Is the public health aim of antibiotic reduction overriding AB usage in China?

Exploring the moral considerations of antibiotic usage and restriction in China

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Executive Summary

Worldwide humans are threatened by the growing antibiotic microbial resistance problem. Recently the WHO, global infectious diseases researchers and AMR experts have gathered together to set global targets to reduce AB usage for fighting AMR worldwide.¹ This thesis explores whether the global antibiotic reduction policy aim overrides antibiotic usage now in China. The main research question entails whether the global public health aim of antibiotic reduction overrides AB usage in China? The study's direct relevance is the global antimicrobial resistance problem. China is of particular interest because of it's huge total consumption of Abs in combination with it's massive amount of citizen's.

In fact, recent statistics from the Academy of Sciences of China showed that China consumes 162 thousand tons of ABs, which is more than half of the world's total consumption. 52% of these ABs are used in their farming, and 48% are used by people.² More than 50 thousand tons of ABs flow to the soil and water, affecting the ecosystem. These amounts are worrisome as, according to the World Economic Forum, antimicrobial resistance constitutes one of the main risks to human health.³ AMR is threatening the health of both present and future humans.⁴

Hence to reduce the harm and damage from AMR, world renowned experts and global governments have recently announced a global public health AB reduction aim.⁵ Interestingly although there is a shared interest of inducing an AB reduction aim, no common agreed public health ethics framework excists to guide and justify actions. Until now ethicists have mostly ignored the AMR problem. Only a few ethicists have provided an ethical assessment of the AMR-related threats, which only entail clinical medicine practices. Within this case, the underlying ethical question is whether this public health aim of reducing AB usage overrides current AB usage in China. Because of the lack of in-depth conceptual ethical analyses and public health ethics framework to weight arguments and guide policy decisions, more attention to this topic is needed.

Research design

Aim of this thesis

The mission of this research is to investigate whether the global public health AB reduction aim overrides current AB usage in China.

¹ United Nations high-level meeting on antimicrobial resistance. World Health Organization.

http://www.who.int/antimicrobial-resistance/events/UNGA-meeting-amr-sept2016/en/. Published September 26, 2016. Accessed April 17, 2018.

² China Consumes Almost Half of World's Antibiotics. China Consumes Almost Half of World's Antibiotics---Chinese Academy of Sciences.

http://english.cas.cn/newsroom/mutimedia_news/201506/t20150623_149222.shtml. Accessed April 17, 2018. ³ The Dangers of Hubris on Human Health. Global Risks 2013. http://reports.weforum.org/global-risks-

^{2013/}risk-case-1/the-dangers-of-hubris-on-human-health/. Published 2016. Accessed April 17, 2018.

⁴ Michael CA, Dominey-Howes D, Labbate M. The Antimicrobial Resistance Crisis: Causes, Consequences, and Management. *Frontiers in Public Health*. 2014;2. doi:10.3389/fpubh.2014.00145.

⁵ World Health Organization. *Global Action Plan on Antimicrobial Resistance*. Geneva, Switzerland: WHO Document Production Services; 2015.

Thesis outline

Because of the lack of thorough conceptual ethical assessments about AMR I have chosen to explain why AMR is a public health problem based on scientific knowledge from the field of the life sciences. The purpose is to visualize the magnitude of the problem and show why it must be considered a public health problem and thus to indicate that it needs a public health ethics assessment. Based on this description I have outlined why AMR must be considered a public health problem. Based on this understanding, in chapter 2 I have given a description and ethical assessment of the moral dimension of the AMR problem. I have used various normative theories to identify the moral dimensions of the AMR problem from multiple perspectives, including arguments from human rights, deontology, teleology, and sustainability. In chapter 3 I explored whether there are legitimate context specific arguments that override the AB reduction aim. In order to answer the research question I also explored whether there are any legitimate context specific arguments that could override the AB reduction aim. Based on empirical research these are outlined and weighted against the ethical considerations that have been found in the previous chapter. Finally, based on the findings of both empirical and literature research I have concluded that the public health aim overrides AB usage in China. The two-legitimate context specific arguments are important to be recognized in the reduction policy, but they do not override the devastating effects of AMR. By reducing AB usage we would be able to save billions of lives, including the lives of future humans, and protect humanity against a horrible future scenario in which ABs are not working anymore. Lastly, I have given final remarks regarding the implementation of a public health framework to implement AB reduction policies in China. These include stewardship and collective action goals as further described by REACT group.⁶

Methods

Because there are no common agreed upon public health ethics framework to weight arguments and guide policy decisions regarding AMR, and no ethical analyses of AB usage in China, I decided to combine writing this thesis with performing empirical research myself (read more about this in the appendix). Because of the lack of any context specific ethical assessment of AMR in China I have choosen to discuss the most important and interesting findings from the empirical research after the ethical assessment of the AMR problem. The empirical research has been performed at Peking Health Science Center, University Peking, China. During this research I experienced the culture first-hand, Chinese citizen's motivational reasons and norms and values regarding AB usage and the AMR problem. By becoming part of their community, I gained an insider's perspective on the AMR problem. I have traveled to multiple cities throughout China and talked with many stakeholders from different levels of society. My time in China allowed me to explore the intuitions, assumptions and (moral) considerations behind their AB usage behavior. I used various research methods to collect data, including empirical research, random interviewing, storytelling and natural observation with medical students, medical doctors and random people from the local Chinese population. Notably, to some degree there was a language barrier, as many of the Chinese do not speak fluent English (such was generally spoken only by the professors, teachers and students). Therefore, questionnaires were translated by a

⁶ The ethics of antibiotic resistance – 2017 – ReAct. ReAct. https://www.reactgroup.org/news-and-views/news-and-opinions/year-2017/the-ethics-of-antibiotic-resistance/. Accessed April 18, 2018.

Chinese PhD student. Also, because of the lack of literature about the AMR problem in China I have used a considerable amount of information gained by the interviews and quotations of participants that I have interviewed during my study to answer the research question. Of which the most relevant are highlighted within this thesis and some of them are outlined in the appendix.

Ethical assessment

Based on the outcomes of the empirical research and the comprehensive conceptual analyses of AB usage and the AMR problem in China I proceeded with the ethical assessment to answer the research question. Because of the lack of ethical assessment, this thesis strongly focusses on describing the various moral dimensions of the AMR problem first. The final ethical assessment has been performed based on argument deriving from various normative theories, including the human rights, deontology, and teleological approaches. I will also consider the related concept of sustainability, which must guide all long term public health inquiries.

Conclusions

Based on the empirical research and my contextual analyses, I conclude that the global public health aim overrides current AB usage in China. Facts are informing us that the AB efficiency is rapidly decreasing every time AB is used. This is an important fact once we consider ABs a common good and non-renewable resource.

According to the deontologist and human right approach every person deserves access to healthcare and access to medication. China as a country represents a complex case as the way that Chinese citizen's living in urban places are using Abs differently (e.g. preventative drugs) rather than people living in poor and rural areas (e.g. AB might be their only resource to protect their health). Because of this huge inequality, it's unfair and unjust to deny those people access to ABs. For the deontologist this would not even be a question to consider. Contrary, as AB are a non-renewable resource, the teleological and sustainability approach believe that we have a duty to reduce ABs to preserve their efficacy. Because we also have future people and they deserve an equal chance on a healthy life too. Moreover, differently than the teleological and sustainability approach, the consequentialist view argues in favor of bringing about the biggest benefits for the largest amounts of people. This theory justifies denying some set of people taking ABs if that would lead to billions of other people whose lives could be saved (in the future).

During this study, we have seen that AB usage does not only affect the individual, but the entire system. Because AB efficiency is relevant to every human, and taking Abs is lowering the total AB efficiency. Using the non-consequentialist approach of deontology and human rights I have shown that the AB reduction aim in China might be ethically problematic based on the principles of fairness, equality and justice. From a teleological / sustainable view I have shown that we need to include both present and future people into the moral weighting regarding AB usage. Considering the context specific arguments given by Chinese citizens, I have showed that many of these arguments do not hold in relation to the devastating consequences of AMR. The most legitimate argument from all context specific arguments to justify current AB usage in China is the cultural beliefs over health and diseases. Though in a broader scope, this argument does not override the public health AB reduction policy. As by reducing AB usage we would be able to save billions of lives,

including the lives of future humans, and protect humanity against a horrible future scenario in which ABs are not working anymore.

Based on these findings I conclude that the global AB reduction aim must override current Chinese AB practices. This, however, doesn't mean that we should not take the arguments in favor of current practices into account as we cannot ignore the deontological norms and values that are at stake. Especially for the most disadvantaged among us – the people who do not have access to AB's nor healthcare. In the final chapter I have provided some recommendations regarding implementing stewardship programs. Because a careful balance to be found between curtailing current AB usage, while ensuring appropriate availability for the vulnerable.

AB	Antibiotic
AMR	Antimicrobial resistance
HIC	high income country
LMIC	low middle income country
Оор	Out of pocket (expenditure)
OtC	Over-the-counter (sale
MDGs	Millennial Development Goals

Abbreviation

Operational definitions

Access (excluding rational usage) refers to a person's ability to obtain the right medication, treatment and/or resources when needed.

Rational usage follows the WHO's definition: "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period, and at the lowest costs to them and their community."⁷ There is a rational usage to the prescribing, dispensing and consumption of antibiotics. Affected stakeholders are expected to refrain from irrational AB usage.⁶

AB prescriber means any person working in healthcare that is eligible to issue a valid prescription for a medicine (in this case AB). In the context of AB in China this mostly refers

⁷ World Health Organization. Promoting Rational Use of Medicines: Core Components. *WHO Policy Perspectives on Medicines*. 2002;005. http://apps.who.int/medicinedocs/en/d/Jh3011e/.

to physicians or people working at a pharmacy (who are responsible for over-the-counter sale).

Chapter 1: The Global Antimicrobial Resistance Problem

Introduction

According to Cars et al., antibiotic resistance is considered one of the greatest public health challenges that must be addressed in the 21st Century.⁸ In 2015 the World Health Assembly (WHA) adopted several resolutions concerning antibiotic resistance.⁹ In 2000 the WHO presented a global strategy to work against antimicrobial resistance, calling for a global, multidisciplinary and coordinated approach. This resolution also urges all engaged member states to ensure the development of a coherent, comprehensive and integrated global approach.¹⁰ The causes of antibiotic resistance are complex and include human behavior at many levels of society, across different continents. Its consequences affect us all. But what do these causes entail and why is it a public health problem?

In this chapter I will first discuss the scientific logic behind AMR. Understanding AMR is essential both to understand why it is a public health problem and to distinguish between various moral considerations of the AMR problem. I will first explain the process of how AMR developed over time. I will then discuss the burden of AMR on individuals and society as a whole and outline the underlying drivers. Within this chapter I will discuss why AMR is a public health problem that needs the perspective of public health ethics to determine what must be done.

Antimicrobial Resistance and evolution

Antibiotics have been one of the most important discoveries in human history.¹¹ They have been considered as magic drugs that could cure every disease, "the magic bullets."¹² After their discovery in 1940 they have been used extensively within both human and animal healthcare.¹³ Their existence has contributed greatly to the improvement of human health and living standards and therefore must be considered one of the most significant medical breakthroughs in history. Antibiotics have been used to prevent and treat all kinds of bacterial infections, such as tuberculosis, as well as bloodstream, wound, respiratory-tract and sexually transmitted infections. Antibiotics are still the most important drugs within today's healthcare.

⁸ Cars, Otto, Anna Hedin, and Andreas Heddini. "The global need for effective antibiotics—moving towards concerted action." *Drug Resistance Updates* 14, no. 2 (2011): 68-69.

⁹ World Health Assembly addresses antimicrobial resistance, immunization gaps and malnutrition. World Health Organization. http://www.who.int/mediacentre/news/releases/2015/wha-25-may-2015/en/. Published August 22, 2016. Accessed April 17, 2018.

¹⁰ World Health Organization, April 17, 2018.

¹¹ Davies J, Davies D. Origins and Evolution of Antibiotic Resistance. *Microbiol Mol Biol Rev.* 2010;74(3):417-433. doi:10.1128/MMBR.00016-10./

¹² Aminov RI. A Brief History of the Antibiotic Era: Lessons Learned and Challenges for the Future. *Frontiers in Microbiology*. 2010;1(134). doi:10.3389/fmicb.2010.00134.

¹³ Aminov 2010;1(134).

However, every time ABs are used, bacteria become less sensitive to their functional working mechanism.¹⁴ The process by which microorganisms become resistant to medication to which they were previously sensitive is called antimicrobial resistance (AMR; see figure 1 below). AMR occurs via a natural process of adaptation.^{15,16} AMR develops when a microorganism mutates (e.g. changes the genes affecting its sensitivity for certain ABs) or acquires a resistance gene (e.g. by for example taking up a particle from another microorganism that has resistance gene).¹⁷ The AMR process of adaptation means that the effective lifespan of antibiotics is limited.

Due to AMR, resistant organisms, including some bacteria, fungi, helminthes, viruses and protozoa, are able to survive attacks by antimicrobial medicines such as antibiotics, antivirals and antimalarias. This means that over time standard treatments become ineffective, infections persist and may spread to other people. Both unnecessary use and inappropriate usage (e.g. overuse, misuse and underuse) of antibiotics favor the emergence and spread of resistant bacteria. The figure below shows the process by which this occurs. If people take too many ABs too often, called overuse, the emergence of AMR increases. Similarly, underusage through inappropriate choice, inadequate dosing, poor adherence to treatment, and substandard antimicrobials, also plays an important role in the emergence and spread of AMR.^{18,19}



Figure: The biological process by which antibiotic resistance occurs (CDC)¹

In order to limit AMR, policies mention the adoption of 'rational-usage AB policies'. Such policies are meant to address how AMR impacts the availability and thus overall utility of ABs for other persons. Entailing the provision of guidelines to protect against unnecessary

¹⁴ Davies 2010.

¹⁵ World Health Organization. *The Evolving Threat of Antimicrobial Resistance: Options for Action*. Geneva: World Health Organization; 2012.

¹⁶ Davies 2010.

¹⁷ Davies 2010.

¹⁸ World Health Organization. *WHO Global Strategy for Containment of Antimicrobial Resistance*. Geneva: World Health Organization; 2001.

¹⁹ Xiao Y, Zhang J, Zheng B, Zhao L, Li S, Li L. Changes in Chinese Policies to Promote the Rational Use of Antibiotics. *PLoS Medicine*. 2013;10(11). doi:10.1371/journal.pmed.1001556.



Figure 2: explaining the human and financial cost of failing to address antibiotic resistance. ¹

use and inappropriate usage - providing proper resources of knowledge to caregivers and persons.²⁰ In this case, as the effectiveness of the drug decreases, its effective lifespan also decreases, which has significant impact on these so-called 'rational usage of antibiotics'.^{21,22}

The burden of AMR

Whereas AMR could have been understood as a future concern for past people, it cannot be anymore²³ According to the World Economic Forum (2013; 28) AMR constitutes one of the main risks to human health. AMR threatens the health of both present and future humans. Greater infectious disease spread is an increased burden worldwide and leads to billions of dollars in direct health costs and lost productivity (figure 2).²⁴ In the WHO European Region the resistance of some pathogens now reaches over 50% in some countries. New resistance mechanisms are rapidly emerging and spreading. For example, in the European Union 400.000 resistant infections are estimated to occur every year. These resistant infections lead to about 25.000 deaths.²⁵ AMR gives rise to considerable health costs because of longer hospital stays and more expensive treatment, as well as direct and indirect costs to society. Additionally, bacterial multidrug resistance is increasingly threatening the outcome of many common medical interventions and diagnostic procedures that until recently were considered safe or low-risk.²⁶ According to the American Centers for Disease Control and Prevention (CDC) annually 2 million people are infected with resistant bacteria of whom 23.000 die as a direct

²⁰ Antimicrobial Stewardship. Society for Healthcare Epidemiology of America. https://www.sheaonline.org/index.php/practice-resources/priority-topics/antimicrobial-stewardship. Published 2018. Accessed April 17, 2018.

²¹ Gyssens I, Monnier A. The global definition of responsible antibiotic use: Three highlights. AMR Control. http://resistancecontrol.info/2016/rational-use-of-antibiotics/the-global-definition-of-responsible-antibiotic-use-three-highlights/. Published September 9, 2016. Accessed April 17, 2018.

²² Levin BR, Perrot V, Walker N. Compensatory Mutations, Antibiotic Resistance and the Population Genetics of Adaptive Evolution in Bacteria. *Genetics*. 2000;154:985-997.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1460977/pdf/10757748.pdf.

²³ CDC, 2013; Smith and Coast, 2013; Review on Antimicrobial Resistance, 2014.

²⁴ Antibiotics: One of the Greatest Discoveries of the 20th Century. *Antibiotics: One of the Greatest Discoveries of the 20th Century*. https://www2c.cdc.gov/podcasts/media/pdf/Antibiotics_Short.pdf. Accessed April 17, 2018.

²⁵ Centers of Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2013.

Atlanta: Centers of Disease Control and Prevention; 2013.

²⁶ Wong D, Sande-Bruinsma N. WHO European strategic action plan on antibiotic resistance: How to preserve antibiotics. *Journal of Pediatric Infectious Diseases*. 2015;09(03):127-134. doi:10.3233/jpi-140426.

result.^{27,28,29.} However, while global amounts of resistance are increasing, the number of effective antibiotics is decreasing.³⁰ Experts expect that by 2050 10 million people will annually die because of infections with resistant bacteria (see figure 3).³¹ Even more concerning is the fact that there is no realistic chance of a timely medical or technological solution to the problem. Currently there are only a few new antibiotics under development, and those that lack novel action mechanisms will not effectively circumvent existing AMR.³²



Figure 3: Expected deaths attributable to antimicrobial resistance every year by 2050.¹

Drivers of AMR

According to experts, AB usage is dependent on varied factors, such as access to healthcare resources in less-developed countries, ³³ health literacy and adherence to treatment, ³⁴ economic considerations of cost-effective treatments and psychological insights into

²⁷ CDC 2013; World Health Organization - Regional Office for Europe. *European Strategic Action Plan on Antibiotic Resistance*. Baku, Azerbaijan: World Health Organization; 2011.

²⁸ Smith R, Coast J. The true cost of antimicrobial resistance. *Bmj*. 2013;346(3). doi:10.1136/bmj.f1493.

²⁹ Review on Antimicrobial Resistance. *Antimicrobial Resistance: Tackling a Crisis for the Future Health and Wealth of Nations.* London: Review on Antimicrobial Resistance; 2014.

³⁰ The Center for Disease Dynamics, Economics and Policy (DDEP). *The status of the world's antibiotics 2015*. CDDEP: Washington, D.C.; 2015

³¹ Review on Antimicrobrial Resistance. *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. United Kingdom: Review on Antimicrobial Resistance; 2016.

³² Nathan C, Cars O. Antibiotic resistance—problems, progress, and prospects. *The New England Journal of Medicine*. 2014;371:1761-1763. doi:DOI: 10.1056/NEJMp1408040.

³³ Byarugaba D. Antimicrobial resistance in developing countries and responsible risk factors. *International Journal of Antimicrobial Agents*. 2004;24(2):105-110. doi:10.1016/j.ijantimicag.2004.02.015.

³⁴ von Wagner C, Steptoe A, Wolf M, Wardle J. Health Literacy and Health Actions: A Review and Framework from Health Psychology. *Health Education & Behavior*. 2009;36(5):860-877. doi:10.1177/1090198108322819.

antibiotic prescription patterns and expectations and individual usage patterns.^{35,36} While excessive usage of antibiotics remains a major problem, it also illustrates the fact that people in poorer parts of the world are doubly disadvantaged because of their lack of access to education to understand the problem, and how to use ABS and access to essential and effective life-saving antibiotics.³⁷ This last argument is essential because of increasing bacterial resistance levels, older and cheaper antibiotics are losing their efficacy. Oftentimes newer, more effective and significantly more expensive drugs are unavailable due to their high costs.³⁸ Because of these dimensions of the AMR problem, it must be considered highly complex. There are many contributing and causal factors which counteract attempts to reduce AMR. One reason for the difficulty of addressing the AMR problem is that, for most people, AMR represents a non-tangible futuristic concept rather than a disease. And because of the very limited attention from the ethics field, it is not clear which ethical framework should be used. This leads to a lack of guidance and justification of actions and public health policy decisions. Notably until now ethicists have not sufficiently addressed the ethical issues that are at stake. Because of this lack of research, there is also a lack of ethical guidance when addressing individual use cases, and so it is currently unclear what should be done in any particular case.

AMR, a public health problem

From a public health perspective, the threat of progressing AMR puts all of us at a tangible risk of harm. Failure to reduce AMR also imposes risks on future generations.³⁹ If more antibiotics are used, there is a higher risk of resistance developing, which reduces the number of effective antibiotics. Antibiotic use by one person may affect another person's future access to effective antibiotics. Allowing AMR to progress while knowing the massive difficulty it poses to both saving lives and reducing healthcare costs means, as will be shown, that we are falling short of our moral obligations to provide safe medical care to millions of people while protecting sustainable healthcare for all.

The trouble with AMR developed from AB usage is not only due to human medical application. ABs are also used in food-producing animals. Through their feces the Abs are also influencing

³⁵ Bbosa GS, Wong G, Kyegombe DB, Ogwal-Okeng J. Effects of intervention measures on irrational antibiotics/antibacterial drug use in developing countries: A systematic review. *Health*. 2014;06(02):171-187. doi:10.4236/health.2014.62027.

³⁶ Knobler S. *The Resistance Phenomenon in Microbes and Infectious Disease Vectors Implications for Human Health and Strategies for Containment: Workshop Summary*. Washington, D.C.: National Academies Press; 2003.

³⁷ Knobler 2003.

³⁸ ReAct - Action on Antibiotic Resistant. *ReAct Strategic Plan 2015 – 2019*. Uppsala, Sweden: Uppsala University; 2014.

³⁹ Littmann, Jasper, and A. M. Viens. The ethical significance of antimicrobial resistance. *Public health ethics* (2015): phv025.

our ecosystem from that perspective^{.40,41,42,43} Shockingly the American Food and Drug Administraton published data that there are more kilograms of antibiotics sold in the United States for food-producing animals than for people.⁴⁴ Such use of ABs highly contributes to the emergence of (new) antibiotic-resistant bacteria in food-producing animals. This is worrisome as resistant bacteria in food-producing animals serve as carriers.⁴⁵ Carriers as 'hosts' to contaminate humans through food. People who consume these foods can then develop antibiotic-resistant infections.^{46,47} Therefore it is necessary to reduce AB usage in both humans and animals as both uses contribute not only to the emergence but also to the persistence and spread of antibiotic-resistant bacteria (see figure 4).⁴⁸



Figure 4: The full cycle by which AMR is developed, including our food, animals, humans and healthcare institutes.

⁴⁰ Vázquez-Moreno L, A. MB, Languré A, Higuera-Ciapara I, Aguayo MD, Flores E. Antibiotic Residues and Drug Resistant Bacteria in Beef, and Chicken Tissues. *Journal of Food Science*. 1990;55(3):632-634. doi:10.1111/j.1365-2621.1990.tb05194.x.

⁴¹ Roura E, Homedes J, Klasing KC. Prevention of Immunologic Stress Contributes to the Growth-Permitting Ability of Dietary Antibiotics in Chicks. *The Journal of Nutrition*. 1992;122(12):2383-2390. doi:10.1093/jn/122.12.2383.

⁴² Rassow D, Schaper H. The use of feed medications in swine and poultry facilities in the Weser-Ems region [Article in German]. *Dtsch Tierarztl Wochenschr*. 1996;103(7):244-249.

⁴³ Waxman HA, Corr B. Waste from pharmaceutical plants promotes antibiotic-resistant superbugs. Waste from pharmaceutical plants in India and China promotes antibiotic-resistant superbugs.

https://www.statnews.com/2016/10/14/superbugs-antibiotic-resistance-india-china/. Published October 14, 2016. Accessed April 17, 2018.

⁴⁴ National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS). Centers for Disease Control and Prevention. https://www.cdc.gov/narms/resources/threats.html. Published April 14, 2014. Accessed April 17, 2018.

⁴⁵ Cantas L, Shah SQA, Cavaco LM, et al. A brief multi-disciplinary review on antimicrobial resistance in medicine and its linkage to the global environmental microbiota. *Frontiers in Microbiology*. 2013;4. doi:10.3389/fmicb.2013.00096.

⁴⁶ National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS). Centers for Disease Control and Prevention. https://www.cdc.gov/narms/faq.html. Published January 26, 2018. Accessed April 17, 2018.

⁴⁷ Economou V, Gousia P. Agriculture and food animals as a source of antimicrobial-resistant bacteria. *Infection and Drug Resistance*. April 2015:49. doi:10.2147/idr.s55778.

⁴⁸ Andersson DI. Persistence of antibiotic resistant bacteria. *Current Opinion in Microbiology*. 2003;6(5):452-456. doi:10.1016/j.mib.2003.09.001.

FACTS: The Burden of AB usage in China

From the general description of AB usage and AMR risks above, we can move to the specific Chinese context. Examining this particular data will make clear that the world's AMR challenges are especially exemplified by China's AB usage habits. The Academy of Sciences of China showed that China annually consumes 162 thousand tons of ABs, which is more than half of the world's total consumption. 52% of Chinese ABs are used in farming, and 48% are used medicinally for humans.⁴⁹ More than 50 thousand tons of ABs flow to the soil and water, affecting the ecosystem. Moreover, ABs commonly used include low quality ABs that are without prescription dispensed and thus are used excessively on a regular basis. Worldwide, China uses the most AB per capita, with a steep increase in AB usage each year. The consequences of high AB usage include negative impact to both the health of individuals and society, as the working mechanism of antibiotics is decreasing and the country becomes more prone to dangerous infectious disease outbreaks with catastrophic outcomes.⁵⁰

AMR and AB usage requires a public health ethics assessment

Understanding AMR as a global public health problem means that we need a public health ethics perspective to identify and assess the problem's moral dimensions. Public health ethics includes normative issues in epidemiological research, health promotion, screening, population genetics, infectious diseases control, resource allocation, vaccinations, health care system reform, environmental and lifestyle factors, among others. For the purpose of a public health ethics analysis, these elements are considered in terms of both global and individual health, equity and justice. Such a systematic analysis will also evaluate the moral problems in population health and preventive medicine. Public health ethics contrasts with the liberal perspective of classical biomedical ethics by its focus on such factors as the collective, the production of (maximal) benefits, avoiding (collective) harm, producing a maximal balance of benefits over harms, distributive justice, fairness, equality and public participation.⁵¹ Where the biomedical ethicist sees how the individual is affected by any particular decision or policy, the public health perspective attempts to see further interconnections, to understand how the world's many elements—from people to plants, animals, natural resources, and beyond—are all affected by health decision-making. As you have read the AMB problem is caused by AB usage for both humans and animals. But because the total AMR problem is too comprehensive and complex, in this thesis I will only focus on the AMR risks of AB usage by humans.

⁴⁹ China Consumes Almost Half of World's Antibiotics. *China Consumes Almost Half of World's Antibiotics*. June 2015. http://english.cas.cn/newsroom/mutimedia_news/201506/t20150623_149222.shtml. Accessed April 17, 2018.

⁵⁰ World Health Organization. *Antibiotic Resistance: Multi-Country Public Awareness Survey*. Geneva, Switzerland: World Health Organization; 2015.

⁵¹ About the Journal. Public Health Ethics. https://academic.oup.com/phe/pages/About. Accessed April 17, 2018.

Clinical ethics vs Public health ethics

When the AMR problem is seen as a public health problem, there are important conceptual and practical ethical implications, especially in terms of clinical practice. Whereas medical ethics is focused mainly on the special nature of the doctor-patient relationship (e.g. the obligation of doctor versus the rights of the individual patient), public health is more focused on larger populations and not so much on the individual. Public health ethics is targeted at the possible health benefits of groups of people (e.g. the population), not just at individual patients. This shift in orientation results in the following key differences: First, in public health the initiative for preventive care and public health programs usually comes from the public health professional, not 'the patient'.⁵² Whereas personal autonomy is the key value in modern individual healthcare, other values such as the protection of the health of the public, the prevention of harm to others and the promotion of health equity are more central in public health. Taking a public health perspective often shows that physicians face dilemmas between the welfare of the patient and the directive of healthcare systems.

Consider how one might feel in such a difficult scenario: Imagine that one is a doctor who is facing an ill patient, suffering from severe disease and pain. The person looks into your eyes and asks for the best medication to relieve his pain and save his life. One might automatically wish to give the patient what he wants, especially if he is asking for antibiotics by name. However, taking his current condition into account, there is no obvious evidence that providing ABs would significantly increase his chances to survive. Rather, AB usage will probably lead to the development of more harmful resistant bacteria that could potentially be spread to other patients, putting their lives at risk. But, there might still be a small chance that this patient's AB use would be lifesaving. What is the right thing to do? Providing ABs to this one patient or reducing this individual's AB usage for the greater good? Such an example shows the difficulty of the aim to restrict AB usage in clinical practice. It also shows how the public health perspective always looks beyond the individual patient's expressed desires.

A second difference between public health and individual medicine is that public health interventions aim to protect and promote health at a group or population level.⁵³ Public health programs may not be beneficial for each individual person as there might well be a conflict between protecting the health of the public and the well-being of particular individuals. Ethical reflection about public health therefore requires discussion of the tension between individual and public interests.

Third, preventive programs are potentially highly pervasive.⁵⁴ If public health interventions come to impact our ability to lead our own lives, or if the pervasive public concerns for health would negatively impact upon our private lives and individual choices, then further ethical questions arise. These questions for example include disease surveillance measures such as, isolation of individuals.

⁵² Dawson A, Verweij MF. *Ethics, Prevention, and Public Health*. Oxford, UK: Oxford University Press; 2009.

⁵³ Dawson 2009.

⁵⁴ Dawson 2009.

Newly arising ethical questions

Taking a public health perspective about AB usage means that we will be confronted with ethical dilemmas concerning the AB prescription behavior of doctors and patients. Particularly challenging questions arise whether individual persons can be denied ABs if doing so will put their lives at risk but potentially benefit the lives of others, including future people. It is also important to determine whether physicians should take into account only the interests of the individual patient in front of them or if other patients' interests matter too. According to the reasoning of classical bioethics, doctors must act in the best interest of their current patient.⁵⁵ Similarly patients expect to be treated according to their best individual interests. However considering AMR as a public health problem, which may indicate an obligation to lower AB usage, physicians and patients are faced with further, pressing ethical questions and complications.

These ethical questions do not regard only the current situation but also concern the future. For example, consider the next AB to be developed. A scientific case can be made that without taking steps toward AB reduction and adopting effective stewardship policies, resistance will arise within a few years. Similar phenomena have been witnessed over the history of antibiotic usage, from penicillin through all classes of antibiotics. If stewardship measures are applied, the resistance will develop slower, which means the antibiotic may be useful for a longer period.

Concluding remarks

In this chapter I argued that to answer the research question we need to consider AMR as a public health problem. AMR is a very complex issue and many questions remain unanswered or have not been addressed previously. This chapter identified the following factual knowledge: 1) AMR is threatening the health of citizens on a global scale to a degree never before seen (e.g. it is one of the major threats to human health in the 21st century), 2) both under- and over usage (i.e., misuse) is driving AB resistance, 3) access to (high quality) ABs for LMICs is not equally distributed compared to access in HLICs, 4) there is a lack of knowledge about rational AB usage among both doctors and citizens, 5) there is a lack of infrastructure and research facilities in rural areas to identify people that need ABs), 6) more than 50% of ABs are used by farmers and 7) there are no incentives for new AB development. Notably, China has a very unregulated animal husbandry business, in which a lot of AB's is used to prevent diseases in animals. Although this is an important factor, because of the scope of this thesis I will only restrict myself to the AB usage by humans in China.

⁵⁵ Beauchamp TL, Childress JL. *Principles of Biomedical Ethics*. New York, NY: Oxford University Press; 1979.

Chapter 2: Ethical description and analyses of the moral dimensions of the AMR problem

In the previous chapter I discussed why AMR is a public health problem and outlined some of the factors that cause AMR to arise. In this chapter I will proceed with an ethical description of the moral dimensions of AB usage and then apply these theories to the AMR case in order to provide an ethical analysis. I will discuss various normative theories in order to identify the different moral dimensions of the AMR problem. These systems will help us to provide an ethical weighting of the relevant arguments and factors occurring in the tension between among others patient autonomy and reducing the risks of AMR. We will use these arguments to provide an ethical weighting of the situation regarding the public health AB reduction aim and to provide a context sensitive analyses to investigate if there are other ethical considerations and whether they support current AB usage in China and if they are overriding the public health AB reduction aim. Apart from discussing the theories I will also apply the theory within the case of the current worldwide AMR crisis and provide an ethical weighting at the end of the chapter. In the next chapter I will discuss the specific ethical considerations within the Chinese context that impact further evaluation of the AB reduction policy and whether they induce ethical weighting to the overall research question.

Method

The ethical analysis below as well as the ethical weighting are based on findings from both the empirical study as well as literature review. Articles for the literature review were obtained through searches for "ethics", "antibiotics" and "Antimicrobial resistance" on Google Scholar and PubMed. I excluded non-English articles and articles and books that were not accessible through the Utrecht University online licenses and subscriptions. Articles discussing specific instances of antibiotic usage as part of treatment and disease mechanism reviews were also ruled out. I performed more research using Google, in part by searching for well-known bioethicists from the field, such as Jasper Littmann and Marcel Verweij. Through this research, I found that only very recently have research projects begun to perform ethical assessment on AMR as a global problem. I also consulted WHO bulletins, and information about the scientific working mechanism of AMR was obtained through simple Google searches.

Using various normative theories

To provide an ethical weighting of the considerations underlying worldwide AB usage, I consider various ethical theories to identify the norms and values that are at stake. Such an evaluation will provide the context necessary both to understand the factors that must be considered with respect to worldwide AMR problems and Chinese AB usage and to decide what decision should be made regarding AB use in China. Below I will discuss various normative theories that can be used to answer the research question of whether AB reduction aim overrides AB usage in China. These theories are separately used by different ethicists – each based on their own fundamental believes, norms and values that are relevant for the normative theory. In my work, I combine their positions and evaluations in

order to examine the relationship between AMR and AB usage from multiple perspectives. Below I will provide a short introduction of each and describe how this theory could be applied to assess and weight the varied ethical considerations.

Harm principle

A central tenet of much ethical thinking is known as the harm principle. It holds that the actions of individuals should only interfere with the freedom of others to prevent harm being done to other people. J.S Mill argued that, "The only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others."⁵⁶ The harm principle underlies various public health interventions such as physical examinations, treatment, isolation, and quarantine. In liberal democracies, the harm principle is viewed as the most convincing justification for public health policies that interfere with individual liberty, such as isolation and quarantine in case of infectious diseases. The global AMR problem affects everyone. Any one of us taking ABs is contributing to the global threat, and hence placing other people at risk and/or contributing harm. However, as with all such principles, questions remain about its specification. How significant must the threat of harm be, regarding both its likelihood and magnitude?

According to Littman et al. it is only recently that any concrete information about risks and harm related to the global AMR problem have become available. As previously there were no studies performed that could offer guidance within the decision-making process. Because of this no standard has been found and more ethical assessment of various situations is needed. Nevertheless, the availability of research on the global AMR problem provides a concrete starting place for this ethical evaluation.

Risk for Harm

Besides the actual harm done in any case, there is also the risk of doing further harm which is not the same as the actual harm. In the case of AMR, everyone is at a tangible risk to develop AMR during his or her life. And every time a patient takes ABs, he or she puts him or herself and other people around them at risk. But placing oneself, or even another person, at risk does not yet harm them e.g. neither physically nor mentally. Using a risk-based assessment intuitively we can understand that there are certain thresholds of the amount of risk that can be placed on patients and people that are highly context specific and dependent on both personal, medical and environmental factors. Verweij et al. state that the higher the threat, the more risk we are willing to take and the more restrictions of individual liberty we tend to justify protecting people from harm.⁵⁷ However, Garau argues that balancing the risks of treating or not treating with AB considering the global AMR problem is complex. He emphasizes the negative implications of AB restriction leading to suboptimal treatment which exposes the patient to the risk of poor outcome, adverse events and the wider risk of AMR. Failure to treat the risk of a poor outcome exceeds the

⁵⁶ van Mill, D. Freedom of Speech. Stanford Encyclopedia of Philosophy.

https://plato.stanford.edu/entries/freedom-speech/. Published May 1, 2017. Accessed April 18, 2018. ⁵⁷ Verweij M, Dawson A. Ethical principles for collective immunisation programmes. *Vaccine*. 2004;22(23-24):3122-3126. doi:10.1016/j.vaccine.2004.01.062.

risk of an adverse event due to ABs is also ethically unacceptable. Besides that, information that is relevant to the actual context is very important to provide an accurate ethical assessment of the context-specific situation.⁵⁸ From a medical point of view, appropriate treatment depends on whether the person is young or old, the kind of infection and the environmental conditions. It also depends on the availability of life-rescue resources, the total number of patients and the hygienic state of the care institute. These context sensitive factors are important to take into consideration as they all contribute to the risk for harm and the actual harm that is performed on any person by, for example, denying access to ABs.

What the harm approach implies regarding AB usage

We have seen that one's decision to take AB does not have an impact on only one's own economy and health, but also on the future health of other people as the result of the emerging resistance to ABs. There is a broad consensus among scholars in public health ethics about the idea that prevention of harm to others offers a moral basis for coercive measures. This may imply justifying the waiving of individual liberties and autonomy to prevent harm to others.⁵⁹ Based on the increasing threat of AMR on both present and future humans, the harm principle states that it is legitimate to reduce individual liberties, such as implementing individual AB reduction policies.

Harm versus harm dilemma

To reduce AMR and maintain AB effectiveness to treat diseases, we should accept that dependent on the context, sacrifices need to be made. We cannot make unrestricted use of ABs, as doing so may cause harm to ourselves or to the people around us. Nowadays looking at the context of the global AMR problem, we have reached the point that avoiding harm is no longer a relevant fact: all AB usage contributes to the AMR problem. The situation of preventing harm to others has now become a matter of weighing harms in a harm versus harm dilemma. That means that the morally correct thing to do is to find how to avoid the greater harm. Given AMR's disastrous consequences both currently and the future, we have an obligation to reduce AB usage to prevent more severe harms.

Human rights / Deontology

Ethical systems based on duties, rights and justice are the main alternative to consequentialist theories.⁶⁰ The consequentialist view argues that the right thing to do in all cases is that which leads to the most overall positive outcome. Against this, other ethical theories are rooted in an underlying assumption about the existence of universal rights,

⁵⁸ Garau J. Impact of antibiotic restrictions: the ethical perspective. *Clinical Microbiology and Infection*. 2006;12:16-24. doi:10.1111/j.1469-0691.2006.01527.x.

⁵⁹ Kass NE. An Ethics Framework for Public Health. *American Journal of Public Health*. 2001;91(11):1776-1782. doi:10.2105/ajph.91.11.1776.

⁶⁰ Alexander L, Moore M. Deontological Ethics. Stanford Encyclopedia of Philosophy.

https://plato.stanford.edu/entries/ethics-deontological/. Published November 21, 2007. Accessed April 17, 2018.

wrongs and responsibilities. These theories argue for principles that are valid for every person on this planet. Insofar as one is a person, one must act in certain ways to be morally right. These theories emphasize what people ought to do in contrast to those approaches that guide people into being a particular kind of person (for example, Aristotelian virtue ethics) or evaluate the consequences of some act (consequentialist theories such as the utilitarian approach which we will discuss later).

A right is a justified claim against another person's behavior, an expectation that others will not act in certain ways. Hence rights and duties are related, as the rights of one person imply the duty of someone else not to violate that right. With respect to AMR case, consider the Universal Declaration of Human Right: people have rights of access to medicine, access to healthcare and fair distribution based on the principles of fairness, equality and justice. The World Health Organization (WHO) constitution states that any impediment of access to health care undermines the enjoyment of the highest attainable health standard. This last sentence shows that the WHO holds that such impedance is a failure of duty and a violation of people's rights to health care.

Access to ABs

According to the Human Rights theory every person should have access to healthcare and medication. However, people in low middle income countries do not always have access to Abs. Public health research in low middle income countries show that more than one third of all children with pneumonia do not receive antibiotics, with the children of poor and rural patients being worst off.⁶¹ Research has also shown that due to sinking GDPs, people in LMICs suffer from higher child mortality rates, shorter lifespans, higher burdens of communicable diseases, less access to basic healthcare with skilled personnel and quality medicines, greater health inequities and less spending on healthcare. A higher proportion of medical spending in LMICs is out-of-pocket (OoP), further increasing inequities.^{62,63} In sum, LMICs have limited access to medicine and healthcare, and their citizens suffer from a higher burden of disease and are at greater risk of developing life-threatening infectious illnesses. In many places, especially rural areas, the lack of access to medicines is a great source of mortality and morbidity. As a result, there is excessive AB misuse, as ABs are taken to protect against and treat all kinds of diseases and disease outbreaks.

Daniels argues that justice in the medical field requires that all receive equal access to care.⁶⁴ This implies that there must be access to healthcare and available resources for all human beings, both current identifiable people as well as future ones. On this view, we have a right to health and preservation of life in the years ahead. This indicates that all people have a right to have access to AB, as this is an important resource in health care. If this is correct, then we have an obligation to preserve the effectiveness of ABs for both current

⁶¹ UNICEF. Pneumonia and Diarrhoea: Tackling the Deadliest Diseases for the World's Poorest Children. UNICEF; 2012.

⁶² Lindstrand A. *Global Health: an Introductory Textbook*. Lund: Studentlitteratur; 2010.

⁶³ Gapminder. https://www.gapminder.org/. Accessed April 17, 2018.

⁶⁴ Daniels N. Justice and Access to Health Care. Stanford Encyclopedia of Philosophy.

https://plato.stanford.edu/entries/justice-healthcareaccess/. Published October 20, 2017. Accessed April 17, 2018.

and future people.⁶⁵ However, LMICs such as China have a high burden of diseases and are at greater risk for developing infectious diseases. Insofar, Chinese citizen's have a claim to use Abs in case they are in need to keep themselves healthy. As according to the above human rights and deontology principles, restricted access to medication and healthcare cannot be merely be justified. As every person has a right to medicine and healthcare.

Lack of fair distribution

China is a LMICs in which both <u>distribution and access to working ABs are impeded</u> for a large part of the population, especially in rural areas. Whether people have fair access to medicine and healthcare depends mainly on the rules and boundaries of the distribution system as formulated by policy and legislation. In the case of AB usage in China, ABs are not fairly distributed among citizens. Prescribing medical professionals diagnose patients to the best of their knowledge, and if ABs are needed, they will then prescribe a drug according to guidelines. Dispensers such as pharmacies and drug sellers also provide patients with pharmaceuticals, usually without prescription needed. Patients are responsible for compliance with dispensed therapies as well as for their own care seeking behavior. This might appear that residents have easy access to the medicine they need.

However, in practice the system fails in many ways. Drug regulatory bodies are weak, nonexistent or non-enforcing.⁶⁶ Research shows that, in the Chinese context, there is a lack of surveillance on therapeutic efficacy. Because of this lack, people cannot initiate timely counter-resistance measures, lack of access to quality ABs (i.e. many ABs used are locally made, poor quality, or black market with fake components) and dispense medicines without performing or following the results of laboratory diagnosis (which is required for rational AB usage). According to research in LMICs, less than half of all medicine dispensed are taken according to the clinical guidelines, as instructions do not reach people, because of high rates of out-of-pocket (OoP) sale and black-market of high quality medicine.⁶⁷

These features place a higher burden to the AMR problem in China. AMR is even more problematic as when resistance to earlier generation antibiotics emerges and spreads, patients have to move on to newer, more expensive antibiotics. There are economic implications that follow for the already-strained health systems in LIMCs as well as the overall level of AB efficiency worldwide.⁶⁸ Adding to this, the speed for ABs losing their efficacy is dramatically greater than the speed of new antibiotic development. In the meantime, no new ABs are being developed due to a lack of economic incentives for

Availability, and Affordablility. Geneva: World Health Organization; 2011.

⁶⁵ Daniels 2017.

⁶⁶ WHO report finds systems to combat antibiotic resistance lacking. *WHO | WHO report finds systems to combat antibiotic resistance lacking*. April 2015.

http://www.who.int/mediacentre/news/releases/2015/antibiotic-resistance-lacking/en/. Accessed April 17, 2018. ⁶⁷ Cameron A, Ewen M, Auton M, Abegunde D. *The World Medicines Situation 2011: Medicines Price*,

⁶⁸ United States Pharmacopeia Drug Quality and Information Program. *Ensuring the Quality of Medicines in Resource-Limited Countries: An Operational Guide*. Rockville, MD: The United States Pharmacopeial Convention (USP); 2007.

pharmaceutical corporations. According to Littman et al., this shows an ethical conflict of norms and values between medical needs and the current pharmaceutical business model.⁶⁹

From a rights-based egalitarianism approach, fair distribution should allocate material goods (in this case, working ABs) equally to all members of society who need them. This means that all people, from all layers of society, should have equal access (fair distribution) to working ABs. This latter factor is really important, as working AB's include high quality AB that are meant to treat specific diseases. As described above, China is a LMIC with a socially hierarchical organization in which both distribution and access to working ABs is impeded among much of the population in various geographic areas. Hence this shows great injustice and a violation of some Chinese people's rights.

According this view, implementing the AB reduction aim in China would lead to more injustice as fewer people would have access to working ABs. People in LMICs are most often double disadvantaged as 1) they do not have access to (the high quality) ABs, and 2) they might be the ones who are in high need (i.e., they already have the highest rate of (deadly) disease outbreaks). Resources such as high quality Abs are centralized in modern hospitals and pharmacies in urban areas. But the countryside is really poor and highly depended on local fabricants or distribution (eg. Black market) of medicines from urban places to the countryside. As described in chapter 2, there is a huge inequality of wealth between urban and rural areas. And because of the huge population of China the people living in rural areas still include 590 million people. To place this in perspective, this is almost double of the number of US citizens all together. Hence from a human rights point of view, these disadvantages emphasize the need for better access to medication, healthcare, regulation and/or measures taken by third parties such as the government.

This injustice can also be illustrated by applying John Rawls' Difference Principle. Rawls argues that part of what justice requires is a reckoning of the way in which unequal distribution occurs. The Difference Principle, which is Rawls' idea for understanding unequal distribution, permits diverging from strict equality so long as the inequalities in question would make the least advantaged in society materially better off than they would be under strict equality.⁷⁰ In the case of AB usage, that means that people who do not have access to working ABs and/or healthcare in poor and rural areas, should be compensated in other manners.

Fighting AB Mis-usage

The lack of fair distribution, access to medicine and poor education leads to heavy misuse of ABs, which lowers AB efficiency for all. Daniels argues that every person has a right to health and the preservation of life in the years ahead. However, current heavy misuse of ABs is the main driver of the global AMR problem, especially in LMICs. Because of incorrect AB usage, AMR levels are increasing. Hence ethical questions arise about who should take ABs and under which conditions. These questions also point to the responsibilities of people in

⁶⁹ Littman J, Buyx A, Cars O. Antibiotic resistance: An ethical challenge. *Int J Antimicrob Agents*. 2015;4:359-361. doi:10.1016/j.ijantimicag.2015.06.010.

 ⁷⁰ Lamont J, Favor C. Distributive Justice. Stanford Encyclopedia of Philosophy.
 https://plato.stanford.edu/entries/justice-distributive/. Published September 26, 2017. Accessed April 17, 2018.

relation to each other: every person's AB-taking behavior can affect future patients' access to effective antibiotics and health.

As shown by empirical research, rural people in China use ABs in ineffective ways, such as for viral illnesses such as diarrhea and the common cold.⁷¹ Self-medication with ABs is common because of over-the-counter (OtC) sales to patients without any prescription or doctor's advice. But if prescription-only status is enforced on antibiotics and/or if stringent AB reduction policies are enforced, the poor and rural population will be <u>deprived of access to antibiotics</u>, which may cause irrational usage increases.

This phenomenon has been witnessed in the past: controlled drugs lowers health equities even further.⁷² In the context of AMR, lowering AB usage in general must be understood and balanced against the current excessive or inappropriate use of ABs. In terms of distributive justice this means that, on the one hand, we need to safeguard AB efficiency by lowering AB usage (to maintain working ABs for all) but, on the other hand, we also need to remember maintaining access to ABs for all. This is essential because poor access leads to AB misuse and thus lowers AB efficiency level overall.

To address this tension, according to Daniels, we should seek for more rational AB policies in practice. Developing these practices must remain attentive to differences in needs, namely who needs ABs and in what circumstances.⁷³ Littman argues that considering the high burden of AMR and the general lack of implementation capacity in LMICs, we need to raise ethical questions about the obligations of high income countries. Because of the interdependencies of people's AB-taking behavior in relation to the overall AMR problem, the current situation is a matter of deep ethical concern. However, based on the findings from empirical research and the literature we have found that many people are not aware of the working mechanism of ABs and thus about AB misusage. If people are not aware of this, they can't take responsibility for the problem or perhaps do their share to slow AMR development. If the AMR problem is exacerbated by poor education, then major players such as the Chinese government and third parties must provide better (access to) education in order to show people that they are part of the problem.

What the deontologist suggests regarding AB usage

As seen above, according to the deontologists all people have a right to equal access to medicine and healthcare. The deontologists believes that it is a fundamental right to have equal access to healthcare. Moreover, some ethicists go beyond this, stating that we even have a right to equal access to care based on the principle of fairness. Contrary to the risk approach, the deontologist is against reasoning based on risk assessments. For example, it can be questioned whether it is ethically justified to place other people at unnecessary risks and if yes, to what extend this holds true. If one believes these are not important concerns

⁷¹ World Health Organization 2011.

⁷² Ganguly NK, et. al. Rationalizing antibiotic use to limit antibiotic resistance in India. *Indian J Med Res.* 2011;134:281-294.

⁷³ Rawls J. A *Theory of Justice*. Cambridge, MA: The Belknap Press of Harvard University Press; 1999.

and each person's desires for antibiotics should be met, then access to new antibiotics should be granted to anyone who needs it, even in the face of excessive total usage.

Access, excess and ethics

Lack of access

But what does all of this mean for access to ABs and the WHO's AB-usage reduction aim? As articulated above, drawing on the Universal Declaration of Human Rights, people have a right to (equal) access to medicine, access to healthcare and fair distribution based on the principles of fairness, equality and justice. From the human rights and deontology perspective this proposal of restricted access to medicine and healthcare cannot be justified, as every person has an absolute right to medicine and healthcare. Daniels argues that justice requires that everyone receives equal access to care.⁷⁴ This implies assurances of access to healthcare and available resources for all human beings, including both current and future people.

Lack of fair distribution

Based on the deontologist principles of fair distribution and justice, there is clearly great injustice, as every person should have an equal right to medication and healthcare. The lack of fair distribution and access to medicine is one factor that leads to heavy misuse, which is the main driver of AMR. Implementing the AB reduction aim in China might lead to even more injustice as more people would be kept from accessing ABs, and thus the fair distribution would be even less existent, exacerbating the above misuse issue.

Fighting AB misusage

China is doubly disadvantaged as 1) they do not have equal and safe access to ABs, and 2) they may be the ones who are in highest need of such care (because of, e.g., their high incidence of disease outbreaks, etc.). As argued above, Rawls' Difference Principle permits diverging from strict equality while still maintaining a just situation. So long as the inequalities in question would make the least advantaged in society materially better off than they would be under strict equality, this disadvantage could be justified.⁷⁵ However, there are practical concerns: in China there are no protection mechanisms in place, which would ensure better access and outcomes to the poor. This emphasizes towards duties of the government and/or third parties to provide better access to medication, healthcare and regulation and/or protection measures.

⁷⁴ Daniels 2018.

⁷⁵ Ibid.

Consequentialism

Consequential ethicists argue that the morally correct duty or obligation is to bring about what is ultimately good or desirable. This theory is opposed to the earlier-described deontological theory, which argues that the basic standards for an action's being morally right are independent of the good or evil generated in the final analysis.

Cost-efficiency approach to AMR

The consequentialist way to approach the AMR problem is by using the cost-effectiveness argument, a utilitarian approach.⁷⁶ Utilitarian theory holds that actions and policies are right if they promote the greatest good in general. Utilitarianism is often assumed to be the normative theory that best "fits" the aims of public health and thus the AMR problem, because both utilitarianism and public health operate and evaluate from the broadest possible perspective. Given that the present human and economic costs of AMR already amount to thousands of casualties each year, leads to increased infectious disease burden around the world and billions of dollars in direct health costs and lost productivity, utilitarian theories holds that we need to reduce AMR.⁷⁷ Less AMR is one way to achieve greater overall good, the utilitarian aim. Considering this theory, the underlying considerations are focused on the collective rather than individualistic considerations, such as the right to receive treatment. From this perspective, the individual person's desire or right to treatment may be set to the side in order to ensure less AMR.

This is contrary to the human right/ deontologist approach, which derives from individual duties, rights and justice. Whereas the deontological approach implies that every person has a right to receive the right treatment. The consequentialist approach would justify an action that excludes a person access to the right treatment (e.g. for example AB to a person in the hospital with pneumonia) if another collective action will result into a bigger collective gain (e.g. protecting 10 other patients in the same hospital room to be infected by resistant bacteria of this person).

What the cost-efficiency approach implies regarding AB usage

According to the cost-effectiveness argument we need to act to decrease AMR, as that will decrease costs and increase effectiveness of medicine and care in society. This does not simply mean, however, that people must stop using ABs. After all, given the biological developmental process of AMR, resistance also develops when there is a lack of appropriate ABs. Research shows that the long-term outcome of patients given appropriate empirical treatment is better than that of patients given inappropriate treatments.⁷⁸ This shows that

⁷⁶ Davies SE. *Global Politics of Health*. Cambridge: Polity; 2010.

⁷⁷ CDC 2013; Smith and Coast, 2013; Review on Antimicrobial Resistance, 2014.

⁷⁸ Leibovici L. Long-term survival following bacteremia or fungemia. *JAMA: The Journal of the American Medical Association*. 1995;274(10):807-812. doi:10.1001/jama.274.10.807.

there is an advantage to provide appropriate empirical treatment. In a formal model, the cost of future resistance to the patient was less by an order of magnitude than the cost to other, future patients.⁷⁹ The nature of AMR therefore requires what scientists call in biology, "rational AB usage."⁸⁰ For AB usage in China this has the following consequences:

- Chinese citizens cannot use ABs as preventive medicine
- ABs should not be given if they are not necessary
- We cannot randomly decrease AB usage. A context specific assessment is needed to determine who needs to obtain ABs, and specifically, which type of AB.

Sustainability argument

Sometimes, moral obligation has been thought of only in terms of currently living people. This is a relatively small group of people, given the total number who have lived and will live. Often little regard has been given to the needs and moral standing of future generations. A Swedish research group, called REACT, has argued that this way of thinking is reflected in our moral intuitions, as we generally have difficulties seeing the moral implications beyond these smaller groups. However if we expand our perspective so that future generations, including our own children, have the same value in our ethical thinking as current adults do, we can make a sustainability argument that focuses on both present and future generations. The sustainability arguments holds that in our desire to increase our wellbeing, we ought not to act in a manner that deprives future people of the means to do so as well. Besides focusing on present patients, we also need to focus on maintaining a sustainable system of healthcare.

This view is described by, among others, Daniels. He argues that all people have a right to health and preservation of life in the years ahead. As described earlier, on his view, all people have a right to equal access to healthcare. This implies that all people have an equal right to receive medication and thus that we have an obligation to preserve the effectiveness of ABs as a common good for both current and future people. Losing AB efficiency would end currently working ABs and thus modern healthcare, which would make impossible the realization of future people's equal access to healthcare.⁸¹ If this worry is correct, then it implies that decisions about AB reduction should be made before further ABs are lost, so that their use can also be sustained.

The sustainability perspective argues that AB usage must be evaluated from a broad perspective, not be left to each individual doctor-patient encounter.⁸² This view indicates

⁷⁹ Paul M, Andreassen S, Tacconelli E, et al. Improving empirical antibiotic treatment using TREAT, a computerized decision support system: cluster randomized trial. *Journal of Antimicrobial Chemotherapy*. 2006;58(6):1238-1245. doi:10.1093/jac/dkl372.

⁸⁰ Antibiotics Smart Use: a workable model for promoting the rational use of medicines in Thailand. World Health Organization. http://www.who.int/bulletin/volumes/90/12/12-105445/en/. Published November 29, 2012. Accessed April 18, 2018.

⁸¹ Daniels 2018.

⁸² Weinstein MC. Should physicians be gatekeepers of medical resources? J Med Ethics 2001; 27: 268 – 74.

the necessity to aim for more rational AB policies. In particular, it is important to distinguish who, based on their medical needs, requires ABs and in which circumstances.⁸³ ABs cannot be given to all patients in all cases. This ensures the effectiveness of ABs for the health of both current and future human beings.

Millar argues that all people have a right to receive treatment. And thus, that we have an obligation to preserve the effectiveness of ABs for both current and future people. According to him, however, worldwide equal access to antibiotics on the level currently found in highincome countries (HIC) would generally induce resistance quicker. Millar arrives at the conclusion that the suffering of future patients infected with AB resistant bacteria must be considered when regulating AB today. <u>He states that AB should only be used when there is</u> <u>"a substantial risk of irretrievable harm"</u> without their application. Millar applies Scanlon's contractualism to the issue of AB usage and its restriction, showing that AB use is justifiable only if it is based upon principles that no one could reasonably object to, which is the central idea of Scanlon's theorizing. According to Millar, intragenerational justice—the thought that everyone alive right now should get just what they want or need, no matter the damage to the future—comes at the expense of intergenerational justice or sustainability. He thus concluded that equal access to effective ABs worldwide can only occur sustainably if there are multinational agreements on AB restriction paired with programs such as vaccines and improved sanitation.⁸⁴

In a further development of sustainability argumentation, Leibovici et al. combines the four principles of biomedical ethics (beneficence, non-maleficence, autonomy and justice) with a utilitarian approach. The underlying moral reasoning is based on the Rawlsian veil of ignorance construct. Rawls uses a thought experiment to deduce a wide variety of desiderata for a just society. The thought experiment asks each person to imagine themselves into a pre-political moment, without any social-political identity. That is, not only do we not know what position we will have in the society, we do not know what generation we will belong to. From there, we ask what should be done: our own ignorance and desire for ourselves, in whatever role we take up, to have the best outcome, will shed light on what justice is. This gives us a perspective from which to treat all generations equally. This thought experiment shows the unfairness of one generation's depleting resources (such as depleting the working mechanism of AB by wrong usage). Leibovici et al. therefore conclude that individual autonomy must be overruled in favor of the principles of justice and non-maleficence in the case of AB usage. Only a view like this one will balance the rights of different generations and reach the most <u>cost-effective outcome</u>.

But of course, there will be harms to present people who want to use ABs but are not permitted to in order to work against future-AMR. As a way of avoiding some of the present suffering that results from the AB reduction policy Leibivici et al. suggests implementing a rescue rule in case an immediate risk of irretrievable serious harm presents itself. This means that in the case of very serious harms that AB-usage would address, ABs should be used. This seems to imply that this rescue rule is implied to prevent unnecessary usage of AB as much as possible, even if it would induce some harm to the patient. But this rule does not

⁸³ Rawls 1971.

⁸⁴ Battin MP. *The Patient as Victim and Vector: Ethics and Infectious Disease*. New York: Oxford University Press; 2009.

justify the action of sacrificing someone's life by denying a patient's need for AB in the case of life-threatening situation. As some infections will eventually become life-threatening, even if they are not currently. In those cases in which antibiotic use will guarantee a person's life is preserved. In these cases, doctors should allow access to antibiotic treatment to a present patient regardless of how it would affect the collective of future patients.⁸⁵ Leibivici does not mention the criteria of assessing the threshold point. I would just argue that taking AB in cases where there are not effective would be wrong.

Teleological / Sustainability argument

A teleological view provides similar considerations compared to the consequentialist and a complete different ethical assessment of the situation compared to the deontologist. Differently that the consequentialist this view has a clear aim to specifically preserve AB efficiency for future generations. Because of this, the deontological aim of providing equal access to healthcare to any human above all other considerations is in stark contrast with the sustainability view and seems untenable. As excessive use leads to reduced AB efficiency and thus appears to be a clear violation of our responsibilities toward future generations.

Providing access to as many people as possible

From a teleological view, we have an obligation to ensure that as many patients as possible benefit from any new antibiotic over time, because this situation guarantees the most goodness for the most people. This seems to imply that access to the antibiotic should be severely restricted for most low and middle-income countries. Such a restriction would affect millions of people, causing thousands of deaths, but if the long-term outcome would be that more people are cured due to the antibiotic's longer life span, it would be the moral thing to do. This implies that: The morally best outcome is the one with the greatest utility for all. We should decrease AMR as that will improve overall public health, decrease costs and maintain the effectiveness of ABs to maintain healthcare for the future. This situation demands rational AB usage. According to Millar it is ethical justifiable to restrict antibiotic usage to instances where their usage prevents a substantial risk of <u>irretrievable harm</u>.

Most people would consider this position to be irreconcilable with the human rights to life and health; that every human has the right to life and healthcare. As such this view would be untenable for some. There is a clear conflict between consequentialist and nonconsequentialist reasoning in this case.

The sustainability view regarding future generations

According to the sustainability approach we need to take both the present and future context into account when making moral judgments. Our analysis must then focus on the needs and responsibilities of both present and future generations. On this view we have a

⁸⁵ Leibovici L, Paul M. Ethical dilemmas in antibiotic treatment: focus on the elderly. *Clinical Microbiology and Infection*. 2015;21(1):27-29. doi:10.1016/j.cmi.2014.10.013.

duty to preserve (access to) medication and sustainable healthcare, and thus must lower AB usage. Without working ABs we will not be able to treat simple infections in the future, hence healthcare as it is today would be drastically changed. We need to lower AB usage among present people in order to maintain AB efficiency for future generation, even if this entails that millions of people are denied access to ABs now. In terms of distributive justice this means that we need to safeguard AB efficiency by lowering AB usage (to maintain working ABs for all, long-term).

But the sustainability perspective does not only say that we must stop using so many ABs generally; it also stresses the need to <u>avoid AB misusage</u>. Poor access to ABs also leads to AB misuse and thus lowers the overall AB-efficiency level. This means that we are not only not morally permitted to deplete a limited resource for our own wellbeing but also that we should ensure that others will have access to a sustainable future with enough resources. In the case of ABs, this general rule could be translated as an obligation to use new antibiotics sustainably, i.e. only under the best stewardship practices.

Common-good approach

Whereas the deontologist takes ones' duty as a starting point, the common good approach starts from another commitment. This approach is focused on the public good and the collective. The common good approach focuses on what is shared and beneficial for all (or at least most) members of a given community. In the realms of politics and public service, collective action and participation are the consequences of common-good thinking. Solidarity across difference is a key aim, which provides support and guidance when considering the public health AB reduction policy aim.

Littman suggests that we can easily treat antibiotics as a scarce resource based on their limited availability. If having effective ABs would be a public good, their overuse may be likened to the tragedy of the commons scenario.^{86,87} The tragedy of the commons is the most widely used economical and ethical concept to describe the nature of the problem of AMR.^{88,89,90} According to ecologist Garret Hardin (1968) the tragedy of the commons includes the depletion of a common resources through rational utility-maximizing actions performed by rational actors. Even though the actions undertaken are rationally correct for each individual, when evaluated from the perspective of the group, they will suffer in the long run for losing the resource.⁹¹ This concept explains why it might seem rational for patients to take antibiotics even for a minor infection despite the threat of emerging AMR. Despite the benefit for the individuals, there is a risk of emerging resistance (loss of utility)

⁸⁶ Hardin G. Excerpts from "The Tragedy of the Commons." *Environment and Society*. 1968;162(3859):202-212. doi:10.2307/j.ctt1ht4vw6.33.

⁸⁷ Laxminarayan R, Malani A. *Extending the Cure*. Washington, D.C.: Resources for the Future; 2017.

⁸⁸ Swain F. Antibiotic resistance: Bacteria are winning the war | Frank Swain. The Guardian. https://www.theguardian.com/science/2011/apr/07/antibiotic-resistance-bacteria. Published April 7, 2011. Accessed April 18, 2018.

⁸⁹ Battin 2009.

 ⁹⁰ Conly J. Antimicrobial resistance: revisiting the "tragedy of the commons". World Health Organization.
 http://www.who.int/bulletin/volumes/88/11/10-031110/en/. Published March 4, 2011. Accessed April 18, 2018.
 ⁹¹ Hardin 1968.

shared among the entire population. The fraction of resistance that is carried by this individual patient is small while the chance of a quick recovery may be large.

However, the rationality of capricious individual AB use may not be as rational as the above analysis indicates. Battin et al. argues that it is not rational for patients to take ABs in a situation where their condition does not pose a serious threat to their health. These patients would then risk acquiring a resistant normal flora of bacteria due to consuming an antibiotic treatment. According to Battin et al., AMR is not something that will happen in the future. Instead, it is an ongoing process, happening right now. Every time a patient takes ABs he or she may acquire a resistant bacterium due to consuming ABs. This may happen without them knowing until years later, when they get a serious infection that cannot be treated with ABs. In the view of Battin et al, people therefore must refrain from excessive use of antibiotics as it puts them at greater risk than most patients would already have.⁹² However, as many people, especially in LMICs, have misconceptions regarding ABs and their usage, this logic might not be implemented in practice.

Conclusion

Within this chapter I have provided an ethical description of various normative theories and an assessment of the ethical considerations underlying the AB reduction aim. This material allows deeper understanding of what is at stake, ethically speaking, when it comes to evaluating the AB reduction aim. In particular, the chapter showed the conflict of values at play when viewing AB reduction through different ethical frameworks. The main question to answer is whether these cultural contextual considerations hold enough moral value to override the global public health AB reduction aim. As we have seen in evaluating the above views, there is a fundamental contradiction between the sustainability argument, human rights theory and the implications of the various ethical systems. According to the human rights / deontology / virtue view every human should have access to healthcare. While a teleology / sustainability view is more focused on maintaining AB efficiency for the biggest amount of people, among which both present and future people. And then the harm principle is focusing on preventing harm to others. These different views and ethical systems illustrate the classical dilemmas between public health and individual liberties. However, it might be that there are legitimate context-specific Chinese arguments that override the public health aim. Within the next chapter we will explore and discuss the context specific considerations in China.

⁹² Battin 2009.

Chapter 3: Moral weighting of context specific arguments about AB usage in China

Introduction

In the previous section, we have discussed the ethical weighting of the global AB reduction policy versus general AB usage. We have used various theories to guide us towards a recognition and moral weighting of the various ethical norms and values that are at stake. But to provide an accurate ethical weighting we also need to provide an context-sensitive moral weighting of the AB reduction policy dilemma in China. Hence we need to include the various arguments of Chinese citizens into the equation. This chapter will explore to what extent there are legitimate moral considerations to support current Chinese AB usage practices. Each paragraph will briefly explain the context and then provide an ethical weighting of the argument(s) given using the above facts and the above mentioned normative theories. These considerations will then allow us to answer the main research question of this thesis: whether these context specific Chinese arguments morally justify the Chinese manner of using ABs.

Based on my empirical research in China I have performed a system-wide contextual analyses in which I briefly describe the various phenomena and causal relations regarding 1) inequality of access to healthcare, 2) social and 3) medical and 4) cultural believes regarding diseases, 3) Economical argument of a lack of access to resources, 4) fast pace of life argument, 5) Bad Chinese doctor-patient relationship argument and 6) Bad Chinese doctor-patient relationship argument and 6) Bad Chinese doctor-patient relationship argument and believes regarding impact AB usage by humans in China, though, again, the AMR crisis is brought on by use in non-human animals as well.⁹³ In this Chapter most of the writing is freely based on the interviews and impressions from the research I conducted in China.

1. Inequality of access to healthcare

China is (still) a LMIC, in which still many people, mostly in rural areas, are living in poor life conditions. Access to healthcare is limited and unequally dived among the population. Although there is rapid economic growth, only a small percentage of the population benefits from it. The central government has regulated healthcare for some, but not for all.⁹⁴ In the past two decades China has shifted from a system espousing equal access to medical care from state-run providers to one that is increasingly dependent on private options.⁹⁵ Because of this shift, receiving healthcare is not easy for many Chinese. Many Chinese do not receive reimbursement for money spent on their healthcare and medicines. People need to travel long distances to visit a doctor, which costs them a considerable amount of time and money.

⁹³ Note: Details of the research setup, including the customized questionnaire, can be found in this work's appendix.

⁹⁴ Forchielli A. The Chinese Healthcare System: How It Works And Future Trends. The Chinese Healthcare System: How It Works And Future Trends. http://www.albertoforchielli.com/2015/11/13/the-chinese-healthcare-system-how-it-works-and-future-trends/. Published January 7, 2016. Accessed April 17, 2018.

⁹⁵ State Council Information Office. *Medical and Health Services in China.*; 2012.

Because of this the poor and people living in solated and rural areas have access to very limited treatment options.^{96, 97}

Urban vs. rural disparity access to high quality Abs

A major problem of the inequality in access to healthcare is the huge disparity between urban and rural populations, which is part of the general urban-rural disparity.⁹⁸ Although this is a common feature of nations, it is more obvious in China due to their massive population scale: there are an<u>enormous number of people living in China – almost 1.5 Billion people.</u> The disparity is not only due to health access. Within rural areas there is also greater distrust of doctors, as the educational level is relatively lower.⁹⁹ Because of this, doctors tend to provide more ABs to be sure that nothing unexpected will happen with the patient. And similarly patients are demanding higher dosages of ABs as he/she thinks that this will cure them.^{100,101}

Lack of governance access to AB's and the rise of free market forces

AB restriction policies in China are inconsistent across medical providers. Chinese pharmacies can sell all types of medication. Most of these, such as antibiotics, can be bought without a prescription. It is therefore not necessary for Chinese people to go to the hospital for many illnesses. Such treatment accessibility allows poor people to receive medication if they are sick. However, because of low regulation standards and lack of control systems, an unregulated free market has developed: because medication prices are generally kept low, their quality is often doubtful. Many labeled drugs are fake, so they cause no or low treatment response.¹⁰² This represents a huge inequality in access to high quality healthcare and medication. Poor treatment outcomes cause people to buy more and stronger antibiotics than might have originally been needed.

Soft capital influences access to (high quality) healthcare

Another important context specific factor of the Chinese society is its deeply hierarchical attitude. So a patient's occupational status significantly influences their ability to access medical care.¹⁰³ Because these social connections are difficult to quantify and track, there is an intangible quality to access to medical care availability. Although such connections do not, by themselves, have a direct ability to provide good or bad healthcare, they strongly

⁹⁹ Within rural areas there is more distrust in doctors as the educational level is low(er).

 ⁹⁶ Wang H, Yip W, Zhang L, Wang L, Hsiao W. Community-based health insurance in poor rural China: the distribution of net benefits. *Health Policy and Planning*. 2005;20(6):366-374. doi:10.1093/heapol/czi045.
 ⁹⁷ Wilkinson L. Universal Rural Health Care in China? Not So Fast. The Atlantic.

https://www.theatlantic.com/china/archive/2013/09/universal-rural-health-care-in-china-not-so-fast/279429/. Published September 6, 2013. Accessed April 17, 2018.

⁹⁸ Knight J, Song L. *The Rural-Urban Divide Economic Disparities and Interactions in China*. Milton Keynes, UK: Lightning Source UK Ltd.; 2010.

 ¹⁰⁰ Xing M. The Rise of Patient-on-Doctor Violence in China. The Bowdoin Globalist.
 https://bowdoinglobalist.com/2016/04/15/the-rise-of-patient-on-doctor-violence-in-china/. Published May 4, 2016. Accessed April 17, 2018.

¹⁰¹ Tucker JD, Cheng Y, Wong B, et al. Patient–physician mistrust and violence against physicians in Guangdong Province, China: a qualitative study. *BMJ Open*. 2015;5(10). doi:10.1136/bmjopen-2015-008221.
¹⁰² This has been told by multiple destars from both Baijing's third hermital and smaller primairy agra hermital.

 ¹⁰² This has been told by multiple doctors from both Beijing's third hospital and smaller primairy care hospitals.
 ¹⁰³ As Li pointed out in 2006,

guide outcomes. Because of a lack of strong oversight, many doctors act in terms of these social relationships. Some doctors find it difficult to deny personal requests, even if they think that providing ABs is not necessary. Often their patient is a friend or someone they know. If they deny the request, then the patient will think less of them or believe that their social standing has been damaged. For many of doctors, this is not considered to be a choice.¹⁰⁴ Because of factors like these, the AMR problem is made worse through over-prescription.

Ethical weighting legitimacy

Receiving healthcare is not easy for most. The poor have access to very limited treatment options.^{105,106} For the people living outside rural and poor areas, AB are considered to be a wonder drug. Because they are protecting them against potential deadly diseases. Because these people do not have access to high quality AB, nor healthcare in generation, taking these Abs might be the only medication they have. According to the deontological view access to healthcare and medication is essential to every human. In the absence of other options and/or to protect themselves against life threatening diseases, taking ABs can be considered legitimate. However, from a teleological view this argument does not justify the situation: using ABs incorrectly leads to bad outcomes via AMR. After all, we also need to think about the health of other people, including future people.

2. Cultural beliefs about health and medication usage

In China there is a deep-rooted cultural fear of disease, which stimulates medicine usage. This further stimulates AB prescription by doctors and intake by patients, even if ABs are not necessary for recovery from disease. Traditional Chinese culture supports taking medicine for any kind of ailment. It also argues that the more medicine is consumed, the faster it will work. Because of the culture of Chinese medicine usage, people have not learned to rely on their body's own healing mechanisms, so they feel insecure when they are denied any desired medicine. It is important to note that traditional Chinese medicine includes use of herbal medicine along with western drugs such as ABs. Chinese people measure their health status to the amount of happiness or comfort they experience. People fear disease because it is very uncomfortable and may last for a long time. Hence the more discomfort they feel, the more worried they become. They feel very dependent on their doctor. And if the doctor does not want to provide medicine to them, they will be stressed.

"You can't know what the disease will do to you. The only thing you know is that disease is bad. Taking medicine will take make you feel better. That is important because that is less harmful". – Professor Peking University

¹⁰⁴ This argument has been given by medical students from Peking University.

¹⁰⁵ Wang, et al. 2015.

¹⁰⁶ Wilkinson 2018.
Ethical weighting legitimacy

How we treat our health and how we respond to disease and risks are highly influenced by cultural and geographical factors. From the old Chinese traditions people believe that medicine is able to cure every disease. In their ancient past they would have taken herbs for everything. Some interviewees explained to me that if a doctor would not provide them medication, they would be stressed and worried. Taking medicine is a way for Chinese to feel safe. One underlying reason for this relies on an inner fear of Chinese to rely on the healing mechanism of their own body, which is something that they never have learned. Because of this they will take medication even before they get sick. Their motives reside from an inner protection mechanism. Another observation is that the behaviors of Chinese often relate to the amount of pain and pleasure, where pleasure means "happiness". This is a kind of utilitarianism based on individual pleasure, which is just egoism interested in one's own happiness. With regard to AB usage – or health in general – they think that their health is most precious to them. They are afraid of disease and fearful for death. Feeling sick is causing pain, discomfort and stress and hence it should be treated with medication as soon as possible. Because of this Chinese justify using AB as a preventive drug. Without such a preventive measure, the thought of disease and what will happen to them makes them stressed and fearful. From all factors that play a role, this one might be the **most legitimate** reason to justify Chinese AB usage patterns. Apparently Chinese citizen feel they are in direct need to protect themselves based on an underlying fear / insecurity. This illustrates a basic human need that drives them to take ABs. However, considering the scope of the global AMR problem, even like the above reasons, this argument doesn't justify their actions regarding the overall ethical assessment of the global AMR problem.

3. Economical argument lack of access to resources

China is a LMIC and hence a lot of people do not have access to a lot of resources. Because of this lack of access to resources the decision making might be changed and justified dependent on other factors. In the light of this thesis I will only discuss the educational disparity (e.g. healthcare disparity has been mentioned before).

Educational disparity

In general, both the elderly and the poor are not well educated.^{107,108} They, generally, are not aware of the medical world's changing knowledge of ABs. The Chinese government has, through propaganda, taught that ABs are magic bullets. Further, these individuals often see the positive results of AB use. Especially children are often encouraged to take ABs to maintain good health. Most people do not know ABs are harmful for their health and how their use affects the health of others. A new, multi-country survey performed by the WHO

¹⁰⁷ Facts about China: EDUCATION. Education in China. http://www.china-mike.com/facts-about-china/facts-chinese-education/. Accessed April 17, 2018.

¹⁰⁸ Education in China. Wikipedia. https://en.wikipedia.org/wiki/Education_in_China. Published April 16, 2018. Accessed April 17, 2018.

among 1.002 participants illustrates that people are confused about the major threat to public health that is AMR. Further, they do not understand how to prevent it.¹⁰⁹

Ethical weighting legitimacy

Most Chinese have a very low educational level. They do not know about the harm that ABs can cause for their health and that of others. They think ABs are magic bullets, protecting them from developing disease. This is based on false beliefs which make them demand the wrong sort of medicine. These mistaken desires cause a negative feedback circle as doctors continue to fulfill give incorrect medicines. This emphasizes the duty of the government to provide clear guidance and surveillance systems for doctors and hospitals and to increase general awareness among citizens regarding good AB usage and healthy living (e.g. to protect them against the harm they cause on their own health). The lack of education explains why Chinese citizens currently wrongly use ABs. The explanation, though, **does not justify the situation**. Ignorance may be a moral defense against claims of responsibility, but it cannot be a reason not to change. We cannot accept the current situation while facing the risks of losing AB efficiency. Improving education represents a general duty to fulfill. It stresses the moral obligation of the Chinese governments and/or high income countries to provide tools to improve the educational level about AMR and the risks that we are facing. Whereas education can be improved, AMR cannot be reversed.

4. Fast pace of life argument

"We have learned to sacrifice our interest for the interest of the collective. That's our value." – young professional in metroline China.

There are also great societal problems which contribute to excessive AB usage. One is the culture's fast pace of life. Chinese citizens from various levels of society use this cultural element as an argument for justifying AB usage to prevent them from becoming sick or to recover faster. Another factor is China's single child policy: Chinese people need to take care of their parents, which puts a high burden on their lives. Illness means that people can't work, do not earn money and cannot take care of maintaining their family. In their perception, ABs are a kind of magic drug that provides them with a cheap and fast cure and protection against harm. For both patients and doctors, taking ABs seems to be a rational course of action. "I don't have time to be sick" is a common slogan for why Chinese people take ABs. Because of the fast developments and high work pressure within China, people are experiencing life to be very 'fast paced'. Everything needs to be fast in order to produce more, better or cheaper. This "fast pace of life" argument is so prominent in individuals' perception that it is a societal problem in general. For Chinese, to be sick and to stay away

¹⁰⁹ WHO multi-country survey reveals widespread public misunderstanding about antibiotic resistance. *WHO / WHO multi-country survey reveals widespread public misunderstanding about antibiotic resistance*. November 2015. http://www.who.int/mediacentre/news/releases/2015/antibiotic-resistance/en/. Accessed April 17, 2018.

from work is not an option. Chinese people believe they will be less respected by their boss or get fired if they fail to show up to work. Going to the hospital to see a doctor is an enormous hassle that takes them at least a full day of travellign and waiting. Buying cheap antibiotics in the pharmacy next to their homes is affordable, without risk of loosing their job and potentially a quick way of getting better.

Now for then argument

Because of how Chinese people experience sickness, and the fast pace of life argument Chinese people are more focused on direct and fast results. Therefore, taking ABs as a rescue drug perfectly suits their expectation pattern: to release discomfort and being able to proceed once practices. By taking AB's people are experience fast positive results and it protects them from suffering.

Fast recovery as medical standard argument

In the Chinese medical context, fast recovery is considered the Holy Grail. This has important implications for clinical practice. Differently than in the West, Chinese patients expect their doctors to do anything possible to make them better as soon as possible. As in the West, doctors are supposed to act in the best interest of the patient, but there is a difference in understanding what "best interest" means. In both cases, this concept has to be understood contextually. For example, the Chinese take ABs as a fast recovery drug. But in the long run, because of AMR, it will put their health and that of others at risk. Chinese doctors believe that there should be not be any risk for the current patient and/or the current medical condition. Contrary, Western doctors might also consider the long-term efficiency of Ab – whether the patient will become less sensitive at a later moment of time. Therefore, taking AB efficiency into account affects clinical decision-making.

Competition argument

Chinese citizens, from birth, understand what a fast pace of life entails. Chinese citizens typically experience life this way: There are so many Chinese people, competition is extremely high and working hard is considered as a universal moral value. In general, Chinese citizens take ABs faster (e.g. as preventive medicine) and in higher doses (to get better faster) compared to citizens of other countries. From birth, Chinese people are taught that they are not allowed to be sick. Competition in all domains of life is extremely high. If children cannot go to school due to illness, their education and development will be perceived to be "behind" other kids. Hence parents regularly bring their children to doctors, and likewise, doctors feel justified to provide ABs to prevent people from getting ill⁻

^{110,111,112,113} In the past – and still a lot - doctors infuse children with medicine in order to ensure they can continue going to school. They understand the pressure of competition and the harm of being sick means for children.

Fear of loss of face argument

"If we ask for sick leave just because we got a cold, other people will think that we aren't strong and we will feel ashamed about ourselves." – an ethics student at Peking University

This is a deep-rooted cultural believe for all Chinese. Independent whether people are rich or poor. Most people will choose to keep on working, even if others advise them to have a good rest. The person will still stick to his choice because his value or the sense of responsibility.

One-child family planning

Chinese persons feel strongly responsible for their family. Because of the one child family planning, Chinese citizens experience a high burden of taking care of their families and ensuring their children get a good life. To this end, they sometimes take excessive ABs to ensure continued personal and familial performance. Although this might be very stressful for the individual and family, it does not justify lowering AB efficiency; private stress is not a trump card on all other people's needs, rights and goods. Fortunately, the Chinese government has recently changed their policy, allowing additional children for families, which may take off some of the burden

Ethical weighting legitimacy

Their argument for this behavior is that they cannot be sick for even one day because of fast pace of life. Going to the hospital to see a doctor is an enormous hassle. They need to take a day off work (risking the chance of getting fired or losing respect), need to pay for transportation (hospitals are usually not next door) and pay for healthcare (not everyone has health insurance and if they do, they first need to pay themselves before getting reimbursement). Buying cheap antibiotics in the pharmacy next to their home is an

¹¹⁰ Yu M, Zhao G, Lundborg CS, Zhu Y, Zhao Q, Xu B. Knowledge, attitudes, and practices of parents in rural China on the use of antibiotics in children: a cross-sectional study. *BMC Infectious Diseases*. 2014;14(1). doi:10.1186/1471-2334-14-112.

¹¹¹ Woodhead M. China Medical News. Infusion madness: patients in Nanchang hospitals consuming gallons of IV antibiotics. http://www.chinesemedicalnews.com/2014/03/infusion-madness-patients-in-nanchang.html. Accessed April 17, 2018.

 ¹¹² Zhang Z, Zhan X, Zhou H, et al. Antibiotic prescribing of village doctors for children under 15 years with upper respiratory tract infections in rural China. *Medicine*. 2016;95(23). doi:10.1097/md.000000000003803.
 ¹¹³ Hairong W. Overdosing on Antibiotics: New research yields insight into China's antibiotics abuse and its impact on the environment. The Beijing Review. http://www.bjreview.com.cn/nation/txt/2015-07/20/content_696697.htm. Published July 20, 2015. Accessed April 17, 2018.

affordable and quick way of getting better. "The fast pace of life" represents a deeper societal problem. Although it is a high (mental) burden to Chinese citizens to experience life this way, it does not justify the ineffective ways they take ABs. From both the views of deontology and teleology, taking ABs to prevent diseases and/or to accelerate disease recovery **does not override** the loss of AB efficiency for the greater good of humanity.

Hard working as moral value

Chinese are educated from an early age that it is not good to be sick. Hard working is a key cultural and moral value. Chinese citizens consider themselves to be better people if they continue working, no matter what. Even if they are not sick, parents bring their children to doctors in order to keep them healthy, and likewise, under this pressure, doctors justify their decision to provide ABs to prevent children from getting ill or to let them go to school. In this way, antibiotics have become a prevention drug. For them, taking ABs is similar to how paracetamol is taken in the west, as an easy and cheap innocent cure. The hardworking argument illustrates a cultural value that has broad purchase among Chinese individuals and in their decision-making to take ABs. However, taking ABs only to guarantee that one is seen as a hardworking or strong person **cannot be justified**, given the global AMR threat. The argument of preserving AB efficiency to save lives and reduce healthcare costs clearly overrides this argument.

Now-for-then decision making

Most Chinese are very focused on the 'here and now', the current moment. What is happening right now is more real compared to events that might happen in the future. If people feel discomfort, stress or fear they want to act to solve this straight away. Taking ABs provides a quick, positive result versus waiting for a disease to be eliminated by itself. AMR is something that most people have never heard of, and most people are not aware of their resistance status or anyone's else. Further, AMR is not seen as a current concern; instead, it is a non-tangible future concern. Because of these limitations, they provide less weight to it compared to current, seemingly pressing issues that are at stake. For them, the AMR is like a "concept" rather than a disease state from which they will suffer. This argument explains Chinese behavior towards ABs usage, but it is **not a legitimate reason** to justify current practice. It is thus the obligation of the educated west to inform them, to educate and empower average people and doctors alike.

Social alienation

Because of the lack of protection mechanisms in society and the emergent social alienation of industrialization and technology, people have lost connectedness with other people and with society as a collective system in general. They have learned to be focused on their own lives. Notably, the Chinese have a long history in which they have learned to act in favor of the collective. Some norms and values arrive from the respect people receive regarding the

collective. However, this kind of sense of the collective has other roots compared to collective norms and values built on reciprocity, trust and care about others. These ideas have been eroded, and now the social web containing social goods is lacking in the Chinese society. There is no community feeling, purpose, responsibility and/or common interests, whereby in the spirit of cooperation, people are concerned about those who are less fortunate or vulnerable and strive for equity and justice for all. It is difficult to justify the option to take care for a social good, as this perception no longer even exists within the experience of Chinese citizens. The above situation explains why Chinese citizens at this moment, feel less willing to take any risk to their own health to protect the health of others. However, this argument **does not justify** current AB usage in China. Rather than accepting the current state of affairs as justification for individualistic AB decision-making, a new framework for thinking must be encouraged. This new framework must understand people's relationships as primary, that one person's medicine-taking habits affect other people's health. There is a need for the government to address this problem in society, to create greater trust in the system and in other citizens. Interestingly this argument about the community and the collective considerations can be used in the fight against AMR, to lower AB usage. Because of this collective approach China needs a leader who is making them aware of the harmful consequences of taking Abs and praise people who lower AB usage. If performed in an ethical responsible and honest manner, this could create a powerful effect causing an entire population to lower AB usage.

5) Bad Chinese doctor-patient relationship argument

Contrary to doctors in the west, Chinese doctors have low rank in society and hence a lack of perceived expert authority. According to the participants I interviewed, Chinese people expect to go to a doctor and get medicine. Because of this cultural difference, the doctorpatient relationship also has different dimensions in China than in the West. Instead of being seem as an expert, the doctor is instead a medical salesman. In China patients treat doctors and hospital services like a business. Their way of thinking is: "I pay you to make me better. I pay you to give me medicine. And I pay you to become better as soon as possible. Doctors believe patients have their authority to ask for individual healthcare." If the doctor does not provide these, people believe that the doctor deliberately withholds medication from patients, not that medication was not necessary after all. Therefore, patients do not believe the doctor and ask for medicine again. If the doctor does not provide it to them, they will go to another doctor, engaging in "doctor-shopping." Because of this some doctors have become fearful losing their patients and/or being accused of being blamed and feel they need to fulfil all patient's requests for medicine. Moreover, many people get emotional if they do not get what they want or if something happens to their health or to the health of their family members. If something bad happens to the health of a patient, then doctors fear that 1) the doctor will get blamed, 2) the patient will do bad things to the doctor, 3) some doctors are afraid of losing their jobs because of the lack of protection provided within healthcare protocols or from their workplace. In the past decade multiple public outrage events of angry patients have turned out very badly for doctors. Because of this experience, doctors believe that something really bad will happen to them and they don't dare to take risks. Because of this fear, doctors may find themselves in a conflict of interest between the

interests of the patient, protecting their own position and the public's health. Because of the expectation pattern of patients, doctors are changing their behavior accordingly. Doctors do not want to argue with the patient and hence they will provide them medication or a higher dose. In case of ABs, if doctors think that their Chinese patients want to get medicine, whether ABs or something else, they feel they should give it to them to make the patient happy. All these factors cause harm to the integrity of the doctor's work. Further, such factors make the application of rational AB usage policies almost impossible.

Ethical weighting legitimacy

In China, doctors have very low status and are distrusted by their patients.¹¹⁴ Patients do not respect doctors because of their expertise, instead expecting them to provide medicine for the patient to get better as soon as possible. Some doctors feel that they need to obey patient requests in order to be a good doctor, as doing so would satisfy the patient and fulfill their wishes. This represents a loyalty problem of doctors towards patients. The soft capital and bribe culture adds to this problem. However, being a good doctor according to their medical oaths is something different than satisfying the patient's wish. The patient is not the expert and does not know what is best for their health. It is up to the doctor as a specialist to protect the health of the patient respectively future patients, as best as possible. In such an analysis, the doctor needs to take both short and long term considerations into account. Considering the global AMR problem and the risks that we are facing, accepting soft capital and bribes for individuals to receive ABs are wrong ethical conduct. This argument cannot be justified using any moral theory, short of egoistic self-promotion. It rather illustrates the need to provide better protection policies within healthcare institutions to avoid such practices. Second, some doctors are afraid that something bad will happen to them if they would not prescribe ABs.¹¹⁵ Situations occurred in which patients are attacking their doctor. They blame them for getting sicker or for the death of a family member. This has huge implications for the traditional doctor patient relationship, which used to be built upon trust. Like the previous argument, this argument illustrates the need to provide better protection policies within healthcare institutions towards such practices. So that doctors would feel safe and protection against wrongful acting of patients. Allowing them to make rational choices instead of being driven by fear. Hence this argument **does not justify** the current way of AB usage in China.

Another important aspect to consider is the Chinese attitude towards healthcare in general. Healthcare is a business in which every service can be bought. This mentality partly derives from a strong desire of Chinese individuals to find their identity via the choices they make, including their medical choices. They believe that their choice relates to their autonomy. Many Chinese refer to the liberal thought of free choice and self-determination. They feel it

¹¹⁴ Duckett J, Hunt K, Munro N, Sutton M. Does distrust in providers affect health-care utilization in China? *Health Policy and Planning*. 2016;31(8):1001-1009. doi:10.1093/heapol/czw024.

¹¹⁵ Wu HY-J. Deep reflection needed on Chinas medical-help-seeking culture. *The Lancet*. 2013;381(9863):e2. doi:10.1016/s0140-6736(13)60131-2.

is up to them to decide what they think is important and what should be done. Such a consumer-based approach in general illustrates a more modern technological conception, including in choices about obtaining healthcare services, but it **does not justify** random/ excessive AB usage in the light of the global AMR threat. As ABs are a scarce resource, serving a public good, they require proper guidelines for distribution and prescription practices.

6) Other Cultural argument

"Individualism is selfish. My understanding of this is that you need to take care for yourself first, to take responsibility for yourself. Then you have the power to help others. In china individualism is treated as a very bad thing. It is very selfish." – Student Peking University

According to interviewed PhD students in ethics at Peking University, the difference between western and eastern conceptions of medicine comes down to ideology. In the west, individualism sets the stage. To further illustrate this point I will share the following anecdote. According to students from the research group at the ethics department of Peking University the Chinese government always talks about collaboration and "making sacrifices for the collective."

"Two decades ago the government gave orphan home children Abs every morning to prevent disease outbreaks. Hence taking AB within this context is considered a good thing if it would prevent something bad for another person." – Student Peking University

The same way of reasoning is reflected in the doctor patient relationship. Doctors do not only take the patient in front of them into account, but also the risks for other patients. For example, doctors feel comfortable providing Abs to reduce the chances of other patients to become infected by each other. The Chinese doctor strongly believes that they should not take any risk regarding another person's health. Despite the above cultural beliefs, especially about what one person owes to the collective, there is a strange individualism in Chinese medicine. Because of the lack of governance, comprehensive regulation, surveillance and protection mechanisms within society, in practice many Chinese have learned to focus mainly on their own lives and that of their families. A so called 'social alienation.'

Chinese have learned not to question

Having a long history of suppression Chinese individuals have learned to obey and not to question. "We are raised not to think and talk about politics. We have learned to obey to the rules. This is how the government wants it. The government wants to control everything. It is all about controlling; all media is controlled. These are propaganda machines. So for most people they don't even realize what is going on in society. Even if they do, then they will not care, because they feel they don't have any power to do something." Realizing this is important. Because understanding our history and how this has affected the culture within population, we can better anticipate on today's challenges. It provides us clues on the root cause of the problem, in this case, AB usage and how we can reduce it.

Mistrust in each other

"This 'kid' is huge, fat, but it does not learn anything. The 'kid' does not have sympathy. The 'kid' does not have a kind of heart. Although more people are making money – people are still suffering. We have learned 'not to care', we do not have religion, we are not afraid of anything. We do not worship anything. Nothing will protect us....so we should protect ourselves. Hence people start worshipping money. In these circumstances, it is so scary. Some people are doing everything to make money. They pollute the environment or do very 'bad' things. For example, look at food security (e.g. adding acid substances) and other things as well. Because of this development, China as a society has become a mess." – Professor Peking University

The above quotation shows how one Chinese academic understands his nation. It is large, powerful, and ignorant. Despite its strength, greed has made it difficult to launch interventions that benefit the common good. There are many social factors that both cause and result from this social framework. This last decade China has experienced various negative incidents on the news where random people who offered public support to people in need became publically accused of being accountable.^{116,117,118,119,120,121} These cases have created a deep rooted fear that reaching out to assist a person in need will lead to personal financial loss and harm.¹²² Examples of such incidents also occurred in medical settings, which I will discuss later. Mistrust in one another has created complications in social life, including in medicine. As a reaction to mistrust, people have become introverted and learned to live their 'own live'. The social alienation of people from one another contributes to the culture's attitude toward AB usage. As people are focused on their own health they have less empathy with other people around them, which means that ABs are taken without care for consequences. Hence the AMR problem becomes worse.

¹²² Elderly falls ... 2018.

¹¹⁶ Minter A. In China, Don't Dare Help the Elderly: Adam Minter. Bloomberg.com.

https://www.bloomberg.com/view/articles/2011-09-08/in-china-don-t-dare-help-the-elderly-adam-minter. Published September 8, 2011. Accessed April 17, 2018.

¹¹⁷ Explaining Chinese kindness and reserve: Nanjing Peng Yu. Guangzhou Stuff.

http://www.gzstuff.com/forum/topics/explaining-chinese-kindness. Accessed April 17, 2018.

¹¹⁸卫生部:老年人跌倒后是否扶起要分情况[Ministry of Health: Does the elderly person raise the situation after falling?] http://huati.weibo.com/zt/s?k=9739&hasori=1. Accessed April 17, 2018.

¹¹⁹ Elderly falls in the middle of the road, no one helps because fear of being framed. ChinaHush. http://www.chinahush.com/2010/07/12/elderly-falls-in-the-middle-of-the-road-no-one-helps-because-fear-of-being-framed/. Published July 12, 2010. Accessed April 17, 2018.

¹²⁰ Rahman K. Shocking moment three-year-old boy is brutally beaten on the street by passerby... and pedestrians walk past as if nothing is happening. Daily Mail Online.

http://www.dailymail.co.uk/news/peoplesdaily/article-3072032/Shocking-moment-three-year-old-boy-brutallybeaten-street-passerby-pedestrians-walk-past-happening.html. Published May 7, 2015. Accessed April 17, 2018. ¹²¹ To Help or Not to Help, a Dilemma in China. www.theepochtimes.com.

http://www.theepochtimes.com/n3/1493926-to-help-or-not-to-help-a-dilemma-in-china/. Published March 16, 2018. Accessed April 17, 2018.

Ethical weighting legitimacy

Although the above cultural arguments are important to acknowledge as such, they do not justify actions that override AB usage. They do not hold in relation to the devastating consequences of AMR.

Of course there are reasons for Chinese AB usage habits. They are not random or irrational. Indeed, the above paragraphs show that there are historical, economic, social, and personal motivations for the problematic usage of ABs that is prevalent in China today. To understand these reasons in the context of the AMR crisis, though, an ethical analysis is necessary. And that evaluation is what the dissertation has provided. By understanding both sides of the debate—arguments in favor of current Chinese usage as well as arguments against—an individual is able to weigh the sides.

The two sides may be summarized thus: on the one is individualism and traditionalism; on the other is community and scientific evidence. The starkness of this distinction, especially in this dangerous era of increasing AMR, should make clear what must be done.

Conclusion

The above paragraphs have provided a context-sensitive weighting of the moral considerations underlying AB usage in China. It is clear that AB usage happens for many reasons, some legitimate but many not. These factors provide the necessary background for the essential debates about AB utilization in the contemporary world. Despite the importance of the Chinese arguments, they must be examined with and met by responses from moral theory. The cultural context matters, but it cannot be a defense against any possible critique. This is especially the case when AMR continues to risk worldwide health. Only this sort of work will show individuals—patients, academics, medical professionals, a clear path forward in considering AB usage and the AB reduction prioritization. The next chapter will focus on answering the research question and the conclusion that we can draw from taking the moral weighting of the AB reduction policy and the contextual moral considerations into account.

Chapter 4: Conclusion

The direct relevance of writing this thesis is an acknowledgement of the global AMR threat for humans and the statistics of over-consumption of ABs in China. The mission of this thesis was to investigate whether the global AB reduction aim overrides AB usage in China now. The research question of this thesis is whether the public health aim of antibiotic reduction overrides AB usage in China? Based on the findings of both empirical research and literature research I conclude that the public health reduction aim overrides AB usage by Chinese citizens. Because of the lack of previous agreed upon public health ethics framework and conceptual analyses of AB usage in China, I have performed both empirical and literature research. To assess the research question in its context I have also investigated context specific arguments derived from the Chinese economic, political, social and cultural situation regarding AB usage in China.

The first part of the thesis has shown that AB usage does not only affect the individual, but the entire system. Because AB efficiency is relevant to every human, and taking Abs is lowering the total AB efficiency. Because of this we can consider antibiotic efficacy as a common good and a potentially non-renewable resource. Because once AMR arises, we cannot undo the efficiency. As such, some ethicist pointed to the "tragedy of the commons" situation. Depicting a scenario where the self-interest of individual stakeholders collectively cause depletion of working Abs, damaging the group's good (responsiveness to Abs; health). This model illustrates why we need a public health ethics framework that tackles AMR on a global scale.

According to the deontologist and human rights theory the AB reduction aim in China might be ethically problematic based on the principles of fairness, equality and justice. Directing towards the right to equal access to healthcare for every human. Access to healthcare is a human right regardless of who you are or where you live. Notably, China as a LMIC has a double disadvantage to overcome because of its lower education, the low awareness about the bad consequences of taking Abs and the restricted access to healthcare, including the right ABs, in many parts of the country and according to its geographic location highly restricted access to high quality ABs. This means that, besides the public health aim to reduce AB's, we also have a moral obligation to promote equal access to AB for those who do not have access to this common good. However, the right to equal access to AB does not override the public health AB reduction aim. As not acting to reduce AB usage would eventually account for potentially millions of other sick people (e.g. of some equally without access to health), deaths and tremendous amounts of healthcare costs on a global scale.

Apart from the deontologist theory, the teleologic and sustainability approach have provided me with arguments in favor of the AB reduction aim to take preserve AB efficiency for both present and future people. It is the right to provide equal access to future people that changes the perspective. As billion of other humans will derive on earth after us. Moreover, this is in line with the consequentialist view which focusses on maintaining AB efficiency for the greatest amount of people. The aim is to save as many lives as possible and reduce healthcare costs. Both theories stresses that we need to maintain AB efficiency and hence argue in favor of the public health AB reduction aim as overriding to current AB usage in China. Based on those arguments I conclude that we have a duty to preserve the AB efficiency and all have a moral duty to lower AB usage.

Though that doesn't mean that we do not need to take into account the deontological arguments. And we certainly cannot ignore what's at stake for the most disadvantaged

among us. In this situation, the people in poor and rural areas. In order to lower AB usage in China, a careful balance has to be found between curtailing current AB usage and still ensuring appropriate availability and the attitude of third parties, such as the Chinese government and developed countries towards low middle income countries who are lacking the resources to provide access to medication and healthcare to lower the unintended burden. The argument given by some Chinese citizens for taking ABs in such large amounts does not override the global public health AB reduction aim. As by reducing AB usage we would be able to save billions of lives, including the lives of future humans, and protect humanity against a horrible future scenario in which ABs are not working anymore.

Besides using varying normative theories I have also explored whether there are legitimate context-specific arguments that would override the global public health AB reduction aim. Based on empirical research I have shared arguments given by Chinese citizens. I have also showed that many of these arguments do not override the global public health AB reduction aim in relation to the devastating consequences of AMR. Altogether, I found two legitimate argument to justify how some Chinese citizenss are using ABs. These include the argument to improve equal access to healthcare and treatments and the argument regarding deeprooted cultural beliefs about fear for diseases. Lowering the inequalities of access to healthcare is based on a human rights and deontological argumentation. However, although this depicts an important public health aim, it does not override the current research question. Because apart from the AMR problem there are multiple manners to lower access to health inequalities among the general population. It does not only depend on having free access to AB's, but more about access to all kind of resources to protect health, diagnose diseases and taking care of patients. Because of this, the necessity of lowering AMR, with its devastating effects for populations worldwide, is considered more urgent in this situation. The other argument is based on deep rooted cultural convictions related to disease and experiencing discomfort. The quotations used from the empirical research in chapter 3 are visualizing how this fear has become part of Chinese citizen's identity. Although this is an important consideration to be taken serious by policymakers, healthcare institutes and public health experts, within the broader scope of the threat of AMR, this argument does not override the public health AB reduction policy. As by raising education, awareness and access to healthcare resources and services, Chinese citizens would be able to understand the actual threat of AB usage, the bigger AMR problem and the harm it conducts in relation to the discomfort that they are experiences.

In sum, I believe that the public health AB reduction aim overrides current AB usage in China. In general, over usage of Abs is just wrong! Considering the AMR threat in relation to thetotal amount of AB taken by Chinese citizen's and their underlying arguments for taking AB as preventive medicine this is ethically very problematic. As by reducing total AB usage, we can protect us against a horrible future scenario in which ABs are not working anymore, save billions of lives, including the lives of future generations and save trillions of healthcare costs. Though by changing AB usage in China, a responsible public health framework is needed that also considers health inequalities and deep-rooted fear from Chinese citizens for diseases. In the final chapter you can read a few final recommendations regarding the need of more ethics research and stewardship programs to lower AMR at a global scale.

Chapter 5: Final remarks towards a Public Health Framework for the AB reduction Policy aim

To reduce AB usage in China, a context sensitive but global public health ethics framework is needed. This framework is needed to guide the various stakeholders involved through the complexity of this public health problem. And to provide a justification for those actions conducted. Having provided an ethical assessment of AB usage and reduction in China, more ethical assessment is needed to investigate how to implement the AB reduction aim in practice. Based on the research performed, the ethical assessment and further literature research on stewardship measures to reduce AB usage I have outlined a few final remarks for future research.

In depth ethical assessments of varied context are essential

As I have outlined above, the global AMR problem is highly complex and many new situations with new ethical questions are arising every day. We need ethicists to guide us with the exchange of knowledge, translate moral concepts to an appropriate population-level while clarifying the relational and socially embedded normative concepts that will underpin AMR responses. But to provide this guidance, ethicists first need to find a global common agreed upon public health ethics framework to provide concrete guidance and justification of actions and policy decisions in practice. And to be able to guide other professionals and the people in various contexts.

Apart from merely focusing on lowering AB usage by inducing a public health AB reduction aim, we need to take into account the consequences for low and middle income countries to ensure rational AB usage. And hence, our attitude towards these countries. As the ethical assessment showed that we have ethical duties to provide equal access to healthcare to all. The moral principles of justice, fairness and equality stress our moral obligations to improve access to high quality ABs and healthcare in LMICs (called: 'rational AB usage', or within humanities 'AB stewardship'). Because of this, the global public health framework needs to consider two problems: Safeguarding AB efficiency by lowering AB usage and improving access to healthcare by providing people better access to ABs under specific conditions.

Some may object that encouraging China to use fewer ABs, in more responsible manners, will infringe on the status of one of the world's poorest nations. In response, though, it must be said that the reduction of AMR is more urgent than lowering public health inequalities. Lowering public health inequalities is an important issue that must be addressed, but the two factors cannot be weighed against each other. One must first address AMR, as the effect of not reducing AMR is more devastating than solving those healthcare inequalities. Moreover there are multiple manners to reduce inequalities of access to healthcare apart from AMR reduction. These are important, too, and they must be remedied in turn, based

on a careful public health prioritization that acknowledges health risks, efficacy, and other factors.

Stewardship: A sustainable public health AB reduction strategy

To guide the various stakeholders and to justify the actions that are taken to justify AB usage it's essential to have one global public health framework. A framework that will guide decision makers from all countries, including china, while taking their context into account. By applying stewardship measures based on one generic public health framework, all countries can unite forces to achieve one common goal. Whereas low and middle-income countries may not have the structural or financial capacity to apply such rigorous stewardship measures, HICs can support them by building appropriate structures so that stewardship can be applied. By applying stewardship, we fulfill the obligation to not deprive future people of the limited resource of antibiotic efficacy.

This stewardship includes:

- 1. Improving education to the general population and physicians
- 2. Guiding the government/ healthcare institutes to set improved protection measures and AB usage and prescription standards using the European guidelines
- 3. Embracing new technology to invent new and improved ABs for lower costs
- 4. Using improved diagnostic technologies to select the right ABs based on the individual profile of the patient (prevent AB misusage).
- 5. Choosing the right type of ABs according to its specific situation and the individual need of the person.

By taking up these stewardship criteria, we ensure our moral responsibility to provide access to lifesaving drugs while safeguarding the prohibition of excess and unsustainable usage.

Global Guidelines REACT group: Collective global action

Based on the existing guidelines from the REACT group¹²³, the following cornerstones for collective global action are widespread acknowledged among experts and policy leaders:

- Ensuring reliable distribution systems and redundancies in manufactures to minimize shortage of access to affordable, effective antibiotics for all, including low and middle-income countries.
- Implementing stewardship policies: developing and implementing local guidelines for rational antibiotic use and improved diagnostic capacity.
- Taking care of preventing infections. As every averted infection can be a potential course of antibiotics saved. This requires action on both individual and systemic level.
- Embracing new technologies in the field of drug development and health diagnostics. To minimize excess use by guiding therapy, and efficient systems to prevent, control and track infections and epidemics.

¹²³ The ethics of antibiotic resistance – 2017 – ReAct. ReAct. https://www.reactgroup.org/news-and-views/news-and-opinions/year-2017/the-ethics-of-antibiotic-resistance/. Accessed April 18, 2018.

• Providing adequate technical and financial support in these areas for countries with limited resources.

These cornerstones together form a practical framework to fulfill our moral obligations within the field of antibiotic resistance and to promote the development of a world free from fear of untreatable infections. Such a world would ensure a brighter future for all.

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Appendix

Attachment 1: WHO questionnaire AB usage 2016

16 NOVEMBER 2015 \downarrow GENEVA - As WHO ramps up its fight against antibiotic resistance, a new multicountry survey shows people are confused about this major threat to public health and do not understand how to prevent it from growing.¹²⁴

- 57% of respondent's report taking antibiotics within the past 6 months;
- 74% say they were prescribed or provided by a doctor or nurse;
- 5% say they purchased them on the internet.
- More than half (53%) of respondents wrongly believe that they should stop taking antibiotics when they feel better, rather than taking the full course as directed.
- 61% of respondents think, incorrectly, that colds and flu can be treated by antibiotics.
- Two thirds (67%) of respondents are familiar with the term 'antibiotic resistance' and
- three quarters (75%) say it is 'one of the biggest problems in the world'.
- 83% of respondents say that farmers should give fewer antibiotics to animals—the highest proportion of any country in the survey.

Attachment 2: Interview survey and Chinese system analyses

Sampling & Participants

Sampling for the participants was purposive to ensure in-depth knowledge on AMR in China and motives behind AB usage in China. There are some articles about the ethical problems of the AMR problem and AB usage in China, but there are no in-depth ethical or context-specific analyses. In order to answer the research questions, I moved to Beijing to get a better understanding of the Chinese way of living and their reasons and norms and values regarding AB usage. I tried to become part of their community in order to get an insider's perspective on the AMR problem. I have traveled to multiple cities throughout China and talked with many people I have met to explore the personal feelings, intuitions, assumptions and way of thinking and living. Further, I attempted to determine how these correlate to the Chinese context. During my stay I used various research methods to collect data, including empirical research, random interviewing, storytelling and natural observation with medical students, medical doctors and local Chinese population. Notably, sometimes there was a language barrier, as many of the Chinese did not speak English (e.g. generally only the professors, teachers and students). Therefore, questionnaires were translated.

Data collection & Instruments

Prior to our research, we asked permission of the ethical committee of Peking University to perform empirical research using questionnaires and interviews. After permission Chinese doctors and medical students were approached in person and asked to cooperate with our research. A semi structured interview guide was created to cover AMR, AB usage and prescription patterns and use with a scenario as a starting point.

¹²⁴ http://www.who.int/mediacentre/news/releases/2015/antibiotic-resistance/en/

Table 1 – Participants China study

#	Profession	Country of birth	Stakeholder Category
1	Ethics student	Inner Mongolia	Student
2	Nurse	China	Nurse
3	Student	Sichuan	Student
4	Nurse	Peking	Student
5		Guangdong province	High school
6	Student	China	Student
7	Sales Pharma	China	Pharma
	Nurse	China	Nurse
8	English teacher	Xi'an Shaanxi	Teacher
9	Office staff university	Shanghai	University
10	Student	Chengdu, Sichuan.	Student
11	Student	China	Student
12	Product manager	Hebei	Pharma
	pharma		
13	Journalist	China	Journalist
14	Advertisement	China	Sales
15	Sales pharma	China	Pharma
16	Financial manager	China	Manager
17	WHO Beijing	China	Public health
18	Student	China	Student
19	Student	China	Student
20	Doctor	Taiwan	Doctor
21	Doctor	China	Doctor
22	Doctor	China	Doctor
23	Doctor	China	Doctor
24	Doctor	China	Doctor
25	Doctor	Taiwan	Doctor
26	Phd public health	China	Phd
27	Stranger	China	mother
28	Ethics student	China	Student
****5 strangers			

at lunchroom

Interviews were carried out in person, over the telephone (translated by Chinese Phd student) and by email. Most interviews were held in Chinese and lasted for 25-45 minutes. At the end, all findings were translated into English. We performed three interviews with renowned doctors at the Beijing Third Hospital (e.g. most prestigious hospital in China) and a primary care hospital just outside of Beijing city. With the verbal consent of the participants, the interviews were recorded for later transcription by the researcher. Each respondent was promised confidentiality and that his or her name was not to be published within any presentation of the results of the survey. Small changes in the interview guide were made as the survey moved along. Less emphasis was put on the general questions on AMR due to time constraints and more emphasis was put on the underlying (moral) motives of AB usage, this being a reoccurring theme in all the initial interviews.

Data analysis

The audio recordings from the interviews were transcribed verbatim by the researcher. The qualitative method of analysis used was "Framework' analysis. The transcripts were then read through for familiarization. Based on the research notes from the process and initial thematic

framework was created. The attitudes of the respondents towards different key themes and concepts were abstracted, summarized and put into charts to construct an easily read overview of results.

Theoretical analyses

Articles were obtained through searches for AMR and AB usage in China in PubMed and Google Scholar. Research findings and factual information about China, the healthcare system and social economical factors have below been combined with results from the interview and questionnaire to provide an in-depth description of the Chinese context. Which is important to consider the moral considerations underlying the problem.

Research Peking University 北京大学调查 Researcher: Susanne Baars 调查者: Susanne Baars

Topic: Antibiotic usage in today's China 标题:抗生素在今天中国的使用

我们想知道中国的群众对抗生素的普遍看法,以及他们认为健康和疾病较为重要的 因素。你本人不需要对抗生素有很深入的了解,你给我的答案也没有对与错。可以 畅所欲言。

- 1. 所有的答案都会被匿名。
- 2. 所有的数据也将保密,只会对本次调查的调查者以及相关教授开放。
- 3. 如果你有你不想回答的问题,可以不回答。

Age:

年龄:

Education level:

受教育程度:

Current work: 现有工作:

Home town / province; 祖籍:

PART 1

1. How many times do you use AB/year?

- 2. 0-3
- 3. 3-5
- 4. more

您一年服用多少次抗生素?

- 5. 0
- 6. 0-3
- 7. 3-5
- 8. 更多

I prefer infusion of antibiotics above pills

- o yes
- o no

explain:

```
我更愿意输液而不是吃药
是
否
```

请解释:

2. I take AB (multiple options possible)

- 1. only on prescription after being tested for bacterial infection in hospital
- 2. buy them at pharmacy
- 3. use leftover from previous times
- 4. use Abs from friends/family
- 5. use AB cream/ drups if I cut myself / wounds / ear or eye infection
- 6. <u>others:</u>...

我服用抗生素 (可多选)

- 1. 只在医院, 当被告知有系就感染后
- 2. 在药店购买
- 3. 用过去医生开过的剩下的
- 4. 从朋友/家人处获取
- 5. 在划破皮肤/感染眼睛后使用抗生素软膏/滴眼液

3. I take AB to:

- 1. Fasten disease recovery (no time to be sick / become more sick)
- 2. Make me feel better (relief)
- 3. Prevent further sickness
- 4. Easy solution
- 5. Other.....

我选择服用抗生素,因为:

- 1. 想尽快使病情好转(没有时间生病/使病情恶化)
- 2. 使我自己感到放松
- 3. 防止以后的疾病
- 4. 方便简易
- 5. 其他

Do you think the following statements are true or <u>false:</u>

您认为以下观点是否正确:

Statements 观点	True 对	Ealse. 错
"It's okay to use antibiotics that were given to a friend or family member, as long as they were used to treat the same illness" "给家人或朋友服用拉佐春是可以的,日要可以没愈同样的疾病。"		
出家八级加久顺用加工来定可以的"八安可以用巡问件的沃纳"		
"It's okay to buy the same antibiotics, or request these from a doctor, if you're sick and they helped you get better when you had the same symptoms before" "如果生病时有了与上一次同样的症状,可以购买同品种的抗生素或向 医生电谱处方"		
" it's okay to stop taking ABs once patients do feel better" "		
"当症状消失后,可以停止服药"		
"A stronger doses AB will relief sickness sooner" (e.g. especially first days take high doses)?		
史强效的机生素可使病症恢复待更大 (如任弗一人使用人剂重)		
" its okay if patients store left overs from ABs to use them if they need it another time"		
"如果需要,可以存储一些抗生素以便下次使用"		
Patients are not at risk of getting AB resistance if they use AB correctly" "只要使用正确,病人便不会对抗生素产生耐药"		
<i>Many kind of antibiotics already don't work anymore in a lot of people</i> "许多种的抗生素已经对很多人无效"		
Antibiotic resistance is only a problem for people who take antibiotics regularly "许多抗生素已产生耐药,但耐药只会对服药群体产生影响"		
Resistant bacteria can spread from person to person and are hence able to cause resistance directly in other people		
耐药性可以直接在人之间传染,"		
I have always full trust in the doctor / hospital services		

"我一直都信赖医生与医院的服务"	
After visiting a destar I amost to get medicine to sure my disease (
Alter visiting a doctor, i expect to get medicine to cure my disease/	
relief sickness symptoms	
"看完医生后,我会获得可缓解病症的药物"	
In general: If i can choose between taking medicine, or take nothing. I	
would shoose taking medicine	
"忌体米说,任用约或者什么都个用的两种情况下,找会选择用约物进	
行治疗"	
Every time i use antibiotics i put others at risk to become resistant	
towards antibiotics too	
"母伙当我使用机生素的时候,都有可能会给别人带米风险"	
Before i go to the doctor i look on internet and ask to friends/family	
which medicine i need and ask the doctor for specific medicines	
去找医生看病开药之前我会先求助于朋友/家人	
I feel doctors don't have enough time for individual patients	
我觉得医生没有充足的时间给每个病人仔细看病	
I think nationts should have the authority to choose a particular	
treatment or medicine	
我忍忍病人有权利选择被医治的方式	
In general I think doctors know what they do (I trust them), but I do	
think they have bad morals with regard to medicine prescription	
我认为医生们的职业素差很高。但我并不相信他们的职业道德	
I prefer to get medicine in informal way or buy them myself (also	
antibiotics), instead of going to hospital	
我更愿意以非正规的方式开药,而不是去医院	
If I am sick I prefer to take antibiotics if possible, also if I know it would	
not he personal	
not be necessary	
如果生病了,我会服用抗生素,即使我知道可能没有必要	
Doctors best practice means that it is the doctors duty to relief my	
sickness as soon as possible	
医生水平高的表现是很快的治好我的病	
E TAT I HIN A 20 M C IN IN HAILINI 20 HAILI	
If i go to the hospital I try to get more medicine than needed so I can	
use them later on (dont have to go to hospital again)	
如果去医院,我会开很多的药,这样下次就可以不用再去一趟医院	

Note: while answering, please consider both the city hospitals – remote /rural village hospitals

注:回答问题时,请全面考虑市医院和乡村医院

PART 2: Antibiotic problem in China

- Do you think ABs are good? Why? 您认为抗生素是否有益?为什么?
- What does the general population in china think about AB? 您认为中国人群对于抗生素的态度为怎样?
- Do you know about the excessive use of antibiotics in China? 您对于抗生素在中国滥用的情况是否了解?
- 4. What do you think are the main reasons for the high antibiotic usage in china compared to other countries? (Which Specific factors or reasons related to china Chinese culture)?
 相比其他国家,您认为中国为何会出现抗生素滥用情况?(请举出具体原因,如:文化影响)?

Part 3: Chinese cultural context

- For Chinese individuals it seems very important to recover as fast as possible. Why is this so important? 对于中国人群,尽快痊愈是非常重要的事情,为何如此重要?
- 6. Do individuals think and care about the risk of infecting others if they are sick? For example, if they go to work once they are sick? 您认为患者会担心把病传染给他人吗?例如:如果生病,他们会去上班吗?
- Do you think people are scared of being sick? Why. 您认为人们害怕生病吗?为什么?
- 8. Why do Chinese individuals immediately want to take medicine?
 - a. Above mentioned reasons
 - b. From Chinese beliefs: Patients think there is an immediately cure for everything
 - c. Patients do not see the potential harm of using medicines

- d. Patient are focused on direct result and not on long term implications (for example: risk of taking medicines too often)
- e. Patients feel more comforted if they can use a medicine (also if placebo effect)
- f. Cultural myths: (explain)
- g. Other:....

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为何中国患者会选择在生病后立刻吃药?
a.上述原因
b.源于中式思想:患者相信有方法可以立刻使身体恢复
c.患者不知道药物的远期伤害
d.患者不会远期思考风险 (如:长期服药的风险)
e.患者服药后会感到安心
f.文化影响
g.其他
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9. Do you think the above reasons are different for people living in big city / country side?

您认为城市与乡村人口对前一个问题会有不同答案吗?

Part 4: Chinese medical context

10. In china the bad doctor patient relationship (tension between doctor – patient) is a big problem. In what way is the bad-doctor patient relationship influencing over prescription by doctors?

 On behalf of the patient

 •
 On behalf of the patient

 Explain:
 Explain:

• <u>On behalf of the doctor</u> Explain:

.在中国, 医患关系有时会非常紧张, 您认为这种关系会影响医生为患者开的处方吗? 请解释:

11. Do you sometimes ask the doctor for AB?

您会向医生要求开取抗生素吗?

12. Imagine situations:

situation 1: a patient travels from long distance, is sick and wants to recover as soon as possible. He or she hopes to get infusion as he/she thinks this is best treatment.

situation 2: patients know the doctor and request <u>antibiotics</u> (personal request)- infusion.

Maybe infusion is not absolutely necessary. However the patient would recover faster.

What does a patient expect from a doctor? What should a doctor do?

请想像以下情况: 情景1:一个患者在长途旅行中患病并想要尽快恢复,他/她想要尽快恢复 情景2:患者与医生有私人关系,并想要开取一些抗生素

您认为患者在以上状况中回想向医生提出什么要求?医生又会作何反应?

- Imagine, <u>The</u> doctor does not give you the medicine because it is not necessary (maybe you cure by yourself). AB are not always needed. How would you feel going home without doctor's prescription for AB? 因为身体可以自愈, 医生没有给您开取抗生素, 您作何感想?
- 14. Do you think individuals should have the authority to choose a treatment/medicine? For example a patient who travelled a long time to get to hospital. He need to work and therefore needs to recover fast. Should doctors comply to this?

你認為中國的醫生應該有權利去選擇個體化病人的治療方式或是藥物嗎?舉 例說明:一個剛結束一趟長途旅行的病人到了醫院,但是他馬上就要開始工 作所以他需要盡快康復,當你生為醫生你會怎麼看待這件事?

PART 5: Personal behavior towards antibiotic usage

- 15. Do you see AB resistance as a threat for your own health? 您认为抗生素会给健康带来不良影响吗?
- 16. Many people know the harm of ABs. Why do people continue taking ABs, also if they know it is not good? 许多人知道抗生素是有害的,为何人们会选择继续服用抗生素?

12. Imagine situations:

situation 1: a patient travels from long distance, is sick and wants to recover as soon as possible. He or she hopes to get infusion as he/she thinks this is best treatment.

situation 2: patients know the doctor and request <u>antibiotics</u> (personal request) - infusion.

Maybe infusion is not absolutely necessary. However the patient would recover faster.

What does a patient expect from a doctor? What should a doctor do?

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- 16. Many people know the harm of ABs. Why do people continue taking ABs, also if they know it is not good? 许多人知道抗生素是有害的,为何人们会选择继续服用抗生素?
- 17. Do you feel responsible for the AB resistance problem yourself? 您认为您对抗生素滥用问题付有一定责任吗?
- 18. Do you know AB are not only harmful for your own health, but also for others (put them at risk to become resistant)?

您是否知道抗生素不仅影响个人,而且影响他人健康吗?

(If not: AB resistant bacteria can infect everyone and therefore cause disease that are not treatable <u></u>(如果答案为"否",抗生素会使疾病在未来不可治愈)

19. If you know taking AB causes potential harm for your health in the future and can do harm to others, does this change your behavior towards taking antibiotics?

如果您知道服用抗生素会影响您和他人的健康,您会改变服用抗生素的习惯吗?

Part 6: Role of doctor

20. Do you think a doctor should be concerned about the health of the patient in front of him or also about public and global health issues?

a. Please explain: 您认为医生应优先考虑患者的健康,还是公共与全球卫生为题?

21. Do you think there is a conflict between the interest of the individual patient and public health? Please explain:

您认为患者需求和公共卫生需求只见有矛盾吗?

22. Do you think doctors should take public interests into account? Also if this means that doctors should reduce AB prescription to patients? Why? 您认为医生是否抗生素问题付有责任, 医生是否应减少为病人开取抗生素?

23. In practice this could mean that patient are sometimes put on risk (do not get antibiotics) in order to protect public health interests (reduce overall antibiotic usage)"

Do you think this is a good moral (ethics) for doctors? Or should doctors only be concerned about the patient health and do what is best for patients? 有时好的移植方法并不会满足大众需要,例如:减少抗生素的发放 您认为开取抗生素以换取快速疗效是好的医疗道德吗?或医生应该保证病人的健康而减少发放抗生素?

24. Do you agree of disagree:

I think doctors should not take any risk to patient health (always choose safest option – in case of antibiotics: the doctor should provide antibiotics if there are symptoms – instead of waiting if body can do without (take a small risk).

AgreeDisagree

您是否同意医生不应该在患者的健康问题上冒风险,应永远采取安全的方法。 在抗生素的问题上,医生应该给患者抗生素,而不是让他们慢慢恢复。

25. Besides to protect the health of the current generation of people, we also have future humans. Do you think we have the duty to reduce the AB problem in order for future humans to be able to use Abs in the future as well?

除了保护这一代人群,我们对未来子孙也负有责任。您认为我们是否对下一 代减轻抗生素滥用问题负有责任?

Final

- Looking to the Chinese context, at this moment, what do you think is most important to work on? (<u>take home message</u>) 在此刻,您认为什么是需要大家齐心合力来解决的医疗问题?
- Are there any other important points that have not been mentioned but that you think are important? 您认为还有哪些重要的问题此调查没有问到?请补充。
- 3. How do you think about our questions? (any advice / comments)

Attachment 4: Highlighted Quotations Empiric Research

Results III – Interview survey

" I have to admit that using the broad-spectrum ABs and using combination of ABs are in a serious situation in China. Using combination is because many ABs are not working on some patients so we must use another or more ABs. Using broad-spectrum is usually in the primary health care hospital, they don't have the lab equipment so they will use the broad-spectrum ABs." – Chinese doctor Beijing Third Hospital, Beijing.

Most Chinese believe that patients are not at risk of getting AB resistance if they use AB correctly. They believe that AMR is only a problem for people who take antibiotics regularly. They also mention that they will always follow their doctor's advice. And that 9 out of 10 times they visit a doctor, they will get ABs. But most persons don't know how to use them correctly – as resembled by questions about correct AB usage. They don't understand the harm and therefore they don't understand how it affects others. A possible explanation for this is that AMR is a concept rather than a real disease (if you are not resistant). The consequences are not touchable. While the Chinese are very driven by the fast pace of life – relying on quick results and quick solutions.

"They should let them exercise more and have a healthy life style to boost their immune system, rather than use ABs every time. Or they will get resistant, there will be no drug to save them in the future." – Doctor Beijing Third hospital Beijing

The question remained whether people would feel engaged with the problem and if they would change their behavior if they would be aware of the working mechanism of AMR. According a public health professor at PKU:

"Focus is on own health. Health is so important for an individual. Nothing goes beyond this. Even he or she knows. AB will release my symptoms even if people know the harm to others. I don't think people will start to act differently. "

Because persons are so concerned about their own health, thinking about the potential harm in the future or harm for others might not outweigh their decision.

Attachment 3

Stakeholder perspectives

Below I have outlined the various stakeholder perspectives and pointed towards the varied ethical dilemma's. This will help to identify relevant ethical considerations. According to the Utrecht method this requires "to step into the shoes of the other." As you will read, you will understand that performing one action will directly have implications to someone else. Knowing the different perspective is needed to be able to provide an ethical assessment (e.g. weighting ethical considerations) to answer the research question. In the case of the AMR problem and AB usage in China the following stakeholders are involved; they Physician, the patient, the Chinese citizen, the payer's perspective (e.g. pharma, hospitals, pharmacies) and the government.

Physician's perspective

For physicians the Hippocratic oath resembles the universal binding agreement between a doctor and society. Using the traditional biomedical ethics framework in clinical practice, situations are assessed according to the principles of beneficence, nonmaleficence, autonomy and justice. Overall, this means that it is the duty of physicians to act according to the best interest of the patient in front of him/her. However, in case of the global AMR problem the physicians is caught between their responsibility to the patient, the need to preserve antibiotic efficiency for future use and their position as gatekeepers for health systems that may impose incentives and penalties based on prescribing habits. Within this context the doctor needs to weight different (sometimes contrary) ethical considerations which now also include the interests of public health ethics. The relationship between these responsibilities and the lack of guidance are creating tension in practice. As we have seen during the empirical research, Chinese physicians strongly belief that treating the individual patient matters most rather than the preservation of ABs for society and future patients. This is representing a now for then argument). In the Chinese context, acting in the patient's best interests means to provide a clinical cure that makes the patient better as soon as possible, without the need for a return visit for follow up medication or to be treated for adverse side-effects (e.g due to the withdrawal of ABs in the first place). The empirical research also shows that Chinese physicians feel very pressured by the fear of litigation - e.g. being sued for not providing something that might have cured the patient; feeling forced through patient pressure¹²⁵. This depicts a loyalty problem of doctors towards patients that undermines the medical professionalism. Providing ABs to keep the patient and his/her family satisfied. Which is worsening the AMR problem and restricting AB reduction policies in practice. Additionally, besides the above AB drivers, providing ABs might seem very rational for physicians as they have learned about their healing mechanisms by their supervisors (old generation doctors) and experienced ABs to provide a quick cure to their patients in practice themselves. The AB reduction aim might therefore feel unnatural to them, and sometimes even seem to go against their beliefs of doing what's good. It is in their interest to be able to provide the right treatment to patients, to have working medicine, to be the best doctor, to ensure that patients will come back to them (to maintain a good salary to take care of their family), to know what to do in which situation (best practice; to know that risks and benefits are proportionate) and that the patient is informed.

Patient perspective

The interests of patients are to protect their health. In general patients expect to receive the best treatment. However, the context is shaping the interpretation of this value. In China the best interest of a patient entails a cure to become better as soon as possible. Many Chinese patients are not aware of the risks of AB usage. They have not experienced a direct effect of AMR yet and do not know the working mechanism -which leads to misusage. Their decision-making process does not consider the actual harm of ABs and the potential risks in relation to their own health or the people around them. For them other values are at stake and are guiding their behavior.

Notably, China is (still) a LMIC – from which many people are living in poor life conditions. Most rural areas do not have access to medicine and high quality care. People need to travel long distances to visit a doctor, which costs them time and money (harm). Because of the single child policy Chinese need to take care of their parents, which put a high burden to their lives. Being sick means that they can't work, do not earn money and/or cannot take care of the whole functioning of the family. For

¹²⁵ Interviewing

them, ABs are a kind of magic drugs that provide them a cheap and fast cure and protection against harm. Similarly, to the standpoint of physician's, for patients, taking ABs seems to be very rational to them. Nonetheless, considering the AB reduction aim it is in their interest to maintain AB efficiency, to be able to have access to medicine, to have access to healthcare, to be informed and to provide informed consent.

Chinese citizen's perspective

The interest from the Chinese citizen can be multiple. As we have witnessed in the previous chapter, the general awareness among the public about the threats of AMR remain very low. In general, the focus of Chinese Citizen's is put on the fast pace of life. There is high competition to be the best, to get into study and/or to work as hard as possible to maintain their job. In the meantime, they should take care of their family, their parents are often living in the same house and they need to take care of their grandparents. It is in their interest to maintain their health and protect against diseases. In light of the AB reduction aim the Chinese citizen wants to know what harm it will bring them, how they can best take care of their health, whether there would be compensation for the risks of not taking ABs or the harm that it can bring and if there is healthcare and working medicine to rely on in case that their health is endangered. They also need to be informed about the AMR threat and the risks of taking ABs to themselves and others. As being a good citizen, they can only take responsibility for the collective AMR problem if they are informed and if they feel responsible for the problem and the risk that they possess on others (e.g. their own contribution).

Payer perspective

In this context, payers entail respectively hospitals, pharma and pharmacy. Payers are more concerned about considerations related to costs. Costs of the initial AB treatment, the consultation, but also the costs of poor outcomes and the possible downstream costs of resistance. The scope of the problem depends on all payers in the system who all meet different costs. Within healthcare systems payers have therefore a commitment to the collective outcome. In the case of the AB reduction aim considerations include the cost of poor outcome for the individual with the cost of initial treatment plus the cost of resistance. For individual payers the interest is sell as many items as possible (e.g. ABs), while lowering the burden of disease-related costs. Contrary, they also have a duty to ensure the quality of their medicines and to ensure safe drug-policies. However individual payers do usually not have notice for "what lies over the wall". And research results on the true costs of AB reduction on a system level (e.g. burden) are not available yet.¹²⁶

Chinese government

The Chinese government has the responsibility to take care of the health of their citizens (public health). They have a duty to take measures that promotes public health and lower healthcare related costs. They need to protect the universal human rights and ensure that all citizens have access to medicine and healthcare. As being the national authority they have the power to guide people's behavior.¹²⁷ Like the general population, it would the question if these authorities now realize the

¹²⁶ Garau 2006.

¹²⁷ However, in case of AMR it is important to know that with the discovery of ABs as the magic drugs, the government has highly promoted AB distribution by extensive media propaganda and the delivery of ABs at places of big crowds of people to protect against disease outbreaks. Because of this, they have stimulated a culture of AB usage.

scope and threat of AMR at national level. And whether they have set the right state priorities. As they are a LMIC, they have more national threats to consider, among the protection against infectious disease outbreaks (e.g. which they have previously managed by widespread uncontrolled AB distribution).Therefore, the question remains to what extend their efforts will reach.

Concluding remarks

The above paragraphs have shown the various stakeholders that are involved, their perspective and their interests. We have seen that the ethical considerations underlying their perspectives are not as simply as what might have been presumed before. Of which many are inter-related to environmental factors. Now we know the various perspectives, in the next paragraph we will explore the moral considerations of AB usage in China by using various ethical theories.