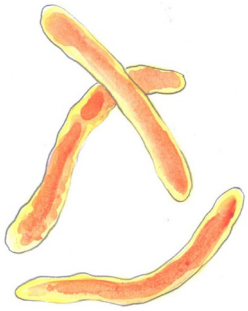
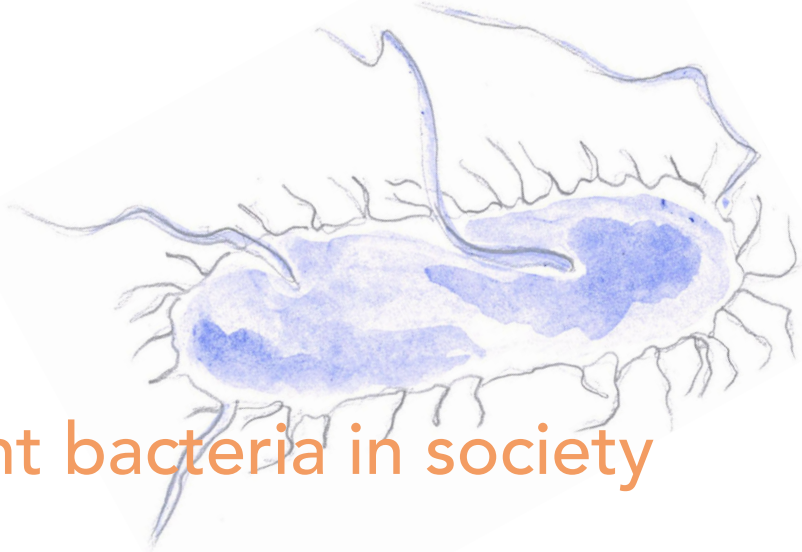
Resistant bacteria in society





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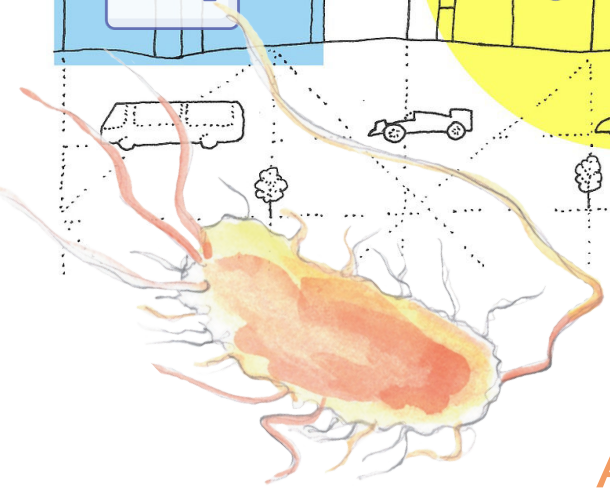
Travelling through practices of policy, healthcare and science



Alena Kamenshchikova

Resistant bacteria in society

Travelling through practices of policy, healthcare and science

Dissertation

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Alena Kamenshchikova

Supervisors
Prof. Dr. K. Horstman
Prof. Dr. C.J.P.A. Hoebe

Co-supervisor:
Dr. P.F.G. Wolffs

Assessment Committee
Prof. Dr. P.H.M. Savelkoul (Chair)
Prof. Dr. P. Martens
Prof. Dr. H. Dijstelbloem, University of Amsterdam
Prof. Dr. C. Chandler, London School of Hygiene and Tropical Medicine

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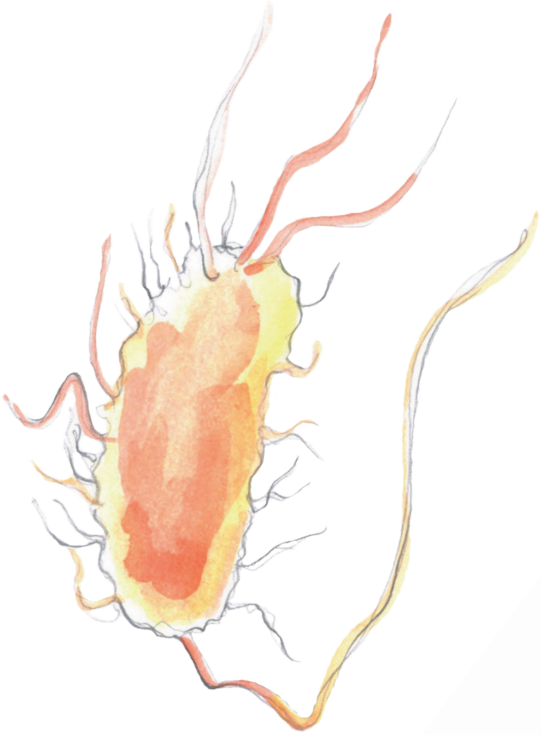

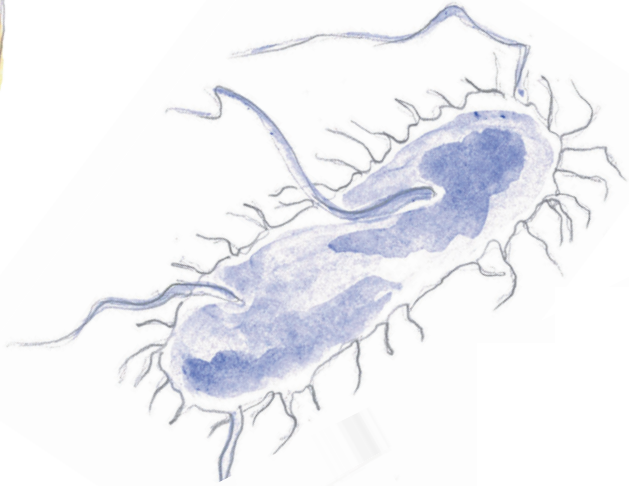

Introduction

Bacteria in society

Down the rabbit hole

This thesis is the result of my journey into the world of antimicrobial resistance (AMR). This journey started in 2017 with a collaboration between philosophers, microbiologists and infectious disease specialists working on a project about AMR screening of refugees in the Netherlands. After having finished a master's in the humanities and social sciences, I joined this project for five months to analyse ethical aspects of such screenings. However, I stayed longer and became part of a team working on transdisciplinary approaches to AMR. I started studying different practices and meanings of AMR, and I travelled through three different settings: 1) international policies on AMR, 2) AMR healthcare practices 3) and microbiological and social science research on AMR. Starting this journey, I did not have a clear map that would guide me through these different settings; therefore, like Alice in Wonderland I went down the rabbit-hole 'never once considering how in the world [I] was to get out again'. In the following thesis, I will lead you through the Wonderland that I discovered during this adventure.

Biology in society and vice versa

Antimicrobial resistance can be understood as both a biological and social phenomenon. As I travelled through the world of microbiology I learned that microbiologists define AMR as an evolutionary ability of microorganisms, including bacteria, viruses and parasites, to adapt to antimicrobials, such as antibiotics and antivirals (WHO, 2018). This ability of microorganisms challenges the treatment of infectious diseases and complicates medical procedures that require immunosuppression, such as chemotherapy or surgery (Martinez, 2014). Such explanation of AMR in microbiology has not always been understood as an established fact – it has been developed only within the last 70 years.

The first effective antimicrobial agents, sulfonamides, were introduced in 1937, and by the end of the 1930s bacteriologists had already announced that bacteria had developed resistant mechanisms to this agent (Davies & Davies, 2010). Similar developments have been recorded with other antibiotics introduced to the market: penicillin was first given to a patient in 1941, and in 1942 penicillin-resistant bacteria were identified (for a further chronology of AMR development see Figure 1). One of the first disciplines interested in the effects of antibiotics on bacteria was genetic science that analysed bacterial mutation processes that led to the development of resistant mechanisms (Landecker, 2015). In the 1940s and 1950s, these mutation processes were believed to be rare events limited to vertical genetic inheritance, meaning that only the offspring of mutant bacteria would acquire resistance. However, by the

end of the 1950s and beginning of the 1960s, the understanding of AMR and its mechanisms had begun to change.

The rise of genetic engineering in the 1960s led to a different vision of AMR: resistant genes can be transferred not only within the same bacterial population but also between different populations of bacteria (Landecker, 2015). This paradigmatic shift took place in biological sciences with the introduction of horizontal gene transfer – the transmission of genetic information both between and within different bacterial populations (Barlow, 2009). Subsequent microbiological research on multidrug-resistant infections argued that bacteria could acquire resistance to antibiotics that they were previously exposed to. In addition, it was argued that bacteria might acquire resistant mechanisms from the environment and other bacteria, even if they had not had previous direct exposure to antibiotics (Levy, 2002).

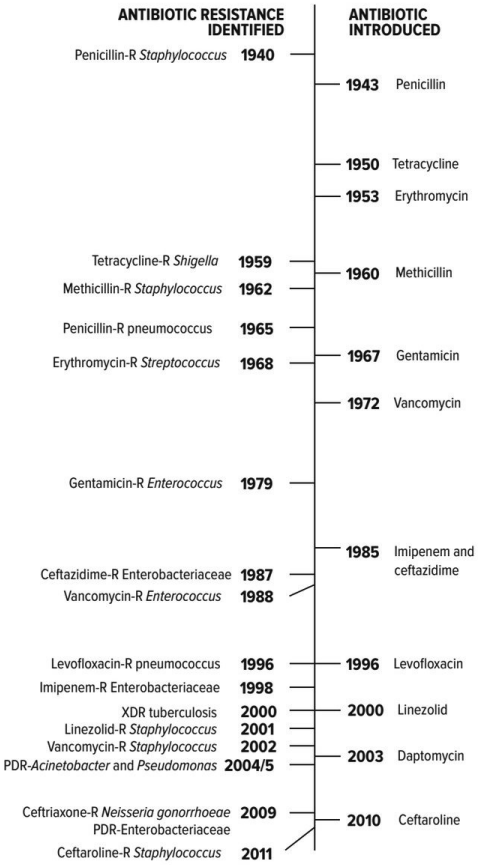

Figure 1: The timeline of the introduction of antibiotics and the appearance of antibiotic resistance (the figure is taken from Malmir et al., 2018)

Since then the phenomenon of AMR has been linked to more and more mechanisms that bacteria can develop, including limiting the uptake of a drug, drug inactivation and drug efflux (Martinez, 2014; Reygaert, 2008). Although microbiology has generated substantial knowledge about the biological life of bacteria and their mechanisms of resistance, many authors stress that this knowledge is incomplete and constantly changing (Cox & Wright, 2013; Martinez, 2014; Reygaert, 2008). This brief history of biological inquiries into AMR shows that this phenomenon is not understood as something static or fixed but that it is a broad term that refers to different and constantly changing knowledge about bacteria.

Travelling through the world of microbiology and learning about the biological mechanisms of AMR, I then returned to my home discipline of social science and philosophy.

There, I looked at the work of social scientists to understand how AMR can be studied as a social phenomenon. Social science scholars have studied various antibiotic practices in humans, animals and agriculture as well as practices of pharmaceutical and clinical waste management – namely, human practices that influence the acquisition of resistance by bacteria (Broom et al., 2014; Larsson, 2014; Rodrigues, 2020; Rutgersson et al., 2014). Apart from that, social scientists have reflected upon and conceptualised human-bacteria relations and their role in economic and political processes at the national and international levels (Brown & Nettleton, 2016; Chandler, 2019; Landecker, 2015). These studies have shown that the practices of antibiotic use are influenced by different processes, including economic and structural accessibility of non-antibiotic treatments, the possibility to take time off work to recover from illness and economic pressures of market demands on farmers to produce more food. Therefore, similar to the microbiological understanding of AMR, social science studies have shown that this phenomenon refers to multiple social practices and processes that may influence the bacterial acquisition of resistance.

The biological and social understandings of AMR can be brought together to create an umbrella biosocial concept of AMR that refers to multiple microorganisms and mechanisms to resist antimicrobials and to multiple social practices and processes that influence resistant mechanisms of bacteria.

The management practices of this biosocial phenomenon have been incorporated into policy, healthcare and science settings. International organisations, like the World Health Organisation (WHO) and the World Organisation for Animal Health (OIE), and national governments develop antibiotic prescription protocols and standards for infection management, introduce quarantine practices for patients with suspected AMR infections and allocate funding for the development of new medicines and scientific research (O'Neill, 2016; WHO, 2015). These actions have been criticized by researchers in both the biomedical and social sciences for being too technical and for not addressing the multi-sectorial nature of AMR (Chandler, 2019; Hinchliffe et al., 2018; Larsson, 2014). The microbiologist Larsson (2014) stresses that it is important to look beyond the prescription of antibiotics and to address the economic and political conditions that allow pharmaceutical companies to establish their factories in countries like India and pollute the local environments with antibiotic waste. The anthropologist Chandler (2019) argues that campaigns targeting the individual behaviour of patients or prescribers do not acknowledge the significance of social, political and economic drivers, like the inability to pay for healthcare services or to take the time off work, which, in

turn, influence behavioural practices. Therefore, the world of AMR presents ambiguities, contrasts and controversies when it comes to defining and dealing with this phenomenon.

Against the background of these discussions about AMR and how to tackle it, in this thesis I aim to gain more insight into how AMR is incorporated and *practised* in different settings of policy, healthcare and science and what kind of reality is *constructed* through these practices.

Before starting the journey into this AMR Wonderland, I will give an overview of relevant background information, which will help in navigating through different settings and practices. I will first sketch how starting from the development of the first antibiotics, bacteriologists and medical professionals aimed to construct AMR as a major public health issue. I will then present how current international health policies deal with this issue. Following this, I will introduce how social scientists have proposed to study AMR. After having explained my methodological approach, I will elaborate on the structure of this thesis.

The historical construction of AMR: from a laboratory to policy agenda

To understand how AMR has become a concern for public health globally, I will give a sketch of the historical constructions of this phenomenon that is related to the invention and use of antibiotics. In his Nobel Prize lecture in 1945, Fleming shared his experience of observing a penicillin production factory in the US:

> I had the opportunity this summer of seeing in America some of the large penicillin factories which have been erected at enormous cost and in which the mould was growing in large tanks aerated and violently agitated. To me it was of especial interest to see how a simple observation made in a hospital bacteriological laboratory in London had eventually developed into a large industry and how what everyone at one time thought was merely one of my toys had by purification become the nearest approach to the ideal substance for curing many of our common infections.

This observation captures the infrastructural transformations and increasing expansion of antibiotics from one laboratory in the UK to industrial factories all over the world. Such expansion was possible due to the integration of antibiotics, starting from penicillin, into all spheres of life, including healthcare, hygiene, policy-making, scientific research, agriculture and animal husbandry. In the 1960s and 1970s, AMR was not considered a major public health problem, to the point that in 1978 Petersdorf, one of the world's leading infectious disease specialists of that time, argued that infectious disease was a speciality that might no longer be needed as antibiotics can easily tackle infections. He stated that 'even with my great personal

loyalty to infectious disease, I cannot conceive of the need for 309 more [graduating trainees in] infectious disease . . . unless they spend their time culturing each other' (Spellberg, 2008). Thirty-three years later the WHO announced that AMR is 'a threat to all branches of medical and public health practice', which requires an increase in infectious disease expertise (Leung et al., 2011).

Several historical studies have provided insights into the dynamics of how AMR has steadily become a public health concern of global importance. In his work *Penicillin: Triumph and Tragedy,* Bud (2007) investigates the history of the discovery and global popularisation of penicillin in the second half of the 20th century, which took place in the broader socio-political context of the post-war era. Bud describes that prevention of infectious diseases before the introduction of penicillin in the UK and the US was characterized by moralistic framings of hygiene. Hygiene and health were associated with the moral character of people. He elaborates:

> Whether qualified as 'personal' or 'social' hygiene, this involved not just a variety of exacting precautions [i.e. 'efficient sewage disposal and clean water supplies'], but also the more general taking of a personal responsibility for one's own welfare. Approved medical practices were linked therefore with moral responsibility for staying healthy and with the implication of moral failure in the case of illness. (p. 5)

The moralistic undertones of infectious disease prevention, as Bud argues, changed with the introduction of penicillin. Infection prevention and treatment became conceptualised as a 'pharmaceutical cure'.

By analysing the creation and global dissemination of the pharmaceutical model for infection treatment in the post-war era, Bud (2007) shows that mass-production of penicillin was introduced in a very specific context immediately after the Second World War, when people were craving positive changes.

> Penicillin became available to patients at a time when publics across the world yearned for good news. It was not just the war itself that was wearying. In many countries, rationing lasted till well after the Second World War. Even in Canada it outlasted the war by two years, and other less well-endowed countries suffered longer. The very word 'austerity' long evoked the legacy of the post-war years. Against the shortage of many luxuries, penicillin was a symbol of the wider range of effective medicines then becoming available. (p. 55)

His study shows that after the war, penicillin, and later other antibiotics, gained tremendous public attention. Pharmaceutical companies advertised the healing capacities of the wonder drugs; scientists published articles describing the newly discovered effects of antibiotics; newspapers published interviews and stories with researchers, doctors and recovered patients. Therefore, patients, medical doctors, industry and science together established a new doctrine which proclaimed that infections were not a moral responsibility but rather 'a technical problem susceptible to a pharmaceutical solution' (Bud, 2007).

Bud (2007) shows that the rise of penicillin popularity in the post-war years was accompanied by warnings from several bacteriologists who pointed out the potential development of resistance in bacteria. However, despite these warnings, in the 1950s and 1960s pharmaceutical companies started a race for new antibiotic types to meet the rising global demand. Bud (2007) states that the first restriction on over-the-counter sales of antibiotics was introduced in the US in 1951, but it was justified by the 'danger of allergic reaction threatening unsuspecting users', rather than by AMR. Although cases of antibiotic-resistant *Streptococcus* have been rising in different parts of the world since the 1950s, with the first recorded lethal case of methicillin-resistant *Staphylococcus aureus* in the US in 1962, the development of new antibiotics remained to be the main instrument for tackling infections.

It was not until the 1980s, according to Bud (2007), that AMR started to gain political attention. He argues that AMR was established as an issue of public concern before entering a policy agenda. He shows that starting in the 1960s several bacteriologists and medical specialists were addressing AMR as an increasing risk to healthcare practices. They argued that due to the increased popularity of antibiotics, the hygienic measures in hospitals had started to deteriorate, and surgeons were performing risky operations without following strict hygienic rules, relying solely on antibiotics. In addition, some medical doctors were criticising patients' demands for antibiotics, which they explained by the influence of antibiotic advertisement campaigns. Bud (2007) concludes that in the 1980s rising concerns about AMR in the biomedical community, as well as the rise of *Staphylococcus*-resistant infections in different parts of the world, including lethal cases, contributed to making AMR an issue of political concern globally; it was then included into the agenda of the WHO.

Similar to Bud (2007), Podolsky (2015) argues in his book *The Antibiotic Era: Reform, Resistance, and the Pursuit of a Rational Therapeutics* that AMR became an issue of global political concern around the 1980s. But while Bud (2007) focuses on the development and use of antibiotics, Podolsky analyses the history of antibiotic regulations from the 1940s onwards, with a focus on *rational therapeutics* advocacy in the US and globally. He starts his analysis

from the regulations of the 'inappropriate pharmaceutical marketing of *inappropriate* drugs', and moves on to the analysis of the regulations of the 'inappropriate prescribing of *appropriate* drugs' (Podolsky, 2015, emphasis original). He gives the following description of the 1940s–1950s social context that sparked the development of antibiotic policies:

> Yet the placidity of the era – when the most frightening situation a clinician would apparently find himself in was as a 'fielder trying to catch a dozen fly balls [pharmaceutical options] at once' – would be shaken by the mid-1950s by several phenomena: the seemingly unfettered proliferation and marketing of the wonder drugs, the increasingly recognised costs and adverse effects (allergic and otherwise) of antibiotics, novel syndromes of 'superinfection' resulting from alterations in patients' microbial florae, apparently correlated diagnostic sloppiness, and finally, increasingly documented antibiotic resistance, particularly among the feared staphylococci. (p. 38)

Podolsky (2015) describes that in the early 1950s policy attention was focused on the efficacy of antibiotics and the development of rational therapeutics practices. He elaborates that clinical trials of medicines were the central concern for early reformers. In addition to the efficacy of medications, medical regimens were a priority question for governing antibiotics. Podolsky (2015) shows that at the beginning of antibiotic reforms there were several actors involved in the construction of rational antibiotic practices – pharmaceutical companies, scientists and policymakers.

Similar to Bud (2007), Podolsky (2015) shows that the rise of political attention to AMR started around the 1980s when biomedical scientists began to actively voice their concerns about this issue. He describes how in 1981 during the Molecular Biology, Pathogenicity, and Ecology of Bacterial Plasmids conference in Santo Domingo, 147 scientists from different parts of the world signed the 'Statement Regarding Worldwide Antibiotic Misuse' where they argued that AMR should be understood and addressed as a 'neglected health problem' (Statement regarding worldwide antibiotic misuse, 1981). According to Podolsky (2015), the rising concerns of the scientific community about AMR attracted the attention of reformers of practices regarding antibiotic use and prescription.

Podolsky (2015) shows that the interest of medical doctors and patients became part of AMR regulations preceding the significant rise of public and policy attention to this issue in the 1990s. He describes how at that time newspapers like the Times and Newsweek started to publish 'hot' stories elaborating on apocalyptic scenarios that might happen as a result of AMR.

Such attention, Podolsky (2015) argues, resulted in an increase in funding for infectious diseases and AMR research and treatment. For instance, he shows how the US Centre for Disease Control increased its funding for emerging infections from '$1 million in 1994 to $7.7 million in 1995 to $59.1 million in 1998'. Apart from the US, since the end of the 1980s and the beginning of the 1990s AMR has gained international attention, and the WHO in 1985 established the Collaborating Centre for Surveillance of Antimicrobial Resistance (WHONET), in 2001 introduced the WHO Global Strategy for Containment of Antimicrobial Resistance, and in 2015 the Global Action Plan on Antimicrobial Resistance.

With the rise of political attention to AMR in the 1990s, the antibiotic behaviours of medical doctors and patients have often been problematised as a cause of this problem (Bud, 2007; Podolsky, 2015). However, several decades before that, AMR in humans had already been explained by the extensive use of antibiotics in animals and agriculture. In his book, Bud (2007) shows that after the Second World War antibiotics not only became important for the treatment of infections in humans but were also a crucial ingredient of a farming industry that was rapidly growing. He argues that since the 1950s, 'antibiotics had become a high technology solution to the problems of newly intensive farming'. Antibiotics were increasingly used for treatment and prevention of infections in animals, growth promotion, and food conservation. Although there were some attempts to control and limit the use of antibiotics in farming and agriculture, Bud (2007) shows that such attempts were not very successful. He mentions two reasons for this: first, resistance by the farming community and involvement of strong economic interests and second, disagreements between scientists and policymakers about the potential AMR risks of antibiotic use in farming on human health.

In line with the analysis of Bud (2007), the German historian Kirchhelle (2018b), in his article 'Swann Song: Antibiotic Regulation in British Livestock Production (1953–2006)', specifically focusses on the scientific and political controversy around the potential risks of AMR that antibiotic use in farming can cause in humans. He analyses the history of this controversy in the UK starting from 1953 and shows attempts to pacify it through the establishment of the Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine in 1968. This committee was coordinated by the molecular biologist Michael Swann, and it was installed to analyse and bring a solution to the sharp increase of antibiotic consumption in farming, which by 1963 had reached the point where 44% of antibiotics in the UK were fed to animals.

After a year of work, in 1969 the committee produced the *Swann Report*. Kirchhelle (2018b) shows that this report became famous for creating a distinction between antibiotics

that were *therapeutically relevant* for human health and antibiotics that were *therapeutically irrelevant* for human health, and for stating that only the latter were allowed to be applied in animal treatment and growth promotion. He argues that this report was a compromise between economic demands of the food production sector and public health concerns, and it gained widespread popularity in and beyond the UK and determined the trajectory of European antibiotic regulations for the next several decades. However, he concludes that the report did not make a significant difference in antibiotic practices in farming.

> Aiming to satisfy all parties within the corporatist decision-making framework, the report's recommendations made little difference on farmers and even less difference for bacteria. (p. 349)

Broadening the focus from the UK to other parts of the world, in his other article 'Pharming animals: A global history of antibiotics in food production (1937-2017)' Kirchhelle (2018a) analyses how antibiotics were used and regulated in different countries, not only in farming but also in agriculture. Similar to his analysis of the UK context, focusing on different food production settings around the world, Kirchhelle (2018a) concludes that increased economic demand for farming products in combination with easy access to antibiotics and poor policy regulations in this area made the use of antibiotics a mundane practice. His work highlights how political economy and demands for food production became intertwined with the antibiotic production industry, which simultaneously provoked the debates about the potential risks of AMR for human health.

The two intertwined histories of antibiotic use in humans and animals described by Bud (2007), Podolsky (2015) and Kirchhelle (2018b, 2018a) provide important insights into how AMR has been constructed in public health and policy arenas. Although several bacteriologists have argued about the importance of AMR for human health since the introduction of penicillin, but the economic demands and healing capacities of this drug superseded these warnings. Interestingly, while human practices of antibiotic use became seen as a cause of AMR only at the end of the 1990s, antibiotic use in animals and agriculture has been considered to be a risk factor for human health since the 1960s. The controversy surrounding antibiotic use practices in non-human sectors and their impact on humans has still not been resolved in microbiology, with new studies arguing that the connection between the two sectors may not be that strong (Wu et al., 2013). Despite this uncertainty, there have been numerous attempts to bring policy solutions to this controversy. The *Swann Report* aimed to separate the two

sectors by allowing them to use different antibiotics, but as we could see from the research of Kirchhelle (2018b) this approach did not make much difference to AMR. In contrast to the *Swann Report*, since the introduction of the Global Action Plan on AMR in 2015, the policy approach of One Health has been introduced to regulate the uncertain connection between human and animal use of antibiotics by addressing it as a shared concern. The influence of this approach to AMR is still unclear, and this is one of the questions that I aim to reflect upon in this thesis.

Construction of the One Health policy approach to addressing AMR

The history of antibiotic development and the increased concern for AMR have shown that this phenomenon has been defined and re-defined by various stakeholders debating its importance and relevance for public health. We can see that different policy control instruments have been implemented to tackle AMR: the prohibition of antibiotic advertisement and self-treatment, attempts to control antibiotic use in farming and control of medical prescriptions. The regulations on antibiotic use in both human and animal health sectors has been one of the major controversies in the history of AMR, which continues to the present day. The *Swann Report* tried to separate the human and animal sectors by allowing the use of different antibiotics, but not much progress has been made in decreasing AMR. Currently, a new policy paradigm is taking the lead in the arena of AMR – the One Health approach – which, contrary to the *Swann Report*, aims to coordinate human and animal health sectors by connecting rather than separating them from each other.

The One Health approach to health highlights the connectivity and interdependency between the human, animal and environmental health. This approach is not new. It can even be traced back to ancient Greek medicine: the Greek physician Hippocrates stressed the dependency of human health on seasonal and environmental factors in 400 BCE (Miller, 1962). The 19th-century German physician Virchow coined the term *zoonosis* to highlight the interdependency between human and animal health, and he introduced the notion of *One Medicine* to underline the importance of collaboration between human and animal medicine. The concept of One Medicine was not widely accepted during his life (Schultz, 2008), but it was picked up again by the parasitologist Shwabe (1984), who argued that human and animal health are interconnected and therefore should be studied in cooperation. Although the concept of One Medicine was not widely accepted in the public health arena, the concept of zoonosis and the idea of dependency between human and animal health did attract the attention of health professionals, but it was not commonly applied to AMR. In 2004, health experts from different

parts of the world, debating different approaches to zoonotic diseases, participated in the international symposium Building Interdisciplinary Bridges to Health in a Globalized World, hosted by Rockefeller University in the US. This symposium resulted in 12 principles of One Health known as the 'Manhattan Principles', which major aim was to emphasize a 'link between human, domestic animal, and wildlife health' (Centers for Disease Control and Prevention, 2004).

Following the conference, the One Health approach became widely adapted to address different zoonoses, and it became a central concept to bridge the work of international organisations such as the WHO, the OIE and the Food and Agriculture Organisation of the United Nations (FAO). Following these developments, the concept of One Health has become gradually incorporated into AMR policy agendas. The 2015 Global Action Plan elaborated that AMR is an interest of everyone's concern that requires collaboration between and within professions from human and animal sectors. The One Health approach in this document is defined through 'coordination among numerous international sectors and actors, including human and veterinary medicine, agriculture, finance, environment, and well-informed consumers'(WHO, 2015). In the 2017 European Action Plan against AMR, the concept of One Health also occupies a central position, it even became a part of its title – *A European One Health Action Plan against Antimicrobial Resistance.* The *European Action Plan* defines One Health as follows:

> One Health is a term used to describe a principle which recognizes that human and animal health are interconnected, that diseases are transmitted from humans to animals and vice versa and must therefore be tackled in both. The One Health approach also encompasses the environment, another link between humans and animals and likewise a potential source of new resistant microorganisms (p. 4).

While in the 20th century microbiologists problematised both the use of antibiotics in humans and animals, which resulted in fierce debates about the connection between human and animal health, the policy regulations of the 21st century made this argument central to addressing AMR and concluded that these health sectors must be coordinated together.

The focus on the One Health approach to AMR has made human-animal relations central to addressing this phenomenon, and it has been analysed and reflected upon by different scholars. In her book *One Health and the Politics of Antimicrobial Resistance,* the physician Kahn (2016) argues that One Health is a necessary approach that should be incorporated in

AMR regulations. She conducted a historical analysis of the controversy related to the regulations of antibiotics in human and animal sectors in different countries. This controversy, as was mentioned in the previous section, centred on the potential of antibiotic use in animals to cause harm in humans. Applying the One Health approach as an analytical framework, she shows that this framework should be dominant in developing policy regulations for AMR. Therefore, she emphasizes that 'ultimately, the goal for both public health and agriculture should be to optimize human, animal, and environmental health: in essence, One Health' (Kahn, 2016).

Other scholars have been more critical about One Health and the connection between the health of humans and animals that it highlights. Studying the history of policy responses to livestock-associated zoonoses in the Netherlands in the 20th century, Haalboom (2017) argues that the agricultural and farming sectors have always held dominance over the public health domain in terms of defining shared health problems. She explains that deep financial interests involved in the farming sector granted them 'primary ownership' over zoonotic diseases, which have been defined as economic rather than public health problems.

At the same time, a different perspective on the concept of One Health in its application to zoonoses was introduced by Craddock and Hinchliffe (2015), who argue that the current formulation of One Health in policy regulations seems to propose a top-down approach between human and animal sectors, where the human sector leads. They point out that instead of building bridges between different sectors, One Health makes the human health sector the authority in the field that can dictate regulations for animal and environmental sectors. Similar arguments have been made by the proponents of the EcoHealth approach who have highlighted that health should be understood and addressed in the context of ecosystems and not only human-animal relations (Mi et al., 2016; Zinsstag, 2012). In contrast to One Health, the EcoHealth approach shifts its focus from disease threats to wider environmental understanding of health and illness (Roger et al., 2016). In addition, Craddock and Hinchliffe (2015) elaborate that the One Health approach to policy regulations tends to prioritise knowledge produced by biomedical professionals in the human health field, while often not taking into account other forms of knowledge produced in animal and environmental sectors and by social sciences.

While the concept of One Health and the different modes of relations that it builds between the human and animal sectors have been reflected in the context of zoonotic diseases, similar reflections in relation to AMR are currently lacking. Applying the One Health approach to address shared health concerns is not new, but it is a relatively recent innovation in AMR

regulations. Therefore, it is still unclear how it may influence the ongoing controversy surrounding the connection between the health of humans and animals.

Social science approaches to the construction of AMR

In biomedical sciences, AMR has been researched and debated since the introduction of penicillin. Bacteriologists have been lobbying for the recognition of AMR as a major public health concern and have been arguing about the biological connections between AMR in humans and animals. Parallel to these constructions of AMR as a biomedical phenomenon, social science scholars have analysed and developed various understandings of the social nature of AMR. Social scientists have been developing knowledge about different practices of antibiotic use by healthcare professionals, patients and farmers (Barden et al., 1998; Boyd, 2001; Mangione-Smith et al., 1999). These studies have articulated that antibiotic practices are shaped by different social processes, including economic access to healthcare and the ability to take sick leave, and by market demands for larger quantities of food.

The same year as the publication of the Global Action Plan, the British professor of health system economics Richard Smith published a commentary in the *British Medical Journal* highlighting the importance of social science research to addressing AMR. He argues that to understand the mechanisms of AMR, it is crucial to analyse how antibiotics are embedded into the daily reality of professionals and laypeople. Along with this call for deeper engagement with social sciences, in 2016 a group of anthropologists from the London School of Hygiene and Tropical Medicine released a report arguing that AMR should be understood as a phenomenon that is made and remade in different settings and practices, rather than as a static biomedical fact (Chandler et al., 2016). Hence, they propose three potential settings where this phenomenon can be analysed: practices of healthcare professionals and laypeople, policy regulations and scientific practices of knowledge production (Chandler et al., 2016). The authors suggest these broad settings as a starting point for understanding how AMR is shaped and, at the same time, how it can influence the settings where it is shaped. This understanding, they argue, is important for addressing AMR as a biosocial phenomenon that is made by different practices depending on the social world where it is situated.

In line with the suggestions in the report, several studies have analysed how patients and prescribers in different settings give meaning to antibiotics in everyday life, and they have shown the range of conceptualisations of this medicine. In an anthropological study, Lambert et al. (2019) show how practices of antibiotic prescription in a rural province of China present a combination of Western ideas about how infections should be treated with antibiotics and

Chinese ideas about how inflammations can be treated with traditional medicines. The authors argue that local practices of antibiotic prescription should be understood as a result of conceptual and linguistic overlaps between the concept of infection and the concept of inflammation. These overlaps mean that medical doctors have to bridge the two different concepts in their antibiotic practices. Such analysis goes beyond the understanding of antibiotic prescription as something based on biomedical knowledge, but it shows how antibiotic practices are embedded in a particular setting.

Similarly, Broom et al. (2014) show how antibiotic prescription practices in an Australian urban hospital are determined by local rules of professional communication. These authors show that the need to prevent AMR has a limited significance in the decision of medical doctors to prescribe antibiotics; rather, antibiotic prescription can be motivated by factors like the fear of undertreating patients or by forms of professional etiquette which imply that decisions of colleague clinicians to prescribe antibiotics should not be questioned. In both cases, in healthcare settings in China and Australia, antibiotic prescription practices were determined by the social worlds in which these practices took place. Therefore, distinctive approaches would be required to address AMR as a phenomenon that is unique depending on the setting. Without the engagement of qualitative social sciences, these crucial nuances could be overlooked in policymaking.

Another setting that Chandler et al. (2016) emphasise as important for social studies of AMR is policy regulations. They argue that analysis of national and international policy discourses gives an important understanding of how AMR is imagined and how responsibilities for control over antibiotic use are distributed. For instance, Brown and Nettleton (2016) show how in UK policies on AMR economic considerations play a major role. AMR is presented as an issue of primarily economic concern that increases the cost of healthcare and that can be addressed through investments in the development of new medications. The same authors demonstrate that, partly in line with economic considerations, AMR is constructed in policy discourses as a foreign threat, which means that incoming migrants are presented as carriers of AMR who can disseminate it among the UK public. Brown and Nettleton (2016) argue that this framing of AMR can be used by policymakers to justify strict migration policies.

Social scientists like Chandler (2019) and Will (2018) have critically analysed the individualist tone of many policies for AMR prevention: these policies focus on changing the individual behaviour of prescribers and users of antibiotics. Both authors highlight that policies that focus on behavioural changes fail to address the structural processes that influence people's behaviour, such as access to healthcare services and the ability to take sick leave. In

addition, these authors argue that focus on behaviour runs the risk of allocating responsibility for AMR development on individuals whose practices can be determined not simply by their lack of knowledge but by their inability to get access to healthcare and non-antibiotic treatment.

The third setting where, according to Chandler et al. (2016), social science research can play an important role is in practices of science and production of scientific knowledge. They argue that the conceptual frameworks developed in science and technology studies (STS) can help analyse the processes of scientific fact production about AMR. STS can be broadly described as an area of study that analyses scientific facts and the production of those facts as intrinsically social and political (Edge, 1995). Chandler et al. (2016) refer to the famous study *Laboratory life: The construction of scientific facts* by Latour and Woolgar (1986). In this study, Latour and Woolgar (1986) argue that scientific facts are constructed through the processes of communication, negotiation and re-negotiation of these facts between scientists, funders and policymakers. The authors conducted a two-year ethnography at the Roger Guillemin laboratory at the Salk Institute for Biological Studies and showed how the knowledge produced in the laboratory was discussed and contested in scientific literature, scientific conferences and meetings before it became stabilised as a fact. Analysing the process of AMR scientific fact production, Nerlich and James (2009) focus on how this phenomenon was imagined by microbiologists at the end of the 1990s and beginning of the 2000s. They show that microbiologists were using the metaphors of catastrophe and apocalypse to communicate scientific facts about AMR to health professionals, policymakers and laypeople. They argued that these specific metaphors were used to construct AMR as an urgent public health phenomenon and to attract policy attention and funding to AMR research (Nerlich & James, 2009).

The analysis of antibiotic practices in the three different settings proposed by Chandler et al. (2016) facilitates understanding into how antibiotics are embedded into policy discourses, scientific knowledge production, and the modern infrastructures of healthcare and farming. In her research on the history of biological developments of antibiotics, Landecker (2015) suggests that antibiotics themselves become infrastructural. She explains that antibiotics have become an inevitable part of the idea of health, hygiene and farming. Medical doctors and patients build their relationships around the prescription of medications where antibiotics themselves become a form of care and an artefact that represents scientific knowledge (Chandler et al., 2017; van der Geest & Whyte, 1989). Similar to the suggestion of Landecker (2015) and following the work of Bowker and Star (2000) on classifications as information infrastructures, Chandler (2019) elaborates on how antibiotics can be analysed through the

concept of infrastructure. She applies a broad definition of infrastructure as something that arranges and organises the work of its heterogeneous users. These infrastructures can be physical tools like surgical instruments, the organisation of a hospital on different wards, or an idea or a concept, like etiquette rules for communication with others. These infrastructures are usually invisible to their users unless there is an inversion – a breakage of the infrastructure; for instance, if there are more patients with infectious diseases than there are beds in a hospital, we recognise the limits and gaps of the existing hospital infrastructures.

Chandler (2019) shows that antibiotics can be understood as infrastructure because they construct the modern concepts and practices of health, productivity and sufficient convalescence. In this context, AMR can be seen as an inversion of these infrastructures – something that breaks them down and makes them visible. She concludes that the rise of AMR concerns has led to the deconstruction of antibiotic infrastructures – it shows the dependency of modern economic, social and political processes on these medicines.

> The present moment of antimicrobial resistance as a major topic of global concern can be understood to represent a moment of inversion—when antimicrobials have been rendered visible where previously they have been a part of the woodwork (p. 9).

Working with the concept of infrastructure, Chandler (2019) suggests that AMR makes the work of antibiotics visible – it shows how different antibiotic practices have been established and function in various settings. AMR, Chandler (2019) argues, disturbs the established practices and infrastructures in which antibiotics are embedded. Social science scholars have developed extensive expertise on the study of antibiotic practices in different settings and by various stakeholders (Broom et al., 2015; Hinchliffe et al., 2018; Lambert et al., 2019). However, the number of studies focused on the inversions of antibiotic infrastructures and adaptive practices shaped by AMR have been limited. Therefore, this thesis shifts the focus from antibiotic practices to infrastructural disturbances introduced by AMR and the biosocial world that these disturbances shape.

Methodological approach

The literature on AMR shows that this phenomenon can take various shapes and produce different practices depending on the social world where it takes place. Informed by these studies, I visited practices shaped in policies, healthcare and science to study how AMR is defined, framed, lived with and dealt with. To that purpose, I chose methodological approaches

from the social sciences and humanities. I applied different qualitative methods, including observations, interviews, focus groups, discourse analysis and conceptual analysis.

To study policy practices, I used discourse analysis. I focused the analysis on the emerging concept of One Health and analysed the meanings of this concept for international policy regulations on AMR.

During my journey through practices of healthcare, I combined different methods. This journey brought me to a refugee centre in the Netherlands and the hospitals and pharmacies in Russia. In both settings, I conducted in-depth interviews with local residents – refugees, microbiologists, nurses, clinicians, patients and pharmacists. In the Dutch study, I also conducted two focus groups with public health professionals and I performed observations in two refugee centres to understand the daily routines of their residents.

To study scientific practices about AMR, I also combined several methods. I conducted a discourse analysis of microbiological research articles to gain a deeper understanding of how microbiologists imagine AMR and travelling. I analysed semi-structured interviews with students who travelled from different parts of the world to India, in which they discussed how they understood AMR and travelling. I also conceptualized how microbiological data based on the analysis of stool samples from these travelling students could come into a dialogue with the analysis of the interviews and what such dialogue would mean for AMR.

In each of the chapters, I will present more details about the methods that I applied in that specific study.

Outline of the thesis

This thesis focuses on how AMR is practised in different settings – in policies, healthcare and science. In **Chapter 1** I study how the idea of One Health and specifically the relations between the health of humans, animals and environments are constructed to address AMR in the international policy arena. To that purpose, I analyse influential international AMR policy regulations and study how the One Health approach is conceptualized in these documents. The analysis is conducted in two steps: first, I analyse general international health policy regulations that form the basis for AMR One Health policies and second, I analyse international policies that consider One Health the main approach for addressing AMR.

The next two chapters are dedicated to different antibiotic practices exercised by health professionals and laypeople. In **Chapter 2** I analyse practices of AMR control in public health. Against background discussions about AMR screening of refugees, this chapter explores different perspectives on this practice in the Netherlands. Based on interviews with refugees,

public health doctors, public health nurses and microbiologists, I analyse the perspectives of these stakeholders on AMR screening. **Chapter 3** moves from public health to clinical settings, namely primary care clinics in Russia. I analyse how medical doctors, pharmacists and patients shape communication and everyday antibiotic practices in a context of increasing control of over-the-counter antibiotic sale and the introduction of obligatory medical prescriptions.

The next two chapters deal with the scientific arena of AMR. In **Chapter 4,** I analyse how microbiological research imagines AMR and its dissemination through human travelling. Focusing on the analysis of metaphors in microbiological discourses of AMR in travellers, this chapter elaborates how different elements – travellers, bacteria, countries of origin and countries of destination – shape the notions of health and health risks concerning AMR. In the context of the increasing calls for transdisciplinary research in AMR, **Chapter 5** explores the possibility to combine microbiological and social science methods and insights to address AMR. This combined methodology allows the investigation of the potential of transdisciplinary approaches for addressing AMR as a biosocial phenomenon. **Chapter 6** is a short commentary-reflection on my own journey through the worlds of AMR as a member of a transdisciplinary research team.

In the conclusion**,** I summarise the results of my travels through different AMR practices and I will reflect upon the added value of these travel insights.

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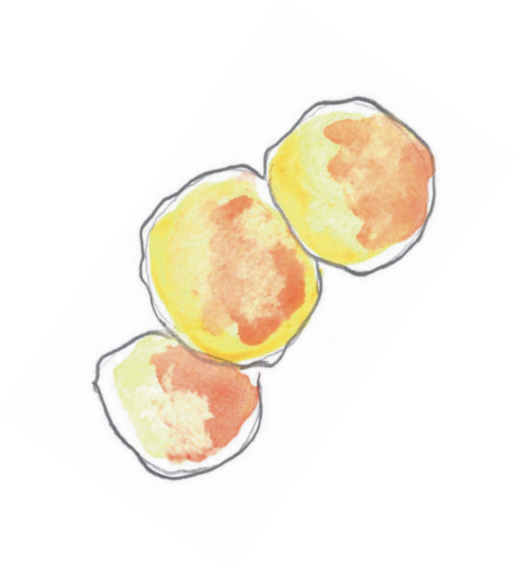
Policy

Chapter I

Anthropocentric framings of one health



Based on: Kamenshchikova, A., Wolffs, P. F. G., Hoebe, C. J. P. A., & Horstman, K. (2019). Anthropocentric framings of One Health: an analysis of international antimicrobial resistance policy documents. *Critical Public Health*, 1-10. doi:10.1080/09581596.2019.1684442

Abstract

One Health (OH) is an increasingly popular approach for addressing antimicrobial resistance (AMR) which is often presented as a shared health concern at the interface of human-animal-environment relations. OH is widely adopted as a framework for collaboration between organisations like the World Health Organisation and the World Organisation for Animal Health; furthermore, it occupies a central position in international AMR policy documents. Scholars like Craddock and Hinchliffe have raised questions about whether a unified OH understanding of health allows us to comprehend the diversity of practices and knowledge involved in transdisciplinary and inter-organisational collaborations. In this article, we aim to explore how the OH idea as a shared health concern is conceptualised in international responses to AMR. Therefore, we conducted a constructivist policy analysis of two types of international policy documents – 11 documents dedicated to AMR and a OH approach to it, and 12 documents with a focus on more general health issues that AMR regulations are built upon. The analysis of this policy arena makes clear that both sets of documents put human health at the centre, while the animal and environmental sectors are primarily framed as a risk for human health. Although human health is, more or less explicitly, considered to be the main problem, the animal and environmental health sectors are assigned responsibility for addressing this problem.

Introduction

Within three decades after the introduction of penicillin, antibiotics have occupied an essential role not only in human medicine but also in the veterinary and agricultural sectors. The history of the interrelations and conflicts between the human and non-human health sectors in Europe, as it was described by Kirchhelle (2018b, 2018a), shows how antibiotics became intertwined with health, sanitation, and food infrastructures, thus also shaping 'antibiotic infrastructures'. Antibiotics as infrastructure – 'usable systems that are unnoticeable unless disrupted (Bowker & Star, 2000) – have been elaborated upon by Chandler (2019) and Chandler et al. (2016) to highlight how antibiotics are embedded into health and economic infrastructures through the ideas of sanitation, food production, healthy body, and human productivity. Such infrastructures can be seen as platforms that bring together the human, animal and environmental sectors. For instance, the spread of zoonotic diseases has led to close collaboration as well as shared health and sanitation practices between stakeholders dealing with human health, farming, and wildlife (Chien, 2013). At the same time, the rise of concerns over antimicrobial resistance (AMR) can intensify the competition between these sectors over the scarce resources of antibiotics (Chandler, 2019). Although both the human and animal sectors share a common aim to address zoonotic diseases, the means to achieve this aim may vary. While the human sector may focus on the optimisation of antibiotic prescription to maximise healthy living, the animal sector can be more economically driven and focuses on the maximisation of meat production (Degeling et al., 2017).

In an attempt to develop a comprehensive regulatory mechanism of inter-sectoral cooperation, a One Health (OH) policy framework has been adopted by international organisations such as the World Health Organisation (WHO), the World Organisation for Animal Health (OIE), and the Food and Agriculture Organisation of the United Nations (FAO). Starting from 2008 this framework has been explicitly utilised to address avian influenza (Chien, 2013). Since then, OH has become increasingly popular in the scientific and political arena for addressing such health issues as food safety, zoonoses, and AMR (Bidaisee & Macpherson, 2014; Coker et al., 2011; Kakkar & Abbas, 2011; Lee & Brumme, 2013).

While the OH framework for collaboration has occupied a central position in international health policy, health professionals have demonstrated different interpretations to this approach. A Delphi survey among human and animal health practitioners conducted in Australia by Degeling et al. (2017) revealed a variety of disagreements when prioritising between human health, animal health, and economic considerations. For instance, the survey showed that when formulating priorities for addressing AMR, human health professionals were keen to give a

higher ranking to the emotional wellbeing of people, while those from the animal health sector gave greater consideration to animal health and economic concerns. In addition, in public health literature OH is described in different ways: as 'a seamless interaction between veterinary and human medicine' (Calistri et al., 2013), or as a 'perspective, covering animals and humans [...] as well as the environment' (O'Neill, 2016). Therefore, a tension arises in the AMR field between the search for a unified OH approach to address shared health concerns and the diverse priorities within this approach.

The OH search for consensus in explaining and addressing shared health concerns has been scrutinised by Hinchliffe (2015). He argues that a unified 'One World One Health approach runs the risk of reducing the diversity of knowledge, practices, and values, i.e. the diversity of worlds, that are involved in the process of health making. Hinchliffe (2015) elaborates that through the attempt to give a unified explanation and propose a single solution for a shared health issue, OH has a tendency of reducing the complexity of interrelations between practices that take place in farms, clinics, or laboratories. Another social science researcher, Craddock (2015), argues that inter-organisational collaborations may reflect conflicting values and interests of the involved organisations. She gives an example of product development partnerships for a tuberculosis vaccine and explains that pharmaceutical companies involved in such partnerships often focus on 'markets rather than diseases burdens. An example can be found in the 2010 response to Q-fever in the Netherlands that caused substantial damage to Dutch farmers. Because Q-fever is not severe in animals, no mandatory vaccination was required, however, after the 2009 Q-fever outbreak in humans, it was decided to cull 40,000 pregnant goats in the hope that it would prevent further human outbreaks (Enserink, 2010). Craddock (2015) argues that the OH framework for collaboration can underline the power-dynamics between involved actors, such as pharmaceutical companies and small research centres, or, as illustrated in the second example, farmers and medical professionals.

Despite the ambiguous nature of OH discussed by Hinchliffe (2015) and Craddock (2015), Chien (2013) explains that it can be a suitable collaboration framework for international health agencies, such as the WHO, the FAO, and the OIE. This framework, she argues, can help to reduce conflicting interests and to improve communication between these organisations. Drawing on interviews with officials from international health organisations, Chien (2013) shows that OH has been perceived as a fruitful strategy for collaboration that allows the expertise of different organisations to complement each other without prioritising one over another.

Inquiries into the way OH aims to shape a unified understanding of health, and the ambiguities involved in such unified concepts raise the question of how the notion of OH is conceptualised in international health policy. To explore this question, we will focus on a product of OH collaborations, that is, international health policy documents. We will narrow our analysis to AMR policy documents, which is one of the areas where OH has become increasingly popular. Inspired by social science literature regarding the ambiguity of OH, here we aim to understand whether OH policy documents shape a unified AMR world, how it links and incorporates the diversity of human-animal-environmental knowledge on AMR, and what kind of collaborations and solutions to address AMR it suggests.

Theoretical approach

To analyse policy documents, we draw from constructivist policy analysis, and especially the work of Gusfield (1984) and Stone (2012). Both scholars have demonstrated how policy discourses are not neutral technical representations of problems and solutions, but specific normative constructions of reality. In his analysis of traffic regulation policies in the US, the sociologist Gusfield (1984) demonstrated, for instance, how dominant policy discourses implicitly constructed traffic accidents as being caused by the drivers, and not by, for instance, technological characteristics of the cars or motorway infrastructures. These policies presented 'drunk driving as the cause of accidents. At the same time, a city infrastructure, which implied that all pubs could only be reached through the highway, was not at the focus of attention. It is not to say that drivers who consume alcohol were not contributing to traffic accidents, or that car characteristics did not cause these problems, rather, in his analysis Gusfield (1984) demonstrated how by focusing on a particular aspect of a problem (i.e. drinking and driving), policies shaped a certain reality of this problem that may exclude alternative framings, explanations, and solutions.

The political scientist Stone (2012) criticised the so-called 'rationality project' that assumed that policies were developed by 'rational' and 'analytical' methods. She argued that policies were the result of struggles, conflicts and negotiations about values and definitions of problems and solutions. Policies were developed by continuously 'fighting with words and by mobilising narrative plots, metaphors, numbers, analogies and symbols. Policy documents were an important actor in these fights: through articulating problems and solutions in a specific way, they aimed to shape specific realities and futures. According to (Asdal, 2008), policy documents were performative, in a sense that they not only described but also created a specific reality. This reality was organised through the work of a network constituted by policy

documents that were interconnected and co-dependent. Scholarship in the actor-network theory demonstrated how networks of diverse actors (including documents) both established an 'issue' and formulated rules for addressing this 'issue' (Asdal, 2015; Latour, 1988; Latour & Woolgar, 1986). Therefore, these networks became obligatory passage points that cannot be avoided when developing new strategies for tackling an 'issue' formulated by a network (Callon, 1986). In the context of AMR, policy regulations can be seen as such a network that builds a certain discourse about antibiotics, AMR and OH, thus establishing an obligatory passage point in addressing AMR in practice. Drawing from constructivist policy approaches, our analysis of international policy documents on AMR focuses on the specific meanings of OH, which entail particular causes and responsibilities for addressing AMR.

Methods

Our analysis of the OH policy arena deals with two types of international policy documents – eleven documents dedicated to AMR and OH, and twelve documents that focus on more general health issues. To select the documents dedicated to AMR and OH, we first identified thirty-three documents that were fully or partially devoted to AMR and that were produced by four major international agencies – WHO, FAO, OIE, and the European Commission. Second, we examined these documents based on the following criteria: 1) the document was fully devoted to AMR; 2) it proposed recommendations/ standards for tackling AMR; and, 3) it incorporated OH as an approach to address AMR. From this, eight documents were selected for the main analysis. Third, following the same criteria, we examined references from the selected documents to identify other international documents that deal with AMR though the OH approach. In total, eleven international policy documents were included in the analysis (see Table 1).

Table 1. Selected international One Health policy documents and EU regulations on AMR

Title of policy documents	Author(s)	Year
A European One Health action plan against antimicrobial resistance	European Commission	2017
EU Guidelines for the prudent use of antimicrobials in human health	European Commission	2017
Global framework for development & stewardship to combat antimicrobial resistance. Draft roadmap	FAO, OIE, and WHO	2017
Antimicrobial resistance: A manual for developing action plans	FAO, OIE, and WHO	2016

Declaration by the pharmaceutical, biotechnology and diagnostics industries on combating antimicrobial resistance	International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)	2016
UN Draft political declaration of the high-level meeting of the General Assembly on AMR	General Assembly of the United Nations	2016
Final report and recommendations: Tackling drug-resistant infections globally	J. O'Neill	2016
The OIE strategy on antimicrobial resistance and the prudent use of antimicrobials	OIE	2016
The FAO action plan on antimicrobial resistance 2016-2020: Supporting the food and agriculture sectors in implementing the global action plan on antimicrobial resistance to minimise the impact of antimicrobial resistance	FAO	2016
EU Guidelines for the prudent use of antimicrobials in veterinary medicine	European Commission	2015
WHO Global action plan on antimicrobial resistance	WHO	2015

International policy documents on AMR and OH were not developed from scratch, but they stemmed from existing health policy discourses, initiatives, and practices. In the selected AMR documents, we found systematic references to more general health documents produced by the same organisations – the WHO, the FAO, the OIE, but also the World Trade Organisation (WTO), the United Nations International Strategy for Disaster Reduction (UNISDR), and the United Nations Environmental Programme (UNEP). These documents provided context and were part of the network from which AMR OH policies have originated. Therefore, in order to understand AMR OH policies within the context of international health policies and to trace a rationale in its thought style, we decided to include those general policy documents that focused on the health of humans, animals, and the environment in the analysis. In total, twelve general health documents were analysed (see Table 2).

Table 2. Selected general international health documents

Title of policy documents	Author(s)	Year
Aquatic animal health code	OIE	2017
Terrestrial animal health code	OIE	2017
Bangkok principles for the implementation of the health aspects of the Sendai framework for disaster risk reduction 2015-2030	UNISDR	2016
Frontiers 2016 report: Emerging issues of environmental concern	UNEP	2016

Sendai framework for disaster risk reduction 2015-2030	UNISDR	2015
Operational framework for good governance at the human-animal interface: bridging WHO and OIE tools for the assessment of national capacities	WHO and OIE	2014
Rapid risk assessment for acute public health events	WHO	2012
One Health: Food and agriculture organisation of the United Nation strategic action plan	FAO	2011
The FAO-OIE-WHO Collaboration: Sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces	FAO, OIE, and WHO	2010
International health regulations	WHO	2005
International plant protection convention	FAO	1997
The WTO Agreement on the Application of Sanitary and Phytosanitary Measures	WTO	1995

First, we double-read each document to define categories for analysis. Second, following our goal to understand how OH is conceptualised in AMR policies, the following analytical categories were established: types and kinds of relationships between human, animal, and environmental health; causal relations between AMR practices in the different health sectors; and roles and responsibilities of various professionals to control and prevent AMR. Then, using the NVivo 9 qualitative data analysis software (QSR International Pty Ltd, Doncaster, Victoria, Australia), we analysed each document in accordance with the established categories.

Roots of One Health: general international health regulations

Although general health policy documents are not focused on AMR and often do not mention the concept of OH, they play an important role in the making of OH. In order to become part of the international health policy network, OH regulations for AMR have to be aligned, in defining problems and solutions, with already established documents. Therefore, to better understand the content of AMR documents, in this section, we will first give an overview of the context in which these documents originated. In our analysis, we found four main characteristics of these general international health regulations.

First, general health documents, not surprisingly, predominantly focus on improving, sustaining, and promoting the health of humans. Human health is understood quite broadly; as it involves not only the biological wellbeing but also the 'environment, health status, behaviours, social or cultural practices, health infrastructure and legal and policy frameworks' as factors that can shape human health (WHO, 2012). These health policies often describe humans as vulnerable and those who must be protected from various environmental hazards.

For instance, one of the documents emphasises the necessity to protect humans by trying to 'stimulate people-centred public and private investment in emergency and disaster risk reduction, thus putting human health at its centre (UNISDR, 2016).

Second, animal health is recognised as being important in two different ways. On the one hand, animals are understood to be a resource for human health; on the other hand, they are considered as potential carriers of diseases. Animal health has to be secured because threats to animal health may transform into health risks for humans. One of the documents stated that 'good veterinary governance is key to improving national productivity and income generation as well as contributing to human health (WHO & OIE, 2014). Another document – *Frontiers 2016 report: Emerging issues of environmental concern* – raises a question about the consequences of inappropriate practices towards animals, such as the illegal smuggling of wildlife animals, which can influence human health. Although this document raises a concern about the appropriate behaviour with respect to animals, it mostly focuses on how misconduct towards animals can influence humans,

> But the attempt to smuggle an exotic animal through a major international hub only hints at the massive and lucrative illegal trade in live animals that threatens to decimate wild populations and ecosystems, even as it exposes entire cities and regions to corruption, violence and deadly diseases (UNEP, 2016).

Third, as far as international health documents deal with animal health, they largely focus on domesticated animals. These documents are looking at human practices dealing with animals as part of the human food chain, such as farming and veterinary medicine, while pointing to the responsibility of animal professionals, including farmers and veterinarians, for potential human health hazards coming from the animal sector. One of the documents, for example, states '*veterinarians* have a dual responsibility – the epidemiological *surveillance* of animal *diseases* and ensuring the safety and suitability of *meat* (OIE, 2017, emphasis original).

Fourth, most health policy documents do not mention how the environment affects human health. The notion of the environment, if it is mentioned in a document at all, is not operationalised, so it is quite difficult to grasp the meaning of what is understood as the 'environment'. The documents that do mention the environment point to the interdependencies between human, animal, and environmental health. One of the documents discusses environmental health as something both valuable in itself and important for human and animal health (UNEP, 2016). This document states that long-term sustainable development is essential

for healthy living, where health is understood broadly as an ecological phenomenon. The notion of the environment is understood through human practices, such as agriculture, manufacture, and waste production, which can influence and shape a healthy environment. It is stated that 'changes in the environment are usually the result of human activities, ranging from land use change to changing climate' (UNEP, 2016).

International health policy documents can be seen as providing a context for a developing OH framework in AMR. These policy documents are dedicated to improving human health, thus emphasising human exceptionalism over animals and the environment. When animal or environmental health is mentioned, it is often in terms of a function of human health. In the international AMR arena, important OH policy documents refer to and build upon these general health policy regulations. Analysis of these general regulations helps us to understand a rationale for developing international AMR documents that we will explore in the next section.

Continuity of human exceptionalism: One Health policies to tackle AMR

Although AMR is recognised by many international health organisations as a major problem that requires an OH solution, a closer look at the policy documents reveals that they define this problem in various ways. While some documents define AMR as a major threat for human health, arguing that 'it [AMR] needs to be seen as an economic and security threat' (O'Neill, 2016), other documents argue that AMR is a threat for both human and animal health. For instance, the *EU Guidelines for the prudent use of antimicrobials in veterinary medicine* states that 'AMR is not only an animal health and economic concern [. . .], but is also a public health concern'. Other documents broaden the problem definition even further, describing AMR as a multispectral problem that 'pose[s] an extraordinary threat to human and animal health, and to the world ecosystem' (OIE, 2016). Different policy documents construct AMR differently, as either a problem of human health, of human and animal health, or of human, animal, and environmental health. In contrast, however, our analysis of these documents shows that they construct OH in a very specific way.

First, one of the most pressing problems in the policy documents is that of antibiotic use in clinical health care as well as in the animal and agricultural sectors. Many documents emphasise that antibiotic use in clinical settings is a contributing factor to the rise of AMR in humans. Some of the documents make a circular link between the contamination of the environment with antimicrobials (that is, the result of animal, human, and manufacturing waste) with the potential risks of AMR transmission though the environment to humans,

> Antibiotics can reach the environment through three principal channels: animal waste, human waste and manufacturing waste. They can contaminate soil, crops and water sources and encourage the development of drug resistance amongst the pathogens with which they interact (O'Neill, 2016).

Second, similar to general health regulations, AMR OH policy documents focus on human health, framing the causality of human-animal relations as one-directional. Humans are those who suffer from AMR, in terms of their physical wellbeing as well as economic prosperity, while animals are presented mainly as potential risk factors for human health. In the documents, these risks are connected to the direct transmission of resistant bacteria from animals to humans and to the economic losses due to animals' illness and death from AMR. As one of the documents states

> [T]he overarching principle for addressing antimicrobial resistance is the promotion and protection of human health within the framework of a One Health approach, [and] . . . this requires coherent, comprehensive and integrated multisectoral action, as human, animal and environmental health are interconnected (General Assembly of the United Nations, 2016).

In other words, animal health is part of OH, but only as a means to human health. This implicit causal relation is also expressed in the slogan of the OIE which reads 'Protecting animals, preserving our future' whereby animals are described as a necessary element for human health but not vice versa (OIE, 2016).

Third, the AMR OH world described in policy documents includes mostly domesticated and food-producing animals. To be sure, AMR OH policies do not consider domesticated animals as a threat to human health in itself, instead, they focus on human practices like the use of antimicrobials in farming and veterinary medicine,

> Regarding food safety, standards have been developed by the FAO/WHO Codex Alimentarius Commission [. . .]. They provide methodologies to appropriately reduce the risk of the emergence of resistance or spread of resistant bacteria through food that result from the use of antimicrobial agents in food-producing animals (FAO et al., 2017).

Consequently, AMR documents assign a particular responsibility for human health to the animal sector. According to OH policies, the animal sector specialists have a duty to take care

of animals in accordance with the needs of human health. Therefore, the potential risks that human practices can pose on animals and wildlife are not widely considered.

Fourth, similar to the general health policy documents, AMR OH regulations do not provide a clear definition of the environment or environmental health. Not every document considers the environment, and when it is mentioned the operationalisation of what is considered to be 'environment' is often lacking. Some documents refer to the environment including elements such as water, air, soil, as well as wildlife that can be harmed through human and animal practices, and that can also constitute a substantial risk for human and animal health,

> The environment is increasingly acknowledged as a contributor to the development and spread of AMR in humans and animals, in particular in high risk areas due to human, animal and manufacturing waste streams, but strong evidence is still required to better inform decision-making in this area (European Commission, 2017).

Drawing from the international health policy discourses, policy documents that argue for the urgency of OH to deal with AMR globally stress, on the one hand, the interdependency between human, animal, and environmental health. However, on the other hand, these sectors are associated with each other in a very specific, asymmetrical way. OH policy documents tend to assign different roles to different sectors in AMR control and prevention. Humans are usually portrayed as those who experience the burden of AMR, while animals and environments are often defined as sources of this threat. In line with this, initiatives and actions proposed by the OH approach unintentionally reflect the asymmetrical and hierarchical relations between human, animal, and environmental health. AMR can be caused by different factors, including the use of antimicrobials by humans, clinical waste and the use of antimicrobials in the animal and environmental sectors, that involve farming, veterinary, agriculture and manufacturing. However, OH documents unintentionally frame the risks to human health as a driving force underlining the need for greater control and prevention of AMR in the human, animal, and environmental sectors (See Figure 1).

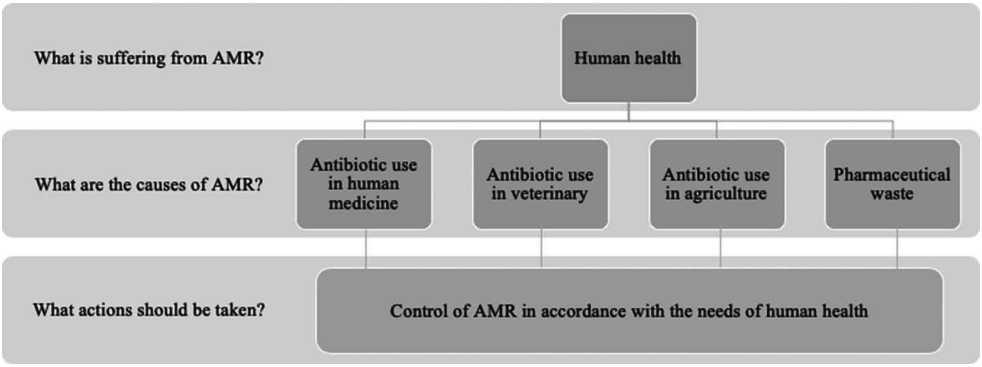


Figure 1. The hierarchical structure of AMR policies.

Discussion

In the context of social science research on OH, we used insights from constructivist policy studies to analyse the specific conceptualisations of OH in the international policy arena of AMR. Our study makes clear that AMR OH policy documents follow the discourses present in general international health regulations: they put human health at the centre stage, and the animal and environmental sectors are presented primarily as risks to human health. Moreover, veterinary and environmental practices are framed from a human-centred perspective – animals that have not been domesticated are given minimal attention compared to livestock and pets. Although this framing might seem logical, as people are confronted with AMR initially as a human health problem, our analysis demonstrates the ambiguity of the OH policy framework for AMR. While the ideal of OH is presented as a collaboration between professionals from the human, animal and environmental sectors, this collaboration is, simultaneously but unintentionally, framed as hierarchical. This specific framing entails that the values of the human health sector prevail above the values of other non-human sectors.

Studying how OH has been adopted in the context of international cooperation against avian influenza, Chien (2013) shows that this framework for collaboration has been well perceived by officials of international organisations such as the WHO, the FAO, and the OIE. She describes that the representatives of these organisations understand OH as a framework that can help to reduce tensions between diverse interests and expertise, and that it can help to build a balanced approach to a shared health concern. However, focusing on a product of inter-organisational collaborations in AMR, which is policy documents, here we showed that the ideals of a balanced and unified approach have not been fully translated into the documents utilising OH. On the contrary, AMR OH policy documents institutionalise the hierarchical

relations between organisations working in the human, animal, and environmental sectors. As such, OH policies do not explicitly open up or create a discursive space for exploring and acting upon different values that are at stake in AMR prevention.

As we mentioned in the introduction, the ambiguous nature of OH has already been scrutinised by researchers like Craddock (2015), Hinchliffe (2015), and Wolf (2015). With Hinchliffe (2015) as well as Wolf (2015) arguing in their works that the OH framework runs the risk of oversimplifying and reducing the diversity of approaches and methods of various disciplines. Other authors highlight that OH can undermine certain values and motives of different sectors and local contexts (Craddock, 2015; Giles-Vernick et al., 2015; Smith et al., 2015). Our analysis provides similar findings with respect to AMR. While OH, in theory, may enable collaboration between the human-, animal- and environmental sectors, its implementation in policy documents, runs the risk of legitimizing the unequal, hierarchical structure of addressing AMR in these sectors.

The formulation of such hierarchical cooperation with human health interests at the top of the pyramid is in parallel with the historical discourses on AMR. Works on the history of antibiotics and antibiotic regulations by Bud (2007), Kahn (2016), and (Kirchhelle, 2018a, 2018b) showed how starting from the 1930s, antibiotics became an essential part of not only human medicine, but also farming and agriculture. Since then, the heated debates with regards to the roles and responsibilities of non- human sectors in the growing issue of AMR have been taking different shapes – from the separation of burdens and responsibilities faced by the human and non-human sectors to the interrelation of these burdens and the allocation of responsibilities exclusively to the animal and environmental sectors. The OH framework can be seen as an attempt to balance these debates and to distribute the AMR burdens and responsibilities between and within various sectors. However, the power to give definitions and to make decisions with respect to burdens and responsibilities still lies within the human health sector.

We can find attempts to reformulate an anthropocentric OH approach in works on post-humanism, for instance in Murdoch (2004) and Rock (2017) articulated that ‘human problems cannot be understood accurately without taking non-humans into account’ drawing attention to the inevitable multi-species entanglement in the understanding of health. Proponents of post-humanism provide a critical vision on the anthropocentric structures of modern science and politics, drawing attention to the complexity of multi-species communities that are interlinked with each other (Badmington, 2004; Murdoch, 2001; Rock, 2013). In line with this, Law (2015) develops a critique towards a one-world metaphysics, arguing that the unification of multiple

realities enacted in practises of various professionals silences the least dominant of these realities (e.g. ecological aspects of AMR). Instead, he argues, we should focus on crafting encounters across different practices, knowledge, and thus worlds. As opposed to the idea of a unified understanding of health, Law (2015), as well as Rock (2017), provoke us to rethink the concept of health through its multiplicity, which is exercised in the different realities of the human-animal-environmental sectors.

In the network of AMR policy documents, we can see that OH discourses have been predominated by anthropocentric ideals. Therefore, other ontologies that might exist in the animal and environmental sectors are not given an opportunity to establish a politically legitimate understanding of AMR that would be based on their practices, knowledge, and, therefore, their realities. Following the way Stone (2012) and Asdal (2015) understand policies – as performative documents that can shape a discursive space to deliberate new routes of dealing with urgent public problems – we may conclude that the discursive space shaped by OH AMR policy documents is rather narrow and would benefit from a broaden approach.

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Healthcare

Chapter II

Complex narratives of healht, stigma and control

Based on: Kamenshchikova, A., Wolffs, P. F. G., Hoebe, C. J. P. A., Penders, J. and Horstman, K. (2018). Complex narratives of health, stigma and control: Antimicrobial resistance screening among non-hospitalised refugees. *Social Science & Medicine* 212: 43- 49. doi:10.1016/j.socscimed.2018.07.012

Abstract

Antimicrobial resistance (AMR) is often presented as a major public health problem globally. Screening for AMR usually takes place in clinical settings. Recent developments in microbiology stimulated a series of studies focusing on AMR in communities, and particularly in travellers (any mobile individual), which was argued to be important for identifying potential public health risks. Against this background, microbiologists have become interested in non-hospitalised refugees as one of the traveller groups. However, this attention to refugees has provoked some professional debates on potential stigmatisation of refugees as dangerous 'others'. To contribute to these debates, and to explore the idea of AMR screening of non-hospitalised refugees from different perspectives, we conducted a qualitative study among four groups of stakeholders who were chosen because of their associations with potential microbiological screening: microbiologists, public health physicians, public health nurses, and refugees. The study took place in a Dutch city from June to August 2016 and had 17 participants: five microbiologists, two public health nurses, four public health physicians, and six refugees. While microbiologists and public health physicians demonstrated a de-contextualised biomedical narrative in arguing that AMR screening among non-hospitalised refugees could be important for scientific research as well as for AMR prevention in communities, public health nurses displayed a more contextualised narrative bringing the benefits for individuals at the centre and indicating that screening exclusively among refugees may provoke fear and stigmatisation. Refugees were rather positive about AMR screening but stressed that it should particularly contribute to their individual health. We conclude that to design AMR prevention strategies, it is important to consider the complex meanings of AMR screening, and to design these strategies as a process of co-production by diverse stakeholders, including the target populations.

Introduction

The ever-increasing global level of antimicrobial resistance (AMR) is often presented as a major public health threat, resulting in an estimated number of human deaths that will dramatically increase from 700,000 in 2015 to 10 million in 2050 if left unresolved (O'Neill, 2016). AMR is defined by the WHO (2018) as an evolutionary process of development of microorganisms that acquire the ability to withstand antimicrobial drugs, thus making treatment of infections ineffective, and increasing the risk of resistant microorganisms spreading among people, animals, and the environment. Microbiologists cite different sources of the emergence and dissemination of AMR, such as misuse of antibiotics in humans, animals, and the environment; mobility of human populations between regions and between care facilities (Selgelid, 2007).

Microbiological studies have focused on the emergence, control, and prevention of AMR within health practices. Scientists have studied the prevalence of resistant microorganisms in different groups of patients, for instance, in paediatric and intensive care units (Gaspari et al., 2006; Khurana et al., 2017). Based on similar studies, countries have developed their national guidelines on the prevention of AMR in hospital settings. For instance, the Netherlands developed a so-called 'search and destroy' policy for AMR, that involves AMR screening of all hospitalised patients and isolation of those patients who are considered to be at risk groups (Kluytmans-Vandenbergh et al., 2005). Such risk groups include patients who received treatment in a foreign hospital within two months prior to hospital admission in the Netherlands, and farmers and members of their families who have contact with pigs, calves, or chickens (Werkgroep Infectiepreventie, 2017).

Recently, microbiologists in the Netherlands (Arcilla et al., 2017), Sweden (Tangden et al., 2010), and Australia (Kennedy & Colliqnon, 2010) conducted AMR studies among non-hospitalised populations such as international travellers (where 'travellers' are understood as people who move from one territory to another, crossing national borders regardless of the purpose of their travel), and showed that travel can contribute to the dissemination of resistant bacteria from endemic to non-endemic parts of the world (J. Penders et al., 2013). In this regard, since 2014, refugees have attracted the attention of microbiologists and public health professionals as a mobile demographic group travelling between geographic areas (de Smalen et al., 2016; Heudorf et al., 2016).

Refugee studies on AMR have been conducted among hospitalised refugees upon their admission to clinics (Reinheimer et al., 2016; Tenenbaum et al., 2016). For example, in their research on AMR among hospitalised refugees in Germany, Reinheimer et al., (2016) showed

that 61% of 143 refugees carried AMR, compared to 17% in the German population. Based on these data, the authors proposed that refugees admitted to hospitals be required to undergo a compulsory AMR screening, which entailed a departure from regular AMR control practices in Germany (we have to add, however, that since the end of 2016, individuals that have been in a refugee centre in the past two months are screened for AMR upon hospital admission in the Netherlands and several other European countries, including Germany). Other scientists have also suggested that AMR screening should be compulsory for refugees admitted to hospitals (de Smalen et al., 2016; Maltezou et al., 2017). Considerably fewer studies (Angeletti et al., 2016; Heudorf et al., 2016) have been conducted among healthy refugees ('healthy' and 'non-hospitalised' will be used as synonyms for the remainder of the article), and therefore the data on the prevalence of AMR among healthy refugees is scarce.

AMR screening involving both healthy and hospitalised refugees provoked discussions about vulnerability and potential stigmatisation of refugees as subjects of AMR screening (Walter et al., 2016). The question of stigmatisation of refugees with regards to AMR has been analysed by social scientists and anthropologists. For instance, in their analysis of politics of AMR in the UK, Brown and Nettleton (2016) demonstrate how the political discourse of AMR is framed in the concepts of 'trauma' and 'catastrophe'. They argue that the meaning of AMR in British politics has been shifted from being understood as 'biological resistance' into 'resistance of economies', creating a platform for articulation of new political discourses, which associate the 'catastrophic' threat of AMR with politics of immigration. In addition, the same authors, in their analysis of debates about antibiotics and AMR that take place among 'lay people' on a popular online forum, showed how debates on antibiotics resistance became entangled with debates on public politics and personal responsibility (N. Brown & Nettleton, 2017). AMR, they argue, provokes a moral reflection on bio-political responsibility of citizens for their individual immunitary practices, such as antibiotic use, hygiene, or immunisation (N. Brown & Nettleton, 2017). Other scholars have analysed the use of the notion of responsibility with regard to carriers of communicable diseases like SARS, Ebola, and HIV, transforming victims into agents (Wald, 2000, 2007). In her work, Wald reflects on the theory of Douglas (1966) who described how the dichotomy between 'dirt' and 'pure' relates to the distribution of power in society. Douglas explained that social order entails the construction of controlling mechanisms that restrict potential dangers and 'sources of disorder' caused by 'others', and the dirt-pure dichotomy helps to facilitate that.

These studies show the complex relationship between health, stigma and control as a fruitful lens to study AMR screening among refugees as a travelling group. Discourses of

catastrophism and responsibility for acquisition of AMR may create a potential danger that refugees coming from endemic areas are held responsible for disseminating resistant bacteria to host countries and imposing a danger upon other people. AMR screening of refugees can be seen as a mechanism that helps to control the dangers coming from 'others' who bring potential threats to the bacterial order of a host community. From the perspective of these studies, discussion about AMR screening may construct refugees not merely as people seeking asylum but as bodies polluted by foreign bacteria (Chandler & Hutchinson, 2016). Therefore, when speaking about AMR screening of refugees, it is important to analyse the complex meanings of such an intervention.

Current debates regarding justification or non-justification of AMR screening among non-hospitalised refugees take place in scientific journals between different scientists (Kempf & Heudorf, 2016; Walter et al., 2016). Refugees, however, do not often have a voice in these debates. The present article aims to fill that knowledge gap and to explore the voices of different professionals as well as refugees regarding the idea of AMR screening. For this purpose, we conducted a qualitative study involving microbiologists, public health physicians, public health nurses, and refugees. We explored how these four groups give meaning to potential voluntary AMR screening among healthy refugees, and how they consider the possible rationale, benefits, and harms of such screening. To be sure, when discussing AMR screening, we mean voluntary microbiological screening among non-hospitalised refugees. Although we acknowledge the complexity of the concept, for our study we opted for a broad definition of screening. When discussing it with participants, we spoke about AMR screening as a broad practice that included collection of stool samples for research and/or public health purposes.

Methodology

We studied four stakeholder groups who are already involved with health issues of refugees, and who potentially could be involved in AMR screening among healthy refugees: microbiologists, public health physicians, public health nurses, and refugees originating from Syria. Refugee participants included both people who had already obtained their official status of refugees and received their residence permits, and those who were still in the process of applying for asylum. The study was conducted in a Dutch city from June to August 2016. It involved a variety of qualitative methods, including observations of participants in their daily life and professional activities, in-depth interviews, group interviews, and informal discussions with participants. We decided to use qualitative methods as they provided us with an

opportunity to analyse in-depth meanings that different stakeholders gave to the phenomenon of AMR and to the idea of AMR screening of refugees.

Research participants

Microbiologists who participated in the study had experience working with AMR in clinical (diagnosis, therapy, and prevention) and research settings, including microbiological screening of travellers. At the time of our study, two microbiologists were actively involved in developing a research proposal for AMR screening of non-hospitalised refugees in the Netherlands. Therefore, the interviews and discussions were of particular interest for them.

The public health physicians and nurses have practical experience and knowledge in working with hospitalised patients who carry resistant bacteria, as well as experience in working with national AMR prevention programs. In addition, participants from these two groups have experience in communicating with refugees in the context of implementation of prevention strategies in asylum centres. It is important to note that public health physicians and public health nurses who participated in the study worked at the same organisation in one office, and therefore they knew each other and collaborated with each other on various public health programs.

With regard to refugees, we chose to narrow our focus to Syrian refugees, because at the time of the study they comprised the largest refugee group in Europe (UNHCR, 2017). We collaborated with one of the master's program students from Maastricht University in the Netherlands, who himself was Syrian and worked as a physician in a hospital in Syria before his arrival in the Netherlands. His background and knowledge of the Arabic language helped us to build contacts with people in the asylum-seeker centres. He assisted as a translator during two interviews with refugees and explained language nuances.

Qualitative study

The study involved 17 participants: five microbiologists (two female and three male), two public health nurses (two female), four public health physicians (two female and two male), and six refugees (three female and three male). The number of participants was determined by data saturation. The age distribution at the year of the study among refugees was between 24 and 60 years old, and among professionals between 35 and 63 years old. The first author visited microbiologists and public health professionals at their offices, and refugees were interviewed at asylum-seeker centres, either in their private rooms or in interview rooms. All interviews

were conducted in English, apart from two interviews with refugees that were conducted in both English and Arabic at the request of the interviewees.

All interviews were tape-recorded after written informed consent was provided, and participants received a copy of the consent form with the researchers' contact information and affiliations. Interviews were coded for anonymity and transcribed verbatim. Interviews were read and discussed with all authors. Based on the literature from sociology of diagnosis and anthropology of AMR, the first author defined categories for interview analysis that were relevant to the study. These categories were discussed with the other authors, and subsequently modified. The final analysis of the interviews was discussed with and modified by all authors.

The process of inviting refugees to take part in the qualitative study required several steps. After having obtained permission to visit two asylum-seeker centres from the centres' administration, we visited the centres four to six times over two weeks to introduce ourselves, our study, and the issue of AMR to potential participants. During these weeks, we met the administration of the centre and refugees from various countries, not only Syria. In the next months, we visited the asylum-seeker centres one to three times per week. During this fieldwork, we heard stories about the process of immigration and the previous lives of refugees in their countries of origin.

During our initial visits to asylum centres we introduced ourselves as researchers and approached people whom we met in communal areas, such as kitchen, common rooms with tennis table and TV, and communal spaces outside the buildings of the centres. Syrian refugees who expressed their interest in participating in the qualitative study were provided with detailed oral and written information about the research, and its aims and objectives. Information was provided in both English and Arabic. In addition to voice-recorded qualitative interviews, the first author conducted observations of the daily life of refugees and asylum seekers and made notes on the informal discussions with participants.

After the study was completed, a report was sent to all the participants in order to receive their agreement or disagreement with the authors' interpretations of the data collected. We received feedback from all public health nurses and physicians, and four microbiologists provided their comments. However, none of the refugees replied to the report. One of the participants explained that he did not have time to read through it; another person commented that it was too difficult for her to read long texts in English. In addition, some of the people who participated in the study moved to other asylum centres or received their housing by the time the report was sent out, and therefore we could not trace them.

Ethical clearance

According to Dutch regulations, qualitative studies do not require a legal approval from an ethics committee. However, we made a decision that it was crucial that the study be conducted in an ethical way and therefore applied for ethical clearance. The study was approved by the Medical Review Ethics Committee of the Maastricht UMC+ (approval number METC 16-4-117.1/ab).

Findings: understanding AMR from different perspectives

Screening is required for prevention and research

Both the microbiologists and the public health physicians presented AMR as an alarming public health problem, and therefore, generally supported the idea of AMR screening of healthy refugees. They provided a rather de-contextualised justification of AMR screening, arguing that screening of refugees entering the country can be essential for public health as well as for the necessity of research. In interviews, microbiologists argued that non-hospitalised refugees are an important and large population that cannot be ignored when it comes to potential health threats.

> There are so many people [refugees] coming in right now, it should not be ignored, it is public health and it should be studied (M2).

> It is research [AMR screening of healthy population] that has a rationale in knowing more about to which extent resistance is threatening us and will threaten us in the future. (M3).

By the time the study was conducted, unless a refugee had been treated in a foreign hospital in the last two months before her hospital admission in the Netherlands, she did not need to undergo obligatory screening for AMR. Public health physicians argued that the AMR study among non-hospitalised refugees would help to determine whether refugees should be added to the category of a risk group for obligatory AMR screening during their admission to a hospital regardless of whether they were in a foreign hospital before.

> It is useful to have some background information about the risk levels within our community, or within our region. … If we find that AMR is high in refugees that would necessitate hospitals to deal with them in the same way as with people who spent some time abroad or who were admitted to a hospital in a foreign country – isolate them, screen them, and treat them if necessary (PHD3).

In addition, microbiologists pointed out that AMR studies among healthy populations, including refugees, could be important for developing scientific knowledge in the field of microbiology.

> The data not primarily used for the participants [healthy populations], it primarily used to get further in the professional field. And that is something which also has to be considered, which research should be done which is good for the professional field. (M3).

While the participants came up with a biomedical justification of AMR screening of refugees and do not refer to political issues, social scientists have demonstrated that this distinction between science and politics is difficult. Brown and Nettleton (2016) described how in the mid-2000s in the UK, conservative politicians were trying to lobby a policy that would impose 'compulsory screening of migrants prior to departure from their countries of origin'. Such policies, as the authors emphasised, merge discourses of bio-politics of race with those of infectivity, thereby stigmatising newcomers as dangerous, and shaping the image of AMR as a threat coming from the outside.

Although ideas about the scientific rationale for AMR screening of healthy refugees were widely accepted by microbiologists and public health physicians, not every interviewee agreed with them. One of the microbiologists, who was working as an internist in infectious diseases, was not particularly convinced about the potential clinical benefits of AMR screening of non-hospitalised refugees. While he agreed that the data from such screening might be interesting, he emphasised that it was hard for him to see why microbiological screening of healthy refugees would be necessary.

> When there is no problem [when refugees are healthy], well, it's a lot harder for me to see the importance of screening. Because why should you screen, there is no problem there. No, there is no problem there. Maybe you might screen them just as a baseline. For example, we do not know anything about refugees and about antimicrobial resistance prevalence so you want to know at the baseline what is actually the prevalence of antimicrobial resistance among healthy refugees. When it is 0, then we do not have to be afraid, but when it is 80%, maybe we have a problem there. So for research, maybe it is interesting just to know, is the carriage of resistance a problem there, in that population. (M5).

However, the same participant indicated that microbiological screening of healthy populations who are not refugees might be beneficial for public health in general and clinical practice in particular.

> With regards to the screening of the healthy population, well, I think we all want to better understand, for example, how resistance is transmitted. Is it taken from abroad and then introduced for example to the Netherlands? And how is it, by hand contact, or by faecal contamination, or by air? You can think of all kind of things. So I think when you want to fight against antimicrobial resistance and you see that as a problem, I think it is really wise to understand how does it really spread among the population. And one way to look at it might be to screen healthy volunteers who have travelled all over the world, and screen if they carry antimicrobial resistance bacteria. (M5).

One of the limitations of AMR screening among healthy refugees that was mentioned in the interviews was the lack of any personal benefits for participating refugees, because there is no treatment for resistant bacteria in healthy people. The screening may, for instance, indicate that a healthy refugee carries the β-lactamase gene, but this knowledge will not benefit her, as she cannot be treated for it. One of the microbiologists explained this difficulty while talking about the AMR study conducted with international travellers:

> We screened them [travellers] for antimicrobial resistant bacteria in gastrointestinal tracts of healthy subjects basically, and if a person is positive, we know that. Before travel 6% of the travellers were positive, when they came back, 34% were positive so there was a huge increase. But we cannot do anything with that, we can only tell them that you have antimicrobial resistant bacteria and that's it, people don't have any benefits from it, there is no treatment from it, there is also not any harm as far as we now know as long as they are healthy. … We were very reluctant in telling people whether they are positive for antimicrobial resistant bacteria, we did not want to worry them … We really think it was not very wise to scare people with something. …. Then we decided not to communicate results individually to people. (M2).

However, other microbiologists and public health physicians emphasised that the decision to not report individual results back to participants might also be problematic, because people often want to know their data. Emphasising this complexity, one of the microbiologists

described how she herself felt uncomfortable not knowing her individual results from the AMR study in which she participated.

> We are mainly studying resistance in the total community, so also in common cells, so we are saying to also the people that help us in the study, and to participants, that we don't really know yet what it means if you have this. And of course, I mean, like I participated in some of our own studies as well and all of a sudden, you know, then you start wondering like, 'Hmm, do I have a resistance in me or not?', you know. It is, it is just strange, what does it mean and I tell everyone, 'Oh, it does not mean anything, we do not know, we have not seen any evidence yet that you have more risk of infection', but still when it was all of a sudden, when it was about me, I thought, 'Hmm, I actually want to know if I have or not have it.' So yes, but in general, since we do not know what it means we do not report it back to people. (M1).

Microbiologists understand that while the technology of screening may provide them insight in the bacterial world of a healthy person, it does not give them an instrument to control this world. In this context, AMR screening of healthy individuals reveals unruly 'intolerant bodies' that pose potential risks to these persons themselves and to others (Anderson & Mackay, 2014). Both microbiologists and public health physicians emphasised that the knowledge from AMR screening can be used in developing medical guidelines for healthcare practice, and they generally expressed support for the potential AMR screening of healthy refugees. The arguments for such screening are rooted in a de-contextualised biomedical discourse that does not anticipate the contextual risks of associating refugees with AMR.

Screening is not fruitful for healthy persons

As opposed to the discourse of microbiologists and public health physicians, public health nurses expressed a more personal and contextualised orientation to AMR, and they were hesitant about the idea of AMR screening of healthy refugees. They doubted whether such a study could bring any benefits to refugees, and whether possible public health benefits outweighed personal considerations. Public health nurses argued that microbiological screening would only stimulate worries among refugees about their health status as well as uncertainties regarding the screening itself, because AMR is not a common medical concept. According to nurses, AMR screening is a technique that is used in hospital settings, but one that should not be offered in the context of a general, non-hospitalised population.

> The population is not ill at the refugee centre; there is no need to do screening. It [AMR] does not do anything with healthy people. … If you test them at refugee centre, what would you do? You can't do anything with this knowledge, you can't treat them. (PHN1).

Public health nurses who participated in our study always worked with individuals (e.g. for STD or TB testing), and they had experience as nurses in hospitals, as well as in providing AMR training for nurses, and in providing educational programs about AMR in secondary schools. The direct interactions with diverse publics may explain why they were rather negative about the idea of offering microbiological screening to all refugees for public health purposes. Based on their experience of educating laypeople about AMR, public health nurses expressed that the lack of knowledge about AMR among the general public can cause prejudice, hostility, and stigma toward people with AMR or groups that would be offered AMR screening. They argued that this could particularly affect refugees, who are already presented by many media channels as dangerous others. This worry is mirrors the understanding of stigma as fear of otherness and 'anomaly' (Douglas, 1966; Goffman, 1968). As Douglas (1966) points out in her analysis of the notion of dirt, societies marginalise people if they have been in contact with unknown 'danger'. In the context of AMR, this danger comes from resistant microbes. However, as microbes are embodied within bodies of people, they transform carriers from being 'victims' of microbial activity to 'agents' that represent bacteria-host relationships (Wald, 2007). One of the examples given was about a boy with AMR who had problems with going to a school for people with disabilities because he was claimed to be dangerous to other children.

> One child who has MRSA [resistant bacteria], and he is going to new school and there is some rumours, some negative excitement about it in the school. Really, really bad. It is a school for children who are disabled, and some people worried a lot about consequences of MRSA for other people and for themselves. (PHN2).

Moreover, public health nurses emphasised that there is a lack of knowledge about AMR among nurses in hospitals who often do not fully understand what AMR means and why some actions must be taken, for example, isolating patients with AMR:

> When I was a nurse in the hospital, I just got the instructions that this is the person with MRSA, here is your coat, and your gloves, and your mask. But they did not explain to me really what the point was, I was a bit concerned that if it is MRSA, then I have to be very

> careful, and I was tested afterwards if I was clean or not. But they never explained to me well why I had to do it, I just did it very carefully because I was scared. And it is also stress for the patient because even the nurse can't explain him why these measures are taken. (PHN2).

With this background of communicating with different patients who carry AMR and must be isolated in hospitals, public health nurses applied more contextualised approach to patients and potential volunteers in AMR screening. When speaking about the idea of AMR screening of refugees, they were focusing not merely on public health benefits, but rather on the complexity involved in the concept of AMR. They point to the lack of familiarity with AMR among both patients and nurses and the potential for provoking fear among both refugees, who are not able to do anything about their AMR status, and the general public, who may perceive refugees as carriers of dangerous microorganisms.

What kinds of benefits does it bring us?

All refugees who participated in the qualitative study had been living in the Netherlands for at least six months. All participants came to the Netherlands through Turkey and Italy, travelling from Italy to the Netherlands by train or car. Two of the participants had a high school education, and another four had either finished higher university education or not yet finished (because of the war in Syria).

The phenomenon of AMR was introduced to refugees in two steps. First, we had informal conversations in small groups in both English and Arabic about AMR, its causes and possible health consequences for a person with resistant infection. Then, written information in both languages was provided. Most of our participants had never heard the English term ‘antimicrobial resistance’ before; however, some of them were familiar with its Arabic analogue. They explained that AMR is a bodily condition that relates to the ability to fight a disease.

> Antimicrobial resistance is a resistance of your body against microbes, if you have enough white blood cells your body will fight the disease, but if you have less white blood cells you have immune deficiency and your body will not fight the disease. (R5).

Another person elaborated the reasons for AMR by making a connection between the development of resistance and consumption of antibiotics:

> In Syria we take a lot of antibiotics. So maybe the genes they have immunity for this medication. … Because we take a lot of antibiotics in Syria, our body gets used to it. So how much stronger from antibiotic [no matter how strong the antibiotic], it will not affect us. (R1).

At the same time, refugees argued that they had to consume antibiotics anyway because they help in treating diseases. One participant explained that although he understood that overuse of antibiotics may harm his body, he still wanted to use them because it can help alleviate pain. Such idea, as they explained it, is rooted in practices that people followed in Syria, where they could access and use antibiotics whenever they thought they were needed.

> In our country, we were taking antibiotics when we had something, or even a small pain in our body. (R4).

This way of understanding antibiotics as something essential for healthy living is not unique. Scientists in anthropology use the metaphor of 'charm' to describe how different people understand this medicine as 'magic bullets that have the power to heal (Chandler & Hutchinson, 2016). Unwanted effects of antibiotics, such as AMR, are either unknown or deemed to be unimportant in comparison with the treatment capacity of the drug. The Dutch system of antibiotic regulation was foreign to our participants who arrived from Syria. They preferred to consult their pharmacists instead of general practitioners, and to buy medications directly from a pharmacy while avoiding medical consultations.

> Our pharmacy is our own doctors … I hate Dutch hospitals because when you call them they tell just to take paracetamol. … Paracetamol will not make any difference if you are sick. Some people in Syria take antibiotics every day for headaches, most people have headaches. (R2).

When discussing the idea of AMR screening among healthy refugees, some participants were rather positive about potential participation, because they considered participation in screening as a way to get more insights into their personal health problems and to get advice that would help them to maintain their health.

> It [screening] would be helpful for me, I can take care about myself. If there is something bad with me, the researcher will tell me. (R1).

> It [screening] will be helpful to take care of myself if there is any problem. So it is good for me. (R2).

One of the participants explained that potential AMR screening is an important preventive health measure for individuals, and thus he would like to participate in it:

> If person has something wrong they [researchers] try to fix it, they are trying to make him better. … Research is for the person. They will do research to know what medicine is good for the person. … If someone has something not good they will try to get him better, to get him in a hospital, it [screening] is better for us. (R1).

People participating in our qualitative research considered it necessary that potential information obtained through the AMR screening be shared with them and that it should benefit them. They pointed out that the practices of antibiotic use in their home country were the only ones that they knew and believed to be right, but they argued, if these practices may actually harm them, researchers must tell them and share their knowledge about better practices.

> You should tell us what to do to make us feel better without taking antibiotics, because I don't know how. (R4).

We also explored concerns and worries about potential harms of AMR screening. When we discussed general medical checks that refugees are required to undergo upon their arrival in the Netherlands and the possibility of voluntary microbiological screening, it became clear that people felt a little awkward: One person said: ‘We are clean, really’ (R2). Another person mentioned: ‘… do not tell the media about it [AMR screening]. Because if you tell the media, media will tell it all wrong’ (R1). In this context, all Syrian interviewees questioned why potential AMR screening was discussed only with respect to refugees. They argued that if this screening has important health benefits, it must be offered to everyone and not exclusively to refugees. One of the participants raised a number of questions about the rationale of offering AMR screening exclusively to refugees.

> What will affect me, what will I have, what the benefit from it on me, does it help me, does it help all the refugees, is there anything wrong, did you suspect something, I have all these questions. So, did you suspect something from me as a refugee, why you are doing this research only for Syrians, are you suspect something, or just trying to help us? (R1).

Some people worried that if they showed some signs of a serious health problem, their asylum applications would be rejected. In fact, one of the refugees was reluctant to ask for medical assistance for her son before they arrived to the Netherlands.

> My son [4 years old] had a very high temperature [during their travel to the Netherlands], but I had medicines with me. Also, you know, when we had a problem, we were afraid to go to the doctor because we have to arrive to Europe without any problems. … So I just gave him some antibiotics, he felt better, and we continued. (R4).

The refugees with whom we spoke demonstrated a complex narrative about AMR screening. They consider the benefits of screening for public health, but they also add that then AMR screening should be offered not only to refugees but to other travellers as well. They also consider the benefits of AMR screening for the individual health of refugees, but they express fears that promises of anonymity will be broken and that results of AMR screening could affect their asylum applications in a negative way.

Discussion and recommendations: complex narratives about health, stigma and control

The purpose of our study was not to judge which perspective on microbiological screening of healthy refugees was the most scientifically sound or ethically justifiable. Instead, our aim was to understand how different stakeholders give meaning to AMR screening, and how they understand 'proper' AMR screening of healthy refugees.

It is important to note some limitations of our study. First, the study involved a small number of participants – 17 people. However, this allowed us to make an in-depth analysis of the complex narratives of the participants. Second, we decided to focus on four stakeholder groups who may be actively involved in the process of AMR screening of healthy refugees, although the spectrum of perspectives on this issue can be broader. Third, we deliberately involved only English-speaking refugees who had experience of direct communication with Dutch health professionals, although it excluded other potential participants who might have different perspectives on AMR and AMR screening. In addition, as was emphasised at the beginning of the article, our study was focused on voluntary AMR screening, because microbiological studies are currently at the stage of studying the prevalence of AMR among refugees. However, if microbiological screening demonstrates a high level of AMR among refugees, it is probable that obligatory AMR screening will be recommended for this group.

Therefore, we would like to elaborate that further studies and ethical reflections on the potential stigmatisation are important in this developing field.

While biomedical discourses about AMR tend to distinguish the scientific insights about AMR from the political issues, social scientists have shown that AMR discourses are more complex and that symbolic meanings about purity and danger, and self and others are intertwined with AMR policies and practices (N. Brown & Nettleton, 2016; Chandler & Hutchinson, 2016). Our study shows that stakeholders engaged in discussing AMR screening among refugees express different perspectives: we found a narrative about screening that emphasises the problem of AMR and the benefits for science and public health, but also narratives that articulate the ambiguities of screening healthy refugees, pointing to the health benefits for refugees and communities as well as to the risks of stigmatisation and exclusion. When discussing making AMR screening of healthy refugees a national or European practice, it is important to realise that policies are always developed in concrete contexts where complex narratives are operative.

Following the work of Fleck (1979) on thought styles and thought collectives, B. Penders et al. (2009) argued that different thought styles also produce different notions of 'proper' science. From this perspective, we can interpret the different perspectives of the stakeholders as reflecting different thought styles, different practices, and different notions of 'proper AMR screening'. For microbiologists as well as for public health physicians who worked mainly with public health issues on the level of the laboratory and statistics, the crucial argument for screening was the potential threat of AMR to the community and the opportunity for monitoring on a population level. For them, this could be done anonymously, and the subject of screening with her social status, cultural background and political affiliations may be unknown. The practice of public health nurses, on the contrary, entails meeting and caring for individual patients. Therefore, they considered AMR screening to be important on the level of detecting personal health risks, not merely on the statistical level of public health. From this perspective, AMR screening of healthy refugees was not considered fruitful. At the same time, Syrian refugees saw AMR as a bodily, personal health condition that affects people when they are ill but that could be prevented if a person has appropriate information about, for instance, antibiotic use. From this perspective, the refugees could see the benefits of screening of healthy refugees, but only when the results will be made beneficial for broadening AMR screening to larger populations.

These different perspectives on proper AMR screening that stem from different everyday practices and thought styles mirror broader ethical discussions about AMR, known as 'the

tragedy of the commons'. Whether AMR is recognised as a public or a personal problem would require putting either the community before an individual or vice versa (Foster & Grundmann, 2006; Hardin, 1968). Various studies have demonstrated that professionals in the medical and public health fields have different ideas about this dilemma and give preference to either personal health (Broom et al., 2014; Metlay et al., 2002)or public health (Oczkowski, 2017). However, our study suggests that the debate about potential AMR screening among healthy refugees should not only consider prioritising an individual or society, but also *how* eventual AMR screening of a healthy population is framed and organised. In that respect, the input of the refugees is illuminating. While they demonstrated a belief in antibiotics as 'magic bullets', they also argued that they would like be informed about their individual AMR status and potential ways to protect their health (such as proper intake of antibiotics). Moreover, refugees stressed the importance of framing AMR screening among healthy refugees in a non-stigmatising way, for instance by labelling it 'AMR screening among travellers' instead of 'AMR screening among refugees'.

Science and Technology Studies (STS) (Jasanoff, 2004; Rabeharisoa & Callon, 2004) stresses that production of knowledge and technologies requires co-production of science and society. More specifically, Oudshoorn and others have demonstrated that 'users matter' (Oudshoorn et al., 2004; Oudshoorn & Pinch, 2003): interaction with diverse users is crucial for designing and developing robust knowledge and 'working' technologies. Several studies have emphasised that co-production requires constructing a dialogue and interaction between different styles of practices that in turn may lead to the creation of new collective identities around a particular issue (P. Brown, 1992; Rabeharisoa & Callon, 2004). Because public health has developed as a policy-driven field that is dominated by epidemiology, it has difficulty relating to diverse publics (Horstman, 2013). The lessons of STS are highly relevant for this field. Our study can be considered a first step toward co-production around the discussion of AMR screening of healthy refugees. Instead of assuming what is scientifically or ethically proper AMR screening, we explored thought styles and practices among different actors, because the making of scientifically, socially, and ethically proper screening depends on collaboration and dialogue between these actors. Instead of relying only on technical experts, including the voices of others reminds us that the tragedy of the commons is not an immutable problem, but is one that can be shaped and reshaped through engaging diverse actors representing different styles and practices in processes of co-production.

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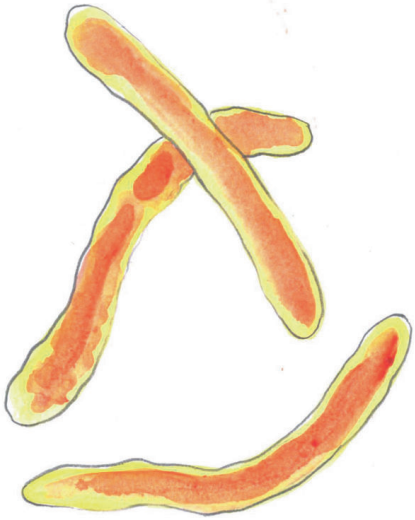
Chapter III

Obligatory medical prescription of anibiotics in Russia



Based on: Kamenshchikova, A., Fedotova, M. M., Fedorova, O. S., Fedosenko, S. V., Wolffs, P. F. G., Hoebe, C. J. P. A., Horstman, K. Obligatory medical prescription of antibiotics in Russia: Navigating formal and informal healthcare infrastructures. (second round of revisions)

Abstract

Antimicrobial resistance control programmes often aim to 'fix' the behaviour of antibiotic users and prescribers. Such behavioural interventions have been widely criticised in social science literature for being non-efficient and too narrow. Drawing on these critics, this article analyses how the political programmes for fixing antibiotic behaviour were adapted in practices of healthcare professionals and patients in Russia. In 2018 we conducted interviews with medical doctors, pharmacists and patients in a Russian city, focusing on their practices around the policy requirement for obligatory medical prescriptions of antibiotics introduced in 2017. We conceptualised the obligatory medical prescription as a political technique that aimed to change practices of self-treatment and over-the-counter sales of medications by establishing doctors as obligatory passage points to access antibiotics. Our analysis shows that the requirement for medical prescriptions has not reflected the infrastructural gaps that influence antibiotic practices. These gaps include a lack of medical specialists, long wait times for medical appointments and difficulty for patients to take time off work to go to the hospital. To compensate for these infrastructural gaps, healthcare professionals and patients adopt informal networks of antibiotic care within the requirement for an obligatory prescription.

Introduction

Control and regulations of antibiotics in healthcare, including prescriptions, over-the-counter sales and self-medication, have been a priority for national and international programmes for addressing antimicrobial resistance (AMR) (Chandler, 2019; Will, 2018). In the Global Action Plan, published in 2015 by the World Health Organisation, the World Organisation for Animal Health and the Food and Agriculture Organisation of the United Nations, individual behaviour regarding antibiotic use is considered to be one of the leading causes of AMR. Following the international lead, national policies against AMR have focused on the reduction of 'unnecessary use' of antibiotics in healthcare (European Commission, 2017; O'Neill, 2016). The behavioural focus of AMR policies has been scrutinised by various social scientists who highlight their narrow capacity and limited effectiveness (Haenssgen et al., 2018; Pearson & Chandler, 2019). Scholars like Chandler (2019) and Will (2018) argue that it is necessary to understand the underlying social, economic and political processes that influence antibiotic practices, rather than focusing on the individual behaviour of users.

Despite this critique, behavioural interventions have continued to play an essential role in AMR control programmes (Broom, Kenny, Prainsack, et al., 2020). To understand what kind of work these interventions perform in the world of healthcare, we studied practices of medical doctors, pharmacists and patients in a Russian city. The Russian context is especially interesting because AMR is a relatively new object in the policy agenda of this country, and over-the-counter sales of antibiotics became strictly prohibited only in 2017 (Government of the Russian Federation, 2017). This means that our research was conducted in a context of policy changes that were aiming to influence antibiotic practices. In particular, we analysed how practices of medical doctors, pharmacists and patients have been adapting to the introduction of an obligatory, standardised antibiotic prescription as part of the national action plan against AMR that was introduced in 2017. Contributing to discussions on behavioural interventions against AMR, we will analyse the obligatory, standardised medical prescription in Russian healthcare as a political technique to manage antibiotic behaviour of heterogeneous actors.

Below we will introduce the theoretical background of our study. Then, we will describe our research setting and methodology. In the results, we will present the analysis of how obligatory medical prescriptions mediate the practices of doctors, pharmacists and patients in a Russian city. In the discussion, we will reflect upon the findings in the context of current theoretical debates to control individual antibiotic behaviour.

Theoretical background

Behavioural interventions, including awareness campaigns for healthcare professionals and patients and practices of antibiotic surveillance and control over individual behaviour, have been deliberately scrutinised by social science scholars. The research conducted by Pearson and Chandler (2019) in Ethiopia, India, Nigeria, the Philippines, Sierra Leone and Vietnam demonstrates that awareness about AMR among healthcare professionals does not automatically translate into the reduction of antibiotic prescriptions. The authors show that despite the awareness about AMR, healthcare professionals prescribe antibiotics due to infrastructural constraints, such as lack of diagnostics and shortages of medical staff, and social constraints, such as economic access to antibiotics and overall level of hygiene and sanitation in communities and clinical settings. Pearson and Chandler (2019) argue that rather than reducing antibiotic prescriptions, high levels of awareness about AMR among healthcare professionals has given them confidence in prescribing broad-spectrum antibiotics, which are believed to be more effective in a setting with poor hygiene and limited diagnostic capacity.

In a special issue of this journal, Will (2018) scrutinises individual behaviour interventions as a solution for AMR, and she argues for the need of a more nuanced understanding of the 'routines and logic' that shape organisations and delivery of care. She elaborates that the antibiotic prescription behaviour of medical doctors can be influenced by multiple processes, including their relationships with particular patients, the socio-economic status of these patients, their communication with colleagues and their feelings of responsibility towards an individual patient and society as a whole. Following criticism of the behavioural approach to AMR, Chandler (2019) argues that the focus on behavioural changes tends to overlook infrastructural conditions that often shape the behaviour of antibiotic users in a particular way. She elaborates that the question of antibiotic use is not a simple, rational question of choice and availability of knowledge, which is often argued by behaviour-oriented policies, but depends on larger infrastructural processes that define social, economic and political inequities.

Case studies from different parts of the world demonstrate how antibiotic practices are the results of multiple processes, including the availability of particular infrastructures to which professionals and laypeople have to adapt. Studying the social world of urban Australian hospitals, Broom et al. (2014) show that AMR as such does not play a significant role in clinical decision-making. Rather, doctors make their decisions about antibiotic prescriptions following the 'rules of the game' within a hospital. These rules can reflect professional hierarchies between more- and less-experienced doctors and a constant negotiation of immediate clinical risks versus long-term population burdens. In a similar study in a rural Australian hospital

Broom et al. (2017) show that doctors have to adapt their prescription practices to the social and infrastructural realities of the rural area. This includes high mobility of patients who come to rural areas for seasonal work and large distances between a hospital and residential areas, conditions that challenge the continuity of treatment and stimulate prescriptions of antibiotics. Another study in Australian healthcare shows that inter-professional relationships between doctors and pharmacists can also contribute to antibiotic practices, including the informal negotiations about the appropriateness of a particular treatment (Broom et al., 2015). Several studies state that antibiotic prescriptions can be influenced by the intricate relationships between a doctor and a patient and between a pharmacist and a patient (Broom, Kenny, Kirby, et al., 2020; Cabral et al., 2015; Lambert et al., 2019). Depending on how healthcare professionals perceive the expectations of patients, they may feel obliged to prescribe or sell antibiotics to preserve a trusting relationship with a patient and to provide a physical symbol of care in the form of a prescription.

Antibiotic practices of patients can also be influenced and shaped by different processes, beyond immediate knowledge about AMR. In her study of self-medication practices in Maputo, Mozambique, Rodrigues (2020) analyses the different rationales of patients for using antibiotics. She argues that communication between healthcare professionals and patients plays an important role in patients' decisions for self-treatment. She shows how standardised practices of diagnosis and treatment exercised by doctors become familiar to patients. After visiting a doctor several times with reoccurring complaints, patients become acquainted with medical practices of diagnosis and treatment, including medical prescriptions. As a result, Rodrigues (2020) shows, by learning the practices of doctors, patients feel confident enough to perform self-treatment with medications that were previously prescribed to them.

Another study on antibiotic use behaviour among patients was conducted by Willis and Chandler (2019) with participants from Tanzania and Uganda. The researchers show that these behavioural practices are influenced by structural dimensions. These dimensions include limited access to non-pharmaceutical forms of care, economic demands for productivity and thus inability to sufficiently convalesce after an illness and poor sanitary conditions in certain settings, which require people to use antibiotics for prevention. Willis and Chandler (2019) argue that within these dimensions antibiotic use can be understood as an attempt to quickly 'fix' access to care, individual productivity and poor hygiene.

In these various settings, researchers have highlighted the importance of analysing antibiotic practices as influenced by diverse social, political and economic processes. This approach to antibiotic practices allows us to unpack the infrastructural dimensions in which

antibiotics have become an invisible steering wheel for guiding the understanding of health, hygiene and permissible time for illness and recovery. The analysis of antibiotics as infrastructural was proposed by Chandler (2019) to highlight how antibiotics are embedded into the different spheres of modern living, defining hygiene as non-bacterial, healthcare as based on pharmaceutical care and productivity as not disrupted by prolonged illnesses. AMR, she argues, is performing an inversion of these infrastructures by challenging conventional practices of antibiotic use and making visible the dependencies between these medicines and modern ideas of health and productivity.

Grounding our research in these theoretical insights, we will analyse obligatory medical prescription in Russia as part of the antibiotic infrastructure that organises modern ways of care delivery. Focusing on practices of medical doctors, pharmacists and patients, we will entangle this infrastructure and make visible practices and dependencies that antibiotics create in Russian healthcare.

AMR, antibiotics and Russian healthcare

Following the global movements in developing national plans to tackle AMR, in 2017 Russia launched its national strategy to prevent the spread of AMR lasting until 2030. Similar to the Global Action Plan on AMR, the Russian strategy highlights the importance of tackling the misuse of antibiotics in healthcare practice, articulating the need for behavioural changes among antibiotic users and prescribers. Since 2017, the federal government has introduced several changes into the federal regulation on drug circulation (Federal law №61). In particular, surprise inspections (i.e. unplanned and unnotified inspection of a pharmacy) have been implemented to enforce control of the over-the-counter sale of medications, including antibiotics, in pharmacies (Federal law №61, Article 9). In addition, pharmacists have been obliged to collect and file patients' prescriptions for inspection purposes (Decree N 647н). Although there has been a prohibition on the sale of antibiotics without a prescription since 2006, there were no mechanisms to control this regulation. The introduction of surprise inspections and the requirement to collect and file patients' prescriptions in a pharmacy in 2017 restricted the over-the-counter sale of medications and thus enforced patients to seek an official standardised prescription from a medical doctor.

The Russian healthcare system has often been characterised by informality (Temkina & Rivkin-Fish, 2019; Zvonareva et al., 2018). This informality is rooted in different types of personal relationships between a patient and a doctor and between a patient and a pharmacist. These relationships can be both financial and economic (non-monetary presents) or based on

friendship and favours. In contrast to the Soviet Union, where private payments for healthcare services were not allowed, at the beginning of the 1990s, while preserving the principle of universal free-of-charge healthcare by introducing compulsory medical insurance, Russia legalised some private payments for various health services. However, official channels to distribute these legal payments from a hospital's administration to doctors and nurses were often distrusted. In this context, informal payments to doctors and nurses started to play an important symbolic role in establishing trusting and caring relationships with a particular doctor (Cook, 2014; Rivkin-Fish, 2005).

By the late 2000s, informal payments in Russian healthcare dropped significantly – the number of people who informally paid for diagnostic services decreased from 36% in 2001 to 17% in 2011 (Shishkin et al., 2014). Shishkin et al. (2014) explain this drop by referring to the launch of the national priority project Health, implemented in 2006, that included a salary increase for medical professionals and legalisation regarding various pay-for-service practices which, before, were conducted under the table. Although informal payment practices decreased, Temkina and Rivkin-Fish (2019) argue that contemporary Russian healthcare preserves part of its informal organisation. Despite the liberalisation of the healthcare provision that allows patients to choose free or paid medical services, patients continue to rely on personal networks for establishing trusting doctor-patient relationships.

Methodology

To understand the work of obligatory medical prescription of antibiotics in healthcare practices, we conducted a qualitative study of the daily antibiotic realities of doctors, pharmacists and patients. To that purpose, we engaged five types of doctors from different specialities: general practitioners (GPs), paediatricians, ENTs, gynaecologists and urologists. Being a part of primary care settings, GPs and paediatricians are in continual contact with communities, which make them primarily responsible for providing information about antibiotic treatments and AMR to patients. In addition, they play a vital role as gatekeepers who refer patients to specialised doctors in case more intensive treatment is necessary. At the same time, ENT, gynaecology and urology are among the medical specialities where the most antibiotics are prescribed. All doctors involved in this study had been working in state polyclinics and primary care institutions.

We included pharmacists as it is a common practice in Russia to go to a pharmacy for medical consultation instead of going to a doctor, and pharmacists play an important role in informing people about different drugs, their benefits and their potential burdens (Kaae et al.

2020; Strachunsky and Andreeva 2004). All pharmacists except one who took part in the study were employed by private organisations as they constitute the majority of the pharmacological market in Russia.

Patients were engaged in the study to understand how the requirement for a standardised medical prescription of antibiotics has or has not influenced their treatment practices and their relationships with doctors and pharmacists. All patients that participated in the study were in the process of treatment with one of the medical specialists that were included in the study. The study took place in a Russian city of medium size between June and August of 2018.

To understand antibiotic practices, we conducted semi-structured interviews. In total, we conducted 53 interviews: 21 interviews with the doctors – five GPs, four paediatricians, four ENTs, four gynaecologists and four urologists. The age of the doctors who participated in the study varied from 25 to 60, and only three were men, which reflected the gender distribution of doctors in Russia. The average number of years of experience for doctors was 19.5. We conducted interviews with 16 pharmacists; their age varied from 21 to 47, and only one was a man. The average number of years of experience for pharmacists was 14. We conducted 16 interviews with patients, and their age varied from 21 to 78; three of them were men. From 16 patients, seven were mothers of paediatric patients. The number of interviews conducted was determined by data saturation. All interviews lasted between 15 and 60 minutes.

Analysis

To recruit doctors and pharmacists for interviews, we sent letters with information about the study to several primary care settings and pharmacies in one Russian city. For those doctors and pharmacists who responded to the call, we provided further details about the aim and methods of the research and obtained informed consent from participants who agreed to give interviews. Patients were recruited from the waiting rooms of the polyclinics. They were provided with detailed information about the study (aim, methods, researchers, their contacts and affiliations). Those patients who agreed to take part in the study signed informed-consent forms. In the case of paediatric patients, parents were invited to take part in the research.

All interviews were conducted in a private space and were subsequently anonymised. Questions in the interviews were developed by the transdisciplinary team of sociologists and medical doctors, different questions were developed for the three groups of participants and pilot interviews were conducted with each of the group. Pilot interviews were not included in the analysis. All interviews were voice-recorded and transcribed verbatim. The language of the interviews was Russian; quotes in the article were translated into English by the first author.

Thematic analysis was used on the transcripts of interviews. Different themes were determined for the three groups of participants. Each transcript was carefully analysed line by line and separated on themes using the qualitative data software NVivo 9 (QSR International Pty Ltd, Doncaster, Victoria, Australia).

Ethical clearance

The study was approved by the ethical committee of the Siberian State Medical University in Russia (№5916 on 22 May 2018).

Results

'We cannot always provide quick care'

With the new antibiotics policy of 2017, medical doctors became an obligatory passage point for accessing antibiotics. The requirement for a standardised medical prescription can be seen as a re-articulation of the clinical authority of medical doctors over pharmacists, who were then restricted to providing antibiotics by prescription only. The requirement for a medical prescription can be seen as an attempt to regulate the professional distribution of responsibilities to those who prescribe and those who sell medications. Some of the doctors reflected on this work of medical prescription:

> L101: It is very good [that antibiotics can be only sold with prescription]! And not only antibiotics but other medications should also be sold only with prescriptions. Doctors know the value, and patients know the value that without doctors they are nobody. And pharmacists think that they are doctors already. All medication should be sold only with doctors' prescriptions. (ENT, age 34)

> P106: Actually, I think that most of the medications should be sold with medical prescriptions because now we have a total absence of authority [*vsedosvolennost*]. And such absence of authority leads to uncontrolled use of medications. (Gynaecologist, age 60)

Although enthusiastic about the re-articulation of their medical authority over pharmacists, the doctors explained that this change did not introduce major transformations to their daily routine. Rather, as no further changes in official standards of healthcare delivery were made, the amount of their work increased. The requirement for a standardised prescription meant that they had to write an additional paper, although the time for a patient visit remained unchanged

(about 15 min per patient):

> U106: Now, apart from medical recommendations that we print on computers, we have to write a prescription. But, we put our stamps and signatures on both of the documents. It takes more time. (GP, age 37)

Discussing the meanings of the obligatory prescription, we asked the doctors about their diagnostic practices and about the kind of evidence that they used to decide about antibiotic treatment. By giving doctors the ultimate authority over diagnostic and treatment procedures, the prescription became a symbol of evidence-based decisions about antibiotic treatment. Similar to other studies in the field of antibiotic prescription practices, like the research of Broom et al. (2014) or Lambert et al. (2019), the doctors explained that they based their diagnoses on a combination of experience, personal clinical knowledge and institutionalised clinical recommendations. Apart from this, one of the ENTs explained that because a patient would only come to a specialist after a GP's referral, this would be taken as evidence that a patient was eligible for antibiotics:

> L101: You know, patients will not immediately come to an ENT; they will always come from a GP or a paediatrician. They will get treatment at home for a common cold, and then they will come to us with complications. For example, there is no point in treating angina without antibiotics. The same is for sinusitis, it is impossible to treat without antibiotics. (ENT, age 34)

Drawing on evidence-based decisions, a doctor could prescribe antibiotics to a patient. However, some of the doctors stressed that the notion of evidence included not only the clinical characteristics of patients but also their social and economic circumstances. As we noted before, apart from the introduction of a standardised medical prescription, no other changes occurred in the daily work of doctors. However, the requirement to go to a doctor for a prescription had stimulated an increase in the number of patients seeking a consultation. In addition, while a medical prescription aims to restrict practices of self-treatment it does not have the flexibility to incorporate potential reasons for this behaviour. Doctors who know the limitations of the healthcare system, including the limited amount of medical staff, and who are familiar with the economic restraints of patients who may be not able to take the time off work to visit a doctor have to compensate for these limits by adapting their antibiotic practices:

U107: It happens sometimes that a child got ill on Friday. Saturday and Sunday are holidays, and the child has a high fever. I know that we should wait for 2–3 days [before prescribing antibiotics], but I don't know whether they will call an ambulance or not on the weekend, so I can give them an antibiotic prescription and instruct how to use it in case the child feels worse. Either this way or if they don't use the prescription now, they might use it next time if the child gets very ill. (Paediatrician, age 53)

P102: I support this decision [change in antibiotic sale regulations]. However, patients will probably now have problems visiting doctors. Unfortunately, we cannot always provide quick care as patients, and also us doctors, often want. But still, taking the growing resistance to many antimicrobials, I think that most medications should be sold with prescriptions. (Urologist, age 45)

The introduction of the obligatory medical prescription of antibiotics established medical doctors as an obligatory passage point to access these medicines to restrict practices of self-treatment. It has also increased the workload and pressure on doctors as other elements of the healthcare delivery system have stayed intact: doctors have the same amount of time to receive a patient, and the number of medical staff have stayed the same. In our research we could see that, instead of restricting self-treatment with antibiotics, doctors might use their authority to prescribe medicines as a compensatory mechanism for the limits in the healthcare systems and for economic restraints of patients. The requirement for a medical prescription created informal networks of care delivery where evidence for an antibiotic prescription included the availability of medical staff and the opportunity for patients to visit a doctor.

'This system had started from the wrong end'

The requirement for a standardised medical prescription has restrained pharmacists' authority to recommend and sell antibiotics. From a policy perspective, the introduction of this requirement into the healthcare system could be seen as a necessary step to establish a clear hierarchy where doctors give a prescription and pharmacists sell the antibiotics that are prescribed. In practice, however, pharmacists do something different. The obligatory prescription of antibiotics has allowed pharmacists to negotiate the practices and conditions of antibiotic prescription in a hospital. One of the pharmacists explained that prescriptions often missed a certain detail or were unclear, which meant that the pharmacist was put in a situation where he or she had to guess what medication was intended by the doctor. At the same time, the pharmacist was legally responsible for selling any incorrect medicine. One of the

pharmacists explained:

> F106: Very often doctors confuse forms [of medications]. For instance, cefixime can be in two different forms with different dosages, but they [doctors] only write 'cefixime for seven days'. And you have to think and guess – should I give a regular one in capsules where there are six capsules in a box, or another one, where there are seven capsules. In the end, you sell regular capsules because they are cheaper, and people prefer to buy them. But actually, the doctor meant another form. This will result in a return of medication, and this is a conflict because nobody is praising us for returns [returns may cause financial conflicts between pharmacists and the administration of a pharmacy]. And actually, according to the law, we are not allowed to do returns. But it is 600 or 700 rubles [around 10 euros], and it is essential for people. (Pharmacist, age 28)

In addition, some pharmacists explained that doctors may not have used the standardised forms for prescriptions, but they are not allowed to sell antibiotics to patients with prescriptions on other forms:

> F104: I think that the situation with the requirement for a standardised medical prescription is good, and there should be some connection between a doctor and a pharmacist. But it is important to solve the problem with the standardised prescription forms because patients often comment that doctors don't have those. (Pharmacist, age 32)

This example indicates an interesting moment in the work of prescriptions. While they are intended to separate the responsibilities of doctors and pharmacists, instead they re-mediate their relationships, where pharmacists can observe certain pitfalls in the work of doctors, including the lack of necessary infrastructures like prescription forms. In addition, pharmacists are positioned as mediators between doctors and patients; in the interviews they reflected on the working infrastructures of the new antibiotic policies through the stories of their clients:

> F101: [Q: for what reasons do people ask to sell them antibiotics without a prescription?] They don't have time to go to a doctor, that is the first reason. There is a very long wait time to get an appointment with a doctor. For example, you cannot get to an ENT specialist because you need to have an appointment a month in advance. A child might have an acute exacerbation of sinusitis right now, but an appointment with an ENT specialist is only in a month. Also, it is impossible to go to a private doctor, for instance, because it is

> expensive. Actually, I think that this system [of control over the sale of antibiotics] started from the wrong end because it is necessary to first fix the system of appointments with doctors so that they [patients] can get a consultation the same day they need it. (Pharmacist, age 35)

The requirement for a standardised medical prescription has influenced the communication between pharmacists and their clients. Several pharmacists described that since the introduction of the standardised prescription and the implementation of the control mechanism of surprise inspections they have been distinguishing between formal communication with new patients and informal communication with familiar patients. One pharmacist elaborated that familiar relationships with a customer may blur the line between the role of a doctor and the role of a pharmacist. In this situation, a pharmacist performed both diagnostics and selection of medical therapy:

> F103: To tell the truth, if it is our regular customer, maybe a child of a co-worker, then we can [sell antibiotics without a prescription]. So if there are no unfamiliar people in a line, if I am alone with a client, then I can do it [sell antibiotics without a prescription]. But if I see a person the first time, then of course not. (Pharmacist, age 20)

Therefore, the requirement for a standardised prescription had stimulated the emergence of a grey zone, where antibiotics were manged between a pharmacist and a patient without the control of the state or the involvement of a doctor. This grey zone was justified by pharmacists as a necessary response to the current gaps in the infrastructure of healthcare delivery, including the lack of doctors in hospitals that made timely delivery of care problematic. It was presented as a form of care for patients whose social and economic situation might not allow them to take time off work to go to a doctor:

> F102: There are sometimes cases when we [pharmacists] recommend prescribed medications, but it is usually, for example, eye drops or something like that. Something for what a patient would not go to a doctor, but of course all antibiotics for eyes can only be sold with a prescription. But in these cases, we take responsibility because a person with conjunctivitis [eye infection] will not go to a doctor and will infect other people. (Pharmacist, age 30)

The introduction of standardised medical prescriptions for antibiotics in practices of pharmacists has made visible the tensions between the work of doctors and the needs of patients. Although unable to officially recommend and sell antibiotics, through the use of prescriptions pharmacists can observe the infrastructural realities of doctors and highlight the gaps in these infrastructures, such as the lack of official prescription forms and lack of medical personnel to timely accommodate all patients. The standardised medical prescriptions coordinate the official channels of communication between a pharmacist and a patient, and they stimulate the creation of parallel grey zones. These grey zones can be understood as a response to AMR control programmes that aim to discipline patients' behaviour without considering the social and economic context of these patients.

'Not everyone can take a day off work'

The presentation of patients as those exercising unhealthy behaviours of self-treatment with antibiotics is common in policy discourses on AMR (Haenssgen et al., 2018; Will, 2018). In this context, the requirement for a medical prescription often functions as a technique to prevent such unwanted behaviour. However, as studies of Rodrigues (2020) and Willis and Chandler (2019) show, self-treatment with antibiotics is not a question of choice but is influenced by social, economic and political processes, such as access and affordability of healthcare, non-therapeutic forms of care and the opportunity to take time from work to visit a doctor and convalesce. In our interviews with patients in Russia, we observed similar processes.

Some of the patients saw the requirements for a prescription as a positive move that would protect people from the overuse of antibiotics. For instance, one of the patients told us that 'the body of each person is different, and it means that you must do it [take antibiotics] only under a doctor's supervision' (P110, age 42). Other participants explained that it was difficult for them to accept the new requirements. Complexities regarding long wait times for clinical appointments, which was mentioned by both doctors and pharmacists, were further elaborated upon by patients. Having an appointment with a doctor would mean long wait times and the necessity of taking a day off work, which was a significant obstacle for some of the patients to access antibiotics:

> PT101: To tell the truth, when it all just started [stricter requirements for antibiotic prescriptions], I did not like it. I did not like that it was now necessary to go to a doctor every time. (Patient, age 31)

PT102: Now I am ok about it [stricter requirements for antibiotic prescriptions], but when this requirement first took place [I did not like it]. Before you could just go and buy medications, because for some it was difficult to go for an appointment with a doctor; not everyone can take a day off work. (Patient, age 30)

One patient was particularly critical about an antibiotic's prescription requirements. She explained that instead of going to a doctor she preferred to rely on her pharmacist as it saved her time and money from potentially expensive antibiotic alternatives:

PT107: It [amoxicillin] was once prescribed to me by a doctor. But it was a long time ago. Then I started to always buy it in a pharmacy; it is not expensive. And now it is very bad that I can buy it only with a prescription. It is really terrible for me! Because now you need to go to a doctor, pay money, and a doctor will prescribe you very expensive medications, very expensive – he will not prescribe a cheap one! And then I would have to run to a pharmacy. (Patient, age 49)

In the Russian context, antibiotics can be understood as an economic tool, or as Pearson and Chandler (2019) call it, a 'quick fix'. This tool is seen as something that can fix the body to make it productive again. While the requirement for a medical prescription aims to regulate the biological body of a patient and prevent self-treatment practices, the economic body of the patient perceives antibiotics as a requirement to stay productive in society, to earn money and to prevent poverty. Therefore, adapting to the new conditions which require a visit to a doctor as an obligatory passage point to access antibiotics, some of the patients explained that they would prefer to use leftover antibiotics rather than go to a doctor if their health conditions were not severe. Most of the patients from our study had leftover antibiotics at home from their previous prescriptions as in Russia you have to buy a whole package of medicine and not the exact amount that was prescribed by the doctor. A mother of a paediatric patient described a situation that was similar to the one described by one of the doctors – if a patient got ill on the weekend, she would not be able to receive specialised care on Saturday or Sunday. In this scenario, patients preferred to not wait until they would be able to see a doctor, but to start treatment with antibiotics if they had a chance:

PT101: For example, it was a case that we had some leftover antibiotics. He [a child] recently had a tooth problem – he had gumboil. And it was a weekend and nobody could receive us [at a hospital]. It was 4 pm, and they receive patients only until 2 pm. I have

> some friends who are clinicians and they recommended me to give him antibiotics to prevent any complications. And I had those leftover antibiotics, and I gave him one pill. Then, on Sunday, we came in an ambulance to a paediatric dental clinic. They told us there that we did good to give him an antibiotic. (Patient, age 31)

Although self-treatment with antibiotics is presented in policy regulations, including the Global Action Plan on AMR, as a major problem in resistance development, several of our participants were very cautious about these medications (World Health Organization, 2015). Contrary to some studies arguing that patients demand antibiotics from doctors (Ashworth et al., 2016; Little et al., 2004), our participants expressed that they would prefer to avoid antibiotic treatment when possible as they thought of them as a strong medicine with serious side-effects. Those patients explicitly asked doctors to not prescribe them antibiotics and requested alternative treatment:

> PT102: If it is for kids, I ask whether it is possible to have treatment without antibiotics. Because I am worried. They probably have some side effects, such as milk fever or something like that. (Patient, age 30)

> PT103: [Q: Have you ever disputed a doctor's prescriptions?] Yes, I asked for something else. I do not feel so bad as to need antibiotics. (Patient, age 67)

Aiming to control the practices of self-medication, the requirement for a standardised medical prescription presents patients as potentially irresponsible users. However, our research shows that patients' relationships with antibiotics reflects the broader social and economic realities of their life, rather than a simple lack of knowledge. Antibiotics were perceived as a necessity for their functioning in society, while at the same time many patients were cautious with them. Some of the reasons for avoiding official channels to access antibiotics were similar to the ones already articulated by doctors and pharmacists: while the introduction of the prescription required patients to coordinate their treatment practices with a doctor and a pharmacist, existing limits in healthcare delivery could not accommodate this requirement, leading to the creation of informal channels of coordination between those actors.

Informal infrastructure to compensate for policy gaps

In this article, we studied how the requirement for a medical prescription had affected practices of doctors, pharmacists and patients. The analysis showed that while this requirement

aimed to establish a clear distribution of responsibilities between doctors and pharmacists to prevent patients' self-treatment, in practice, it unpacked the infrastructural gaps that influenced self-treatment practices. The analysis showed that the requirement for medical prescriptions obliged patients to seek an appointment with doctors instead of going to the pharmacy to buy antibiotics. This, however, increased the pressure on the limited number of medical staff and stimulated the practice of just-in-case prescription of antibiotics by doctors. The system of over-the-counter sales of antibiotics did not disappear but became more clandestine and accessible only to friends and acquaintances. These informal practices involving doctors and pharmacists, which considered the socio-economic realities of patients, can be understood as compensating for infrastructural gaps, such as the limited number of doctors and corresponding insufficient availability of medical appointments, lack of official forms for prescriptions and the constrained economic situation of patients that does not allow them to take time off work to visit a doctor.

The insights from our study confirmed the arguments of other scholars about the infrastructural embeddedness of antibiotic practices. Similar to the study of Broom et al. (2017), we could see that doctors, as well as pharmacists, adapted their antibiotic practices to the infrastructural conditions that might hinder patients' access to timely medical appointments. Also, along with the study by Willis and Chandler (2019), some of our patients understood antibiotics as quick fixes that enabled faster recovery and return to their social and economic responsibilities. However, our study demonstrated that antibiotic practices are not driven by economic factors exclusively. Rather, the organisation of healthcare delivery (e.g. the timetable for when the ambulance is working) and structural limits for access to certain specialists stimulated medical doctors to prescribe precautionary antibiotics in case a patient would not be able to access timely care. In addition, several of our patients-participants expressed that they would prefer a non-antibiotic treatment if they had a choice as they were worried about the potential side effects of these medicines. While the study of Little et al. (2004) demonstrated that doctors perceive pressure from patients to prescribe antibiotics, our findings showed that patients themselves would prefer alternative ways of treatment if that would help them to recover in their specific socio-economic reality.

Analysing how AMR is constructed as a problem in public health, Chandler (2019) stresses that antibiotic practices are shaped by the infrastructural conditions in which they are situated, including physical organisation of care delivery (e.g. availability of diagnostic technology or number of medical staff) and social and economic demands to stay healthy and productive. Understanding practices of doctors, pharmacists and patients through the lens of healthcare

infrastructure provides insights into the obligatory medical prescription of antibiotics as a boundary object of such infrastructure, which coordinates and aligns the work of the main actors.

The concept of boundary objects was originally developed by Star and Griesemer (1989) in their analysis of the work of the Museum of Vertebrate Zoology at the University of California. They propose this concept to explain the processes of coordination between heterogeneous actors that were required to run this museum and to make exhibitions, such as amateur naturalists, professional scientists and philanthropists. They argue that the notion of boundary objects helps to understand how the complex work of diverse actors can be performed. An example of a boundary object is, for instance, a standardised system for disease classification (Bowker & Star, 2000). Such a system is simple enough that different actors, including medical doctors, technicians, nurses and insurance agents, can understand it; at the same time, the coding provides specific information for each of the actors: for a medical doctor a system of disease classification can indicate the line of treatment, and for an insurance agent it provides information about the applicability of an insurance policy to a concrete case. As such, this system aligns the work of both.

In the context of new antibiotic policies to reduce AMR in Russia, the requirement for a standardised medical prescription can be seen as a boundary object facilitating the coordination between doctors, pharmacists and patients. However, some of this coordination work takes place outside of the officially established infrastructures to informally compensate for the gaps in care delivery. Imposed to coordinate new hierarchical relationships between patients, doctors and pharmacists, the obligatory medical prescription unpacks the current political economy in Russia. In this system, doctors and pharmacists have to informally accommodate the socio-economic conditions of patients who cannot afford to take time off work to be sick and sometimes live far away from healthcare facilities. This informally organised system of antibiotic care indicates that the officially established healthcare infrastructure does not reflect the economic and social realities of its patients. This coordination of obligatory antibiotic prescriptions escapes the hierarchy between medical doctors, pharmacists and patients when it comes to diagnosis and treatment. By navigating the antibiotic prescriptions, doctors, pharmacists and patients informally compensate for the gaps in this antibiotic infrastructure.

While international and national policies continue to initiate behavioural interventions aimed at antibiotic users and prescribers, these users have to adopt practices to fix the gaps that become visible through these interventions. These frictions between the policy understanding of AMR and its everyday practical articulations indicate a gap between policy and practice.

While the former imagines AMR as problem defined by the lack of knowledge among antibiotic users, the latter defines it as a consequence of economic and healthcare infrastructures that limit patients' ability to be sick and take time off work.

In his study of pasteurisation in France, Latour (1988) argues that for an intervention to work, it has to be aligned with everything that allows it to work, in a process of mutual translation – the co-production of ideas and practices. In other words, to make AMR policies more efficient, the conditions that allow them to be efficient have to be adapted through the cooperation of local and national actors. As we saw in our research, the informal practices involving doctors, pharmacists and patients indicated the need for infrastructural changes like the increased availability of medical staff, increased time for a medical appointment and legal protections for patients as economic subjects that could fall ill and needed time for recovery. To reassemble the socio-economic and temporal infrastructures that influence antibiotic practices, it is important to take seriously the realities and practicalities that are communicated by public health professionals and patients.

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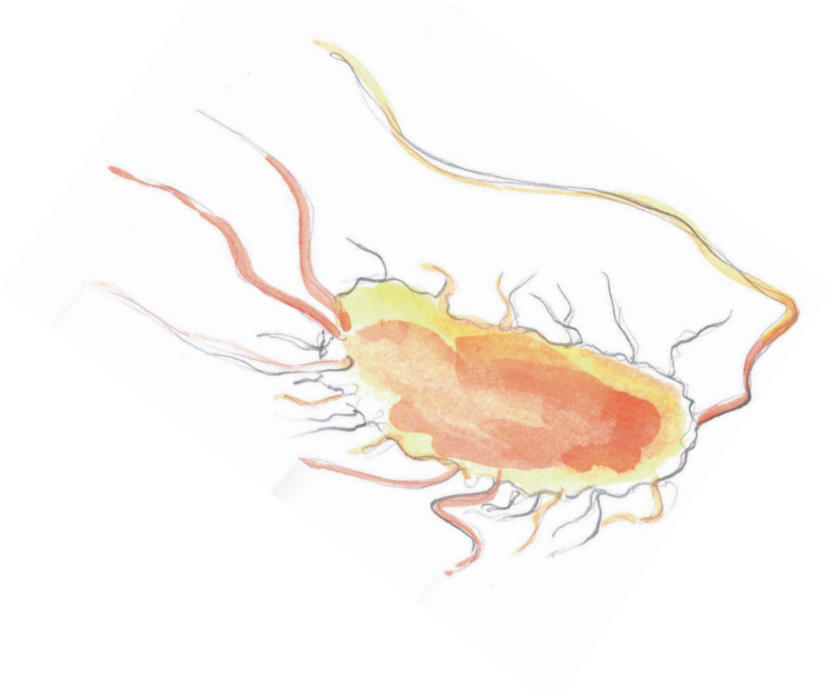
Science

Chapter IV

Global travelling and the 'import' of bacterial 'intruders'



Based on: Kamenshchikova, A., Wolffs, P. F. G., Hoebe, C. J. P. A., Penders, J. and Horstman, K. Global Travelling and the 'Import' of Bacterial 'Intruders': The work of Metaphors in Microbiological Scientific Practices. (submitted)

Abstract

Metaphors are an inevitable ingredient of scientific research practices. This article studies metaphors in microbiological research about transmission and dissemination of antimicrobial resistance (AMR) globally. The authors conducted a discourse analysis of nine microbiological research articles published from 2016 to 2018 about AMR and travelling. The metaphors of AMR 'reservoirs' were attributed to both countries of travellers' destinations and travellers returning from a trip, and the metaphor of 'intruders' was used to describe bacteria that 'colonise' travellers. The authors analyse how these metaphors shape and potentially limit the microbiological imaginings of AMR.

Introduction

Antimicrobial resistance (AMR) is a phenomenon that is often defined in metaphors such as 'apocalypse' (Nerlich & James, 2009) and 'return to the dark ages' (N. Brown & Nettleton, 2016). While scholars in sociology and anthropology have scrutinised the use of such metaphors in public and policy discourses (B. Brown & Crawford, 2009; N. Brown & Nettleton, 2017; Chandler et al., 2016), the microbiological conceptualisations of antibiotics and AMR have rarely been discussed. However, it is important to engage with microbiological conceptualisations of AMR to understand how scientists frame and attempt to address it. Whether a metaphor of a catastrophe plays a role in science or whether alternatively, less alarmist presentations of AMR prevail can play a significant role in defining policy priorities for addressing the issue. In this article, we present the results of a discourse analysis of microbiological scientific writings focused on the transmission and dissemination of resistant bacteria through international human travelling, which has been identified by different microbiologists as a crucial reason for the global rise of AMR (Angue et al., 2015; Arcilla et al., 2017; Ricotta et al., 2014).

Although the metaphor of a catastrophe for presenting AMR has been dominant in the international policy arena, social science scholars have criticised this conceptualisation (Chandler et al., 2016; Nerlich & James, 2009). For instance, the use of catastrophic metaphors was reflected on by Chandler et al. (2016) in their report on sociological and anthropological approaches for addressing AMR. They argued that catastrophic metaphors can convey only 'selective scientific facts' that present AMR as a biomedical problem that can be controlled through the regulation of antibiotic use and the production of new antibiotics, thus overlooking potential economic and political processes that influence antibiotic practices. Such selective representation, they elaborated, often leads to the blaming of different actors, such as patients, physicians and farmers who use antibiotics, and it does not allow for alternative imaginings of AMR as a multifactorial and bio-social phenomenon.

Researchers present and discuss their work through language, in which metaphors are an inevitable ingredient. This also counts for scientific discourses about AMR. In this article, we present a study of microbiological discourses of AMR in the context of international travelling. We analysed research articles on microbiology, understanding them as scientific artefacts. Such an approach to analysing scientific papers has been elaborated on in science and technology studies (STS) by various researchers studying processes of scientific knowledge production (Latour, 1987; Latour & Woolgar, 1986; Law, 2009). For instance, Latour (1988) argued that the establishment of a scientific fact about microbes causing infections is a result

of argumentations, negotiations and renegotiations of a claim, and, simultaneously, it is a creation of a scientific, political and social context in which this claim can become a fact. For instance, for Louis Pasteur to convince his fellow countrymen that a microbe caused infections, he had to redefine the relations amongst farmers, hygienists, medical doctors and politicians and convince them they had a vested interest in microbes, and as a result, the claim became an undisputed fact, and society became ready to act upon that (Latour, 1988). Scientific articles are an important ingredient in the dynamics of global argumentative work that co-shapes scientific facts as well as a context in which these facts can flourish. To understand how scientific articles co-shape facts and contexts, it is important to study the metaphors that are used in their language.

Below, we introduce a rich field of metaphor analysis in biomedical research and the work of sociologists and anthropologists who have studied metaphors of AMR in policy and public discourses. Then, we describe the methodology for analysing scientific discourses of AMR and travelling. After presenting the results of our analysis, we discuss the role of metaphors used in microbiology to explain the importance and the connection between AMR and travelling.

Metaphors in Biomedical Research

Metaphors are important linguistic instruments in scientists' toolkits that help them to describe and act upon the world (G. Lakoff & Johnson, 1980; van der Geest & Whyte, 1989). Olson, Arroyo-Santos and Vergara-Silva (2019) distinguished two main functions that metaphors play in science: firstly, metaphors allow communication and collaboration amongst scientists from different fields; secondly, they can navigate the research process in a novel and innovative way. For instance, the fields of genetics and genomics have described DNA as a 'book of life', a 'blueprint', a 'language' or a 'code', which has allowed scientists to communicate the complexity of genetics to other researchers in ethics and social sciences as well as to policymakers. At the same time, these metaphors have guided biomedical researchers to look for potential ways to 'read', 'edit' and even 'break the code' of DNA (Nerlich, 2015). Therefore, the work of metaphors is embedded in the thinking process through which scientists imagine the world and the various ways of accessing it.

Metaphors not only connect different researchers and social worlds but also play a crucial role in conducting science. In his book on metaphors in cell biology, Reynolds (2018) argued that these metaphors should be understood as the 'third lens' of a microscope that supports knowledge production processes. He noted that the concept of a cell in biology was originally understood as a metaphor that described a space with 'walls'. Currently, in biology, the cell is

understood as a fact, rather than a metaphor. This, according to Reynolds (2018), indicates that the metaphor has been positioned in a kind of limbo where it stopped being directly associated with its origin, however, it kept some of its characteristics such as being a space with ‘walls’.

The choice of metaphors guides the understanding of the scientific phenomenon and how it is further investigated. For instance, Reynolds (2018, p.7) showed how social and engineering metaphors are put together to describe the cell in biology as ‘a being with particular characteristics, which may change over time as a result of its history of social interactions with other cells, but it is also a machine that performs some kind of work or fulfils some function as a result of the properties and behaviour of its component parts (e.g., proteins, DNA)’. Therefore, the choice of metaphors, either conscious or unconscious, has significant importance in how the world is imagined in biomedical research, and how it is further acted upon.

Metaphors of AMR in Policy Discourses: A Future Catastrophe

Metaphors are not simply figures of speech that do not act upon the real world. They inform practices by actively ‘working upon, modifying, and transforming’ the political reality in which a discussed phenomenon is situated (Asdal, 2015, p. 74). In analyses of AMR policy discourses, it has become clear that the metaphors of catastrophe and apocalypse have been dominant (B. Brown & Crawford, 2009; N. Brown & Nettleton, 2016). According to Nerlich and James (2009), presenting AMR as an apocalypse creates a reality where current medical treatments are facing future failure. Such a presentation of AMR requires immediate economic investments and policy actions to produce new medicines and preserve current ones. In this section, we introduce several social science studies that reflect on the policy implications of the catastrophic framings of AMR. These metaphors can be found in local and international policy discourses, in the media and in scientific communications. Although these contexts are diverse, it can be seen that they present AMR as a ‘worse to come’ phenomenon.

Catastrophic conceptualisations of AMR can transform and justify certain economic policies as reacting to potential future dangers. Brown and Nettleton (2016) showed that catastrophic formulations of AMR helped to justify UK immigration policies restricting entrance to immigrants who were thought to carry potentially dangerous bacteria. The same authors described how the presented dangers of AMR transformed the economic and market priorities in the UK, steering investments towards research into new and alternative antimicrobial treatments. Similarly, in her analysis of catastrophic metaphors utilised in microbiology at the beginning of 2000s, in particular in the popular writings of the

microbiologist James, Nerlich (2009) showed how such metaphors help to attract economic investments into AMR research. She argued that, at the end of the 1990s and beginning of the 2000s, microbiologists intentionally presented AMR as a catastrophe to attract funding for research in this area.

Apart from transforming AMR into a political and economic concern, catastrophic metaphors allow establishing AMR as an urgent issue not only in clinical settings but also in the public arena. In their research on the media reports of methicillin-resistant *Staphylococcus aureus* (MRSA) from 1992 to 2007 in the UK, B. Brown and Crawford (2009) determined how catastrophic presentations of this phenomenon shaped a reality that constituted an inevitable threat to 'modern medicine'. Such an inevitable threat, the authors argued, was presented not only in clinical settings but also in 'gyms, [and] non-NHS [United Kingdom National Health Service] nursing homes' where bacteria could be transmitted and acquired.

In her analysis of AMR in the international policy arena, Chandler (2019) applied the concepts of the sentinel and the actuarial styles of reasoning developed by A. Lakoff (2017). The sentinel style of public health reasoning aims to prepare for 'potentially catastrophic events' that cannot be predicted or calculated beforehand. This means that, while we might not have the tools to calculate the timing and the severity of a potential outbreak, we should anyways take precautions to prepare for such an outbreak. The actuarial style of reasoning refers to a situation when threats are known through statistical calculations and epidemiological data (A. Lakoff, 2017). In such a scenario, the preparedness for an outbreak would be based on the experiences gained in the previous outbreaks, such as those of seasonal flu. Chandler (2019) argued that attempts to address AMR through the actuarial approach are met with two major challenges. First, calculating the risks of AMR is complicated as this phenomenon refers to multiple microorganisms, including bacteria, viruses and fungi, and to different mechanisms of resistance, such as limiting the uptake of a drug, drug inactivation and drug efflux as well as mutations and subsequent alterations of the antiviral target. Second, calculating the risks of AMR is difficult because of 'technical and resource' challenges in collecting and calculating information about AMR globally as not every country has the equipment to collect and analyse such data. Therefore, Chandler (2019) noted, AMR has been defined in international policies 'as a threat in the future tense, that must be acted upon in anticipation'. She elaborated that, on the international level, 'AMR is presented as one of the most pressing global threats – articulated in terms of a threat to health, economies, security and modernity'. The metaphor of a catastrophe, Chandler (2019) concluded, adds a sense of dire urgency to addressing AMR, thus attracting economic and policy interests to this phenomenon.

Although the use of metaphors in science and policy is inevitable, the choice of specific metaphors is especially important as it steers scientific and policy attention in a specific way. The dominance of alarmist metaphors in the AMR policy field raises the question about which metaphors are used in microbiological studies of AMR.

Methodology

We conducted a discourse analysis of microbiological articles focusing on the use of metaphors in describing AMR and its mechanisms in the context of international travelling. Analysing metaphors in microbiology, we focused on recently published key articles to understand current discourses of AMR. The key articles were defined as relevant papers measured by the number of citations and the relatedness to the topic of the current study based on the expert opinion of two microbiologists. Articles that were included in the analyses were published from 2016 to 2018, and they were focused on the acquisition of multidrug-resistant *Enterobacteriaceae* (MDR-E) in healthy travellers as microbiological research has defined it to be a rising global health concern (Arcilla et al., 2017; Lübbert et al., 2015). In addition, focusing on AMR in the context of travelling allowed us to understand how this issue has been analysed and communicated in the global health arena. Von Wintersdorff et al. (2014) and Hattem et al. (2019) have defined international travel as having the potential for becoming colonised with resistant bacteria that may cause an infection if given an opportunity, for example, amongst immunocompromised travellers. Analysing the acquisition and transmission of MDR-E, Arcilla et al. (2017) argued that travellers who go to areas that present a high risk of acquiring AMR may carry it for up to 12 months after their return from a trip.

The process of article selection was organised in five steps: 1) through the database Web of Science (https://apps.webofknowledge.com), we selected articles that included the terms 'Enterobacteriaceae' and/or 'MDR-E' and/or 'ESBL (Extended Spectrum Beta-Lactamases)' and/or 'travel' and/or 'resistance' and/or 'healthy' and that had been published from 2016 to 2018; 2) the articles were ranked by citation to capture the most discussed papers; 3) we screened titles and abstracts of the articles to determine their relevance to our study, which meant that an article should focus on the acquisition and dissemination of MDR-E across international borders by healthy, non-hospitalised travellers; 4) we selected three articles from each year from 2016 to 2018 with the highest number of citations; and 5) the list of selected articles was discussed with two experienced microbiologists to ensure their relevance to their field. See the list of articles in Table 1.

Table 1. List of Microbiological Articles for Discourse Analysis.

- Vading, M., Kabir, M. H., Kalin, M., Iversen, A., Wiklund, S., Naucler, P., & Giske, C. G. (2016). Frequent acquisition of low-virulence strains of ESBL-producing *Escherichia coli* in travellers. *Journal of Antimicrobial Chemotherapy*, *71*(12), 3548–3555.
- van Hattem, J. M., Arcilla, M. S., Bootsma, M. C. J., Van Genderen, P. J., Goorhuis, A., Grobusch, M. P., Molhoek, N., Oude Lashof, A. M. L., Schultsz, C., Stobberingh, E. E., Verbrugh, H. A., de Jong, M. D., Melles, D. C., Penders, J. (2016). Prolonged carriage and potential onward transmission of carbapenemase-producing Enterobacteriaceae in Dutch travellers. Future Microbiology, 11(7), 857–864.
- Reuland, E. A., Sonder, G. J. B., Stolte, I., al Naiemi, N., Koek, A., Linde, G. B., van de Laar, T. J. W., Vandenbroucke-Grauls, C. M. J. E., van Dam, A. P. (2016). Travel to Asia and traveller's diarrhoea with antibiotic treatment are independent risk factors for acquiring ciprofloxacin-resistant and extended spectrum β-lactamase-producing Enterobacteriaceae—a prospective cohort study. Clinical Microbiology and Infection, 22(8), 731.e1-731.e7.
- Arcilla, M. S., van Hattem, J. M., Haverkate, M. R., Bootsma, M. C. J., van Genderen, P. J. J., Goorhuis, A., Grobusch, M. P., Lashof, A. M. O., Molhoek, N., Schultsz, C., Stobberingh, E. E., Verbrugh, H. A., de Jong, M. D., Melles, D. C., Penders, J. (2017). Import and spread of extended-spectrum β-lactamase-producing Enterobacteriaceae by international travellers (COMBAT study): A prospective, multicentre cohort study. The Lancet Infectious Diseases, 17(1), 78–85.
- Woerther, P. L., Andremont, A., & Kantele, A. (2017). Travel-acquired ESBL-producing Enterobacteriaceae: Impact of colonization at individual and community level. *Journal of Travel Medicine*, *24*(suppl_1), S29–S34.
- Kantele, A., Mero, S., Kirveskari, J., & Lääveri, T. (2017). Fluoroquinolone antibiotic users select fluoroquinolone-resistant ESBL-producing Enterobacteriaceae (ESBL-PE)–data of a prospective traveller study. *Travel Medicine and Infectious Disease*, *16*, 23–30.
- Schwartz, K. L., & Morris, S. K. (2018). Travel and the spread of drug-resistant bacteria. *Current Infectious Disease Reports*, *20*(9), 29.
- Ruppé, E., Andremont, A., & Armand-Lefèvre, L. (2018). Digestive tract colonization by multidrug-resistant Enterobacteriaceae in travellers: An update. *Travel Medicine and Infectious Disease*, *21*, 28–35.
- Nakayama, T., Kumeda, Y., Kawahara, R., Yamaguchi, T., & Yamamoto, Y. (2018). Carriage of colistin-resistant, extended-spectrum β-lactamase-producing *Escherichia coli* harbouring the mcr-1 resistance gene after short-term international travel to Vietnam. *Infection and Drug Resistance*, *11*, 391.

The primary aim of our analysis was to determine which metaphors were used to introduce the phenomena of AMR, to describe the relationship between AMR and travelling and to explain specific findings about AMR and travelling. The analysis was conducted in the NVivo 9 qualitative data analysis software (QSR International Pty Ltd, Doncaster, Victoria, Australia).

Results

The analysis revealed that most microbiological articles distinguished between travelling from a country of origin to a country of destination and travelling from a country of destination

back to a country of origin. In the process of distinguishing these two types of travelling, we found different metaphors were notable in describing the *acquisition* of AMR while travelling 'abroad' and *transmission* of AMR when travelling to a 'home country'. This separation provided an important context for understanding how travelling is problematised as an AMR risk. The process of travelling was defined in the analysed articles as a movement of people accompanied by bacteria from one part of the world to another part of the world and back, a process considered as vital for the transmission and dissemination of AMR.

> International travel is one of the central means by which resistant intestinal bacteria spread across the globe. (Kantele et al., 2017, p. 23)

> The bottom line is that hundreds of millions of people visit tropical regions annually – and a substantial proportion of them do contribute to the transport of ESBL-PE worldwide. (Woerther, Andremont, & Kantele, 2017, p. S32)

As it is illustrated in the second statement, travelling abroad often means travelling to tropical regions. At the same time, travelling back to a home country means travelling to countries in Europe, North America, Australia or Japan. This distinction is not accidental, but it reflects the organisational setups of microbiological research described in the articles. The research laboratories noted in the articles were located in countries such as the Netherlands, Sweden, Finland, Japan, the US and Australia, and most research participants were recruited in those countries through travel clinics or travel agencies, which people visit only when travelling to tropical regions such as South and Southeast Asia, the Caribbean, Central America and sub-Saharan Africa. Below, we analyse the microbiological metaphors following the two directions of travelling: going abroad and coming home.

Travel Destinations as 'Reservoirs' for AMR

The travel destination is a major risk for acquiring AMR according to the analysed articles. Describing these destinations, microbiological articles focus on particular parts of the world, such as Southeast Asia, Eastern Africa, South America and Southern Asia (Arcilla et al., 2017; Kantele et al., 2017). The Indian subcontinent was specifically presented as a destination having 'the greatest risk' for colonisation with resistant bacteria (Schwartz & Morris, 2018). For example, some authors generalised these travel destinations under the category of subtropics:

> Travel to (sub)tropical countries is a well-known risk factor for acquiring resistant bacterial strains. (Reuland et al., 2016, p. 731.e1)

Other parts of the world were also mentioned in the process of dissemination of resistant bacteria, but they were considered less risky:

> The MRE acquisition after a trip to North America, Europe or Oceania seemed rare, although few studies reported that travelling to Southern Europe, especially to Greece, would be riskier that travelling to other regions of the continent. (Ruppé, Andremont, & Armand-Lefèvre, 2018, p. 29)

Interestingly, comparing the risks of AMR acquisition in different parts of the world, one of the articles drew parallels between geographic locations and the economic status of these locations:

> This study compared travellers to temperate zones (North America, Europe and Oceania) to those who travelled to tropical and subtropical zones as surrogates for higher and lower-income countries, respectively. (Schwartz & Morris, 2018, p.6)

The travel destinations, therefore, were defined not only by their geography, but by the economic labelling of these areas, and they were often referred to as 'regions with poor hygiene' (Woerther et al., 2017) or as 'low-income countries, where poor hygiene and uncontrolled antibiotics consumption by humans have likely set favourable conditions for the dissemination of these resistant bacteria' (Ruppé et al., 2018, p. 28). It was also noted that:

> The risk is particularly high in regions with *poor hygiene* and *weakly implemented* [*emphasis added*] antimicrobial policy. (Kantele et al., 2017, p. 23)

These various descriptions of poor hygiene and uncontrolled antibiotic use in travelling destinations were summarised in one of the articles by using the metaphor of a 'reservoir' for AMR. This metaphor combines the various geographic and non-geographic characteristics involved in the problematisation of a travel destination as a risk for AMR acquisition:

> The Indian subcontinent has been identified as an important reservoir of carbapenemase-producing Enterobacteriaceae (CPE). (van Hattem et al., 2016, p. 857)

> Greece is known as an important reservoir for KPC [*Klebsiella Pneumoniae Carbapenem*]. (Van Hattem et al., 2016, p. 861)

Apart from travel destinations, microbiological articles stated that travellers and the practices that they exercise in destination countries contribute to the risk of acquiring AMR. These practices often relate to hygiene and eating behaviour that may lead to the development of diarrhoea. In addition, the use of antibiotics during travel was described as an important contributor to AMR acquisition. For example,

> Travellers who had occasionally consumed food from street vendors were at increased risk of acquiring ESBL-E compared with those who had avoided street food vendors, and the risk increased further in travellers who *consumed food from street vendors daily* [*emphasis added*]. (Arcilla et al., 2017, pp. 81-82)

> One study identified *antibiotic use* and another reported *vegetarian diet* and *owning a cat* [*emphasis added*] as risk factors for prolonged intestinal carriage by resistant bacteria. (Woerther et al., 2017, p. S31)

One of the studies mentioned that 'travellers have little knowledge of the risks of acquiring MRE [*multi-resistant Enterobacteriaceae*] during a trip' (Ruppé et al., 2018, p. 33). Although these authors added that travellers are often provided with information about the treatment of diarrhoea and that antibiotics are not necessary for non-severe diarrhoea, they concluded that 'travellers . . . are likely to ignore the recommendations'. While presenting travellers as potentially ignorant about health recommendations concerning antibiotic use, the same authors highlighted that these travellers are often 'unaware' about the potential risks:

> Provided that ESBL-E were acquired during travels, they could be easily transported from one country to another in the guts of millions of *unaware* [*emphasis added*] travellers. (Ruppé et al., 2018, p. 29)

In opposition to such ignorant but unaware travellers, bacteria were often presented in the literature as actors that define travel destinations to be risky. The countries of travel destinations that were presented as being risky for travellers were defined as countries of the origin of the bacteria. For example,

> NDM-1 [*New Delhi metallo-b-lactamases*] is thought to have originated in the Indian subcontinent and tends to spread between bacterial species on a transposon. (Schwartz & Morris, 2018, p. 3)

> Another participant was admitted to a foreign hospital in India and was colonised with a ciprofloxacin-resistant strain. (Reuland et al., 2016, p. 731.e5)

> Most CTX-M-9 strains (8 out of 12) were acquired in South-East Asia (Vading et al., 2016, p. 3549).

Bacteria were conceptualised based on their capacity to 'intrude' (Woerther et al., 2017) and 'colonise' 'millions of unaware travellers' (Ruppé et al., 2018). Resistant bacteria were described as 'a major concern worldwide' that is associated with 'higher mortality, longer hospitalization and higher costs' compared with non-resistant infections (Vading et al., 2016, p. 3548). In the analysed articles, bacteria were presented as actors who cause health risks:

> By altering the intestinal microbiota, antibiotics disrupt its ability to resist colonization by new *intruders* [*emphasis added*], a phenomenon well known as colonization resistance. (Woerther et al., 2017, p. S30).

> The presence of the antibiotic favours growth and colonisation by drug-resistant organisms and, occasionally, such bacteria *succeed* [*emphasis added*] in causing a clinical infection. (Kantele et al., 2017, p. 23)

The process of bacterial colonisation of travellers have led researchers in microbiology to propose several pre-travel measures to prevent the acquisition and potential spread of bacteria. These measures include 'pre-travel advice' on the prevention of diarrhoea and suggestions to refrain from unnecessary antibiotic use during travel (Kantele et al., 2017; Reuland et al., 2016; Ruppé et al., 2018). Some researchers suggested including, in the pre-travel advice, the description of potential risks of AMR acquisition during travel:

> Patients should be counselled regarding the risk of ESBL colonisation during pre-travel assessments. This is important information for travellers when evaluating the risks associated with potential itineraries. (Schwartz & Morris, 2018, p. 3)

In summary, the microbiological articles created a specific discourse regarding travelling abroad: a country of destination was presented as a cumulative reservoir for AMR, which was defined by poor hygiene and misuse of antibiotics in this country. When arriving at this reservoir, although travellers may ignore the health advice provided to them before the departure, they can be defined as unaware victims of bacteria. Moreover, these bacteria are in fact organised in colonies that reside in countries of travel destinations. Metaphors such the 'reservoir' for AMR referring to the countries of destinations, and 'intruders' and 'colonies' referring to bacteria are common concepts in the scientific discourse found in the literature. In the discussion, we will further reflect upon these metaphors after we analyse the following discourse of travelling from abroad to a home country.

Travelling to Home Countries and the 'Import' of AMR

After visiting a foreign country, travellers return to their countries of origin, which are described in microbiological articles as being primarily located in Western Europe, North America and Australia (Arcilla et al., 2017; Reuland et al., 2016; Ruppé et al., 2018). These countries are 'high-income countries' with 'better hygiene' and 'controlled antibiotic consumption'. One article defined travelling as a 'movement of persons from low- and middle-income countries in Asia, Africa, and South America, to high-income countries in Europe plus USA, Canada, Australia, and New Zealand' (Schwartz & Morris, 2018, p. 1).

Returning to their countries of origin, travellers are presented as 'potential carriers' that may serve as vehicles for the transportation of bacteria that have colonised them during a trip (Arcilla et al., 2017). These potential carriers are differentiated as either asymptomatic healthy carriers, for whom the risk of infection is 'not yet well known' (Vading et al., 2016), or as 'risk patients', travellers who have been hospitalised at home after their return from a trip (Kantele et al., 2017). At the moment of hospitalisation, an important shift in the microbiological discourse takes place: when a returning traveller is admitted to a hospital in a home country, it is this traveller that becomes a 'reservoir' for AMR, which was acquired abroad (Nakayama, et al., 2018).

> Travellers can represent potential *reservoirs* [*emphasis added*] for the dissemination of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae. (Nakayama et al., 2018, p. 391)

> If hospitalized at home, returning travellers having treated TD [*traveller's diarrhoea*] with antimicrobials while abroad should be considered *risk patients* [*emphasis added*]. (Kantele et al., 2017, p. 29)

In parallel with metaphors of 'risk patients' that refer to travellers who were hospitalised after returning to their home countries, we also found the metaphor of a 'sentinel': by travelling to a different country, travellers acquire and transport a piece of the local environment in them. Thus, apart from being presented as potential risks for a home country, travellers are understood as a source for acquiring knowledge about AMR prevalence in their destination countries. For instance, some researchers described this as follows:

> Travellers may act as a sentinel for emerging local resistance in developing countries like Indonesia and Myanmar. (van Hattem et al., 2016, p. 861)

> Even though the details of these [ESBL-producing *E. coli* harbouring *mcr-1*] carriage mechanisms are not clear, our results indicate that travellers may come to resemble Vietnamese residents, a percentage of whom are carriers of mcr-1-positive bacteria (unpublished data), during their stay in Vietnam. (Nakayama et al., 2018, p. 394)

By travelling to another country and, consequently, acquiring AMR, a returning traveller then becomes a person who resembles the local population of a visited country and its bacterial environment. By being colonised with local bacteria, travellers themselves become biologically local to the environment of travel destination countries. This approach to a traveller, as a sentinel to a foreign bacterial environment, goes together with a shift in applying the metaphor of a 'reservoir'. While in the first part of the microbiological discourse, a country of destination was described as a 'reservoir' for AMR, when a traveller returns from abroad to a home country, it is they who become this 'reservoir'.

The process of bacterial colonisation of travellers is conceptualised through the metaphors of the 'import and spread' of AMR (Arcilla et al., 2017; Reuland et al., 2016) and 'transportation' of resistant bacteria (Nakayama et al., 2018; Ruppé et al., 2018). Along with elaborating on these trade metaphors, one article investigated the route of bacteria to identify their country of origin:

> International travel has been implicated as the origin in both patients and hospital staff. This was highlighted by a neonatal intensive care unit outbreak in the UK of PVL+ MRSA

> infections traced back to a nurse who brought this clone from the Philippines. (Schwartz & Morris, 2018, p. 4)

The language of colonisation evokes respective metaphors and practices of decolonisation of returning travellers from bacteria, such as active screening of hospitalised travellers and the collection of patients’ travel histories (Arcilla et al., 2017; van Hattem et al., 2016; Woerther et al., 2017). The articles suggested various actions that can be taken in a country of origin to tackle the potential AMR spread by travellers into healthcare settings; for example:

> Active screening for ESBL-E and CPE and adjustment of empirical antimicrobial therapy should be considered for returning travellers as increased risk of ESBL-E carriage. (Arcilla et al., 2017, p. 79)

> In may be useful to advise returning travellers regarding personal hygiene to decrease the risk of transmission of acquired ARB to household members. (Reuland et al., 2016, p. 731.e6)

In addition, one article emphasised the need to take preventive measures not only at the local level of a country of origin but also at the global level and particularly in countries of destinations:

> This review highlights the importance of antimicrobial stewardship, infection control and surveillance; particularly in low- and middle-income countries. International leadership with global coordination is vital in the battle against antimicrobial resistance. (Schwartz & Morris, 2018, p. 1)

The second part of these microbiological discourses on AMR and travellers that dealt with returning to a country of origin, which was characterised as that having a higher level of hygiene and antibiotic use standards, described the transition of travellers from being ignorant or unaware when travelling abroad, to becoming ‘reservoirs’ for AMR that ‘import’ risks to a home country. However, this transition was also noted as being a means to opening up an opportunity to learn about foreign bacterial environments.

Discussion

Medical microbiology is a world shaped by metaphors that allows us to describe and act upon the world of microorganisms. Focusing on the very specific aspect of microbiological

work – acquisition and dissemination of MDR-E by healthy travellers – we analysed how scientists imagine bacteria, their relations to different geographical and political contexts and their interactions with human travellers. Distinguishing between travelling abroad and travelling to a home country, scientists describe a two-dimensional world where 'ignorant' and 'unaware' travellers go to 'reservoirs' of AMR and become 'colonised' by bacterial 'intruders'. This process turns travellers themselves into AMR 'reservoirs' when they are travelling back to their 'home countries' and 'importing' there 'colonies' of 'intruders'. The shifting metaphor of a 'reservoir' as well as colonising metaphors can facilitate an understanding of global concern and spread of AMR as something coming from one place to another.

Our research had several limitations, however. We deliberately decided to narrow the focus of the discourse analysis to the international transmission and dissemination of MDR-E in healthy travellers to grasp the coherent discourse that has been shaped in a distinct field in microbiology. This focus allowed us to reflect upon the understandings of AMR as a global concern that travels from one part of the world to another. At the same time, our analysis did not allow us to reflect upon how microbiologists imagine AMR in a national context in clinical and public settings, or a context of national travelling from one city to another. For the discourse analysis, we included only nine articles, which cannot possibly represent the entire field of microbiological research on AMR and travelling. In addition, we included several articles by the same authors who belong to particular study groups, such as the group of Anu Kantele, the COMBAT group and the VOYAGE-R study group. However, these groups have conducted some of the most comprehensive studies in this scientific field. Therefore, we think that this analysis is an important contribution to understanding the role of metaphors in microbiology, in general, and in AMR and travelling, in particular.

Studies of metaphors in scientific and policy arenas have shown that AMR is commonly conceptualised as a catastrophe, an imaginary that allows for the presentation of this issue as an urgent economic and public health concern (B. Brown & Crawford, 2009; N. Brown & Nettleton, 2016). Interestingly, in our analysis of microbiological articles on AMR and travelling, apocalyptic notions that were present in microbiology in the 1990s are no longer present. Metaphors of an 'apocalypse' and a 'return to the dark ages' have been substituted for by the precautionary warnings about future uncertainties of global AMR transmission and dissemination.

Chandler (2019) showed that in the international policy arena AMR is articulated through a sentinel approach, presenting AMR as an uncertain future threat that is difficult to estimate, to predict and to control. Our analysis showed how microbiologists in the field of AMR and

travel, without being alarmist, paint travellers as potential ‘sentinels’ that can help to resolve the uncertainties about AMR. The microbiological articles suggested that, by acquiring and carrying bacteria from the countries of travel destinations, travellers can contribute to the collection of microbiological knowledge about the territories where this knowledge is limited.

The metaphor of a ‘sentinel’ to define returning travellers was used in these articles alongside the metaphor of a ‘reservoir’ to describe these travellers. The concept of a reservoir is usually referred to as a source of something such as a water reservoir which refers to a pool that serves as a source of water. This metaphor was used in microbiological discourses to describe both countries of travel destinations and returning travellers. In both cases, the ‘reservoir’ was presented as something problematic that should be tackled through travel advice and quarantine measures. Countries of destination were presented as reservoirs due to their ‘poor hygiene’ situations, and by visiting those countries, travellers themselves were considered as being ‘reservoirs’ for AMR.

The two-dimensional world with AMR ‘reservoirs’ and countries with ‘better hygiene’ described in these articles involves colonial metaphors that are used to describe bacteria and their relations with environments and travellers. These metaphors are not uncommon in natural sciences. Taylor and Dewsbury (2018) showed that metaphors of ‘colonies’ are widely used in biology to describe non-humans and their relations amongst each other, such as colonies of ants or monkeys. The same authors have also argued that these metaphors run a risk of building analogies with ‘systems of dominance and hierarchy’, which may lead to ‘dehumanizing colonial representations of historically subjugated groups’ to whom the word ‘colony’ was originally referred (Taylor & Dewsbury, 2018, p. 3). A similar argument was made by Herbers (2007) who emphasised that, although scientists might not intend to build parallels between human and animal practices, historically and racially loaded metaphors can suggest similarities that might be given different interpretations.

Analysing the work of historians of colonial medicine, Anderson (2006, p. 293) highlighted the metaphor of a ‘reservoir’, which he argued was used in colonised territories to describe ‘local fauna, which included native races’ as ‘natural reservoirs of germs’. In our analysis of microbiological discourses, the metaphor of a ‘reservoir’ occupied a central role that was attributed to both countries of travel destinations and travellers returning from those countries. The colonial metaphors were directly attributed to the description of bacteria intruding upon ‘unaware’ travellers. It is also relevant to note that the entire setup of microbiological research mirrors the colonial separation on the ‘West’ or home countries where research laboratories were based and ‘East’ or countries abroad that travellers were visiting.

Colonial metaphors in microbiological discourses do not necessarily indicate that scientists using them imply their problematic historical backgrounds. On the contrary, according to Reynolds (2018), such metaphors are situated in limbo where they become biomedical concepts without a direct link to the original object of comparison (e.g. 'colony'). However, although metaphors do not simply describe an object of study, they are part of knowledge production processes (McLeod & Nerlich, 2017; Reynolds, 2018). In this context, it is important to reflect upon how colonial metaphors in microbiology help to perform science and whether they hinder some potential alternatives.

In their study of the histories of colonial science, Chambers and Gillespie (2000) showed that, although these histories were written about 'Indian' or 'Chinese' science, they were still 'European' in their focus. In our analysis of microbiological discourses, we observed a similar tendency. While AMR was defined as a global health issue, its global nature was imagined in rather linear relations between countries of travellers' destinations and home countries, as well as between travellers and bacteria. Dichotomies of bad hygiene versus good hygiene and ignorant/unaware travellers versus intruding bacteria allow only a particular type of reasoning – to protect one country from another. We could see this reasoning in different propositions designed to tackle AMR spread and dissemination – inform departing travellers and screen them on their return. Although these measures might indeed be necessary to address AMR, we can also imagine potential alternatives where the 'global' is understood as something networked and interdependent. Separation along the lines of home countries and those that are abroad may overlook this interdependency, where all countries can be imagined simultaneously as those representing a traveller's origin and destination.

Departing from a dichotomous separation of the world, we might think of AMR as an issue of interdependency amongst travellers, microbes, antibiotic policies and environments as well as geographies that can be understood as non-static elements that influence each other. Such understanding of the world as interconnected is not new and has been suggested by several scholars in the field of global health (Hinchliffe et al., 2013; Kehr, 2018; Landecker, 2015). For instance, in a study analysing budget cuts for tuberculosis (TB) treatment in Berlin, Kehr (2018, p. 5) argued that while 'North-South boundaries are permeable for disease through migration, . . . the actual location of TB is imagined to be in the South, among poor people of colour'. Kehr also noted that such geopolitical division lowers the importance of TB for the German context, which leads to cuts in funding and has a consequential impact on health care access for the poorest part of the German population. In their work on the multispecies ethnography in the UK farms, Hinchliffe et al. (2013) made a similar argument for rethinking

the dichotomy between health and disease as co-producing each other. Landecker (2015) took a step further and argued against a linear understanding of human-bacteria relations. Instead, she stated that not only bacteria influence the life of humans, but also vice versa.

Applying this non-dichotomous way of thinking and practising AMR and travelling can add a different angle for understanding this issue – how travelling from countries with ‘better hygiene’ can contribute to AMR in countries of sub-tropical regions and how the process of travelling can shape the global distribution of AMR. For instance, it can be important to understand how the process of travelling activates and shapes infrastructures surrounding travellers and their practices, such as separate food industries for travellers and separate health services and local policies for dealing with health complaints of foreign visitors. All these infrastructures are interdependent and connected into the continuous process of shaping potential AMR risks for both local populations and local environments as well as for travellers and their countries of origins. However, these infrastructural nuances can be overlooked due to the dichotomous metaphors of static ‘reservoirs’ ‘importing’ risks to countries with ‘good hygiene’. In addition, these metaphors might hinder potential opportunities for alternative research setups where home countries of travellers are located in sub-tropical regions of former colonies.

Metaphors help to communicate complex scientific objects to wider publics, including policymakers and funders, and they also guide the performance of scientific research. These two roles of metaphors are connected. The use of metaphors such as ‘reservoirs’, ‘intruders’ and ‘import’ may help to attract funding for research that would determine linear travelling patterns from a ‘healthy’ part of the world to an ‘unhealthy’ part and back. But alternative metaphors to communicate science may also attract funding for research that can offer different ways of imagining the global spread of AMR. Introducing the metaphor of ‘export’ along with the metaphor of bacterial ‘import’ and communicating the geopolitical dependencies and movements of people from all parts of the world may bring different imageries of AMR. In addition, we may think of the term mobility instead of travelling to broaden the research context to various movements of people, including mobilities amongst and within countries and regions. These metaphors may suggest that there is a need to build laboratories in sub-tropical regions and connect them to other laboratories in different parts of the world. It may also bring a new vision for understanding AMR as something that is constantly changing and deeply embedded in the modern lifestyles. In addition, it can offer alternative policy practices for addressing AMR as a phenomenon that requires action beyond international borders, that

connects different territories and people and that needs to be addressed as a result of such connectedness.

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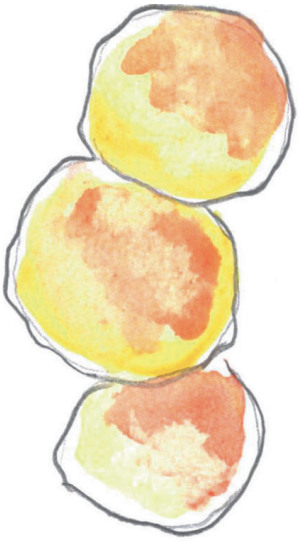
Chapter V

Stool and stories



Based on: Kamenshchikova, A., Wolffs, P. F. G., Hoebe, C. J. P. A., Penders, J., Park, H. Y., Kambale, M. S., Horstman, K. Combining 'Stool and stories': Exploring antimicrobial resistance among a longitudinal cohort of international health students. (submitted)

Abstract

Background

Antimicrobial resistance (AMR) is a public health concern that requires transdisciplinary approaches. However, there is a lack of transdisciplinary studies. Focusing on the acquisition of multidrug resistance genes, encoding extended-spectrum betalactamases (CTX-M) and carbapenemases (NDM-1) among a travelling population of health students, we present a methodology of 'stool and stories' that combines microbiological and sociological methods.

Methods

A longitudinal study with 64 health students travelling to India was conducted in 2017. The study included multiple-choice questionnaires (n=64); a collection of faecal swabs before travel (T0, n=45), in the first week India (T1, n=44), the second week in India (T2, n=41); and semi-structured interviews (n=11). Stool samples were analysed by a targeted metagenomic approach.

Results

The incidence of ESBL- and carbapenemase resistance genes significantly increased during travel; for CTX-M from 11% before travel to 78% during travel and for NDM-1 from 2% before travel to 11% during travel. The interviews showed that participants considered AMR mainly in relation to individual antibiotic use or to its presence in a clinical environment but not to travelling.

Conclusion

The microbiological analysis confirmed the previous research showing that international human mobility is a risk factor for AMR acquisition. However, sociological methods demonstrated that travellers understand AMR primarily as a clinical problem and do not connect it to travelling. These findings raise questions about the potential effectiveness of biologically driven AMR stewardship among the social groups of travellers. Further development of the 'stool and stories' approach is important for a transdisciplinary basis of AMR stewardship.

Introduction

Antimicrobial resistance (AMR) is a growing global public health concern, which has been defined by its bio-social nature (Smith, 2015). Although AMR is a biological phenomenon, the mechanisms leading to the development and dissemination of resistance genes are deeply social and include practices of antibiotic prescription and use (Broom et al., 2014; Rodrigues, 2020), practices of antibiotic production as well as waste management (Larsson, 2014; Larsson et al., 2007). Responding to this complex nature of AMR, calls for transdisciplinary approaches to AMR have been formulated by various researchers and public health institutes (Greenhough et al., 2020; Kamenshchikova et al., 2020; World Health Organization, 2015). The Global Action Plan for AMR published in 2015 by the World Health Organisation (WHO) states that 'everybody – in all sectors and disciplines – should be engaged' in addressing this issue (World Health Organization, 2015). A policy brief from 2019 by the WHO emphasized the importance of cultural contexts for understanding and developing solutions for AMR (Ledingham et al., 2019). Despite these calls, there have been a lack of studies that engage with both biological and social nature of AMR. To this end, we propose and present the results of a transdisciplinary methodology that combines methods and concepts of microbiology and sociology, we called this methodology 'stool and stories'. Stool and stories, we argue, should help to understand AMR in its bio-social multiplicity.

To present the methodology of stool and stories, in this article we focus on the acquisition of multidrug resistance genes encoding the extended-spectrum beta-lactmase (ESBL) enzymes of the CTX-M group and the NDM-1 carbapenemases among a population of health students who travelled to India from different parts of the world. The mobility of healthy human populations has been shown to contribute significantly to the dissemination of AMR globally (Findlater & Bogoch, 2018; Schwartz & Morris, 2018). Microbiological research from the Netherlands showed that international travellers have a high risk of acquiring AMR bacteria which persisted for up to 12 months after return from a trip in part of the travellers (Arcilla et al., 2017). Multiple social, biomedical and environmental factors can increase the risk of resistant bacteria acquisition during travel, including antibiotic use, diarrhoea during travel, as well as eating behaviour, hygiene practices and overall sanitary conditions (Angelin et al., 2015; Arcilla et al., 2017; Collignon et al., 2018; Vading et al., 2016).

Applying the methodology of stool and stories to study AMR in travelling groups we aim to understand both incidence of AMR in a particular travellers' group, and perceptions of this group towards AMR and potential risks for its acquisition during travel. Therefore, we aim to illustrate and get a preliminary understanding of potential linkages between the two worlds of

laboratory and society. Learning about such linkages is crucial for the understanding of AMR and for the development of coherent and comprehensive AMR control programs. In this article we bring this diverse expertise into a dialogue to show how the acquisition of AMR during international travel can be understood and addressed in a systemic way.

Methods

Study participants

The study involved 64 people from a total cohort of 207 health master students from a university in the Netherlands and a university in Canada of different nationalities. In 2017 these students were travelling from the Netherlands, Canada, Colombia, and Thailand to the south of India to participate in a two-week education symposium. From microbiological research on travelling groups, we know that India is considered to be a country with high prevalence of AMR (Arcilla et al., 2017; van Hattem et al., 2016). This leads to the high level of AMR acquisition among non-hospitalised travellers. The research cohort we focused on presented a unique travelling group because they had a prior health education background and could be familiar with AMR and potential routes of its acquisition.

Study design

The stool and stories approach included three methods of data collection: laboratory analysis of faecal swabs samples, multiple-choice questionnaire, and semi-structured open interviews. To invite students for participation in the research, we provided all the study related information to the potential participants (names and affiliations of research team, study methodology, and ethical clearance), and informed them about the use of anonymized microbiological data and deidentification of interview data. Students could choose whether they are willing to participate in the whole study protocol, or only in one of the methods of data collection. All students who agreed to take part in the study signed written informed consent.

Multiple-choice questionnaire

The aim of this method was to collect information about previous travelling history; previous antibiotics use history; health related preparation for a trip to India; and demographic characteristics of the study group. The data was analysed using the software IBM SPSS Statistics Desktop Version 25.0. (IBM corp., Armonk, New York, USA). From 64 students, all participants filled in the questionnaire. Most of the students filled in the questionnaire when they were in India (70%).

Laboratory analysis of specimen

From 64 participants, 45 students participate in specimen collection. We provided participants with collection kits for faecal swabs, and this enabled them to collect samples themselves. The faecal samples were collected and stored in DNA/RNA shield (Zymo research, Irvine, USA) to ensure the stability of the metagenome during unrefrigerated transport and during travel. Sampling timepoints were: before travel (T0), during the first week in India (T1), and at the second week in India (T2). There was a small difference in participation for the faecal swabs at the moments in time. Before travel (T0), a total of 45 stool specimens were collected, from which 28 were collected in the Netherlands and 17 were collected directly at arrival to India for students coming from Colombia, Thailand, and Canada. During the first week in India (T1), 44 specimens were collected. At the second week in India (T2), 41 specimens were collected.

Faecal swabs were processed at the medical microbiology laboratory in the Netherlands after travel as follows: For the extraction of metagenomic DNA, 200 µL of the suspended faecal swabs were added to a 2 mL vial containing 0.5g of 0.1mm zirconia/silica beads (BioSpec, Bartlesville, OK, USA) and 1 mL of lysis buffer from QIAmp DNA stool kit (Qiagen). Samples were disrupted in a Magna Lyser device (Roche, Basel, Switzerland) in 3 cycles of 1 min. at 5,500 rpm. Subsequently metagenomics DNA was isolated from the samples by using the QIAamp DNA stool kit according to the manufacturer's instructions. DNA was eluted in 200 uL elution buffer and stored at -20 C until further analysis.

Real-time PCR was performed to detect and quantify the β-lactamase-encoding genes $bla_{\text{CTX-M -1}}$, $bla_{\text{CTX-M -2}}$ and $bla_{\text{CTX-M -9}}$ and bla_{NDM}. These genes were amplified using a 7900HT Fast Real-Time PCR Detection System (Applied Biosystems) in 25 µL reactions containing 12.5 µL Absolute QPCR ROX Mix (Thermo Scientific, Waltham, MA, USA) and 5-µL template DNA. The PCR was performed as described previously(von Wintersdorff et al., 2014).

After determining how many samples were positive for a resistance gene after travel, McNemar's test for paired samples was used to compare resistance gene frequencies between the results from before and during travel. A p-value of <0.05 (2-sided) was used as a significant cut-off. Statistical tests were performed by using IBM SPSS Statistics Desktop Version 25.0.

Semi-structured open interviews

The semi-structured interviews were conducted with 11 participants from the main cohort to get a deeper understanding of how the participants give meanings to the relationships

between travelling, antibiotics, and AMR. In addition, we explored stories of participants about their health preparation for a trip to India, and eventual precautionary health measures they thought are necessary before and during travelling. The number of interviews was determined by data saturation. All interviews were conducted in person with the use of voice-recorder and transcribed verbatim. The analysis of the transcribed data was conducted in the NVivo 9 qualitative data analysis software (QSR International Pty Ltd, Doncaster, Victoria, Australia).

Ethics

The study protocol was approved by the Medical Review Ethics Committee of the Maastricht University Medical Centre+ (approval number).

Results

Sharp increase in AMR genes after travelling

A total of 45 students participated in fecal sampling. Before travel, 5 of 45 (11%) students showed a faecal swab positive for $bla_{CTX\text{-}M}$ genes, of which 4 swabs contained genes from $bla_{CTX\text{-}M\ \text{-}1}$ group and 1 swab $bla_{CTX\text{-}M\text{-}\ 9}$ group. During the stay in India, 35 students tested positive for $bla_{CTX\text{-}M}$ genes leading to a total positivity rate for these genes of 78%, which is a significant increase ($p < 0.001$). 31 of 45 students (68%) acquired a new or additional type of $bla_{CTX\text{-}M}$ gene. Of the 45 students, 40 were tested at both time-points during the trip (T1 and T2). Of this subset 26 acquired $bla_{CTX\text{-}M}$ during the trip and the majority: 15/26 (58%) were positive at both timepoints, 5 only acquired $bla_{CTX\text{-}M}$ in week 2 and 6 students acquired $bla_{CTX\text{-}M}$ or an additional type of $bla_{CTX\text{-}M}$ at T1, but lost them again at T2. For bla_{NDM}, only 1 of 45 had a faecal swab positive for this gene prior to travel. An additional 4 students acquired bla_{NDM} during the stay and also this was a significant increase ($p<0.05$). Of these, 2 students were tested at both T1 and T2 and showed a persistence of bla_{NDM} positivity.

Global travellers and precautionary purchase of antibiotics

The analysis of the questionnaires showed that median age of the participants was 27, and the majority of students were women (73%). The cohort of respondents represented a very mobile group, which was shown by their travelling practices. The majority (83%) of respondents visited more than 2 countries within the last three months before their arrival to India. The primary travel destinations were within Europe and included Belgium (37%), Germany (35%), and the Netherlands (30%), but also Canada (13%) and Thailand (10%). All of the participants visited India. These travelling trajectories can be explained by the international nature of the education program that students were involved in. Canada, Thailand

and India were the three countries students could opt to go to for an elective. In addition, close proximity of the Netherlands to Belgium and Germany could also have contributed to the high students' mobility between these countries.

Most of the participants did not take any antibiotics within the last year prior to the study (66%, n=42), only quarter of people took one course of antibiotics (25%, n=16), and several people took 2 or 3 courses (9%, n=6). Among those who did take antibiotics within the last year prior to the study, more than a half was prescribed by a physician (59%, n=13). However, 41% (n=11) from those who used antibiotics within the last year informed us that they used non-prescribed antibiotics, which they got either from a family member or from a pharmacist without prescription in countries where it is possible.

With respect to their travel preparation to India, 14 out of 64 respondents reported that they brought antibiotics with them to the trip. The most popular antibiotics were azithromycin (42%, n=5), amoxicillin (33%, n=4), and ciprofloxacin (25%, n=3). Two students indicated that it is important to take some antibiotics with them when travelling to India as a precautionary health measure.

Travelling is not considered to be a risk for AMR

Accompanying the quantitative data from the microbiological analysis and survey, the qualitative interviews were aimed to gain a deeper socio-cultural understanding of the daily practices of students that were problematised by the quantitative data as potentially risky. Exploring the meanings of AMR, the interviewees often described this phenomenon in biomedical terms – as an evolution of bacteria to resist antibiotics. Such descriptions were not surprising as our participants had background education in health, and therefore could be familiar with this phenomenon. In addition, the interviewees were also participating in the collection of stool samples and the survey, and therefore they were previously exposed to the information about AMR.

Building on a biomedical understanding of AMR our participants described several ways of how AMR can be developed and acquired. We distinguished two of such interrelated ways: first, AMR as an individual responsibility, and AMR as a medical phenomenon that can be acquired in clinical settings. This means that students associated mechanisms of AMR development with antibiotic use, and they connected AMR acquisition with clinical facilities, which they presented as potential sources of resistant bacteria.

In the interviews, students explained that the development of AMR is determined by individual use of antibiotics, including self-treatment, interruption of prescribed antibiotic treatment and its overuse. For instance, our participants explained,

> *Specific bacterial strains are becoming resistant to antibiotics because of the really often use of antibiotics (S21)*

> *Antibiotic resistance is due to the fact that some people in many countries just taking many multi-resistant* [antibiotics]. *... The other reason is that many people don't take the whole prescription that they're supposed to take (S36)*

Individual behaviour with respect to antibiotic use was defined by students as a major cause of AMR. In particular the excessive amount of antibiotic use was associated with risks of resistance development.

Apart from the individual use of antibiotics, several students highlighted that environmental and infrastructural factors may play a role in AMR acquisition. Some students distinguished between a 'risky country' where antibiotics are used inappropriately, and a 'risky environment' like hospitals where AMR can be easily acquired by visitors and patients. During the interviews, students argued that a person can acquire AMR if she gets admitted to a hospital in a particular country. Although several students mentioned that individual use of antibiotics can contribute to the high level of AMR in a country, they narrowed the risks for AMR acquisition to clinical settings:

> *I know that especially some parts of the world, there is a lot of antibiotic use and because of this, this create like the bacteria that are already resistant to antibiotics and stay alive, and if this happened too much you create a resistance strain of antibiotics and I think this is becoming more urgent issue. (S47)*

> *So I am aware of different countries have different levels of antibiotic resistance. Probably if I get treated in a country where there is like hospital where there is a lot of bacteria around that are resistance and I am exposed to this, then I might not be able to have them treated. (S20)*

AMR, therefore, has been understood by our participants as rooted in individual practices of antibiotic use and in clinical practices of certain countries that create risks for AMR acquisition. These understandings were mirrored in students' reflections on their personal

health practices and travel preparations. Participants were surprised by our questions about the connection between AMR and travelling and they explicitly elaborated that they do not see such as a connection:

> *I always think about it [AMR] if I ever prescribed antibiotics and when I take it, not when I think of it when I am travelling or some kind, no, no, no. (S42)*

While been aware of AMR, its biomedical nature and mechanisms, our participants argued that AMR as a problem was located in clinical settings rather than in public spaces. They did not associate and connect their routine travelling practices with potential risks of acquiring resistant bacteria, unless they were admitted to a foreign hospital. This may indicate that while microbiological data highlight the importance of travellers' social practices for understanding AMR, travellers themselves do not see AMR as a part of their social worlds but rather locate it in the clinical world.

Discussion and conclusion

In 2018, more than 6 billion people moved across the world, which included more than 4.3 billion air travellers (International Air Transport Association, 2018), approximately 1.4 billion international tourists (United Nations World Tourism Organization, 2019), as well as about 68.5 million forcibly displaced people (United Nations High Commissioner for Refugees, 2018). Accompanying human travellers, bacteria are spread and disseminated to different parts of the world, which contributes to the global rise of AMR (Ruppé et al., 2018; Vading et al., 2016; van Hattem et al., 2019). In this article we explored the fruitfulness of a stool and stories approach to understand the biological and social dimensions of AMR among a traveling group of international health students.

The microbiological findings from our study confirmed previous research (Arcilla et al., 2017; von Wintersdorff et al., 2014) pointing to the fact that travelling can be seen as a substantial risk factor for acquisition of resistant bacteria. While overall microbiological data was not drastically different from other research with travelling groups, the acquisition of bla_{NDM} during the trip was higher as compared to other studies (Arcilla et al., 2017; von Wintersdorff et al., 2014). We suggest that this can be partially explained by the high level of mobility among the study population. The data from the survey showed that international students are frequent travellers who come in contact with diverse environments.

The analysis of the interviews showed that our participants constructed AMR as a biomedical phenomenon. They were explaining this phenomenon through the practices of

antibiotic use or through its presence in clinical settings in particular countries. At the same time, public spaces and travelling practices were not associated with AMR health risks. Reflecting on their travelling and daily practices in a foreign country, our participants explained that as long as there were not taking antibiotics and they were not hospitalised, they would not be exposed to AMR.

Our research has limitations. The sample size for all three methods was relatively small and the population was rather specific: health students who have prior knowledge on AMR. We understand that different results can be obtained from another group of travellers without education background in health. Moreover, the sample size for microbiological analysis was not equal at each moment as not all of the students who participated in before travel (T0) were able to further participate in the study. However, this research demonstrates the fruitfulness of a transdisciplinary methodology of 'stool and stories'.

Although this is a small study, the results suggest that laboratory-methods represent AMR differently compared to the analysis of stories among these highly mobile health students (Vries & Horstman, 2008). These different results indicate potential difficulties for preventing AMR, as many preventive strategies depart from a biomedical perspective on risks and lack a social science understanding of risks in everyday life. To develop an adequate prevention for AMR, it is important – instead of turning the biomedical perspective into a standard for social scientists – to put the biological and societal perspectives into a dialogue to create a new transdisciplinary understanding of AMR and travelling. Instead of imposing biomedical knowledge on society and trying to change social behaviour to attune to this knowledge (practice, which often showed to be unsuccessful (Pearson & Chandler, 2019; Will, 2018)), transdisciplinary approaches open an opportunity for a dialogue and a compromise between the two worlds. This way AMR can become part of the world of travellers where some bacteria exist beyond the clinical settings and the world of travellers can become part of the laboratory where not all travelling practices are considered to be risky. Without the integration of diverse perspectives on AMR the health risks and preventive strategies highlighted by the laboratory can fail to be attuned to the social realities of travellers that may not see bacteria to be part of their daily life. We suggest that to improve the alignments of laboratory and societal practices, and to get more insight in the added value of transdisciplinary research, it is important to further develop the stool and stories approach. This also includes the further development of much closer linkages between laboratory research and social-cultural analysis in a systematic way.

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Chapter VI

Transdisciplinary work against antimicrobial resistance

Based on: Kamenshchikova, A., Wolffs, P. F. G., Hoebe, C. J. P. A. and Horstman, K. (2020). Transdisciplinary work against antimicrobial resistance. *The Lancet Infectious Diseases,* 20 (5): 526-527. doi: 10.1016/S1473-3099(20)30137-7

In 2015, WHO issued a Global Action Plan emphasising One Health as an essential approach to tackle antimicrobial resistance (AMR). One Health aims to bridge human, animal, and environmental sectors to address shared health concerns (Craddock & Hinchliffe, 2015). One of the gaps in knowledge articulated by the Global Action Plan is scant understanding of social science and behaviour. In that context, One Health offers a potential for transdisciplinary collaborations, including between social and biomedical disciplines. WHO states that the role of social sciences in the One Health approach to AMR is dedicated to support effective antimicrobial stewardship programmes in human and animal health and agriculture. Although this role is essential for the success of AMR control programmes, it limits the potential of social science studies to support such programmes rather than to co-develop them based on both biomedical and social knowledge.

Also in 2015, Smith wrote that AMR is a social problem; social science research has to be taken seriously in addressing the issue of AMR. Cultures of prescription, sale, and use of antibiotics in human and animal sectors, and practices of antibiotic production and waste management, are essential for understanding drivers of emergence and dissemination of multidrug- resistant bacteria (Broom et al., 2014; Chandler & Hutchinson, 2016; Kirchhelle, 2018). Study findings substantiate the claim that AMR is not only a biological problem but also a social problem. Research by Collignon and colleagues shows that social and economic inequalities, poverty, and public health expenditures are major factors driving the global level of AMR (Collignon et al., 2018).

If AMR can be considered a biosocial issue, solutions should neither lie exclusively within the biomedical disciplines nor fall into the social disciplines, but should reside on their intersections. In principle, the One Health approach offers an opportunity to develop a transdisciplinary and trans-sectoral agenda for AMR. However, findings of a study suggest that the One Health governing framework has an anthropocentric focus, positioning animal and agricultural sectors under the dominance of human health governing organisations (Kamenshchikova et al., 2019). Moreover, at the moment there are not enough conceptual, physical, and financial infrastructures to undertake transdisciplinary and trans- sectoral work. To create possibilities for transdisciplinary research, combining sociological and anthropological studies with microbiological research, funding needs to be organised; moreover, opportunities are needed to publish the results of transdisciplinary research, which combines very different types of data. It is important to think about concepts and approaches

that go beyond One Health in capturing the multiple biosocial complexity of AMR, without prioritising one discipline over the other. Without a research infrastructure to build and sustain transdisciplinary collaborations, we are locked in disciplinary paradigms and will not understand AMR as a biosocial issue.

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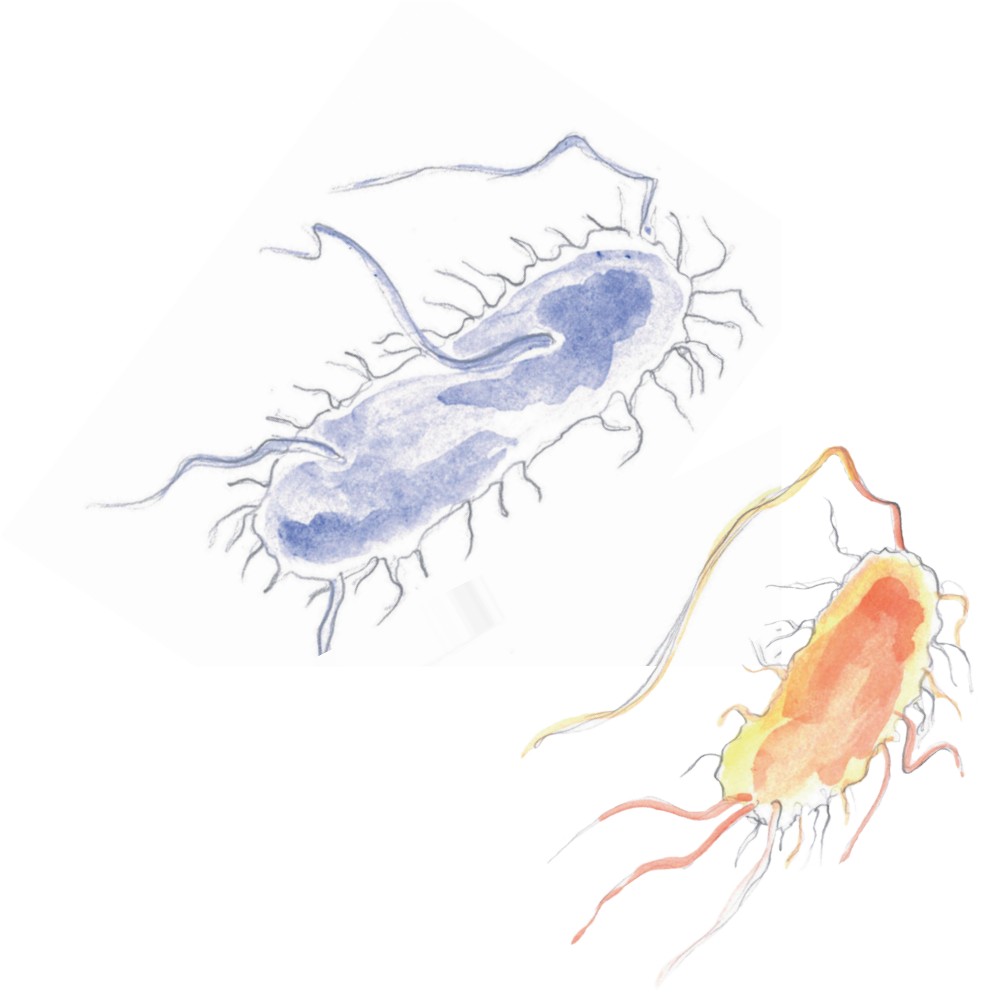

General discussion and conclusion

How are bacteria changing the world?

Alice: Would you tell me, please, which way I ought to go from here?
The Cheshire Cat: That depends a good deal on where you want to get to.
Alice: I don't much care where.
The Cheshire Cat: Then it doesn't much matter which way you go.
Alice: ...so long as I get somewhere.
The Cheshire Cat: Oh, you're sure to do that, if only you walk long enough.

Lewis Carroll, Alice in Wonderland

Being a philosopher and entering the terrain of AMR, it has been fascinating to observe how this phenomenon is negotiated between different stakeholders. The WHO presents AMR as a global health concern that should be addressed on the national and international levels through increased surveillance, the development of new medications and control over the behaviour of antibiotic users (WHO, 2015). This perspective on AMR can also be found among biomedical and public health professionals (Pouwels et al., 2019). At the same time, social science scholars argue for a different perspective on AMR. While they also present it as a global health concern, they suggest that solutions should be found beyond the production of new medications and development of behavioural interventions (Hutchinson et al., 2018; Will, 2018). In the field of social science, researchers argue that to address AMR as a global phenomenon, policymakers need to pay attention to the problem of access and distribution of current medicines, to the modern ways of production and trade and to the modern ways of understanding productivity and necessary time for convalescence. Observing these negotiations in the pages of scientific journals, I was inspired by the theoretical approaches of STS that allow for the analysis of facts as constructed (Latour & Woolgar, 1986; Mol, 2002). Instead of joining the debates on how to present AMR, I took a step aside and analysed how AMR is practised in different settings where various presentations of this phenomenon are constructed.

This thesis is a report on my travels to different AMR settings and practices that have not yet been explored in the existing field of social studies on AMR. Without having a strict travel plan or detailed travel guide, I analysed the arenas of international policy, healthcare practices and scientific work. In this last chapter of the thesis, I will first summarise the main lessons of my travels. Next, I will reflect on the limitations of these travels and elaborate on how the characters in my travels enabled or hindered specific insights into understanding AMR. Then, I will explore the meaning of the results in relation to relevant theoretical discourses.

Exploring diverse AMR settings

I started my journey with an analysis of AMR practices in the international policy arena. This arena has been dominated by the One Health policy approach that aims to address AMR as a shared health concern between the human, animal and environmental sectors (European Commission, 2017; WHO, 2015). In chapter one, I explored how this approach influences AMR policies at the international level. In line with Asdal (2015), I theorised policy documents as an arena that does not simply describe AMR and One Health but constructs them as policy objects and influences practices of professionals working in the field of human, animal and environmental health.

My analysis showed that One Health policy regulations, while aiming to unite the human, animal and environmental sectors, implicitly prioritise AMR as a human health issue, while animal and environmental health are presented as being potentially responsible for AMR risks that could influence humans. Reflecting on this analysis, I explored the potential of post-humanism theories in understanding One Health because these theories suggest different non-anthropocentric approaches to health. Rock (2017), in her critical analysis of the concept of *public* in public health and One Health promotion, argues that the health of different species should be understood as co-shaping each other because they all depend on and share the same environment. Hinchliffe and Ward (2014) propose the concept of *folded life* to understand human-animal-bacteria relations as making one another – they are folded together. The application of post-humanism theories to One Health policy regulations of AMR has highlighted how these regulations stimulate hierarchies between humans, animals, environments and between professionals who work in these sectors. I have concluded that the construction of such hierarchies can be rooted in the larger health policy arena from which One Health policy regulations of AMR are derived, which are primarily focused on human health. The analysis showed that it is quite difficult to develop symmetry between the health of different species and knowledge practices of different professionals.

The next setting that I introduced in this thesis to study AMR practices was healthcare. I analysed two cases: AMR screening of refugees in the Netherlands and antibiotic control practices in Russian outpatient clinics. In chapter two I analysed how practices of AMR screening of refugees were perceived and constructed by different actors – Syrian refugees, microbiologists and public health professionals. This study was conducted in 2016 in a context of increasing policy attention to the incoming refugees in Europe, where this group had become an object of biomedical scrutiny for posing potential risks for disease dissemination (Maltezou et al., 2017). My analysis showed the diversity of perspectives on AMR screening of refugees.

Microbiologists and public health doctors presented this screening as a potentially important public health measure, describing the importance of generating information about the overall AMR level in the community. At the same time, public health nurses dismissed AMR screening as potentially stigmatising for refugees, and they argued that screening had no clinical relevance. Refugees themselves perceived screening as permissible, but only if it benefited their personal health, not only public health. They stressed that if AMR screening is an important public health measure, it should be required from all travellers and not exclusively from refugees.

I proposed to analyse the different perspectives on AMR screening of refugees through the concept of the tragedy of the commons; this concept refers to a situation where individual users of shared resources exercise practices that may be beneficial for them personally but harmful for the whole community that shares those resources. Applying this concept to AMR would mean that health is understood as a shared resource and AMR can be perceived either as a public health or individual health concern (Foster & Grundmann, 2006). In this context, AMR screening might be not justified if understood from the perspective of individual health because the screening of non-hospitalised people will not bring any benefits to these particular people. At the same time, if AMR screening is understood from a public health perspective, different individuals can be regarded as subjects of screening without considering potential individual harms to these individuals.

I concluded that while AMR screening was often presented as a public health concern, screening practices that specifically focused on refugees separated this group from the public and presented them as being risky to this public. I suggested shifting the discussion from debates about the necessity of screening to the question of *how* this screening was organised. This meant the inclusion of refugees' perspectives, as they were members of the public, and integration of their needs into the public health concerns for AMR.

In chapter three I explored how AMR prevention was practised by medical doctors, patients and pharmacists in the context of Russian outpatient care. I analysed practices of healthcare professionals and patients in a context of changing policy regulations in Russia, where the over-the-counter sale of antibiotics has been strictly prohibited since 2017, when the requirement for obligatory medical prescriptions of antibiotics were introduced. In my research, I observed the adaptive practices that doctors, pharmacists and patients exercised in this new policy context. On the one hand, they argued that AMR was a serious problem and that antibiotics were important medications that should not be misused. On the other hand, their social and economic realities, including patients' difficulties in taking sick leave and getting

timely appointments with doctors, led to informal practices that allowed access to antibiotics without prescriptions.

In my analysis, I engaged with social science literature, critically evaluating policies that defined AMR primarily as a behavioural problem of inappropriate prescription and use of antibiotics. Scholars like Chandler (2019) and Will (2018) argue that such policy approaches tend to overlook infrastructural conditions that determine antibiotic practices. These infrastructural conditions refer to the economic possibilities for patients to access non-pharmaceutical forms of care and their ability to sufficiently convalesce, as well as non-economic conditions, like personal relations between patients and doctors and between patients and pharmacists. Reflecting on this critique, in my analysis I concluded that while policies to control the over-the-counter sale of antibiotics in Russia were focused on the behaviour of antibiotic prescribers and users, the informal practices of these users compensated and adapted to the lack of infrastructural changes in the economic and social realities of healthcare providers and patients. These infrastructural realities included a lack of medical staff in hospital settings and the inability of this staff to deliver timely treatment within the officially established standards for care delivery. It also included the economic context of patients, including difficulties in taking the time off work to visit a doctor and thus staying ill.

The last setting in my journey was the biomedical practices of AMR. Inspired by studies on metaphors in fields like synthetic and cell biology (McLeod & Nerlich, 2017; Reynolds, 2018), in chapter four I presented the results of a discourse analysis of microbiological articles on AMR and travelling published between 2016 and 2018. In line with Reynolds (2018), who argues that metaphors in science should be understood as the 'third lens' of a microscope, I focused on metaphors in microbiology as tools that did not simply describe complex scientific phenomena but guided research processes and framed results. Language is not only descriptive but is also performative and political; that applies to scientific language as well as other types of language use (Asdal, 2015; Reynolds, 2018). I analysed how researchers described AMR and its transmission in travels between different parts of the world.

I showed that microbiological articles described AMR transmission as a process in which 'ignorant' and 'unaware' travellers 'import' bacterial 'intruders' from countries that are presented as 'reservoirs' of AMR to 'high-income' countries. Microbiological studies on AMR and travelling imagine a very specific notion of the world, where 'healthy' countries are separated from 'unhealthy'. I have concluded that such presentations might overlook the potential imaginary of AMR as a networked phenomenon that highlights interdependencies between different places and practices of travelling. The separation of healthy and unhealthy

countries implicitly reinforces the notion of national borders in a microbial global world where these borders offer limited protection when it comes to AMR. Therefore, the metaphors in microbiological research may threaten effective global policies to deal with AMR and travelling as a networked phenomenon that ties different places together.

Calls for transdisciplinarity in AMR research have been predominant since the publication of the Global Action Plan in 2015 and the introduction of the One Health approach for addressing AMR. Following the Klein's (2017) definition of transdisciplinarity as a system of knowledge that 'transcends the scope of disciplinary worldviews through an overarching synthesis', in my thesis I worked in the transdisciplinary interface of the social sciences, humanities and biomedical sciences. In chapter five, where I presented the methodology of stool and stories, I explored the potential of transdisciplinary research combining methods of different disciplines. On a research team that included sociologists, microbiologists and public health specialists, we experimented with transdisciplinarity by putting two very different types of data – stool samples and stories – into a dialogue about AMR acquisition during international travel. This dialogue was organised around the data that we collected among a cohort of graduate students who travelled from different parts of the world to India for an education symposium.

The result of this transdisciplinary dialogue shows that microbiology and social science speak very different languages when communicating about AMR. While microbiological data showed that students arriving in India had acquired a higher level of AMR than before their arrival, the sociological data demonstrated that students did not consider AMR to be relevant to their travel practices. In my analysis of the cooperation between microbiology and social science, I concluded that despite the aim to understand AMR as a biosocial phenomenon, biomedical and social science data existed in parallel to each other, but not yet connected as there was a lack of concepts, instruments, funding and infrastructural possibilities to co-produce biosocial knowledge. Reflecting on this complicated dialogue, I argued that continuous practices of co-production of the biosocial methods and concepts for understanding AMR were crucial for bridging the laboratory and society. This bridging can open an alternative imaginary of infection preventions and surveillance, one that balances the social acceptance of such preventions and the biomedical approaches to it. Although it can be seen as speculative, transdisciplinary experimentation with microbiological and social science methods may result in democratisation of infection prevention, where social practices and understanding play equally important roles as the microbiological samples.

In line with this, the last chapter of the thesis was a commentary about infrastructural gaps – namely in transdisciplinary concepts and methods, in accessibility of funding, and intransdisciplinary journals and platforms for knowledge co-creation – that may hinder the development of transdisciplinary work. This commentary can be considered a reflection on the whole journey of this thesis that I walked together with my supervisors from different disciplines. It indicated certain difficulties that we met in our research practices and highlighted the necessity of increasing funding and creating transdisciplinary platforms to stimulate the co-production of knowledge about different aspects of AMR.

The chapters of this thesis focused on very different settings and involved different actors, such as policy-makers, healthcare professionals, laypeople, microbiologists and scientific articles. In each of these settings, I described how resistant bacteria acted and were acted upon by society. In a sense, I showed how resistant bacteria became *socialised* differently depending on the setting and context where they were positioned. This diversity of social practices that surround and shape resistant bacteria highlights the necessity to approach AMR as multiple biosocial phenomena that cannot be addressed by universalistic and technical approaches that can often overlook the diverse social contexts where resistant bacteria are constructed.

Travelling without a map

I started this study as an Erasmus philosophy student working on a project about AMR screening of refugees, and I did not have a completed study design available I had to follow. The Erasmus project slowly developed into a PhD and studies of different settings were designed rather incrementally. Chapters of this thesis focused on different settings where I applied different methodologies and theoretical angles. A disadvantage of such an approach, this thesis does not present an in-depth analysis of AMR practices in one particular context, and it does not explore in-depth one specific theoretical approach. At the same time, the diversity of settings and practices that I explored allowed me to engage and highlight the differences showing that AMR was not a static, unified and standardised phenomenon, as often suggested in policy discourses (O'Neill, 2016; The Wellcome Trust, 2019). Rather, the diversity of case studies in this thesis points to the necessity for addressing AMR as multiple phenomena that are shaped by the biosocial worlds in which they are situated. The different theoretical perspectives that I applied in this thesis indicate various angles from which AMR can be approached. Therefore, the diversity of methods and theoretical concepts opened up an arena of diversity and experimentation where new biosocial approaches to AMR can be developed.

During my travels through AMR worlds, I connected to different disciplinary backgrounds – my supervisors represented the disciplines of STS and social sciences, public health and microbiology – and I engaged with different disciplinary and theoretical approaches during the research. Throughout my PhD work, I learned some basic knowledge about microbiology and public health – about different types of bacteria and their behaviour, about different mechanisms of AMR and different laboratory tests and public health measures to control these bacteria. In STS it is important to stick to the symmetry principle: this means that beliefs (false or true) should be treated as equal and a researcher must remain impartial when explaining the causality of these beliefs. This also means that scientific phenomena are explained as intrinsically social and political. Learning about AMR as a member of a transdisciplinary team, rather than a sociologist observing biomedical practices, I was challenged to maintain this symmetry and to preserve a neutral position towards different types of knowledge. Studying practices of laypeople, doctors, pharmacists and policymakers, I was already 'contaminated', in the words of Zuiderent-Jerak and Bruun Jensen (2007), by certain perspectives from microbiology and biological understandings of AMR. This means that I was already embedded in knowledge practices and beliefs of microbiologists and public health professionals with whom I was working. This often made it challenging to impartially analyse AMR and antibiotic practices as neither good nor bad.

Simultaneously, my philosophical perspectives influenced and contaminated the perceptions of my supervisors from microbiology and public health. One example is a conversation I had with my microbiology supervisor about the different types of knowledge of AMR. In one of the chapters in this thesis I wrote about a 'perspective from the laboratory', to which she argued that laboratories produce facts rather than perspectives. Interestingly, after this conversation, she commented that after several years working in such a transdisciplinary team, in which we critically analyse AMR knowledge production practices, she had started to question whether the laboratory actually produces facts, or perspectives that are argued to be facts.

Studying different AMR practices, I simultaneously participated in the transformation of these practices as a philosopher and as a member of the transdisciplinary team. Another memorable example of such co-contamination that we had in our team was a discussion about the potential title of this thesis as 'Peace Treaty with Resistant Bacteria'. While the social science part of the team was quite intrigued by this idea, its biomedical counterpart argued that such an idea went against the aims of modern science and medicine to tackle these resistant bacteria. After an hour of discussion, we came to common ground with the idea of 'Peace

Treaty with Bacteria' – a result of our co-contamination. We agreed that while modern medicine tries to tackle AMR, it does it through the practices of peace with other bacteria, like the development of probiotics or faecal microbiota transplantations.

While it was challenging throughout my travels to stay impartial towards microbiological knowledge, to which I was constantly subjected, being part of a transdisciplinary team had important benefits. By working together, we subjected each other to different knowledge and practises, which allowed the co-production of hybrid knowledge that incorporated the diverse biosocial nature of AMR. Therefore, it opened up an important field for deeper research inquiries into the processes of socialisation by resistant bacteria. A combination of methods, metaphors and approaches created the opportunity for experiments, and I am convinced that we should continue with these experiments to overcome the separation between bacterial and human social worlds.

Opportunity for theoretical experiments

Although AMR has been studied by microbiologists since the discovery of the first antibiotics, it is a relatively new object of research in social sciences, and it has stimulated several theoretical developments. In different chapters of the thesis, I engaged with theories on post-humanism to describe human-bacteria relations, the concept of the tragedy of the commons to understand the ambivalent position of AMR in health practices and the concepts of infrastructures and informality to reflect on how health professionals and laypeople adapt to AMR policies. In addition, I explored practices enabled by scientific metaphors and theoretical approaches to transdisciplinarity. Although these approaches and the five chapters of this thesis analysed very different settings, they can be conceptualised in terms of the inversion of antibiotic infrastructures.

The concept of antibiotic infrastructure has been elaborated by Chandler (2019) to explore the role of antibiotics in society. She builds on the work of Bowker and Star (2000), who introduced the concept of infrastructure in their analysis of classification systems. Bowker and Star (2000) argue that systems of classifications and standardisations are embedded and shape the social infrastructures that define our ways of living; thus, they define the 'work practices, beliefs, narratives, and organizational routines'. The authors refer to the examples of infrastructure described by Becker (1982): the established standards for how music keys are written and how long a music concert should last define what kind of music can be written and what kind of concerts can be performed. Similarly, the established conventions about the dimensions of painting canvases (that it should fit onto a wall) pre-determine the type of

paintings that can be drawn. These standards, rules, conventions and physical dimensions of musical instruments or art galleries are examples of infrastructures that are embedded into the daily routines and mundane understandings of what music should sound like and how big the paining should be. These infrastructures are invisibly interwoven into the conventions of living.

Bowker and Star (2000) develop this line of reasoning further and apply it to healthcare practices. Classification of patients as infectious and non-infectious define infrastructures of hospitals that have separate wards for different patients and different specialists working with these patients. These infrastructures are invisible and they guide the daily routines of a hospital. Classifications and standards that are shared between several groups, like standards for patient classification, are presented by the authors as boundary objects. These objects facilitate communication between heterogeneous actors, like doctors, nurses, insurance agents and patients, and allow them to work together while performing their individual tasks. For instance, while both doctors and insurance agents refer to the same system of patient classification, they use it differently – doctors develop treatment schemes, and insurance agents assess reimbursement plans. But it is these boundary objects that help different actors involved in the process of healthcare delivery coordinate their work practices. Boundary objects may include systems of patient classification, personal medical records, medical prescriptions or ultrasonograms that can be read by various professionals, who extract different information from it.

The work of infrastructures can become visible, Bowker and Star (2000) elaborate, through the process of *infrastructural inversion*, which can be understood as a conceptual method to re-assemble the 'depths of interdependence of technical networks and standards, on the one hand, and the real work of politics and knowledge production on the other'. Infrastructural inversion aims to unpack the nets of dependencies between different elements of infrastructure that make it work. Trying to diagnose a patient with signs of illness that have not yet been described and classified in medical protocols untangles the infrastructural organisation of how such classifications are produced and how they are embedded into the practices of healthcare delivery. Infrastructural inversion allows the challenge of existing, often invisible, conventions. The COVID-19 pandemic, which started at the beginning of 2020 and led to quarantine measures in different parts of the world, has challenged conventional ways of education delivery. In a way, this pandemic can be seen as an infrastructural inversion that unpacks conventional knowledge of communication practices (i.e. the length of a lecture, the maximum number of students in a class and the importance of laboratory work and practicums)

and shows its dependencies from physical structures (lecture halls) and instruments (laboratory equipment) that currently define education processes.

Building on this theoretical work, Chandler (2019) suggests analysing AMR as an inversion of antibiotic infrastructure. She aims to show that antibiotics are invisibly intertwined with modern understandings of healthcare and farming and more broadly with current political and economic processes that shape ideas of productivity and influence socio-economic inequities. Antibiotics influence modern understandings of hygiene and safety as non-bacterial and conventional healthcare practices of surgery and cancer treatment that would not be possible without antibiotics. Antibiotics are also embedded into the modern idea of productivity. In other words, the capacity of antibiotics to treat infections within a particular number of days defines how long a patient can stay ill before returning to work, which is translated into medical protocols and health insurance policies for covering a standardised treatment. Antibiotics also define the possibility of industrial farming by allowing a large number of animals in the same territory. Elaborating on these different examples, Chandler (2019) argues that antibiotics, as a biomedical phenomenon, should be understood as an infrastructure that shapes modern ways of living. Following this, she suggests conceptualising AMR as an inversion of such infrastructures as it allows questioning the modern social, political and economic processes that are shaped by antibiotics.

Reflecting on the chapters in this thesis and engaging with the work of Bowker and Star (2000) and Chandler (2019), I would like to suggest a further analytical endeavour regarding the concept of infrastructure. Apart from understanding AMR as an inversion of antibiotic infrastructure because it shows our dependency on antibiotics in many ways, it can be fruitful to analyse bacteria, including resistant bacteria, as an infrastructure. Bowker and Star (2000) argue that 'infrastructure does not grow de novo; it wrestles with the inertia of the installed base and inherits strengths and limitations from that base'. In addition, infrastructure is 'never changed from above. Changes take time and negotiation, and adjustment with other aspects of the systems involved' (Bowker & Star, 2000). Therefore, while resistance mechanisms of bacteria can be understood as an inversion of antibiotic infrastructure, bacteria themselves can also be analysed as infrastructure that establishes new connections and builds new boundary objects between new stakeholders who might have previously not been a part of the antibiotic infrastructure. In a sense, this conceptual alternative will shift the focus from antibiotic capacities to bacterial mechanisms and their manifestations. In the concluding section of this thesis, I would like to reflect upon this analytical experiment.

Bacteria as a manifesting infrastructure

Different chapters of this thesis showed how resistant bacteria have shaped new practices of various actors who had to adapt to new biological realities. Referring to the work of Bowker and Star (2000) it can be argued that bacteria turned into a material-objective force that creates and mediates actions and practices. In this context, bacteria can be understood as boundary objects. The concept of boundary objects was originally developed by Star and Griesemer (1989), who analysed how different actors with their diverse interests and goals can work in cooperation with each other. They studied how amateur naturalists, professional biologists and philanthropists built cooperations between each other that allowed the formation of the Museum of Vertebrate Zoology at the University of California from 1907–39. Star and Griesemer (1989) argue that the cooperation between different actors was possible because of two elements of translation between the work of these actors: the standardisation of methods and the development of boundary objects. The standardised methods allowed for communication between different actors involved in the process of knowledge production. The standardised way of labelling specimens connected the work of amateur collectors and the work of professional scientists; while the former collected specimens in nature, the latter could analyse them only if they were properly labelled according to the standards. However, standardised methods are not enough to ensure cooperation between different actors. Star and Griesemer (1989) elaborate that to cooperate, different actors create boundary objects that facilitate translation between their heterogeneous interests and values without diffusing them. A boundary object is an analytical concept that refers to 'objects which both inhabit several intersecting social worlds and satisfy the informational requirements of each of them'. A library can be understood as a boundary object: diverse actors can use a library as a source of information or as a workspace, though they do not necessarily have to negotiate these differences between each other.

Following this line of argument, bacteria, both resistant and non-resistant, can be analysed in terms of infrastructure. This means analysing how bacteria and their mechanisms are interwoven into the conventional infrastructures related to health and illness. For instance, we clean our hands with soap to keep bacteria out and to stay healthy; we also eat yoghurt and take probiotics to have bacteria inside our bodies and to stay healthy. By defining health and illness, bacteria influence the conventions of interpersonal relations and the notion of social living with bacterial others. They also shape economic and policy processes, disturbing or opening up opportunities for international trade and mobility.

Being part of different worlds and work practices, bacteria enable multiple processes of cooperation between heterogeneous actors, like healthcare professionals and farmers, or refugees and microbiologists. These processes involve both the creation of boundary objects to allow for cooperation between these actors and – simultaneously – the creation of boundaries between them. While bacteria connect the health of humans, animals and the environment, they simultaneously create infrastructural, hierarchical boundaries between these sectors and between different species. Similarly, in scientific research, bacteria can be seen as connecting the different geographical territories highlighting their routes of transmission. But this can also stimulate the creation of boundaries between those territories as 'healthy' or 'unhealthy'.

To conceptualise the work of bacteria as infrastructure, it is important to recognise that infrastructure is never neutral. Bowker and Star (2000) elaborate on the political nature of any infrastructure that brings forward certain perspectives while silencing others. They give an example of how school systems classify students based on their standardised test results that valorise only certain knowledge skills while making other skills invisible; for instance, a test may show that a student can calculate a certain mathematical formula, but it does not show that a student can also critically reflect on this formula as faulty. Another example from their work is the infrastructure of the US Immigration and Nationalisation Service. This service classified particular social classes and people in terms of skills, and in the classification system specific skills like computer engineering were considered desirable. The use of this classification resulted in a quota system where people from more affluent countries were preferred over people from poorer countries.

In line with this, Law and Mol (2008) argue that material artefacts and processes can be understood as political. Analysing practices of boiling pigswill in UK farms, they show that a material object or material practices can be analysed as performing political work. Elaborating on the technique of boiling pigswill, the authors explain that this technique aims to protect pigs from bacteria, which could be present in illegally imported meat from countries where foot and mouth disease is endemic. However, not all farmers follow it, which means that infected illegally imported meat can reach pigs. Thus, Law and Mol (2008) show, boiling pigswill can be seen as a political technique that implicitly divides the world into 'disease-free countries', like the UK, and 'countries where foot and mouth are endemic', like Bangladesh.

Considering infrastructure as political, it is important to reflect upon the politics of bacteria. Analysing bacteria as an infrastructure that performs material politics allows for scrutiny of what kind of hierarchies are developing, what perspectives are dominant and which are silenced. Therefore, an infrastructure of bacteria stimulates a further analytical endeavour

towards new social, economic and political relations moving beyond antibiotic-related practices. This means that we shift the focus from antibiotics to bacteria, analysing how these microorganisms influence and shape our societies: what the role of bacteria is in the organisation of healthcare practices, the practices of inter-personal relations and practices of animal husbandry; how bacteria move across national borders and what conditions they establish for trade and human mobilities and how the prevalence of bacteria in different areas of the world shape international relations and immigration law between these areas – to answer these questions we need to untangle bacterial infrastructures.

Becoming a part of the One Health policy arena, resistance bacteria have stimulated new practices and standards for professionals working in healthcare, animal husbandry and agriculture. As any emerging infrastructure, bacteria have connected to the already established basis of international health regulations that focus on human health control and prevention and, in line with that, bacteria have stimulated a policy trajectory to protect the health of humans. In the already existing context of One Health, the bacterial infrastructure brings forward the interests of some actors while backgrounding others. Certain sectors, like wildlife, have become predominantly silenced in the political arena of infection management. Different knowledge practices have also been arranged in an unequal way where biomedical knowledge about human health has prevailed over social science insights. Reflecting on One Health as a boundary object within bacterial infrastructure unpacks the emerging processes of cooperation between different sectors and assignation of different values and responsibilities to each of them.

We can observe similar processes in public health and clinical settings. The potential threat of resistant bacteria that became associated with some mobile groups, in particular with refugees, has stimulated the development of screening practices. These screening practices can be analysed as both consequences of public health control and as a cause of potential stigmatisation of refugees as dangerous others. Engaging with practices of refugees, microbiologists, public health doctors and public health nurses, I showed how these groups were engaging with resistant bacteria. AMR screening, while being contested by some actors and supported by others, navigates the relationships and practices between these heterogeneous actors. Although it was debated upon by different participants in my research, the technique of screening applied to refugees has already brought forward the health risk voices of the biomedical community and silenced those from public health nurses and refugees.

In clinical settings, the problematisation of AMR as self-treatment with antibiotics has stimulated policy developments to control the prescription and use of these medicines. The

analysis of emerging control policies, particularly obligatory medical prescriptions, as boundary objects that navigate the collaboration between doctors, patients and pharmacists opens up an interesting perspective on this collaboration. My analysis showed that obligatory medical prescription has stimulated informal collaborations amongst doctors, patients and pharmacists to deliver care beyond governmental restrictions. In a way, Bowker and Star (2000) highlight that infrastructure is 'never changed from above' and that 'changes take time and negotiation, and adjustment with other aspects of the systems involved'. These adjustments can be seen in the case of Russian healthcare practices that utilise informal communication to adapt to the new realities manifested by resistance bacteria.

In the scientific arena of AMR research, heterogeneous actors, including researchers, medical professionals, funders, policymakers and laypeople, contribute to the process of knowledge production. Research technology, methodology and protocols and scientific language and its metaphors can be considered boundary objects that influence the processes and the results of knowledge production. An emerging concern for resistant bacteria has been reflected in the developments of new diagnostics, new microbiological lab equipment and new metaphors that describe the 'import' of bacterial 'intruders' from countries with 'low level of hygiene' to 'high-income countries'. The presence of resistant bacteria enables hierarchical imaginings of a world that has become divided into 'healthy' and 'unhealthy'.

Expanding the focus from antibiotic infrastructure to bacteria as infrastructure provides insights into how these bacteria have established different social worlds. Studying the history of antibiotic development and the use of these medications, Landecker (2015) shows how this history has manifested itself in the biology of bacteria that acquire resistant mechanisms. She shows how human history and modern ways of living have been built on the opportunities that were opened up by antibiotics. Many studies in social science have demonstrated the functioning of the antibiotic world: the concept of illness as something technical that can be quickly tackled, the concept of hygiene as something sterile and non-bacterial and the various practices of mobility as something safe and non-risky (Hinchliffe & Ward, 2014; Newman et al., 2016; Willis & Chandler, 2019). However, these studies also show that the antibiotic world is slowly losing the war against bacteria. Therefore, the shift, both analytical and political, from antibiotics to bacteria enables the imagining of a different type of social living and the adjustments that are necessary for this living. Focusing on the mechanisms and capacities of bacteria rather than the opportunities of antibiotics allows the exploration of potential peace with bacteria that make our living possible.

When my supervisors and I were debating the idea of a peace treaty with bacteria, we concluded that many current practices of dealing with infectious diseases could already be understood as steps towards this peace (e.g. a delay in antibiotic treatment or the development of probiotics or faecal microbiota transplant). Reflecting on my journey through the different settings and practices related to AMR, I came to the realisation that being a part of a transdisciplinary research team was one of the most important elements of this journey. Discussing various social practices that I was analysing in my fieldwork, I was in a continuous dialogue about the role and mechanisms of bacteria in these practices. This focus on bacteria was something I found to be limited in many policies and social science debates about AMR. Understandably, social scientists would not debate about the biology of bacteria but I think we, as a research community, need to take important steps towards the integration of bacteria into the social world and vice versa. The socialisation of bacteria, not only antibiotics, is a crucial step in understanding how to make the micro and macro worlds coexist.

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Appendices

VALORISATION

Societal relevance is an important component of scientific research, and Maastricht University encourages explicit reflection upon this aspect in a separate chapter of a PhD thesis. Therefore, here I will outline how my journey through different AMR practices has contributed and will contribute to the development of practical and analytical tools for understanding and communicating this phenomenon. I will reflect upon new opportunities for research and policymaking that can be opened up by transdisciplinary collaborations, and I will describe how the results of this thesis have been disseminated among health professionals and laypeople.

New opportunities for transdisciplinary understanding of AMR

In the arena of health policy, AMR has often been understood as a biological fact, the solution for which can be found in laboratories that produce new technologies for AMR screening and new medications for the treatment of infections (O'Neill, 2016; WHO, 2015). In this context, human practices of antibiotic use have been problematised as something that needs to be fixed through awareness campaigns and behavioural control programmes (Rodrigues, 2020; Will, 2019). We can see such conceptualisations of AMR in the *Global Action Plan on AMR* by the WHO, OIE and FAO (2015), in the *European One Health Action Plan against AMR* (2017), and in the influential report on AMR by the British economist Jim O'Neill (2016). However, as I have shown throughout this thesis, such approaches to AMR have been widely criticised by scholars in the biomedical and social sciences (Chandler, 2019; Larsson, 2014; Will, 2018). One of the major points of this criticism is that AMR is not only a biological but also a social phenomenon, which is shaped through various social, economic and political processes (Chandler, 2019). In addition, neither the biological nor the social nature of AMR can be understood as a fixed fact because knowledge about bacteria and their social embeddedness is constantly changing. Therefore, scholars in both the biomedical and social sciences have argued for more nuanced approaches to AMR that reflect the social context and the biological uncertainties of this phenomenon (Chandler et al., 2016; Collignon et al., 2018; Smith, 2015).

Following the traditions of STS that suggest analysing knowledge as constructed through different practices (Latour & Woolgar, 1986), this thesis unpacked several systemic and infrastructural nuances that have influenced AMR practices and shaped AMR in different settings. This approach did not dismiss the biological nature of AMR, but it engaged with bacteria as a social phenomenon that influences and is influenced by policymaking practices, the organisation of healthcare delivery and epistemic practices. Analysing AMR knowledge as

constructed, this thesis also tried to bring together biological and social constructions of bacteria.

The analysis of the *social life* of AMR opens up opportunities for alternative research and policymaking, where AMR is conceptualised as a biosocial phenomenon that can be addressed through transdisciplinary collaborations. Transdisciplinarity is often understood as an ambitious project for systemic integration of knowledge that 'transcends the scope of disciplinary worldviews' (Klein, 2017). This integration allows the development of more comprehensive, holistic understandings formed by a diversity of languages, methods and epistemic practices (Hackett et al., 2017). The importance of transdisciplinarity in AMR research and policymaking is emphasised by the urgent need for transformation of the current practices, policies and economic organisations that are not able to respond to the growing concern about AMR. AMR is a complex issue, and different specialist approaches are not able to resolve it on their own. Transdisciplinary approaches and the integration of biosocial perspectives to address the biosocial phenomenon of AMR are crucial steps that require the transformation of research infrastructures and policy choices that present AMR as static and universal in every social context.

Studies in microbiology have shown that AMR refers to various microorganisms and various mechanisms of resistance, which can be natural or acquired (Cox & Wright, 2013; Reygaert, 2008). Studies in social sciences have demonstrated how various social and political processes shape different antibiotic practices, including antibiotic use, distribution and waste management (Collignon et al., 2018; Lambert et al., 2019; Willis & Chandler, 2019). However, the insights from these two very different disciplines have rarely been put into a dialogue with each other, which hinders the production of adequate explanations of AMR (Smith, 2015). The lack of such dialogue can be seen in policy approaches to AMR that neither fully engage with the biology of bacteria nor with its diverse social practices. Namely, environmental aspects of AMR are largely outside the political scope as are economic and social inequalities that hinder access to antibiotics. Instead, national awareness campaigns, as well as international policy regulations, narrow their approaches to AMR as something technical that can be solved by the production of new antibiotics and changes in antibiotic use by implementing guidelines and protocols (Hinchliffe & Ward, 2014; O'Neill, 2016; Will, 2019).

Engaging with the biosocial diversity of AMR, rather than focusing on its selective features, is a necessary shift for the development of comprehensive and meaningful approaches to resistant bacteria. To allow this shift, biomedical and social sciences should be engaged in a closer transdisciplinary dialogue to exchange and question each other's epistemic practices of

knowledge production, including the use of scientific language, methods and theoretical instruments. This questioning of epistemic practices will provide a basis for 'co-contamination' of these practices – introducing the insights of the social science world into the world of the laboratory and vice versa. Although the concept of co-contamination may go against the methods of different disciplines that have their established vocabulary and conventions of dealing with research topics, it opens the window for innovation and alternative approaches that may be impossible within the frames of one discipline.

The current disciplinary separation of biological and social studies of AMR hinders the potential integration of knowledge produced in these disciplines. By studying the biology of bacteria, microbiologists also learn about the biological dynamics of social worlds from where these bacteria came from and what practices they were a part of. In a similar way, by studying social practices and the processes related to health and hygiene, social scientists learn how bacteria become part of social, political and economic processes. The biological and the social nature of AMR is manifested in the bacteria themselves; however, the epistemic practices that produce knowledge about the biosocial nature of bacteria are currently separated.

To open up the opportunity for transdisciplinary research between the biological and social aspects of AMR, we need to revisit the epistemic distinction of knowledge production practices. The work of the STS scholar Latour (1983) may serve as a helpful guide here. Reflecting on the transformative capacity of a laboratory, Latour (1983) rephrased the famous Archimedean expression into the following: 'Give me a laboratory and I will raise the world'. By rephrasing a famous Greek motto, he aimed to address a crucial distinction between the micro and macro level of social studies of science, where the former refers to the analysis of the interpersonal relationships between people or social groups, and the latter refers to the analysis of social institutions. To show the meaninglessness of this distinction, Latour (1983) refers to his analysis of the laboratory work of Louis Pasteur and his development of the anthrax vaccine.

Following the work of Pasteur, Latour shows that the introduction of the vaccine was not a clear and linear process from the laboratory to society. Rather, Latour (1983) argues, Pasteur first had to convince farmers, veterinarians and hygienists that anthrax was caused by bacteria – he had to make this bacteria visible for others in his laboratory. He then had to convince them that there was a cure that could tackle this bacteria – he did experiments in his laboratory showing the vaccine worked. Then he had to convince them once more that the vaccine worked not only in his laboratory but also on farms, if farmers followed his instructions. Given this example, Latour (1983) argues that by studying the work of one laboratory of Pasteur – a study

that would usually be referred to as micro-level – a researcher can see the social (or macro) transformations of society. Latour shows how, by convincing different actors in society (e.g. veterinarians, farmers and hygienists), Pasteur introduced the *Bacillus anthracis* as a new actor in this society, which he could control. But to establish this control, Pasteur did not just release the vaccine to society for free use, he turned society into his laboratory by setting the conditions under which this vaccine would work. That's the motivation for the Latour's alteration of the Archimedean motto – for Pasteur to introduce an anthrax vaccine, he had to turn the world into his laboratory and make the *Bacillus anthracis* a part of this world.

The reason I introduced the work of Latour (1983) here is to highlight once again that the laboratory and society do not exist in two parallel worlds, where the scientific facts from a laboratory are simply transferred to society. Rather, these two worlds co-create each other. A laboratory can raise the world by turning it into a laboratory and introducing new inhabitants to it. But the world can be turned differently, depending on what laboratory it is. Pasteur turned the world into a microbiological laboratory, introducing microorganisms with their biological mechanisms as the new inhabitants. These biological microorganisms, according to Pasteur, could be conquered with his vaccine. However, the laboratory world that Pasteur introduced did not incorporate the socio-economic divisions and inequalities that can be shaped by these microorganisms via access to vaccines. Establishing transdisciplinary laboratories and allowing the co-contamination of biological and social sciences may result in the creation of a different world where micro-organisms and their biological mechanisms have to co-exist with macro-organisms and their social practices. This is a necessary step for understanding bacteria and their socialisation processes.

Communicating antimicrobial resistance

Throughout my research, I organised several events to communicate my findings on AMR to professionals and laypeople. One of these events was Antibiotic Awareness Day, which took place at the Siberian State Medical University on 21 March 2018. Organising this event, I invited professionals from three different disciplines: medicine, microbiology and philosophy. Such disciplinary diversity enabled discussion of AMR as a biosocial phenomenon, highlighting different nuances from every discipline. The event took place at the building of a

medical university, which attracted many medical students who often did not work with non-biomedical dimensions of AMR. In total, about 50 people participated in the event.

Following Antibiotic Awareness Day, in collaboration with a medical doctor from the Siberian State Medical University, I organised two social science student research projects on AMR. Both projects aimed to understand antibiotic practices of patients and medical doctors in Tomsk, Russia. Throughout these projects, I provided students with several workshops on qualitative methods and transdisciplinary approaches to AMR. The major aim of these projects was to introduce students to the importance of knowledge diversity in understanding and addressing such phenomena as AMR.

Poster from the Antibiotic Awareness Day at Siberian State Medical University on 21 March 2018, Tomsk.

Apart from education projects in Russia, I developed a case study on AMR for one of the learning activities within the Philosophy in Action course at Maastricht University. This course was taught in the health sciences bachelor's programme, and it invited students to reflect on different biomedical topics by applying the theories of ethics. In addition, I developed two case studies for the course Communicable and Non-communicable Disease in the EU and WHO European Region for the European public health bachelor's programme at Maastricht University. These case studies aimed to show students the importance of transdisciplinary communication and collaboration in addressing such phenomena as AMR. Bringing together the insights from both biological and social sciences, I showed students the various angles that different knowledge practices can bring into their future professional practice.

The insights from my research have also been communicated to different professionals in the field of microbiology. I was invited to participate in the research day of the Microbiology Department of Maastricht University where I presented the results of the project that was described in Chapter 2. This engagement stimulated some important conversations on how we can bridge different types of knowledge that have been produced in various disciplines.

Assembling a biosocial puzzle of knowledge practices

Within the last decade transdisciplinarity has increasingly become an important component of much research and one of the requirements for funding (Hessels et al., 2010; Mattsson, 2015). Transdisciplinarity was also at the core of my research in that I collaborated with microbiologists and public health professionals. Many studies that aim to combine different types of knowledge run the risk of co-existing on the same project without co-producing results (Parker, 2010). To address this risk, one of the aims of my research was to build a coherent collaboration with professionals working with the biological side of AMR. The methodology of stool and stories that was presented in chapter five is a result of this collaboration where I aimed to bring microbiological and social science knowledge into a dialogue with each other.

Picture from a transdisciplinary symposium on the cross-border movements of microorganisms, 22 November 2018, Maastricht.

To stimulate the development of transdisciplinary knowledge production practices, I co-organised a symposium on the cross-border movements of microorganisms. The symposium took place in Maastricht on 22 November 2018, and it brought together professionals from anthropology, microbiology, art, infectious diseases and sociology. As a result of this symposium, together with six other participants, I applied and received the Mingler scholarship to conduct a collaborative research project that will combine insights from microbiology, epidemiology, sociology and art. Following the insights from my thesis work, this research project will develop an understanding of the cross-border movements of microbes and propose alternative epidemiological mappings of these movements.

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SUMMARY

Introduction. Antimicrobial resistance (AMR) is a growing public health concern globally that calls for comprehensive transdisciplinary approaches. Although AMR refers to biological mechanisms of bacterial resistance, it is a deeply social phenomenon that is influenced by economic, political and cultural processes. Studies in microbiology have provided important insights into the biology of bacteria and their different ways of acquiring resistance. In turn, studies in social sciences have shown how antibiotic-related practices, including prescription, use, production as well as utilisation of antibiotic waste may influence the development of AMR. In this thesis, I took a step forward from studying antibiotic-related practices and analysed how AMR is incorporated and *practised* in different settings of policy, healthcare and science, and what kind of reality is *constructed* through these practices.

This thesis is a report of my journey through settings where I studied how AMR has been changing the social worlds of different actors. These settings included the world of international policy regulations on AMR and One Health approach to it; the world of public health AMR screening of refugees in the Netherlands; the world of antibiotic practices among medical doctors, pharmacists and patients in Russia; and the world of science with its diverse metaphors and methods to address AMR. The different chapters of this thesis elaborate on my findings from the journeys to each of the social worlds and their practices.

Chapter 1 analyses the policy world of AMR where the One Health approach has been gaining popularity since the publication of the Global Action Plan on AMR in 2015. Analysing international policy regulations on AMR, as well as more general health regulations from which AMR documents are derived, this chapter reflects on how the One Health approach shapes AMR in the international policy arena. Policy documents are understood here as performative – they are not simply describing the reality about AMR and One Health approach to it, but they construct this reality and influence practices of individuals involved in the human, animal and environmental sectors. The chapter engages with the theories of post-humanism to critically examine the modes of relations between the human, animal and environmental sectors that One Health approach to AMR proposes. It shows that despite the One Health ideal to build inter-sectorial collaborations for addressing shared health concerns, AMR policy regulations that implement One Health shape hierarchies between the health of different species and between knowledge practices of professionals working with these species.

Chapter 2 shifts the focus from the policy arena to public health practices of AMR screening of refugees in the Netherlands. This chapter analyses how AMR has been constructed

as a potential risk posed by the incoming refugees. Focusing on different perspectives of microbiologists, public health doctors, public health nurses and refugees, AMR screening is shown to be a constructed phenomenon that can be understood as either a necessary public health measure, an unnecessary stigmatising technique, or a potential for the improvement of personal health. While the debates about the necessity of AMR screening of refugees have been taken place on the pages of scientific journals, this chapter reflects on a different question: how to perform an AMR screening of refugees to accommodate the diverse perspectives of different actors? The chapter is arguing for the need for co-production processes in developing and implementing the technique of screening, where the public health needs and potential risks of stigmatisations are equally considered.

Chapter 3 moves from the world of public health in the Netherlands to the world of healthcare practices in Russia. This chapter analyses antibiotic practices of medical doctors, pharmacists and patients against the background of the recently introduced policy requirement for the medical prescription on antibiotics. While this requirement aims to tackle the over-the-counter sale of antibiotics defining AMR as a problem of self-treatment, the chapter provides a more nuanced reflection on how AMR is practised and how antibiotic care is organised in Russia. Self-treatment practices with antibiotics are the results of different processes, including the lack of medical personal in the clinical settings that hiders a timely provision of care, and the inability of many patients to take time off work to visit a medical doctor. Recognising these different processes, medical doctors, pharmacists and patients adopt informal techniques to deliver and access antibiotics beyond the policy requirement for medical prescription. The chapter analyses these informal techniques as compensatory responses of healthcare professionals to the gaps in the official healthcare system.

Chapter 4 focuses on how microbiologists imagine AMR as a global phenomenon, which can be transmitted and disseminated from one country to another. Analysing metaphors that microbiologists use in their scientific articles on AMR and travelling, this chapter shows how the notion of global is presented in a very specific way. Using such metaphors as AMR ‘reservoirs’ and bacterial ‘intruders’, the metaphors in microbiology imagine the global transmission of AMR as a linear process where bacteria from low-income countries are transmitted to high-income countries with ‘better hygiene’. The chapter argues that metaphors are not just figures of speech, but they help in navigating scientific research processes. Describing certain countries as AMR reservoirs and other countries as those with better hygiene may lead to the one-sided research processes, where the potential transmission of AMR from incoming travellers to countries-reservoirs is overlooked as less significant.

Chapter 5 describes an experimental methodology 'stool and stories' that was developed by Maastricht University team to study AMR as a biosocial phenomenon. Following the cohort of graduate students who travelled from different parts of the world to India, this chapter brings together the data from microbiological stool sample analysis and the data from semi-structured interviews conducted with the same cohort. The two diverse sets of data focus on the same research question about the importance of AMR for international travelling but give different answers to this question. While microbiology highlights the potential risks for acquiring AMR when travelling internationally, social science data shows that travellers themselves do not consider AMR to be a relevant health problem in the context of travelling. This difference in answers demonstrates the important gap between the biological and social constructions of AMR, which are currently not connected.

Chapter 6 is a short reflection on my PhD journey as a transdisciplinary practice. This reflection argues for the infrastructural changes in the current ways of organising knowledge production practices that separate biomedical and social science approaches to AMR. Rather, the collaborative platforms, including academic journal and conferences, and transdisciplinary funding for understanding AMR should be established and promoted at the national and international levels.

General discussion and conclusion. The six chapters of this thesis focus on different settings and various practices of AMR. This diversity highlights that AMR is not a static and universal phenomenon that can be addressed in a similar way regardless of the context. On the contrary, the different insights from each of the chapters show that AMR acts and is acted upon in various ways depending on the hierarchies between different species and disciplines, the perceptions of risks, the available opportunities for treatment, and the language and methods of scientists who analyse and address AMR.

Departing from the analysis of antibiotic practices and focusing on how AMR is practised in different settings, this thesis offers an alternative analytical and political shift in understanding this phenomenon. It is a shift from antibiotics as a leading focus for understanding social and political processes related to AMR, to bacteria and changes that they introduce to social where they are situated. This shift allows for the understanding of AMR beyond antibiotic-related practices, AMR is analysed as constructed through the language of scientists and as a part of the daily reality of travelling and human mobilities. This has also political implications as it requires a change in the paradigm where social worlds with their daily practices of travelling, healthcare and farming have to be adapted to the biological mechanisms of bacteria, rather than to the opportunities offered by antibiotics.

SAMENVATTING

Inleiding. Antimicrobiële resistentie (AMR) is wereldwijd een groeiend probleem voor de volksgezondheid dat vraagt om een transdisciplinaire benadering. Microbiologische studies hebben belangrijke inzichten geleverd in de verschillende manieren waarop bacteriën resistentie verwerven. Onderzoek in de sociale wetenschappen heeft op haar beurt aangetoond hoe sociale-, politieke- en economische processen antibiotica productie, gebruik, en afval beïnvloeden en daardoor de ontwikkeling van AMR bevorderen dan wel remmen. Tegen de achtergrond van dit onderzoek heb ik geanalyseerd hoe AMR wordt geconstrueerd in verschillende settingen – beleid, gezondheidszorg en wetenschap. Het proefschrift is als het ware een verslag van mijn reis door deze verschillende werelden van AMR. Ik bestudeerde de ontwikkeling van de One Health-aanpak in de internationale beleidsarena; perspectieven op AMR-screening van vluchtelingen in Nederland in het kader van de volksgezondheid; omgang met antibiotica-richtlijnen door artsen, apothekers en patiënten in Rusland; en het gebruik van metaforen in microbiologisch onderzoek naar de relatie tussen AMR en internationaal reisgedrag. De verschillende hoofdstukken van dit proefschrift zijn een verslag van mijn reis naar een van deze werelden.

Hoofdstuk 1 analyseert de beleidsarena waarin de One Health-aanpak, die sinds de publicatie van het Global Action Plan on AMR in 2015 aan populariteit wint, werd ontwikkeld. Ik analyseer de internationale beleidsdocumenten op het gebied van AMR en het internationale gezondheidsbeleid waarvan AMR-documenten zijn afgeleid, en bekijk hoe de One Health-aanpak voor AMR in deze documenten wordt vormgegeven. Beleidsdocumenten worden hier opgevat als performatief – ze beschrijven niet alleen de realiteit over AMR maar ze construeren deze realiteit en ook de handelingspersdpectieven van betrokkenen uit de gezondheidszorg, de veeteelt en de milieusector. Het hoofdstuk gebruikt theorieën van het post-humanisme om de relaties tussen deze sectoren in de One Health-benadering van AMR kritisch te onderzoeken.

De analyse laat zien dat de One Health-benadering voor de aanpak van AMR, ondanks de doelstelling om intersectoraal te werken, impliciet hiërarchieën creëert tussen de gezondheid van mensen, dieren en ecosystemen, en ook tussen professionals die in deze domeinen werken. De gezondheid van mensen wordt als het meest centrale probleem gezien, en de andere sectoren moeten bijdragen aan de oplossing ervan. De gezondheid van dieren, gedomesticeerd en wild, en van het ruimere milieu verschijnt onbedoeld als ondergeschikt aan dat van mensen.

Hoofdstuk 2 verschuift de focus van de beleidsarena naar de volksgezondheid, en onderzoekt perspectieven op AMR-screening van vluchtelingen in Nederland. De

vluchtelingen crisis leidt in 2015 zichtbaar in Europa tot discussies over nut en dilemma's van AMR-screening van vluchtelingen. Tegen de achtergrond van deze discussies heb ik verschillende perspectieven op de mogelijke constructie van vluchtelingen als een gezondheidsrisico onderzocht. Ik heb interviews gedaan met microbiologen, volksgezondheidsartsen, verpleegkundigen en vluchtelingen, en het blijkt dat AMR-screening vanuit hun perspectieven een verschillende betekenis krijgt. Microbiologen en artsen werkzaam in de publieke gezondheidszorg zien screening als een noodzakelijke maatregel in het kader van het onderzoek naar de volksgezondheid, verpleegkundigen zien het als een onnodige stigmatiserende interventie die weinig bijdraagt aan de volksgezondheid, en veel vluchtelingen zien screening als een potentiele techniek voor verbetering van de persoonlijke gezondheid en als er geen individuele uitslagen worden gegeven zien zij het over stigmatiserend. Terwijl de debatten over de noodzaak van AMR-screening van vluchtelingen primair een debat was van microbiologen in wetenschappelijke tijdschriften, heb ik geprobeerd de actoren te onderzoeken die er in de praktijk mee te maken zouden kunnen krijgen. Het hoofdstuk pleit voor meer samenwerking bij de ontwikkeling en implementatie van de screening, waarbij volksgezondheidsrisico's en risico's van stigmatisering beide worden gewogen.

In **hoofdstuk 3** gaat de reis verder naar de wereld van de gezondheidszorg, en wel de gezondheidszorg in Rusland. Rusland is een interessante setting omdat recentelijk maatregelen zijn getroffen om wetgeving die antibiotica gebruik zonder doktersvoorschrift tegen moet gaan, te gaan implementeren en handhaven. Tot voor kort konden mensen antibiotica bij de apotheker halen: aan deze vorm van 'zelfmedicatie' moet nu een einde komen. We hebben interviews gedaan met artsen, apothekers en patiënten om te onderzoeken hoe zij omgaan met deze eis van antibioticagebruik op medisch voorschrift. De analyse geeft een reflectieve blik op de organisatie van antibioticagebruik en zorg voor bacteriële infecties in Rusland. De zogenaamde zelfmedicatie met antibiotica moet begrepen worden in de specifiek Russische context die gekarakteriseerd wordt door gebrek aan medisch personeel in de klinische setting, lange wachttijden, de gebrekkige mogelijkheden van veel patiënten om vrijaf te nemen en dus inkomen te derven om een arts te bezoeken. Omdat iedereen dit weet en artsen toch 'goede zorg' willen leveren, ontstaan er informele infrastructurele antibiotica praktijken om ''het verplichte recept'' werkbaar te maken. Dokters schrijven recepten voor een langere duur, voor het geval dat de klachten verergeren, of een hogere dosis zodat patiënten vooruit kunnen. Deze informele praktijken compenseren de hiaten en de problemen in de formele gezondheidszorg.

Hoofdstuk 4 analyseert metaforen die microbiologen gebruiken om hun wetenschappelijk onderzoek over AMR en reizen te presenteren. Metaforen zijn interessant omdat ze geen onschuldige beeldspraken zijn, maar verbeeldingen van de realiteit en als zodanig een basis om te handelen. Metaforen geven als theoretische concepten richting aan wetenschappelijk onderzoek, ook aan disciplines die het imago hebben dat ze ‘’de natuur’’ representeren. Ook in deze disciplines speelt taal echter een sleutelrol in de verbeelding van onderzoeksresultaten. Voor de analyse heb ik een specifieke set belangrijke wetenschappelijke artikelen van microbiologen onder de loep genomen. De analyse laat zien dat onderzoekers met behulp van metaforen als AMR ‘reservoirs’ en bacteriële ‘indringers’, de overdracht van AMR op wereldschaal schetsen als een proces waar gevaarlijke bacteriën uit lage-inkomenslanden worden overgedragen aan landen met een hoog inkomen met een ‘betere hygiëne. Hiermee worden landen impliciet als ‘goed’ en ‘slecht’ voorgesteld. Het beschrijven van bepaalde landen als AMR-reservoirs en andere landen als landen met een betere hygiëne, leidt er toe dat de overdracht van AMR van inkomende reizigers naar deze landen-reservoirs minder aandacht krijgt. Ook worden landen als homogene entiteiten voorgesteld terwijl grensgebieden bijvoorbeeld vaak andere patronen laten zien. De conclusie luidt dat het belangrijk is om te reflecteren op metaforisch gebruik van kernconcepten in AMR onderzoek en wat zij doen in beeldvorming en in de verdere ontwikkeling van onderzoek, omdat ze impliciet sommige zaken naar de voorgrond en de achtergrond duwen.

Als onderzoeksteam zijn we overtuigd van de waarde van transdisciplinair onderzoek naar AMR. **Hoofdstuk 5** beschrijft het gebruik van een experimentele transdisciplinaire methodologie ‘stool and stories’ die we hebben ontwikkeld om AMR te bestuderen als een bio-sociaal fenomeen. Dit hoofdstuk presenteert de microbiologische analyse van ontlastingsmonsters en de sociologische analyse van semi-gestructureerde interviews, beide uitgevoerd binnen een cohort van studenten die de Global Health master volgden en uit verschillende delen van de wereld naar India reisden voor een symposium. De twee verschillende datasets richten zich op dezelfde onderzoeksvraag over het belang van AMR voor internationale reizen, maar geven verschillende antwoorden op deze vraag. Terwijl de microbiologische analyse (stool) laat zien hoe internationaal reizen samenhangt met het verwerven van AMR, toont de sociale wetenschappelijke analyse (stories) dat reizigers zelf AMR niet als een relevant gezondheidsrisico van reizen beschouwen. Dit verschil wijst erop dat de biologische en sociale constructies van AMR – ook in een cohort van hoogopgeleide en in de gezondheidsdisciplines geschoolde studenten - niet met elkaar verbonden zijn. De

conclusie is dat het voor een beter begrip van AMR en AMR-preventie noodzakelijk is dergelijke verschillende resultaten met elkaar in dialoog te brengen.

Hoofdstuk 6 is een korte reflectie op mijn promotietraject als een transdisciplinair onderzoek. Deze reflectie pleit voor infrastructurele veranderingen in de huidige organisatie van het AMR-onderzoek, waarbij biomedische en sociaalwetenschappelijke benaderingen van AMR sterk gescheiden zijn. In plaats daarvan moeten er transdisciplinaire samenwerkingsplatforms, wetenschappelijke tijdschriften, conferenties, en financieringsvormen gecreëerd worden op nationaal en internationaal niveau, om AMR te begrijpen.

Discussie en conclusie. De zes hoofdstukken van dit proefschrift laten zien dat AMR niet een ding is, maar in verschillende contexten als een ander fenomeen wordt geconstrueerd, en op verschillende manieren wordt behandeld: de aanpak van AMR wordt uitgedrukt in termen van hiërarchieën tussen soorten, sectoren en disciplines, risico's voor gezondheid en voor stigmatisering, relaties tussen gezonde en riskante werelddelen. Op basis van mijn onderzoek stel ik voor om meer aandacht te besteden aan de politiek, economische en sociale infrastructuren die door AMR in het leven zijn geroepen. Een transdisciplinaire benadering is daarbij noodzakelijk.

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AUTHOR DETAILS

Alena Kamenshchikova (1992) is a researcher at the Department of Health, Ethics and Society, Maastricht University. She began her PhD studying the bio-social worlds of AMR in 2017 after receiving an Erasmus+ grant for recent graduates. Before starting to work at Maastricht University, Alena was working as a junior researcher at the Research Centre for Policy Analysis and Studies of Technologies in Tomsk, Russia.

Alena obtained a Master's degree in Philosophy from the University of Tartu in Estonia in 2017 (*cum laude*), and a Bachelor's degree in Sociology from Tomsk State University in Russia in 2014. She also attended several MA courses on Global Health at Maastricht University in 2014, and courses on Migration Studies at Lund University in Sweden in 2016.

Starting from 2015, Alena received several grants and scholarships, including the tuition waiver scholarship at the University of Tartu in 2015 (€7,480), the NordPlus Higher Education Programme for mobility for the Nordic and Baltic countries in 2016 (€1,330), the Estonian government program Dora Plus for talented international Master's students in 2017 (€3,500), and the Erasmus+ traineeship grant for nine months at Maastricht University in 2017 (€6,800).

Following her PhD research, Alena works on the development of a transdisciplinary agenda for understanding the bio-social worlds of AMR and infectious diseases. She is currently involved in a collaborative project titled 'Bacteria & borders. Experimental cartography between art, lab & (daily) life' where together with microbiologists, public health specialists, philosophers and artist, she is working in developing alternative imaginings of bacterial border-crossing movements. This project was supported by the Mingler Scholarship in 2020 (€10.000). In parallel, Alena is developing her line of research, conceptualising bacteria as infrastructure that influences and shapes the modern ways of living.

LIST OF PUBLICATIONS

Will, C., & **Kamenshchikova**, A. (2020). From universal frames to collective experimentation? Pursuing serious conversations about antimicrobial resistance. *Wellcome Open Research*, 5(192), 192. (Open letter)

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