciences of the USA* **108**, 4554-4561.

Dixon, R., Nussbaum, M. (2011). 'Abortion, Dignity and a Capabilities Approach'. In Baines, B., Barak-Erez, D., Kahana, T. (eds). *Feminist Constitutionalism*. Cambridge: Cambridge University Press.

Dwyer, J. (2009). 'How to connect bioethics and environmental ethics: health, sustainability, and justice'. *Bioethics* **23**, 497-502.

Easton, PM., Marwick, C.A., Williams, F.L., Stringer, K., McCowan, C., Davey, P, Nathwani, D. (2009). 'A survey on public knowledge and perceptions of methicillin-resistant Staphylococcus aureus'. *Journal of Antimicrobial Chemotherapy*, **63**(1), 209-214.

Enne, VI. (2010). 'Reducing antimicrobial resistance in the community by restricting prescribing: can it be done?' *Journal of Antimicrobial Chemotherapy* **65**, 179-182.

Entwistle, V.A., Watt, I.S. (2013). 'Treating patients as persons: using a capabilities approach to support delivery of person-centered care.' American Journal of Bioethics

European Surveillance of Antibiotic Consumption Centre. (2009). 'Summary of Latest European Data on Antibiotic Resistance and Antibiotic Use'. Available at www.nvu.nl/uploads/d9/C-/d9C.../Samenvatting-EARSS-2009.pdf (accessed August 2011).

Faden, R.R., Powers, M. (2006). *Social justice: the moral foundations of public health and health policy*. Oxford: Oxford University Press.

Finnis, J. (1994). 'Natural Law and Legal Reasoning'. In George, R.P (ed). *Natural Law Theory: contemporary essays*. Oxford: Oxford University Press.

Fiscella, K., Franks, P, Zwanziger, J., Mooney, C., Sorbero, M., Williams, G.C. (2000). 'Risk aversion and costs: a comparison of family physicians and general internists'. *Journal of Family Practice* **49**, 12-17.

FitzGerald, M., Bedford, C. (1996). 'National standards for the management of gonorrhoea'. *International Journal of STD & AIDS* **7**, 298-300.

Fitzpatrick, T. (2008). 'From contracts to capabilities and back again'. *Research Publications* **14**, 83-100.

Fluss, S.S. (1992). 'National AIDS Legislation: An Overview of Some Global Developments'. In Gostin, L., Porter, L. (eds). *International Law and AIDS* Washington: American Bar Association

Foster, K.R., Grundmann, H. (2006). 'Do we need to put society first? The potential for tragedy in antimicrobial resistance'. *PloS Medicine* **3**,e29. Epub 2006 Jan10.

Francis, L.P, Battin, M.P, Jacobson, J.A., Smith, C.B., Botkin, J. (2005). 'How Infectious Diseases got left out – and what this omission might have meant for bioethics'. *Bioethics* **19**, 307-324.

Frei, T. (2009). 'The Redundancy Objection, and Why Scanlon is Not a Contractualist.' *Journal of Political Philosophy* **17**, 47-65**.**

Fukuda, H., Lee, J., Imanaka, Y. (2011). 'Variations in analytical methodology for estimating costs of hospital-acquired infections: a systematic review'. *Journal of Hospital Infection* **77**(2), 93-105.

Gardoni, P., Murphy, C. (2009). 'Capabilities-Based Approach to Measuring the Societal Impacts of Natural and Man-Made Hazards in Risk Analysis.' *Natural Hazards Review* **10**, 29-37.

Gardoni, P., Murphy, C. (2010). 'Gauging the societal impacts of natural disasters using a capability approach.' *Disasters* **34**, 619-636.

Gasper, D., van Staveren, I.P (2003). 'Development as Freedom – and as What Else?' *Feminist Economics* **9**(1),
137-162.

General Medical Council. (2006). *Good Medical Practice*. General Medical Council.

General Medical Council. (2008). *Good practice in prescribing medicines – guidance for doctors*. General Medical Council.

Ghafur, A. (2010). 'An obituary – on the death of antibiotics!' (editorial). *Journal of the Association of Physicians of India*. Available at http://www.japi.org/march_2010/article_01.html (accessed December 2012).

Givens, J.L., Jones, R.N., Shaffer, M.L., Kiely, D.K., Mitchel, S.L. (2010). 'Survival and comfort after treatment of pneumonia in advanced dementia'. *Archives of Internal Medicine* **170**, 1102-1107.

Gleckman, R.A., Madoff, M.A. (1969) 'Environmental pollution with resistant microbes'. *New England Journal of Medicine* **281**, 677-678.

Gordon, J.I., Stappenbeck, T.S., Hopper, L.V. (2003). 'Commensal bacteria make a difference'. *Trends in Microbiology* **11**, 150-151.

Gostin, L.O., Lazarinni, Z. (1997). *Human Rights and Public Health in the AIDS pandemic*. Oxford: Oxford University Press.

Gould, D.J., Drey, N.S., Millar, M., Wilks, M., Chamney, M. (2009). 'Patients and the public: knowledge, sources of infection and perceptions about healthcare-associated infection'. *Journal of Hospital Infection* **72**(1), 1-8.

Graves, N., Harbarth, S., Beyersmann, J., Barnett, A., Halton, K., Cooper, B. (2010). 'Estimating the cost of health care-associated infections: mind your p's and q's'. *Clinical Infectious Diseases* **50**, 1017-1021.

Greenwood, B. (2008). 'A global action plan for the prevention and control of pneumonia'. *Bulletin of the World Health Organization* **86**, 322-322A.

Groenewegen, P, P. (2006). 'Trust and the sociology of the professions'. *European Journal of Public Health* 16: 3-6.

Gruskin, S., Tarantola, D. (2005). 'Health and Human Rights'. In Gruskin, S., Grodin, M.A., Annas, G.J., Marks, S.P (eds.). *Perspectives on Health and Human Rights*. New York: Routledge.

Halton, K.A., Cook, D., Paterson, D.L., Safdar, N., Graves, N. (2010). 'Cost-effectiveness of a central venous catheter care bundle'. *PLoS one* **5**, e12815.

Hansson, S.O. (2006). 'Economic (ir)rationality in risk analysis'. *Economics and Philosophy* **22**,231-241.

Hansson, S.O. (2007). 'Philosophical problems in cost-benefit analysis.' *Economics and Philosophy* **23**, 163-183.

Hardin, G. (1968). 'The Tragedy of the Commons.' *Science* **162**,1243-1248.

Hare, C. (2007). 'Voices from another world: must we respect the interests of people who do not, and will never, exist?' *Ethics* **117**, 498-523.

Hartzell-Nicols, L. (2012). 'Intergenerational Risks'. In Roeser, S., Hillerbrand, R., Sandin, P, Peterson, M. (eds). *Handbook of Risk Theory.* London: Springer.

Hayenhjelm, M. (2012). 'What is a fair distribution of risk?' In Roeser, S., Hillerbrand, R., Sandin, P, Peterson, M. (eds.). *Handbook of Risk Theory.* London: Springer.

Health Protection Agency. (2012[a]). 'Epidemiological data (carbapenem resistance and NDM-1)'. Available at

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/CarbapenemResistance/EpidemiologicalData (accessed January 2013).

Health Protection Agency. (2012[b]). 'English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011'. Available at http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317134304594 (accessed December 2012).

Heffner, A.C., Horton, J.H., Marchick, M.R., Jones, A.E. (2010). 'Etiology of illness in patients with severe sepsis admitted to hospital from the emergency department'. *Clinical Infectious Dieases* **50**, 814-820.

Hehemann, J.H., Correc, G., Barbeyron, T., Helbert, W., Czjzek, M., Michel, G. (2010). 'Transfer of carbohydrate-active enzymes from marine bacteria to Japanese gut microbiota'. *Nature* **464**, 908-912.

Hessler, K. (2010). 'Exploring the philosophical foundations of the human rights approach to international public health ethics'. In Selgelid, M.J., Pogge, T. (eds). *Health Rights*. London: Ashgate Publishing.

Hills, A. (2009). 'Utilitarianism, contractualism and demandingness'. *The Philosophical Quarterly* **60**, 225-242.

Hurtig, A.K., Porter, J.D.H., Ogden, J.A. (1999). 'Tuberculosis control and directly observed therapy from the public health/human rights perspective'. *International Journal of Tuberculosis and Lung Disease* **3**, 553-560.

Hvistendahl, M. (2012). 'Public health. China takes aim at rampant antibiotic resistance'. *Science* **336**, 795.

Institute of Medicine of the US National Academy of Science Workshop. (2005). *Ending the War Metaphor: The changing agenda for unravelling the Host-Microbe relationship* Washington DC: The National Academies Press.

Jakobsson, H.E., Jernberg, C., Andersson, A.F., Sjölund-Karlsson, M., Jansson, J.K., Engstrand, L. (2010). 'Short-term antibiotic treatment has differing long-term impacts on the human throat and gut microbiome'. *PloS One* **5**, e9836.

Jarvis, W.R. (2007). 'The United States approach to strategies in the battle against health-care associated infections, 2006: transitioning from benchmarking to zero tolerance and clinician accountability.' *Journal of Hospital Infection* **65**, 3-9.

John, S.D. (2007). 'How to take deontological concerns seriously in risk-cost-benefit analysis: a re-interpretation of the precautionary principle.' *Journal of Medical Ethics* **33,** 221-224.

Jones, K.E., Patel, N.G., Levy, M.A., Storeygard, A., Balk, D., Gittleman, J.L., Daszak, P. (2008). 'Global trends in emerging infectious diseases'. *Nature* **451**, 990-993.

Judson, O. Microbes 'R' Us. (2009). New York Times. July 21st.

Kamm, F.M. (2008). *Intricate Ethics: Rights, Responsibilities, and Permissible Harm*. USA: Oxford University Press.

Kaufman, A. (2006). Capabilities Equality Basic Issues and Problems. Volume 18 of Routledge Innovations in Political Theory. Oxford: Routledge .

Kumar, R. (2000). 'Defending the moral moderate: Contractualism and Commonsense'. *Philosophy and Public Affairs* **28**, 275–309.

Kumarasamy, K.K., Toleman, M.A., Walsh, T.R., Bagaria, J., Butt, F., Balakrishnan, R., Chaudhary, U., Doumith, M., Giske, C.G., Irfan, S., Krishnan, P, Kumar, A.V., Maharjan, S., Mushtaq, S., Noorie, T., Paterson, D.L., Pearson, A., Perry, C., Pike, R., Rao, B., Ray, U., Sarma, J.B., Sharma, M., Sheridan, E., Thirunarayan, M.A., Turton, J., Upadhyay, S., Warner, M., Welfare, W., Livermore, D.M., Woodford, N. (2010). 'Emergence of a new antibiotic resistance mechanism in India, Pakistan and the UK: a molecular, biological and epidemiological study.' *Lancet Infectious Diseases* **10**, 597-602.

Kuppula, V.S., Meinzen-Derr, J., Morrow, A.L., Schibler, K.R. (2011). 'Prolonged initial empirical antibiotic treatment is associated with adverse outcomes in premature infants'. *Journal of Pediatrics* **159**, 720-725.

Lakoff, G., Johnson, M. (1980). 'Conceptual metaphor in everyday language'. *Journal of Philosophy* **77**, 453-486.

Larson, B. (2011). *Metaphors for Sustainability: Redefining our relationship with nature*. Yale: Yale University Press.

Law, I., Widdows, H. (2008). 'Conceptualising Health: insights from the capability approach.' *Health Care Analysis* **16**, 303-314.

Laxminarayan, R., Malani, A., Howard, D., Smith, D. (2007). 'Extending the cure: Policy responses to the growing threat of antibiotic resistance.' Available at http://www.rff.org/Publications/Pages/PublicationDetails.aspx?PublicationID=9575 (accessed September 2012).

Lenman, J. (2008). 'Contractualism and risk imposition'. *Politics, Philosophy & Economics* **7**, 99-122.

Levin, P.D., Simor, A.E., Moses, A.E., Sprung, C.L. (2010), 'End-of-life treatment and bacterial antibiotic resistance: a potential association' . *Chest* **138**, 588-594.

Levy, S.B. (1993). 'Confronting multidrug resistance: A role for each of us'. *Journal of American Medical Association* **269**, 1840-1842.

Liberati, A., D'Amico, R., Pifferi, S., Torri, V., Brazzi, L., Parmelli, E. (2009). 'Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care'. *Cochrane Database of Systematic Reviews* CD000022

Lipsitch, M., Riley, S., Cauchemez, S., Ghani, A.C., Ferguson, N.M. (2009). 'Managing and reducing uncertainty in an emerging influence pandemic'. *New England Journal of Medicine* **361**, 112-115.

Mainous III, A.G., Everett, C.J., Post, R.E., Diaz, V.A., Hueston, W.J. (2009). 'Availability of antibiotics for purchase without a prescription on the internet'. *Annals of Family Medicine* **7,** 431-435.

Mandell, L.A., Wunderink, R.G., Anzueto, A., Bartlett, J.G., Campbell, G.D., Dean, N.C., Dowell, S.F., File, T.M., Musher, D.M., Niederman, M.S., Torres, A., Whitney, C.G. (2007). 'Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of Community-acquired pneumonia in adults'. *Clinical Infectious Diseases* 44: S27-72.

Mangan, J. (1949) 'An Historical Analysis of the Doctrine of Double Effect'. *Theological Studies* **10**, 41-61.

Mann, J.M. (1997). 'Medicine and public health, ethics and human rights'. *Hastings Centre Report* **27**(3), 6-13.

Mann, J.M., Gostin, L., Gruskin, S., Brennan, T., Lazzarini, Z., Fineberg, H.V. (1994). 'Health and Human Rights'. *Health and Human Rights* **1**(1), 6-23.

Manson, N.C., O'Neill, O. (2007). *Rethinking Informed Consent in Bioethics*. Cambridge: Cambridge University Press.

Marcus, E.L., Clarfield, M., Moses, A.E. (2001). 'Ethical Issues in Antibiotic Therapy'. *Clinical Infectious Diseases* **33**, 1697-1705.

Marks, S. (2004). 'Human Rights'. In Post, S.G. (ed). *Encyclopedia of Bioethics* (3rd edition). New York: Macmillan Reference.

Marquis, D. (1991). Four versions of double effect. *The Journal of Medicine and Philosophy* **16**, 515-44.

Martinez, J.L. (2009). 'Environmental pollution by antibiotics and antibiotic resistance determinants'. *Environmental Pollution* **157**, 2893-2902.

Mckie, J., Richardson, J. (2003). 'The rule of rescue.' *Social Science and Medicine*. **56**(12), 2407-2419.

Metlay, J.P, Shea, J.A., Asch, D.A. (2002). 'Antibiotic prescribing decisions of generalists and infectious diseases specialists: thresholds for adopting new drug therapies'. *Medical Decision Making* **22**, 498-505.

Mid Staffordshire NHS Foundation Trust Inquiry report. (2013). Available at http://www.midstaffsinquiry.com/documents.html (accessed January 2013).

Mill, J.S. (1859). 'On Liberty'. In Collini, S. (ed). *On Liberty and Other Essays (1989).* Cambridge: Cambridge University Press.

Mill, J.S. (2004). 'Utilitarianism'. Project Gutenberg Online Edition. Available at http://www.gutenberg..org (accessed December 2012)

Millar, M.R., Grover, M., Butler, P, Antoniou, A. (1991). 'Multi-resistant Streptococcus pneumoniae in Romania'. *Lancet* **ii**, 323.

Millar, M.R. (2009). 'Should we screen low risk patients for meticillin resistant *Staphylococcus aureus*?' *British Medical Journal* **339**, b4035. doi: 10.1136/bmj.b4035.

Millar, M. R. (2010). 'Thresholds for antibiotic resistance at which we change empirical treatment choices'. *Archives of Disease in Childhood* **95**, F463.

Millar, M. (2011). 'Patient rights and healthcare-associated infection'. Journal of Hospital Infection 79(2), 99-102.

Morel, C., Mossialos, E. 'Stoking the antibiotic pipeline'. *British Medical Journal* **340**, 1115-1118.

Morgan, D.J., Diekema, D.J., Sepkowitz, K., Perencevich, E.N. (2009). 'Adverse outcomes associated with contact precautions: a review of the literature'. *American Journal of Infection Control* **37**, 85-93.

Moser, K., Macfarlane, A., Chow, Y.H., Hilder, L., Dattani, N. (2007). 'Introducing new data on gestation-specific infant mortality among babies born in 2005 in England and Wales'. *Health Statistics Quarterly* **35**, 13-27.

Muller-Pebody, B., Johnson, A.P, Heath, PT., Gilbert, R.E., Henderson, K.L., Sharland, M., iCAP Group. (2010). 'Empirical treatment of neonatal sepsis: are the current guidelines adequate?' *Archives of Disease in Childhood* **96**(1), F4-8

Munthe, C. (2008). 'The Goals of Public health: An integrated, multidimensional model'. *Public Health Ethics* **1**, 39-52.

Murphy, C., Gardoni, P. (2012). 'The Capability Approach in Risk Analysis'. In Roeser, S., Hillerbrand, R., Sandin, P, Peterson, M. (eds). *Handbook of Risk Theory*. London: Springer.

Murphy, D.M. (2007). 'Go to zero then pay it forward'. APIC News. Available at http://www.infectioncontroltoday.com/articles/2008/01/zero-tolerance-for-infections-a-winning-strategy.aspx (accessed January 2013).

Murthy, A., De Angelis, G., Pittet, D., Schrenzel, J., Uckay, I., Harbarth, S. (2010). 'Cost-effectiveness of universal MRSA screening on admission to surgery'. *Clinical Microbiology and Infection* **16**, 1747-1753.

National Health Service Standard Contract 2012/2013. Section E – Core Legal Clauses and Definitions, Gateway Reference 16953, E31. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131988 (accessed October 2012)

National Institute for Health and Clinical Excellence (2006). *The clinical and cost-effectiveness of drotrecogin alfa (activated) Xigris™ for the treatment of severe sepsis in adults: a systematic review and economic evaluation*. Available at http://www.nice.org.uk/nicemedia/live/11545/32951/32951.pdf (accessed October 2011)

National Institute for Health and Clinical Excellence. (2009). *The Guidelines Manual*. Available at www.nice.org.uk (accessed November 2012)

National Institute for Health and Clinical Excellence. (2012). *Measuring effectiveness and cost-effectiveness*. Available at http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenesstheqaly.jsp (accessed October 2012)

Neonatal Staffing Study Group. (2002). 'Patient volume, staffing, and workload in relation to risk-adjusted outcomes in a random stratified sample of UK neonatal intensive care units: a prospective evaluation'. *Lancet* **359**, 99-107.

Nerlich, B., James, R. (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**, 574-590.

New Catholic Encyclopedia. (1967). 'The Principle of Double Effect'. New York, McGraw-Hill. **4**, 1020-1022.

Newman, L.M., Moran, J.S., Workowski, K.A. (2007). 'Update on the management of gonorrhoea in adults in the United States'. *Clinical Infectious Diseases* **44**, S84-101.

NHS London. (2013). *Reducing infection: Infection prevention is everyone's business.* Available at http://www.london.nhs.uk/what-we-do/our-current-projects/reducing-infection (accessed March 2013).

Nicholson, J.K., Holmes, E., Kinross, J., Burcelin, R., Gibson, G., Jia, W., Pettersson, S. (2012). 'Host-Gut Microbiota Metabolic Interactions'. *Science* **336**, 1262-1267.

Nightingale, F. (1863). *Notes on hospitals* (3rd edition). London: Longman, Green, Longman, Roberts and Green.

Nuffield Council on Bioethics. (2007). *Public Health: ethical issues.* Cambridge UK: Cambridge Publishers. (Report available at www.nuffieldbioethics.org).

Nugent, R., Back, E., Beith, A. (2010). 'The race against drug resistance. Global Development Report 2010'. Available at www.whenmedicinesfail.org (accessed August 30th 2010).

Nussbaum, M. (1995). 'Human capabilities'. In Nussbaum, M., Glover, J. (eds). *Women, Culture & Development: a study of Human Capabilities*. Oxford: OUP, Clarendon Press.

Nussbaum, M. (2000). *Women and human development: The capabilities approach*. New York: Cambridge University Press.

Nussbaum, M. (2004). 'Beyond the Social Contract: Capabilities and Global Justice'. An Olaf Palme Lecture, delivered in Oxford on 19 June 2003. *Oxford Development Studies* **32**, 3-18.

Nussbaum, M. (2005). 'Capabilities as fundamental entitlements'. In Kaufman, A. (ed). *Capabilities Equality Basic Issues and Problems*. *Volume 18 of Routledge Innovations in Political Theory*. Oxford: Routledge.

Nussbaum, M. (2006). *Frontiers of Justice: Disability, Nationality, Species Membership* London: Harvard University Press.

Nussbaum, M. (2007). 'Human rights and human capabilities'. *Harvard Human Rights Journal* **20**, 21-23.

Okeke, I.N., Lamikanra, A., Edelman, R. (1999). 'Socioeconomic and behavioural factors leading to acquired bacterial resistance to antibiotics in developing countries'. *Emerging Infectious Diseases* **5**, 18-27.

O'Neill, O. (1996). *Towards Justice and Virtue*. Cambridge: Cambridge University Press.

O'Neill, O. (2004). 'Informed consent and public health'. *Philosophical Transactions of the Royal Society of London* **359**, 1133-1136.

O'Neill O. (2005). 'The dark side of human rights'. *International Affairs* **81**, 427-439.

Ostrom, E. (1990). *Governing the Commons: the Evolution of Institutions for Collective Action*. New York: Cambridge University Press.

Parfit, D. (2011). *On What Matters* (volume 1). Oxford: Oxford University Press.

Pearl, J. (2009). *Causality* (2nd Edition). Cambridge: Cambridge University Press.

Peterson, M. (2006). 'The precautionary principle is incoherent'. *Risk Analysis* **26**, 595-601.

Peterson, M. (2007). 'Should the precautionary principle guide our actions or our beliefs?' *Journal of Medical Ethics* **33**: 5-10.

Pierce, J.J. (2002). 'Can Bioethics Survive in a Dying World?' *Medical Humanities* **23**, 1-6.

Plant, A.J. (2009). 'When action can't wait: investigating infectious diseases outbreaks'. In Bammer, G., Smithson, M. (eds). *Uncertainty and Risk*. London: Earthscan.

Planta, M.B. (2007). 'The role of poverty in antimicrobial resistance.' *Journal of the American Board of Family Medicine* **20**: 533-539.

Podolsky, S.H. (2010). 'Antibiotics and the social history of the controlled clinical trial, 1950-1970.' *Journal of the History of Medicine and Allied Sciences* **65**(3), 327-67.

Pogge, T. (2002). 'Can the capability approach be justified?' *Philosophical Topics* **30** (2), 167-228.

Pogge T. (2006). 'Relational Conceptions of Justice: Responsibilities for Health Outcomes'. In Anand, S., Peter, F., Sen, A (eds). *Public Health, Ethics, and Equity*. Oxford: Oxford University Press.

Pogge, T. (2008). *World Poverty and Human Rights (*2nd edition). Cambridge: Polity Press.

Powers, M. Faden. R. (2006). *Social Justice: The Moral Foundations of Public Health and Health Policy*. Oxford: Oxford University Press.

Prosser, J.I., Bohannan, B.J.M., Curtis, T.P, Ellis, R.J., Firestone, M.K., Freckleton, R.P, Green, J.L., Green, L.E., Killham, K., Lennon, J.J., Osborn, A.M., Solan, M., van der Gast, C.J., Young, J.P. (2007). 'The Role of Ecological Theory in Microbial Ecology'. *Nature Reviews Microbiology* **5**, 384-392.

Public Accounts Committee of the House of Commons. (2009). *Reducing Healthcare Associated Infection in Hospitals in England* (HC 812). (52nd Report of Session 2008-09). London: The Stationery Office.

Public Health Leadership Society. (2002). 'Principles of Ethical Practice of Public Health 2002'. (Report available at www.phls.org) (accessed December 2012).

Public Health (Scotland) Act. (2008). Available at www.opsi.gov.uk/legislation/scotland/acts 2008 (accessed January 2012)

Quinn, W.S. (1989). 'Actions, Intentions, and Consequences: The doctrine of double effect'. *Philosophy and Public Affairs* **18**: 334-351.

Rawls, J. (1971). *A Theory of Justice*. Harvard: Harvard University Press.

Raymont, V., Bingley, W., Buchanan, A., David, A.S., Hayward, P, Wessely, S., Hotopf, M. (2004). 'Prevalence of mental incapacity in medical inpatients and associated risk factors: cross-sectional study'. *Lancet* **364**, 1421-1427.

Raz, J. (1986). *The Morality of Freedom*. Oxford: Clarendon Press.

Rees Jones, I., Urwin, G., Feldman, R.A., Banatvala, N. (1997). 'Social deprivation and bacterial meningitis in North East Thames region, three year study using small area statistics.' *British Medical Journal* **314**, 794-795.

Rescher, N. (1983). *Risk*. Lanham: University Press of America.

Rescher, N. (2006). *Presumption and the Practice of Tentative Cognition*. New York: Cambridge University Press.

Rifkin, J. (1983). *Algeny: A New Word - A New World*. New York: Penguin Books.

Robeyns, I. (2005). 'The capability approach: a theoretical survey'. *Journal of Human Development* **6**(1), 93-117.

Rodriguex-Garcia, R., Akhter, M.N. (2000). 'Human Rights: the foundation of public health practice'. *American Journal of Public Health* **90**, 693-694.

Rollins, B. (2001). 'Ethics, Science and Antimicrobial Resistance' *Journal of Agricultural and Environmental Ethics* **14**, 29-37.

Rowe, R., Calnan, M. (2006). 'Trust relations in healthcare: the new agenda'. *European Journal of Public Health* **16**: 4-6.

Rowlands, M. (1997). 'Contractarianism and animal rights'. *Journal of Applied Philosophy* **14**, 235-247.

Royal College of Paediatrics and Child Health. (2004). *Withholding or Withdrawing Life Sustaining Treatment in Children: A Framework for Practice*. London: Royal College of Paediatrics and Child Health.

Saigal, S., Doyle, L.W. (2008). 'An overview of mortality and sequelae of preterm birth from infancy to adulthood'. *Lancet* **371**(9608), 261-269.

Sandel, M. (1997). 'It's immoral to buy the right to pollute'. *New York Times* **15th December 1997 A23**.

Sandin, P (2007). 'Common-sense precaution and varieties of the precautionary principle'. In Lewens, T. (ed.) *Risk*. Abingdon: Routledge.

Scanlon, T. M. (1998). *What we owe to each other*. Harvard: Harvard University Press.

Scanlon, T.M. (2008). *Moral Dimensions: Permissibility, Meaning, Blame*. London: Belknap Press of Harvard University Press.

Scanlon, T.M. (2009[a]). 'Being realistic about reasons: Epistemological worries.' *The John Locke Lectures*. Available at http://www.philosophy.ox.ac.uk/_data/assets/pdf_file/0010/25858/Lecture_4.pdf

Scanlon, T.M. (2009[b]). 'Being realistic about reasons: Normative Structure.' *The John Locke Lectures*. Available at http://www.philosophy.ox.ac.uk/_data/assets/pdf_file/0011/25859/Lecture_5.pdf

Scanlon, T.M. (2011). 'How I am not a Kantian'. In Parfit D. *On What Matters.* Volume 2. Oxford, Oxford University Press.

Schwaber, M.J., Carmeli, Y. (2008). 'Antibiotic therapy in the demented elderly population'. *Archives of Internal Medicine* **168**, 349-350.

Schwarz G. (2004). 'Hippocrates Revisited'. *Einstein Journal of Biology and Medicine* **21,** 33-34.

Scottish Parliament. (2010). *Patient Rights (Scotland) Bill 2009*. Crown Copyright.

Sedgwick, W. (1868). 'On some Analogies of Cholera, in which Suppression of Urine is not accompanied by symptoms of Uraemic Poisoning'. *Medico-Chirurgical Transactions* **51**, 1-43.

Selgelid, M.J. (2007). 'Ethics and drug resistance.' *Bioethics* **21**(4), 218-229.

Selgelid, M.J. (2008). 'Ethics, Tuberculosis and Globalization'. *Public Health Ethics* **1**, 10-20.

Sen, A. (1982). 'Rights & Agency'. *Philosophy & Public Affairs* **11**, 3-39.

Sen, A. (1993). 'Capability and Well-being'. In Nussbaum, M.C., Sen, A. (eds). *The Quality of Life*. Oxford: Clarendon Press, pp 30-54.

Sen, A. (1999). *Development as Freedom*. Oxford: Oxford University Press.

Sen, A. (2004). 'Elements of a theory of human rights'. *Philosophy & Public Affairs* **32**, 315-356.

Sen, A. (2005). 'Human rights and capabilities'. *Journal of Human Development* **6**,151-166.

Sen, A. (2010). *The Idea of Justice*. London: Penguin Books.

Shiloh, A.L., Eisen, L.A., Savel, R.H. (2010). 'Selective decontamination of the digestive tract: what outcomes matter?' *Critical Care Medicine* **38**, 1386-1387.

Slovic, P. (2006). *The Perception of Risk*. London: Earthscan,

Smith, G.E., Smith, S., Heatlie, H., Bashford, J.N.R., Hawker, J., Ashcroft, D., Millson, D., Verlander, N.Q., Warren, R. (2004). 'What has happened to antimicrobial usage in primary care in the United Kingdom since the SMAC report? – Description of trends in antimicrobial usage using the General Practice Research Database'. *Journal of Public Health* **26**, 359-364.

Smith, R. (1998). 'Action on antimicrobial resistance'. *British Medical Journal* **317**, 764.

Smyth, E.T.M., McIlvenny, G., Enstone, J.E., Emmerson, A.M., Humphreys, H., Fitzpatrick, F., Davies, E., Newcombe, R.G., Spencer, R.C., Hospital Infection Society Prevalence Survey Steering Group (2008). 'Four Country Healthcare Associated Infection Prevalence Study 2006: overview of the results'. *Journal of Hospital Infection* **69**, 230-248.

So, A.D., Carr, O., Gupta, N. (2010). 'Tackling antibiotic resistance'. *British Medical Journal* **340**, c2071.

Soll, R.F. (2010). 'Probiotics: are we ready for routine use?' *Pediatrics* **125**,1071-1072.

Sontag, S. (1988). *Illness as Metaphor & AIDS and its metaphors*. New York: Farrar, Straus, and Giroux.

Souza, T.B., Morais, M.B., Tahan, S., Melli, L.C., Rodrigues, M.S., Scaletsky, I.C. (2009). 'High prevalence of antimicrobial drug-resistant diarrheagenic *Escherichia coli* in asymptomatic children living in an urban slum'. *Journal of Infection* **59**, 247-251.

Spence, D.P.S., Hotchkiss, J., Williams, C.S., Davies, PD. (1993). 'Tuberculosis and poverty.' *British Medical Journal* **307**: 759-761.

Standing Medical Advisory Committee (SMAC). Sub-Group on Antimicrobial Resistance. (1988). *The Path of Least Resistance*. London: English Department of Health.

Stelfox, H.T., Bates, D.W., Redelmeier, D.A.(2003).'Safety of patients isolated for infection control'. *Journal of the American Medical Association* **290**, 1899-1905.

Stewart, S., Taylor, J., Marshall, M., Christie, P. (2001). *Health Protection Scotland, National Services Scotland, NHS Scotland MRSA Screening; Economic Analyses*. Health Protection Scotland [Report].

Stiel, S., Krumm, N., Pestinger, M., Lindena, G., Nauck, F., Ostgathe, C., Radbruch, L., Elsner, F. (2011). 'Antibiotics in palliative medicine – results from a prospective epidemiological investigation from the HOPE survey'. *Support Care Cancer* DOI: 10.1007/s00520-011-1084-1.

The Sun. Individual reports available at http://www.thesun.co.uk/sol/homepage/showbiz/bizarre/2229443/Michael-Jackson-is-suffering-from-an-MRSA-type-infection-that-could-EAT-his-flesh.html; http://www.thesun.co.uk/sol/homepage/features/2893696/NHS-crisis-The-killer-bugs-that-infect-hospital-wards.html; http://www.thesun.co.uk/sol/homepage/news/104197/I-caught-MRSA-font-colorrednine font-times.html (accessed July 2012)

Tomlinson, T. (2008). 'Caring for risky patients: duty or virtue?' *Journal of Medical Ethics* 34, 458-62.

Tremmel, J.C. (2009). *A Theory of Intergenerational Justice*. London: Earthscan.

United Nations. (1948). *Universal Declaration of Human Rights*. G.A. res. 217A (III), U.N. Doc A/810. United Nations.

United Nations Document A/6316. (1966). *International Covenant on Economic, Social and Cultural Rights*. Geneva: United Nations.

United Nations Economic and Social Council, U.N. Sub-Commission on Prevention of Discrimination and Protection of Minorities. (1984). *Siracusa principles on the limitation and derogation of principles in the International Covenant on Civil and Political Rights*. Annex, UN Doc E/CN.4/1984/4. United Nations.

United Nations. (2011). *Human Development Index*.
Available at http://hdr.undp.org/en/statistics/hdi (accessed December 2012).

United Nations Environment Programme. (1992). *Rio declaration on environment and development*. Geneva: United Nations. Available at www.uneporg (accessed July 2009).

US Centre for Disease Control. 'Get smart for healthcare: why in-patient stewardship?' Available at http://www.cdc.gov/getsmart/healthcare/inpatient-stewardship (accessed September 2012).

US Department of Health and Human Services. (2012). 'National Action Plan to Prevent Healthcare-Associated Infections: Roadmap to Elimination'. Available at http://www.hhs.gov/ash/initiatives/hai/infection.html (accessed April 2012)

US Department of Veterans Affairs. (2012). 'Infectious diseases and gulf war veterans.' Available at http://www.publichealth.va.gov/exposures/gulfwar/infectious_diseases.asp (accessed July 2012).

US Public Health Leadership Society. (2002). 'Principles of Ethical Practice of Public Health'. Available at http://www.phls.org (accessed December 2011)

van Asselt, M.B.A. & Vos, E. (2006). 'The precautionary principle and uncertainty paradox'. *Journal of Risk Research* **9**, 313-336.

Van Delden, J.J., Ashcroft, R., Dawson, A., Marckmann, G., Upshur, R., Verweig, M.F. (2008). 'The ethics of mandatory vaccination against influenza for health care workers'. *Vaccine* **26**(44), 5562-5566.

Venkatapuran, S. (2011). *Health Justice*. Cambridge: Polity Press.

Verghese, A. (2004). 'What is in a word?' *Clinical Infectious Diseases* **38**, 932-933.

Verhagen, F.C. (2008). 'Worldviews and metaphors in the human-nature relationship: An ecolinguistic exploration through the ages'. *Language & Ecology* **2**, 1-15.

Versluys, Z., Leeuw, R. (1995). 'A Dutch report on the ethics of neonatal care'. *Journal of Medical Ethics* **21**, 14-16.

Warren, J., Abrutyn, E., Hebel, J.R., Johnson, J.R., Schaeffer, A.J., Stamm, W.E. (1999). 'Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women'. *Clinical Infectious Diseases* **29** 745-758.

Warye, K.L., Murphy, D.M. (2008). 'Targeting zero health care-associated infections'. *American Journal of Infection Control* **36** (10), 683-684.

Wasserman, D. (2006). 'Disability, capability, and thresholds for distributive justice'. In Kaufman, A. (ed). *Capabilities Equality Basic Issues and Problems.* Volume 18 of Routledge Innovations in Political Theory. Oxford: Routledge, 214-234.

Winslow, C.E.A. (1920). 'The untilled field of public health'. *Modern Medicine* **2**, 183-191.

Wolff, J. (2006). 'Risk, Fear, Blame, Shame and the Regulation of Public Safety'. *Economics and Philosophy* **22**, 409-427.

Wolff, J., De-Shalit, A. (2007). *Disadvantage*. Oxford: Oxford University Press.

World Health Organisation. 'Bacteraemia Zero: Preventing bloodstream infections from central line venous catheters in Spanish ICUs'. Available at http://www.int/patientsafety/implementation/bsi/bacteraemia_zero/en/index.html# (accessed September 2012).

World Health Organisation. (1946). *Constitution of the WHO*. Geneva: World Health Organisation.

World Health Organisation. (1994). *A Declaration on the promotion of patients' rights in Europe*. Copenhagen: World Health Organisation.

World Health Organisation. (2002). *25 Questions and Answers on Health and Human Rights*. Health and Human Rights Publication Series 2002. Geneva: World Health Organisation.

World Health Organisation. (2005). *International Health Regulations*. Available at http://www.who.int/ihr/9789241596664/en/index.html (accessed December 2012).

World Health Organisation. (2007). *A human rights-based approach to neglected tropical diseases.* Geneva: World Health Organisation. http://www.who.int/hhr/activities/NTD%20information%20sheet%20-%20English.pdf (accessed December 2012).

World Health Organisation. (2009). *Global tuberculosis control – epidemiology, strategy, financing: WHO report.* Geneva: World Health Organisation.

World Health Organisation. (2010). *Treatment and prevention of pneumonia*. Geneva: World Health Organisation.

World Health Organisation. (2011). 'Combat drug resistance: no action today means no cure tomorrow.' http://www.euro.who.int/en/who-we-are/whd/world-health-day-2011-antibiotic-resistance-no-action-today,-no-cure-tomorrow (accessed august 2011).

Yorkshire Evening Post. (2011). 'Hospitals MRSA fines to reach half million mark.' http://yorkshireeveningpost.co.uk/news/latest-news/leeds_hospitals_fined_over_superbugs_1_3340724 (accessed November 2012)

Zhou, J.S., Pillidge, C.J., Gopal, C.K, Gill, H.S. (2005). 'Antibiotic susceptibility profiles of new probiotic lactobacillus and bifidobacterium strains'. *International Journal of Food Microbiology* **98**, 211-217.

PUBLICATIONS COMING FROM THIS WORK

Millar, M.R., Coast, J., Ashcroft, R. (2008). 'Are MRSA blood stream infection targets fair to those with other types of healthcare associated infection or cost-effective?' *J Hosp Infect* **69**, 1-5

Millar, M. (2009). 'Do we need an ethical framework for hospital infection Control?' *J Hosp Infect* **73**, 232-8

Millar, M. (2009). 'Should we screen low risk patients for meticillin-resistant *Staphylococcus aureus*?' *Br Med J* **339**, 949-951

Millar, M. R. (2010). 'Tackling Antibiotic Resistance: International Action Required'. *Br Med J* **340**, 1262

Millar, M. R. (2010). 'Thresholds for antibiotic resistance at which we change empirical treatment choices'. *Arch Dis Child* **95**, F463

Millar, M.R. (2011). 'Can antibiotic use be both just and sustainable…..or only more or less so?' *J Med Ethics* **37**(3),153-7

Millar, M. (2011). 'Patient rights and healthcare-associated infection'. *J Hosp Infect* **79**, 99-102

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

Millar, M. (2012). 'Moral permissibility and individual responsibility for the spread of infectious diseases'. *Public Health Ethics* **5**(3), 314-317

Millar, M. (2012). ''Zero Tolerance' of Avoidable Infection in the English National Health Service: Avoiding the Redistribution of Burdens'. *Public Health Ethics* doi: 10.1093/phe/phs035

Millar, M. (2013). 'A capabilities perspective on Healthcare Associated Infection.' American Journal of Bioethics **13** (8), 53-54