Antibiotic Resistance: A Multimethod Investigation of Individual Responsibility and Behaviour

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Abstract
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The rapid development of antibiotic resistance is directly related to how antibiotics are used in society. The international effort to decrease and optimise the use of antibiotics should be sustained by the development of policies that are sensitive to social and cultural contexts.

The overarching aim of the thesis was to explore and discuss the Swedish public's beliefs, values and preferences influencing engagement in judicious antibiotic behaviour.

Study I explored through focus group discussions lay people's perceptions and beliefs about antibiotics and antibiotic resistance. The Health Belief Model was used to identify factors that could promote or hinder engagement in judicious antibiotic behaviour. Participants found antibiotic resistance to be a serious problem but were not equally worried about being affected by it. There was a tension between individual and collective reasons for engaging in judicious behaviour.

Study II explored lay people's views on the moral challenges posed by antibiotic resistance through focus group discussions. Participants identified in the decreasing availability of effective antibiotics a problem of justice, which involves individual as well as collective moral responsibility. Different levels of policy demandingness were discussed in light of these results.

Study III investigated, through an online Discrete Choice Experiment, public preferences regarding antibiotic treatment and the relative weight of antibiotic resistance in decision-making. Public behaviour may be influenced by concerns over the rise of antibiotic resistance. Therefore, stressing individual responsibility for antibiotic resistance in clinical and societal communication may affect personal decision-making.

Study IV clarified the notions of collective and individual moral responsibility for antibiotic resistance and suggested a virtue-based account thereof. While everyone is morally responsible for minimising his/her own contribution to antibiotic resistance, individuals do or do not engage in judicious antibiotic behaviour with different degrees of voluntariness.

The findings suggest that people could change their behaviour due to concerns over their own contribution to antibiotic resistance. Effective health communication should be developed from an appraisal of people's attitudes, beliefs and social norms that influence antibiotic resistance related behaviours. Policy demandingness should take into account socioeconomic factors characterising local realities.

Keywords: Antibiotic resistance, Behavior, Health Behavior, Health Belief Model, Discrete Choice Experiment, Preferences, Bioethics, Empirical bioethics, Moral responsibility, Justice, Policy demandingness, Virtue ethics

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A Leonardo

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I   Ancillotti, M., Eriksson, S., Veldwijk, J., Nihlén Fahlquist, J., Andersson, D. I., and Godskesen, T. (2018). Public awareness and individual responsibility needed for judicious use of antibiotics: a qualitative study of public perception and behavior. *BMC Public Health*, 18:1153.

II   Ancillotti, M., Eriksson, S., Godskesen, T., Andersson, D. I., and Nihlén Fahlquist, J. (2020). An effort worth making: A qualitative study of how Swedes respond to antibiotic resistance. *Public Health Ethics,* phaa033.

III   Ancillotti, M., Eriksson, S., Andersson, D. I., Godskesen, T., Nihlén Fahlquist, J., Veldwijk, J. (2020). Preferences regarding antibiotic treatment and the role of antibiotic resistance: A discrete choice experiment. *International Journal of Antimicrobial Agents,* 56(6):106198.

IV   Ancillotti, M., Nihlén Fahlquist, J., Eriksson, S. (2021). Individual moral responsibility for antibiotic resistance. *Submitted.*

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Contents

Abbreviations

AR	Antibiotic Resistance
COREQ	Consolidated Criteria for Reporting Qualitative Studies
DALYs	Disability-Adjusted Life-Years
DCE	Discrete Choice Experiment
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EMEA	European Medicines Evaluation Agency
EQF	European Qualifications Framework
FGD	Focus Group Discussion
HICs	High-Income Countries
HBM	Health Belief Model
LCA	Latent Class Analysis
LMICs	Low- and Middle-Income Countries
MDR	Multidrug Resistant
NGP	Nominal Group Process
OECD	Organisation for Economic Co-operation and Development
PEW	Pew Research Center
RIS	Relative Importance Score
RUT	Random Utility Theory
SVARM	Swedish Veterinary Antibiotic Resistance Monitoring
SWEDRES	Swedish Antibiotic Sales and Resistance in Human Medicine
WHO	World Health Organization
WTP	Willingness to Pay

Introduction

Antibiotic resistance (AR) is a global health and development threat. The World Health Organization (WHO) has declared it one of the top ten global public health threats facing humanity (WHO, 2019a). The capacity to treat infections and some of the most remarkable achievements of modern medicine, such as cancer treatment or surgery and transplantations, are all dependent on the availability of effective antibiotics. Due to the ease of travel — of both pathogens and carriers — the capacity to treat infection is threatened even in countries with effective disease control programmes. In Europe alone, AR causes about 33,000 deaths per year and extra healthcare costs and productivity losses estimated between EUR 1.1 and 1.5 billion each year (European Centre for Disease Prevention and Control [ECDC] & European Medicines Evaluation Agency [EMEA], 2009; Organisation for Economic Co-operation and Development [OECD] & ECDC, 2019).

What should be done to solve the problem of AR and whose responsibility it is?

Antibiotic resistance is a complex problem, whose solution (i.e. its mitigation) requires the engagement and collaboration of multiple sectors and stakeholders. Our chances of maintaining acceptable levels of antibiotic effectiveness depends heavily on the design and implementation of conservation programmes, policies and legislation. At the same time, research and development of new antibiotics, vaccines, and diagnostic tools are needed. I think it is fair to assume that securing antibiotic effectiveness through stewardship and coordinated actions is the duty of national governments and international bodies.

Considering that the situation of the antibiotic pipeline is that there are not enough antibiotics in development for current and expected patient needs (Pew Research Center [PEW], 2020), it is unlikely that the AR problem can be solved only in the laboratories. In the words of the Wellcome Trust Director, Jeremy Farrar, 'We can do all the science and innovation we want but if we can't take society with us, then we won't land the science or the challenges, and we won't access the maximum number of people' (Farrar, 2019). To some extent, the feasibility of effective conservation programmes and surveillance of AR depends on what people actually do. While AR is a natural process, this is accelerated by human behaviour. Antibiotic resistance is a collective problem, and a shared responsibility. Among a multitude of other causes, misuse and overuse of antibiotics are major drivers in the development of multidrug

resistant (MDR) bacteria. The fact that the current AR situation is mostly caused by human behaviour can be particularly frustrating for some. Furthermore, given that the future situation depends on what we will be able to do to mitigate AR, and therefore our capacity to change behaviours that are particularly noxious, this may also be disheartening to some.

In my doctoral project, I focused on the behaviour of lay people and on their responsibility for AR. All empirical studies were conducted in Sweden. I used qualitative research methods to explore lay people's health beliefs, looking for factors that could influence, and partially explain, antibiotic behaviour. I have also looked at what they considered morally challenging with the AR situation. Thereafter, I used quantitative research methods to elicit public preferences regarding antibiotic treatment and the relative weight of AR in decision-making. I found that people consider AR to be a serious threat, that is unfair to deploy the antibiotic 'resource' and that they are willing to act responsibly, even if this comes at some personal cost and not only for egoistic reasons, but because of other-regarding preferences. Finally, I developed a notion of individual moral responsibility for AR as a virtue. The possibility for individuals to develop a sensitivity towards the AR theme and engaging, actively and voluntarily, in judicious antibiotic behaviour, depends on the circumstances that characterise their existence. These circumstances are represented by their political, socio-economic and cultural contexts. The cultural context influences individual behaviour through moral and social norms that regulate the life of a community.

Background

A global threat to public health

Antibiotic resistance is a form of antimicrobial resistance, where bacteria can survive exposure and continue to proliferate in the presence of therapeutic levels of antibiotics. Bacteria can be intrinsically resistant to certain antibiotics or can develop resistance via mutations in chromosomal genes and by horizontal gene transfer (Blair, Webber, Baylay, Ogbolu, & Piddock, 2015). Antibiotic resistance is an inevitable process speeded up due to human action, as the usage of antibiotics enriches and select for it in humans, animals, and the environment (ECDC, European Food Safety Authority, & European Medicines Agency [EMA], 2017).

International agencies, such as the WHO and the World Economic Forum (WEF), identify the rapid development of MDR bacteria as one of the most significant threats to public health globally (WHO, 2019a; WEF, 2020). Indeed, antibiotics are a cornerstone of modern medicine. We need them to prevent and treat infections associated with cancer treatment, surgery and transplantations; in the treatment of burns; and in neonatal care (Teillant, Gandra, Barter, Morgan, & Laxminarayan, 2015; Ventola, 2015). Thanks to the use of antibiotics, it has been possible to reduce childhood mortality and increase life expectancy (Blair et al., 2015). However, if we fail to diminish the progression of AR, the morbidity and mortality associated with infections due to MDR bacteria will vertiginously increase.

Worldwide, AR is increasing at the same time as antibiotic consumption. In recent years, there has been an increase in access to antibiotics, especially in low- and middle-income countries (LMICs), which has posed the challenge of widening access to antibiotics, while restricting inappropriate and excessive use (Laxminarayan et al., 2016). Over a 15-year study period, between 2000 and 2015, recent research have shown that use per capita increased by 26.2% in Access antibiotics and 90.9% in Watch antibiotics – researchers adopted the WHO's 'AWaRe' antibiotic classification framework: Access (first- or second-line therapies), Watch (only with specific indications due to higher resistance potentials), or Reserve (last resort) (Klein et al., 2021; WHO, 2019b).

Over the past decades, at the same time that efficacy of antibiotics alarmingly decreased, the development of new antimicrobial agents also decreased (Morel & Mossialos, 2010). The situation of the antibiotic pipeline is that there are not enough antibiotics in development for current and anticipated patient

needs (PEW, 2020). However, the production of antibiotics is massive and represent in itself a source of antibiotic pollution (Malmqvist & Munthe, 2020). Some experts warn that we may soon enter in a post-antibiotic area (Davies, Grant, & Catchpole, 2013).

In Europe, it has been estimated that the overall societal cost of AR results in extra healthcare costs and productivity losses between EUR 1.1 and 1.5 billion each year (ECDC & EMEA, 2009; OECD & ECDC, 2019). Meantime, AR is also found to be the direct cause of about 33,000 deaths per year and 875,000 DALYs (one DALY can be thought of as one lost year of "healthy" life) (Cassini et al., 2019). With an estimated combined cost of up to $100 trillion to the global economy – pushing a further 28 million people into extreme poverty – this is one of the most pressing challenges worldwide (O'Neill et al., 2016).

Antibiotic resistance in Sweden

In Sweden, consumption of antibiotics in outpatient care is lower than in other European states, and Swedes show to be more knowledgeable about correct antibiotic use and AR than other European counterparts (European Commission, 2018). Indeed, studies on Swedish population confirm good levels of public awareness but also find common confusion about mechanisms and spread of AR (André, Vernby, Berg, & Lundborg, 2010; Vallin et al., 2016). A study on Swedish travellers found that low level of knowledge about MDR bacteria and AR spreading influenced travellers' behaviour and risk-taking, which resulted in unwitting exposure to risk situations (Wiklund, Fagerberg, Ortqvist, Broliden, & Tammelin, 2016). Swedes also show rather solidaric or altruistic attitudes towards the collective; research have shown that most people are in principle willing to abstain from using antibiotics for the common good (Carlsson et al., 2019; Sveriges kommuner och landsting, 2015)

Yearly, about 60 tonnes of antibiotics are sold for human use and about 10 tonnes for animal use (Swedish Antibiotic Sales and Resistance in Human Medicine [SWEDRES]- Swedish Veterinary Antibiotic Resistance Monitoring [SVARM], 2019). These quantities are inferior to most other European countries (ECDC, 2020b; EMA, 2019). Although the AR situation can be considered favourable from an international perspective, most types of AR keep increasing (SWEDRES-SVARM, 2019). Currently, there are about 16,000 cases of AR per year, which is expected to become 32,000 in 2030 and 70,000 in 2050. The estimated additional total cost to society is approximately SEK 16 billion by 2050 (Folkhälsomyndigheten, 2018).

Local and national cooperation characterises Swedish containment work and, since 1989, there are County Medical Officers for communicable disease control. The Swedish Strategic Programme against Antibiotic Resistance (Strama), whose overall aim is to preserve effectiveness of antibiotics, has worked at regional and national levels since 1994. Starting in 2000, there has

been a plan for coordinated work towards the containment of AR and healthcare-associated diseases, jointly run by the National Board of Health and Welfare and the Swedish Board of Agriculture. As a result of such early commitments to curb AR, antibiotic consumption started to decrease already in the 90s (Holmberg, 2012). Sweden hosts the ECDC (European Union's main surveillance system on AR) and is the headquarters for ReAct (an international network that has been working on the containment of AR in several countries since 2005). In recent years, new academic interdisciplinary centres have been founded, such as the Centre for Antibiotic Resistance Research in Gothenburg and the Uppsala Antibiotic Center in Uppsala, which include humanities and social sciences research in their vision.

Human behaviour

As mentioned, human actions influence AR, i.e. human behaviour worsens the resistance situation. Considering that increasingly more people have access to antibiotics, that AR is rising and that the development of new antibiotics is not estimated to cover health care needs, it is unlikely that the AR problem could be solved only in the laboratories. In recent years, the social sciences literature on AR has improved and its input has started to be increasingly recognised (Lu, Sheldenkar, & Lwin, 2020). However, historically, this contribution has been lacking and still is a negligible share of the total academic contributions (Frid-Nielsen, Rubin, & Baekkeskov, 2019).

Over the last years, the One Health approach has gained popularity as a way to intend and tackle AR. One Health defines an approach to design and implement local, national and global programmes; policies; and research characterised by the communication and collaboration of multiple sectors to attain optimal health for people, animals and the environment (American Veterinary Medical Association, 2008). One Health recognises that the health of people, animals and the environment are connected, and the clear connections AR has to each of these three domains make it the quintessential One Health issue (McEwen & Collignon, 2018; Robinson et al., 2016). In fact, the WHO promotes the One Health approach in the global action plan and framework on antimicrobial resistance (WHO, 2015, 2017b). In Sweden, the One Health approach for the containment of AR has been a guiding principle for the last 20 years and, at present, engages 25 governmental agencies and organisations working in different fields, including human health, animal health and food (Folkhälsomyndigheten & Jordbruksverket, 2020)

Most research including the public have focused on knowledge and identified gaps in people's knowledge about proper use of antibiotics and scarce awareness of AR as the main problems explaining non-judicious use of antibiotics (Kosiyaporn et al., 2020; McCullough, Parekh, Rathbone, Del Mar, & Hoffmann, 2016). It is implicit that national and international strategies for

the management of AR, which recommend awareness education, aim not only to provide information but also to change behaviour (Stålsby Lundborg & Tamhankar, 2014). The problem is that although we can consider it a pre-requisite for judicious behaviour, filling the knowledge gap is not enough to induce behaviour change (Huttner et al., 2019). Antibiotic use and other human behaviour that affect AR are part of a micro level system of health beliefs and lifestyle habits, which must be addressed by theories, frameworks and methods from behavioural and psychological sciences (Haenssgen, Charoenboon, & Khine Zaw, 2018; Lu et al., 2020; Stålsby Lundborg & Tamhankar, 2014; Thorpe, Sirota, Juanchich, & Orbell, 2020). The One Health approach, with its multidisciplinary character, also inspires social sciences to address AR from the societal, historical and economic perspectives (Lu et al., 2020).

Health behaviour

A variety of behaviours, usually called health-related behaviour or health behaviour, such as smoking, alcohol use, diet and physical activity, have a part in all major leading causes of death, e.g. ischaemic heart disease, stroke and chronic obstructive pulmonary disease (Conner & Norman, 2017). Behaviours that have the potential to affect AR can also be considered health behaviours. The understanding of the fundamental role played by health behaviour has become a central component of and has grown together with public health. Health behaviour has been defined as:

> 'those personal attributes such as beliefs, expectations, motives, values, perceptions, and other cognitive elements; personality characteristics, including affective and emotional states and traits; and overt behavior patterns, actions and habits that relate to health maintenance, to health restoration and to health improvement'. (Gochman, 1982, p. 169)

Considering the focus of this thesis, the goodness of Gochman's as a working definition of health behaviour lies in its emphasis on the individual; it includes observable, overt, actions but also the mental events and feeling states (Glanz, Rimer, & Viswanath, 2008). Regarding AR, the focus on the individual should not be interpreted merely as egoistic reasons individuals have to engage in proper 'health antibiotic behaviour'. Additionally, the emphasis on the individuals aims at empowering them and accounts for the fact that what they do matter, for themselves and for the collective. Clearly, individuals and communities are interrelated. Individual behaviours are determined by specific factors such as one's genetics, age, gender and many social determinants like social status, social support network, education, employment/working conditions, etc. In a nutshell, health behaviours reflect the interplay between people and contextual factors (Short & Mollborn, 2015). Health behaviour can be

distinguished from lifestyle: health behaviours can include occasional actions, such as being vaccinated, while sustained patterns of complex behaviour, such as doing regular physical exercise, eating a healthy diet or having proper hygiene routines are called lifestyle behaviours (Glanz et al., 2008). In the present context, I refer to health behaviour generally, thus including periodic actions as well as medium- and long-term patterns of action.

Behaviours influencing antibiotic resistance

With no ambition of compiling an exhaustive list, a simple method to distinguish behaviours, which hold the potential to worsen the AR state, is to consider situations that are conducive to the use of antibiotics. The management of AR involves many national and international actors; in this context, I am only referring to laypeople's behaviour.

Antibiotic use within the community

Antibiotic use is the main driver of AR (Costelloe, Metcalfe, Lovering, Mant, & Hay, 2010; Holmes et al., 2016). Most antibiotics in human medicine are prescribed in the outpatient sector. In Europe, antibiotic consumption is tenfold higher in the community than in the hospital sector (ECDC, 2020a). As the mere usage of antibiotics, even if it is proper usage, contributes to worsen AR, then the more antibiotics are used, the worse the situation.

Patients can influence antibiotic prescription by showing that they expect an antibiotic treatment, but it is also the case that prescribers assume that patients want to be prescribed these drugs. It has been shown that prescribers tend to prescribe antibiotics more often when they believe that their patients expect them or when the patient openly demands antibiotics (Gaarslev, Yee, Chan, Fletcher-Lartey, & Khan, 2016; Lucas, Cabral, Hay, & Horwood, 2015; Mangione-Smith, McGlynn, Elliott, Krogstad, & Brook, 1999; Thompson et al., 2019). In countries where antibiotics can de facto be bought over the counter, pharmacists lament that patients often insist on getting antibiotics and that they have a low perception of pharmacists' competence (Gartin, Brewis, & Schwartz, 2010; Kotwani, Wattal, Joshi, & Holloway, 2012). These behaviours are modifiable, but they need to be comprehended in their complexity. Besides individual features such as demographic and socio-economic characteristics (Zanichelli et al., 2019), antibiotic use is influenced by contextual and collective determinants (Schmiege, Evers, Kistemann, & Falkenberg, 2020). For instance, due to historical and cultural reasons, some patients seem to trust the antibiotics more than the words of the doctors and pharmacists (Gartin, Brewis, & Schwartz, 2010; Morel & Mossialos, 2010).

Some key drivers of antibiotic use are of a socio-economic nature. Socio-economic disadvantages, such as precarity or living in deprived areas, may sometimes directly affect and explain non-judicious antibiotic use, but in general it is a proxy for other factors, e.g. drivers of infectious diseases for which

antibiotics are necessary (Haenssgen, Charoenboon, Xayavong, & Althaus, 2020; Schmiege et al., 2020). Patients try to recover as quickly as possible from illness and return to work, or to their usual activities (Bagnulo, Muñoz Sastre, Kpanake, Sorum, & Mullet, 2019; Wickström Östervall, Hahlin, & Lundevall, 2019). Some simply cannot afford a medical visit and try to obtain antibiotics without prescriptions or resort to self-medication, using already available antibiotics (Grigoryan et al., 2008; Roque et al., 2013). Consequently, strategies to decrease antibiotic use must involve welfare policies and social interventions, such as work environments and social support structures. This is vital to create circumstances that can facilitate individual engagement in judicious antibiotic behaviour.

While each use of antibiotics can contribute to worsening the resistance situation, misuse, overuse and diversion of prescription are glaring examples of misbehaviour. To start with, there is a diffuse non-adherence with prescribed or oral indications. Such behaviours typically include delays and failures in taking the prescribed drugs or treatment interruption upon improvement in condition (Fernandes et al., 2014; Pechère, Hughes, Kardas, & Cornaglia, 2007; Tong, Pan, Lu, & Tang, 2018). It is noteworthy that also the opposite of antibiotics abuse, i.e. underconsumption, contributes to accruing AR and exposing the patient to the risk of poor outcome and adverse events. Untreated bacterial infections increase the rate of complications and mortality and create the best environment for bacteria proliferation (Andersson & Hughes, 2014). An unfortunate sign of general public misbehaviour is the presence of antibiotics in domestic waste, which contributes greatly to antibiotic pollution (Anwar, Iqbal, & Saleem, 2020; Bound, Kitsou, & Voulvoulis, 2006).

Food consumption

Using antibiotics in veterinary, aquaculture and agriculture contributes to the clinical problem of resistant disease in human medicine (Chang, Wang, Regev-Yochay, Lipsitch, & Hanage, 2015). Globally, much of the antibiotics are used for growth promotion and disease prevention, and not to treat sick animals (WHO, 2017c). In Europe alone, about 7,000 tonnes of antibiotics are sold for use on animals, with the vast majority in animal husbandry (EMA, 2019). Food production is expected to use two-thirds of all antibiotics by 2030 (Van Boeckel et al., 2015).

Antibiotic resistance can spread through the environment and via the food chain through direct or indirect exposure. Direct exposure occurs following human-animal contact, for instance, through slaughtering and processing. Indirect contact occurs as a consequence of the consumption of contaminated food. This includes fruits and vegetables, which can also be contaminated by bacteria at the farm or later through cross-contamination (Hashempour-Baltork et al., 2019).

The WHO recommends an overall reduction in use of antibiotics in food production to preserve their effectiveness. Although the WHO's primary audience is policy makers and regulatory officials overseeing food production, they underline the important role that consumers can play. They can be a driving force in the market and have strong influence on how foods are produced through their choices (WHO, 2017c). Consuming factory-farmed meat is an example of behaviour that can have repercussions on AR. An individual who makes well thought out food choices would display a healthy and conscientious behaviour for themselves and the collective. How can a lay person engage in judicious antibiotic behaviour about food consumption? As pointed out by Direk Limmathurotsakul and colleagues, food labelling is contentious: food should not contain antibiotics even when they have been used in the production process. Therefore, terms such as 'antibiotic-free' and 'organic' are misleading and actually used in different ways (Limmathurotsakul et al., 2019). However, reducing one's consumption of meat would surely represent a step in the right direction.

International travel

Due to the ease of travel — of both pathogens and carriers — the capacity to treat infection is threatened even in countries with effective disease control programmes. In Sweden, this is acknowledged as a major threat, as the currently favourable situation can change quickly as a result of travel and trade (Government Offices of Sweden, 2020). As a matter of fact, MDR bacteria can endanger even isolated populations who never used antibiotics (Clemente et al., 2015). Travellers to regions with high AR can be exposed to MDR bacteria and return to their countries colonised and be vectors.

International travel involves risks that may be beyond the travellers' control and other risks arising from personal behaviour, which can be decreased by, for instance, the development of proper pre-travel advice for tourists and corresponding advice seeking behaviour (Angelin, 2015). Recommendations to individuals travelling to regions with high prevalence of AR include having up to date vaccines, being aware of ways to treat and prevent diarrhoea and being informed on safe sexual practices (Frost, Van Boeckel, Pires, Craig, & Laxminarayan, 2019). Any action that is related to disease prevention and health maintenance can be considered as health behaviour: taking steps to inform oneself and adopting other preventive measures before and during the travel, such as using probiotics and prebiotics (Riddle & Connor, 2016), can be labelled as health-directed behaviour (Glanz et al., 2008).

Prevention

There are many evidences that domestic and community settings are important for infection transmission and for the acquisition and spread of AR (Maillard et al., 2020). The WHO and many national governments, including the Swedish one, emphasise the role that the public can play in mitigating AR through

the adoption of preventive measures, such as compliance with basic hygiene practices and having vaccines up to date (Government Offices of Sweden, 2020; WHO, 2017a). Examples of basic hygiene practices typically include hand hygiene and food safety rules to avoid food poisoning. However, the picture is not simple, and it calls for individuals to understand the private and public health reach of simple, everyday actions. Crucial risk moments comprise using the toilet, changing a baby's nappy, touching common surfaces (e.g. on the public transportation), coughing or sneezing, caring for domestic animals, etc. (Maillard et al., 2020). Everyone has an obligation not to infect others, for instance, staying home and adopting adequate prevention when ill (Verweij, 2005).

Social norms

As stated, public campaigns focusing on awareness-raising as a behavioural tool are problematic because they are seldom developed from an adequate appraisal of the attitudes, beliefs and social norms that influence antibiotic use. Instead, behavioural studies highlight their role, which are key in bringing about desirable behaviour modification (Nyborg et al., 2016; Pinder, Sallis, Berry, & Chadborn, 2015).

Social norms can be divided into two sorts: descriptive and injunctive. Descriptive norms comprise behaviours the way they are performed by the people, namely what is done. Injunctive norms reflect behaviours that are approved or disapproved by the community, indicating what ought to be done (Wagner et al., 2020). Given the consensus that moral norms and social norms are formally distinct (Brennan, Eriksson, Goodin, & Southwood, 2013), it must be acknowledged that morality and culture relate to one another and that moral norms contribute to the making, and to the judgment, of social norms (Turiel, 2002).

An ethical issue

There are many ethical questions connected to AR. Here are some of the main issues in connection with the studies.

Global inequalities

The fact that human behaviour worsens AR implicates intragenerational and intergenerational justice issues. Intragenerational justice rests on the assumed equality of people's moral status. Recently, there has been an increase in access to antibiotics, especially in LMICs, resulting in the challenge of widening access to antibiotics while at the same time restricting inappropriate and excessive use (Laxminarayan et al., 2016). In some areas in LMICs, unrestricted

access to antibiotics would cause resistance problems, of course, but in the short-term can potentially lead to substantial health gains for the population (Mendelson et al., 2016). Constructing a sustainable, yet accessible, model of antibiotic distribution for LMICs is a global health task; while excessive and incorrect use of antibiotics must be reduced in some regions of the world (high-income countries (HICs), but not only), access must be ensured in others (Heyman, Cars, Bejarano, & Peterson, 2014). At present, inequalities increase the risk that some individuals or groups will suffer more from issues related to AR and antibiotic access than others. According to Michael Millar (2019), there are pragmatic and moral reasons for developing international agreements designed to control AR. A pragmatic reason comes from the fact that inequalities in access to health and health outcomes contribute to the overall population burden of infectious disease and then to the spread of AR. Moral reasons come from the fact that the current distribution of benefits of effective antibiotics and burdens of infectious diseases and AR is unfair and, in part, could be improved by international actions (Millar, 2019). Without proper surveillance, AR in LMICs can be conducive to greater inequalities because it will entail health costs, which a large segment of the population cannot afford or make it difficult to sustain livestock agriculture and produce enough food. Therefore, 'antibiotic resistance can breed poverty, while poverty feeds the problem of antibiotic resistance' (Van der Heijden et al., 2019). The divide between HICs and LMICs is not the only source of intragenerational issues. For instance, low income in HICs is associated with the risk of contracting infectious diseases and therefore higher risks from exposure to antibiotics (Alividza et al., 2018).

Intergenerational justice relies on the assumption that current and future generations are equal in moral status. The core of the intergenerational justice problem is that present use of antibiotics leads to increasing pathogen resistance, that is, a decreasing antibiotic effectiveness for future patients. This progressive loss of antibiotic effectiveness poses an ethical dilemma at the societal level; if people in the future are as entitled to effective antibiotics as those living here and now, there is a prima facie moral obligation for people now to preserve antibiotic effectiveness for as long as possible. It has been described that the erosion of antibiotic effectiveness is analogous to the 'tragedy of the commons' (Foster & Grundmann, 2006; Hollis & Maybarduk, 2015; Levin, 2001). This concept describes how the exploitation and gradual depletion of a common resource result in a loss of utility distributed equally among the population, while the gain becomes concentrated on the people doing the exploiting. This process was first conceptualised by Garrett Hardin, who illustrated this by farmers overgrazing a shared field to maximise their own benefit at the expense of other farmers (Hardin, 1968).

The ethics of AR involve many areas of bioethics, with an overlap between fields such as clinical ethics and public health ethics (Verweij & Dawson,

2018). In the following, I will first highlight some of the dilemmas closer to clinical ethics and then address the public health and policy issues.

Clinical ethics

Clinicians and others who can prescribe and administer antibiotics feel the pressure to treat those who may be perceived as particularly vulnerable. This causes higher prescription rates of broad-spectrum agents to kill potential resistant organisms (Lee, Cho, Jeong, & Lee, 2013; Means et al., 2014). These perceptions and feelings can be deeply rooted and amount to a deontological imperative that Albert R. Jonsen called the 'Rule of rescue', namely a moral, more instinctive than rational, response to the imminent death of identifiable people (Jonsen, 1986). It can also be grounded more in moral reason: Antibiotics prescribers have sometimes explained their non-judicious prescription behaviours in deontological terms, i.e. the obligation to give the best possible treatment to their patients (Leibovici, Paul, & Ezra, 2012; Means et al., 2014; Price, 2006). In the ethics literature, the 'rescue rule' has been used to explain healthcare personnel's preferences for antibiotic treatments believed to benefit present patients, rather than future ones (Garau, 2006; Krockow & Tarrant, 2019; Leibovici et al., 2012). While there are other explanations, e.g. legal demands upon care services, in general there is a strong moral impetus for helping a person in need here and now and to disregard the abstract group of people possibly affected in the future (McKie & Richardson, 2003).

Typically, intergenerational justice highlights the problem that present use of antibiotics decreases the availability of effective antibiotics for future patients, whose interest in effective cure should be taken into account. Another challenging aspect is that there is a risk that present patients receive less than optimal treatment to benefit future patients, which in turn may cause an increase in present morbidity and mortality rate (Leibovici et al., 2012; Littmann & Viens, 2015; Paul et al., 2010). A situation in which patients receive suboptimal treatments raises, among others, ethical concerns in relation to informed consent, if it is assumed that patients should be informed about the quality of the treatment received and about the alternatives, even if these are not endorsed by the healthcare system (Wagstaff, 2006).

Other issues concern antibiotic treatment of individuals as a way to protect the public interest. Michael Selgelid claims that effective antibiotic treatment of individuals, irrespective of their capacity to afford the cure, could be justified as a measure to control the secondary spread of infections (Selgelid, 2007). Carl H. Coleman recently took on the thorny issue of non-consensual treatment of serious infectious diseases, such as tuberculosis, made on the grounds that curing the patients would be necessary to protect the safety of the collective (Coleman, 2020).

Public health ethics

Antibiotic resistance raises many questions concerning the justification of different possible stewardship policies and how to resolve moral dilemmas that arise because of such policies (Munthe, Nijsingh, de Fine Licht, & Larsson, 2019). The essence of the problem may be represented as a trade-off between promoting patients' health and preserving antibiotic effectiveness for future use.

Millar suggests a principle for the distribution and constrain of antibiotics based on Thomas M. Scanlon's contractualist approach:

> [A]ntibiotics should be used to prevent some substantial risk of irretrievable harm in patients or their contacts, where a substantial risk is a level of risk that can be reduced by the use of antibiotics, and which exceeds the range of risks of irretrievable harm that we tolerate in our day-to-day lives. (Millar, 2012, p. 467).

The principle should prevent completely inappropriate use of antibiotics and the use of antibiotics for infections that do not involve a risk of irretrievable harm. The principle implicitly assumes that antibiotics are a common good and that misusing them goes against the principle of justice. According to Millar, limiting the use of antibiotics to the prevention of irretrievable harms would entail, for example, not using them for self-limiting conditions, or in situations when antibiotics do not substantially impact the outcomes (e.g. final stages of terminal illness), or for animal growth (Millar, 2012).

As overprescription and overconsumption are among the major causes of AR, national and international preservation programmes include surveillance, infection control and promotion of the rational – or proper or justified – use of antibiotics. The focus on reducing unnecessary prescriptions of antibiotic treatments includes delaying or withholding access to antibiotics that are known to be beneficial. These practices place some patients at risk of harm (Daneman, Low, McGeer, Green, & Fisman, 2008; Littmann, Rid, & Buyx, 2020). Considering the issue of when it is justified for clinicians not to promote the best clinical interests of their patients, Annette Rid and colleagues found limitations on the existing guidance on acceptable public health risk and proposed an analogy with clinical research (Rid, Littmann, & Buyx, 2019). The authors claim that the fundamental ethical justification for exposing participants in clinical research to some risks lies in the potential benefits of the research for future patients. Similarly, rational use programmes that involve delaying or withholding antibiotics expose patients to some risks for the potential benefits of future patients (Rid et al., 2019). The authors have also developed a six step systematic framework for evaluating the risks of rational antibiotic use programmes that involve delaying or withholding antibiotics from patients and determine whether the risks to the patient are justified by, i.e. if they are proportionate to, the policy's social value. Minimal risks to the

individual would be acceptable and such a minimal threshold would allow the implementation of the programme without the need to inform the patients (Littmann et al., 2020).

A substantial difference between the two approaches described above is that in the former (Millar's), a quite high threshold is set for allowing antibiotic use; in the latter, a quite low threshold is set for allowing antibiotic non-use. Preservation programmes that would enforce one or the other proposal would probably lead to different results, in terms of maintenance of antibiotic effectiveness but also in terms of different demands on the patients.

Although all preservation programmes should aim for the conservation of antibiotic effectiveness, national health programmes cannot be the same everywhere. Eva M. Krockow and Carolyn Tarrant have recently highlighted how socio-economic, organisational and cultural differences between countries can influence the design and feasibility of antibiotic stewardship policies (Krockow & Tarrant, 2019). Similarly, the perception and the role of ethical aspects can differ greatly. A finding of particular interest is that the extent to which AR is a visible threat (i.e. affects present patients) influences the extent to which doctors make decisions that aim to preserve antibiotic efficacy for the future. The authors thus argue in favour of a contextualised approach to policy justification, in which local specificities would be taken into due consideration (Krockow & Tarrant, 2019).

Policy demandingness is a central notion in Alberto Giubilini and Julian Savulescu's analysis of what antibiotic preservation programmes should impose on patients (Giubilini & Savulescu, 2019). The authors argue that policymakers should only impose requirements on citizens that they, as citizens, would have a moral obligation to fulfil, irrespective of the state making it mandatory, i.e. something for which citizens can be considered responsible (in the sense of responsibility as a moral obligation, see page 27 of this thesis). This would usually result in requirements that would not be too demanding – as it may be the case of a programme based on a low threshold to permit antibiotic non-use – or else in individuals receiving compensation for something very demanding or even supererogatory – as it may be in the case of a high threshold for permitting antibiotic use. Indeed, Giubilini and Savulescu consider foregoing antibiotics something that may be very demanding, in some instances. For this reason, a system of incentives would be a preferable option with respect to punitive measures, or even coercion. Incentives could be of an economic nature but could also consist of increased medical attention to monitor the infection. In addition, the positive influence of social norms suggests that social recognition and praise could be good options (Giubilini & Savulescu, 2019).

Moral responsibility

The focus of this section is on moral responsibility: responsibility that is grounded in moral considerations and not in other notions of responsibility (e.g. legal or organisational). Morality is here understood as a normative framework for practical reasoning and acting provided by human social practice (Cane, 2012).

One basic conceptual distinction to be drawn here is between backward-looking responsibility, which concerns accountability for the current situation, and forward-looking responsibility, which concerns current accountability for the future situation. Forward-looking approaches to moral responsibility focus on the consequences that different practices could bring about. Another essential distinction is between descriptive and normative accounts of the different concepts of responsibility. Descriptive claims assert that such-and-such is the case or not, while normative claims assert that such-and-such ought to be the case, so that they imply a normative evaluation or a prescription.

Another due distinction is that between collective and individual moral responsibility. Whether it is reasonable to hold collectives responsible is controversial and much debated (May & Hoffman, 1991). Intuitively, preserving antibiotic effectiveness is a matter of collective responsibility, which many people agree upon (Jamrozik & Selgelid, 2020b). On the one hand, all people can be deemed accountable for adopting (or failing to adopt) judicious behaviour towards AR, which can be mitigated only if sufficiently large groups of people contribute to the common good and refrain from harmful behaviour. On the other hand, there is a collective interest in the maintenance of antibiotic effectiveness. Notwithstanding that, each individual also has a responsibility to contribute to the maintenance of antibiotic effectiveness.

In his taxonomy of responsibility, Ibo van de Poel distinguishes nine concepts, which are hence used as a baseline for discerning useful notions of responsibility and their applicability to the case of AR (van de Poel, 2011).

Responsibility as a cause

Causality is one of the most intuitive conditions for holding an agent responsible (Driver, 2008). Responsibility as a cause is mainly backward-looking and descriptive: the responsibility lies on the fact that an agent has somehow contributed to the state of affairs, e.g. the driver is responsible for the accident because he/she did not stop at the red light. Although bacteria did not evolve in response to human use of antibiotics but started evolving millions of years ago, the process is accelerated by human behaviours. We can consider the current state of affairs something that we all have potentially contributed to, e.g. by taking or prescribing antibiotics (Abbo et al., 2011; Giubilini, 2019), travelling (Millar, 2015), being an asymptomatic carrier of resistant bacteria (Jamrozik & Selgelid, 2020a). Although causality is a major modulator in peo-

ple's judgments and is traditionally considered a condition for moral responsibility, the latter should not be simply inferred from an assignment of causal responsibility (van de Poel, 2011).

Responsibility as a task

Sometimes referred to as role-responsibility (Hart, 1968), responsibility as a task is mainly backward-looking and descriptive: it refers to an agent's duty to provide some services for the benefit of others as part of the distinctive position or office that that agent occupies, e.g. the train driver is responsible for driving the train. This kind of responsibility especially falls on those involved in AR stewardship, such as public health officials and healthcare professionals in medical and veterinary communities (Lloyd & Page, 2018; Trivedi & Pollack, 2014; WHO, 2018).

Responsibility as authority

Responsibility as authority is mainly backward-looking and descriptive: it indicates that it is an agent's bailiwick to make decisions or that an agent is in charge and for which one can be held accountable. As for responsibility as a task, this concept of responsibility is also tightly connected with agents' job or position. Securing antibiotic effectiveness through stewardship and coordinated actions is primarily the national government's duty. There are evidences of the link between lack of appropriate governance and high AR (Collignon, Athukorala, Senanayake, & Khan, 2015). Unfortunately, it is a fact that financing and capacity constraints in many countries are inadequate to implement proper stewardship programmes (Interagency Coordination Group on Antimicrobial Resistance, 2019).

Responsibility as capacity

van de Poe defines responsibility as capacity as the ability to act in a responsible way, e.g. 'the ability to reflect on the consequences of one's actions, to form intentions, to deliberately choose an action and act upon it' (van de Poel, 2011, p. 39). It is a common view that moral competence is a condition of moral responsibility and that agents morally impaired cannot be held fully responsible for their actions (Fischer & Ravizza, 1998; Wolf, 1987). In this sense, responsibility as capacity is mainly backward-looking and descriptive. However, in a prospective or remedial sense, responsibility as capacity has forward-looking connotations, especially in consideration of AR.

Connected to the issue of countries' different capacities to tackle AR mentioned in 'Responsibility as authority', it is worth considering the "Common But Differentiated Responsibilities" principle. This was formalised in the United Nations Framework Convention on Climate Change in 1992 (United Nations, 1992). The principle states that HICs should bear a larger proportion of responsibility for climate change because: 1) HICs have contributed more to climate crisis and 2) these countries have greater capacities to address the

climate crisis. The same considerations can be applied to the global threat of AR (Millar, 2019). Whereas the first justification emphasises the backward-looking concept of responsibility, the second is based on a forward-looking notion of responsibility. The latter can be applied to individuals as well as to countries. If an individual can contribute to curb AR, for instance, engaging and promoting judicious behaviour in relation to antibiotic use and AR, he/she has a responsibility to do so. If an individual is less capable of doing so, then he/she is not responsible to the same extent.

Responsibility as a virtue

Responsibility as a virtue refers to an agent cultivating certain character traits that make him/her a responsible person (Nihlén Fahlquist, 2019b). It is normative and forward-looking in that it relates to responsibilities that an agent actively assumes. It has been described as a 'readiness to respond to a plurality of normative demands' (Williams, 2008). In the case of AR, individual responsibility as a virtue could mean, for instance, actively developing a sensitivity to when antibiotics are necessary and to the judicious use of antibiotics. Indeed, the complexity of the AR problem could be seen as requiring a certain sensitivity in relation to the plurality of normative demands involved and to discern what actions could have undesirable consequences for AR. Responsibility as a virtue is applicable to antibiotic prescribers. It would mean, for instance, for physicians to consider whether prescribing antibiotics in certain circumstances is likely to affect the availability of effective antibiotics for the community, in the face of unproportioned gain for the patient (Oakley, 2020). Further, responsibility as a virtue is also applicable to lay people; it would entail actions such as complying with the prescriptions and not interrupting the course of antibiotics as soon as the symptoms disappear, not self-medicating with drugs bought online or using leftovers as soon as symptoms appear. Furthermore, it could include an idea of the right balance between protecting individuals and being fair to both current and future patients.

Responsibility as a moral obligation

Responsibility as a moral obligation, in van de Poel's words means: 'to see to it that something is the case [...] e.g. he is responsible for the safety of the passengers, meaning he is responsible to see to it that the passengers are transported safely' (van de Poel, 2011, p. 39). As noted by van de Poel, the concept seems very close to responsibility as task. The differences are essential, however. Responsibility as a task is mainly backward-looking and descriptive; its focus is on the agent's correct performance of his/her duties. The notion of responsibility as a moral obligation, on the other hand, is normative and forward-looking; the focus is on the foreseeable consequences of the actions and on its moral implications.

As for responsibility as a task, this notion of responsibility can also be primarily laid at the feet of those involved in AR stewardship. They are supposed to know about AR and foresee the implications of different actions.

Responsibility as accountability

Responsibility as accountability is mainly normative and backward-looking: it is about 'the (moral) obligation to account for what you did or what happened (and your role in it happening)' (van de Poel, 2011, p. 39).

To ensure that an agent is in the kind of relation with his/her own actions and related consequences, so that he/she can be properly held accountable, some criteria have to be satisfied. Responsibility as a cause and responsibility as capacity are often regarded as prerequisites for holding someone accountable. This is because for an agent to be in the right relation with his/her own actions and related consequences (i.e. to be considered accountable), there must be a connection of causality and a condition of moral competence, which are the bases of responsibility as a cause and responsibility as capacity, respectively.

Regarding lay people and their behaviours, considering that (1) there is a causal connection between AR and people's behaviours and that (2) the majority of people are morally competent, it could be inferred that most people are morally accountable for AR.

Responsibility as blameworthiness

Responsibility as blameworthiness constitutes a large part of the literature on responsibility. It is mainly normative and backward-looking: an agent is held responsible for something happening and is blamed for it. Holding an agent accountable does not necessarily imply blame (or praise). It is often believed that other elements are needed, besides causality and competence, to attribute blame. Typically, these are knowledge, freedom and wrongdoing (Nihlén Fahlquist, 2019a; van de Poel, 2011).

Traditionally, an agent who is in the kind of relation with his/her own actions and related consequences, such that he/she could be held accountable, can be excused if it is demonstrated that he/she acted under compulsion or if he/she lacked relevant knowledge about his/her actions. Therefore, if the agent was not free to act, he/she is not blameworthy – this scenario, together with agents intentionally misbehaving to increase AR, appears too remote and thus is deemed not relevant in this context. The case of the agent who lacked relevant knowledge, however, is less straightforward. The concept of culpable ignorance needs to be taken into account (Smith, 1983). In some cases, an agent might not have had the relevant knowledge, but he/she should have known or taken action to get the relevant knowledge, when information can be collected effortlessly and is easily retrievable. Although at present there is a certain ignorance about AR (McCullough et al., 2016), this may soon be considered

inexcusable, especially in HICs (Littmann & Viens, 2015). As stated, judicious antibiotic behaviour takes more than just knowledge. As individual antibiotic use and other behaviours that affect AR are part of a system of health beliefs and lifestyle habits, it is relevant to mention that in the philosophical debate on the epistemic conditions of moral responsibility, it is also debated whether we should hold people responsible for their beliefs. Briefly, there are positions for which agents are considered to be in control of, and therefore are responsible for the beliefs they form and hold (Montmarquet, 1995), and other positions which, on different grounds, deny such control (Zimmerman, 1997).

Responsibility as liability
Responsibility as liability is mainly normative and backward-looking: an agent is liable to remedy. This notion of responsibility follows other notions of responsibility: typically, an agent is considered liable if he/she is blameable, or even only accountable, for a given situation.

The notion of responsibility for AR as liability is not analysed further as it hardly applies to the individuals and its application to institutional agents goes beyond the scope of the present thesis.

Rationale

Improvement of public awareness and understanding of proper antibiotic use is a global strategic objective to curb AR. This objective largely depends on effective communication, education and training strategies, which should be developed together with the involvement of the public. Promoting public awareness is fundamental because people who better understand the rationale of antibiotic use may be more inclined to take responsibility for both themselves and the community. Nonetheless, merely providing the public with information is inadequate to promote and establish judicious behaviour.

Local policies that are sensitive to social and cultural contexts should support the international effort to decrease and optimise the use of antibiotics. Therefore, research on public beliefs, preferences and values is key for developing messages that can promote individual engagement in judicious behaviour and for implementing effective public health programmes.

Aims

The overarching aim of this thesis was to explore and discuss public beliefs, values and preferences that can influence engagement in judicious behaviour relating to antibiotics.

Here are the specific aims of each study:

Study I: To explore Swedish lay people's perceptions and beliefs in order to find factors that influence antibiotic use behaviour.

Study II: To explore Swedish lay people's views on the moral challenges posed by antibiotic resistance.

Study III: To investigate Swedish general public preferences regarding antibiotic treatment and the relative weight of antibiotic resistance in decision-making.

Study IV: To analyse and discuss the notion of individual moral responsibility for antibiotic resistance and suggest a virtue-based account thereof.

Methodologies and methods

The AR challenge, as other global threats to humanity, transcend boundaries of single disciplines and cannot be adequately addressed through a mono-disciplinary approach. This is because these challenges are phenomena characterised by a multitude of dimensions, which require a synergic effort from multiple disciplines in order to be understood and addressed (W. Janssen & Goldsworthy, 1996). The Centre for Research Ethics and Bioethics is a multidisciplinary research environment wherein PhD students are encouraged to learn and experience beyond their fields of origin. In my PhD project, I have tried to reflect on this. Thus, within the limits of my capacities, I attempted to learn and apply theories and methods outside of my philosophical background. Multi-disciplinarity can sometimes lead to inter-disciplinarity. While in multi-disciplinary research, knowledge from different disciplines is gathered to offer a multi-faceted understanding of, or solution to, the issue in question, inter-disciplinary research aims at integrating – synthetically and not only synergically – the knowledge and methods from different disciplines. There is no room in the present context to delve into the semantic and conceptual differences in the definition of the possible relations between disciplinarities (e.g. intra-, cross-, multi-, inter- and trans-disciplinary). However, reflecting on my doctoral journey, I think that my work is somewhere in between multi-disciplinary and inter-disciplinary research. In studying the impact of human behaviour on AR, I have employed methods and theories from different disciplines – especially from the social sciences – and used them in my research to gain a holistic perspective of the problem, and of the possible ways to mitigate it.

Study I

Methodology

Qualitative research is a systematic scientific inquiry, which aims at generating a holistic, largely narrative, description of a social or cultural phenomenon and in which the researcher is an integral part (Astalin, 2013; Holloway & Galvin, 2017). Therefore, researchers should make an effort to give a circumstantial picture of their research. To this end, in the publication of the study, I

adhered to the consolidated criteria for reporting qualitative studies (COREQ) (A. Tong, Sainsbury, & Craig, 2007).

The study was exploratory, an approach often used to investigate a phenomenon that is not clearly defined. The study of public behaviour (starting from perceptions and beliefs) that holds the potential to affect antibiotic use and AR is one such phenomenon. Moreover, exploratory research is commonly used to identify questions and select types of measurements prior to large-scale investigation. In this sense, Study I laid the foundation for programmed further research (Study III) but also prompted a new line of research (Study II).

Qualitative content analysis

Content analysis is a family of quantitative and qualitative techniques for systematic text analysis (Mayring, 2000). Analytic approaches range from impressionistic, intuitive and interpretive analyses to organised, strict textual analyses (Rosengren, 1981). The type of content analysis approach chosen, qualitative or quantitative, depends on the theoretical and practical aims of the research and the problem studied.

In this study, I resorted to a directed approach to qualitative content analysis, i.e. a strict deductive analysis informed by a theory, in which I used pre-identified variables for the organisation and analysis of the text (Hsieh & Shannon, 2005). The theory used was the Health Belief Model (HBM), and its six constructs constituted the themes under which the text was categorised (see Table 1).

Health Belief Model

I used the HBM to develop the interview guide, as well as in the analysis and discussion of the results.

The HBM is a psychological theoretical model, which has been extensively used to explain changes and maintenance of health-related behaviour. The HBM states that personal demographic and psychological characteristics influence how people perceive the seriousness of and susceptibility to a threat, as well as barriers to and benefits of treatment or the adoption of judicious habits. One can gain an understanding of health behaviour by weighing these health beliefs against possible cues for action and the individual's perceived self-efficacy (N. K. Janz & Becker, 1984; Nancy K Janz, Champion, & Strecher, 2002).

The HBM has been used before in research on antibiotics to understand how parents' beliefs influence their decision to consult primary care (Cabral, Lucas, Ingram, Hay, & Horwood, 2015), and how patients' perceptions affect their involvement in antimicrobial stewardship (Heid, Knobloch, Schulz, & Safdar, 2016), as well as to assess physicians' motivations for preventing AR in hospitalised children (Brinsley, Sinkowitz-Cochran, & Cardo, 2005). To

my knowledge, Study I was the first use of the HBM in the exploration of the behaviour of the general population in relation to antibiotic use and AR.

Methods

Design

The design of the study is qualitative and exploratory. I used the focus group discussion (FGD) because it provides insight into behaviour by generating a process that helps participants to self-disclose (Khan et al., 1991). The interview guide, structured according to best practice guidelines (Krueger & Casey, 2015), was based on a review of the existing literature about antibiotic awareness, knowledge, attitudes, beliefs and behaviour. The interview guide was tested in a pilot (see Appendix 1).

Participants

I recruited participants from the general population through a site-based approach and purposive sampling (Arcury & Quandt, 1999). Inclusion criteria were legal age and Swedish proficiency. Potential participants who might have negatively affected the FGD dynamics because of their education or profession in healthcare, were excluded. Twenty-three respondents were distributed heterogeneously into four groups according to gender, age and education level. Participants received a gift card of approximately EUR 25 after participating.

Data collection

As exploratory research benefits from multiple sources of evidence, I used different methods of data acquisition in the course of the FGDs. Group moderation was facilitated by two experienced researchers with different backgrounds who used follow-up and probing questions, and Nominal Group Process (NGP) techniques were employed. The NGP is a method encompassing a number of steps and techniques to explore the qualitative and quantitative elements, patterns and structure of a health care issue under preliminary investigation (Van de Ven & Delbecq, 1972). The following techniques were used: Silent generation of ideas in writing, Round-Robin listing of ideas on white board and Serial discussion of ideas on white board. The meetings were held in a meeting room at Uppsala University in the period October–November 2016. The meetings lasted between 90 and 120 minutes. Participants watched a short video about AR after a pause during which refreshments were served (Nyhetsmorgon, 2016). The interviews were audio recorded and transcribed verbatim by a professional transcription service.

Data analysis

Data were analysed using a directed approach to qualitative content analysis (Hsieh & Shannon, 2005), in QSR International's NVivo 11 Software.

The HBM key constructs were employed as a coding tree (Table 1). Another researcher and myself analysed the transcripts independently of each other, compared outcomes and discussed inconsistencies. The results were then critically discussed with the rest of the research team until consensus was reached.

Table 1. Application of the Health Belief Model constructs

Construct	Application
Perceived susceptibility	Participants' subjective perception of the likelihood of being affected by AR
Perceived seriousness	Participants' perception of the severity of the AR situation
Perceived benefits	Participants' perception of the benefits of engaging in judicious behaviour in relation to antibiotics
Perceived barriers	Participants' perception of barriers in engaging in judicious behaviour in relation to antibiotics
Perceived self-efficacy	Participants' perceived competence in engaging in judicious behaviour in relation to antibiotics
Cues to action	Trigger mechanisms to prompt engagement in judicious behaviour in relation to antibiotic use

Study II

Methodology

About empirical bioethics

Bioethics established itself as a discipline between the end of the 1960s and the 1970s (Jonsen, 1998). The first bioethicists mainly made philosophical-normative claims about bioethical problems. In this period, the four principles of medical ethics – the 'Georgetown mantra' of autonomy, beneficence, non-maleficence and justice – exerted a great influence on the bioethical debate. Between the end of the 1980s and the 1990s, the discipline increasingly involved empirical methods (Salloch, Schildmann, & Vollmann, 2012). According to Arthur Caplan, this 'empirical turn' is the consequence of including social scientists and empirically trained clinicians in bioethics; the methods of the new scholars' disciplines gained importance within bioethics, which no longer consisted of normative analyses only, but also of empirical investigations of bioethical questions (Caplan, 2007). Others pinpoint this change to

deeper and less circumstantial origins, i.e. in pragmatism. According to Wayne Shelton, applying ethical theory for solving practical bioethical problems is a difficult task. Thus, Shelton, among others, turned to John Dewey's influence on philosophy and ethical theory to find possible solutions (Shelton, 2008). Dewey criticised the philosophical traditions that perpetuated the reason-experience dichotomy, which considered the latter to be an unreliable source for deriving moral obligations. Dewey believed that there was a need for a pragmatic understanding in which human experience would be the basis of ethics (Dewey, 1960).

Although I do not advocate for pragmatic ethics and nor do I see empirical bioethics as a direct consequence thereof, I share an assumption with many in the field, namely that empirical knowledge can provide an essential contribution to the understanding and analysis of bioethical questions. One risk for empirical bioethicists is that of 'practice without theory' – or of being under suspicion of it. For instance, Sabine Salloch and co-authors warn that while '(e)mpirical studies on people's moral attitudes regarding ethically challenging topics' – as it may be the case for Study II – can provide a great contribution to bioethical research, they are sceptical about the possibility that 'ethical judgements can be based on empirical work alone' (Salloch, Vollmann, & Schildmann, 2014, p. 597). This harks back to one of the fundamental, meta-ethical reasons explaining the (progressively decreasing) resistance to accommodating empirical bioethics and for considering it peripheral to bioethics: the distinction between descriptive and normative ethics (Borry, Schotsmans, & Dierickx, 2005). The distinction serves the purpose of making the roles clear: descriptive ethics gathers empirical data about moral issues, about how reality *is*, normative ethics tell people how they *ought* to behave. Inferring an *ought*-conclusion from premises that consist entirely of *is*-statements is a logical mistake, often referred to as the naturalistic fallacy. What this distinction fails to reflect is that the data gathered through empirical methods describe people's values, norms and preferences that guide their actions and shape their relations in reality. This *'is'* matters and often actually shapes people's behaviour. The provision of recommendations on what *ought* to be done without knowledge of the circumstances of reality but in adherence to philosophers' interpretation of an ethical theory, is dogmatic. As is often the case, one-sided interpretations lay themselves open to criticism and nowadays, at least in bioethics, are less common. As pointed out by Kimberly A. Strong and co-authors:

> 'Normative ethics inevitably draws upon assumptions and evidence about the world, human nature and behaviour, while empirical ethics describes aspects of the world that are, in turn, value laden and socially constructed' (Strong, Lipworth, & Kerridge, 2010)(p.319).

I would conclude with a truism about the importance of integrating knowledge to inform sound bioethical claims: theory with practice (and vice versa).

Thematic content analysis

Methodologically, between qualitative content analysis (used in Study I) and thematic content analysis, used in this study, there are minor differences and many commonalities. Using these qualitative methods is suitable for research aiming at employing a relatively low level of interpretation (Vaismoradi, Turunen, & Bondas, 2013). Indeed, I did not try to elaborate any theories from these analyses, but I tried, as objectively as possible, to describe the phenomenon studied through participants' words and categories.

Probably, the major differences between the two studies' data analysis are those between deductive (Study I) and inductive (Study II). Qualitative content analysis is closer to the quantitative tradition, and one of its tenets is the systematisation of the texts into themes and categories according to criteria such as the recurrence of words or, as in our case, the liability to fall under predetermined classifications. As the structure of analysis was operationalised based on previous knowledge, in Study I, I adopted a deductive approach. On the other hand, thematic analysis is keener to make the classifications (categories and themes) emerge from the concepts expressed in the text. As the object studied is not well known and no theoretical framework was used in Study II, an inductive approach was preferred. Arguably, this implied more interpretation from our side with respect to Study I, but still less than other content analysis methods, such as grounded theory or hermeneutic phenomenology, which demand higher levels of interpretive complexity (Vaismoradi et al., 2013).

Methods

Study II was a secondary analysis of the material gathered in Study I. Due to the richness of the material and considering that FGD participants discussed moral aspects of antibiotic use and AR at length, I performed another analysis to pursue interests distinct from those of Study I (Hinds, Vogel, & Clarke-Steffen, 1997). Information about the design, participants and data collection of Study II overlap with Study I and are not repeated.

Data analysis

Transcripts were analysed inductively with thematic content analysis (Burnard, Gill, Stewart, Treasure, & Chadwick, 2008), in QSR International's NVivo 11 Software.

In the first stage, another researcher and I independently coded the transcripts. While I analysed all the transcripts, the other researcher analysed a representative one-fourth of all the group transcripts. In order to familiarise ourselves with the content, we read the transcripts multiple times. At the same time, we started to open code the material. Open coding means identifying themes and categories as they emerge from the text and taking note of words

and phrases from the participants that could sum up relevant content. At the end of this stage, we had a meeting to compare our coding decisions. In the second stage, duplications and overlapping or too similar categories were crossed out. In the third stage, sorting the remaining categories into groups served to refine the distinctions. The other researcher and myself compared our outcomes and critically discussed inconsistencies. Then, the whole research team met to discuss the results and to find a consensus. The resulting categories were descriptive, recalling the participants' terms. The themes, instead, were obtained from a final abstraction process and were thus interpretative.

Study III

Methodology

Discrete Choice Experiment

Traditionally, methods for measuring benefits in health care have focused on improvements in health outcomes. However, while health outcomes are crucial, they are not the only benefits of a health care intervention or service that interest patients. Patients' appraisal of health care interventions and services includes non-health outcomes (e.g. type, amount and understandability of information) and process characteristics (e.g. treatment location and duration or route of drug administration) (de Bekker-Grob, 2009). Because of the progressive aversion of medical paternalistic attitudes and the rise in shared decision-making approaches in health care, patients are increasingly encouraged to deliberate and express their preferences (Elwyn et al., 2012). Therefore, methods for quantifying patients' preferences have gained popularity.

The Discrete Choice Experiment (DCE) is a stated preference method widely and increasingly used in health research (Soekhai, de Bekker-Grob, Ellis, & Vass, 2019). The method provides participants with several hypothetical but realistic choice sets, and it is used to elicit individuals' preferences for a medical intervention, such as an antibiotic treatment. Discrete Choice Experiments rely on certain cardinal assumptions. First, the intervention can be divided into separate characteristics, called attributes, which are further specified by variants called attribute levels. Second, the individuals' preference for such intervention is determined by the selection of the combination of attributes and attribute levels that give the highest utility (Ryan, 2004).

The theoretical pillar of DCEs is the Random Utility Theory (RUT) (Hensher, Rose, & Greene, 2015; Louviere, Hensher, & Swait, 2000). According to RUT, individuals seek to achieve the highest utility, which reflects their individual valuation of an alternative. Moreover, it is assumed that rational

individuals choose the alternative that provides them with the greatest value. This utility is latent as it is not directly observable. Latent utility comprises a measurable systematic element and an unmeasurable random element. The measurable systematic element comprises the attribute levels and covariates (such as demographics) that determine the decisions that individuals make. The latent utility 'U' of individual 'n' concerning scenario 'j', can be estimated by taking the sum of the systematic element 'V' and the random error 'ε'. 'V' represents the utility of 'n' in 'j', based on all attributes, levels and covariates. 'ε' represents all unobserved and unobservable factors influencing the utility of 'n' in 'j'.

This can be represented as follows in Equation 1: $U_{nj} = V_{nj} + \varepsilon_{nj}$

Discrete Choice Experiments enable the investigation of both health outcomes and non-health outcomes through the analysis of respondents' multiple choices between the alternatives. Furthermore, by analysing their choices, trade-offs can be inferred such as the magnitude and direction of the attribute-level estimates, the relative importance score (RIS) of the attributes, and willingness to pay (WTP) – including health outcomes, non-health outcomes and process characteristics (Hauber et al., 2016).

A DCE was used to investigate the preferences heterogeneity as well as the trade-offs that people are willing to make between different typical antibiotic treatment features (health outcomes and process characteristics) and their potential contribution to AR (non-health outcome).

Methods

Design

This was a cross-sectional study based on an online survey consisting of a three-part questionnaire (see Appendix 2). Light House Studio 9.6.1 software was used to design the questionnaire and conduct the survey in April 2019.

Below follows a description of the questionnaire parts and the DCE design, including development phases of the attributes and levels.

Questionnaire – Part I

The first part consisted of socio-demographic, background and antibiotic-related questions. Socio-demographic questions concerned age, gender, education, occupation and financial vulnerability. Financial vulnerability describes the individual's ability to recover from sudden financial shocks. High financial vulnerability means that such individual's ability is low. It was necessary to have a question about the financial capacity of the respondents because one of the attributes in the DCE was out-of-pocket cost. Financial vulnerability was preferred over other options (e.g. household or individual income), because it was assumed to be a better measure to capture the financial situation of the respondents at that specific point in time.

Background questions concerned self-reported health status; altruism, which was measured using the Adapted Self-Report Altruism Scale (Duerden, Witt, Fernandez, Bryant, & Theriault, 2012); health literacy; and numeracy. Health literacy describes the ability to access, understand, appraise and apply health-related information. Numeracy describes the ability to apply and manipulate numerical concepts. Health literacy and numeracy were evaluated through two subjective rating scales: the Communicative and Critical Health Literacy Scale – Swedish Version, and the 3-Item Version of the Subjective Numeracy Scale (McNaughton, Cavanaugh, Kripalani, Rothman, & Wallston, 2015; Wångdahl & Mårtensson, 2014). Subjective measures were chosen because they involve less cognitive effort than objective measures, which is a substantial benefit in DCE studies.

Antibiotic-related questions aimed at evaluating respondents' knowledge about correct use of antibiotics and AR.

Questionnaire – Part II
The second part of the questionnaire comprised the DCE choice tasks preceded by instructions about the DCE scenario. In the instruction section, each attribute was explained and all the attribute levels described. Respondents were asked to imagine having a bacterial infection and that the doctor prescribed antibiotics to avoid complications. To specify the type and seriousness of the bacterial infection was not deemed necessary, nor helpful. Preliminary testing suggested that information and scenario were understandable and believable. Table 2 describes the attributes and levels as they were presented in the instructions for completing the DCE choice tasks.

Table 2. Attributes (bold) and levels (italic) in the DCE instruction section

Contribution to antibiotic resistance Bacteria that can withstand an antibiotic treatment are antibiotic resistant bacteria. The main cause of resistance is treatment with antibiotics. Antibiotic resistance is a serious and growing public health problem. It results in longer care times, higher care costs and an increased risk of complications with infection. The contribution to antibiotic resistance of the antibiotic treatments you choose is:

Low 15,000 cases per year: In 10 years, the number of cases in Sweden would remain the same.

Medium 30,000 cases per year: In 10 years, the number of cases in Sweden would double.

High 70,000 cases per year: In 10 years, the number of cases in Sweden would more than quadruple.

Treatment duration You must take three tablets a day throughout the treatment period prescribed by your doctor.

3 days
7 days
14 days

Side effects All medicines have side effects, including antibiotics. Since they not only kill harmful but also beneficial bacteria in the body, they can cause mild to moderate side effects such as nausea, stomach upset, headache and tiredness. The choice situations state how likely the antibiotic treatment is to cause side effects.

1% (1 in 100 people taking this antibiotic get side effects, whereas 99 do not get side effects)

5% (5 in 100 people taking this antibiotic get side effects, whereas 95 do not get side effects)

10% (10 in 100 people taking this antibiotic get side effects, whereas 90 do not get side effects)

20% (20 in 100 people taking this antibiotic get side effects, whereas 80 do not get side effects)

Treatment failure An antibiotic treatment can fail to treat an infection for many reasons. If a treatment fails, it means that you have to be treated with another course of antibiotics.

5% (5 out of 100 people need a further course of antibiotics)
10% (10 out of 100 people need a further course of antibiotics)
15% (15 out of 100 people need a further course of antibiotics)
20% (20 out of 100 people need a further course of antibiotics)

Cost Antibiotic treatments are not reimbursed and you have to pay out-of-pocket.

10 euro
25 euro
40 euro
100 euro

Respondents chose between two unlabelled alternatives ('Antibiotic A' or 'Antibiotic B') in 16 consecutive choice tasks (see Figure 1).

In case the respondents could not recollect the exact meaning of the levels while completing the DCE choice tasks, they could place the mouse over the attribute or attribute levels and a hover box would appear as a popup window. For the attribute levels in which there were percentages, an icon array was shown in addition to the textual information (see Figure 2).
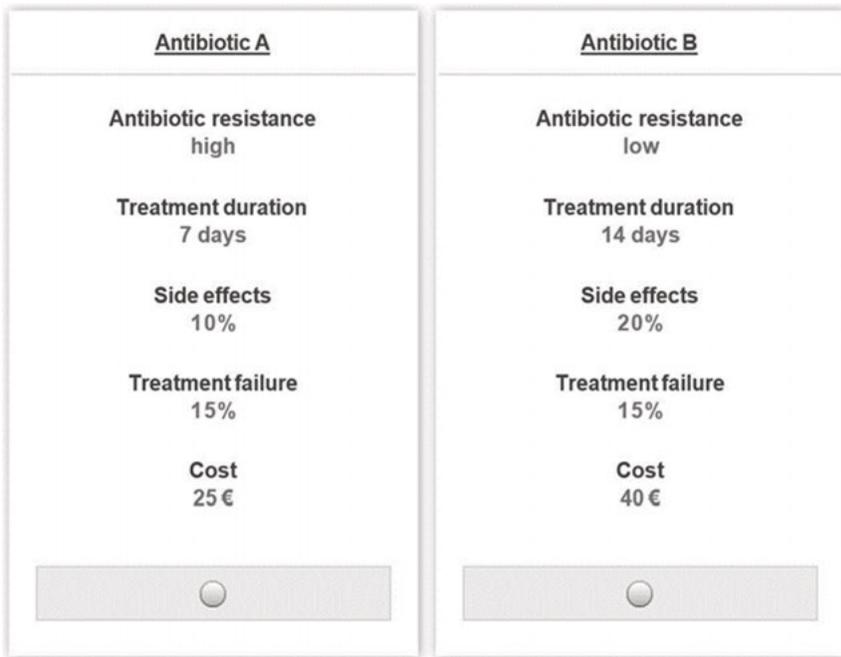

Figure 1. Example of a choice set.
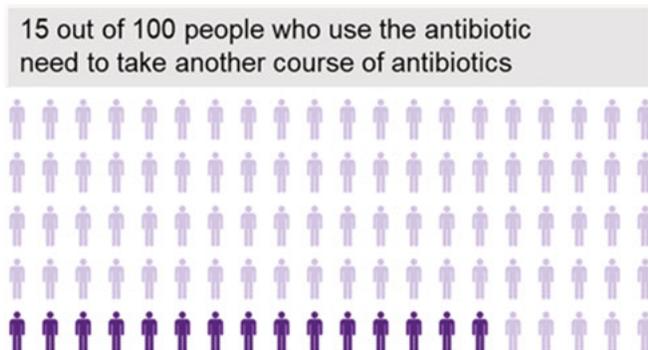
Figure 2. Example of hover box. Treatment failure 15%.

About 'Contribution to antibiotic resistance'

As shown in Table 2, the attributes were 'Treatment duration', 'Treatment failure', 'Cost', 'Side effects' and 'Contribution to AR'. There was affinity between the antibiotic features identified through the FGD ranking exercises and those found in the literature (see below *Phase I – Literature review –* and *Phase II – Focus groups*), except for 'Contribution to AR'. This was highly ranked in the FGDs but nearly untraceable in the literature. It was added to the list of attributes because it actually represents the reason the survey was made and the DCE method chosen: to see whether the public can encompass an additional feature that is not a typical drug attribute (as the other four attributes), in their consideration of antibiotic treatment.

Questionnaire – Part III

The third part comprised a subjective measure of antibiotic-related perceptions based on the HBM including 12 questions, risk attitude measured using the Health-Risk Attitude Scale (van Osch & Stiggelbout, 2007), feedback questions about length and difficulty of the questionnaire, and an optional comments box.

Development of questionnaire, attributes and levels

I developed the attributes and attribute levels adhering to best practice guidelines (Bridges et al., 2011; Kløjgaard, Bech, & Søgaard, 2012). The number of attributes was kept as low as possible because it is the factor most influencing response rate and accuracy, together with cognitive burden (Watson, Becker, & de Bekker-Grob, 2017). In the following, the development phases are described.

Phase I – Literature review

A literature search conducted in PubMed through combinations of search terms such as antibiotic, AR, DCE, behaviour, etc. produced 343 hits (from 1999 to 2019). An assessment of titles and then abstracts restricted the sample to 26 documents. Following an analysis, I created a preliminary list of 12 potential attributes and relative levels.

Phase II – Focus groups

As already mentioned, the exploratory character of Study I also served the purpose of generating knowledge for further investigation. In fact, the participants in FGDs took part in a ranking exercise, aiming at producing a list of attributes and levels for the DCE. After the literature review, I retrieved the material from Study I. Thereafter, by adopting uniform terminology to eliminate different formulations for the same attribute, I identified seven additional potential attributes and relative levels.

Phase III – Attribute features checklist

I tested the 19 potential attributes (12 from the literature review and 7 from the FGDs) against a checklist of desirable attribute features. The checklist was created based on the methodological literature on DCEs and researchers' experience (Bridges et al., 2011; Kløjgaard et al., 2012). The attributes features were: to be realistic, plausible, tradable, clear and unambiguous, distinctively different from others, comprehensive, not a proxy for utility, unlikely to dominate, and relevant to respondent's choice. Thereafter, I shortened the potential attributes list to 10 items.

Phase IV – Stakeholder interviews

I held interviews with two general practitioners, a nurse, and a pharmacist to discuss the attributes, levels and the whole questionnaire. The number of attributes was decreased to five items, and major changes were made to the rest of the questionnaire.

Thereafter, I tested and refined the DCE choice tasks and instruction, together with the rest of the questionnaire. This was done to develop a DCE part that was: understandable, would not cause excessive fatigue, and would be well integrated within the questionnaire.

Phase V – Pre-testing

An early version of the survey was answered by 12 colleagues, who gave their feedback in a peer-debriefing in a seminar of the Open Higher Seminar series at the Centre for Research Ethics and Bioethics. The primary focus of this pretest was on the question format, wording and order. Consequently, I made some minor changes.

Successively, four people (non-colleagues) participated in think-aloud interviews. The think-aloud method implies verbalising thoughts that come to mind while completing a task (Charters, 2003); in this case, an early version of the survey. The interviews encompassed both the concurrent and the retrospective phase. In the concurrent phase, participants verbalise their thoughts during the task. In the retrospective phase, participants can add something that they did not mention earlier and the interviewer can ask questions, both related to contents that emerge in the concurrent phase and from a pre-defined list of questions. The primary aim of the interviews was testing understandability and general usability. Hence, a few improvements were made.

Finally, 44 respondents from the public participated in a pilot test run in February 2019. In the pilot, the same recruitment method and research population as in the final survey were used. The whole questionnaire was tested. Data were analysed using multinomial logit (MNL) models, and estimates were used as priors for the final DCE design.

DCE design

Two attributes with three levels ('Contribution to AR' and 'Treatment duration') and three attributes with four levels ('Side effects', 'Cost' and 'Treatment failure') can be combined into 576 ($3^2 \times 4^3$) potential antibiotic alternatives, and into 165,600 ($576 \times 575 \times \frac{1}{2}$) different choice tasks. As said, choice tasks consisted of two unlabelled antibiotic alternatives. The 'opt out' alternative was regarded as unnecessary and unrealistic, considering that it was asked participants to imagine they had a bacterial infection and that the doctor prescribed antibiotics to avoid complications. As it is not feasible to present a respondent with 165,600 choice tasks, a 'Bayesian efficient design' was chosen as an alternative. Such a design minimises the effort (respondent's burden) to arrive at reliable parameters, i.e. the group's preference weights assigned to the attribute levels. This design maximises the D-efficiency criterion (Reed Johnson et al., 2013). Ngene 1.0 (ChoiceMetrics, 2011) was used to create this design. The design was set to be optimal to estimate a standard multinomial logit (MNL) model, based on a main-effects utility function. In designing the pilot, I used Bayesian priors based on best guesses from the literature and expert opinions, to optimise the variance-covariance matrix. This helped, therefore, to minimise the sample size and the number of choice tasks every respondent was asked to complete. Priors are also important because they enable Ngene 1.0 to eliminate dominant alternatives. Afterwards, data from the pilot were analysed using MNL models, and estimates were used as priors for the final design. The final Bayesian D-efficient design comprised 48 unique choice tasks divided over 3 blocks of 16 choice tasks, to which respondents were randomly assigned.

Participants

Participants were recruited through Dynata, a commercial survey sample provider. The sample was representative of the Swedish population in terms of age, gender and geographical region. The inclusion criteria were 18-65 years of age and proficiency in Swedish language. Respondents were excluded if they could not take antibiotics. To calculate DCEs sample size, there is a generally accepted rule of thumb as in Equation 2 (Marshall et al., 2010):

$$Sample\ size > \frac{500l}{TA}$$

As shown in Equation 2, sample size depends on the number of choice tasks (T), the number of alternatives in a choice set (A) and largest number of levels in any attribute (l). This DCE had three blocks, which included 16 choice tasks in each block, with 2 alternatives per choice task, and there were maximum 4 levels. Therefore, the survey required at least 63 respondents per block

(500*4/16*2=62.5) to estimate the main effects only. As 3 blocks were included in the design, there was a need to have at least 189 respondents (63*3=189). In order to identify differences in preferences but also to perform an analysis of subgroups, there was a need for a larger sample. Based on the DCE design, the pilot test, and using current insights related to optimal sample sizes for DCE studies (Soekhai et al., 2019), a sample size of 350 respondents was deemed sufficient.

Data collection
Data were collected in April 2019. Data collection was performed by Dynata and terminated when the predetermined sample size was reached.

Data analysis
All variables were analysed using descriptive statistics in the Statistical Package for the Social Sciences (SPSS) version 25. Choice data were analysed in Nlogit 5.0 (Econometric Software, 2012).

Choice data were analysed using Latent Class Analysis (LCA) models. LCA assumes that respondents differ with respect to their preferences. The classes are defined latent because class membership is not a priori determined. This is expressed as class probabilities, depending on respondents' characteristics. It is the researcher's prerogative to decide upon the number of classes. The decision is based on the model fit (Aikake information criterion, Bayesian information criterion, pseudo-R2) and sound interpretation of classes (Hensher et al., 2015). The modelling procedure resulted in a three-class model, based on the utility function in Equation 3:

$$
\begin{aligned}
U_{rta|c} = {} & \beta_{1|c} Contrib\ to\ AR_{medium\ rta|c} + \beta_2 Contrib\ to\ AR_{high\ rta|c} \\
& + \beta_3 Treatment\ durat_{7\ days\ rta|c} \\
& + \beta_4 Treatment\ durat_{14\ days\ rta|c} \\
& + \beta_5 Side\ effects_{5\%\ rta|c} + \beta_6 Side\ effects_{10\%\ rta|c} \\
& + \beta_7 Side\ effects_{20\%\ rta|c} + \beta_{8i} Failure\ rate_{rta|c} \\
& + \beta_{9i} Cost_{rta|c} + \varepsilon
\end{aligned}
$$

In Equation 3, U represents the observable utility that a respondent 'r' belonging to class 'c' selected alternative 'a' in choice question 't', β1 – β9 are variable weights (coefficients) associated with each attribute of the DCE. 'Failure rate' and 'Cost' attributes were considered as linear attributes, whereas 'Contribution to AR', 'Treatment duration' and 'Side effects' were categorical and dummy coded. The reference level for 'Contribution to AR' was "low", for 'Treatment duration' was "3 days" and for 'Side effects' was "1%". A significant coefficient ($P \leq 0.05$) indicates that the attribute or level has a significant impact on antibiotic treatment preferences. That an attribute estimate within a certain class is significant means that the attribute contributes to the decision-

making process of respondents who belong to that class. The sign of the coefficient reveals whether this impact has a positive or negative effect on utility.

After fitting the utility function, a class assignment model was estimated. Potential explanatory variables were tested for a significant contribution to the class assignment model. The final class assignment resulted in the utility function in Equation 4:

$$U_{rta|c} = \beta_1 Age_{rta|c} + \beta_2 Financ\ vulner_{rta|c} + \\ \beta_3 Health\ literacy_{rta|c} + \beta_4 Numeracy_{rta|c}$$

Significant estimates in Equation 4 indicate that the variables contribute to the class assignment. For instance, if numeracy is negative and significant for Class 1, respondents with inadequate numeracy are more likely to belong to Class 1.

Relative importance score and willingness to pay

I calculated the difference between the most preferred level of an attribute and the least preferred level of the same attribute to estimate the relative importance of each attribute. The attribute with the highest difference score in each class is most decisive in the choice of antibiotic treatment. An importance score of 1 was given to the most important attributes in each class. Every other RIS was calculated by dividing the difference value with the largest difference value, which gave the relative distance of each attribute to the most important attribute. Relative importance scores were calculated separately for each of the classes in the model.

Broadly conceived, WTP is the valuation of health benefits in monetary terms. In the present context, WTP is a technique to derive WTP valuations, which is another way to understand the importance of an attribute for the participants. Willingness to pay values were determined for 'Contribution to AR'. To calculate respondents' WTP, the estimate of the 'Cost' attribute was used as a measure of the marginal utility of money. The ratio of the estimates of 'Contribution to AR' and 'Cost' was calculated to elicit respondents' WTP for the 'Contribution to AR' attribute.

Study IV

Methodology

Normative bioethics

Typically, doctoral students at the Centre for Research Ethics and Bioethics apply themselves to their theoretical studies at either the beginning or the end of their projects.

When the theoretical study is at the beginning of the project, it usually helps the student to: 1) map an already conspicuous literature, 2) suggest that in the existing debate there is a neglected but relevant aspect or a new perspective, and then 3) the empirical studies try to fill that void or to contribute to settling the debate. The underlying assumption is that empirical evidences can support or justify the theoretical claims. These research projects can be loosely described as deductive, and they contain theoretical studies that are primarily descriptive.

When the theoretical study concludes the project, the empirical evidences are foundational and contribute to the formulation of the theoretical claims, explicitly (the empirical evidences partly inform and lead to the theoretical construction) or implicitly (without necessarily representing the legs sustaining the theoretical construction, they help the students to understand the topic and give them 'food for thought'). The underlying assumption is that empirical knowledge can contribute to the understanding and analysis of theoretical questions. These research projects can be loosely described as inductive, and the theoretical studies tend to be primarily normative.

My concluding study belongs to the second type of research projects.

Methods

Conceptual analysis and normative ethics

In Study IV, I performed a conceptual analysis of responsibility in relation to AR, whose main output is the characterisation of it as 'individual moral responsibility for judicious antibiotic behaviour'. First, I focused on the clarification of concepts that I considered of special relevance – that AR actually is an ethical issue, the difference between individual and collective moral responsibility and between backward-looking and forward-looking responsibility in relation to AR.

Conceptual analysis is an umbrella term for a series of conceptual devices employed to reach conceptual clarity. This is needed to promote understanding and avoid unnecessary disagreement. In the words of J. Clint Parker: '[w]ithout a shared understanding of how interlocutors are using terms, dialogue devolves into equivocation and emotivism' (Parker, 2020, p. 2). In the

pursuit of clarity, I attempted to define how key concepts were employed while trying to anticipate possible objections, i.e. to resist falsification.

The second part of the study contains normative claims and advocates a virtue ethics-based notion of responsibility as a way forward to contrast AR. The virtue based approach was not a consequence of the conceptual analysis but a choice made starting from the study of the different notions of responsibility as they could be applied to the AR discourse. I deemed that responsibility as a virtue had the potential of meeting people's views on AR and that offered a meaningful guise for desirable antibiotic behaviours to be embedded in social norms, i.e. to account for the relational aspects and the diversity of demands involved by AR.

Ethical considerations

All the empirical studies adhered to Swedish research regulations and were approved by the Uppsala Regional Ethical Review Board (Dnr 2016/154 and Dnr 2018/293 for Study I-II and Study III, respectively).

Participants in FGDs received information before the meetings via email. The information letter included a presentation of the research institution, the researchers involved and their contacts. Participants were informed about the aim of the study, its significance and the intention of publishing the results in peer-reviewed international journals. They also received information about meetings procedures, data management, and about the fact that withdrawal was possible at any time before and during the meetings. Additionally, they were informed that the meetings would be recorded and then transcribed but that to protect their confidentiality, transcripts would be anonymised. Prior to the meetings commencing, the participants were informed again orally and gave their oral consent to participate.

The theme discussed were not particularly delicate, as they did not involve disclosure of sensitive data about their health, political opinions or religious beliefs etc. However, as it is typical in social and behavioural research, also FGDs involve an informational risk, i.e. a potential for harm from the disclosure of information about the participant or other people.

The respondents in Study III gave their consent to participate in two steps. They received the same information of participants in FGDs but this was repeated twice; at the beginning of the survey, before starting the questionnaire, and at the end, before submitting the survey. In order to 1) start and 2) submit the survey, the respondents needed to click on a button after reading the information section. Taking and submitting the survey were considered as the actual expression of participants' will to participate in the research. Incomplete surveys, namely surveys that were not submitted, were not considered.

Summary of findings

Study I

Focus group discussions saw the participation of 23 people: 13 women and 10 men, age range 20-81. Education was measured using the European Qualifications Framework (EQF): 12 participants' highest attained education level was equal to EQF 4-5, indicating high school, vocational school and university diplomas; 8 participants had EQF 6-7, which reflects bachelor's degree, vocational universities and master's degree; and 3 participants had EQF 8, indicating a doctoral degree.

Individual perceptions	Modifying factors	Likelihood of action
	Demographic (culture/tradition) Sociopsychological (socioeconomic factors, peers pressure) Knowledge (awareness)	**Perceived benefits of judicious use of AB** ◦ Preserving AB ◦ Individual gain ◦ Collective gain *vs.* **Perceived barriers to judicious use of AB** ◦ Individual effort ◦ Overprescribing
Framing		
Perceived susceptibility to AR Generally low, higher in relation to travelling and food **Perceived seriousness of AR** High, mostly a future concern	Perceived threat of AR	Likelihood of engaging in judicious use of AB
	Cues to action ◦ Global effort ◦ Information ◦ Public involvement	

Figure 3. Focus group participants' perceptions of antibiotic use and resistance mapped through the HBM.
AB=Antibiotics; AR=Antibiotic resistance.

Participants perceived AR as a serious but unlikely threat to their health. The likelihood of using antibiotics judiciously was positively influenced by the aim of maintaining antibiotic effectiveness but was negatively influenced by

bad habits (as demanding antibiotics and overprescribing) and the disadvantage potentially involved for the individual. Empowerment through effective health communication could motivate behaviour change (see Figure 3).

Perceived susceptibility and perceived seriousness

Participants viewed AR as an important, current health problem that could have severe future consequences. They perceived the severity of the problem more strongly than individual susceptibility. After watching the video, participants who were not aware of the risks associated with food and travelling, considered AR an even greater problem. Information on the risks associated with imported food and travels promoted the idea that living in Sweden and consuming Swedish food represented the safest available option. Participants repeatedly resorted to metaphors and analogue frames of reference to describe the AR situation. The most recurring simile related AR to climate change, with reference to the likelihood of being affected by it and its seriousness.

Perceived benefits and perceived barriers

Overall, antibiotics were associated with a positive perception. However, this positive perception of antibiotics would involve a risk that people get "spoiled" and demand antibiotics unnecessarily. Using antibiotics as little as possible, refraining from asking for antibiotics, and compliance with prescriptions were considered beneficial to the individual but also a way to place "society first". Indeed, the most important benefit of engaging in judicious use of antibiotics was the preservation of antibiotic effectiveness.

Considering the barriers to engaging in judicious behaviour, this can conflict with individual interests as it can involve effort and cost. The participants perceived overgenerous prescribing as another barrier. The apparent isolation of Sweden in trying to curb AR and a lack of international commitment could also hinder judicious behaviour.

Perceived self-efficacy and cues to action

The participants expressed good levels of self-efficacy and willingness to engage in judicious behaviour. Their willingness often had altruistic reasons and arose from their individual duties towards the collective.

Increased awareness of the international effort to fight AR and effective communication from health authorities and family physicians were the main cues to action for engaging in judicious behaviour.

Study II

A secondary analysis of the material collected in Study I highlighted that for participants: the decreasing availability of effective antibiotics implies justice-related issues; AR management involves both individual and collective moral responsibility; and difficulty of setting the appropriate level of demandingness. Table 3 provides a list of the inductively identified themes and categories.

Table 3. Overview of themes and categories

Theme	Category
Justice	Limited resource
	Questioning the need
	Distribution criteria
	Society first
	Protect everyone's life
Responsibility	Moral sentiment
	Stigma risk
	Collective responsibility
	Future generations
	Individual responsibility
	Uncertainty of risk
Demandingness	Increase control
	Personal struggle
	Worth the effort
	Effort not worth making

Justice

As the use of antibiotics contributes to the decrease of antibiotic effectiveness, the non-judicious use of antibiotics poses a series of justice-related ethical issues. The participants considered non-judicious use of antibiotics to be unfair and immoral. They identified as major problems 1) the selection of criteria for distinguishing between justified and unjustified use and 2) who should set such criteria.

The participants discussed whether the collective should take precedence over the individual. Although they prioritised the common good, this was counterweighted by the concern that prioritising the collective may lead to undesired and perhaps fatal consequences, such as antibiotic treatments being withheld from some patients.

Responsibility

Participants believed that everyone, themselves included, has a responsibility for AR and should contribute to curb AR. They thought of it in terms of moral responsibility, which can trigger moral sentiments. For instance, foregoing antibiotics would provoke relief while non-judicious use would cause a sort of antibiotic shame. The moralisation of antibiotic use would imply risks of phenomena such as the stigma of using antibiotics, or of using them in non-judicious ways.

The participants argued that there is a responsibility, calling for collective action to ensure the effectiveness of antibiotics for those who need them the most, now and in the future, including future generations. They also emphasised the role of bottom-up initiatives, such as conscientious consumerism. Individual responsibility was the primary focus of the discussions, however. The participants blamed the behaviour of patients demanding antibiotics and of doctors eager to please patients.

According to the participants, people should adopt a series of precautions to minimise their need for antibiotics. For instance, people should inform themselves, take hygienic measures to prevent exposure to bacteria and to avoid spreading infections. People should also assume responsibility for other behaviours that can contribute to worsening the AR situation, such as their food consumption or travelling to countries known to have high resistance records.

A notion emerging from the appraisal of consequences of AR was that of uncertainty. Spatial and temporal proximity to the effects of AR would promote a recognition of one's moral responsibility and trigger action. On the contrary, the uncertainty of the risk would dilute one's moral feelings. For the individual, the possible or foreseeable consequences of the present non-judicious use of antibiotics may not represent a sufficient reason to adopt judicious behaviour.

Demandingness

The participants viewed the imposition of stricter regulations as positive, mostly regarding medical prescriptions and the livestock industry, to curb AR. Imposing more austere regulations is not unproblematic, however. They would impose higher demands on individuals, who may struggle in being compliant. For example, the idea of restricting freedom of movement was acceptable to the participants as a self-imposed sacrifice, but they debated on whether it should be a top-down initiative.

Notwithstanding such notions of a struggle, participants' attitude was that of a readiness to make personal efforts, such as foregoing antibiotics and staying home from work longer, revising food and travel habits, and even to suffer more pain because of non-treatment. What participants absolutely rejected

was putting their own or others' lives at risk as a consequence of theirs or others' effort to comply with stricter regulations to manage AR.

Study III

Mean age of respondents was 43 years, where 55.0% were women. Highly educated respondents represented 51.9%. Furthermore, 17.5% had some type of health-related education. Sufficient health literacy was reported by 46.6% of respondents and sufficient numeracy by the 23.3%. Financial vulnerability (low wealth) was reported by 33.6% of respondents, and 10.8% were unemployed. While about 66% of respondents showed sufficient knowledge about antibiotic use, they demonstrated less knowledge regarding AR questions (6.1% and 29.1%). Tables 4 and 5 present the specific characteristics of the participants.

Most participants understood the questionnaire well; only 4.2% thought it was too long and 1.6% thought that it was too difficult.

Table 4. Characteristics of respondents (1/2)

	Respondents (N=378)	
	mean	sd
Age 18–65 years	43.3	13.5
	N	(%)
Women	208	55.0
Health		
Bad	44	11.6
Moderate	113	29.9
Good	221	58.5
Education		
Low	26	6.9
Medium	156	41.2
High	196	51.9
Healthcare education	66	17.5
Tertiary healthcare education	39	10.3
Health Literacy		
Inadequate	41	10.8
Problematic	161	42.6
Sufficient	176	46.6

Table 5. Characteristics of respondents (2/2)

	Respondents (N=378)	
	N	%
Numeracy		
Inadequate	108	28.6
Problematic	182	48.1
Sufficient	88	23.3
Occupation		
Employed	248	65.6
Students	36	9.5
Retired	34	9
Unemployed	41	10.8
On disability living allowance or leave	19	5.0
Financial vulnerability		
High	127	33.6
Medium	105	27.8
Low	146	38.6
Knowledge (sufficient)		
About antibiotics		
AB effective against (multiple response): *Bacteria, Virus, All microbes, DK*	257	68.0
ABs effective against influenza (single resp.) *Agree, Disagree, DK*	244	64.6
About AR		
Human body resistant to AB (single resp.) *Agree, Disagree, DK*	23	6.1
AR spread through contact with (mult. resp.) *Human carriers, Animal carriers, Infected surfaces*	110	29.1

AB=Antibiotics; AR=Antibiotic resistance; DK=Don't Know.

Health Belief Model statements

Most participants perceived low to medium susceptibility of the AR risk (32.8% and 39.9% respectively), and 50.0% perceived AR as a future issue. The perceived severity of the AR threat was higher than the perceived susceptibility, but 15.1% of respondents could not say whether AR is currently a substantial problem in Sweden. A minority of respondents did not perceive using antibiotics properly as beneficial, for themselves (19.9%) or for the col-

lective (22.2%). Regarding the barrier of engaging in a judicious use of anti-biotics, only 2.9% of respondents found it difficult to adhere to prescriptions, and 9.3% did not think that their use of antibiotics contribute to AR. Concerning self-efficacy, respondents showed a lower propensity to make sacrifices (30.9%) than to, more generically, use antibiotics properly (21.4%). Most participants agreed that more knowledge and greater awareness of Sweden's commitment to curb AR would work as trigger mechanisms towards judicious use of antibiotics (9.8% and 14.8% disagreed, respectively). See Table 6.

Table 6. Health Belief Model perceptions

	Levels							
	Low		Medium		High		DK	
	N	%	N	%	N	%	N	%
Susceptibility/Severity								
A) AR is a potentially big threat to my health	124	32.8	151	39.9	76	20.1	27	7.1
B) AR is primarily a problem for the future	189	50.0	92	24.3	65	17.2	32	8.5
C) Nowadays, AR is a big problem in Sweden	78	20.6	162	42.9	81	21.4	57	15.1
D) Afraid to get resistant bacteria	119	31.4	131	34.7	110	29.1	18	4.8
Benefits								
E) Correct use of antibiotics is good for myself	75	19.9	176	46.6	104	27.5	23	6.1
F) Correct use of AB is good for the collective	84	22.2	137	36.2	121	32	36	9.5
Barriers								
G) Difficulty to adhere to prescriptions	272	72	72	19.0	11	2.9	23	6.1
H) Individual use of antibiotics does not affect AR	206	54.5	65	17.2	35	9.3	72	19.0
Self-efficacy								
I) Can take responsibility to use antibiotics correctly	81	21.4	143	37.8	130	34.4	24	6.3
J) Can make some sacrifices to reduce AR	117	30.9	157	41.5	73	19.3	31	8.2
Cues to action								
K) Awareness of Sweden's committment	56	14.8	166	43.9	116	30.7	40	10.6
L) Better understanding of AR	37	9.8	164	43.4	156	41.3	21	5.6

AB=Antibiotics; AR=Antibiotic resistance.

Each HBM-related question is scored on a 4-point Likert scale plus DK: 1 (agree), 2 (partially agree), 3 (partially disagree) and 4 (disagree). Questions are coded as follows: 1 high, 2 medium and 3–4 low. Question B) is reverse coded.

Preferences for antibiotic treatment

All attributes showed a significant estimate, meaning that all attributes contributed to the decision process (see Table 7). Overall, participants mostly preferred antibiotics with the lowest contribution to AR, medium-course treatment durations (7 days), and the lowest risk of side effects (1%). The negative signs of failure rate and cost show that participants preferred treatments with a lower failure rate and a lower price.

Table 7. Preferences for antibiotic treatment based on latent class analysis

	Class 1		Class 2		Class 3	
	Estimate	*SE*	*Estimate*	*SE*	*Estimate*	*SE*
Contribution to AR						
Low (ref.)						
Medium	-0.49***	0.11	-1.69***	0.12	-0.10	0.09
High	-0.81***	0.19	-4.21***	0.24	-0.51***	0.14
Treatment duration						
3 days (ref.)						
7 days	0.15	0.10	0.11	0.11	0.05	0.08
14 days	-0.39***	0.10	-0.25**	0.11	-0.17**	0.08
Side effects risk						
1% (ref.)						
5%	-0.13	0.12	-0.24*	0.13	-0.33***	0.10
10%	-0.01	0.13	-0.20	0.14	-0.77***	0.10
20%	-0.23	0.16	-0.71***	0.16	-1.59***	0.13
Failure rate (linear)	-0.17	0.14	-0.59***	0.14	-0.95***	0.12
Cost (linear)	-0.43***	0.03	-0.15***	0.02	-0.05***	0.02
Class probability model						
Constant	1.44*	0.83	1.05	0.76		
Age	-0.01	0.01	-0.03***	0.01		
Financial vulnerability	-0.42**	0.18	0.05	0.17		
Health literacy	0.58**	0.24	0.26	0.23		
Numeracy	-0.62***	0.22	0.08	0.20		
Average class probability	0.33		0.38		0.29	

*P<0.10, **P<0.05, ***P<0.01.
AR=Antibiotic resistance.

Relative importance and willingness to pay

On average, 'Contribution to AR' was the most important attribute but only slightly more important than 'Cost'. Then followed 'Side effects', 'Failure rate' and 'Treatment duration'. However, participants showed heterogeneous preference patterns, corresponding to the three identified classes: to respondents in Class 1, the most important attribute was 'Cost'; in Class 2, 'Contribution to AR'; in Class 3, 'Side effects' (see Figure 4).

Respondents with lower numeracy, and higher financial vulnerability and health literacy were more likely to belong to Class 1. Younger respondents had a greater likelihood of belonging to Class 2. Older respondents with lower financial vulnerability and health literacy, and higher numeracy were more likely to belong to Class 3.

Respondents' WTP for an antibiotic contributing as little as possible to AR was 389 SEK (approximately €36.50) on average, to have an antibiotic that has a low instead of medium contribution to AR, and 940 SEK (approximately €88) on average, to have an antibiotic that has a low instead of high contribution to AR.
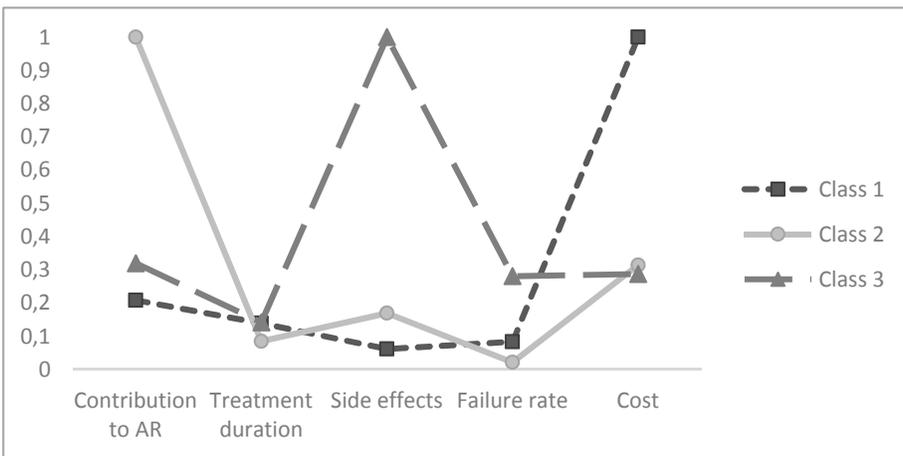
Figure 4. Relative importance of the attributes stratified by class. Values reflect the relative distance of all attributes to the most important attribute on a 0 to 1 scale.

Discussion

Judicious antibiotic behaviour

Judicious antibiotic behaviour is a blanket term that I adopted to describe a set of behaviours in relation to antibiotic use and AR.

I chose the word *judicious,* instead of alternatives such as appropriate and rational, because it reflects the important role of those making antibiotic decisions. *Judicious* means having, showing or doing with good judgement or sense. Ideally, there is only one medically adequate use of antibiotics; "the right drug for the right condition for the right amount of time" (Wilson & Tan, 2010). In practice, actual decisions about antibiotic treatment are made under suboptimal conditions, from both the side of who prescribes, sells or administrates antibiotics and the side of antibiotic consumers (Heyman et al., 2014; Ledingham, Hinchliffe, Jackson, Thomas, & Tomson, 2019). While in some circumstances, to guarantee proper use would be sufficient to take antibiotics only when and how prescribed, in others, antibiotics are commonly bought over the counter without any, or only little, recommendations for use (Heyman et al., 2014; Kotwani et al., 2012). To make an example, antibiotic leftovers should not be disposed of as regular domestic waste. Some communities have "pharmaceutical take-back" programmes but generally, people do not know what to do with unused or expired antibiotics and about environmental contamination (Anwar et al., 2020; Bound et al., 2006).

Besides the issues arising in the private context, AR is hugely influenced by relational dynamics within communities (Ledingham et al., 2019; Lin, Alam, Fearon, & Hargreaves, 2020). For instance, patients' attitude towards antibiotic prescription (resisting or insisting on the prescription) and prescribers' perception of patients' attitudes are factors known to negatively influence antibiotics prescription rates, and therefore AR (Lucas et al., 2015; Thompson et al., 2019).

Behaviour that can potentially contribute to AR is not limited to human medical use. Using antibiotics in veterinary medicine, aquaculture and agriculture contributes to the global AR problem because resistant bacteria spread through the environment and the food chain via direct or indirect exposure. Through their choices, individuals as consumers affect the market and can influence how food is produced (WHO, 2017c). Similarly, travelling to countries with high AR records (Millar, 2015), keeping or not keeping vaccinations

updated in accordance with one's lifestyle (Jansen, Knirsch, & Anderson, 2018), are all instances of behaviours that have an influence on AR.

Although there are other examples, the point is that there are plethora of ways in which human behaviour can affect AR. Thus, judicious antibiotic behaviour is the best use of antibiotics or other AR-related behaviour according to individuals' best judgement and under the prevailing circumstances. Clearly, individuals' capacity for assessment, as well as their circumstances, vary.

The starting point: knowledge, perceptions and beliefs

This discussion section mirrors and deepens aspects from Study I and Study III.

Data from the last Eurobarometer reports on antimicrobial resistance showed that: consumption of oral antibiotics in Sweden was lower than in most European states, the Swedish population was comparatively more knowledgeable about AR, and Swedes used antibiotics more appropriately (European Commission, 2016, 2018). Therefore, testing Swedes' knowledge was never the object of this doctoral project as the convergence between the Eurobarometer reports and other national studies was convincing (André et al., 2010; Vallin et al., 2016). In fact, I assumed it was reasonable to explore the perceptions and beliefs of Swedes because they had relatively good levels of knowledge and awareness. Knowledge was tested in Study III but only through four questions and with the sole purpose of assessing whether it could explain heterogeneity in the preferences pattern. The results showed a rather low knowledge of the correct use of antibiotics and of AR mechanisms. Although I still believe the assumption was reasonable and that perceptions and beliefs found through the FGDs were informative (virtually no one has perceptions and beliefs only based on perfect knowledge), I found the results on Swedes' knowledge a bit surprising. First, there is no doubt that four questions cannot represent a reliable measure. Second, as there are no reasons to believe that the participants in Study III were less knowledgeable than average or that they answered incorrectly due to negligence or on purpose, I must deduce that the results can be explained by the relative difficulty of the questions asked. Even though these results warn caution, there is a datum that I found of special interest, namely that 93.9% of participants agreed with the incorrect statement "The human body can become resistant to antibiotics, giving free space to bacteria". Previous research on the Swedish public found that 88% answered incorrectly to the statement "People can become resistant to antibiotics", which is also a low score (Vallin et al., 2016). The Swedish public likely have good knowledge of the dos and don'ts of using antibiotics and know that AR exists and it is problematic because it hinders antibiotic efficacy. This reflects the goodness of the Swedish work on containment of AR, including awareness-raising and education campaigns (Mölstad et al., 2017). So, one may

wonder if there is any issue at all in the fact that most people do not know how resistance spreads. Actually, it can be an issue worth some attention. The misconception that the body can become resistant to antibiotics has global diffusion (Brookes-Howell et al., 2012; Cambaco et al., 2020; Gaarslev et al., 2016; McCullough et al., 2016). The belief that the individual becomes resistant to antibiotics and not the bacteria involves the risk that people see AR as a threat to the person and fail to understand the threat posed to public health by non-judicious antibiotic behaviour. This risk may be better characterised considering the results from Study I and Study III about participants' perceptions about the threat of AR.

The analysis of FGDs revealed that participants perceived AR as a severe threat to health but did not perceive this as a peril to themselves. While this is credible, and previous studies have reported on the divergence between the perception of seriousness and of susceptibility in relation to AR (Brooks, Shaw, Sharp, & Hay, 2008; Wiklund et al., 2016), it must be noted that the interview guide was created ad hoc to facilitate the discussion on these topics: Do people really feel threatened by AR or only when they focus on it they find it a threat? The results from Study III questionnaire show that, in the end, there is not so much fear and that AR is believed to be foremost a future problem. Indeed, participants in Study I often resorted to climate change to express their perception of AR: a potentially serious threat to human life which goes unnoticed in everyday life but that is continuously progressing until it may be too late to remedy, a 'slowly emerging disaster' (Viens & Littmann, 2015). In the HBM, perceived susceptibility and seriousness are of fundamental importance: if one does not perceive AR as a health threat, there may be little motivation to engage in judicious antibiotic behaviour as it would not be perceived as a health behaviour useful to avoid illness or harm.

How can the importance of taking action in the present be communicated? Apocalyptic narratives should be avoided in public health messages because they may be ineffective, inducing a sort of 'disaster fatigue' in the public (Nerlich & James, 2008). The disaster language may even be counterproductive, as it may provoke opposite but equally detrimental reactions in the public: people may just refuse because of it being overwhelming, or misbehave in fear of extraordinary use of severe restrictive measures on antibiotics (Nisbet, 2009; Viens & Littmann, 2015), or react with fatalism and embrace the idea that what they do does not matter. A preferable approach is emphasising that AR is a threat to the individual and already a significant public health issue. Framing it as a sort of dilemma for the sake of future generations could lessen individual responsibility and engagement in judicious antibiotic behaviour. On the contrary, I believe that stressing the relevance of individual behaviour and individual responsibility, for one's health and for the collective, may bring some positive results. Indeed, it is one of the indications from Study I that health communication should empower. Focus group participants believed in their efficacy to engage in judicious antibiotic behaviour. They also held the

belief that, in general, the public should be involved, and play a role, in the mitigation of AR. Research investigating public views on the role of lay people reported contrasting results (Dao et al., 2019; McCullough et al., 2016; Worthington, MacGeorge, & Foley, 2020). Research conducted in Sweden found that people believe that they have their share of responsibility and showed to believe in their self-efficacy (Carlsson et al., 2019; European Commission, 2018). This may be the effect of the Swedish work on AR containment; one known source of self-efficacy is that of vicarious experiences provided by social models. Modelling influences build self-efficacy by the provision of a social standard against which individuals can judge their own capabilities and transmit knowledge (Bandura, 1994). Participants in the FGDs perceived receiving accurate information as a factor that would promote self-efficacy and thereby motivate people to take responsibility and engage in judicious antibiotic behaviour against AR (cue to action). In the health behaviour literature, the association between effective communication, self-efficacy and health behaviour is evidenced (Coulter & Ellins, 2007).

The importance of modelling influences is confirmed by the cues to action identified in Study I and confirmed in Study III. Participants in the FGDs claimed that they would feel more motivated to act against the threat posed by AR if they received more information and felt involved. Information of relevance to induce behaviour change were not only those about antibiotic use and resistance but also about the national and international strategies for containment of AR. Engagement by authorities and clear communication help citizens to understand the seriousness of AR.

The most poignant results from the analysis of FGD participants' perceptions about benefits of and barriers to engage in judicious antibiotic behaviour point at that individual and collective interest may be at odds, at times. Participants felt that turning to antibiotics would allow for faster recovery from illness and for them to return to work as soon as possible. Economic barriers can be overcome through welfare policies, such as more generous temporary parental benefit (Wickström Östervall et al., 2019). Results from Study III support the idea that antibiotic behaviour is influenced by financial factors. Although DCE participants were willing to pay sizeable amounts of money for antibiotic less contributing to AR, 'Cost' was the second most important attribute and the most important for respondents whose preference pattern was represented by Class 1. It is worth remarking that Class 1 respondents had higher financial vulnerability, with respect to the other respondents. Research on socio-economic determinants of outpatient antibiotic use suggest that antibiotics are normal goods, influenced by individual financial situation (Filippini, Masiero, & Moschetti, 2006; Masiero, Filippini, Ferech, & Goossens, 2010). In the questionnaire, on which Study III is based, there was the possibility for respondents to leave a comment, at their own discretion. It impressed me that one respondent used it to express that he would have really preferred to choose more alternatives with low 'Contribution to AR', but that

due to his financial difficulties, he often had to prioritise a low 'Cost' alternative. This is just anecdotal, of course. However, it can be a token of the tension between individual effort and collective needs identified in Study I. The relatively high figures about WTP may be of interest for decision makers. However, caution is warranted. As the group whose preferences were mainly influenced by 'Cost' showed financial vulnerability, there is a risk that policy aiming at contrasting antibiotic misbehaviour through financial incentives and disincentives may hinder access to treatment and cause, or worsen, health inequalities. The promotion of judicious antibiotic behaviour should go together with improvements in welfare policies, as aforementioned.

The major benefit of engaging in judicious antibiotic behaviour was contributing to the maintenance of antibiotic effectiveness. This was expressed in numerous ways. The FGD participants emphasised the individual benefit of being less likely to be affected by health issues related to AR as well as the benefit for the collective, including future generations. Data from HBM-related questions in Study III essentially corroborated the qualitative findings.

The interest of the collective was given high consideration in both Study I and Study III. In Study I, participants' emphasis on altruistic or solidaric reasons obliged me to take a deviation from the orthodox application of the HBM, which assumes that health-related behaviour results only from one's own health concerns. In Study III, the importance of 'Contribution to AR' points to the same: individuals can engage in judicious antibiotic behaviour because of altruistic or solidaric attitudes about the health threat posed by AR to others. The results of Study III are discussed in further detail below.

Preferences

From Study I and Study II emerged that lay people may be capable of making decisions and engage in judicious antibiotic behaviour due to altruistic or solidaric reasons. They claimed that they would make personal efforts because of other-regarding preferences, i.e. behaviours and decisions that are not solely motivated by self-regarding preferences. However, Study I and Study II were based on a relatively small sample and participants expressed themselves in front of other participants and the researchers. There was therefore the risk that some participants expressed what they assumed to be the 'right answers', which is a typical bias in qualitative research. Study III was designed to investigate antibiotic treatment preferences and test whether a larger sample would confirm or not that people can be motivated also by other-regarding preferences in their decision-making about antibiotic use.

The findings showed that all attributes of antibiotic treatments ('Contribution to AR', 'Cost', Side effects', 'Failure rate' and 'Treatment duration') influenced respondents' preferences. Therefore, they can all be considered as potential drivers of antibiotic use. As said, the most influential attribute was 'Contribution to AR', which not only shows that people's appraisal of health

care interventions and services can include, and sometimes give paramount importance to non-health outcomes, but it corroborates the previous studies findings about the role of other-regarding preferences. Probably the results would have been different if the respondents were patients or if the attributes were described in other ways. Indeed, this is the salient point: If we bring AR to people's attention, they may be able to include it in their decision-making and be willing to engage in judicious antibiotic behaviour. It is noteworthy that 'Contribution to AR' was explained to respondents as a collective threat and not as a problem to the individual (see Table 2).

Younger respondents were relatively more concerned about their contribution to AR. While this finding is in line with previous research in Sweden (Vallin et al., 2016), research conducted in other countries gave opposite results (Hawking et al., 2017; Napolitano, Izzo, Di Giuseppe, & Angelillo, 2013), which reinforce the idea that regional and cultural differences need to be acknowledged. It makes sense that older respondents tended to be more influenced by side-effects, as the willingness to take (health, financial etc.) risks declines with age (Bonem, Ellsworth, & Gonzalez, 2015; Mather et al., 2012), but it is somehow comforting that the second most important attribute for them was 'Contribution to AR'.

Moral responsibility for judicious antibiotic behaviour

This discussion section mirrors and deepens aspects from Study II and Study IV.

Justice

Focus group participants discussed at length their moral views about the progressive loss of antibiotic effectiveness due to human behaviour. They considered maintaining antibiotics working a matter of justice; they thought it would be unfair to deplete a resource and leave those who need it, or will need it, without.

A rather common view is that when individual actions, laws or public policies are unjust, there is a strong reason to reject them (Miller, 2017). Therefore, the attempt to interpret people's ideas about justice in relation to AR is made to anticipate potential claims between individuals or groups – issues of justice typically arise when people advance claims, e.g., to antibiotic effectiveness, that are potentially conflicting (Miller, 2017). To take into account the public sentiment may also provide useful information for the design of tolerable and suitable policy aimed at constraining the use of antibiotics.

Following Joerg C. Tremmel's work, I distinguish between three main theories of justice that can be applied to issues that involve intergenerational jus-

tice: justice as impartiality, justice as equal treatment of equal cases and unequal treatment of unequal cases, and justice as reciprocity (Tremmel, 2009). The latter does not seem to apply at all to the contents of FGDs. The other two are worth being considered further.

Justice as impartiality, at least in modern and influential versions, is based on contractualist approaches and can be explained in Brian Barry's words as follows:

> [J]ustice should be the content of an agreement that would be reached by rational people under conditions that do not allow for bargaining power to be translated into advantage. [...] The motive for behaving justly is, on this view, the desire to act in accordance with principles that could not reasonably be rejected by people seeking an agreement with others under conditions free from morally irrelevant bargaining advantages and disadvantages. [...] The significance of speaking of 'justice as impartiality' is that this approach, however it is worked out in detail, entails that people should not look at things from their own point of view alone, but seek to find a basis of agreement that is acceptable from all points of views. (Barry, 1989, pp. 7,8)

What Barry describes, can be called a procedural approach to justice: The condition of impartiality is guaranteed by the application of a (just) method, which produces just outcomes (Tremmel, 2009). Contract theories of justice often resort to the thought experiment of an 'original position': an imagined situation about what people would do, prefer or agree upon without existing legal and state systems (Tremmel, 2009). One of the most known and influential is the 'Veil of ignorance' developed by John Rawls (1971). Rawls aimed to describe what free and equal persons, unaware of their personal skills, psychological characteristics, conception of the good and position in society, would consider a fair agreement on the fundamental principles of justice in society. In such a situation, Rawls argued, people would be able to agree on basic principles of justice (Rawls, 1971).

Considering antibiotic treatment and the maintenance of antibiotic effectiveness: People who do not know whether they would be healthy or affected by an infection or whether they would be patients now or in the future, what choices would they make? Krockow and Tarrant argue that "people would generally agree on making appropriate efforts to preserve antibiotic efficacy for future patients through limiting antibiotic use with current patients". The authors claim that in line with Rawls idea of minimising the worst outcome from behind the 'veil of ignorance', exceptions would be justified only in extreme cases. Leonard Leibovici and colleagues also resort to the 'veil of ignorance' but they draw different conclusions (Leibovici et al., 2012). According to Rawls, agents in the original position should rely on maximin reasoning (Rawls, 1971). The maximin principle, which has been much debated (Angner, 2004; Harsanyi, 1975), is supposed to guide agents reasoning when the outcomes of the choices are uncertain. In such situations, the principle says

that each option should be evaluated considering the worst possible outcome that could result from the choice of that option, and decide for the option that is estimated to imply the best worst outcome and discard the other. The focal point about the original position applied to AR is the different interpretation of what constitutes the best worst and the worst outcome, and therefore what people would choose and what they would try to avoid. According to Leibovici et al. (2012), the worst outcome would be to provide (living) patients with suboptimal treatments and to expose them to higher morbidity and mortality to benefit future patients who would be equally, or worse, exposed to morbidity and mortality. There is no way to know what people would really do from behind the 'veil of ignorance' and that is not even the point because, in fact, it is a thought experiment. However, if one considers that the FGD participants' were not only concerned about the maintenance of antibiotic effectiveness for as long as possible but thought that antibiotic effectiveness should be maintained for as long as possible insofar the common good is not sought at the expense of individual patients, then the empirical indication from Study II is that the public sentiment does not tally well with the notion of justice as impartiality.

Participants in FGDs thought it was fair to prioritise social interest for the preservation of antibiotic effectiveness but, at the same time, they expressed concerns about individuals' needs potentially being overlooked. This tension between the interest of the individual and the collective was detected already in the previous analysis, in Study I. Participants' ideas seemed closer to a notion of justice as 'equal treatment of equal cases and unequal treatment of unequal cases'. Namely, patients who have special needs should receive special treatments. While in general, the participants were willing to weigh collective risks and benefits against individual needs, including being positive towards individuals foregoing antibiotics when possible, they always wanted to keep a door open for individuals' special needs and the interest of those who are vulnerable. Participants rejected the option that someone could be not treated and, instead, were in favour of actively taking responsibility. This resonates with the promotion of a virtue-based notion of responsibility, as developed in Study IV: focusing on the creation of capacities and resources that could induce responsible behaviour and a society that promotes and facilitates such capacities.

Moral responsibility

Focus group participants envisioned both collective and individual responsibility for AR. Their focus was on a forward-looking notion of responsibility, i.e. on what can be done to mitigate AR and by whom. They conceived of collective responsibility as being shared by everyone in society, citizens and authorities alike.

The conception of individual responsibility was highly relational: since the behaviour of the individual entails consequences for the collective, behaviours can be object of social judgment. Indeed, when we hold someone accountable, an important factor in our assessment of whether his/her conduct is to blame or praise is if his/her conduct conforms to what we require of one another. This assessment includes normative assumptions about the moral and social norms shared by a community. As highlighted by empirical research, what we do with the information on AR, once it is attained, is influenced by cognitive factors, such as people's attitudes, beliefs, and social norms (Fletcher-Miles & Gammon, 2020). The latter, in the form of injunctive norms, reflect the type of behaviours that a community approves or disapproves, which provide indications to the individuals about what ought to be done (Wagner et al., 2020). The fact that FGD participants interpreted foregoing antibiotics as a potential source of relief and non-judicious use of antibiotics as a possible source of shame, suggests that addressing the moral dimension of antibiotic use and other behaviours could be part of effective health programmes communication. One of the potential challenges of including moral contents within public campaigns or even in the doctor-patient communication was readily identified by the FGD participants themselves: given that the behaviour of the individual who non-judiciously uses antibiotics is blameworthy, there is a risk of stigmatization of socially undesirable behaviour. As participants voiced their concerns over the vulnerable and patients actually receiving needed treatments, it seems they would readily accept providing them with large amounts of antibiotics while also in general condemning overuse and misuse of antibiotics. Similarly, if AR would become a more present and/or tangible threat in people's life, other behaviours such as travelling and food choices may become the object of social judgements and potential stigma. Indeed, when the sensitiveness towards a specific theme spread, individual irresponsible behaviour that holds the potential to be detrimental to the collective can become the object of blame and a source of interpersonal tension. In Sweden, for instance, an expression has been coined, 'flygskam', which translates as 'flight shame'. It refers to a feeling of guilt and therefore shame over the environmental consequences of flying (Wolrath Söderberg & Wormbs, 2019). Flight shame and flight shaming have brought some people to rethink their behaviours, i.e. to reduce or stop flying, either as a result of their own understanding, or as a social desirability response (Mkono, 2020).

As FGD participants regarded the use of antibiotics as morally acceptable when necessary for one's care, and morally questionable in all other cases, presumably, they implicitly referred to *informed* wrongdoing, i.e. when one is aware of proper use of antibiotics and of AR. Indeed, they expressed the view that it is one's duty as citizen to inform oneself. In the literature on moral responsibility, the role of epistemic ignorance and the extent to which it can excuse agents is debated (Rudy-Hiller, 2018). According to Jasper Littmann

and Adrian M. Viens, antibiotic ignorance may soon be considered inexcusable, especially in HICs (Littmann & Viens, 2015). Participants' views that individuals should behave in certain ways, have a duty to educate themselves and develop certain attitudes can be conceptualised in terms of virtue ethics.

In Study II and Study IV, I suggested the idea that social norms hold the potential to contribute to the adoption of judicious antibiotic behaviour and advocated a notion of responsibility as a virtue. The notion of responsibility as a virtue is primarily normative – namely, it implies a normative evaluation of behaviours in relation to AR and prescriptions concerning desirable behaviours and the conditions for their fulfilment – and forward-looking, which is in line with FGD results. The focus on a forward-looking notion of responsibility is also consistent with the conceptual analysis carried out in Study IV. In fact, although virtually everyone can be considered accountable for contributing or having contributed to AR, at present holding agents responsible, in the sense of being blameworthy, makes little sense. In order to attribute blame, usually other elements in addition to causality and competence are needed. Typically, these elements are knowledge, freedom and wrongdoing (Nihlén Fahlquist, 2019a; van de Poel, 2011). I have already written about knowledge and explained that it needs to be seen in context with other cognitive factors and social determinants of health. However, at present, it is difficult to blame anyone based on that he/she knew about correct antibiotic use and other behaviours that can be related to AR. Concerning freedom, it is beyond the scope of this thesis to discuss the notions of free will and determinism. Here I conceive freedom as the agent's possibility to act as he/she chooses, simply intended as the absence of external constraints (Schlick, 1939). Of course, an individual who receives antibiotics against his/her will should not be blamed.

The case of wrongdoing is more nuanced. It is uncontroversial that an individual who, for instance, would take or force another to take antibiotics only to contribute to AR should be blamed. However, this, as the precedent case, is a bit airy-fairy. There is a component that is partially missing for people blaming the irresponsible behaviour of the individual who contributes to AR; while in theory virtually everyone would blame antibiotic misbehaviours, in practice these are not established objects within the realm of moral and social norms yet, and there is a consequent lack of normative assumptions, which could be transgressed or adhered to. Differently from the environmental case, the times are not ready for 'antibiotic shame'. However, when people discuss the moral dimension of behaviours that can have an influence on AR as in Study II, or when they take into account their potential contribution to AR as in Study III, the importance of conserving antibiotic effectiveness and the moral wrongness of non-judicious antibiotic behaviour emerge clearly.

Conceiving responsibility in terms of virtue ethics, as suggested in Study IV, entails focusing on the agent but also on the society of which he/she is part. Responsibility as a virtue refers to an agent cultivating character traits

and habits that make him/her a responsible person (Nihlén Fahlquist, 2019). At the same time, as the desirability of specific character traits is contextual, awareness of AR and of its public health and ethical dimensions should be promoted.

Antibiotic resistance is a complex issue, which can be influenced by a large set of human behaviours. Therefore, responsibility towards it requires the development in the individual of a certain sensitivity to the plurality of normative demands involved (Williams, 2008). The aim would be individual engagement in judicious antibiotic behaviour. This, should be conceived dynamically, i.e. the best course of action under the prevailing circumstances. Individuals who experience favourable socioeconomical, cultural, and political contexts, have a bigger responsibility to engage in judicious antibiotic behaviour. The opposite is also true.

National and international institutions have a responsibility to create the circumstances that can facilitate agents' engagement in judicious antibiotic behaviour, designing campaigns developed from an appraisal of people's attitudes, beliefs and social norms, and designing programmes that take into account people's resources, e.g., socioeconomic factors. Policy demandingness should be set according to local realities.

Policy demandingness

In Study II, two different theoretical proposals for the preservation of antibiotic effectiveness were discussed in light of the study results. The proposals were Millar's principle of antibiotic use, and Giubilini and Savulescu's proposal for an incentive-based policy (Giubilini & Savulescu, 2019; Millar, 2012). Both have already been explained in the Background section of this thesis. Millar's principle:

> [A]ntibiotics should be used to prevent some substantial risk of irretrievable harm in patients or their contacts, where a substantial risk is a level of risk that can be reduced by the use of antibiotics, and which exceeds the range of risks of irretrievable harm that we tolerate in our day-to-day lives. (Millar, 2012, p. 467)

The major issue with the principle is that preserving antibiotics only for the treatment of infections that could cause irretrievable harm would result in leaving many patients untreated. This may be very demanding for some patients and, as already discussed, may be in stark contrast with the moral views expressed by FGD participants, who believed that the common good should not be sought at the expense of individual patients.

Giubilini and Savulescu acknowledge that foregoing antibiotics can sometimes be very demanding. Therefore, people should not be coerced into foregoing antibiotic treatments that could be beneficial to them (Giubilini &

Savulescu, 2019). I consider not offering available antibiotic treatment options to be as morally problematic and equally demanding for the patients than co-ercing them into foregoing antibiotic treatments. Giubilini and Savulescu argue that, instead of compulsory measures, incentives would be a preferable option to encourage a *virtuous* approach to antibiotic use (*virtuous* is my expression). Incentives could be financial but could also consist of improved medical attention. Moreover, the positive influence of social norms suggests that social recognition and praise could be incentives too (Giubilini & Savulescu, 2019). I consider this second proposal more compatible with lay people's views on what they owe to society and on what justice, interpreted as equal treatment of equal cases and unequal treatment of unequal cases, demands.

Discussion of methodology

Studies I–II

To reach trustworthiness of qualitative research findings, credibility, transferability, dependability and confirmability should be pursued. They are described in the following, considering Andrew K. Shenton' recommendations (Shenton, 2004).

Credibility is the extent to which the study has captured the truth of the subject under investigation. It was improved by:

1. Examining previous research findings: first, to build an interview guide to contribute scientifically relevant information and, second, to assess the degree to which the study results are congruent with those of previous studies;
2. Adopting research methods well established both in the design phase and in the analyses phase, using content analyses and the HBM for developing the interview guide, in the analysis and discussion of Study I;
3. Adopting iterative questioning (follow-up and probing questions);
4. Having qualified and experienced researchers with different backgrounds to facilitate the FGDs;
5. Debriefing sessions between the researchers and multiple peer scrutiny;
6. Pursuing triangulation by: A) making the groups heterogeneous (age, gender and education and through site based sampling) as a way of triangulating via data sources; B) two researchers with different backgrounds analysed the transcripts independently.

Transferability is the extent to which the findings can be applied to other situations. It was improved by adhering to the COREQ in order to provide the readers with as detailed information as possible (A. Tong et al., 2007).

Dependability is the consistency of findings across similar settings and/or similar research subjects, i.e. the extent to which the findings would be similar if the study was repeated. This aspect is partially dependent on credibility and seeks to enable readers to potentially reproduce the study, using transparent description of the different phases of the study, which was improved by adhering to COREQ (A. Tong et al., 2007).

Confirmability is the extent to which findings reflect the respondent and context, with limited influence from the researchers (i.e. scientific objectivity). This aspect is partially dependent on credibility. Moreover, confirmability was improved by having an audit trail (with a data-oriented approach, i.e. observers were shown how the data lead to the formation of findings).

The major limitations of this study relate to the fact that the sample was small and relatively homogeneous with mostly Swedish-speaking middle class from an urban area. Thus, the results might not be transferable to other populations and contexts, particularly those in a rural community or those with other cultural or ethnic diversity or social class. Another limitation is the fact that although saturation was reached, data were only gathered within the FGDs and the findings are not matched with data collected through alternative sources (e.g. individual interviews).

Study III

To reach trustworthiness of quantitative research findings, validity and reliability should be pursued. These aspects of the performed DCE are described in the following, considering Ellen M. Janssen and co-authors (2017).

Validity is the extent to which the study measures the outcome of interest. In DCEs, the concepts of face validity, convergent validity and external validity are applied to identify how accurately the DCE measures preferences and how generalizable these are.

Face validity is the extent to which the results are consistent with a priori expectations. In DCEs, attributes and attribute levels that are important for the majority of participants should be captured. Face validity was sought through adherence to best practice guidelines (Bridges et al., 2011; Kløjgaard et al., 2012) and, content-wise, through stakeholders' interviews, peer debriefing, think-aloud exercise and the pilot. Face validity was tested by setting a priori hypotheses between the attribute levels and then checking the (positive or negative) direction of the estimates. All theoretical assumptions were confirmed, and all attributes were significant.

Convergent validity is the extent to which the study results are consistent with other studies or instruments used to do similar measures. This was inter-

nally tested, measuring WTP. Externally, comparisons made with similar previous studies gave contrasting results, which were interpreted as a sign of socio-cultural different contexts (the findings are in agreement with similar Swedish studies).

External validity is the extent to which the results reflect actual decision-making behaviour. It is a difficult concept to test as the best way to do it would be to observe real-life choices about antibiotic treatments (but patients are not presented with antibiotic treatment options in real life). Studies investigating the predictive value of DCEs in public health, thus comparing stated preferences with actual behaviour, have shown between 80% and 93% accuracy (de Bekker-Grob, Donkers, Bliemer, Veldwijk, & Swait, 2020; Lambooij et al., 2015; Salampessy et al., 2015).

Reliability is the extent to which the study produces similar results under consistent conditions. Due to the novelty of this study, there is not an immediate way to compare results. However, the study was designed according to best practice guidelines and indications in the literature to ensure the quality of the instrument (e.g. manners to optimise choice tasks layout, to minimise cognitive burden, to rationally clean the data), so that other researchers can repeat it (although preferences can change over time).

Choice validity and choice reliability, which are concepts specific to examining assumptions in preference studies, were measured by testing the attribute dominance (i.e. when participants' choices are dominated by one attribute, which is against the DCE assumption that all attributes are considered) and left-right bias (tendency to always choose a column).

Concerning generalisability, novelty of the study, sampling and potential specificity of Swedish results warrant caution. Concerning sampling, it should be considered that it was used an online panel recruited through a commercial company.

Conclusion

The international effort to decrease and optimise the use of antibiotics should be supported by the design of local policies sensitive to social and cultural contexts. The fact that AR is taken as a serious matter and that national and international actions are taken to contrast it, should be clearly communicated by the authorities. Public campaigns should include messages on individual health behaviour, but also on the public health and moral dimensions of AR, as people can include them in their decision making.

The empirical findings in this thesis allow drawing conclusions only about Swedish reality. However, it is reasonable to expect that some of the results and of the conclusions drawn may hold value also in other contexts.

The findings point at the importance of involving the public for designing and implementing effective conservation programmes. There are indications that emphasising the fact that AR is already a significant public health issue, for instance in public campaigns or in the doctor-patient communication, may contribute to the engagement in judicious antibiotic behaviour. Although actions against the decrease of antibiotic effectiveness depends on the actions of the collective, the relevance of individual behaviour should be highlighted: individual's behaviour in relation to AR not only contribute to mitigate or worsen the general situation of AR but entails consequences for the individual and his/her close ones. Everyone's behaviour matters.

The exploration of people's moral views showed that maintaining antibiotic working is a matter of justice and that it is considered unfair to deplete a resource and leave those who need it, or will need it, without. The collective responsibility of maintaining antibiotic effectiveness is mirrored in the individual's responsibility to engage in judicious antibiotic behaviour. The findings suggest that people, in reason of other-regarding preferences, could engage in such behaviours even if they imply personal disadvantages.

Individuals have a moral responsibility for AR, which could be conceived as a virtue. According to this notion, individuals have the opportunity to develop a sensitivity towards AR and, consequently, are capable of engaging in judicious antibiotic behaviour. However, individuals engage, or fail to engage, in judicious antibiotic behaviour with different degrees of voluntariness: the influence of socio-economic, contextual and collective determinants need to be acknowledged, because engagement in judicious antibiotic behaviour should not be merely reduced to a matter of individual awareness and good

will. Institutions need to create circumstances that can facilitate individual engagement in judicious antibiotic behaviour.

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Appendix 1. Study I - Interview guide

Opening	1) What is your name and why did you decide to partake in this discussion?
Introductory	2) What is the first thing that comes up in your mind about antibiotics?
Transition	3) What is your experience with antibiotics?
Key questions	4) Please write down a list of what you think are advantages and disadvantages of using antibiotics.
	5) Do you think that you should have the right to buy antibiotics by yourself without prescription? *Probing question:* What the others think?
	- Break and short movie -
	6) How would you react if you had fever and cough and the doctor says no to prescribe antibiotics to you? *Probing questions:* Group reflection about whether this is perceived as dangerous, about buying antibiotics online and using leftovers.
	7) As you saw in the movie, there are risks related to antibiotic resistance. What do you think about it and why?
	8) Thanks to antibiotics, healthcare has had great success in treating infections. We know that increased resistance is of particular concern for groups at risk, such as immunocompromised patients, those who undergo major surgery, patients in cancer treatment, etc. For their sake, it is important that we all use antibiotics responsibly. What do you think about this? *Probing questions:* Group reflection about whether responsible use is difficult/burdensome, about who is or should be held responsible and about future generations.
	9) Some researchers said: "The solution may ultimately require us to put society before the individual. That is, halting the rise of resistance may only be achievable if some patients go untreated". Is this reasonable?
	10) What are you prepared to do to counter antibiotic resistance? *Probing questions:* Group reflection about whether they could do more vaccines, travel less.
Ending	11) If you could give a suggestion to decision makers about antibiotics use, what would be your advice?

Appendix 2. Study III - Questionnaire

Part 1. Questions about you and your knowledge on antibiotics

Have you ever used antibiotics?

- ○ Yes
- ○ No
- ○ I don't know
- ○ I can't use antibiotics (for instance, because of allergy)

How old are you?

Please insert your age: [ ]

⇐ ⇒

What describes you best?

○ Woman
○ Man
○ Prefer not to answer
○ Prefer to self describe: [   ]

⇐ ⇒

What is the highest level of education you have completed?

- ◯ Primary school or equivalent
- ◯ Secondary education (max 2 years)
- ◯ Secondary education (max 3 years)
- ◯ University/high education (3 years or less)
- ◯ University/high education (more than 3 years)
- ◯ Other, namely: [   ]

⇦　⇨

Do you have medical/health-related education (medicine, nursing, dental care etc.)?

- ◯ Yes
- ◯ No

⇦　⇨

What is your main occupation?

- ◯ Unemployed
- ◯ Student
- ◯ Pensioned
- ◯ Permanent employment
- ◯ Entrepreneur
- ◯ Fixed-term employment
- ◯ Other, namely: [   ]

⇦ ⇨

How often would you do the following? (1/2)

	Never	Once	More than once	Often	Very often
I would give directions to someone I did not know	◯	◯	◯	◯	◯
I would make changes for someone I did not know	◯	◯	◯	◯	◯
I would give money to a charity	◯	◯	◯	◯	◯
I would donate clothes or goods to a charity	◯	◯	◯	◯	◯
I would help carry belongings of someone I did not know	◯	◯	◯	◯	◯
I would delay an elevator and hold the door for someone I did not know	◯	◯	◯	◯	◯
I would allow someone I did not know to go in front of me in line	◯	◯	◯	◯	◯

⇨

How often would you do the following? (2/2)

	Never	Once	More than once	Often	Very often
I would point out a clerk's error in undercharging me for an item	◯	◯	◯	◯	◯
I would let a neighbor I did not know well borrow an item of value to me	◯	◯	◯	◯	◯
I would help a classmate who I did not know well with a homework assignment when my knowledge was greater than his/hers	◯	◯	◯	◯	◯
I would voluntarily look after a neighbor's pet or children without being paid	◯	◯	◯	◯	◯
I would offer to help a handicapped or elderly person across the street	◯	◯	◯	◯	◯
I would offer my seat on a train or bus to someone who was standing	◯	◯	◯	◯	◯
I would help an acquaintance move houses	◯	◯	◯	◯	◯

⇦　⇨

UPPSALA UNIVERSITET

How often have you been without money before the end of the month in the past year?

- ⚪ Every month/always/often
- ⚪ Sometimes/seldom
- ⚪ Never
- ⚪ Can't/Don't want to answer

⇦ ⇨

UPPSALA UNIVERSITET

Suppose your household has an unforeseen expense of SEK 20000 that must be paid within a few weeks

Can your household handle such a huge expense without having to take out new loans, sell property, sell securities or through any other major financial sacrifice?

- ⚪ Yes
- ⚪ Not sure
- ⚪ No
- ⚪ Can't/Don't want to answer

⇦ ⇨

How would you describe your health?

- ◯ Very good
- ◯ Good
- ◯ Fair
- ◯ Poor
- ◯ Very poor

⇦　⇨

Can you find and use health-related information if you need to?

Check the option on each line that best matches your answer

	Disagree strongly 1	Disagree 2	Partially agree 3	Agree 4	Agree strongly 5
I can retrieve information from many different sources such as newspapers, internet, books, health services, family and friends etc.	◯	◯	◯	◯	◯
I can choose just the information I need from a variety of sources of information	◯	◯	◯	◯	◯
I can understand the information and share it with others	◯	◯	◯	◯	◯
I can judge if the information is credible	◯	◯	◯	◯	◯
With the help of the information, I can plan and decide what I need to do to improve my health	◯	◯	◯	◯	◯

⇦　⇨

How good are you at managing numbers? Assess your ability while answering the following questions:

	Not good at all 1	2	3	4	5	Extremely good 6
How good are you at working with fractions?	○	○	○	○	○	○
How good are you at figuring out how much a shirt will cost if it is 25% off?	○	○	○	○	○	○

	Never 1	2	3	4	5	Very often 6
How often do you find numerical information to be useful?	○	○	○	○	○	○

⇦   ⇨

UPPSALA UNIVERSITET

Antibiotics are powerful drugs that help fight...

Check one or more alternatives

- ⚪ Virus
- ⚪ Bacteria
- ⚪ All microbes
- ⚪ I don't know

⇐ ⇒

UPPSALA UNIVERSITET

Antibiotics are effective against the flu

- ⚪ I agree
- ⚪ I don't agree
- ⚪ I don't know

⇐ ⇒

The human body can become resistant to antibiotics, giving bacteria free space

- ⚪ I agree
- ⚪ I don't agree
- ⚪ I don't know

⬅ ➡

Antibiotic resistant bacteria can spread to humans through...

Check one or more alternatives

- ⚪ Contact with a person who has an antibiotic-resistant infection
- ⚪ Contact with something that has been touched by a person who has an antibiotic-resistant infection (for instance, an instrument in a healthcare facility with poor hygiene)
- ⚪ Contact with a living animal, food or water that carries antibiotic resistant bacteria
- ⚪ I don't know

⬅ ➡

Part 2. Hypotetical choice tasks

In the upcoming choice situations, you must choose between two different antibiotic treatments.
Each treatment option has five characteristics. The characteristics of the choice situations occur in several different combinations. The characteristics are:

1. Contribution to antibiotic resistance
2. Treatment duration
3. Side effects
4. Treatment failure
5. Cost for you

In the following pages the characteristics are explained in more detail.

⇦ ⇨

Contribution to antibiotic resistance (1/5)
Bacteria that can withstand antibiotic treatment are called antibiotic resistant bacteria. The main cause of resistance is treatment with antibiotics. Antibiotic resistance is a serious and growing public health problem. It gives longer care times, higher care costs and an increased risk of infection complications.

In the choice situations that you will soon be facing, the antibiotic treatments you choose between will have low, medium or high contribution to resistance:

• **Low** (15,000 cases per year: in 10 years the number of cases in Sweden would remain the same)
• **Medium** (30,000 cases per year: in 10 years the number of cases in Sweden would double)
• **High** (70,000 cases per year: in 10 years the number of cases in Sweden would more than quadruple)

⇦　⇨

Treatment duration (2/5)
You must take three tablets a day throughout the treatment period prescribed by your doctor.

In the choice situations, the treatment duration can be either:

• **3 days**
• **7 days**
• **14 days**

⇦　⇨

Side effects (3/5)

All medicines have side effects, including antibiotics. Because they not only kill harmful but also beneficial bacteria in the body, they can cause mild to moderate side effects such as nausea, stomach upset, headache and tiredness.

In the choice situations, we will state how likely the antibiotic treatment is to cause side effects. The probability may be, for example:

1% (1 in 100 people taking this antibiotic get side effects, 99 do not get side effects)
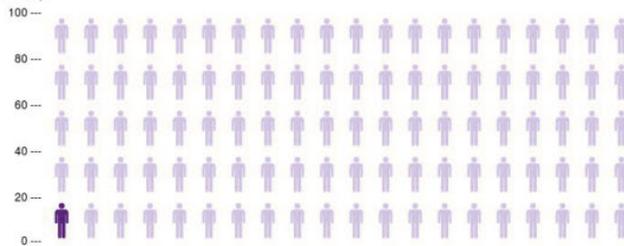
10% (10 in 100 people taking this antibiotic get side effects, 90 do not get side effects)

⇦   ⇨
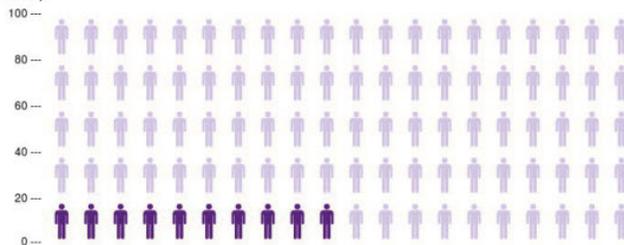
Treatment failure (4/5)

An antibiotic treatment may fail to treat an infection for many reasons. The failure of the treatment means that you have to be treated again, with another antibiotic.

The likelihood that antibiotic treatment will fail can be, for example:

15% (15 out of 100 people need a further course of antibiotics)
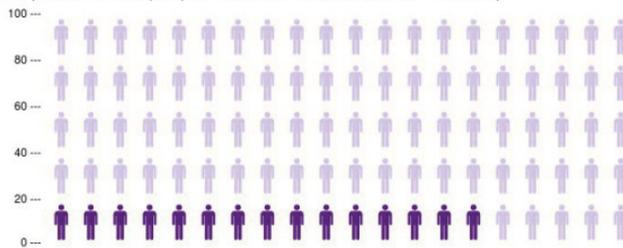
20% (20 out of 100 people need a further course of antibiotics)
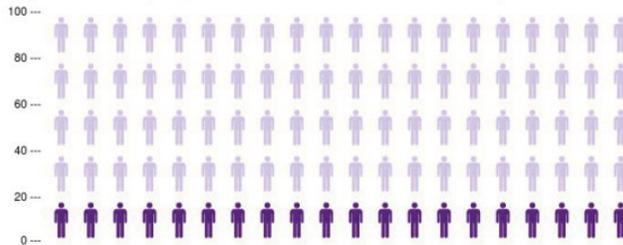
Cost for you (5/5)

Antibiotic treatments in the upcoming choice situations are not subsidized through high-cost protection / drug benefits. You have to pay the full cost yourself.

In the choice situations, there are the following costs for antibiotic treatment:

- **100 SEK**
- **250 SEK**
- **400 SEK**
- **1,000 SEK**

⇐　⇒

Time to start choosing!

Choose between Antibiotics A and Antibiotics B.
Choose the treatment you would prefer.

Antibiotics are used for infections caused by bacteria. Imagine you have a bacterial infection. Your life is not in danger, but your doctor recommends that you take antibiotics. In the choice situations that come, you will be asked how you would do if you had the opportunity to choose between different antibiotic treatments.

Note! If you are not sure about what something means, hover over the text for an explanation.

⇐　⇒

Which do you prefer (1 of 16)
Note! Hover over or press the text for an explanation.

Antibiotika A	Antibiotika B
Contribution to antibiotic resistance low	**Contribution to antibiotic resistance** high
Treatment duration 3 days	**Treatment duration** 7 days
Side effects 10%	**Side effects** 20%
Treatment failure 20%	**Treatment failure** 5%
Cost for you 250 kr.	**Cost for you** 100 kr.
◯	◯

Which do you prefer (16 of 16)
Note! Hover over or press the text for an explanation.

Antibiotika A	Antibiotika B
Contribution to antibiotic resistance medium	**Contribution to antibiotic resistance** high
Treatment duration 14 days	**Treatment duration** 7 days
Side effects 10%	**Side effects** 5%
Treatment failure 20%	**Treatment failure** 5%
Cost for you 100 kr.	**Cost for you** 400 kr.
○	○

⇨

That was the last choice situation!

Now we just want to ask a few more questions to better understand your views.

Your opinion on antibiotics (1/2)

Select the option on each line that suits you best

	Strongly agree	Agree	Disagree	Strongly disagree	I don't know
Nowadays, antibiotic resistance is a big problem in Sweden	○	○	○	○	○
I feel antibiotic resistance as a potentially major threat to my health	○	○	○	○	○
Using antibiotics properly feels good because I know I'm doing something good for myself	○	○	○	○	○
Sometimes it can be difficult to adhere to prescriptions	○	○	○	○	○
That Swedish authorities take the problem of antibiotic resistance seriously makes me more inclined to use antibiotics correctly	○	○	○	○	○
I think I can take responsibility for using antibiotics correctly	○	○	○	○	○

⇦ ⇨

Your opinion on antibiotics (2/2)

Select the option on each line that suits you best

	Strongly agree	Agree	Disagree	Strongly disagree	I don't know
I believe that antibiotic resistance is mainly a problem for the future	○	○	○	○	○
I'm afraid of getting resistant bacteria	○	○	○	○	○
Using antibiotics correctly feels good because I know I'm doing something good for others	○	○	○	○	○
I believe that my use of antibiotics has no effect on antibiotic resistance	○	○	○	○	○
Better understanding of antibiotic resistance helps me use antibiotics correctly	○	○	○	○	○
I can give up things I like (like a holiday trip) if it would reduce resistance	○	○	○	○	○

⇦　⇨

How do you think about your health and taking risks? (1/2)

Select the option on each line that suits you best

	Strongly agree 1	Agree 2	Somewhat agree 3	Neither agree nor disagree 4	Somewhat disagree 5	Disagree 6	Strongly disagree 7
I think I take good care of my body	○	○	○	○	○	○	○
I don't want to have to consider the consequences for my health in everything that I do	○	○	○	○	○	○	○
It is important to me that I organize my life so that I will later enjoy good health	○	○	○	○	○	○	○
If it concerns my health, then I see myself as someone who avoids risks	○	○	○	○	○	○	○
Uncertainty about the consequences of a medical intervention is, in general, part of the game	○	○	○	○	○	○	○
My health means everything to me	○	○	○	○	○	○	○

⇦ ⇨

How do you think about your health and taking risks? (2/2)

Select the option on each line that suits you best

	Strongly agree 1	Agree 2	Somewhat agree 3	Neither agree nor disagree 4	Somewhat disagree 5	Disagree 6	Strongly disagree 7
When I look back at my past, I think that, in general, I did take risks with my health	○	○	○	○	○	○	○
If the doctor cannot offer me certainty about the possible consequences of a medical intervention, then I would rather not undergo it	○	○	○	○	○	○	○
Safety first, where my health is concerned	○	○	○	○	○	○	○
To enjoy good health now and in the future, I am prepared to forego a lot	○	○	○	○	○	○	○
People say that I take risks with my health because of my habits	○	○	○	○	○	○	○
I'm not very fussy about my health	○	○	○	○	○	○	○
In general I would estimate that I would not have much of a problem with undergoing a high risk operation	○	○	○	○	○	○	○

⇦ ⇨

How long was the survey?

◯ Very long   ◯ Long   ◯ Fair   ◯ Short   ◯ Very short

How difficut was to answer the survey?

◯ Very difficult   ◯ Difficult   ◯ Fair   ◯ Easy   ◯ Very easy

Comments (optional)

Please write if you have any suggestions for improvement or if you have detected errors in the survey. Your comments will of course be treated anonymously.

⇦   ⇨

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