

**Influences on healthcare providers' and parents' behaviours with
respect to the use of antibiotics for children: An exploratory study
in urban China**

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Abstract

Background: Antimicrobial resistance is a global public health threat, with antibiotic resistance (ABR) increasing rapidly. In China, the high rate of antibiotic use is a key contributor to the country's ABR problems, and the paediatric use of antibiotics by healthcare providers and parents has been identified as a particular challenge. However, limited research has examined providers' and parents' antibiotic-related behaviour, with particularly few qualitative studies having been conducted, and none in urban China. This research examines influences on healthcare providers' and parents' behaviour regarding the use of antibiotics for children in urban China.

Methods: Informed by a review of English-language and Chinese-language studies, a qualitative study of healthcare providers and a multi-method study of parents were conducted in Chinese to explore factors influencing their antibiotic-related behaviour. The study site was Taiyuan city, a medium-sized city in central China. Qualitative data were transcribed verbatim, translated from Chinese to English, and analysed using framework analysis. Quantitative data were analysed using difference tests and regression analysis.

Results: The two key influences on the paediatric antibiotic-related behaviour of healthcare providers were: (i) parental influences, including public understandings of disease and treatment within traditional Chinese medicine (TCM) and Western medicine, and maintaining trust and good relationships with parents, and (ii) the organisational context relating to China's healthcare system and national policies. The main influences on the paediatric antibiotic-related behaviour of parents related to their lack of antibiotic-related knowledge, their understandings of TCM and Western medicine, and their access to and interactions with healthcare providers.

Conclusions: Although it is a small-scale study located in one urban setting, this research highlights influences on healthcare providers' and parents' paediatric antibiotic-related behaviour operating from individual to organisational and cultural levels. Promoting more appropriate paediatric use of antibiotics in China will require better understanding of the provider-patient relationship and the wider cultural and healthcare contexts, especially in relation to the relative influence of TCM and Western medicine.

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Preface

This thesis describes an exploratory study of the influences on paediatric use of antibiotics by healthcare providers and parents in China. Antimicrobial resistance has become one of the most serious global public health problems causing substantially increased infectious disease mortality and morbidity, as well as a considerable economic burden (Chan *et al.*, 2012; Neill, 2014; WHO, 2015). With respect to human antimicrobial resistance, it is antibiotic resistance (ABR) that has increased most rapidly around the world. Low and middle-income countries with the highest burden of infectious disease are seriously affected by human ABR, particularly China (Bartoloni, 2007; ESRC, 2014; WHO, 2015A). In China, the resistance rates of the most common bacteria to clinical antibiotics are very high, with the prevalence of many antibiotic resistant strains ranking amongst the highest in the world (Xiao *et al.*, 2011). Data from China's hospitals and primary care institutions, retail pharmacies and the public indicate that antibiotics are widely and inappropriately used by all of these groups, and inappropriate use of antibiotics for children is a particular concern (Currie *et al.*, 2013; Fang, 2014; Zeng *et al.*, 2012). This suggests that healthcare providers and parents are key constituencies related to paediatric antibiotic use and ABR in China; factors influencing their behaviours with respect to the use of antibiotics are therefore important research areas.

This thesis develops a social ecological framework (SEF) to inform and guide the review of literature and empirical studies. The SEF is a concentric causative 'web', which has a range of influences on the outcome of interest (the use of antibiotics) situating it within multiple layers from micro (individual)- to macro (policy)- level (Schneider & Stokols, 2009). Under the

guidance of the SEF, a review of both English- and Chinese-language records relating to influences on healthcare providers' and the public's use of antibiotics was undertaken, and empirical studies were conducted with healthcare providers and parents living in one city in central China. Study sites, including hospitals, community health institutions, retail pharmacies and nurseries, and participants were contacted through personal networks, an approach that is sensitive to China's Confucian-based cultural contexts and organisational background (Liu, 2006; Park & Lunt, 2015). There were in total 26 healthcare providers, 12 parents of nursery children, and 98 parents of ill children recruited in this doctoral research. A qualitative approach was used for the study of healthcare providers, with semi-structured interviews conducted with 26 healthcare providers. The study of parents was undertaken using a multi-method design, including a qualitative component of three focus groups on parents of nursery children (12 parents in total), and a quantitative component of a questionnaire survey undertaken in two hospital paediatric clinics and completed by a total of 98 parents of ill children.

This thesis consists of seven chapters. **Chapter 1** provides an overview of the background relevant to the thesis' focus on factors contributing to the paediatric use of antibiotics by healthcare providers and parents in China. **Chapter 2** then describes the theoretical perspectives and the review of literature in the thesis, followed by a brief introduction of the research questions and approaches in **Chapter 3**. Chapters 4, 5 and 6 describe the empirical studies of healthcare providers and parents undertaken for the thesis. Specifically, the qualitative study of healthcare providers is discussed in **Chapter 4** and **Chapter 5**, each chapter focusing on an important influence on healthcare providers' paediatric use of

antibiotics. These two chapters have also contributed to two journal papers. **Chapter 6** then turns to the multi-method study of parents. Finally, findings from the thesis are drawn together in **Chapter 7**, which provides a synthesis of the key study findings and discusses implications, future research and conclusions.

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Author's declaration

I hereby declare that the research presented in this thesis is my own work. This work has not previously been submitted for any other award at this University. Information included from other sources (e.g. journal articles and books) has been fully acknowledged and correctly referenced.

- **Publications arising from chapters of this thesis**

Chapter 4: Zhang, T., Graham, H. & White, P. C. L. (2018). Healthcare providers' accounts of parental influence on their behaviour with respect to the use of antibiotics for children: a qualitative study in China. *Journal of Community Medicine and Public*, 5(1), 036.

Chapter 5: Zhang, T., Graham, H. & White, P. C. L. (2018). Healthcare providers' accounts of influences of antibiotic-related reforms on their behaviour with respect to the use of antibiotics for children: a qualitative study in China. *Public Health Open Access*, 2(1), 000122.

Chapter 1. Overview of human antibiotic resistance and the use of antibiotics with a focus on China

1.1 Introduction

Antibiotic resistance (ABR) has become a major specific challenge within the larger problem of human antimicrobial resistance (AMR), which has serious public health impacts and causes a major economic burden worldwide (WHO, 2015, 2015A; Neill, 2014). The use of antibiotics is the most important factor contributing to ABR problems, relating to both the volume of antibiotic consumption and the way antibiotics are used (Barbosa & Levy, 2000; Byarugaba, 2004; Levy, 1982, 1998, 2001; Pettersson, 2011). Similar to other low and middle-income countries (LMICs), China is seriously affected by ABR (Xiao *et al.*, 2011). In China, the healthcare system consists of the health supervision system, the health service delivery system, and the health financing system, which are independent but inter-related, and traditional Chinese medicine (TCM) and Western medicine are practised alongside each other in China's healthcare system (Mossialos *et al.*, 2016). Research has shown that antibiotics have been widely and inappropriately used, especially for children, in hospitals, primary care institutions, and retail pharmacies among China's healthcare system, as well as by the public (Currie *et al.*, 2013; Fang, 2014; Zeng *et al.*, 2012). Concerned about these problems, the Chinese government launched a set of antibiotic-related policies in the 2011 antibiotic-related reforms, which extended policies introduced during the 2009 healthcare reforms and other wider policies (Mossialos *et al.*, 2016; Xiao & Li, 2013, 2015).

This thesis includes two reviews of literature: a broader review on antibiotic use and resistance in China (discussed in this chapter) and a more systematic search and review on influences on healthcare providers' and parents' antibiotic use in China (discussed in Chapter 2). For the broader review presented in Chapter 1, relevant research and background material

about ABR and antibiotic use in China was identified using the University of York Library search tool – Yorssearch; this search tool was used to identify paper-based books and PhD theses. For journal papers, three search tools – the MEDLINE Ovid, Wan Fang database (an online database of Chinese journals accessed through <http://www.wanfangdata.com.cn/>) and Google Scholar – were mainly used (see the search strategies in Appendix A). For the focused review (Chapter 2), the MEDLINE Ovid and Chinese National Knowledge Infrastructure (CNKI) were used. More detail on the more systematic search and review using MEDLINE Ovid and CNKI is provided in section 2.2.2. In addition, websites including the World Health Organisation (WHO), the World Bank, and GOV.UK were used to identify relevant evidence published in English, including empirical data and policy documents. Some official Chinese websites, such as the National Health and Family Planning Commission (NHFPC) website, were used to identify relevant Chinese data and policy documents. The initial review (conducted in 2015/2016) was updated in June 2017 by reference checking and citation searching from the most relevant studies.

There are five sections in this chapter:

- 1.1 provides an introduction;
- 1.2 describes the development of ABR and the use of antibiotics and ABR in LMICs and China;
- 1.3 provides the context of China and reviews antibiotic use in hospitals and primary care settings, pharmacies and among the general public;
- 1.4 describes the recent reforms and policies relevant to antibiotic use in China; and
- 1.5 concludes this chapter.

1.2 Human antimicrobial and antibiotic resistance, with a focus on low and middle-income countries and China

1.2.1 Antimicrobial and antibiotic resistance in humans

Although global deaths caused by infectious diseases have continued to decrease gradually in recent decades, some infectious diseases remain a human health challenge worldwide, particularly for populations in LMICs (WHO, 2007, 2011, 2014). Considering the health burden caused by infectious diseases, antimicrobials (Box 1) have become one of the most important forms of treatment to reduce the spread and impact of infectious diseases (PAIH, 2015). However, while antimicrobials are widely used by humans to treat infections, and have saved many lives over the past decades, AMR in humans has emerged and rapidly spread across a wide range of microorganisms, and has become an increasingly serious global problem (PAIH, 2015; WHO, 2015). AMR is defined as the ability of microbes to survive an attack by antimicrobials that were previously effective against them (Bebell & Muiru, 2014; WHO, 2015). This means the infectious diseases become harder, or even impossible to, treat by the standard treatment; in consequence, the prevention of infectious disease will be less effective and the period of illness will be prolonged, which increases the risk of the spread of disease to others and to the social and economic cost of the disease (WHO, 2014B; Bartoloni, 2007; Chan *et al.*, 2012; Neill, 2014). Because of human AMR, infectious diseases that were previously treatable by antimicrobials are again becoming major threats. AMR in animals, such as food-producing animals and pets, has also emerged following the introduction of antimicrobials into agriculture (Lloyd, 2007; Wallinga & Burch, 2013). However, there are only a few confirmed cases where animal-related AMR has been the cause of AMR among humans

(less than 4%), and the most of antimicrobial-resistant human microorganisms are not from animal sources (Lloyd, 2007).

Box 1 What is an antimicrobial?

The term 'antimicrobial' refers to any substance, of natural or synthetic origin, that works to destroy or inhibit the growth of microorganisms, for example by disrupting the synthesis of proteins within the cell. Antimicrobials include all agents used to treat infectious diseases caused by microorganisms, such as antibiotics, antivirals, and antifungals, among others (MSU, 2011; WHO, 2015).

According to a study carried out by RAND Europe and KPMG, human AMR is estimated to cause 700,000 deaths annually worldwide and, without urgent action, the number of global deaths due to human AMR is projected to increase to 10 million by 2050 (Neill, 2014). A systematic review also found that, for certain microorganisms (*Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*), patients infected by resistant strains have worse clinical outcomes compared with patients infected by susceptible strains (WHO, 2014A). In addition, it is estimated that the economic burden caused by human AMR will contribute to a reduction of 2-3.5% in Gross Domestic Product (GDP) by 2050, which would be equal to 100 trillion US\$ (Neill, 2014). Human AMR threatens the effective treatment of infectious diseases caused by various pathogens¹. Among bacterial diseases, a growing number of common diseases such as pneumonia, tuberculosis (TB) and diarrhoea have become harder or even impossible to treat. There were 480,000 new cases of multidrug-resistant TB worldwide

¹ This includes bacterial diseases like tuberculosis (TB), viral diseases like HIV and influenza, and parasitic diseases like malaria (WHO, 2015).

reported in 2013, which are associated with higher healthcare expenditure and higher risk of death (WHO, 2015). Antibiotic (Box 2) resistant strains such as *Escherichia coli* and *Staphylococcus aureus* are increasingly widespread around the world (Bebell & Muiru, 2014; WHO, 2014A).

Of the different forms of resistance to antimicrobials, the development of ABR has increased most rapidly around the world and has become one of the biggest global health threats (ESRC, 2014; WHO, 2015A). Meanwhile, there are major gaps in ABR-related knowledge, as this problem is complex and multifaceted (WHO, 2014B). Although data from different regions of the world have not yet been coordinated, surveillance carried out by the WHO indicates that resistance of common human pathogenic bacteria has reached levels with huge costs for human health and the economy (WHO, 2014A). For instance, human ABR is estimated to cause 25,000 deaths and cost more than US\$1.5 billion every year in the European Union alone (WHO, 2015A). Therefore, ABR in humans is a very important dimension of AMR that is causing concern worldwide.

Box 2 What is an antibiotic?
The antibiotic is a type of antimicrobial that is produced by microorganisms to inhibit the growth of other microorganisms, and therefore used to prevent and treat bacterial infections. (MSU, 2011; Sengupta <i>et al.</i> , 2013).

1.2.2 The origins and factors contributing to antibiotic resistance

Like antibiotics, ABR was a naturally-occurring phenomenon long before antibiotics were used by humans (D'Costa *et al.*, 201; Martínez, 2008). A recent study identified ABR genes

from 30,000-year-old Beringian permafrost sediments (D'Costa *et al.*, 2011). Indeed, considering antibiotics have been produced by environmental microorganisms for millions of years, it is not surprising that the ABR should be similarly ancient. The mechanisms of ABR originating from the natural environment include inherent resistance and acquired resistance (Sjölund, 2004; Van Wyk, 2015). Through many millions of years of evolution in an environment with antibiotics, some bacteria today are intrinsically resistant to some types of antibiotics as, for example, there is a lack of a target in the bacteria's body for antibiotics to work against (Martínez, 2008). Meanwhile, ABR genes are carried by most antibiotic producers, and even by some bacteria that do not produce antibiotics themselves (Allen *et al.*, 2010; Fajardo *et al.*, 2008). Acquired resistance means that the ABR genes could be acquired from other bacteria through spontaneous mutation or horizontal transfer (Davies, 1994; Martínez, 2008; Martínez & Baquero, 2000).

Although ABR is an inevitable biological process that originates from nature, its development, such as how rapidly the resistance evolves among bacteria, is strongly influenced by the selective pressures that can be either natural or social (Allen *et al.*, 2010; Barbosa & Levy, 2000; Sjölund, 2004). Among the different selective pressures, an especially important one is related to human antibiotic use, which can drive the development of ABR through either mutation or transfer (Barbosa & Levy, 2000; Martínez, 2008). The use of antibiotics has been identified as the single most important factor contributing to ABR in many studies (Byarugaba, 2004; Huttner *et al.*, 2010; Simonsen *et al.*, 2004).

While it is widely accepted that antibiotic use is a major factor in ABR, the pathway from antibiotic use to resistance is complex and multifaceted, and is heavily influenced by societies

and human activities (Goossens, 2009; Rubin & Samore, 2002). In general, the selective role of antibiotic use related to ABR is associated not only with the volume of antibiotic consumption, but also the way antibiotics are used (Barbosa & Levy, 2000; Levy, 1982, 1998, 2001; Pettersson, 2011). It is clear that increased antibiotic use in human treatment is a driving force behind human ABR, with evidence from both empirical studies and a long history of observation (Gerding *et al.*, 1991; McGowan, 1983; Møller, 1989; Rubin & Samore, 2002). For example, a study in Iceland demonstrated that antibiotic use in the community was strongly associated with the resistance to penicillin in pneumococci in children (Arason *et al.*, 1996). The positive correlation between antibiotic use and resistance has been confirmed by ABR surveillance studies in Europe (Goossens, 2009; Goossens *et al.*, 2005). Animal ABR also emerged after antibiotics were used in agriculture either as a growth promoter or for treatment (Lloyd, 2007).

Another factor related to the use of antibiotics that contributes to human ABR is the way antibiotics are used; inappropriate use of antibiotics is a key factor accelerating the development of ABR (Hildreth *et al.*, 2009; Rubin & Samore, 2002; Van Wyk, 2015). Based on the definitions of rational medicine use (Holloway & van Dijk, 2011) and inappropriate medicine use (Zuckerman *et al.*, 2006), inappropriate antibiotic use is defined here as the use of antibiotics that should be entirely avoided, antibiotics that are used in dosages or for durations that not meet patients' individual requirements, or the use of antibiotics that is not at the lowest cost to patients and the community. The forms of inappropriate antibiotic use contributing to human ABR include both the overuse and misuse of antibiotics. Overuse of antibiotics is when antibiotics are unnecessarily used in human treatments, such as unnecessary antibiotic prescribing practices. Misuse of antibiotics includes the inappropriate

dose, duration, and/or frequency of antibiotic use in human treatment (Low, 2001). For instance, the risk of resistance to penicillin pneumococci in humans has been found to be associated with antibiotic use at a low dose and for a long duration (Guillemot *et al.*, 1998).

In conclusion, although ABR is a natural phenomenon, the spread and scale of this natural biological process is social and shaped by human activities. This, in turn, is highly related to both the total amount of antibiotic consumption and inappropriate use of antibiotics (WHO, 2015).

1.2.3 Human antibiotic resistance and antibiotic use in low and middle-income countries

Although human ABR is a global public health issue, this problem is more serious in LMICs, which are also referred to as developing countries² (Bartoloni, 2007). The WHO has highlighted that the use and inappropriate use of antibiotic drugs accelerate the development of ABR, while some issues such as inadequate healthcare resources and ineffective control measures encourage the further spread of ABR (WHO, 2012, 2015).

Compared with high-income countries (HICs), LMICs suffer from a higher infectious disease burden³ (Bartoloni, 2007; Bebell & Muiru, 2014; Murray *et al.*, 2013). In LMICs, infectious

2. There is no established convention for the designation of 'developed' and 'developing' countries or areas in either the World Trade Organization or United Nations (UN, 2013; WTO, 2015). World Trade Organisation (WTO) members can define themselves as 'developed' or 'developing' countries (WTO, 2015). The World Economic Situation Prospects classifies all countries in the world into three categories: developed economies, economies in transition and developing countries (UN, 2015). The World Bank uses 'developing' to denote LMICs when classifying countries by region, but it also notes that it is not implied that countries in the same income groups are experiencing the same development status (World Bank, 2015).

3. 'Disease burden' refers to the overall impact of disease and injuries at the individual level, society level, or to the disease cost for the economy. The WHO global burden of disease measures disease burden by a time-based method of disability-adjusted-life-year, which combines years of life lost from premature death and years of life lived in less than full health states (WHO, 2015B).

diseases remain a major cause of morbidity and mortality, which has led to a huge amount of antibiotics being used (Sosa *et al.*, 2010; WHO, 2011). Adding to the infectious disease burden, the burden from ABR and healthcare-associated infections⁴ has been very high in all LMICs (Bebell & Muiru, 2014). In LMICs, the frequency of healthcare-associated infections among risk populations, such as patients in intensive care units (ICUs) and new-borns, is several times higher than in HICs (WHO, 2011A). For instance, a systematic review of the burden of healthcare-associated infection in LMICs indicated the pooled healthcare-associated infection density⁵ in adult ICU was as high as 47.9 per 1000 patient-days⁶, which was at least three times higher than the densities reported by the USA (Allegranzi *et al.*, 2011). Evidence also suggests that the inappropriate use of antibiotics is very common in enteric infections and respiratory tract infections among LMICs. ABR resulting from the misuse of antibiotics in treating pathogens, such as *Salmonella enterica* serotype Typhi, *Streptococcus pneumoniae* and *Mycobacterium tuberculosis*, poses a grave public health threat in LMICs, especially for neonates, patients with acquired immune deficiency syndrome (ADIS) or in ICUs (Bebell & Muiru, 2014; Kollef & Fraser, 2001; Okeke *et al.*, 2005). The burden from ABR also includes a great economic burden, which contributes to poverty in LMICs, which can, in turn, lead to increased ABR. In addition, there are other issues that may adversely influence the use and

4. Health care-associated infections, which are also called 'nosocomial' and 'hospital' infections, usually affect patients in a hospital or other health-care facility, and are not present or incubating at the time of admission. They also include infections among health staff, as well as infections that patients acquire in the hospital or facility, but appear after discharge. Data about health care-associated infections are often limited and low quality in LMICs (WHO, no date).

5. 'Health care-associated infection density' refers to the number of infection episodes per 1000 patient-days or device-days (Allegranzi *et al.*, 2011).

6. 'Patient-day' is a unit used by health care facilities or planners for accounting, each day represents a unit of time during which the health services are used by a patient. So 10 patients in hospital for 1 day is equal to 10 patient-days.

inappropriate use of antibiotics, such as poor regulation and an inadequate ABR surveillance system, as well as limited health care resources.

1.2.4 Human antibiotic resistance and antibiotic use in China

As noted above, ABR is a challenge in all LMICs. Based on published ABR studies, the Asian region has become the epicentre of ABR worldwide with a high prevalence of drug resistance in some globally important strains (Zellweger *et al.*, 2017), such as hospital-acquired and community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *Staphylococcus aureus* (VISA), and multi-drug resistant *Pseudomonas aeruginosa*, among others (Kang & Song, 2013; Lai *et al.*, 2014; WHO, 2014A). China is one of the largest countries and the second largest economy in the world, with a population in 2015 of 1.371 billion (World Bank, no date; World Bank, 2017). With the fastest sustained GDP growth (averaging around 10% growth per year) over the last three decades, China has been reclassified by the World Bank from its initial position as a low-income country to an upper-middle-income country (Schellekens, 2013; World Bank, 2015, 2017). However, in common with other Asian countries, China has a serious human ABR problem.

The modern antibiotic era began around 1930s-1940s when sulphonamides and penicillin were introduced (Aminov, 2010). Antibiotic discovery then came into a 'golden age' between the 1950s and 1970s, with nearly half of the classes of antibiotics known today being discovered in that period (Silver, 2011; WHO, 2014A). In China, although data about the evolution of antibiotic use since the founding of the People's Republic of China are limited, the widespread and inappropriate of human antibiotic use is likely to related to China's first stage health reform (from the mid-1980s to the end of 1990s) and the economic reforms from

1978. During this period, the old public healthcare system nearly broke down as the economic reforms led to the collapse of the foundations of healthcare system – people’s communes in rural areas and state-owned enterprises in cities (Chan *et al.*, 2008; Dong, 2001; Mossialos *et al.*, 2016). The subsequent first-stage health reform mainly focused on introducing market incentives and highlighted privatisation and localisation of healthcare services, dramatically reducing national subsidies to the healthcare system and allowing it to earn income from sales of services and drugs (Chan *et al.*, 2008; Hsiao, 1995; Wang & Wang, 2007). As a consequence, hospitals in cities and independent entrepreneurs, who were formerly ‘barefoot doctors’ in rural areas, soon began to compensate for the losses of subsidies and enhance their income by prescribing and selling unnecessary drugs. Because providers are the dominant partner in the provider-patient relationship, patients are entirely powerless when dealing with providers’ inappropriate use of drugs but just purchase their decisions (Ramesh *et al.*, 2014; Xu *et al.*, 2010). It is likely that the widespread and inappropriate use of antibiotics started in this time period.

As the privatisation initiated by health reform progressed, pharmaceutical enterprises also came out of direct governmental control and eventually became business entities, which made China’s pharmaceutical market more competitive (Li *et al.*, 2014). Moreover, with the policies and regulations introduced in economic reforms, such as the ‘open door’ policy, the Chinese pharmaceutical market gradually became attractive to foreign multinational ‘pharma’ companies and started to grow rapidly from early 1990s (Chan & Daim, 2011; Sun *et al.*, 2008). For instance, the gross sales of drugs maintained a growth rate around 20% per year from 1986 to 1990, and the growth rates in the pharmaceutical industry had become much faster than other kinds of industry in China by the end of 1990s (Dong *et al.*, 1999; Li *et al.*, 2014).

The fast growth of pharmaceutical market and drug sales would also promote the wide use of antibiotics in China.

Nowadays, human ABR has become a serious problem in China, with high total antibiotic consumption and widespread inappropriate use of antibiotics and, in turn, high resistance rates of most common bacteria to clinical antibiotics. For instance, the proportion of MRSA and carbapenem-resistant *Acinetobacter baumannii* has reached nearly 50% of isolates in recent years (Xiao *et al.*, 2011). China also had the fastest average growth rate of human ABR between 1994 and 2000 worldwide (Heddini *et al.*, 2009).

1.2.4.1 Human antibiotic resistance in China

While Chinese ABR surveillance started in the 1980s, it was only carried out in a few hospitals with particular strains (Xiao *et al.*, 2011). Since then, China has established two nationwide ABR surveillance networks named Mohnarin and CHINET, which operate alongside some provincial ABR surveillance programmes (Wang *et al.*, 2006; Xiao, 2008; Xiao *et al.*, 2011). The Mohnarin has been overseen by the University of Zhejiang, and provides the widest set of AMR data from 84 member hospitals across China in 2008 (Xiao, 2008; Xiao *et al.*, 2011). The CHINET is overseen by the University of Fudan, and includes AMR data from 16 tertiary hospitals (14 general hospitals and 2 children hospitals) in 2009 (Hu *et al.*, 2014; Xiao *et al.*, 2011). However, as the main sources of Mohnarin and CHINET's AMR data come from their member hospitals, data on ABR in primary care settings are still limited in China (Xiao, 2008). Based on the reports from Mohnarin and CHINET, there is an upward trend in ABR in clinical

bacterial isolates in China, with a serious threat from multi-drug resistant and pan-drug resistant strains in some specific regions (Hu *et al.*, 2014, 2015; Wang *et al.*, 2013).

In China, the most common gram-positive strains are *Staphylococcus aureus*, *Enterococcus* spp. and *Streptococcus pneumoniae*, with a prevalence of 9.13%, 8.73% and 1.8% in 2014, respectively (Hu *et al.*, 2015; Xiao *et al.*, 2012). Resistance to methicillin of *Staphylococcus aureus* has been identified as a particular problem in China. The MRSA was first detected in China in the 1970s with a prevalence of approximately 20% (Li *et al.*, 2001). Since then, studies carried out by Mohnarin indicate that the prevalence increased rapidly and reached a peak in 2008, when more than 60% of *Staphylococcus aureus* isolates were resistant to methicillin; by 2011, it had decreased to 50.5% (Xiao *et al.*, 2011; Xiao *et al.*, 2012). More recent data from CHINET suggest that the prevalence of MRSA gradually decreased to 44.6% in 2014 (Hu *et al.*, 2015). However, it is still high in global terms, compared with a prevalence of 17.4% and 11.0% in the EU and the UK in 2014, respectively (ECDC, 2015). In addition, the distribution of MRSA is distinctive in the eastern regions and big cities, such as Beijing and Shanghai, which are regarded as highly-developed areas in China (Xu *et al.*, 2010). Alongside the problem of MRSA, CHINET suggested that the rate of methicillin-resistant coagulase negative *Staphylococcus* (MRCNS) has also been very high in China, and increased to 83.0% in 2014 (Hu *et al.*, 2015).

For gram-negative bacteria, based on data from Mohnarin and CHINET, the most common species in China are *Escherichia coli* and *Klebsiella* spp. (all belonging to the Enterobacteriaceae family), *Acinetobacter* spp. and *Pseudomonas aeruginosa* (Hu *et al.*, 2015; Xiao *et al.*, 2012). The *Escherichia coli* and *Klebsiella* spp. are the strains most widely

distributed in China and have a strong association with hospital-acquired infections. Generally in China, the resistance of *Escherichia coli* and *Klebsiella pneumoniae* to cephalosporin and fluoroquinolones is high (Xiao *et al.*, 2011). The mechanism of resistance to cephalosporin in the Enterobacteriaceae family (including *Escherichia coli* and *Klebsiella pneumoniae*) is their production of extended-spectrum β -lactamases (ESBLs). Based on the Mohnarín report of 2011, the rates of ESBLs producing *Escherichia coli* and *Klebsiella pneumoniae* have been 71.2% and 50.3%, respectively (Xiao *et al.*, 2012). The CHINET 2014 report also indicated that the ESBLs producing strains accounted for 55.7% of *Escherichia coli* and 29.9% of *Klebsiella* spp., and the resistance rates of *Escherichia coli* to first-generation⁷ cephalosporin (Cefazolin), second-generation cephalosporin (Cefuroxime) and third-generation cephalosporin (Cefotaxime) were 71.1%, 62.8% and 62.0%, respectively. Moreover, the resistance rates of *Escherichia coli* to ciprofloxacin, gentamycin, piperacillin and trimethoprim/sulfamethoxazole have all been higher than 50% in China (Hu *et al.*, 2014, 2015; Wang *et al.*, 2013). In addition, multi-drug resistance becomes more common among Enterobacteriaceae in China. The carbapenem resistance, multi-drug resistance and pan-drug resistance in *Pseudomonas aeruginosa* and *Acinetobacter* spp. also emerged in China, which is similar to some Western countries (Xiao *et al.*, 2011; Hu *et al.*, 2014, 2015; Wang *et al.*, 2013). For instance, Xiao *et al.*'s (2011) study indicated that the rate of pan drug-resistant *Pseudomonas aeruginosa* was 2.1% in 2008 in China.

⁷ Generation terms come only in case of Penicillin and Cephalosporin, which are classified depending on (i) their action on the cell wall of gram positive and gram negative bacteria and (ii) their spectrum.

1.2.4.2 Human antibiotic use in China

As noted in the previous section (section 1.2.2), the most important contributor to ABR is the wide and inappropriate use of antibiotics, a pattern that is found across Asia as well as in China specifically (Cars *et al.*, 2008; Goossens, 2005; Song, 2015). China has an extremely high total antibiotic usage. Data from the Chinese Academy of Sciences estimated that 162,000 tons of antibiotics were consumed in China in 2013, which accounted for half of the total global antibiotic usage. Among total antibiotic usage in China, human consumption accounted for approximately 48%, which was equivalent to 77,760 tons (Zhang *et al.*, 2015). The per capita consumption of antibiotics and frequency of antibiotic use are very high in China as well. In 2013, the per capita antibiotic consumption in China was nearly 6 times than that of the UK⁸. For antibiotic use frequency (Box 3), based on a systematic review of antibiotic usage in China, the overall outpatient antibiotic use frequency was 50.3% between 2000 and 2012, compared with the antibiotic use frequency of 15.3% in the USA at the same time. The average antibiotic use frequency ranged from 40% to 50% in other LMICs (Yin *et al.*, 2013). Other issues that are common in other LMICs also appear to be exacerbating the spread of human ABR in China, such as inadequate control measures, poor accessibility to health care resources and undeveloped national ABR surveillance systems (Alubo, 1994; Verma *et al.*, 2014; Xiao, 2008).

⁸ Author's calculation. In the UK, the population was 64.1 million in 2013, and the usage of antibiotics by humans in 2013 was 641 tons. In China, the population was 1.357 billion in 2013 while the usage of antibiotics by humans in 2013 was 77,760 tons (World Bank; Zhang *et al.*, 2015).

Box 3 What is the antibiotic use frequency?

Antibiotic use frequency is the proportion of encounters (between a patient and a healthcare provider) with an antibiotic prescribed, and it could be used in inpatient, outpatient, and emergency situations, among others (Zou *et al.*, 2014).

The proportion of encounters with an antibiotic prescribed is an indicator used to measure the performance of health practitioners related to rational or irrational use of drugs, which is developed by the International Network for Rational Use of Drugs (Li *et al.*, 2012). This indicator is calculated by '*dividing the number of encounters during which an antibiotic is prescribed, by the total number of encounters surveyed*' (WHO, 1993, pp.14). It is only concerned with whether antibiotics are prescribed for a patient; therefore, for a patient prescribed antibiotics, no matter how many types of antibiotics are prescribed for them, the number of patient encounters during which an antibiotic is prescribed is still one (He, 2013).

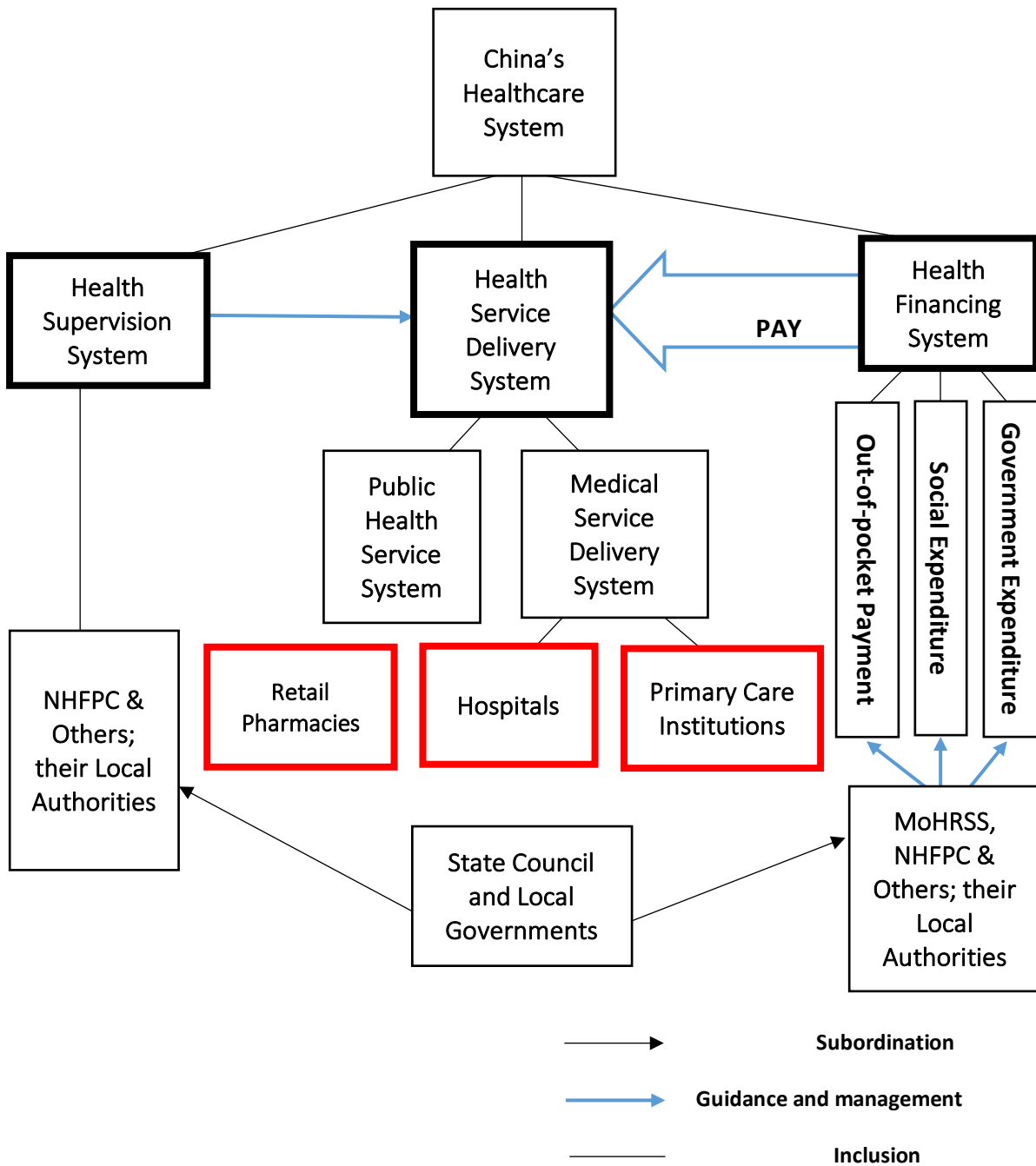
Recent studies also point to widespread inappropriate use of antibiotics in China, particularly in the provision of medical services to patients, in pharmacies and among the public, which highlights the important role of healthcare providers and the public in relation to antibiotic use and resistance in China (Chan *et al.*, 2012; Lv *et al.*, 2014; Mao *et al.*, 2015; Sun *et al.*, 2015; WHO & MoH, 2013). Therefore, the next section will describe China's healthcare system and consider evidence on antibiotic use and inappropriate use in different key parts of China's healthcare system.

1.3 The context and antibiotic use in China

1.3.1 Healthcare system in China

Since the founding of the People's Republic of China in 1949, the healthcare system has experienced several waves of reforms as part of China's wider economic reforms (Meng, *et al.*, 2012). Today's healthcare system is comprised of three independent but inter-related sub-systems: a health supervision system, a health service delivery system, and a health financing system (Chan *et al.*, 2008; WHO, 2015C) (see Figure 1).

Figure 1 Structure of China's healthcare system



Bold black boxes show the three sub-systems in healthcare system;
 Bold red boxes show the institutions focused in this study;
 MoHRSS: Ministry of Human Resources and Social Security;
 NHFPC: National Health and Family Planning Commission.

Source: adapted from Ma et al., 2014; NHFPC, 2014; WHO, 2015C.

China's **health supervision system** exerts tight control over the healthcare system through the NHFPC. This national-level administration governs local authorities at provincial, municipal and county levels. There is no independent health administration at the township level. In consequence, the State Council, NHFPC and their local authorities govern the overall healthcare system in China. The **health service delivery system** mainly consists of a public health service system and a medical service delivery system (WHO, 2015C). The public health service system includes disease control and prevention institutions, maternal and child health institutions, and public education institutions, among others. The medical service delivery system consists of hospitals from ministerial to county levels and primary care institutions (Ma *et al.*, 2014; NHFPC, 2014). The **health financing system** is based around three basic medical insurance schemes⁹ and related administrative departments. Total health expenditure (THE) in China consists of government expenditure, social expenditure, and out-of-pocket payments in the health financing system (Mossialos *et al.*, 2016; WHO, 2015C).

The retail pharmacy is also an important part of China's health service provision and provides pharmaceutical services. Although most drugs in China are still distributed from pharmacies within hospitals and primary care institutions, the retail pharmacy sector is rapidly growing (Mossialos *et al.*, 2016; WHO, 2015C). All drug-related activities in retail pharmacies are supervised by the China Food and Drug Administration (CFDA) and its local authorities at

⁹ They included Urban Employee Basic Medical Insurance (UEBMI) and Urban Resident Basic Medical Insurance (URBMI) for urban areas, and New Rural Cooperative Medical Scheme (NRCMS) for rural areas.

provincial, municipal and county levels (WHO, 2015C). In 2012, the total pharmaceutical expenditure accounted for approximately 40% of THE in China (Mossialos *et al.*, 2016).

Health is an important component of the Chinese social welfare system. Despite the remarkable success of healthcare reforms and the expansion of the Chinese social welfare system, health inequities are still long-standing problems, with the most evident imbalance in healthcare provision being that between urban and rural areas (Chan *et al.*, 2008; Gao *et al.*, 2018). In 2004, the per capita health expenditure was CNY 1,261.9 (US\$ 203.4) in cities while only CNY 301.6 (US\$ 48.6) in rural areas (MoH, 2006). Although the Chinese government has introduced three basic medical insurance schemes since 1998, a marked urban-rural differential in the insurance benefit is still evident (e.g. the 50%-80% inpatient reimbursement in urban areas compared with 20%-60% in rural areas in 2010) (Barber & Yao, 2010; Gao *et al.*, 2018; Meng *et al.*, 2012). Additionally, there is a particular lack of health human resources, including both doctors and nurses, in rural areas (Hou & Ke, 2015; NBSC, 2016; Yang & Dong, 2014). Along with the inequities between rural and urban areas, the low coverage of basic medical insurance schemes for migrant workers in the cities is still a problem (Chan *et al.*, 2008; Yip *et al.*, 2012), although UEBMI was expanded to cover them during 2009-2011 (Hu *et al.*, 2013). The Chinese government has identified benefiting migrant workers as a particular goal for their basic medical insurance scheme-related work in 2018 and beyond (Lancet, 2018). These inequities, therefore, lead to significant differences with respect to the health benefits and health conditions between non-migrant urban residents and rural and migrant populations, such as the high malnutrition and underweight rates for rural children in comparison with children in urban areas (Gao *et al.*, 2018; Tang *et al.*, 2018).

In conclusion, China's healthcare system is a web of complex interactions among different sub-systems, and continues to face challenges in terms of health inequities. Within this healthcare system, the thesis of the present study is mainly related to the medical service delivery system (hospitals and primary care institutions) and retail pharmacies, marked in red in Figure 1. More detailed information on these institutions is therefore provided below; while details in relation to the health supervision and health financing systems are provided in Appendix B.

1.3.1.1 Hospitals

China's hospitals provide both inpatient and outpatient care services. In China, hospitals are subdivided according to size and function; i.e., primary hospitals (20—100 ward beds), secondary hospitals (101—500 ward beds), and tertiary hospitals (>501 ward beds). Primary and secondary hospitals primarily provide basic medical services and preventive health care whereas tertiary hospitals focus more on severe and complicated diseases, as well as responsibilities for conducting medical education and research. Hospitals are then divided into three classes at each level; the A class hospitals are the best, the B class hospitals are intermediate, and the C class hospitals are general and basic, according to medical standards, hospital management, the availability of certain equipment and whether medical research is performed (Xie *et al.*, 2010). Apart from the classification based on the size and functions, hospitals can also be categorised into public hospitals, which are owned and overseen by the

government, and private hospitals, as well as general hospitals and specialized hospitals according to their target diseases (Xie *et al.*, 2010).

Within the medical service delivery system, hospitals are the cornerstone, delivering more than 90% of China's inpatient, and a substantial amount of outpatient, services (Yip *et al.*, 2012). In 2008, more than 50% of urban patients and 17.3% of rural patients chose to directly visit hospitals for healthcare services (MoF, 2009). Among all hospitals, the general tertiary hospitals are the main healthcare provider. Data suggest that, among all hospitals, most healthcare services were delivered by tertiary hospitals in China. In 2013, almost half (49.4%) of hospital healthcare services were delivered by tertiary hospitals, whereas 43.4% and only 7.2% were delivered by secondary and primary hospitals, respectively (NHFPC, 2014A). At same time, compared with private hospitals, 89.8% of hospital visits took place in public hospitals in 2013 (NHFPC, 2014A). In addition, most of China's health resources, such as healthcare institutions'¹⁰ bed and health staff, are concentrated in hospitals (Statistical Information Centre of NHFPC, 2016). For instance, 73% of healthcare institutions' beds were located in hospitals in 2012 (NHFPC, 2014). Additionally, about 70-80% of pharmaceutical sales in China come from hospitals (Mossialos *et al.*, 2016).

¹⁰ The healthcare institution refers to any institution that obtains the *Practice License of Healthcare Institution* of the People's Republic of China or certificates from relevant authorities, and provides medical and healthcare related services or undertakes medically related research. The healthcare institutions include hospitals, primary care institutions, professional public health institutions such as the specialized disease prevention and treatment centre, and other relevant healthcare institutions (MoH, 1994; NHFPC, 2014; NHFPC, 2017).

1.3.1.2 Primary care institutions

The primary care system is a relatively weak, but rapidly growing, sector of China's healthcare system (Chan *et al.*, 2008; Mossialos *et al.*, 2016; Wang *et al.*, 2012). Still in a roll-out stage, knowledge about the primary care system, as well as the effects of policies focused on it, remain insufficient (Li *et al.*, 2017). This system includes community health institutions (CHIs) in the city and township health centres, as well as village clinics in rural areas; the CHIs further consist of community health centres and community health stations. In the urban areas, these community-based institutions are a new type of healthcare institution in China, introduced beginning in 1997 and strengthened in 2006 (Bao, 2007; Li, 2012). Through delivering both public health services and primary care services, the CHIs are defined as combining functions of prevention, health care, general medical care, health education, rehabilitation and supervision of family planning into one (Hao, 2007). The community health centres are the main element of the CHIs in China, whereas the community health stations, one level below community health centres, serve as a supplement to healthcare services and are overseen by CHIs (Zhongyangbianban *et al.*, 2006). In China, there are mainly four kinds of organizational types of CHIs, including government operated CHIs, hospital operated CHIs, social organizations operated CHIs and individual CHIs (Bao, 2007; Hao, 2007). The CHIs can also be divided into public institutions and private institutions in line with their registration types (Statistical Information Centre of NHFPC, 2016).

As strengthening the primary care system has been defined as one of five pillars of China's 2009 health reforms (discussed below in section 1.4.3), the number of primary care

institutions is rapidly increasing (Mossialos *et al.*, 2016; Yip *et al.*, 2012). In 2012, the total number of CHIs has reached 33,562 in urban areas, and the numbers of township hospitals and village clinics were 39,097 and 653,419 in rural areas, respectively (NHFPC, 2014). By 2016, the total number of CHIs further increased to approximately 34,000 (NHFPC, 2017A), which has increased around 100% from 2005 to 2014 (Statistical Information Centre of NHFPC, 2016). In addition, the proportion of primary care visits among all healthcare institution visits reached 57.4% in 2014 (Statistical Information Centre of NHFPC, 2016); in 2016, primary care institutions provided 55% of outpatient care services and 18% of inpatient care services (Li *et al.*, 2017).

However, there are still weaknesses in China's primary care institutions, such as the limited provider facilities. A national survey of 3,602 primary care institutions pointed to a very high proportion of village clinics that could not provide basic clinical tests; for example, 96% were unable to conduct a blood test (Li *et al.*, 2017). Moreover, the general practitioners (GPs) and village doctors, the backbone of primary care institutions, are often inadequately trained and underpaid. Data from the National Statistics Yearbook indicated that, in 2015, still 31% of GPs failed to meet the educational level requirement (junior medical college) in CHIs and township health centres, while 12% of village doctors did not meet the educational level of a technical school in village clinics¹¹ (NHFPC, 2017B). Li *et al.*'s (2017) national survey further indicated

11 There are three educational levels required for providers in primary care institutions: medical college, junior medical college and technical school. Completing medical college or the lower level – junior medical college, are required to become a licensed GPs or licensed assistant GP, respectively, in CHIs and township health centres; people with these educational levels then need to pass the national doctor practicing exam in order to be licensed. After completing technical school one is able to become a so-called village doctor without a formal licence in village clinics (Li *et al.*, 2017).

that over one-fifth of GPs among CHIs and township health centres were unlicensed, with a particularly high proportion (37%) of unlicensed GPs working in community health stations; moreover, the post-qualification training for GPs was insufficient. Additionally, GPs and village doctors were found to have the incomes lower than the average in China, along with low job satisfaction and high occupational burnout (Li *et al.*, 2017). The policies issued under the 2009 healthcare reforms, such as increases in the total subsidy for the primary care system and providing a subsidy to compensate for the loss of income resulting from zero mark-up (ZMU) policies¹², appeared insufficient in improving the incomes of primary care institutions (Gao *et al.*, 2012; Li *et al.*, 2017).

The quality of healthcare services delivered by primary care institutions was questioned by many studies, specifically related to incorrect diagnosis and unnecessary treatments (Su *et al.*, 2017), including antibiotic treatment (Li *et al.*, 2017; Yin *et al.*, 2013). The public also distrust the primary care institutions. Duckett *et al.*'s (2016) study noted that 13% and 88% of 3,680 participants would go directly to hospitals for minor and major illness, respectively, and the higher rates of hospital utilization were associated with a higher distrust in primary care institutions (Duckett *et al.*, 2016). Another national survey also referenced the lower trust levels in primary care institutions as one of major reasons patients choose to go to hospitals directly for healthcare services (Li *et al.*, 2017).

¹² ZMU policies are discussed in section 1.4.3 in more detail.

1.3.1.3 Retail pharmacies

Most hospitals and primary care institutions have their own pharmacies, and these pharmacies are the main drug distributors in China (WHO, 2015C; Mossialos *et al.*, 2016). For instance, it was suggested that, in 2009, drugs sold by hospitals' pharmacies accounted for over 70% of the total drug sales in China (Fang *et al.*, 2013; Sun *et al.*, 2008). Compared with pharmacies within hospitals and primary care institutions, retail pharmacies have developed fast in China since the implementation of China's 2009 healthcare reforms, which forced hospitals to transfer from selling drugs to being more focused on providing medical services (State Council, 2015). Pharmaceutical sales by retail pharmacies grew by an average of 20% each year from 1978 to 2009 (Fang *et al.*, 2013), and, by 2014, there were over 400,000 retail pharmacies (Fang, 2014).

In China, there are two types of pharmacists covered by two different pharmacist qualification systems. The **professional qualification system** is overseen by the CFDA and Ministry of Human Resources and Social Security (MoHRSS), and pharmacists working under this system are called Licensed Pharmacists (MOHR & CFDA, 1999). People who plan to become a licensed pharmacist must obtain the *Licensed Pharmacist Certificate* by passing the national pharmacist licensing exam. After that, they need to register their certificate with the provincial regulatory authorities so that they can work at their registered institutions (MOHR & CFDA, 1999), and they are required to attend post-qualification development in order to gain approval for re-registration every three years (CDFA, 2003; MOHR & CFDA, 1999). In China, the pharmacists permitted to work in retail pharmacies are all licensed pharmacists.

However, the standard set for achieving qualification via the pharmacist licensing exam has been reported as low by some studies (Fang *et al.*, 2013; Huang, 2007), as the minimum qualification for sitting the exam is '*a secondary technical school diploma and a major in pharmacy or related disciplines (e.g., medicine, chemistry, biology or nursing)*' (Fang *et al.*, 2013, pp.524).

Regulations issued in 2012 stipulated that newly-opened retail pharmacies must be staffed by licensed pharmacists; by 2015, licensed pharmacists were required to be present at retail pharmacies during business hours in order to provide pharmaceutical services to consumers (Fang *et al.*, 2013; State Council, 2012). Additionally, it is currently regulated that, in China, the juridical person (person in charge) of retail pharmacies can only be a licensed pharmacist (CFDA, 2015). With respect to the sale of antibiotics, based on earlier regulations and the '*Administrative Regulations for the Clinical Use of Antibiotics*' launched in 2012, antibiotics can only be sold with a prescription by licensed pharmacists in retail pharmacies (MoH, 2012A). However, the phenomena of licensed pharmacists being absent during business hours and selling OTC antibiotics are both still very common in China's retail pharmacies, even after 2012 (Fang, 2014; Jiang *et al.*, 2013; Yu, 2013).

The second pharmacist qualification system is the **specialized system** that is overseen by the NHFPC. NHFPC-qualified pharmacists work in healthcare institutions, mainly hospital pharmacies, and are assigned a special title (ranging from assistant pharmacist, pharmacist, pharmacist-in-charge, and deputy chief pharmacist to chief pharmacist) (Fang *et al.*, 2013). For hospital pharmacists, people with a pharmacy education background can start to get into

this system by being employed by the hospital. After that, they need to take the exam for the particular special title in order to obtain the special title qualification certificate (MoH & MOHR, 2001). The hospital where they work will then assess whether to award the special title to them based on a comprehensive set of qualifications, including the special title qualification certificate, professional performance, English and computer skills and published papers, among others (MOHR, 2000). For CHIs, only pharmacists working at government-operated CHIs are covered by the specialized system (Zhongyangbianban *et al.*, 2006). In addition, a *Licensed Pharmacist Certificate* is not mandatory for pharmacists working under the specialized system (Fang *et al.*, 2013).

1.3.2 Chinese culture and two medical systems in China

1.3.2.1 Chinese culture

The term of culture refers to '*the collection of values, beliefs, behaviours, customs, and attitudes that distinguish a society*' (Fan, 2000, pp.3). In China, despite rapid social changes and marked differences between regions, Chinese culture remains stable and held in common, and continues to shape people's attitudes and behaviour while establishing social norms and standards (Fan, 2000).

Chinese culture is therefore seen as a set of core values underlying China's social interactions in a long period of time and shaping people's behaviour to adapt them to the group where they are embedded (Hofstede, 1980); these core values, which are highly influenced by traditional culture, are related to different dimensions, ranging from interpersonal relations

(e.g. face and *guanxi*), family and society (e.g. loyalty to superiors), to nature (e.g. unity of *yin* and *yang*, harmony between man and nature) (Fan, 2000; Peng, 2003). Shaped by its four-thousand-year history, it is not surprising that traditional culture, with the core of Confucianism, remains central to Chinese society. As Confucianism highlights Five Constant Virtues and five basic human relations (*wulun*) that ensure a harmonious relationship in family and society, a large number of Chinese core cultural values are related to interpersonal relations and family/society rooted in Confucianism, such as hierarchical relationships and observing this order in family and society, keeping harmonious relations with others, and the importance of 'face' – a person's reputation (Fan, 2000). The high proportion of cultural values with an interpersonal and family orientation also underline the importance of the family in Chinese culture and society; moreover, family relations are always defined through the male versions of language, which indicates the predominant position of the male in the family in China (Fan, 2000). Apart from traditional cultural values, there are also some contemporary Chinese cultural values, such as the values of *guanxi*, which means the personal network, in Chinese business philosophy (Fan, 2000).

1.3.2.2 Traditional Chinese medicine and the dual use of medical systems

Chinese culture has endured during rapid social change in China and across Chinese populations within and beyond Mainland China (Fan, 2000), and continues to influence their health and health-related awareness (Chen, 2001). Among various cultural values in China, Taoism is the second major Chinese philosophy and religion that highlights the harmony between human beings and nature, and expands the idea of '*yin-yang*' (Chen, 2001). Based

on the principle, Chinese people divide all phenomena into two contrary components, such as sun and moon, man and women, and hot and cold, and always keep the balance of the two opposite forces, which governs the way of Chinese life (Chen, 2001). TCM is a holistic medical practice system that originates from ancient China and has been practised for more than 2000 years and is also built around this theory. The ultimate goal of TCM is to control the harmony and balance of '*yin-yang*' within the human body and between humans and the wider environment, in order to maintain the source of vital energy and human life – '*qi*' (Cheung, 2011). Specifically, TCM has been used to diagnose, prevent and cure human diseases based on two fundamental theories, *yin-yang* and five elements (*wu-xing*) (Lao *et al.*, 2012; Wang & Li, 2005). It understands the body and life from theories associated with organs (*zangfu*), meridian (*jingluo*), energy (*qi*) and blood (*xue*), and attributes the causes of diseases to six excesses (*liuyin*), seven emotions (*qiqing*) and diet and fatigue (*yinshilaoyi*), among others (Yin & Zhang, 2006). The TCM treatment methods are also different from those of Western medicine. They include herbal medicines, acupuncture and moxibustion, Chinese massage (*tuina*), exercises (*qigong*) and diets, while surgical operation is seldom used (Lao *et al.*, 2012; WHO, 2001).

TCM was the medical practice dominating China until the early nineteenth century, when Western medicine knowledge was brought in by Protestant missionaries and rapidly developed in China after the collapse of the Qing dynasty (Chueng, 2011). It has been noted that, in 2006, over 80% of hospitals in China were the general hospitals, which mainly provide Western medicine services, and the growth rate of general hospitals was much faster than that of TCM hospitals over the last few decades (Xu & Yang, 2009). However, there are

numerous differences between these two medical systems as they evolved from totally different cultural and historical contexts. For instance, focusing on keeping the balance within the human body (*xing shen tong yi*) and between humans and nature (*tian ren he yi*), TCM highlights the important role of the internal relationships between the human mind, human body and environment in preventing and treating diseases; however, Western medicine always tries to identify the specific disease-causing agents (Qiu, 2015). Some key theories, which can be understood within a TCM perspective, such as 'qi', have no equivalent in Western medicine and cannot be measured or explained by modern science and medicine (Qiu, 2015). Additionally, the characteristics of TCM that originate from philosophy and art make its treatment more likely to be an individualized practice, which is difficult to reproduce, whereas Western science and medicine highly emphasize treatment reliability and replication (Bryman, 2008; Qiu, 2015).

In the light of the rapid development of Western medicine and the enduring importance of TCM in China, studies and policies have explored the potential similarities in these two systems and have tried to use them together. For instance, Qiu's (2015) study reported that, even though focusing on opposite aspects, both TCM and Western medicine are systems that integrate medical and social phenomena together; this study also connects TCM's diagnostic process, which is from the whole-organism level, to the Western medicine discipline of structural health monitoring (Qiu, 2015). The official policy since the 1980s has been to promote the dual and equal use of TCM within the national healthcare system, with more ambitious plans to combine TCM with Western medicine initiated in 2007 (Mossialos *et al.*, 2016; Qiu, 2015; WHO, 2001). The State Administrations of Traditional Chinese Medicine

(SATCM) and its local authorities are responsible for supervising the development of TCM in China (WHO, 2001, 2015C). It was established in 1985 and now is directly led by the NHFPC; as noted in Hesketh & Zhu's (1997) study, China is globally unique in that TCM and Western medicine are practised alongside each other at every level of the healthcare system (Hesketh & Zhu, 1997).

With respect to the delivery of TCM services, there were over 40,000 TCM-related institutions in 2014, and TCM services accounted for around 18% of total healthcare services (Qiu, 2015; Statistical Information Centre of NHFPC, 2016). It was also indicated by one study that, among all general hospitals in China, 90% of them had TCM departments, while most TCM hospitals provide both TCM and Western medicine services; TCM outpatient visits made up over 30% of total outpatient visits in China (Xu & Yang, 2009). For primary care institutions, national data indicated that 98% of community health centres and 94% of township health centres provided TCM services in 2016 (NHFPC, 2017A). The wide provision of TCM services in the primary care system was also reported by another nationwide survey that noted 76% of community health centres and 69% of township health centres accessed had a TCM department (Li *et al.*, 2017). The sale of TCM drugs also accounted for about 30% of total pharmaceutical expenditure in 2012, with a particularly higher proportion, 44% of drug sales, in the retail pharmacy (Mossialos *et al.*, 2016). In addition, in professional education, rather than only focusing on TCM theories, the TCM curriculum also includes Western medicine, such as physiology in their curriculum (Xiao, 2004). Therefore, TCM has been regarded as the common philosophy by Chinese people and is well accepted and used alongside Western medicine in China's health-related system.

The use of TCM theory in interpreting illnesses has been reported in studies focusing on both the population of Mainland China and on other Chinese societies, such as Taiwan and overseas Chinese populations (Chung *et al.*, 2014). For instance, a study in Mainland China noted that the majority of the population believed in TCM, even though most of them preferred to seek Western medicine treatment rather than TCM treatment when they are unwell (Xu & Yang, 2009). A large household survey of 42,819 people undertaken in China in 2003 found that, although Western medicine was more popular among Chinese people with 54% of people choosing to use Western medicine alone, 25% of the participants preferred integrated TCM/Western medicine treatment and 12% preferred TCM treatment only, respectively (Xu & Yang, 2009). A more recent study also found that approximately 60% of the population in Hong Kong and Mainland China had consulted a TCM practitioner at least once (Cheung, 2011).

1.3.3 Antibiotic use and inappropriate use by different parts of the healthcare system and the public in China

1.3.3.1 Antibiotic use and inappropriate use in hospitals and primary care institutions

In China, hospitals are a major place where antibiotics are consumed (sales volume of antibiotics accounting for 25% of the total drug sales in hospitals) (Tao *et al.*, 2013), and the antibiotic use frequency (see Box 3) among both hospital inpatients and outpatients is very high (Currie *et al.*, 2013). However, the marked differences in socio-economic development,

such as healthcare resources and the health status across China, mean that the patterns of antibiotic use may be different in urban and rural areas (WHO, 2015C).

Table 1 summarises the reported inpatient antibiotic use frequency among some hospitals in urban areas prior to 2011; the antibiotic use frequency ranged from 45.1% to 85.1% in different cities' general hospitals, which was all much higher than the percentage use of antibiotics recommended by the WHO ($\leq 30\%$) (WHO, 2006). Data from a hospital in the study location for this thesis – Taiyuan city – are included in the studies; antibiotic use is again very high, with an antibiotic use frequency of 67% among 33 inpatients in the respiratory department and 69% among 29 inpatients in the nephrology department of Taiyuan Centre Hospital, respectively (Deng, 2009). Of Taiyuan city, a study also showed that, among 4,399 antibiotic prescriptions collected in 2005 from the sampled hospital in Taiyuan city, 1,889 (42.94%) of them were inappropriate (Dong *et al.*, 2006). A nationwide epidemiological study also found an average antibiotic use frequency of 68.9% among inpatients and an average antibiotic use intensity (Box 4) of 80.1 defined daily doses (DDDs) per 100 patient days in China in 2010 (Wang & Chou, 2013).

To address this high level of antibiotic use, the Ministry of Health (MoH) (NHFPC from 2013) introduced the three-year strategy – '*National Special Campaign for Clinical Use of Antibiotics*' – in 2011 (discussed below in section 1.4.2). This stipulated the limitations on antibiotic use intensity and antibiotic use frequency in hospitals (Bao *et al.*, 2015; MoH, 2012; Tao *et al.*, 2013), and there is evidence that the high inpatient antibiotic use has been gradually decreasing since the introduction of this strategy. One study focused on 65 general hospitals

in China that indicated that the use of antibiotics dramatically decreased from 2010 to 2014 as a result of the strategy, with the average antibiotic use frequency in inpatients and outpatients dropping from 62.9% to 35.3% and from 44.2% to 28.4%, respectively (Bao *et al.*, 2015). The success of the strategy is also supported by data from individual hospitals. For instance, a cross-sectional study indicated that antibiotic use frequency on one particular day in 2014 was 42.4% among 1,306 inpatients in a selected general hospital (Wang & Li, 2015). In addition, a study of 420 hospitals spread across most regions of China reported that, between 2008 and 2011, there was a decline in antibiotic use intensity in both second-line and third-line antibiotics (Tao *et al.*, 2013).

Table 1 Antibiotic use frequency among hospital inpatients in urban areas of China

Region	Hospital Name	Period	Sample Size (cases)	Antibiotic Use Frequency
Luoyang, Henan Province	No. 534 Hospital of PLA	2007.03-2008.02	284	45.1%
Xiangtan, Hunan Province	Xiangtan Centre Hospital	2001.06.30	N/A	48.4%
		2003.06.30		62.9%
		2005.06.30		60.4%
Nanchong, Sichuan Province	Anonymous hospital	2011.09-2011.12	3526	51.67%
Jingzhou, Hubei Province	Anonymous hospital	2005.11-2006.04	479	54.49%
Hefei, Anhui Province	No.105 Hospital of PLA	1996.01-1998.12	9853	57.2%
Datong, Shanxi Province	Anonymous hospital	2010.01-2012.01	500	60.6%
Jiujiang, Jiangxi Province	No.1 Jiujiang Hospital of People	2005.01-2005.12	1315	65.1%
Taiyuan, Shanxi Province (study site for the current study)	Taiyuan Centre Hospital	2008.10-2008.12	33	67%
Taiyuan, Shanxi Province (study site for the current study)	Taiyuan Centre Hospital	2008.10-2008.12	29	69%

Qingdao, Shandong Province	Qingdao City Hospital	2001.04-2001.10	577	74.87%
Guangzhou, Guangdong Province	Centre for Cancer Control & Prevention of Zhongshan Medical University	2001.06-2001-07	739	75.37%
Lanzhou, Gansu Province	Affiliated Hospital of Lanzhou Military Region Lintong Sanatorium	2008.01-2008.06	531	77.4%
Cangnan, Zhejiang Province	Cangnan County Traditional Chinese Hospital	2003.01-2005.01	900	77.78%
Chengdu, Sichuan Province	Sichuan Hospital of People	2002.03-2002.04	602	78%
Chengdu, Sichuan Province	Chongzhou Hospital of People	2002.01-2003.12	1069	85.12%

Source from: Deng, 2009; Li et al., 2002; Liang et al., 2001; Lin, 2004; Liu et al., 2000; Liu et al., 2006; Ren, 2012; Tang et al., 2002; Wang et al., 2010; Wang et al., 2011; Wang & Qin, 2010; Wang & Zhou, 2007; Yi et al., 2006; Zhang, 2005; Zhang et al., 2006; Zhao & Xu, 2014.

Box 4 What is the antibiotic use intensity?

Antibiotic use intensity is measured by the DDDs per 100 patient days, which is a standardized measurement approach of drug usage recommended by the WHO (WHO, 2012; Zou *et al.*, 2014). The WHO's definition of DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (WHOCC, 2009).

However, despite evidence of a reduction in antibiotic use in general hospitals, antibiotic use among children is reported to still be a problem (Zou *et al.*, 2014). China has had an extremely high antibiotic use frequency among inpatient children for a long time, especially in the treatment of upper respiratory tract infections (Cui *et al.*, 2011; Hu, 2006; Zhang *et al.*, 2009). Based on a five-point prevalence survey (conducted in 2001, 2003, 2005, 2008 and 2010) in tertiary hospitals across all 31 provinces of Mainland China, the use of antibiotics remained high in paediatrics departments, despite an overall decreasing paediatric antibiotic-using trend from 2001 to 2010 (Li *et al.*, 2013). The high antibiotic use among children was also identified in a study focusing on the five largest children's hospitals in four highly-developed cities in China, which reported that the mean antibiotic use intensity between 2002 to 2006 was nearly twice as much as France's across a similar period (Zhang *et al.*, 2008; Zou *et al.*, 2014), along with very high antibiotic use frequency reported by individual children's hospitals (He, 2012; Li & Wu, 2007; Wang, 2006; Xie & Wu, 2006; Zheng *et al.*, 2008). For instance, one study of antibiotic use in Shanxi Province (the province where the current study is located) showed that 87.3% of 1,000 child inpatients used antibiotics in the sampled hospital in 2007 (Yang & Shi, 2008).

The high antibiotic use by child inpatients has persisted, even after the three-year strategy. Zou's 2011-2012 study highlighted that antibiotic use remained high in children's hospitals, even though it had declined in other specialist hospitals; specifically, the mean inpatient antibiotic use frequency in children's hospitals increased from 71.91% to 76.86% during this period, and remained much higher than the national standard level ($\leq 60\%$) (Zou *et al.*, 2014). For example, antibiotic use frequency was reported to be as high as 97.7% of 286 child inpatients between 2011 and 2013 in one hospital in Qionghai city, located in the southern area of China (Su, 2013). Furthermore, the use of antibiotics among child outpatients is also very high in China (Zhang *et al.*, 2008A; Zou *et al.*, 2014).

In contemporary China, primary care institutions have become the major healthcare providers, delivering 4.10 billion out of a total of 6.88 billion healthcare services in 2012 (WHO, 2015C). However, compared with antibiotic use in hospitals, the use of antibiotics in primary care settings remains little studied and reliable information is lacking (Wang *et al.*, 2014). A study focusing on urban CHIs across China indicated that, among 230,800 prescriptions collected between 2007 and 2009, there were more than 40% of prescriptions containing antibiotics, with the proportion of doctor-patient encounters resulting in antibiotics being prescribed being twice the WHO standard (20.0%-26.8%) (Li *et al.*, 2012; Isah *et al.*, 1997). Of the total prescriptions prescribed in 24 community health centres across the country in 2009-2011, it also found that 52.5% of 7,311 outpatient prescriptions and 65.4% of 2,888 inpatient prescriptions contained antibiotics (Wang *et al.*, 2014). Extensive antibiotic use in CHIs was also found in studies of individual CHIs, with the reported antibiotic use frequency ranging

from 41.68% to 57.7% (Huang, 2012; Wang & Chen, 2005; Yue & Zhu, 2014). However, unlike hospitals where the use of antibiotics has been controlled by the '*National Special Campaign for Clinical Use of Antibiotics*' and many other programmes, there is still no effective drug management programme focused on primary care settings in China (Xiao, 2012; Xiao & Li, 2013). Although the essential drug list (EDL) policies (discussed below in section 1.4.3) were implemented in primary care settings in 2009, the inappropriate use of antibiotics remained common among primary care institutions in China (Chen *et al.*, 2010; Song *et al.*, 2014; Yang *et al.*, 2013; Yao *et al.*, 2015).

The information about antibiotics use in rural areas of China is limited and less clear than in urban areas (Sun *et al.*, 2010). However, the limited evidence all points to the wide use of antibiotics in the rural areas. A study analysing prescriptions collected from 680 village clinics across 10 western provinces of China in 2005 found that the proportion of prescriptions including antibiotics was 48.43% (Dong *et al.*, 2008). The few studies focusing on antibiotic use in rural areas further indicated the antibiotic use frequency in sampled county hospitals and village clinics was consistently above 60% (Liao & Guan, 2012; Lin *et al.*, 2006; Ma *et al.*, 2002; Wang *et al.*, 2014; Zhang, 2013). In addition, a 2008 study, investigating antibiotic use in rural areas of one wealthy province (Shandong Province) and one poor province (Ningxia Province), also indicated that the proportion of prescriptions in which antibiotics were prescribed were 40.3% of total prescriptions in Shandong's county hospitals and 58.8% of Ningxia's county hospitals, with an increasing trend over time in township hospitals and village clinics of both provinces (Sun *et al.*, 2010). It was reported that antibiotic use was extremely high among children in township hospitals, with evidence that nearly 100% of child

inpatients' prescriptions included antibiotics among 22 township hospitals in Hubei Province (Ma *et al.*, 2013). Antibiotics are also inappropriately used among children, with evidence that, between 2007 and 2008, unnecessary antibiotic prescriptions occurred for 43% of 226 child patients (under 14 years old) in two county hospitals and three township hospitals in two medium-developed provinces of China (Liang *et al.*, 2011).

1.3.3.2 Antibiotic use and inappropriate use in pharmacies

In China, most drugs, including antibiotics, are dispensed from drug companies to wholesalers, and then to the hospital's and primary care institution's pharmacies, or to retail pharmacies, and finally to consumers (WHO, 2015C). Therefore, between antibiotics prescribed by doctors and finally used by consumers, the pharmacies have a very important intermediate and dispensing role. However, information about antibiotic use related to pharmacies is very limited in China.

For pharmacies in hospitals and primary care institutions, one study of 420 hospitals across the country indicated the proportion of sales volume for antibiotics decreased from 23.80% in 2009 to 19.40% in 2011 as a result of the three-year strategy in hospitals (Tao *et al.*, 2013). It has also been suggested that pharmacist interventions can improve rational antibiotic use in China (Penm *et al.*, 2013). For instance, by comparing the total cost of antibiotics in two independent respiratory hospital wards – one with pharmacist intervention and one without – between July 2009 and April 2010, Shen *et al.*'s (2011) study indicated that the total cost of antibiotics in the ward with pharmacist interventions was USD 832.0±373.0, which was

significantly lower than that of the ward without pharmacist interventions (USD 943.9±412.0). A separate study similarly reported that pharmacist interventions on prophylactic antibiotic use are effective, with evidence that, after applying pharmacist interventions from 2011, the rate of using antibiotics in clean operations decreased from 100% of 36 patients in 2010 to 7% of 69 patients in 2013 in the selected hospital (Zhou *et al.*, 2015).

For retail pharmacies, a rural study in Jiangxi Province found that, among all medicines in 8 retail pharmacies, antibiotics had the highest average sales volume (Yu *et al.*, 2013). Although national or provincial data about sales volume of antibiotics in retail pharmacies are rare, studies report that the inappropriate use of antibiotics – selling antibiotics without prescription – is very common. Self-medication with antibiotics is prevalent among the public in China and the retail pharmacy is one of the main sources for the public to acquire non-prescription antibiotics (Fang, 2014; Fang *et al.*, 2012). One study, focusing on 213 retail pharmacies in Shaanxi Province and having one encounter in each pharmacy, showed that 72.8% of 213 encounters relating to paediatric diarrhoea successfully obtained antibiotics without a prescription, while the rate of obtaining non-prescription antibiotics for adult respiratory infections accounted for 95.8% of those 213 encounters (Jiang *et al.*, 2013). Evidence of Liao *et al.*'s (2003) study similarly indicated the rate of obtaining non-prescription antibiotics for paediatric diarrhoea were 37.5% and 95% for adult respiratory infections of 40 encounters in retail pharmacies.

1.3.3.3 Antibiotic use and inappropriate use by the general public

In China, the role of patients in antibiotic use and inappropriate use has been reported to be increasing (Cars *et al.*, 2008). In one study focusing on antibiotic use among the general population of Hong Kong, 80.6% of 465 participants recalled they had been prescribed antibiotics (Chan *et al.*, 2012). Studies based on one particular city in Mainland China also reported that residents commonly used antibiotics. Additionally, antibiotics are widely used by parents for their children in China, with evidence that 85.8% of 183 children (under 7 years old) in a study carried out in Shandong Province were found to be treated with antibiotics when they have colds (Zhao *et al.*, 2013). Another study reported that, among 1,487 rural parents who had children between 0 to 3 years of age in Hebei Province, 88.54% of the 480 parents with educational at high school level or above had used antibiotics on their children when they were feverish, while 91.56% of 1,007 parents with levels at secondary school or below used antibiotics on their children when they were feverish (Yang *et al.*, 2010). As this suggests, antibiotics are widely used among the general public and on children by parents in China.

Alongside the high antibiotic use rate, it has been reported by many studies that the use of antibiotics by patients is often inappropriate. When individuals are not well or symptoms develop, their understandings of what is wrong are likely to be different and the actions they take to seek help will also differ (Gabe *et al.*, 2004); for instance, some people may seek professional health care while others may self-treat or do nothing (Li *et al.*, 2012). In China, because of the long-standing factors related to the high price of healthcare services, low trust

levels in some healthcare institutions and low levels of benefits provided by medical insurance schemes (discussed in section 1.3), self-treatment, including self-medication of antibiotics, is increasing rapidly (Li *et al.*, 2012; MoH, 2004, 2009; Pan *et al.*, 2012; Yip *et al.*, 2012). Data from a survey carried out by the CFDA indicated that, among 7,915 respondents, 1,892 (23.9%) chose to self-medicate with antibiotics when they had symptoms of a cold (Fang, 2014). Different studies suggested a high rate of self-medication with antibiotics among the general public, ranging from 22.09% to 44.8%, and an even higher parental medication rate, with 59.4% of 1,459 children medicated at least once by their parents (Bi *et al.*, 2000; Chen, 2003; Hou *et al.*, 2013; Li *et al.*, 2015). It was noted in Bi *et al.*'s (2000) urban study that, among the parentally-medicated children (59.4% of 1,459 participants), more than half received parental self-medication six or more times during one year. Parental medication of children with antibiotics is also very common in rural areas, with evidence from one study of 854 parents that the rate of parental medication with antibiotics was as high as 62% (Yu *et al.*, 2014). Self-medication and parental medication with antibiotics has been demonstrated to be one of the contributing factors for inappropriate use of antibiotics, which is associated with unnecessary antibiotics and incorrect antibiotics, among other factors (Grigoryan *et al.*, 2010; Jose *et al.*, 2013; WHO, 2012).

Non-adherence¹³ to antibiotic treatment is another common phenomenon related to inappropriate antibiotics used by patients in China. Data from a meta-analysis indicated that

¹³ The adherence is defined as 'the extent to which a person's behaviour-taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider' by the WHO (2003). It could be associated with a wide

poor adherence to treatment was associated with increased mortality (Aronson, 2007; Simpson *et al.*, 2006) and with treatment failure as well as higher costs of treatment (Kardas, 2006; Pechère *et al.*, 2007). With respect to antibiotic treatment, the patterns of non-adherence are various, such as failing to start the prescription, discontinuing an antibiotic before the course is complete, taking more or less of the dose than prescribed and taking a dose at the wrong time, among other issue, which are all examples of inappropriate antibiotic use (Kardas, 2006). In China, non-adherence to antibiotic therapy is common among patients. A global survey of non-adherence to antibiotic treatment showed that, in China, only 2.2% of 284 respondents were defined as adhering to treatment, for example, following dosage instructions and not saving antibiotics, which was much lower than rates in other countries, such as the Netherlands (68.0%) and the USA (54.8%) (Pechère *et al.*, 2007). This was supported by another study indicating that, among antibiotic therapies for outpatients with acute infections in one city of China, only 40.1% of 162 outpatients completely adhered to their therapies (Chen *et al.*, 2015). Another study carried out in Chongqing city in China also reported that 76.92% of 300 respondents chose to stop using antibiotics immediately when they felt better (Zeng *et al.*, 2012).

In conclusion, antibiotics are widely and inappropriately used in hospitals and primary care institutions, pharmacies, and by the public in China. In response to this serious problem, a range of reforms and policies related to the use of antibiotics have been introduced by the

range of health-related behaviour, such as taking medication appropriately, and the quality of the relationship between patients and health care providers is a core element of adherence (WHO, 2003).

Chinese government in order to control antibiotic use and ABR in China. In the next section, information on these reforms and policies is provided.

1.4 Policies related to the use of antibiotics

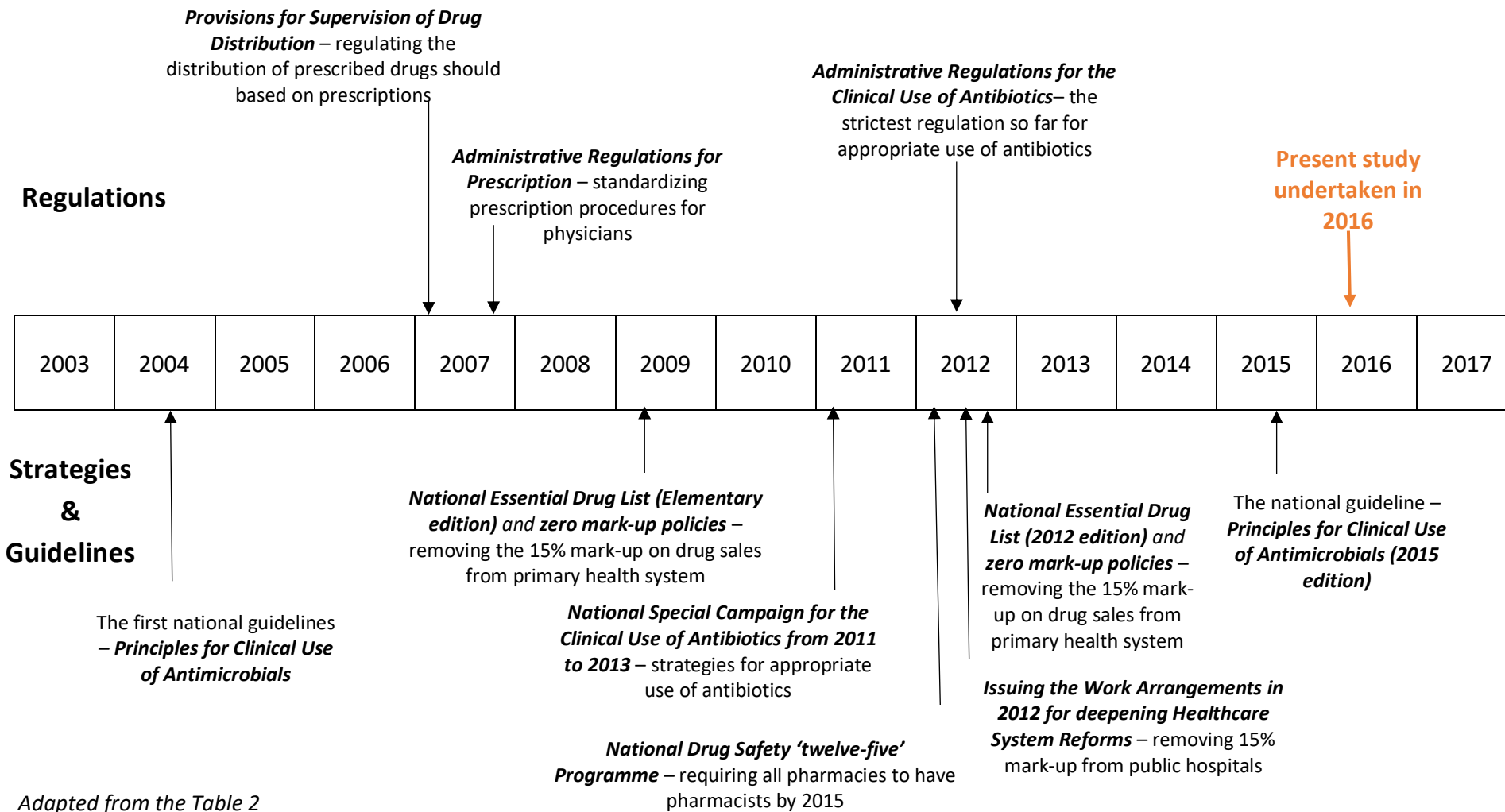
1.4.1 Overview of policies related to the use of antibiotics in China

In China, the development of national-level policies related to antibiotic stewardship began in the 2000s (Zhang, 2011). This included several national guidelines, such as the '*Principles for Clinical Use of Antibiotics*' and the '*National Formulary (2010 edition)*' issued in 2004 and 2010 (MoH *et al.*, 2004; MoH, 2010; Zhang, 2011), respectively, as well as relevant regulations, such as '*Provisions for Supervision of Drug Distribution*' (CFDA, 2007). However, over the past few decades, the inappropriate use of antibiotics was still reported to be very common in China, due to the lack of legal power of these guidelines and the weak enforcement of existing regulations (Xiao & Li, 2013).

The Chinese government began a new round of healthcare system reforms in 2009, seeking to provide universal health coverage to all residents (State Council, 2009). This led to the implementation of a set of policies, such as the EDL and ZMU policies (discussed below in section 1.4.3), which are also relevant to the appropriate use of antibiotics. Along with EDL and ZMU policies, a new strategy that ran from 2011 to 2013 focused particularly on antibiotics use was implemented by the national government, with the issuing of a new regulation in 2012. Following this 3-year period (2011-13), an improvement in hospital antibiotic use was observed (Xiao & Li, 2013; Xiao & Li, 2015). More policies have

subsequently been introduced in order to limit the inappropriate use of antibiotics in China. A timeline of important policies related to the use of antibiotics in China is shown in Figure 2 and a brief introduction to these policies is given in Table 2.

Figure 2 Timeline of policies related to the use of antibiotics in China



Adapted from the Table 2

Table 2 Content and implementation date of policies related to appropriate use of antibiotics in China

Field	Date	Policies	Main content
Regulations	2007	Administrative Regulations for Prescription	<ul style="list-style-type: none"> • Standardizing and supervising physicians' prescribing practices; • Setting punishments and legal responsibilities for violating the regulations.
	2007	Provisions for Supervision of Drug Distribution	<ul style="list-style-type: none"> • Provision of supervision for drug purchase, sale, and storage for different stakeholders, including selling prescribed drugs with prescriptions and under the supervision of licensed pharmacists or qualified staff; • Setting punishments and legal liabilities for violating the regulations.
	2012	Administrative Regulations for the Clinical Use of Antibiotics	<ul style="list-style-type: none"> • Regulating responsibilities, the manner of the work, as well as stricter punishment and legal liabilities related to the use of antibiotics for different stakeholders, from MoH, local authorities, healthcare institutions, and health professionals including physicians, pharmacists and microbiologists.
	2004, 2015	Principles for Clinical Use of Antimicrobials	<ul style="list-style-type: none"> • The principles for the rational use of antibiotics, including the priority given to oral antibiotics over other modes of treatment; • The management of the clinical use of antibiotics; • Pharmacological characteristics of antibiotics and recommendations for antibiotic treatment for infections.
	2009, 2012	EDL and ZMU policies	<ul style="list-style-type: none"> • A list of national essential drugs that should be sold without price mark-ups;

Strategies & Guidelines			<ul style="list-style-type: none"> • Requiring all government-operated primary care institutions to only sell essential drugs, while other medical institutions should procure and use national essential drugs as a priority.
	2011-2013	National Special Campaign for the Clinical Use of Antibiotics	<ul style="list-style-type: none"> • Setting responsibilities related to antibiotic use for MoH and local authorities as well as healthcare institutions; • Setting a range of antibiotic-related targets for healthcare institutions, such as the limitations on proportions of prescriptions with antibiotics; • Setting tasks related to supervision and summary.
	2012	National Drug Safety 'twelve-five' Programme	<ul style="list-style-type: none"> • A set of principles, objectives and tasks related to national drug safety, including one requiring every pharmacy to have pharmacists and ensuring their presence during pharmacy's opening hours by 2015.
	2012	Issuing the Work Arrangements in 2012 for deepening Healthcare System Reforms	<ul style="list-style-type: none"> • A range of tasks in order to deepen healthcare reforms, including one to remove the 15% mark-up on drug sales from public hospitals.

Source from: CFDA, 2007; MoH, 2011, 2012, 2012A, 2013, 2013A; NHFPC, 2015; State Council, 2012; Xiao & Li, 2015.

As shown in Figure 2, the roll-out of antibiotic-related reforms began in 2011, and was influenced by China's 2009 round of healthcare reforms. The present study was undertaken in 2016, in the context of the new antibiotic-related strategies and policies instituted since 2009. Therefore, section 1.4.2 and section 1.4.3 provide more detail about the three-year strategy, the new regulations and related policies.

1.4.2 2011 antibiotic-related reforms

Considering the global public health threat of AMR, the WHO selected '*Antimicrobial Resistance: No action today, no cure tomorrow*' as the World Health Day theme for 2011 (WHO, 2011B). Influenced by the WHO, the MoH in China began a three-year strategy named '*National Special Campaign for the Clinical Use of Antibiotics*' from 2011 to 2013. It was centred on the regulation of '*Administrative Regulations for the Clinical Use of Antibiotics*', with a special focus on the rational use of antibiotics in secondary and tertiary public hospitals (Xiao & Li, 2013; Xiao & Li, 2015). The '*Proposal of National Special Campaign for the Clinical Use of Antibiotics*', an important component of this strategy, was issued as part of its implementation from 2011, and was updated in 2012 and 2013 (MoH, 2011, 2012, 2013). These documents indicate that this strategy is related to all types and levels of healthcare institutions as well as the MoH and local authorities, with a special focus on the secondary and tertiary hospitals; the documents also set several targets during this three-year strategy period, such as:

- With respect to antibiotic procurement, the maximum number of types¹⁴ of antibiotics being stocked should be no more than 50 in the tertiary public general hospital and 35 in the secondary public general hospital; however, there were no limitations set for CHIs and retail pharmacies.
- The MoH set limitations on the proportion of patients prescribed antibiotics for hospitals.

¹⁴ There are hundreds of types of antibiotics, which can be grouped into broader classes (NHS, 2016). For instance, the '*National Essential Drug List (2012 edition)*' in China listed 43 types of essential antimicrobials, and then classified them into 14 classes (discussed below in section 1.4.3).

In general hospitals, the antibiotic use frequency (Box 3) for inpatients should be no more than 60%, and the proportion of prescriptions containing antibiotics should be no more than 20% for outpatients and 40% for emergency patients, respectively. The antibiotic use intensity (Box 4) in the hospitals should be no more than 40DDDs per 100 patient days.

- Required regulars check and evaluation of antibiotic prescriptions and medical records; a range of administrative penalties were introduced for physicians who violated the standards, such as having their level of antibiotic prescription rights lowered.
- Other targets, such as clinical training, building the list of restricted level of antibiotics, accrediting physicians' antibiotic prescribing rights in grades¹⁵, ABR and utilization surveillance, among others, were set (Xiao & Li, 2015; MoH, 2013).

On 13th February 2012, the regulations became tighter. '*Administrative Regulations for the Clinical Use of Antibiotics*' were issued by the MoH; this came into force on 1st August 2012. This regulation only focused on antibiotics, and then clearly set out the roles, responsibilities and liabilities of different stakeholders, including health administrative authorities, medical institutions and healthcare professionals, in order to promote and enforce the rational use of antibiotics (Xiao & Li, 2013; Xiao & Li, 2015; MoH, 2012A). For instance, regulations were designed to encourage physician adherence to guidelines that required examination of patients' clinical presentation and laboratory test results. It was stipulated that physicians

¹⁵ It was stipulated in Action 24 of '*Administrative Regulations for the Clinical Use of Antibiotics*' that, physicians with different special titles could be awarded different antibiotic prescribing rights. Specifically, deputy chief physicians and chief physicians can be awarded the rights to prescribe special restricted antibiotics, while physicians-in-charge can be awarded the right to prescribe restricted antibiotics. Physicians with the lowest special title can only be awarded the rights to prescribe non-restricted antibiotics. All these rights will be awarded after physicians pass the specific training and evaluation (MoH, 2012A).

who violated the regulations would be punished in a range of ways, from a financial penalty to legal liability, depending on the severity of the violation (Xiao & Li, 2015; MoH, 2012A).

The three-year strategy and regulation highlighted the role of the '*Principles for Clinical Use of Antimicrobials*', which led to its update in 2015. The new edition – '*Principles for Clinical Use of Antimicrobials (2015 edition)*' – includes four main parts. These are the general principles of appropriate use of antimicrobials, the management of clinical antimicrobials, the pharmacological characteristics of antimicrobials and recommendations for their treatment of infections and clinical experience-based principles of the antimicrobial selection for common infections. For instance, this guideline indicates that making a diagnosis of a bacterial infection and prescribing antibiotics should be based on relevant indications, such as laboratory test results and that, during antibiotic treatment, oral antibiotics should be given in priority over other modes of treatment, for example, intravenous antibiotics (NHFPC, 2015).

1.4.3 China's 2009 healthcare reforms and other pharmaceutical policies in China

The financial reforms in China have led to a rapid rise of healthcare cost for people, particularly for rural residents, since the 1980s, as a result of the decreased coverage and the low inpatient reimbursement rate of medical insurance schemes (Hsiao, 2007; Meng *et al.*, 2012). The proportion of out-of-pocket expenditures¹⁶ in THE was thus continuously increased from 21.2% in 1980 to 60.0% in 2001 (CNHDRC, 2017). Concerned about these

16. They are the health expenditures paid by patients directly where health insurance does not cover the full cost of health services (OECD, 2011).

problems, in 2009, the State Council launched a three-year national plan, the '*Implementation Plan of the Main Areas of Healthcare System Reform in the Near Future (2009-2011)*', to deepen the healthcare system reform in China. With the first phase goal of achieving comprehensive universal health coverage by 2020, it set up five areas, which were also called the five pillars (Meng *et al.*, 2012). The five pillars include primary care service delivery, essential medicines, public health, insurance and public hospital reforms, that would be the focus in this new round of China's healthcare system reform (State Council, 2009). With the plan, the insurance coverage has expanded and healthcare-related financial burden on people has largely decreased (Fu *et al.*, 2018). For example, the proportion of out-of-pocket expenditures in THE declined from 60.0% to 28.8% in between 2001 and 2016 (CNHDRC, 2017).

One of these five pillars was building the national essential drugs system (State Council, 2009). At its core is the EDL, which is designed to provide basic healthcare services to all residents and promote the rational use of drugs (Xiao *et al.*, 2016). Together with the EDL, the ZMU policy was introduced as part of the national essential drug system to sell drugs at cost, with aims to prohibit healthcare institutions from charging the 15% mark-up on selling drugs¹⁷ (Mossialos *et al.*, 2016; MoH *et al.*, 2009A; State Council, 2009A). The essential drug system, including EDL and ZMU policies, was initially applied at 30% of the government-owned primary care institutions in every province (autonomous region/municipality) in 2009 (Mossialos *et al.*, 2016; MoH *et al.*, 2009, 2009A). The latest version of the EDL is the '*National*

¹⁷ The policy of 15% mark-up on price is discussed in next paragraph.

*Essential Drug List (2012 edition)*¹⁸, which was implemented in 2013; for antimicrobials, there were in total 14 classes¹⁸ of 43 types of antimicrobials included. They all belong to first-line antimicrobials, meaning they can be used without restriction (MoH, 2013A). In order to better enforce the essential drug system, the government then issued relevant documents that required government-owned primary care institutions to all stock and dispense national essential drugs, and further required that other healthcare institutions should procure and use national essential drugs as a priority. A target was set: the proportions of the volume of national essential drugs sold should reach 40%-50% and 25%-30% of total volume of drugs sold in secondary and tertiary hospitals, respectively (NHFPC, 2013). The importance of implementing the essential drug system within the different levels of medical institutions was consistently highlighted by government documents issued in the years that followed (State Council, 2014; NHFPC, 2015; State Council, 2016).

The 15% mark-up policy was introduced in 2006 in China, which allowed county and higher-level healthcare institutions to charge a mark-up of a maximum of 15% on the sales of drugs to compensate for decreases in government funding. However, the 15% mark-up policy also had negative consequences, including overprescription and prescription of expensive drugs by physicians (Mossialos *et al.*, 2016; NDRC *et al.*, 2006). Therefore, in 2009 when China's healthcare system reform, the EDL and ZMU policies, was introduced to gradually remove the incentive of 15% mark-up (Mossialos *et al.*, 2016; State Council, 2009). Another key area of

¹⁸ The 14 classes of antimicrobials are penicillin, cephalosporin, aminoglycoside, tetracycline, macrocyclic lactone, other antibiotics (including clindamycin and fosfomycin), sulfonamide, quinolone, nitro imidazole, nitro furan, anti-tuberculosis, anti-leprosy, anti-fungal and anti-viral drugs, respectively.

the healthcare reform's five pillars – public hospital reform – also required the gradual removal of the 15% mark-up from public hospitals (State Council, 2009). Since then, the ZMU policies began to be implemented in different healthcare institutions. It was found that this policy has almost universally been implemented in government-owned primary care institutions combined with the EDL (Mossialos *et al.*, 2016; Xi *et al.*, 2015). With respect to the public hospitals, by the end of 2014, there were 66% of counties that had removed the 15% mark-up in their county hospitals and an increasing number of urban hospitals began to remove the mark-up (State Council, 2015). The national government also called for the ZMU policies to be implemented in all county hospitals and urban hospitals by 2015 and September of 2017, respectively (Mossialos *et al.*, 2016; State Council, 2015; State Council, 2017).

Additionally, the national government has been concerned about drug distribution, including antibiotics, in retail pharmacies. From 2004, it was required that antibiotics must be dispensed with prescriptions in retail pharmacies (CFDA, 2004). In 2012, a new policy was introduced, the '*National Drug Safety 'twelve-five' Programme*', which required that newly-operating retail pharmacies must be owned or managed by licensed pharmacies; moreover, licensed pharmacists must be presented in the retail pharmacy during its opening hours (State Council, 2012).

1.5 Conclusions

From the above review, it is clear that human ABR is a serious global public health problem, and LMICs, particularly China, are seriously affected by it. As antibiotics are widely and

inappropriately used in the provision of medical services, drug dispensing via pharmacies and among the public, particularly for children, the healthcare providers (including paediatricians, GPs and pharmacists) and parents are key constituencies related to antibiotic use and resistance in China. Therefore, it is important to understand more about the factors influencing their behaviour with respect to use of antibiotics among children, and the next chapter will focus on the relevant literature that sheds light on healthcare providers' and parents' antibiotic-related behaviour related to children.

Chapter 2. A review of factors contributing to the use of antibiotics for children in China

2.1 Introduction

As noted in the previous chapter, the use of antibiotics is the single most important factor contributing to human ABR (Byarugaba, 2004; Huttner *et al.*, 2010; Simonsen *et al.*, 2004), and China, which shows both extremely high total antibiotic consumption and widespread inappropriate use of antibiotics, is a major contributor to global antibiotic use (WHO & MoH, 2013; Zhang *et al.*, 2015). As discussed in section 1.3.3, the rates of antibiotic use and inappropriate use for children by healthcare providers in hospitals, primary care settings and pharmacies, and by parents, are particularly high compared with those of adults in China. However, compared with studies on HICs, much less is known about healthcare providers' and parents' views and experiences of antibiotic use for children in China. Therefore, building on Chapter 1, this chapter provides a review of research studies relevant to understanding factors contributing to the use of antibiotics by healthcare providers and parents for the treatment of conditions in children (hereafter 'the use of antibiotics for children' will be used in the thesis) in China. It reviews studies of the general public alongside studies where the focus is on children.

There are five sections:

- 2.1 provides an introduction;
- 2.2 describes how the research review was conducted;
- 2.3 and 2.4 review evidence on influences on healthcare providers' antibiotic-related behaviour on the public's and parents' antibiotic-related behaviour. In each section,

the evidence is summarised under the spheres of influence highlighted in the framework (e.g. individual level influences, interpersonal influences etc.);

- 2.5 concludes the review and considers limitations and gaps in the evidence.

2.2 Undertaking the review of research literature of factors contributing to the use of antibiotics for children in China

A broad range of research is of potential relevance to this thesis, including studies conducted beyond China. Therefore, a systematic approach was applied. Specifically, there were two stages to the review: (i) identifying and developing a framework through which to understand the influences on the use of antibiotics for children in China, and, using this framework; and (ii) undertaking a review of research relevant to factors influencing the use of antibiotics for children in China. The review included searching for relevant papers in both English and Chinese language journals using two electronic databases.

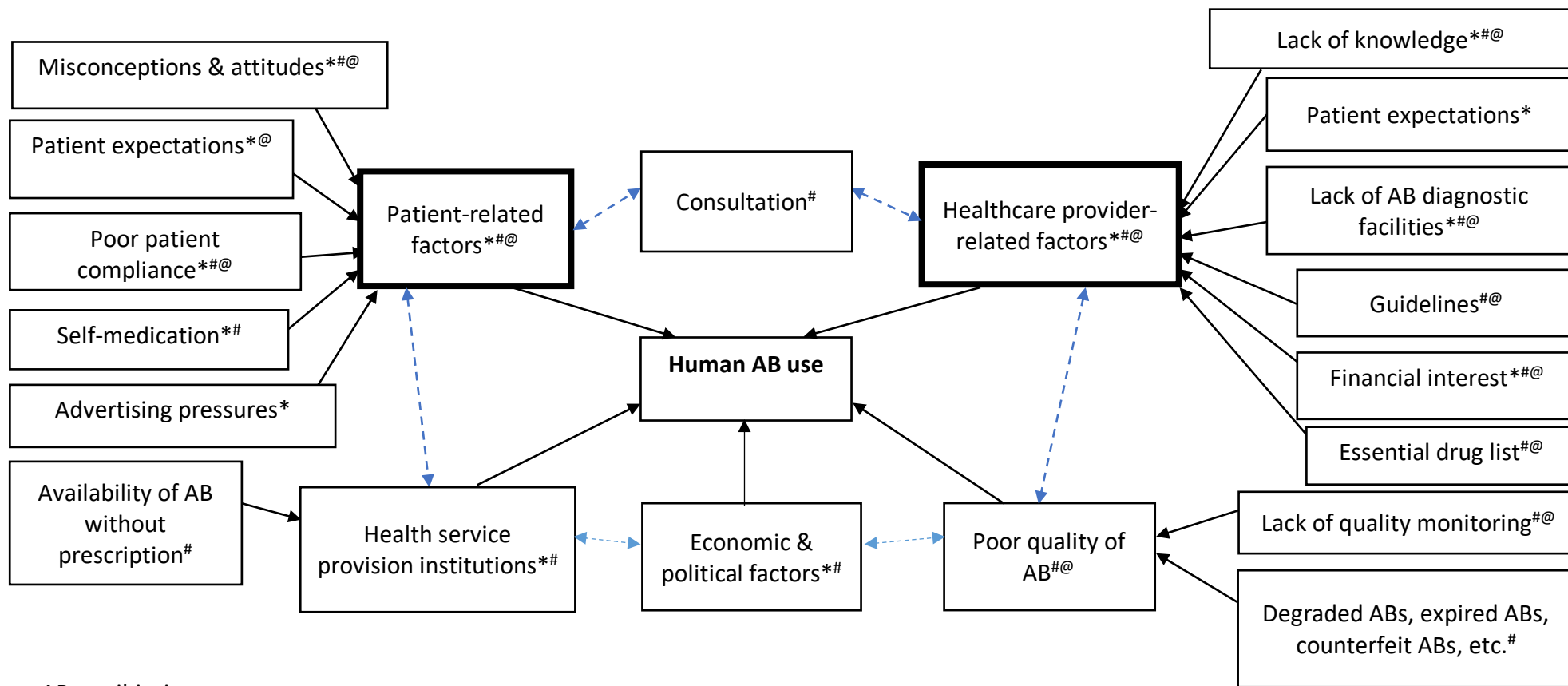
2.2.1 Identifying a framework to capture the influences on the use of antibiotics for children in China

The relevant background reading made clear that there were a wide range of inter-connected factors influencing antibiotic use, and frameworks that represented these influences were very helpful in understanding the context and patterns of use. Therefore, it was decided to use a framework to guide the review. As there was no framework that fitted this research area, a framework was developed using published frameworks and papers concerned more broadly with AMR and ABR. Three widely-cited papers were selected, each providing an

overview of factors from different angles and each with an accompanying framework. They proved to be very helpful in building this research framework and guiding the research review.

Among these papers, the first paper (Byarugaba, 2004) looks at risk factors related to ABR in general, while the second (Okeke *et al.*, 1999) focuses particularly on socioeconomic and behavioural factors contributing to ABR, and the third (Simonsen *et al.*, 2004) discusses ABR risk factors from an ABR containment and surveillance perspective. The first two papers focus on developing countries (which are also referred to as LMICs), countries in the same economic grouping as China, while the third provides a more generic perspective on risk factors for ABR relevant to different geographical and socioeconomic settings (Byarugaba, 2004; Okeke *et al.*, 1999; Simonsen *et al.*, 2004). For reference, the three frameworks derived from the three papers, respectively, are included in Appendix C. By analysing and comparing the factors identified in the three frameworks, it was possible to gain a comprehensive overview of factors contributing to human antibiotic use and then build a framework more relevant to this thesis' focus. Figure 3 presents the framework derived from these frameworks. It includes two key drivers of human antibiotic use (patient-related factors and healthcare provider-related factors, highlighted in bold); as the Figure's key indicates, these were identified in all three frameworks.

Figure 3 Factors contributing to human antibiotic use in low and middle-income countries: A framework developed from three reviews



AB: antibiotic;

*: factors identified from Byarugaba, 2004;

#: factors identified from Okeke *et al.*, 1999;

@: factors identified from Simonsen *et al.*, 2004.

Bold boxes show the key influences that are noted by all three papers



In this framework, a wide range of influences related to human antibiotic use identified by the three papers are grouped into five inter-connected drivers (healthcare provider-related factors, patient-related factors, poor quality of antibiotics, economic and political factors, and health service provision institutions), along with a range of factors that the papers noted as underlying these drivers. Two of these drivers of human antibiotic use (patient-related factors and healthcare provider-related factors) are highlighted in bold. As the Figure's key indicates, **patients** and **healthcare providers** were identified as particularly important influences on human antibiotic use in all three papers. The other three drivers were only mentioned by two papers. Consultation between patients and healthcare providers was noted as a key process mediating the interactions between healthcare provider- and patient-related factors contributing to antibiotic use. In addition, the framework represents the drivers' directions of influence. While all contribute to human antibiotic use, the five drivers can also interact with each other; the set of underlying factors under each driver are identified as influences related to a particular driver.

Some limitations of the framework presented in Figure 3 should be noted. Firstly, some factors could be situated under multiple drivers located at different levels, but these multi-level relationships are not fully represented by this framework. For instance, it was highlighted by papers that government guidelines on human antibiotic use were an influence on healthcare providers' behaviour, and this is where government guidelines is located in Figure 3; however, the guidelines could also be treated as a political factor and located at this more macro level. Secondly, and more importantly, even this simplified framework is too complex to be operationalised within a single doctoral study.

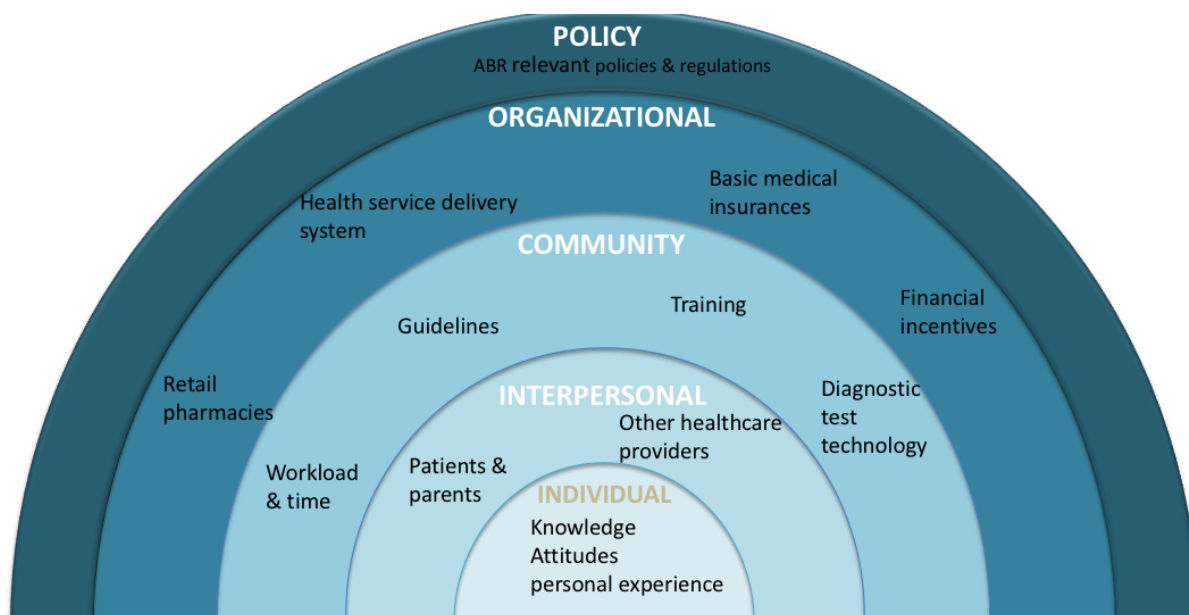
The framework was therefore further refined and simplified. This was done by drawing on the social ecological framework (SEF), which provided an alternative way of representing the influences on human antibiotic use and was found to be particularly helpful. The SEF is a framework that takes into account dynamic and reciprocal interrelationships between individuals and their environments. Therefore, in the SEF, a variety of influencing factors on the outcome of interest (the use of antibiotics) are situated within a causative 'web' which is separated into multiple levels, with the individual level located in the centre and surrounded by a set of concentric circles (or layers) ranging from micro- to macro-level (Schneider & Stokols, 2009). The most well known framework within public health is based around a SEF. This is the Dahlgren and Whitehead's (1991) 'rainbow' model of the main determinants of health, which identifies influences on health as a series of arcs running from the individual level up to the societal level. The SEF is widely used within the public health and healthcare sector, for example by the USA's Centers for Disease Control and Prevention for health promotion (CDC, 2015; Schneider & Stokols, 2009).

Figure 3 was simplified and restructured using Dahlgren & Whitehead's 'rainbow' model, with SEFs developed for this study to represent the complex factors contributing to the use of antibiotics for children in China (Figure 4 presents the SEF for healthcare providers and Figure 5 presents the SEF for parents). This framework was informed by the review of literature of factors influencing the use of antibiotics; it was then revised in light of the findings of the study of this thesis. As the importance of healthcare provider- and patient- (including parent) related factors was highlighted by Figure 3 and the healthcare providers and parents were

identified as key constituencies related to antibiotic use in the review in section 1.3.3, they were regarded as the individual in their own SEF, and therefore located in the centre of the SEF and surrounded by a set of concentric layers influencing their behaviours from micro- to macro-levels (Table 3).

The frameworks were then used to inform the structure of literature review and the design of the data collection instruments (the interviews conducted with healthcare providers and the focus groups and survey questionnaire with parents). As is described below in Chapters 4, 5, and 6, the topic schedules for the interviews either included questions that asked directly about the factors (e.g. for healthcare providers ‘Do you ever find that some parents make clear they wish you to prescribe antibiotics for their child?’ and for parents ‘Do you treat your child with antibiotics by yourself when he/she is ill or symptomatic?’) or enabled these factors to be discussed through indirect questions (e.g. for health care providers ‘What factors do you think usually influence a physician/GP/pharmacist’s antibiotic prescribing behaviour?’).

Figure 4 A social ecological framework representing some of the key factors contributing to healthcare providers' behaviour with respect to the use of antibiotics for children in China



Adapted from: The review of research, findings from this study and Figure 3

Figure 5 A social ecological framework representing some of the key factors contributing to parents' behaviour with respect to the use of antibiotics for children in China



Adapted from: The review of research, findings from this study and Figure 3

Table 3 Factors influencing healthcare providers' and parents' behaviour with respect to the use of antibiotics for children in China

	Healthcare providers	Parents
Individual level	Individual knowledge and attitudes (TCM and Western medicine) toward diseases and antibiotic use, and personal experience	Individual knowledge and attitudes (TCM and Western medicine) toward diseases and antibiotic use, personal experience, age, gender, and socio-economic circumstances
Interpersonal level	Patients and parents, and other healthcare providers	Healthcare providers, particularly physicians and pharmacists, as well as their family members and friends
Community level	Workload and time, guidelines, training, and limited diagnostic test technology	Mass media related factors
Organisational level	Financial incentives, basic medical insurance schemes, retail pharmacies, and health service delivery systems	Pressures from employers and schools, health service delivery system, basic medical insurance schemes, and retail pharmacies
Policy level	Policies and regulations relevant to the use of antibiotics	Policies and regulations relevant to the use of antibiotics

2.2.2 Approach used for reviews of research related to factors influencing the use of antibiotics for children in China

As noted in section 1.1, the broader literature review work started from the first year of the PhD programme (2015/2016), when an initial set of studies related to the use of antibiotics and ABR was identified. Reference checking and citation searching were then undertaken on this set of studies, which revealed that most of the published research on the use of antibiotics and resistance was based on HICs and there were particularly few studies focusing on influences on the use of antibiotics in China. Therefore, more systematic searches for

evidence on influences on antibiotics use in China were undertaken in the second year of the PhD programme (2016/2017). It was then updated in June and July 2017 by reference checking and citation searching from the most relevant studies.

2.2.2.1 Search methods and criteria for identification of papers

The systematic searches included both English and Chinese language research. Chinese language journals were searched because of the study setting (China). There are a large number of Chinese language journals published in China, but the large majority are not indexed in major English language databases; for example, only 82 out of more than 5,000 Mainland Chinese journals were indexed for MEDLINE in 2007 (Fung, 2008). However, the un-indexed papers are particularly likely to contain China-based studies and data related to antibiotic use and ABR, and therefore be a key resource for this doctoral study. Moreover, there is an increasing awareness of a potential language bias in the public health evidence base as major databases largely exclude languages other than English (Fung, 2008; Fung, 2008A). As an example, language bias was found to lead to an underestimation of the protective effect of interventions in random control trials of complementary and alternative medicine (Klassen *et al.*, 2005). However, while there is increasing recognition of the potential contribution of Chinese language studies, concerns have been expressed about study quality (Fung, 2008).

It was decided that, to increase the comprehensiveness and relevance of the review and to avoid potential language bias, both English and Chinese language research would be

systematically searched (Fung, 2008A). Quality appraisal of studies from Chinese language journals included in the review was undertaken. A range of quality appraisal tools was considered (CASP, 2017; Chung *et al.*, 2014; NIH, 2014; Wells *et al.*) and a widely-used tool was identified as suitable (Hawker *et al.*, 2002). It has been developed for appraising the quality of qualitative studies but provides a set of criteria that can also be applied to quantitative studies. It was therefore used for both study designs (qualitative and quantitative). Studies in the review located through MEDLINE were not subjected to quality appraisal as this is built into the selection process for journals in MEDLINE (NIH, 2017).

For the systematic searches (English and Chinese language), two key electronic databases were used: MEDLINE Ovid and Chinese portal of Chinese National Knowledge Infrastructure (CNKI), respectively. MEDLINE Ovid is a major and widely used bibliographic database that is used 'to indicate journals of importance' (Fung, 2008, pp.11). It is updated daily and contains journal citations and abstracts in English covering the international literature on biomedical and life sciences, including healthcare, pharmacy, and the humanities. There were around 5,500 journals published in approximately 40 languages indexed in MEDLINE Ovid (UoY). It is also widely used in systematic reviews on health-related research focusing on China (Chung *et al.*, 2014; Southern *et al.*, 2016).

There are six Mainland Chinese bibliographic databases¹⁹; among them, CNKI, Wan Fang database and VIP are reported to be the most widely used (Fung, 2008; Li, 2011). As noted in

¹⁹ The six mainland Chinese bibliographic databases are Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese National Knowledge Infrastructure (CNKI), VIP information (VIP), Wan Fang database, and iLib (Fung, 2008).

section 1.1, Wan Fan database was used to search for Chinese language research in the broader review. However, when compared with Wan Fang database, CNKI is more comprehensive and better suited to advanced searches (cnki.net; Li, 2011; WANFANG DATA; VIP). For instance, with respect to the journal coverage, CNKI provides more extensive coverage of journals in the Social Sciences and Humanities than Wan Fang database. CNKI also has a faster updating speed than Wan Fang Database and VIP (Li, 2011). Therefore, CNKI was chosen as the database for Chinese language research in this more systematic search and review. Specifically, CNKI (having both a Chinese portal and English portal) is one of the main Mainland Chinese databases that provides not only journal articles, but also degree theses, conference proceedings and newspapers, among others. There were 1,336 and 3,135 Chinese journals in the category of 'Medical, pharmaceutical and hygiene/health sciences' and 'Social sciences I & II', respectively, according to the Chinese portal of CNKI (accessed in August 2017). The Chinese language abstract and links to the authors, journal issue and journal citation are contained in the Chinese portal of CNKI (cnki.net).

There were no restrictions on study design. Therefore, all observational studies, such as cohort studies and cross-sectional studies, and experimental studies (e.g. randomised controlled trials) were included. Quantitative, qualitative and mixed/multi-methods research designs were all included. As the factors influencing on healthcare providers and the public's, including parents', behaviour with respect to the use of antibiotics in China were the outcome of interest, papers which reported any relevant influences were included in this review. Papers whose main outcome did not, or unclearly, related to factors on healthcare providers or the public's antibiotic related behaviour in China were excluded.

2.2.2.2 Data collection

In line with Figures 3 to 5, two systematic searches were undertaken of each database, one searching for records of ‘factors influencing healthcare providers’ behaviour with respect to the use of antibiotics in China’, and the other searching for records of ‘factors influencing the public’s and parents’ behaviour with respect to the use of antibiotics in China’. The keywords used in the searches of MEDLINE Ovid and the Chinese portal of CNKI were as similar as possible. However, compared to MEDLINE Ovid, the Chinese portal of CNKI allowed fewer advanced search strings and searching. For instance, in the advanced search of the Chinese portal of CNKI, although Boolean operators could be used they are restricted to a combination of two words or synonyms, and there are many limitations in combining sets of search terms together to produce more complex search strings. The search strings on the Chinese portal of CNKI and MEDLINE Ovid were slightly adjusted in order to find a manageable number of studies and ensure the studies were as relevant as possible to the topic. The search strategies are provided in Appendix D and the results of the searches are shown below in Table 4.

Table 4 Information on records located and included via searches undertaken on two databases

	Search One			Search Two	
Databases	MEDLINE Ovid	Chinese portal of CNKI*		MEDLINE Ovid	Chinese portal of CNKI
Searching content	Factors influencing the use of AB by healthcare	Factors influencing the use of AB by doctors and in	Factors influencing the use of AB by hospital &	Factors influencing the use of AB by the public	Factors influencing the use of AB by the

	providers in China	retail pharmacies in China	CHI-based pharmacists in China	and parents in China	public and parents in China
No. of records located	217	47	749	222	44
No. of records included	65	8		55	21

* The search one of CNKI for 'factors influencing the use of antibiotics by healthcare providers in China' was separated into two searches to ensure the search terms and search strings on CNKI and MEDLINE Ovid were as similar as possible. It was because: (i) there was no accurately equivalent term of 'healthcare provider' in Chinese; (ii) there were too many records related to clinical pharmacists while only a few on other kinds of providers, such as doctors, based on the result of search one on CNKI.

Among records located via MEDLINE Ovid, via search one 65 out of 217 records related to healthcare providers and via search two 55 out of 222 records related to parents and the public were selected for review. For search one of CNKI for 'factors influencing the use of antibiotics by healthcare providers in China', there were in total 796 (749+47) records identified. Of this set, most (749) were about hospital and CHIs-based pharmacists and only 47 records were about doctors and retail pharmacies. Of the 749 records, the large majority were focused on influences on clinical pharmacists' use of antibiotics in hospitals. Therefore, only the most widely cited papers were reviewed. Finally, among records located through the Chinese CNKI portal, 29 records were selected for review, including 8 out of 796 records identified via search one related to healthcare providers and 21 out of 44 records identified via search two related to parents and the public. In conclusion, there were in total 149 records

included in this review, including 120 (65+55) English language records and 29 (8+21) Chinese language records.

2.2.2.3 Comparison between English and Chinese language records and quality appraisal

Comparing records located via MEDLINE Ovid and the Chinese portal of CNKI, there were a few papers published in Chinese among the records located via MEDLINE Ovid, and most of these papers were also located via the same search on the Chinese portal of CNKI. Most studies found via the Chinese portal of CNKI were published in Chinese and only two were published in English; however, these two English language papers were not located via the same search on MEDLINE Ovid. When compared with records found in MEDLINE Ovid, most records identified from the Chinese portal of CNKI were based on a few or a single institution in a particular city/county, such as an individual hospital in one city. In contrast, records identified from MEDLINE Ovid tended to focus on a wide range of regions across China. In addition, as noted above, there was a particularly high proportion of records found via the Chinese portal of CNKI focusing on influences on antibiotic use in hospitals, while the proportion of records concerned with different kinds of healthcare providers was relatively balanced among records in MEDLINE Ovid.

Chinese language papers can be divided into two types: those with and those without an English title, abstract and keywords. The first (with an English title, abstract and keywords) were usually published in what are referred to as 'core journals'. These are journals indexed in at least one of China's three core journal databases (Comprehensive List of Titles of Chinese

Core Journals; Chinese Science Citation Database; Chinese Science and Technology Paper Citation Database), and indexing in these databases is used to identify top journals in a particular field. The second type (without an English title, abstract or keywords) were usually not published in a core journal. Among the Chinese language papers located via two searches in this review, most papers with an English title, abstract and keywords were published in the national level journals and/or China's core journals, and tended to provide more information (such as more detailed methodology and results) compared with papers without an English title, abstract and keywords.

Quality appraisal was undertaken of 29 Chinese language papers (with and without an English title, abstract and keywords) that were included in this review (Appendix E). The large majority had a low quality score, with those with an English title, abstract and keywords having a higher score; for example, a discussion of ethics and information on ethical approval were absent in almost of all Chinese language papers (only one paper with an English title, abstract and keywords briefly mentioned ethics). However, none of these 29 Chinese language papers were excluded, as they provide local-level evidence from a particular province or city/county that is not available from MEDLINE Ovid. These local-level studies can cover populations of considerable size and, at this sub-national level, can be more accurate than national-level data (Fung, 2008). Moreover, there are other examples of reviews that cover papers published on the Chinese journals even though they have the low quality (Fung & Cairncross, 2006; Chung *et al.*, 2014). In consequence, records found from both MEDLINE Ovid (120 papers) and CNKI (29 papers) were used in the literature review, but most evidence

were drawn on papers located through MEDLINE Ovid for reasons of their higher quality and the more detailed information they provided.

The results of the literature review are discussed in section 2.3 and section 2.4, focusing on factors influencing healthcare providers' behaviour (2.3.2) and the public's and parents' (2.4.2 and 2.4.3) behaviour with respect to the use of antibiotics in China.

2.3 Influences on healthcare providers' use of antibiotics

2.3.1 Factors related to antibiotic prescribing by healthcare providers in high-income countries

Studies in HICs point to multiple influences on healthcare providers (hereafter 'providers') behaviour with respect to the use of antibiotics, with these influences operating across a range of levels in the SEF, including individual factors (e.g. the lack of professional antibiotic knowledge), interpersonal factors (e.g. patients' expectations and demands), organisational factors (e.g. financial incentives offered by different organizations) and policy-level factors (e.g. the basic medical insurance schemes) (Petursson, 2005; Tonkin-Crine *et al.*, 2011). Qualitative studies conducted in either single or multiple HICs indicate that lack of knowledge is an influential factor in inappropriate antibiotic use, along with particular characteristics, such as physicians' professional ethos (Brookes-Howell *et al.*, 2012; Ebert, 2007; Petursson, 2005). Pressure from patients has been identified as a key factor contributing to providers' antibiotic prescribing decisions. A systematic review examining qualitative research on GPs' attitudes and experience of antibiotic prescribing found that, in HICs, GPs' perceptions of

patient-centred care were related to their antibiotic prescribing decisions, with decision making influenced by their perceptions of patients/parents' concerns about their disease (Tonkin-Crine *et al.*, 2011). In addition, workplace pressures, such as a high workload and limited time, pressure from complying with guidelines and other organizational factors (e.g. open access to physicians) were all identified as factors influencing providers' antibiotic prescribing decisions in HICs (Tonkin-Crine *et al.*, 2011; Petursson, 2005).

For factors influencing providers' use of antibiotics for children, further insight is provided by a more recent systematic review of qualitative studies in HICs of prescribing decisions in primary care for acute childhood infections. It indicated that the child's symptoms, perceived pressure from parents, along with broader influences related to financial incentives, workplace pressures, as well as parents' workplace and daycare providers were factors underlying clinicians' decisions to prescribe antibiotics (Lucas *et al.*, 2015). A further cross-sectional qualitative study in the UK also noted that parental influences and the limited time allowed for each consultation affected doctors' antibiotic prescribing behaviour (Horwood *et al.*, 2016).

2.3.2 Factors related to the antibiotic prescribing behaviour of providers in China

In contrast to the extensive evidence for HICs, there are very few studies focusing on factors influencing providers' antibiotic prescribing decisions on patients, including ill children, in China, despite the fact that providers are one of the most important constituencies related to antibiotic use (Chan *et al.*, 2012; Gould, 2008). As noted in section 1.3.3, studies focusing on hospitals, primary care institutions and pharmacies in China have all suggested that the

wide and inappropriate use of antibiotics is very common among providers, particularly for antibiotics used for children. This, in turn, contributes to the consistently high antibiotic overprescribing rate and thus to the very high level of total antibiotic consumption in China (Heddini *et al.*, 2009; Li *et al.*, 2012; Reynolds & McKee, 2008; Sun *et al.*, 2015; WHO, 2006). Below, factors related to antibiotics prescribed by providers in China are described, based on relevant papers published in English and Chinese found through the systematic search undertaken for this thesis.

2.3.2.1 Individual factors related to the use of antibiotics

Similar to studies in HICs, a systematic review on observational studies of irrational use of medicines in China and Vietnam points to the lack of knowledge among providers as contributing to the inappropriate use of antibiotics in China (Mao *et al.*, 2015). The findings from studies undertaken in different individual provinces in Mainland China all demonstrate that doctors' medical knowledge level was related to their use of antibiotics; doctors who had a higher level were more likely to prescribe antibiotics appropriately (Jiang *et al.*, 2012; Rahmanjan *et al.*, 2013; Wang *et al.*, 2013). However, most studies, either focusing on hospitals or primary care institutions, or one particular specialty in the hospital, indicated that the antibiotic-related knowledge among doctors was inadequate (Ding *et al.*, 2014; Du *et al.*, 2009; Su *et al.*, 2012; Wang *et al.*, 2013; Wu, 2009; Zhang, 2015). In a cross-sectional self-administered questionnaire survey of physicians from a range of healthcare institutions (including tertiary hospitals, secondary hospitals and CHIs) in Taiyuan city of Shanxi Province (the location for this thesis' study), overall antibiotic-related knowledge among doctors was

much lower than expected. Knowledge was related to a number of individual factors, and was higher among doctors who worked at tertiary hospitals, who worked in the internal medicine department, who had the professional title of chief physician and who attended antibiotic-related training (Bai *et al.*, 2016). Another questionnaire-based study similarly reported that, among 70 paediatricians from four hospitals in Tai'an city of Shandong province, antibiotic-related knowledge was poor, with evidence that the proportion of participants who passed (threshold for passing is 60/100 points) the antibiotic-related knowledge test was as low as 50% (Xie & Zhang, 2014).

Other individual factors have also been identified as influencing doctors' antibiotic use (Lam *et al.*, 2003; Lin *et al.*, 2010; Wang *et al.*, 2013). For instance, a retrospective cross-sectional study undertaken in 10 county hospitals in Anhui Province found that doctors who were older or more senior tended to prescribe more antibiotics; the explanation given is that the Chinese occupational grading system allowed doctors with higher professional titles to prescribe more types and higher levels of antibiotics (discussed in section 1.4.2, pp. 74) (Wang *et al.*, 2013). In addition to age, the final academic degree and specialty were identified as factors contributing to the differences in doctors' antibiotic usage in this study (Wang *et al.*, 2013). The influence of age and specialty was also reported by a secondary data analysis of the Taiwan National Health Insurance Research Database between 2005 and 2006, with differences in doctors' prescribing practices with respect to broad-spectrum antibiotics on ambulatory care visits for female urinary tract infections related to their age and specialty (Lin *et al.*, 2010). In particular, doctors whose specialty was obstetrics and gynaecology were

found to be more likely to prescribe antibiotics than other specialties in both the studies focusing on Taiwan and Anhui Province of China (Lin *et al.*, 2010; Wang *et al.*, 2013).

A study focusing on 188 doctors in rural areas of Shandong Province pointed to a gap between physicians' reported antibiotic-related knowledge and behaviour and their actual practice in prescribing antibiotics. It compared what the doctors said they would do with respect to cold symptoms with their actual prescribing practice, as reflected in the prescriptions issued via the organisations in which the doctors worked. The study found that, although 87% of the doctors in the study said that they would refuse to prescribe antibiotics to patients with a common cold, even when patients insisted on them, more than half of prescriptions for common cold in their working institutions included antibiotics (Sun *et al.*, 2015).

2.3.2.2 Interpersonal factors related to the use of antibiotics

A postal questionnaire survey of 801 family doctors identified that maintaining patients' and their carers' satisfaction with the medical care they received, and thus avoiding medico-legal problems, were important factors that contributed to family doctors over-prescribing antibiotics for upper respiratory tract infections (Lam *et al.*, 2003). Another postal study in Hong Kong explored the use of antibiotics by 46 primary care doctors; it also found that patients or their carers who demanded antibiotics or who attended follow-up consultations were significantly more likely to be prescribed antibiotics (Lam *et al.*, 2009). In addition, it was reported that children with parents who were healthcare professionals, such as physicians, pharmacists or nurses, were less likely to receive antibiotics than other children, suggesting

parents' medical knowledge has an influence on physicians' antibiotic prescribing behaviour in Taiwan (Hunag *et al.*, 2005).

However, the systematic search of English and Chinese databases located very few studies conducted in Mainland China that focus on patient or parental influence on providers' behaviour. Only four studies conducted in Mainland China were located. Reynolds & McKee's (2009) qualitative study focused on Guizhou Province found that doctors could prescribe unnecessary antibiotics for patients with the common cold in response to patient pressure. Additionally, an experimental audit study carried out in two cities and one rural county in China reported that displaying knowledge related to the appropriate use of antibiotics by patients significantly reduced antibiotic prescription rates (Currie *et al.*, 2011). This finding was confirmed by a similar audit study of hospitals in a large unnamed Chinese city, which reported that doctors' antibiotic prescribing behaviour was related both to patient demand for antibiotics, even for conditions where antibiotics were unlikely to be effective, and to doctors' perceptions that patients want antibiotics (Currie *et al.*, 2014). With respect to factors influencing providers' use of antibiotics for children, only one qualitative study, conducted with 35 village doctors, 12 primary caregivers and 17 healthcare system-related directors, was identified. In that study, the pressure for antibiotic treatment from primary caregivers and the financial pressure to retain patients (rather than lose them to another source for antibiotic treatment) were found to be the main factors contributing to doctors' antibiotic prescribing decisions (Zhang *et al.*, 2016).

Alongside patients and parents, studies also suggested that pharmacists were an important influence on physicians' behaviour with respect to the use of antibiotics in China. A randomised controlled study undertaken in one unnamed tertiary hospital in China found that pharmacist interventions with physicians at ward level significantly reduced the inappropriate use of antibiotics for inpatients with respiratory tract infections (Shen *et al.*, 2011). A larger systematic review focused on clinical pharmacy services' influences on the quality use of medicines in hospitals in China showed that pharmacist interventions had positive impacts on the appropriate prescribing of antibiotics by physicians (Penm *et al.*, 2014). It also noted that antimicrobial stewardship has become an important part of clinical pharmacy services, with 44% of the papers included in this review focusing on antimicrobials (Penm *et al.*, 2014). More recent studies also demonstrate that pharmacists play a key role in the appropriate use of antibiotics in a range of areas, such as antibiotic use in urology or cardiothoracic surgery (Jiang *et al.*, 2014; Zhou *et al.*, 2016; Zhou *et al.*, 2015).

2.3.2.3 Community (workplace) and organisational factors related to the use of antibiotics

In studies in HICs as well as Hong Kong, the pressures of workload and time are commonly identified as factors influencing doctors' antibiotic prescribing behaviour (Lam *et al.*, 2003; Kumar *et al.*, 2003; Horwood *et al.*, 2016; Tonkin-Crine *et al.*, 2011). In the studies focusing on Mainland China found through this review, none identified these workplace factors as a major influence. However, workplace factors related to the implementation of antibiotic stewardship were noted as important. Continuing education programmes, practical guidelines and diagnostic facilities were reported as positively related to doctors' appropriate

use of antibiotics for patients and children (Hou *et al.*, 2014; Li *et al.*, 2013; Liu *et al.*, 2008; Sun *et al.*, 2015; Yang *et al.*, 2014). For instance, a before and after intervention study on the Beijing Children's Hospital reported that, after introducing an antibiotic use guideline and antimicrobial spectrum chart to paediatricians, there was a reduction in both the rate of antibiotic cost per patient day and the most frequently used antibiotics (third-generation cephalosporin) in the paediatric intensive care unit (Ding *et al.*, 2008). In addition, Zhang *et al.*'s (2016) qualitative cross-sectional study focusing on antibiotic prescribing by doctors for children in rural China pointed to avoiding complications and uncertainties as influential factors of village doctors' antibiotic prescribing behaviour, and attributed these uncertainties to the lack of diagnostic tests at village clinic level.

Review of antibiotic use has identified financial factors as contributing to the inappropriate prescribing of antibiotics by providers in China (Mao *et al.*, 2015). A cross-sectional questionnaire survey carried out in the rural areas of three provinces with low, middle and high levels of economic development, respectively, in China reported that doctors' antibiotic prescribing decisions were influenced by the health financing system (whether patients paid through insurance or out-of-pocket payments), health financing methods (whether healthcare facilities were paid by the general budget or a fee-for-service (FFS) method), and payment methods for providers (salary or bonus) (Dong *et al.*, 1999).

As noted in Appendix B, hospitals in China are mainly paid by basic medical insurance schemes and individuals through the FFS structure, while government subsidies for hospitals are very limited. For instance, the government subsidy, insurance, and individual payments accounting

for 21%, 30%, and 49%, respectively, among total funding for public hospitals in China in 2010 (Mossialos *et al.*, 2016). Therefore, studies have uncovered evidence to suggest that some hospitals encourage physicians to sell more and costlier drugs to patients in order to balance hospitals' losses from reduced government subsidies and thus increase financial revenues. In turn, physicians working in hospitals are driven to prescribe more antibiotics by systems of staff bonus tied to the revenues that they bring in (Currie *et al.*, 2014). Audit studies carried out in China by Currie *et al.* (2013, 2014) looking at the influence of financial incentives and patient demand showed that the antibiotic prescription rate in audited hospitals was 10% when patients did not ask for antibiotics and 14% when they did; when combined with a financial incentive, the rate rose to 55% without patient demand and 85% with patient demand.

The influence of financial incentives on providers' inappropriate antibiotic prescribing behaviour has also been reported by studies focusing on primary care institutions (Jiang *et al.*, 2012; Li *et al.*, 2012). For instance, using an interrupted time series design with comparing medical records in community health centres in the Baoan district of Shenzhen city one year before and one year after government structure reform, Liang *et al.*'s (2014) study found that the decrease in prescribing antibiotics was positively related to separating community health centre staff's income from the volume and cost of medical services and prescriptions. It was supported by one matched-pair cluster-randomized study undertaken in rural areas of China, which indicated that implementing capitation with the pay-for-performance method instead of using the FFS led to a 15% reduction in antibiotic prescriptions among primary care institutions (Yip *et al.*, 2014). Furthermore, one study focusing on community health centres

in urban China found that the percentage of prescriptions containing antibiotics prescribed by private community health centres (37.17%) was higher than that among public community health centres (30.14%), which also suggested the influence of financial incentives on overprescribing of antibiotics, as private institutions usually lack government funding and therefore staff incomes rely more on the sales of drugs (Yin *et al.*, 2015). Similar findings related to a significant low antibiotic prescription rate in public sectors were also reported by observational studies of primary care institutions in Hong Kong (Lam *et al.*, 2003; Wong *et al.*, 2016).

Additionally, it has been reported that NRCMS, one of the basic medical insurance schemes in China's healthcare system, could contribute to the overprescribing of antibiotics among doctors in rural areas (Dong *et al.*, 1999; Jiang *et al.*, 2011; Sun *et al.*, 2009). As noted in Appendix B, the NRCMS was introduced by the Chinese government in 2003 with the goal of achieving comprehensive coverage of rural residents by 2020 (Hu *et al.*, 2008). A study, comparing the medical records related to the use of antibiotics among one county with NRCMS and one county without NRCMS in Shandong Province in 2005, pointed to a significantly higher percentage of prescriptions containing antibiotics in the county with NRCMS (the percentage was 74.2% in the county with NRCMS and 59.3% in the county without), suggesting that the inappropriate use of antibiotics was exacerbated by the NRCMS (Sun *et al.*, 2009). However, the review undertaken for this thesis found no paper relating to the influence of two other basic medical insurance schemes, the UEBMI and Urban Resident Basic Medical Insurance (URBMI), on providers' antibiotic prescribing behaviour.

Since China's 2009 healthcare reforms, there have been several policies introduced to tackle financial issues in the healthcare system, such as the EDL and ZMU policies (discussed in section 1.4.3). However, there are few studies that have been undertaken since the most recent healthcare reforms (Gong *et al.*, 2015; Song *et al.*, 2014; Xiao *et al.*, 2016; Yang *et al.*, 2013; Yao *et al.*, 2015), and the impact of EDL and ZMU policies is considered in more depth in the next sub-section.

2.3.2.4 Policy-related factors related to the use of antibiotics

As noted in section 1.4, there have been major policy initiatives in China designed to support appropriate prescribing behaviour by providers, particularly with respect to antibiotics. Evidence relating to these policy changes is summarized below.

The three-year strategy and other antibiotic use-related policies

China's first nationwide antibiotic containment guideline, the '*Principles for Clinical Use of Antibiotics*' was implemented in 2004 (discussed in section 1.4.2) (MoH *et al.*, 2004). An antibiotic-related study analysing five children's hospitals' central computer databases between 2002 and 2006 indicated that this guideline was only effective in reducing the inappropriate use of penicillin and first-generation cephalosporin (Zhang *et al.*, 2008); similar studies also focusing on antibiotic use data in pulmonology wards and outpatients among these five hospitals, and it was found that antibiotics were still overused (Zhang *et al.*, 2008; Zhang *et al.*, 2009). Moreover, because the guideline was not a legal requirement, the

inappropriate use of antibiotics has remained very common in China after 2004 (Xiao & Li, 2013). In 2011, a three-year national strategy, '*National Special Campaign for the Clinical Use of Antibiotics*', backed by China's stricter antibiotic use regulation (discussed in section 1.4.2) was introduced by the MoH (NHFPC from 2013) (MoH, 2013). As reviewed in section 1.3.3, studies demonstrated that this strategy was effective in controlling antibiotic use in some types of hospitals; however, the use of antibiotics in the children's hospitals remained a problem.

The EDL and ZMU policies

Since the implementation of the EDL and ZMU policies (introduced in section 1.4.3) in 2009, there were few studies focusing on its effects on rational use of medicines, including antibiotics, and the outcomes are not clear. With respect to its impact on providers in primary care institutions, a nationwide study of drug use by primary care providers indicated that the EDL and ZMU policies were promoting the appropriate use of antibiotics (Gong *et al.*, 2015). Through comparing prescriptions collected in 35 cities across China from 2007 to 2011, there was evidence that institutions that implemented these policies had a significantly lower proportion of prescriptions with antibiotics and of prescriptions with multiple antibiotics than those that had not implemented the policies. It also found the proportions of prescriptions with antibiotics and with multiple antibiotics decreased by 7% and 2%, respectively, after the implementation of the EDL and ZMU policies (Gong *et al.*, 2015).

However, other nationwide or provincial studies have suggested that, although overall drug use improved and relevant costs decreased following the implementation of the EDL and ZMU policies, the inappropriate use of antibiotics remained common among primary care institutions (Song *et al.*, 2014; Yang *et al.*, 2013; Yao *et al.*, 2015). For instance, it was reported in a retrospective survey of 39 primary care institutions selected to represent a range of socioeconomic development levels that the EDL and ZMU policies had had little effect on the appropriate use of antibiotics (Xiao *et al.*, 2016). Additionally, a cross-sectional survey that assessed the effect of the 2004 version EDL on drug manufacturers, hospital pharmacies and retail pharmacies was conducted in two provinces in 2007, and indicated that there had been relatively little change in the production and supply of medicines. It pointed to the low rates of production of essential drugs (around 50%-60%) and the low availability of essential drugs in drug manufacturers and pharmacies in these two provinces. The reported factors that influenced the behaviour of manufacturers and retail pharmacies were highly related to financial considerations, such as market demand, price, and profit margins, among others (Chen *et al.*, 2010).

2.3.3 Conclusions on this section

In contrast to the extensive evidence for HICs, the systematic search undertaken in two key databases (MEDLINE Ovid and CNKI) located very few studies focusing on factors that influenced providers' antibiotic prescribing decisions on patients, despite the fact they are one of the most important constituencies related to antibiotic use in China. The identified influences on providers' antibiotic prescribing decisions operated across a range of levels in the SEF, indicating influences from the individual (e.g. the lack of professional antibiotic

knowledge), interpersonal (e.g. patients' expectations), and community and organisational levels (e.g. continuing education programmes and financial incentives) to the policy level (e.g. three-year strategy and EDL and ZMU policies). Furthermore, compared with other levels, evidence on the interpersonal level, related to patients' or parental influences on providers' behaviour, was particularly limited, with as few as three studies in Mainland China conducted on patients' influences and only one study on parental influences.

2.4 Influences on the public's and parents' use of antibiotics

2.4.1 Factors related to the use of antibiotics among the public and parents in high-income countries

As ABR has become a serious global public health threat, research on the public's knowledge and attitudes towards antibiotics and ABR has also increased, with most of the studies focusing on HICs. Two recent systematic reviews of the global population's knowledge and attitudes about antibiotics and ABR, respectively, concluded that a lack of knowledge about antibiotics and ABR among the general population was an important factor (Gualano *et al.*, 2015; McCullough *et al.*, 2015). This included misconceptions about ABR as a form of resistance developed in the individual's body rather than in microbes, and a lack of understanding about the kinds of microbes and disease organisms that antibiotics were effective against (Gualano *et al.*, 2015; McCullough *et al.*, 2015). Further studies undertaken in either multi-HICs or the UK only also reported the public's misconception that ABR referred to changes in the human body (Brookes-Howell *et al.*, 2011; Ipsos, 2016). A further study analysed data from a population-based survey (total population 29 million) in the United

States undertaken by FoodNet and found misconceptions that antibiotics were effective against a cold and could prevent more serious diseases after catching a cold; demographic factors, including socioeconomic status, educational level, sex and age, had impact on an individual's knowledge and attitudes related to antibiotics and ABR (Eng *et al.*, 2003).

Along with research on the knowledge and attitudes about antibiotics and ABR, there are numerous studies in HICs exploring interactions between patients and doctors and patients' expectations of antibiotics in relation to their use of antibiotics. Factors located at various levels of the SEF were identified as relevant to patients' expectations of antibiotics in a review of studies in HICs. These factors included patients' symptoms, knowledge and previous experience of antibiotics, the need to return to work organisations or schools, and trust in doctors, while doctor-patient communication also played a key role in reducing patient demand and expectations and improving patient satisfaction (Davey *et al.*, 2002). It was further reported that receiving information or reassurance was positively associated with meeting patients' expectations and with greater satisfaction during the consultation, which highlighted the potential for misunderstanding patients' concerns and the importance of effective communication between doctors and patients in HICs (Butler *et al.*, 1998; Welschen *et al.*, 2004).

With paediatric use of antibiotics recognised as central to the wider problem of antibiotic use and ABR, studies focusing on factors related to the use of antibiotics for children by their parents in HICs are very common. With respect to parents' knowledge and attitudes about antibiotics, a lack of antibiotic-related knowledge was found among 1,247 parents of children

age 0-14 in a multicentre cross-sectional study in Italy, with being male, having a lower educational level and being unemployed associated with lower levels of knowledge (Bert *et al.*, 2016). Similar to studies focusing on the public in HICs, interactions between doctors and parents in the consultation have been widely discussed (Cabral *et al.*, 2015; Cabral *et al.*, 2016; Mangione-Smith *et al.*, 2015). A systematic review of studies focusing on antibiotic prescribing decisions on acute childhood infections in primary care in HICs found that, during the consultation, parents would want antibiotic prescriptions when they perceived antibiotics would be useful to their children's illness and they felt pressures from daycare providers or their employees, while reluctance to accept antibiotics was mainly due to concerns about the side-effects of antibiotics. Moreover, this systematic review identified a gap in the consultation needs of parents and doctors. Parents were more concerned about the medical diagnosis and decision-making but doctors sought to shorten the consultation and, at the same time, satisfy parents (Lucas *et al.*, 2015). A further systematic review of studies particularly focusing on communication in consultations for children's acute illness in HICs also pointed to the different concerns between parents and doctors with the potential to affect antibiotic prescribing decisions in the consultation (Cabral *et al.*, 2014).

Compared with the many studies conducted in HICs, there are very few studies focusing on factors related to the use of antibiotics among the public and parents in China, with studies exploring the interactions between doctors and patients being a particularly noticeable gap. The next two sections will describe factors influencing antibiotic use among the public (section 2.4.2) and parents (section 2.4.3) in China, with evidence again derived from papers published in English and Chinese found from the systematic search of two key databases.

2.4.2 Factors related to the use of antibiotics among the public in China

2.4.2.1 Individual factors related to antibiotic use and resistance

In China, national data relating to knowledge and attitudes on antibiotic use and resistance among the public are very limited; research related to antibiotic use and resistance is usually undertaken at the level of the individual province or area (Gili *et al.*, 2014). Studies undertaken in a range of urban areas in Mainland China all indicated that the public's knowledge related to the use of antibiotics is inadequate (Lin *et al.*, 2015; Tian *et al.*, 2014; Xiong *et al.*, 2015; Ye *et al.*, 2014). For instance, one questionnaire survey conducted between March and August 2014 in Jiangbei district of Ningbo city reported that only 31.5% (560) of 1,778 respondents were able to correctly identify what antibiotics are, even though 72% of them believed they knew (Lin *et al.*, 2015). This study also indicated that 56.5% of respondents believed that antibiotics were helpful for viral infections, which is much higher than the same belief in the UK; a UK-based survey in 2015 of 1,524 adults found that only 38% thought that antibiotics could treat viral infections (Lin *et al.*, 2015; Ipsos, 2016).

Questionnaire surveys looking at rural areas similarly reported that antibiotic-related knowledge among rural residents in China is inadequate (Tan *et al.*, 2014; Zhao *et al.*, 2013). A qualitative study undertaken in four villages in the middle and east of China identified a range of misconceptions and attitudes related to antibiotic use among villagers, such as associating antibiotics with 'xiaoyanyao' (anti-inflammatory drugs) or a belief in a never-ending line of antibiotics, along with very low levels of awareness of ABR among villagers from

poorer households and a common misunderstanding that the human body developed resistance to antibiotics among villagers who had heard of ABR (Jin *et al.*, 2011). It has also been found that people in rural areas have less adequate knowledge and correct attitudes regarding the use of antibiotics, when compared with urban residents (Ma *et al.*, 2014; Wang & Wang, 2013). In addition, studies focusing on particular populations in Mainland China, such as patients or university students, all reported that knowledge was inadequate and attitudes were only moderately accurate with respect to antibiotic use and ABR (Chen & Wang, 2014; Huang *et al.*, 2013; Li & Tong, 2013; Lv *et al.*, 2014; Tian *et al.*, 2015; Wang *et al.*, 2013).

Findings from studies in Hong Kong point to the better antibiotic-related knowledge among the general public. A cross-sectional phone survey carried out in 2006 in Hong Kong showed that, among 1,002 general residents, most of them had adequate knowledge and appropriate attitudes regarding antibiotic use (You *et al.*, 2008). Another more recent mixed method study of more than 2,500 adults in Hong Kong found that the public were aware of the clear message 'not to abuse antibiotics'. It noted, however, that awareness of antibiotic resistance still needed to be improved, pointing to a gap between knowledge of antibiotic use and knowledge of resistance among the public in Hong Kong (Wun *et al.*, 2013).

Based on this thesis' literature review, educational level is the factor most commonly identified across studies in China as related to the public's antibiotic-related knowledge; people who had a higher educational level were more likely to have better knowledge (Lin *et al.*, 2015; Tan *et al.*, 2014; Ye *et al.*, 2014). Factors such as age, gender, history of chronic

diseases and material circumstances have also been identified as related to knowledge of antibiotics (Jin *et al.*, 2011; Lin *et al.*, 2015; Tian *et al.*, 2014; Ye *et al.*, 2014). In addition, studies comparing antibiotic-related knowledge between rural and urban areas, and comparing medical students and non-medical students, emphasized the importance of rural/urban location and having a medical background (Liu *et al.*, 2013; Ma *et al.*, 2014; Zhu *et al.*, 2015).

Antibiotic-related knowledge has been found to be related to antibiotic non-adherence and self-medication. As noted in section 1.3.3.3, non-adherence to antibiotic treatment is a behaviour highly related to the inappropriate use of antibiotics, which is particularly widespread among the public in China (Pechère *et al.*, 2007). Despite its importance, the searches identified very little evidence on non-adherence relating to China. Antibiotic-related knowledge was identified as a factor related to antibiotic non-adherence in a questionnaire survey of 465 Hong Kong urban residents, where there was a significantly higher prevalence of antibiotic non-adherence among residents with poor antibiotic knowledge (Chan, *et al.*, 2012).

Self-medication with antibiotics is another form of inappropriate antibiotic use that may contribute to ABR, and is also demonstrated to be connected to antibiotic-related knowledge (Goossens, 2009; Huang *et al.*, 2013; Jose *et al.*, 2013). A cross-sectional questionnaire survey focusing on Weifang city in China found that, among 354 residents, participants who did not know what antibiotics are were more likely to self-medicate with antibiotics than those who did (Xiong *et al.*, 2015). However, in contrast, university student-based questionnaire surveys

in different regions of China reported that prior knowledge of antibiotics was a risk factor for self-medication with antibiotics (Lv *et al.*, 2014; Pan *et al.*, 2012; Zhu *et al.*, 2015). This finding is further supported by another study comparing university students with and without health-related backgrounds, which suggests that the proportion buying antibiotics without a prescription was significantly higher among medical students (645/791) than non-medical students (207/321) (Liu *et al.*, 2013).

Household circumstances, another individual-level factor, have also been reported to influence people's antibiotic-related knowledge and behaviour related to antibiotic use; however, their specific effects on the use of antibiotics are still not clear. For instance, a questionnaire survey focusing on 558 residents in Nanjing and Suzhou city in China showed that average monthly income was the major predictor of participants' antibiotic knowledge and behaviour; residents with higher average monthly incomes had higher medication use scores in the study, which meant they had better antibiotic use behaviours (Wang & Wang, 2013). This finding was further supported by another cross-sectional study in which, among data collected by questionnaires from 210 inpatients, participants with monthly incomes higher than 3,000 CNY (456 US\$)²⁰ had better knowledge of antibiotics and more appropriate antibiotic use behaviour (Chen & Wang, 2014). However, in Pan *et al.*'s (2012) university student study, a higher income, as measured by a higher allowance (>500 CNY (76 US\$)²¹), was a risk factor for self-medication with antibiotics; students with a higher allowance had a significantly higher rate of self-medication with antibiotics. In addition, studies found that

²⁰ Exchange rate: 1 US\$= 6.5798 CNY (on 30th May 2016)

²¹ Exchange rate: 1 US\$= 6.5798 CNY (on 30th May 2016)

other demographic factors, such as older age, female gender, and area of residence (rural, rather than urban) were risk factors for self-medication with antibiotics among Chinese university students (Liu *et al.*, 2013; Lv *et al.*, 2014; Pan *et al.*, 2012; Zhu *et al.*, 2015). In a global survey that included China, age was found to be a factor that was negatively correlated with antibiotic non-adherence in China, as well as in other countries such as Japan and the Netherlands (Pechère *et al.*, 2007).

2.4.2.2 Interpersonal (patient-provider) factors related to antibiotic use and resistance

Although interactions between providers and patients, with respect to the use of antibiotics, have been widely discussed in studies in HICs, as noted in section 2.3.2.2, research in China focusing on these interpersonal influences is still limited. Providers, including doctors and pharmacists, have been consistently identified as important sources for different groups in China to obtain antibiotic-related information (Lv *et al.*, 2014; Reynolds & McKee, 2011; Zhao *et al.*, 2013). However, the process through which the public gets information from providers, such as the details of interactions and communication between them, are not discussed in these studies. Only one cross-sectional self-administered questionnaire survey, conducted in Hong Kong more than two decades ago, mentioned patient expectations and their influences on consultations with doctors. The study found that, despite common misconceptions that medications and antibiotics were needed for upper respiratory tract infections, the proportion of patients and guardians who came specifically for antibiotics were not high and they would accept doctors' decisions of no medication (Chan, 1996). However, patient

expectations, and the interaction between providers and patients may have changed since the 1990s.

2.4.2.3 Cultural and community-level factors related to the use of antibiotics

This thesis' literature review found little evidence on this 'layer' and the broader layers of the SEF. It only located studies on the influence of TCM and media on the use of antibiotics among the public in China.

Understandings of illnesses and treatments through both the Western medicine and TCM perspectives by the Chinese population has been widely reported by many studies, including research on Chinese people in both Mainland China and in other Chinese societies such as Taiwan, and overseas Chinese populations (Chung *et al.*, 2014). However, only one study focusing on the influence of a TCM perspective on the use of antibiotics among Chinese populations was identified for the literature review. In this study, a questionnaire survey conducted with 2,471 participants in Hong Kong, those who usually attended a TCM practitioner were less likely to use antibiotics and were more concerned about the side effects of antibiotics and ABR than people who usually attended Western medicine providers. They also had a clearer awareness of the types of disease that antibiotics were effective against. However, they were less likely to complete a full course of antibiotic treatment than Western medicine-attenders (Wun *et al.*, 2014). Additionally, Wun *et al.*'s (2014) study found that female participants and those with lower household incomes were more likely to use TCM,

which is similar to findings from other studies on the attitudes and use of antibiotics among Chinese in Hong Kong (Chung *et al.*, 2007; Chung *et al.*, 2009).

In a large qualitative study undertaken in the Guizhou Province of China, factors influencing the overuse of antibiotics in China was one part of the study focus, and the role of media and medical advertising in influencing the use of antibiotics was highlighted by participants (doctors and university students) (Reynold & McKee, 2009, 2011). In this study, one doctor attributed self-medication with antibiotics to the advertising of antibiotics in media, and another doctor believed that people could be adversely influenced by medical advisements because relevant regulations were not enforced. University students who participated in this study acknowledged that people would follow advertisements to purchase drugs including antibiotics to treat minor diseases (Reynolds & McKee, 2009, 2011). Furthermore, another questionnaire-based survey of university students identified the media as a major source of antibiotic-related knowledge, with over 60% of participants reporting that they received information related to antibiotics from the media, such as through TV advertisements and the internet (Lv *et al.*, 2014)

2.4.3 Factors related to the use of antibiotics among parents in China

In China, little is known about factors influencing the parental use of antibiotics for their children. In this thesis' literature review, only five English language studies and ten Chinese language studies were identified. All the studies were cross-sectional and quantitative questionnaire surveys. Among the English language papers, three focused on Mainland China, including two papers reporting on studies conducted in rural areas and one reporting the

results of a study conducted in urban areas; the remaining two English language papers were related to studies in Hong Kong. The Chinese language studies included both rural and urban areas in Mainland China. However, the majority only assessed the antibiotic-related knowledge of parents, and had limitations (noted in section 2.2.2.3, pp.96) which are commonly found in Chinese language papers, such as providing less detailed information on methods and results or being small-scale research; these limitations were particularly evident for studies without an English title and abstract (Fan, 2010; Zheng, 2012). Therefore, evidence about factors influencing the use of antibiotics for children by their parents in China remains very limited, particularly with respect to the urban areas of Mainland China.

Beyond this small set of studies, there is broader evidence of extremely high antibiotic use frequency among children in China over a long period (noted at section 1.3.3). In studies focused on HICs, parental behaviour has been identified as a key factor, with studies noting that a lack of knowledge and awareness of antibiotics and treatment may contribute to inappropriate parental behaviour (Huang *et al.*, 2005; Horwood *et al.*, 2016; Lucas *et al.*, 2015). In China, all the questionnaire surveys located through the search of databases – both those focusing on urban areas and those conducted in rural areas – pointed to low levels of antibiotic-related knowledge among parents, and factors including the age, educational level, and material circumstances were commonly identified as contributors to their knowledge (Ding *et al.*, 2015; Ding *et al.*, 2015A & 2016; Fan, 2010; Wang, 2013; Yu *et al.*, 2014; Zheng, 2012). Furthermore, it was found by Zheng's (2012) study that mothers had better knowledge of antibiotics than fathers; the author explained that this was likely to reflect the fact that

mothers are more centrally involved in the development of children and, therefore, are likely to care more about acquiring information related to their children's health.

As noted in section 2.4.2.1, antibiotic-related knowledge is highly associated with the public's antibiotic use behaviour in China, including antibiotic non-adherence and self-medication with antibiotics, but the effects vary among different groups. Among studies focusing on Chinese parents, it was found that some kinds of antibiotic-related knowledge (Ding *et al.*, 2015A; Wun *et al.*, 2012; Yu *et al.*, 2014) and higher educational levels (Bi *et al.*, 2000; Wang *et al.*, 2017) were positively related to appropriate antibiotic use behaviour. For instance, a cross-sectional study conducted with 854 rural parents indicated that parents who did not know antibiotics should be prescribed by doctors were more likely to purchase OTC antibiotics (Yu *et al.*, 2014). It was also noted in an audit study carried out in 18 hospitals of two unnamed Chinese cities that parents' limited knowledge of antibiotics was a contributor to the inappropriate use of antibiotics for children (Currie *et al.*, 2011). However, Yu *et al.*'s (2014) study also noted that there was no association between parents' total score of antibiotic-related knowledge and their behaviour of self-medicating children with antibiotics.

The review identified one study with evidence about parental medication of children with antibiotics, a questionnaire survey conducted with around 1,500 parents in Hefei city (Bi *et al.*, 2000). Alongside antibiotic-related knowledge and educational level, it was found that maternal characteristics – for example, socio-economic status – were particularly associated with parental medication, while there was no relationship between parental self-medication and the father's characteristics (Bi *et al.*, 2000). The key role of mothers in their children's

development has been highlighted by the WHO; it is also strongly associated with China's social and cultural background, where the mother is commonly responsible for looking after children (Bi *et al.*, 2000; WHO, 2003A). The child's age and the severity of their disease were also identified as being relevant to parental self-medication of children; children who were older or with minor illnesses were more likely to be parentally medicated with antibiotics (Bi *et al.*, 2000; Wang *et al.*, 2017). In addition, studies have demonstrated that the availability of obtaining antibiotics without a prescription, the media and the insurance status of parents all had impact on parental medication with antibiotics of children, which suggested influences from a broader community and organizational level (Bi *et al.*, 2000; Yu *et al.*, 2014).

With respect to another form of inappropriate antibiotic-using behaviour – non-adherence to the child's prescribed antibiotic treatment, factors located in individual and interpersonal level, including parents' age and educational level, concern about side-effects of antibiotics, and better communication between parents and doctors, were found to be influential factors (Ding *et al.*, 2015; Wun *et al.*, 2012; Yu *et al.*, 2014). Furthermore, different to Chan *et al.*'s (2012) questionnaire survey on Hong Kong residents' antibiotic non-adherence and knowledge, Ding *et al.*'s (2015) study pointed to factors (parents' younger age and higher educational level) relating to better antibiotic-related knowledge as contributors to non-adherence to the child's antibiotic treatment by parents. The authors also noted that, for parents who are older or have lower educational levels, although they have higher adherence to the child's antibiotic treatment, they simply follow doctors' decisions rather than purposefully adhering to them (Ding *et al.*, 2015). Finally, it has also been found that parents' poor adherence to doctors' advice was associated with their behaviour with respect to

parental antibiotic medication of their children, suggesting an association between these two types (non-adherence to antibiotic treatment and parental medication) of antibiotic use behaviour (Yu *et al.*, 2014).

In the small number of relevant studies, the doctor was the main source for parents to obtain antibiotic-related information in rural areas of China (Bi *et al.*, 2015; Yu *et al.*, 2014). Although only including evidence from one rural study, it reported that the interaction between doctors and parents was very highly related to parents' antibiotic use behaviour (Yu *et al.*, 2014). Evidence from Yu *et al.*'s (2014) study indicated that parents who the study team assessed as having positive communication with physicians during the consultation had a higher antibiotic adherence rate than those who reported having fewer opportunities to communicate with physicians. It was also reported in a retrospective analysis on National Health Insurance data in Taiwan that children with parents who were well educated in medical matters, such as physicians, pharmacists and nurses, were less likely to receive antibiotics for common colds, upper respiratory tract infections, and acute bronchitis than children whose parents were non-medical personnel (Huang *et al.*, 2005). During the consultation, it was found in Yu *et al.*'s (2014) rural study that over half of parents had directly requested antibiotics from doctors on at least one occasion. In a study of rural parents in Shandong Province, having a child over the age of three was associated with a high level of over-expectation for antibiotics (Ding *et al.*, 2015). However, there were no studies focusing on the influence of parent-provider interaction on parents in the urban areas of Mainland China.

2.4.4 Conclusions on this section

Few studies focusing on factors related to the use of antibiotics among the public and, particularly parents, in China were found through the systematic search of two databases, however many more studies were found in HICs. Moreover, among the identified China-based studies, most focused on the individual level of SEF and noted the public's and the parents' inadequate knowledge and personal characteristics as influences on their inappropriate antibiotic use behaviour. Very few studies focused on interpersonal (patient-provider) and community-level factors and no studies discussed influences from broader levels, including organisational factors and policy-related factors. Therefore, with respect to factors influencing patients' and parents' use of antibiotics in China, the systematic search found very limited evidence and a particular gap in relation to factors influencing antibiotic-related behaviour at 'layers' above the individual level in the SEF.

2.5 Conclusions

In conclusion, the literature review relating to influences on providers' and parents' use of antibiotics for children in China progressed through two stages – identifying a framework and undertaking a review guided by this framework. The search and review identified a major gap in the literature relating to influences on providers' and the public's, particularly parents', use of antibiotics in China in comparison to the extensive evidence presented in high-income country contexts.

When the relevant records were located within the different levels of the SEFs, it was clear that there was particularly limited evidence at the interpersonal level: the influence of providers and patients, including parents, on the behaviour of both groups with respect to the use of antibiotics in China. Another key finding was the dearth of qualitative studies in China, particularly in the setting with a profile of the typical city. Specifically, this review located only two qualitative studies, which both investigated factors influencing providers' antibiotic prescribing decisions in rural areas of China (Reynolds & McKee, 2009; Zhang et al., 2016); no qualitative study focused only on parents was located.

Along with the identification of research gaps, the literature review showed the very low number of Chinese language records indexed in the major international database, particularly in comparison with the huge amount of Chinese language records located in the Chinese database. Therefore, in line with Fung's (2008) study, this literature review points to the importance of searching and reviewing literature published in languages other than English to increase the comprehensiveness of the review and to avoid potential language biases. Despite the large number of Chinese language studies, many were of relatively low quality based on Hawker's quality criteria. Consequently, this review also pointed to the urgency of improving the quality of studies published in Chinese language journals, particularly regarding ethics and the study context, in order to enable them to be more widely indexed in international databases and to provide high quality information.

Chapter 3. Overview of research design

3.1 Overall research question and objectives

The overall research question was informed by the literature review on factors influencing healthcare providers' and the public's behaviour with respect to the use of antibiotics in China in Chapter 2. As discussed in Chapter 1, the inappropriate use of antibiotics for children by healthcare providers in hospitals, primary care settings and pharmacies, and by parents, is a particular challenge in China. The literature review in Chapter 2, however, pointed to a major knowledge gap in relation to influences on providers' and the public's, particularly parents', use of antibiotics in China. It further indicated that research was predominantly quantitative with very few qualitative or mixed/multi-methods studies. Therefore, this thesis aims to shed light on influences on providers' and parents' paediatric antibiotic use behaviours, in relation to the following overall research question, which was established to address gaps identified in the literature review:

- What are the factors influencing healthcare providers' and parents' behaviours with respect to the use of antibiotics for children in China?

The thesis has two specific objectives:

- (i) To undertake a qualitative study of providers to explore factors influencing their use of antibiotics for children
- (ii) To undertake a multi-method study of parents to explore factors influencing their use of antibiotics for their children

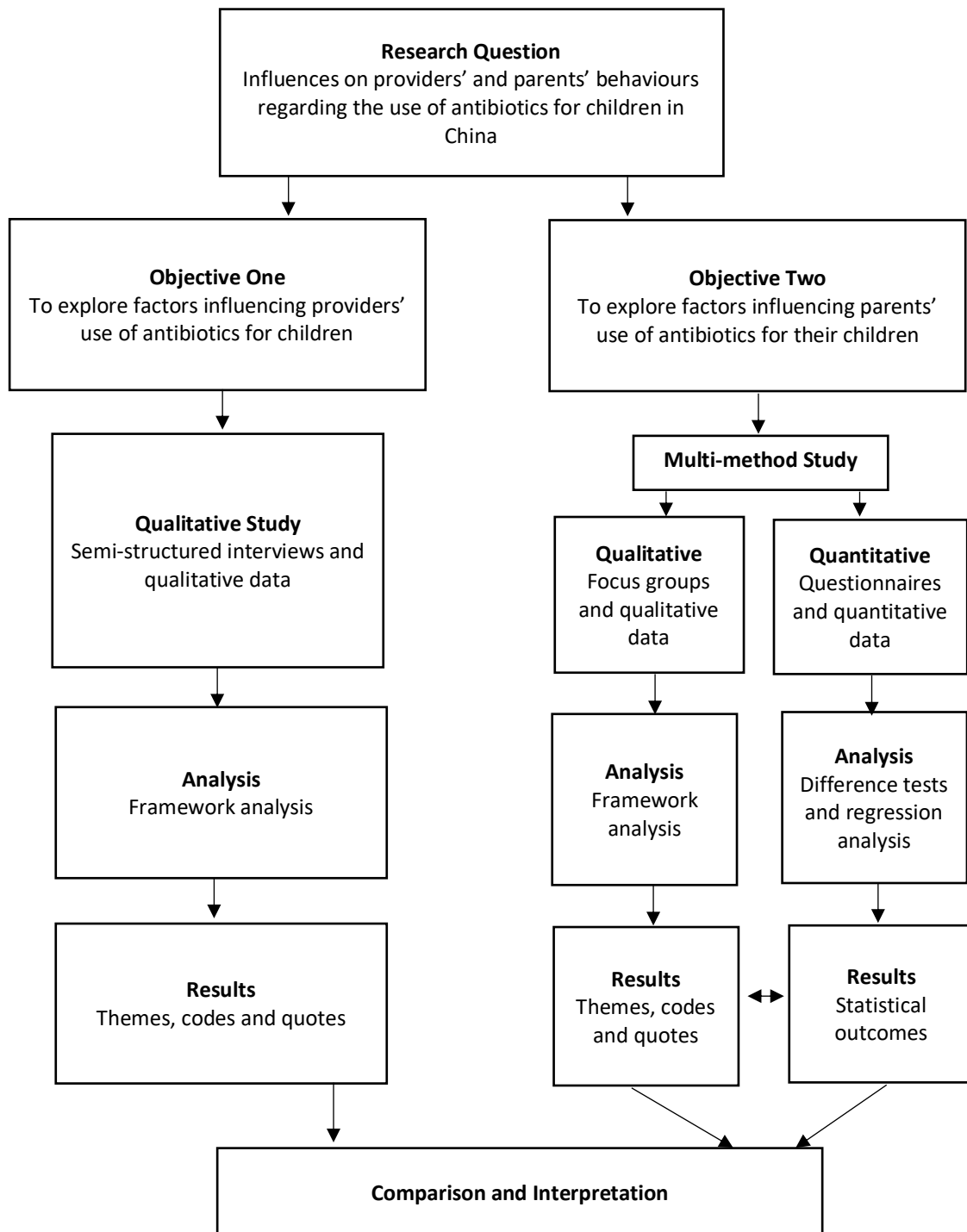
Each objective has its own research questions, which are stated in the Chapters 4, 5, and 6.

3.2 Research approach: Study design

The thesis combines a range of research approaches. As noted in the previous section (section 2.2), the literature review progressed through two stages – identifying a framework and undertaking a review guided by the framework. The broader background reading on AMR and ABR-related research made clear that there were multiple influences operating at different levels. This background reading thus informed an initial SEF, which was then further refined within two SEFs to guide the review and the empirical research. Providers and parents, respectively, were located in the centre of the two SEFs, and were surrounded by a set of concentric layers influencing their behaviours from micro- to macro-level. The systematic searches and review guided by the SEFs were then conducted on two key electronic databases – MEDLINE Ovid and CNKI – to locate English and Chinese language research, respectively. Building on the literature review and the SEFs, the thesis draws on a set of primary studies to address its two objectives. Figure 6 summarises the study design and how the primary studies relate to these objectives.

As shown in Figure 6, a qualitative approach was chosen to explore influences on providers' antibiotic use for children. Such approaches can allow in-depth interpretations of participants' views and experiences (Pope & Mays, 2006; Ritchie & Lewis, 2013), and are well-suited to exploratory studies that focus on specific settings (Hammersley & Atkinson, 2007; Holloway, 2008). In addition, it was not possible to get access to large populations of providers to undertake a broader survey. The qualitative data were analysed by framework analysis. Further details of the methodology are provided in Chapters 4 and 5.

Figure 6 Research methods used to address the overall research question and two objectives in the study



A multi-method study, involving qualitative and quantitative components, of parents was chosen to explore factors influencing parents' antibiotic-related behaviour. Combining the two components in a multi-method design can provide a richer understanding of the research topic (Byrne & Humble, 2007; Morse, 2003; Esteves & Pastor, 2004). Therefore, in this study, the quantitative component focused on parents' knowledge, views and behaviour, in order to provide a broad picture of influences on parental use of antibiotics and the qualitative component was used to explore influences on parental antibiotic-related behaviour in greater depth. The qualitative and quantitative data were analysed separately using framework analysis and statistical methods, respectively. Details of the multi-method study are provided in Chapter 6. Finally, findings from providers and parents are compared and interpreted together in Chapter 7.

3.3 Research approach: Ethics and access in China

China does not have a national research ethics system (an in-country research governance and approval process) (Huang & Pan, 2009) or, as far as the researcher can ascertain, one that operates at an organisational level (e.g. hospital). Furthermore, there is a lack of public and professional understanding of 'research ethics' as the concept and process are understood in Western and high-income countries, and the consequent challenges of adapting the research governance approaches developed in these countries to Chinese culture and ethical principles are little discussed (Huang & Pan, 2009; Liu, 2006). Ethics-related concerns are still limited to medicine and research focusing on specific diseases, such as AIDS (Huang & Pan, 2009). Within medicine and health care as a whole, ethics education is also very limited and,

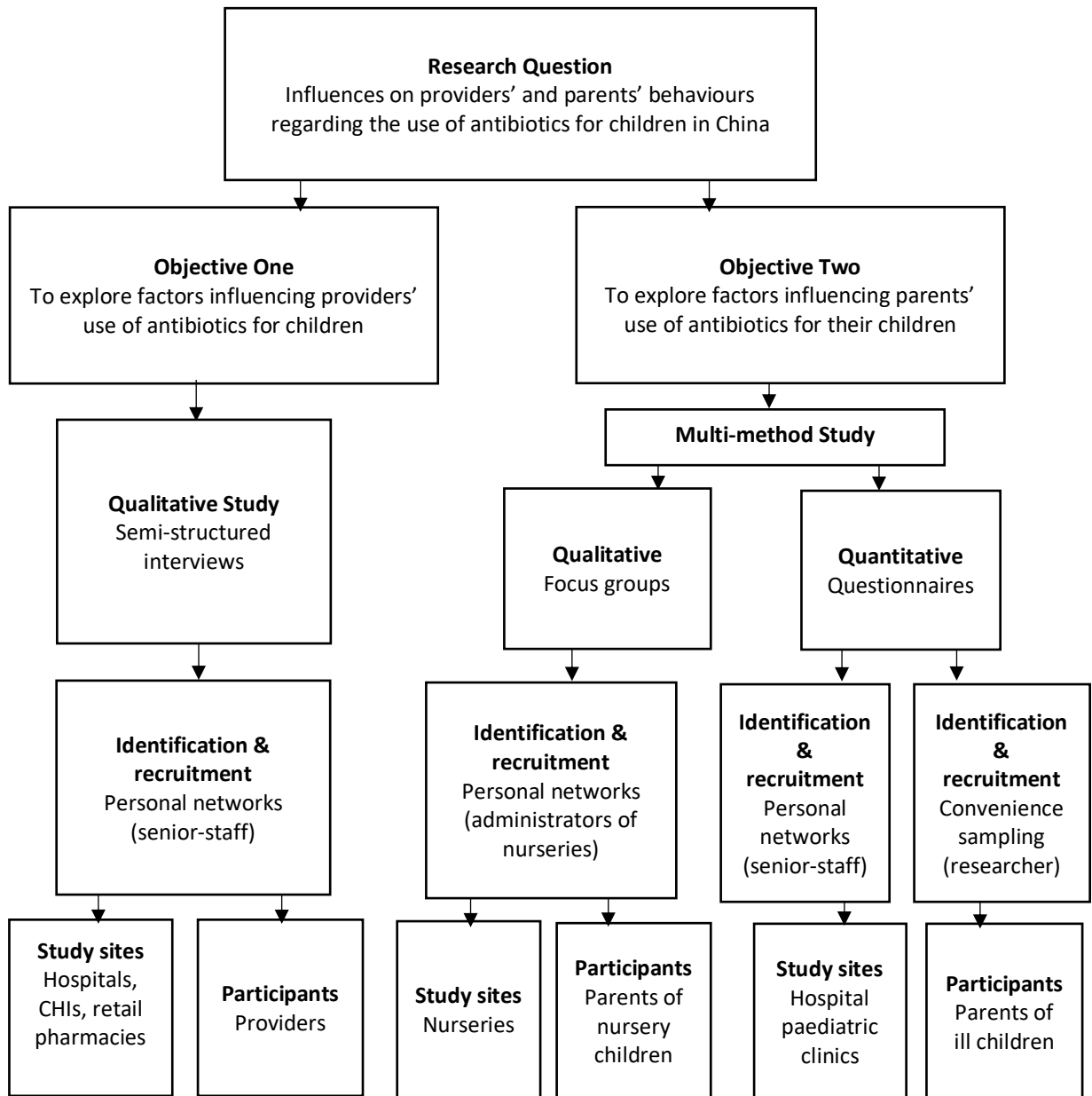
while there is legislation designed to protect patients, implementation lags behind (Gao *et al.*, 2015). Research governance procedures therefore need to take account of, and be sensitive to, these cultural and organisational contexts, with culturally appropriate processes for approval and access to study sites and for informed consent from research participants. These processes, discussed below, were approved by the Research Governance Committee of the Department of Health Sciences at the University of York.

In this study, personal connections and networks were used to gain entry to the study sites and participants, an approach that, as other studies have noted, is sensitive to Confucian-based cultures; these studies also relied on personal contacts to secure support for approval and execution (Liu, 2006, 2007; Park & Lunt, 2015). In China, the anonymous and formal approaches associated with surveys based on random samples can be viewed with suspicion and fear, while trust is engendered by contacts made through personal relationships, particularly those of family and friends (Huang & Pan, 2009; Liu, 2006, 2007). The study validity is reduced when participants are suspicious and stressful, as people are more likely to refuse to participate in the study (Huang & Pan, 2009); moreover, the suspicion increases the social desirability bias, where participants may give what they believe to be the socially acceptable account in a society where there is a strong culture of conformity (Gobo, 2011; Liu, 2006). Therefore, as shown in Figure 7, personal networks were used in all the primary studies.

In the study of providers, study sites, including hospitals, CHIs and retail pharmacies, were accessed through senior staff of these institutions identified through personal networks, and

most of participants were then introduced by these senior staff members. Similarly, for the qualitative part of the parent study, the study sites (nurseries) were accessed through the nurseries' administrators who were identified through personal networks and participants were then recruited by those administrators. For the quantitative part of the parent study, access to the hospital paediatric clinics was secured via the senior clinic staff identified through personal networks. Participants (parents) were then directly recruited by the researcher who approached as many as possible within the clinic opening hours (convenience sample).

Figure 7 Recruitment of participants for the different research methods used in the study



The process of securing informed consent again took account of the cultural context and cultural sensitivities. Official-looking forms and signed consent procedures for research participation are also not part of Chinese culture, and tend to be seen in negative terms (as part of state surveillance) and, therefore, viewed with fear and suspicion (Huang & Pan, 2009;

Liu, 2006). Huang & Pan's (2009) study noted that Chinese people will be wary when required to provide a signature or even to show their handwriting; even if formalised written consent can be obtained, it risks increasing participant stress and burden (Huang & Pan, 2009). These difficulties were confirmed by senior staff and administrators, particularly those working at community health stations and nurseries, during the pilot visit in China in Sept/Oct 2015. They warned that it is not usual to ask participants to sign a consent form, especially for research that does not have a Chinese collaborator. Written consent can also affect data validity by increasing the possibility that participants give socially acceptable accounts (Huang & Pan, 2009; Liu, 2006). Therefore, a culturally appropriate consent process was used in my qualitative and quantitative studies to address these concerns and to protect the validity of data. Participants were given, and individually taken through, the Information Sheet by the researcher, with any queries answered; verbal consent was then requested and, where given, was formally recorded by the researcher (Appendix F). Such alternative approaches to securing informed consent have been noted in other studies (Adams *et al.*, 2007; Bhutta, 2004).

Chapter 4. Healthcare providers' accounts of parental influences on their behaviour with respect to the use of antibiotics for children

A shorter version of this chapter was published in the *Journal of Community Medicine and Public Health Care* (See Appendix G).

4.1 Introduction

Antimicrobial resistance (AMR) is one of the most serious global public health problems (Chan *et al.*, 2012; Neill, 2016; WHO, 2015), and ABR has become a particular challenge (ESRC, 2014; WHO, 2015A). Between 1994 and 2000, China recorded the most rapid increase in rates of human ABR worldwide (Heddini *et al.*, 2009); the prevalence of many antibiotic resistance strains has ranked amongst the highest worldwide (Xiao *et al.*, 2011). A key driver of ABR in China is its high rates of use and inappropriate use of antibiotics (Currie *et al.*, 2011; Heddini *et al.*, 2009; Zhang *et al.*, 2006). China accounts for around half of the world's total antibiotic consumption, of which human consumption accounts for 48% (Zhang *et al.*, 2015). At 138g per person per year, individual consumption in China is 10 times higher than in the United States (Li *et al.*, 2014). Studies point to high rates of inappropriate prescribing by providers, including hospitals (Sun *et al.*, 2015; Xie *et al.*, 2015), primary health care institutions (Li *et al.*, 2012; Wang *et al.*, 2014), and retail pharmacies (Fang, 2014). A study of primary care records across six provinces at different stages of economic development found that over 60% of antibiotics were incorrectly prescribed (Wang *et al.*, 2014).

High rates of paediatric use and misuse are recognised to be a particular challenge in China. Studies of child inpatients report that a very high proportion of patient encounters result in an antibiotic prescription, ranging from 62% to 98% (He, 2012; Li & Wu, 2007; Wang, 2006; Xie & Wu, 2006; Yang & Shi, 2008; Zheng *et al.*, 2008), much higher than the 30% rate recommended by the WHO (WHO, 2006). Retail pharmacies have been identified as a major source for OTC antibiotics for the public (Fang, 2014), with evidence from one study indicating

that over 70% of encounters for paediatric diarrhoea resulted in the sale of antibiotics without prescription (Jiang *et al.*, 2013). Government concerns about the overuse and inappropriate use of antibiotics resulted in the MoH (NHFPC from 2013) in China launching a three-year strategy in 2011, backed by much stricter regulations on antibiotic prescribing (Xiao & Li, 2013, 2015; MoH, 2012A). These are designed to ensure physician adherence to protocols that require examination of the patient's clinical presentation and laboratory test results (Li, 2014; Mossialos *et al.*, 2016; Xiao & Li, 2015).

However, non-clinical factors, and perceived parental pressure in particular, are known to influence providers' behaviour with respect to antibiotic use. A systematic review of qualitative studies in HICs of prescribing decisions in primary care for acute childhood infections indicated that perceived pressure from parents was one of factors underlying clinicians' decisions to prescribe antibiotics (Lucas *et al.*, 2015). Parental influences on doctors' antibiotic prescribing behaviour were also noted in a more recent study in the UK (Horwood *et al.*, 2016). More limited evidence for LMICs suggests that patient and parental pressure are again factors influencing clinicians' antibiotic prescribing decisions (Kumar *et al.*, 2008; Sivagnanam *et al.*, 2004).

However, very few studies have been in China, where TCM is integrated into the healthcare system (WHO, 2001). While qualitative studies can shed a unique light on providers' perceptions and experiences of influences on their behaviour with respect to antibiotic use (Pope *et al.*, 2006; Ritchie & Lewis, 2013), most of these studies are quantitative (Currie *et al.*, 2011; Currie *et al.*, 2014; Huang *et al.*, 2005; Lam *et al.*, 2003; Lam *et al.*, 2009). There were

only two qualitative studies focusing on China located via the literature review undertaken for this thesis. A qualitative study in Guizhou Province found that patient expectations were an influence on providers' use of antibiotics. Guizhou Province is a poor southern mountainous province, with a large ethnic minority population (Reynolds & McKee, 2009), very low life expectancy (Mossialos *et al.*, 2016), and low per capita health expenditure (National Health Development Research Centre, 2013; Statistical Information Centre of NHFPC, 2016). A more recent qualitative study conducted with village doctors, parents and directors in the healthcare system in rural China also identified the pressure for antibiotic treatment from parents, along with the financial pressure to retain patients, as major factors contributing to doctors' antibiotic prescribing decisions for children under 15 years with upper respiratory tract infections (Zhang *et al.*, 2016).

To my knowledge, this is the first qualitative study in a city and one with a profile typical of Mainland China. This study aims to build on the limited existing evidence by focusing on providers' perceptions of parental influences on their behaviour with respect to antibiotic use for children, with research question established as:

- What are the parental influences on providers' behaviours with respect to the use of antibiotics for children in urban China?

Study context

As noted in section 1.3.1.1, hospitals are the cornerstone of China's healthcare system, with more than 90% of China's inpatient and outpatient services delivered by hospitals (Yip *et al.*, 2012), and most of China's health resources, such as inpatient bed and health staff, also

concentrated in hospitals (Statistical Information Centre of NHFPC, 2016). Additionally, about 70-80% of pharmaceutical sales in China come from hospitals (Mossialos *et al.*, 2016). Hospitals operate within a 3-tier system, each tier divided into three levels (A, B and C) (Mossialos *et al.*, 2016). The highest tier is the tertiary A hospitals; they are commonly large public hospitals serving large populations, for example a city and its surrounding rural communities.

Compared with hospitals, the primary care system, including CHIs (including community health centres and smaller community health stations) in cities and township hospital centres in rural areas, is relatively weak, although it is growing rapidly, particularly CHIs with the total number increasing by 100% from 2005 to 2014 (Mossialos *et al.*, 2016; Wang *et al.*, 2012; WHO, 2015C). In addition, the retail pharmacies are another rapidly growing sector, with an average 20% growth in annual pharmaceutical sales from 1978 to 2009 (Fang, 2014).

TCM (discussed in section 1.3.2.2), which has been practised in China for more than 2000 years, is a holistic system used to diagnose, prevent and cure human diseases (Lao *et al.*, 2012; Wang & Li, 2005; Yin & Zhang, 2006). Among its distinguishing features is an understanding of diseases as unbalanced *yin-yang*, which is the fundamental theory, in the human body caused by factors such as six excesses (*liuyin*) (including excesses of heat, wind, cold, dryness, dampness and summer heat) (Yin & Zhang, 2006). TCM understands the body's structure and functioning as the 'constitution', which is associated with interactions among organs (*zangfu*), meridian (*jingluo*), and energy (*qi*) and blood (*xue*). The organs (*zangfu*) can be further divided into five *yin* organs (*wuzang*), including heart, liver, spleen, lungs and kidneys, and six *yang*

organs (*liufu*), including stomach, small intestine, large intestine, gallbladder, urinary bladder and triple energiser, which are connected by the meridian and work together for the body's functioning (Yin & Zhang, 2006). TCM treatment methods include herbal medicines and diets, which are markedly different from those of Western medicine that surgical operation is commonly used (Lao *et al.*, 2012; WHO, 2001).

The integration of TCM into the national healthcare system has been promoted since the 1980s, with the Chinese government supporting equality in the development of TCM and western medicine (Mossialos *et al.*, 2016; WHO, 2001). In 2014 there were over 40,000 TCM-related institutions (Statistical Information Centre of NHFPC, 2016), and TCM services accounted for around 18% of the total healthcare service provision (Qiu, 2015). A survey of all hospitals in China found that 90% had TCM departments, and TCM outpatient visits made up over 30% of total outpatient visits (Xu & Yang, 2009). The sale of TCM drugs also accounted for about 30% of total pharmaceutical expenditure in 2012, with a particularly higher proportion, 44% of drug sales, in the retail pharmacy sector (Mossialos *et al.*, 2016). While the evidence is limited, it indicates that the majority of the Chinese population believes in TCM, although most prefer to rely on Western medicine treatment rather than TCM treatment when they are unwell (Cheung, 2011; Xu & Yang, 2009).

4.2 Methods

4.2.1 Study area and subjects

The study was carried out in Taiyuan city, the provincial capital of Shanxi Province in central China, between April and July 2016. The total GDP of Shanxi Province ranked 24th of all 31 provinces, autonomous regions and municipalities in Mainland China, and its provincial per capita health expenditure was very close to the national average (Statistical Information Centre of NHFPC, 2016). Taiyuan city is a medium-size city of 3.65 million population (in 2014), with an average development among China's cities (Statistical Information of Shanxi, 2015); it is neither among the most prosperous cities like Beijing or Shanghai, nor the poorest cities such as Guizhou or Gansu Province (Pan & Wei, 2015).

Hospitals (the highest tier is tertiary A hospitals), as well as CHIs (including community health centres and the smaller community health stations) and retail pharmacies, are important parts in Taiyuan city's healthcare system. Therefore, participants were recruited from across these healthcare sites: from two of the city's major tertiary A hospitals (one general and one children's hospital), together with six CHIs (three community health centres and three community health stations) and five retail pharmacies; one potential study site (a CHI) refused. The final sample consisted of 20 providers, including six paediatricians from the two hospitals, six GPs, one from each of the six CHIs, together with four licensed pharmacists and four pharmacy staff from five retail pharmacies (Table 5). No invited participants refused. All the paediatricians and GPs were qualified (physician qualification certificate and occupational

certificate); three of the four licensed pharmacists were qualified with a licensed pharmacist certificate and all of the four pharmacy staff were qualified with a retail certificate.

Table 5 Profile of healthcare providers interviewed regarding parental influences on their behaviour with respect to the use of antibiotics for children

	Sex		Age			Position
	Male	Female	30-39	40-49	50<	
Paediatricians	2	4	3	3	0	Physician-in-charge (middle-level)
GPs	3	3	1	2	3	GPs
Licensed pharmacists	0	4	0	4	0	Licensed pharmacist
Pharmacy staff	0	4	3	1	0	Counter staff

As noted in section 3.3, the recruitment method was adapted to the cultural context of the study to avoid low response rates and social desirability biases (Gobo, 2011; Liu, 2006). Both study sites and participants were therefore enrolled via personal connections and networks. Specifically, the study sites were accessed through the gatekeepers identified through personal networks in the pilot work for this study. They were senior-level staff or administrators in the paediatric department of hospitals, CHIs and retail pharmacies. Most of participants in this study were then introduced by the gatekeepers, with additional participants suggested by those already recruited to the study.

4.2.2 Data collection

Semi-structured interviews were undertaken using three interview guides, for (1) paediatricians and GPs (2) licensed pharmacists and (3) pharmacy staff, respectively. The interview guides (see Table 6 for topics relevant to this study) were informed by evidence from earlier studies and revised in the light of the pilot work. Specifically, the topics focused on exploring factors that influenced providers' behaviour with respect to the use of antibiotics for children, which drew on Sun *et al.* (2015) and Reynolds & McKee's (2009) studies focusing on China, as well as studies exploring factors influencing providers' use of antibiotics in HICs (Brookes-Howell *et al.*, 2012A, 2012B; Butler *et al.*, 1998; Petursson, 2005). All interview guides were translated into Chinese.

Table 6 Interview guides: Topics relevant to influences on healthcare providers' behaviour with respect to the use of antibiotics for children

Interview guide for paediatricians/ GPs
1. (<i>Warm-up question</i>) What are the antibiotics most commonly prescribed here for children?
2. What proportion of children who visit here are prescribed antibiotics as part of their treatment?
3. What is the general diagnosis process for ill children who are prescribed antibiotics?
4. For what symptoms or illnesses do you think a paediatrician/GP might consider prescribing antibiotics for ill children?
5. What symptoms or illnesses do you think would lead a parent to expect the prescribing of antibiotics for their children?
6. What factors do you think usually influence a paediatrician's/GP's antibiotic prescribing

behaviour? Are there any circumstances in which you think a paediatrician/GP would prescribe antibiotics to child patients when they are not necessary?

7. Have you ever experienced or heard about parents who make it clear that they want antibiotics to be prescribed to their child during a consultation?
8. If a paediatrician/GP refused a request for antibiotics from a child patient's parents, do you think that the paediatrician/GP would worry about the dissatisfaction of the parents?
9. Do you think that there is sufficient communication between doctors and parents in consultations in Taiyuan city?
10. Have you ever experienced or heard about parents who refuse an antibiotic prescription for their child during a consultation?

Interview guide for licensed pharmacists and pharmacy staff

1. (*Warm-up question*) What are the antibiotics most commonly sold here for children?
2. For what symptoms or illnesses might you consider using antibiotics for children?
3. Have you ever experienced or heard about parents who want to purchase antibiotics for their ill child without a prescription?
4. Have you ever experienced or heard about retail pharmacies that sell antibiotics without a prescription?
5. Have you ever experienced or heard about licensed pharmacists who prescribe antibiotics for ill children?
6. What factors do you think usually influence a licensed pharmacist/pharmacy staff's behaviour in relation to antibiotic dispensing?
7. Have you ever tried to intervene when you become aware of possible inappropriate use of antibiotics for an ill child by his/her parents?

Interviews were conducted face-to-face by the researcher (female) and, in line with participant preference, recorded by either by audio-recorder or notes and the location of each interview was chosen by participants. Generally, interviews with paediatricians and GPs

were undertaken in their clinics, while interviews with licensed pharmacies and pharmacy staff were undertaken in the retail pharmacies. The interviews ranged in length from 15 to 90 minutes. The content related to participants, such as the background setting and the features participants displayed, were also collected by audio-recording and field notes.

4.2.3 Ethics statement

Ethical approval for this study was granted by the Research Governance Committee in the Department of Health Sciences at the University of York. All ethics related documents were translated into Chinese. Participants were made aware that taking part in the study was entirely voluntary and they were free to withdraw at any time. No incentives were offered and informed consent was obtained from all the participants. No identifying information was collected and all transcripts were stored on a secure server at the University of York.

4.2.4 Data management and analysis

All audio-recorded interviews were transcribed and then translated from Chinese to English; translations were checked for ambiguities in meaning (e.g. Chinese concepts without an English equivalent) by researcher's supervisors, Professor Hilary Graham and Professor Piran White (female and male, respectively) prior to data analysis.

Data from the three participant groups (paediatricians; GPs; licensed pharmacists and pharmacy staff) were analysed separately using framework analysis. Framework analysis is a qualitative data analysis method increasingly used in health research and progresses through a set of stages (Brookes-Howell, 2012A; Furber, 2012; Gale *et al.*, 2013; Srivastava & Thomson,

2009). In the first stage, transcripts were read and re-read, and then, in the second stage, views and experiences that recurred within and across the transcripts were noted and collated into themes to build an overarching framework. The draft framework was discussed with my supervisors. Each transcript was then indexed using the themes in the framework. Common themes emerged across the transcripts, indicating data saturation (Saunders *et al.*, 2018). One set of themes related to parental influences on the providers' antibiotic behaviour; this set of themes recurred across the provider groups (paediatricians; GPs; licensed pharmacists and pharmacy staff). The other major theme – related to organisational influences on providers' antibiotic prescribing behaviour – is discussed in Chapter 5. This study was reported following the COREQ (Consolidated criteria for REporting Qualitative research) guidelines (Tong *et al.*, 2007) (Appendix H).

4.3 Results

The results represent providers' perspectives, which capture the perceptions and accounts of parental influences on their antibiotic-related behaviour from all providers. These influences clustered into broad themes (Table 7). Providers discussed how interactions with parents relating to child antibiotic use was influenced, firstly, by the public's understanding of disease and treatment and secondly, by parental trust and, finally, particularly for providers in CHIs and retail pharmacies, by the need to maintain a good relationship with parents.

Table 7 Themes related to parental influences on healthcare providers' behaviour with respect to the use of antibiotics for children

Theme	Sub-theme
Public's understandings of disease and treatment	Public's understandings of the causes and treatment of disease built around TCM
	Public's understandings of disease
	Public's understandings of antibiotics and antibiotic-related treatment
Parental trust	Distrust of the healthcare system
	Maintaining parental trust and avoid complaints
Maintaining a good relationship with patients	Familiarity
	Business concerns

4.3.1 Public's understandings of disease and treatment

Most (18 out of 20) providers referred to the public's understandings of disease and treatment when describing how they made decisions about prescribing antibiotics for ill children. Here, three sub-themes were evident, relating to the public's understanding of (i) TCM, (ii) disease and (iii) antibiotics and antibiotic treatment. These were discussed respectively by 9, 5 and 18 study participants.

4.3.1.1 The public's understandings of the causes and treatment of disease built around TCM

Parents were seen to understand their children's symptoms through a TCM perspective, and providers commonly communicated with parents during the consultation using TCM terms and theories. Providers said parents believed that being ill is associated with a child's constitution, a TCM term refers to relatively stable features related to the structure and

function of the human body; parents also attributed the causes of different diseases to internal excessive heat (*shanghuo*), being cold²² (*zhaoliang*) or spleen and stomach disorders²³ (*piweishitiao*). In the parents' mind, a child's poor appetite was caused by spleen and stomach disorders, being cold was related to catching a cold and internal excessive heat was related to both catching a cold and inflammation.

'They are most interested in why their child suffers from this disease, and whether [it is because] their child's constitution is like that [more susceptible to this kind of disease] during the communication with doctors.'
[Paediatrician 3]

'For the general public, [they believe] anti-inflammatory drugs should be used, without a doubt, when people are suffering from the internal excessive heat and [therefore having] inflammation.' [Paediatrician 5]

'Sometimes consumers' diseases are caused by the internal excessive heat or the inflammation, so we will recommend some drugs which are helpful against internal excessive heat to them.' [Pharmacy Staff 1]

Parents were seen as understanding that a course of TCM treatment would take longer than one based on Western medicine treatment; Western medicine was seen as providing the faster route to recovery. TCM treatments were regarded by parents as more suitable for chronic or minor diseases and the early stage of treatment and, more generally, for health promotion.

22 This term refers to exposure to a low temperature, which is associated with two, the wind and cold, of the six excesses (Yin & Zhang, 2006).

23 The spleen is one of five yin organs and the stomach is one of six yang organs. They are connected by the meridian and work together for digestion and absorption. The spleen and stomach disorder refers to the unhealthy state associated with the spleen and stomach's dysfunction, which will cause symptoms like poor appetite, nausea, digestive issues, diarrhoea, among others (Yin & Zhang, 2006).

'People nowadays like to use the Western medicine [including antibiotics] just because it can cure the disease faster.' [GP 2]

'Overall, some young patients prefer to use Western medicines as they want to recover quickly, while the aged patients and patients with chronic diseases prefer traditional Chinese medicines more.' [GP 4]

'Sometimes you [paediatrician] consider that the ill child's disease is a viral infection, and he/she only needs some [TCM] drugs to relieve symptoms, such as against internal excessive heat. However, they [parents] will feel that you have not taken the disease seriously. ... They will think that you don't prescribe any [useful] drugs... They will also think that these drugs you prescribed cannot cure diseases. Therefore, they will expect antibiotics that they consider can cure the disease quickly.' [Paediatrician 3]

'We will explain to them [people who are keen on using antibiotics] like 'antibiotics are not good when used too much, why would you always want to use them? For sore throat, you can use some Chinese patent medicines, such as Niu Huang Jiedupian and Niu Huang Qingxinwan, which are helpful against your internal excessive heat'. Then they will accept our recommendations and say like 'that's ok. I will try them and come back for anti-inflammatory drugs tomorrow if they are not useful'. [GP 6]

The providers noted that the co-existence of TCM and Western medicine resulted in parents having different degrees of trust in the two systems. A majority of providers considered that trust in TCM was related to parents' concerns about Western medicine, including their resistance to using antibiotics for childhood illnesses. For example, parents may prefer to use TCM treatments because they consider they have fewer side effects.

'...these parents refuse to use antibiotics very firmly and insist on using oral

traditional Chinese medicines. ... There are some parents who insist on using traditional Chinese medicines; they only accept traditional Chinese medicines.' [Paediatrician 4]

'R: I also know some parents who very much prefer to use Chinese massage when their child is ill.

GP1: Yes, there are [parents who refuse an antibiotic prescription]. They all trust traditional Chinese medicine more.' [GP 1]

'Moreover, most patients prefer to use traditional Chinese medicines considering their few side effects.' [GP 4]

In contrast, there were parents who were seen as not trusting TCM, and therefore refusing to use it and only using Western medicines, such as antibiotics.

'There are various kinds of parents. ...Some parents [only accept antibiotics and] say things like 'my child will never recover unless using anti-inflammatory drugs' based on their previous experience.' [Paediatrician 2]

'There are these kinds of patients who really want to use antibiotics. ... [They think] if you [doctors] don't use antibiotics for them, what other kinds of drugs can be used and cure their diseases? In addition, some patients do not trust traditional Chinese medicine, so they will refuse to use this kind of drugs [Traditional Chinese medicines].' [GP 6]

4.3.1.2 The public's understandings of disease

Most providers referred to public misunderstandings of disease aetiology, progression and treatment. Parents were seen as unable to distinguish between pathogens including bacteria, viruses and mycoplasma, which are all potential causes of inflammation and disease. Further,

they were seen as not understanding that some diseases are self-limiting and, while such conditions resolved spontaneously without specific treatment, symptoms could be expected to persist during this period. At the same time, parents were not clear that treatment is a process in which symptom-relief is not instant but takes time.

'Like when you told them [parents] about bacteria, mycoplasma, and virus, they only know those are pathogens but cannot distinguish the differences between them.' [Paediatrician 1]

'Nowadays, parents always require that their child's disease should be cured very quickly when visiting a doctor. But actually, some diseases are self-limiting and their recovery needs a process; so, some diseases will recover without treatment some days later.' [GP 2]

'They [parents] usually cannot understand and accept the idea that the treatment of diseases is a process. The purpose of visiting a doctor for this kind of parent is to control the disease in their children as soon as possible.' [Paediatrician 1]

Fever – symptoms relating to an excess of heat that occupies a central place within TCM – and inflammation were often used as examples to illustrate these misunderstandings. Providers noted that parents believed childhood fever must be caused by inflammation and should not be tolerated, beliefs seen to contribute to parental demand for anti-inflammatory medication.

'Many parents who visit here believe that there are inflammations as long as their children have a fever.' [Paediatrician 4]

'For herpangina, many parents cannot understand it [the treatment of this

disease]. ...However, the fever of an ill child may still persist even though I have used anti-viral drugs for him/her. ...But the parents will say things like 'why don't you prescribe anti-inflammatory drugs to my child as he/she is feverish? Why you don't use them for him/her?' ... They just believe that the fever is wrong even if they understand that the [treatment of] disease is a process.' [GP 3]

4.3.1.3 The public's understandings of antibiotics and antibiotic treatment

Parental understandings of antibiotics were seen as shaped by wider public perceptions of fever, inflammation and anti-inflammatory medication. Providers pointed a common misunderstanding that antibiotics and anti-inflammatory drugs were the same; antibiotics could and should, therefore, be used to treat any kind of inflammations.

'Parents are not very clear about the concept of antibiotics. The public is not clear about it even now. ...the public still believe that the antibiotic is the same as an anti-inflammatory drug and is used to treat inflammation. Actually, the thing they [the public] call an 'anti-inflammatory drug' is an antibiotic.' [Paediatrician 5]

'It might be a habit of Chinese people that they want to use anti-inflammatory drugs whenever they feel a little uncomfortable. Actually, the 'anti-inflammatory drugs' they refer to are antibiotics. People treat antibiotics as a panacea to cure any diseases.' [Paediatrician 1]

'Some parents will [demand antibiotics]! If you don't use antibiotics for ill children who have, for instance, a fever, their parents will think that you don't care about their child, or they may worry that their child's disease may become worse if antibiotics are not used. ...This is related to our national context.' [Paediatrician 6]

'The first one [symptoms that lead a parent to expect antibiotics for their child] is fever. When the ill child's fever has lasted for several days, their parents will definitely demand antibiotics in order to cure their child.' [GP 5]

Alongside the belief that antibiotics were anti-inflammatory therapies, providers pointed to examples of other public misunderstandings about antibiotics. These included the misperception that, to be effective, drugs, including antibiotics, should be administered intravenously and that a full course of antibiotics was three days.

'For many inpatients in our department, their parents will think that you don't treat their child's disease at all if an intravenous infusion is not used.' [Paediatrician 6]

'Some of them only use antibiotics for three days (one course). For example, if I ask them to use antibiotics for three days, they will stop using antibiotics by themselves after three days and not go for a further consultation. When I ask them why they don't come here for further consultation, they say that they think antibiotics should only be used for three days, so they stop using them after that. They believe three days is a full course.' [Paediatrician 4]

Parents were seen to clearly locate antibiotics within Western medicine, and regard imported antibiotics as superior to domestic ones. In contrast to beliefs about TCM, parents were seen as regarding antibiotics as powerful drugs that could cure any disease and, therefore, should be used for any condition, including minor discomfort. Providers pointed to a widespread belief that antibiotics provided the only effective cure for potentially serious childhood ailments; in consequence, parents were keen to use antibiotics when their child had

symptoms like a fever or cough. In addition, parents thought that antibiotics could cure both minor diseases and serious diseases more quickly than TCM methods.

'People nowadays like to use the Western medicine [antibiotics] just because it can cure the disease faster.' [GP 2]

'Moreover, most parents believe that the imported drugs are much better than the domestic one.' [Licensed Pharmacist 1]

'They [patients] think only antibiotics can cure their diseases quickly. If you don't use antibiotics for them, what other kinds of drugs can be used and cure their diseases?' [GP 6]

'They [parents] usually have no concerns about the harm caused by the abuse of antibiotics. They don't know that.' [Licensed Pharmacist 2]

While some parents were seen as concerned about their child taking antibiotics, this was again linked to their lack of knowledge.

'They [parents] only know that antibiotics have side-effects, some parents even believe that antibiotics are very dangerous. ...But they aren't clear about the specific information about antibiotics at all, such as what side effects antibiotics may lead to.' [Paediatrician 2]

'...They [parents] aren't clear about the specific information about antibiotics at all, such as what side-effects antibiotics may lead to. All their information comes from Baidu [the most widely used search engine in China].' [Paediatrician 2]

'After all, most people don't have the medical-related knowledge. Yes, you will not understand this information [antibiotics and ABR] at all if you don't have a medical background. Even for us who have some medical-related background, we are not clear about it.' [Licensed Pharmacist 1]

'As patients don't have antibiotic-related knowledge, generally, they will listen to the doctor's recommendation and comply with the doctor's prescription. ... If doctors prescribe unnecessary antibiotics several times for patients, the patients will be used to it and they may want to use antibiotics as long as they have similar diseases.' [Pharmacy Staff 2]

4.3.2 Parental trust

Fourteen out of 20 providers described how the importance of parental trust influenced their paediatric antibiotic-related behaviour. Within this broad theme, two sub-themes were apparent: distrust of the healthcare system and, maintaining parental trust and avoiding complaints. These two sub-themes were evident in interviews with, respectively, 9 and 13 providers.

4.3.2.1 Distrust of the healthcare system

Providers spoke about a widespread distrust of China's healthcare institutions among parents. All three groups spoke about parental suspicions that the healthcare services were delivered to generate profits for providers rather than treat patients' diseases. GPs also pointed out that parents did not trust the quality of healthcare services provided by CHIs, such as GPs' professional medical skills, when compared with the hospital.

'And now, there is a phenomenon that patients feel the aim of doctors is to earn money from them, such as bringing money out of the patients' pocket and then putting it into the doctors' pocket. Therefore, patients will feel very suspicious of doctors. Yes, it seems that patients do not trust doctors, yes, a lack of trust.' [Paediatrician 5]

'Moreover, we have found some consumers complained that amoxicillin was becoming less effective. Yes, we have met this kind of situation. So we might recommend other drugs that could be combined with amoxicillin to consumers, but they wouldn't trust us. They think that we just want to sell other drugs.' [Pharmacy Staff 2]

'After all, this is only a community health centre, and trust is a problem. Therefore, the problem in the CHI may be that the trust level is relatively low.' [GP 2]

'Many patients will suspect that the antibiotics [you prescribed for them] are not enough as they feel their disease is serious. Therefore, sometimes they will require you to add other antibiotics to their treatment, or have other requirements.' [GP 3]

4.3.2.2 Maintaining parental trust and avoiding complaints

Considering the widespread public distrust, providers noted their concern for building and keeping the trust of parents. In such circumstances, it was seen as not worth jeopardising parental trust for the sake of an antibiotic prescription.

'When parents become dissatisfied or angry with you due to your refusing [them to prescribe antibiotics], they will challenge you in an aggressive way and the things you said. They will not trust you anymore no matter how you explain (your refusal) to them. I think it is a worse situation than prescribing unnecessary antibiotics to them.' [Paediatrician 1]

'If they [consumers] really want antibiotics, we will ... [sell antibiotics to them; otherwise, they will not trust you and buy antibiotics elsewhere]... You see, there are so many pharmacies in this street alone.' [Pharmacy Staff 1]

The majority of providers noted that their antibiotic-related practice was influenced by concerns about avoiding complaints. This could include prescribing antibiotics for children when their parents continued to demand them and when parents were very anxious, citing concerns about their personal safety and about formal complaints. For instance, some paediatricians described how, when a parent continued to demand antibiotics for their child even after it had been clearly explained that antibiotics were not necessary, they would ask the parent to sign the case report notebook, and then acquiesce to their demand.

‘However, for some parents with a low quality²⁴, if you do not use antibiotics for their children straight forwardly and there is an indication of bacterial infection some days later, they will be very angry and ask you like ‘why you did not use antibiotics on the first day I came here?’ or ‘why you use antibiotics so late?’. That is the problem for us. There is a huge variation in population quality in our country.’ [Paediatrician 1]

‘It [parental demand] will definitely influence me. As the relationship between physicians and patients is very bad, it is a lie if I say there is no influence. It is impossible ... It will definitely cause the dissatisfaction of parents [if you refuse their request] ...It will be best if they can understand [when physicians explain the reasons to them]. For those parents who cannot understand, like they strongly demand you do something and sometimes they even threaten your personal safety, I will ask them to sign their signature [and then do as they demand]. I will also write my advice to them on their case report notebook.’ [Paediatrician 2]

²⁴ ‘Quality’ does not have a direct English-language equivalent. It can encompass a parent’s educational level (so ‘low quality’ can include parents with less education), but it has a broader meaning. The closest equivalent to ‘quality’ may be ‘cultural capital’, a concept that refers to individual assets that come with, but are broader than, education, like knowledge, self-confidence, verbal skills, style of dress etc..

'Yes, and we once had a patient who requested us to infuse penicillin. But we didn't want to give him a penicillin infusion considering [the emergency accidents]. Then he became very angry and abused us...Yes, there are this kind of patients who really want to use antibiotics.' [GP 6]

In addition, providers in retail pharmacies mentioned that satisfying consumers' requirements and, therefore, avoiding risk was regarded as a factor influencing their behaviour with respect to antibiotic dispensing.

'For instance, when consumers cannot get the antibiotics they really wanted, some of them will think that you intentionally refuse their requirements and become very angry. Moreover, they will not trust you no matter how you explain it to them, and they will blame you like 'Such a poor pharmacy!''
[License Pharmacist 4]

'Secondly, I think the customer's wishes [requirements] are another factor [influencing the selling of OTC antibiotics from retail pharmacies]. As they are just retailers, we need to satisfy the consumer's requirements.'
[Pharmacy Staff 2]

4.3.3 Maintaining a good relationship with patients

Providers in CHIs and retail pharmacies additionally described how the importance of maintaining a good relationship with patients influenced their antibiotic-related behaviour with respect to children. Two sub-themes were evident, related to (i) familiarity (discussed by 6 providers) and (ii) maintaining their income stream (discussed by 12 providers).

4.3.3.1 Familiarity

The concept of ‘familiarity’ was mentioned by providers in both CHIs and retail pharmacies. These providers described parents with whom they had built a good relationship as ‘familiar parents’, and believed providers and familiar parents trusted each other more. Familiarity, and the harmonious relationship with parents that it fostered, could help to counter the broader public distrust of CHIs.

‘I think it [the trust] is a key factor [in GP’s working with patients in CHIs]. ...So I think the relationship between GPs in the community health station and patients is very harmonious. The GPs in the community health station also said to me like ‘we are just the community health station and we are not famous doctors. If our attitudes (to patients) are bad, no one will come here’. Yes, so their relationship is very harmonious.’ [GP 5]

Accounts from providers in CHIs and retail pharmacies suggested that their decisions about using antibiotics for children would differ depending on their relationship with the parent. The majority thought they were less likely to prescribe unnecessary antibiotics for familiar parents’ children because these parents trusted them and they could, therefore, be persuaded more easily when they demanded antibiotics. However, one provider (quoted below) said she would be more careful about prescribing antibiotics for new patients, as she did not know their case histories. In addition, most providers in retail pharmacies acknowledged that they would sell OTC antibiotics to familiar parents.

‘For some parents where we know each other very well, I can say that it is possible to persuade them [not to use unnecessary antibiotics] through my own efforts; however, for other parents, I will finally prescribe [unnecessary] antibiotics for their child just because of the psychological comfort it brings...

People who are familiar with you will trust you, so they can accept your suggestions that antibiotics are not needed for their ill child.’ [GP 3]

‘For our community health station, I am not familiar with other medical institutions, I will prescribe antibiotics to the returning patients who have previously had infused antibiotics at this station. For the new patients, I will be more prudent in using antibiotics because I am afraid of some emergency accidents.’ [GP 6]

‘Well, they [consumers] should provide prescriptions if you don’t know them. For consumers who are familiar with you, they can get any drugs they want. To be honest, if I am familiar with you, I will try my best, such as asking for help from other people who also work at the retail pharmacies, to provide the drugs you want. Yes, this is the situation. But for the strangers, they must provide prescriptions.’ [Licensed Pharmacist 1]

4.3.3.2 Business concerns

Most providers in CHIs, particularly in community health stations, noted that maintaining good relationships with patients had an economic dimension. Prescribing antibiotics for ill children was seen to help ensure parents’ re-consultation which, in turn, was essential for the CHI’s survival and therefore for their own livelihood. They expressed concern that not prescribing antibiotics for ill children would lead parents to not come back to their CHI if their child’s health deteriorated or if they became ill again. Additionally, providers in the retail pharmacies mentioned that selling OTC antibiotics was related to maintaining the pharmacy’s income and making a profit. In contrast, none of the hospital-based providers (paediatricians) discussed economic concerns as an influence on their behaviour.

'...if you don't prescribe antibiotics to their ill child this time and they find that their child's fever lasts after visiting here, they will not come back here for their next visit, but they will visit another medical institution or buy antibiotics [from retail pharmacies] by themselves. ...The roles of the retail pharmacy and doctor are different. A doctor needs a good reputation and the trust of patients. Only if you cure the patients this time, will they come back again when they are ill next time. Through this process, you can earn your reputation.' [GP 3]

'For the GPs in the CHIs, one of the main characteristics of them [GPs] is that you must control patients' symptoms, and then patients will come back to your clinic when they become ill again.... if no patients come again, you will not be able to survive.' [GP 6]

'They [consumers] can get OTC antibiotics from other places even though we refused their requirement. So how can we deal with this problem?... Anyway, if you firmly refuse their requirements, they can get them from other retail pharmacies...' [Licensed Pharmacist 4]

'The profit [is the main influence on the sale of antibiotics in the retail pharmacies]. They [sell drugs] as they think it can make a profit, particularly for small-scale retail pharmacies. The sale of antibiotics can also make profits, although the profits might not be very high. But if there are not any profits, no retail pharmacy will do it, particularly for small-scale retail pharmacies.' [Pharmacy Staff 3]

4.4 Discussion

To the researcher's knowledge, this is the first city-based qualitative study in China exploring providers' perceptions of parental influences on their antibiotic-related behaviour. Like other

qualitative studies, the sample size was relatively small and it captured providers' accounts of their behaviours (rather than direct observations of their interaction with parents) (Arroll *et al.*, 2002; Björnsdóttir & Hansen, 2002; Brookes-Howell *et al.*, 2012A; Hart *et al.*, 2006). However, its qualitative approach enabled detailed understanding of provider perspectives pointing to three sets of parental influences – the public's understanding of disease and treatment, parental trust, and the need to maintain good relationships with patients, on their behaviour with respect to the use of antibiotics for children.

The use of TCM theory in interpreting illnesses among Chinese populations has been reported by many studies, including in Mainland China, other Chinese societies such as Taiwan, and overseas Chinese populations (Chung *et al.*, 2014). In my study, providers widely understood and accepted that the public interprets illnesses through a TCM perspective, and this appreciation exerted an influence on clinical decision-making. Various TCM terms as well as TCM theories were noted by providers when they described the consultation with parents, such as internal excessive heat, a term that was commonly used to explain and interpret aetiology and symptoms based on the *yin-yang* – a foundational theory of TCM as well as a Chinese core cultural value (Fan, 2000). As noted by other studies focusing on Chinese populations (Bishop *et al.*, 2009; Lwe-Ting, 2005; Xu *et al.*, 2006), providers in the present study also observed that the public's perceptions of the TCM system was often a mirror opposite of Western medicine system and antibiotics. Combined with a lack of knowledge and misunderstandings of disease aetiology, progression and treatment, including antibiotic treatment, the way in which parents viewed TCM and Western medicine resulted in them

becoming particularly keen or reluctant to use antibiotics for their children. This in turn, influenced providers' behaviour with respect to the use of antibiotics for children.

Parents were seen as distrusting China's medical institutions and having particular suspicions about CHIs when compared with hospitals, a finding in line with Duckett *et al.*'s (2016) national survey. This survey pointed to the significant levels of distrust of providers across the Chinese population, but higher levels (26% of participants reported distrust) of clinics, including CHIs, and much lower levels (6% of participants reported distrust) of hospitals (Duckett *et al.*, 2016). Therefore, as the present study found, maintaining parental trust was a key concern among providers. Bosley *et al.*'s (2018) HIC-based systematic review noted trust as the foundation of a high quality relationship between clinicians and parents, which was as one of the main themes relating to influences on parental attitudes toward antibiotic prescribing in children. Another systematic review of qualitative studies related to the patient-doctor relationship in HICs also referred to trust as one key element (Ridd *et al.*, 2009). Similar to these two systematic reviews (Bosley *et al.*, 2018; Ridd *et al.*, 2009), providers noted the importance of maintaining parental trust for parents' acceptance of their antibiotic prescribing decisions, including the depth of the patient-doctor relationship.

A previous HIC-based study reviewing 133 GPs and 3,918 of their consultations noted that familiarity with patients was helpful with respect to GPs' clinical decision-making process (Hjortdahl, 1992). Another noted it was valuable in saving time in consultations with children; familiarity also influenced the overall use of resources in consultations, such as laboratory tests and the degree of medicine use (Hjortdahl & Borchgrevink, 1991). Similarly, providers

in the present study noted that they were less likely to prescribe unnecessary antibiotics to familiar patients, citing that these patients were easier to persuade. The interview data collected for this study further suggested that less familiarity with the child patient would make providers more careful about prescribing antibiotics; this fits with a qualitative study undertaken in nine EU countries that found that clinicians' antibiotic-prescribing decisions were associated with their familiarity with patients' background medical history and continuity of care (Brookes-Howell *et al.*, 2013).

Studies of antibiotic prescribing decisions focusing on HICs as well as rural China have also pointed to providers' concerns about maintaining good doctor-patient relationships and avoiding complaints and/or loss of patients to other providers (Bjornsdottir *et al.*, 2002; Butler *et al.*, 1998; Hart *et al.*, 2006; Horwood *et al.*, 2016; Tonkin-Crine *et al.*, 2011; Zhang *et al.*, 2016). The widespread concern about avoiding complaints among providers, and the broader public distrust of providers in China, has led to an increase of medico-legal problems and mental stress, as well as physical attacks on providers (Gong & Zhang, 2006; Huang *et al.*, 2012; Zheng, 2006).

The present study also found differences among providers with respect to concerns about maintaining a good relationship with parents to ensure their re-consultation, which was only reported by providers in CHIs and retail pharmacies. Because of the status and funding structure of China's hospitals, hospital-based providers have fewer concerns about losing patients and, in consequence, about their job security and the hospitals' survival (Duckett *et al.*, 2016; Mossialos *et al.*, 2016). The workload and time pressures that result from the high

level of demand for hospital appointments also means hospital-based providers have fewer opportunities to be more familiar with parents and therefore to worry about their lack of ‘familiarity’ (Beam, 2014; Woodhead, 2014; Yin 2017). In contrast, providers in the primary care system have to rely heavily on patient retention, which enables them to provide more medical services and increase their incomes²⁵. These financial pressures have increased as the remuneration from drug sales gradually reduced following the implementation of the EDL and ZUM policies in the 2009 healthcare reform (discussed in section 1.4.3), while the subsidy for basic public health services was also reported as modest (Ding *et al.*, 2013; Zhang *et al.*, 2015). In this study, providers in retail pharmacies mentioned that financial incentives – maintaining the pharmacy’s income and making a profit – were influences on their antibiotic-dispensing behaviour. As well as the importance of drug sales for the income of providers in retail pharmacies, studies have noted the weak implementation of regulations and a shortage of well-trained personnel in retail pharmacies in China (Fang 2014; Fang *et al.*, 2013; Reynolds & McKee, 2009).

Alongside the EDL and ZUM policies, China has introduced a set of new regulations aiming to govern antibiotic prescriptions and sales among providers, including stricter antibiotic use regulations in China (*Administrative Regulations for the Clinical Use of Antibiotics*) (MoH, 2012A). These organisational influences were also reported by providers and will be discussed in Chapter 5. However, although these organisational influences could be potential

²⁵ For providers in the primary care system, their income mainly consisted of the basic salary, remuneration and profits from drug sales, the governmental subsidy for providing public health services and a general fee for providing medical services (Zhang *et al.*, 2015).

explanations of providers' recognition of parental influences on their behaviour, they made no reference to these factors when describing parental influences on their behaviour.

4.5 Conclusions

This study provides important evidence on providers' perceptions of parental influences on their behaviour with respect to antibiotic use for children in a city with a profile typical of Mainland China. As noted by providers, antibiotic prescribing decisions on children are directly influenced by the context in which they work: by the public's understanding of disease and treatment, parental trust and, particularly for providers in CHIs and retail pharmacies, the financial imperative of maintaining good relationships with parents. The study therefore suggests that interventions to reduce providers' paediatric use of antibiotics should address these wider cultural and system-level factors. This includes information campaigns to promote public understanding of antibiotics and the risks of misuse, as well as wider health system reforms. Important here are strengthening the primary care system, in line with the Healthy China 2030 plan (CPC Central Committee & State Council, 2016) and reward systems within the retail pharmacy sector that reward the quality of clinical decision making (Mossialso et al., 2016).

Chapter 5. Healthcare providers' accounts of organisational influences on their behaviour with respect to the use of antibiotics for children

A short version of this chapter has been published in the *Public Health Open Access* (see Appendix I).

5.1 Introduction

As noted in previous chapters, China has been seriously affected by ABR (Xiao *et al.*, 2011), which is driven by its high rates of use and inappropriate use of antibiotics (Currie *et al.*, 2011; Heddini *et al.*, 2009; Zhang *et al.*, 2006). The paediatric use of antibiotics by providers is recognised to be a particular challenge (He, 2012; Jiang *et al.*, 2013; Li & Wu, 2007; Yang & Shi, 2008; Zheng *et al.*, 2008). Drawing on data from interviews, it was noted in Chapter 4 that parental influences, including public understanding of disease and treatment, parental trust, and the need to maintain a good relationship with parents, were identified by providers as influences on their antibiotic-prescribing decisions for children. The literature review-based framework used to frame this study (see Figures 4 and 5 in Chapter 2) suggests that these interpersonal factors operate within the context of wider organisational influences. As the SEFs indicated, organisational influences, such as provider facilities and staffing as well as policies, were indeed evident in the interviews. Concerned about the inappropriate use of antibiotics, the MoH (NHFPC from 2013) introduced antibiotic-related reforms in 2011, mainly including a three-year strategy – *National Special Campaign for the Clinical Use of Antibiotics* – and much stricter regulations on antibiotic prescribing (Xiao & Li, 2013, 2015; MoH, 2012). Wider policies removing financial incentives from drug prescriptions were also introduced in the 2009 healthcare reforms to promote the appropriate use of antibiotics (Mossialos *et al.*, 2016; State Council, 2012A). Therefore, an understanding of organisational influences following the reforms from 2011 on providers' behaviour with respect to the use of antibiotics for children is of importance.

Studies have suggested that the high rates of inpatient antibiotic use decreased in China's hospitals after the implementation of three-year strategy in 2011 (Bao *et al.*, 2015; Hou *et al.*, 2014; Wang & Li, 2015). However, there is little evidence on the organisational factors that influence providers' behaviour with respect to the use of antibiotics. There have been only a few quantitative studies undertaken since the rollout of the antibiotic-related strategy in 2011, and none of these have focused on the paediatric use of antibiotics, regarded as a particular challenge in China. One national study of Chinese county hospitals in rural areas suggested that doctors' attitudes to China's EDL policies were an influence on their antibiotic prescribing behaviour (Wang *et al.*, 2013), but otherwise specific evidence on organisational or institutional influence is sparse. A study in rural areas of Shandong Province reported that financial influences, as well as antibiotic-related training, were related with the prescriptions of antibiotics (Sun *et al.*, 2015). An audit study carried out in a large unnamed Chinese city between 2011 and 2012 also pointed to the important influence of financial incentives on providers' antibiotic-prescribing decisions, even when faced with patients' demands. This study noted that, when prescribing and dispensing were carried out in separate institutions, patients' demands for antibiotics had little influence on physicians' antibiotic prescribing rate; however, the antibiotic prescribing rate dramatically increased from 55% (patients did not demand antibiotics) to 85% (patients demanded antibiotics) when physicians believed that patients would purchase these antibiotics at the hospital pharmacy (Currie *et al.*, 2014).

Only one qualitative study undertaken after 2011 focused on the paediatric use of antibiotics. It explored more general factors related to village doctors' antibiotic-prescribing decisions for children under 15 years with upper respiratory tract infections, and pointed to the lack of

diagnostic test technologies as one of the influential factors (Zhang *et al.*, 2016). However, the marked differences in socio-economic development across China – particularly differences in healthcare resources and health-related policies – mean that rural-based studies may not capture influences on providers' behaviour in urban settings (WHO, 2015C).

The present study was undertaken in 2016, five years after the 2011 three-year strategy was instituted. To the researcher's knowledge, this is the first city-based qualitative study undertaken since 2011 that focuses on organisational influences on providers' antibiotic use behaviour. It aims to explore providers' perceptions of organisational influences on their behaviour with respect to the use of antibiotics for children in a city with a profile typical of Mainland China, with the research question as:

- What are the organisational influences on providers' behaviour with respect to the use of antibiotics for children in urban China?

Study context

As discussed in section 1.3.1, China's healthcare system is composed of three systems – a health supervision system, a health service delivery system, and a health financing system (Chan *et al.*, 2008; WHO, 2015C). The health supervision system, including a range of departments from central to local levels, has oversight of the health service delivery system, and the health financing system is based around three basic medical insurance schemes (Mossialos *et al.*, 2016; WHO, 2015C). In China's health service delivery system, hospitals are the cornerstone (Yip *et al.*, 2012), while the primary care system, including CHIs in urban areas, is weak but growing rapidly (Mossialos *et al.*, 2016; Wang *et al.*, 2012; WHO, 2015C).

Hospitals operate within a 3-tier system, each tier divided into three levels (A, B and C) (Mossialos *et al.*, 2016). The highest tier is the tertiary A hospitals; they are commonly large public hospitals serving large populations, for example a city and its surrounding rural communities. CHIs provide both generalist clinical care and basic public health services (Li *et al.*, 2017), and they can be divided into the government-owned institutions and nongovernment-owned institutions (including hospital operated CHIs, social organization operated CHIs and individual CHIs) (SCOPSR *et al.*, 2006; Statistical information centre of NHFPC, 2016). There are still many unclear points for the primary healthcare system in China, as noted in a review, '*despite the importance of primary health care in China and its recent reforms, there is insufficient knowledge about both the current system and the effect of recent policy changes*' (Li *et al.*, 2017, pp.2584). Most hospitals and CHIs have their own pharmacies and they still dominate China's pharmaceutical sales (Mossialos *et al.*, 2016); however, over recent years, retail pharmacies have become a rapidly growing sector, with an average 20% growth in annual pharmaceutical sales from 1978 to 2009 (Fang, 2014).

As noted above and discussed in section 1.4.2, China introduced a three-year strategy in 2011 with several targets to promote the appropriate use of antibiotics (Xiao & Li, 2013). The strategy was then underwritten by the '*Administrative Regulations for the Clinical Use of Antibiotics*' (Xiao & Li, 2013, 2015) and by guidelines for providers ('*Principles for Clinical Use of Antimicrobials*'). A key feature of this set of policies is that they required physicians' adherence to guidelines that physicians should appropriately prescribe antibiotics following a careful check of patients' clinical presentation and laboratory test results (MoH, 2012A).

The appropriate use of antibiotics are supported by EDL and ZMU policies, and public hospital reform, introduced by the national government in 2009 (Duckett *et al.*, 2016; Mao & Chen, 2015) (discussed in section 1.4.3). In summary, the national essential drug system and ZUM policies required all government-owned primary care institutions to stock national essential drugs and dispense them with no mark-up between wholesale and retail price, and further encouraged other types of healthcare institutions, such as secondary and tertiary hospitals as well as nongovernment-owned primary care institutions, to procure and provide national essential drugs with zero mark-up as a priority and ensure a certain use proportion (NHFPC, 2013). The public hospital reform called for the ZUM policies to be implemented in all county public hospitals and urban public hospitals by 2015 and 2017, respectively (Mossialos *et al.*, 2016; State Council, 2015, 2017). By breaking the link between drug sales and income, these policies are also encouraging the appropriate use of antibiotics (Mossialos *et al.*, 2016).

5.2 Methods

5.2.1 Study area and subjects

Details of the study city are given in Chapter 4, together with information on the recruitment method (section 4.2.1). In brief, participants were recruited across the healthcare sites noted in section 4.2.1 (two hospitals, six CHIs and five retail pharmacies), along with another public secondary A hospital. For the six CHIs, two were government-owned CHIs (one community health centre and one community health station) and four were hospital-owned CHIs (two community health centres and two community health stations), as the core roles of

government-owned institutions are highlighted by Chinese government (Bao, 2007; SCOPSR *et al.*, 2006; State Council, 2009B). Moreover, in the study city, the majority of CHIs are government- or hospital-owned (Wang *et al.*, 2009).

The final sample consisted of 26 providers; no invited providers refused. Along with the 20 providers described in section 4.2.1 of Chapter 4, there were three additional pharmacists from two tertiary A hospitals, one pharmacist from the secondary A hospital, and two pharmacists from the two community health centres, among the six CHIs. These six pharmacists were not included in the analysis of Chapter 4 (parental influences), as parental-related factors were not identified as an influence on their behaviour, which was concerned with the dispensing of antibiotic prescriptions issued by the doctors. The profile of the four hospital-based pharmacists and two community-based pharmacists is shown in Table 8. All of them were qualified with an occupational certificate and two of them also had a licensed pharmacist certificate, along with their occupational certificate. The profile of the other participants has been provided in Chapter 4 (see Section 4.2.1 and Table 5).

Table 8 Profile of healthcare providers interviewed regarding organisational influences on their behaviour with respect to the use of antibiotics for children

	Sex		Age			Position
	Male	Female	30-39	40-49	50<	
Hospital pharmacists	1	3	2	2	0	One chief pharmacist
						One deputy chief pharmacist
						Two pharmacist-in-charge
	0	2	0	2	0	One deputy chief pharmacist

Community pharmacists						One pharmacist-in-charge
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5.2.2 Data collection

Semi-structured interviews were undertaken using four interview guides, for (1) paediatricians and general practitioners (GPs) (2) licensed pharmacists (3) pharmacy staff and (4) pharmacists in hospitals and CHIs, respectively. The interview guides for the first three groups are provided in Chapter 4 (Section 4.2.2); the interview guide used for pharmacists in hospitals and CHIs is summarised in Table 9.

Table 9 Interview guide: Topics relevant to influences on healthcare providers' behaviour with respect to the use of antibiotics for children

Interview guide for pharmacists in hospitals and CHIs
1. (<i>Warm-up question</i>) What are the antibiotics most commonly sold here for children?
2. For what symptoms or illnesses might you consider using antibiotics in children?
3. Have you ever experienced or heard about any parents who want to purchase antibiotics for their ill child without a prescription?
4. Have you ever experienced or heard about any pharmacies who sell antibiotics without a prescription?
5. Have you ever experienced or heard about pharmacists who prescribe antibiotics for ill children?
6. What factors do you think usually influence a pharmacist's behaviour in relation to antibiotic dispensing?
7. Have you ever tried to intervene when you became aware of possible inappropriate use of antibiotics for an ill child by physicians or his/her parents?

5.2.3 Ethics statement

All reasonable ethical guidelines were followed in this research, more detail on this is provided in Chapter 4 (section 4.2.3).

5.2.4 Data management and analysis

Data from four provider groups (paediatricians; GPs; licensed pharmacists and pharmacy staff; hospital-based and CHI-based pharmacists) were transcribed and translated, and then analysed separately using framework analysis. Details of the data management and analysis are given in Chapter 4 (section 4.2.4). The set of themes related to the organisational influences reoccurred across all four provider groups. This study was reported following the COREQ guidelines (Tong *et al.*, 2007) (Appendix J).

5.3 Results

Organisational influences on providers' antibiotic-related behaviour were discussed by all 26 study participants. Providers noted how their behaviour with respect to the use of antibiotics for children was influenced by China's healthcare system and national policies. These influences could be located within domains identified in the SEF (Figures 4 and 5 in Chapter 2) relating to the organisational influence layer and policy layer. Although policy-related influences are located at a higher level of the SEF, they influenced providers through their workplace setting, so were generally perceived as organisational factors by providers. Within these two broad layers, themes relating to China's healthcare system clustered around provider facilities and staffing, financial considerations, and interactions between different

healthcare institutions; themes relating to national policies focused on (i) guidelines and regulations on the use of antibiotics, as well as (ii) the enforcement of regulations and protocols. As located in the SEF, these two sets of themes in the organisational and policy layers are inter-related and interactive; however, they are distinguished here as two broader themes for clarity of presentation, and their interactions are discussed later in the discussion section (section 5.4).

5.3.1 China's healthcare system

Most (25 out of 26) providers described how factors related to China's healthcare system influenced their antibiotic-related behaviour for children. Here, three sub-themes were evident, relating to the influence of (i) provider facilities and staffing, (ii) financial considerations, and (iii) interactions between different healthcare institutions. These were discussed respectively by 23, 16 and 16 study participants.

5.3.1.1 Provider facilities and staffing

Most providers, particularly paediatricians and GPs, noted the important role of diagnostic facilities, such as the laboratory-based blood tests, in their decisions related to using antibiotics for children. Their accounts suggested that blood-testing facilities were widely available in hospitals and community health centres, enabling providers to obtain results quickly. For example, in response to questions about the symptoms or illnesses that make a provider consider prescribing antibiotics for ill children, providers noted:

'We will mainly base decisions [to prescribe antibiotics for ill children] on the blood test results. If the result indicate the ill child's disease is a bacterial infection, we will use antibiotics.' [GP 2]

'For the use of antibiotics, we will either base [the decision] on our clinical experience or the results of antimicrobial sustainability test (AST).' [Hospital Pharmacist 3]

'This...one thing is the blood test. If the [result] of the blood test indicates that the disease is bacterial infection, I will consider [prescribing antibiotics]. This is the most important one.' [Paediatrician 2]

'The blood test is fast. [It takes] half an hour to [get the result], generally. For the mycoplasma test... the result will be available in the afternoon if you do it in the morning, and you will get the result tomorrow if you do it in today's afternoon.' [Paediatrician 2]

While some providers regarded the results of laboratory tests as the most important factor in their clinical decision-making, the limitations of diagnostic facilities were also widely noted. These included the limited availability of test facilities in community health stations and their relatively low accuracy; moreover, there was a delay on obtaining results for some types of tests, which led providers to base their antibiotic prescribing decisions only on their clinical experience.

'I will ask them to do the blood test [in the hospital near us if parents demand antibiotics for their ill child]. For community health centres, they can do the blood test in their centre; however, our community health station cannot do the blood test.' [GP 1]

'As the results of the sputum culture and antimicrobial sustainability test (AST) cannot be obtained as quickly when patients come to the hospital –

for AST, the results can only be obtained after three days, [so] the use of antibiotics in the first three days is all based on the physician's experiences.'

[Hospital Pharmacist 3]

The shortage of other relevant healthcare-related resources, such as emergency equipment and inpatient beds, was also mentioned by providers as a factor influencing their antibiotic prescribing behaviour.

'For the new patients, I will be more prudent in using antibiotics because I am afraid of some emergency accidents. You know, we don't have any equipment for the emergency accidents. ... Yes, so I think this factor will influence me towards prescribing antibiotics.' [GP 6]

'Inappropriate prescriptions are relatively common due to the inadequate health resources. For the paediatric department, although there are not so many child patients and parents now, they will crowd into the whole department in the winter. Therefore, antibiotics like cephalosporin, which should be used two or three times per day by intravenous infusion, cannot be achieved.' [Hospital Pharmacist 1]

Alongside the facilities, a majority of providers pointed to the shortage of health professionals when considering influences on the use of antibiotics for children. Compared with hospitals, there was a lack of well-qualified doctors working at CHIs.

'Moreover, the doctors who are capable will usually not choose to work at the community level.' [Community Pharmacist 2]

The shortage of pharmacists was widespread across all healthcare institutions in the study: providers based in hospitals and CHIs spoke of the need for more hospital-based and clinical pharmacists, while those working in the retail pharmacies focused on the need for more

licensed pharmacists. In addition, the professional quality of pharmacists, particularly licensed pharmacists, was questioned by providers.

'For the lack of pharmacists, I think there is a lack of clinical pharmacists, who can guide the use of drugs. ... Uh...in theory, it should have an influence [on the use of antibiotics], as pharmacists should be more professional than physicians with respect to the use of drugs. But...you know... the [professional] level of our pharmacists cannot reach that high [to guide the use of drugs].' [Hospital Pharmacist 3]

'Uh... the lack of pharmacists [is one factor that influences the sale of antibiotics in the retail pharmacies], as many retail pharmacies actually don't have a pharmacist [working at their pharmacies during opening hours], the pharmacists only rent their Licensed Pharmacist Certificate to the retail pharmacies.' [Licensed Pharmacist 2]

'I don't think they [licensed pharmacists working at retail pharmacies] should be called 'pharmacists'. I think they are equal to the retail staff as they don't have a pharmaceutical background.' [Hospital Pharmacist 1]

Providers regarded the training, both that provided in their own healthcare institutions and by the wider healthcare system, as a factor influencing their antibiotic use decisions.

'Another factor [influencing my antibiotic-prescribing decisions] is the training, for example, the frequency of antibiotic-related training held for us.' [Paediatrician 2]

Additionally, when talking about the sources of antibiotic-related knowledge and awareness, most providers noted that they acquired antibiotic- and antibiotic resistance-related

information as part of their training, including their initial training and post-qualification training. Only a few supplemented this with information through the internet.

'Moreover, I can get the information from my post-qualification training, and many people [pharmacy staff] are studying for the Licensed Pharmacist Certificate. Yes, our retail pharmacy staff will also be trained before we can sell drugs in the retail pharmacies, and antibiotic-related knowledge is included into our training.' [Pharmacy Staff 3]

'In addition, we can update our antibiotic related knowledge through the publicity from the drug companies, and some information on the internet.'
[GP 3]

5.3.1.2 Financial considerations

None of the providers referred to financial pressures and incentives as influences on the use of antibiotics in hospitals, even though the ZMU policies had not been implemented in the hospitals in Taiyuan city.

'Well, I think the commercial interests don't have impacts on the hospital. Our hospital will only earn 15% of the retail price of all drugs as a profit²⁶. ...Moreover, a new policy which stops the hospital from earning money by selling drugs has been introduced in many provinces, and it will be implemented in Shanxi province soon.' [Hospital Pharmacist 1]

²⁶ It was noted in the context section that the essential drugs were only a portion of all drugs stocked and dispensed in hospitals, and ZMU policies were to be implemented in all urban hospitals by 2017. Moreover, Hospital Pharmacist 1 discussed in the later part of the interview that the ZMU policies would be implemented soon in this hospital. Therefore, it is indicated that, at the point when the interview was conducted, the ZMU policies were not implemented in the study city's hospitals and they were continuing to mark up the prices of drugs.

Similar to hospitals, the implementation of EDL and ZMU policies in retail pharmacies were not compulsory during the fieldwork period; however, providers in all four groups noted that financial concerns were major factors contributing to antibiotic-related behaviour in retail pharmacies.

'The [retail] pharmacies are run for [profits]. After all, they are heavily influenced by the market, so they will put making a profit in the first place.'
[Paediatrician 2]

'The profit [is the main influence on the sale of antibiotics in the retail pharmacies]. They [sell drugs] as they think it can make a profit, particularly for small-scale retail pharmacies. The sale of antibiotics can also make profit, although the profit might not be very high. But if there are not any profits, no retail pharmacy will do it, particularly for small-scale retail pharmacies.'
[Pharmacy Staff 3]

In CHIs, although providers working at the government-owned institutions noted that EDL and ZMU policies were fully followed and financial factors were no longer an influence on the use of antibiotics in CHIs, the majority of providers still acknowledged that financial considerations would influence CHI-based providers' antibiotic prescribing decisions, particularly those working in community health stations.

'All drugs we use here belong to the 'National Essential Drug List', we can only use drugs from this list. ... We don't earn profit from it [selling drugs], and the retail price of drugs is equal to the purchase price.' [GP 1²⁷]

²⁷ GP1 worked at a government-owned community health station, and therefore, as discussed in the study context section, all drugs stocked and dispensed in this station were to be essential drugs with zero mark-up.

'They [community health stations] should sell drugs mainly based on the 'National Essential Drug List', but actually, they are mainly based on the amount sold and profit [when selling drugs].' [Community Pharmacist 2]

5.3.1.3 Interactions between different healthcare institutions

Providers from all four groups pointed to an appreciation of how antibiotic use was the outcome of interactions between healthcare institutions. They noted that hospitals remained the main providers in China; this more tightly regulated sector was preferred over CHIs by parents who additionally had access to OTC antibiotics from retail pharmacies. In consequence, hospital-based providers suffered from the pressures of high workloads and limited time, which influenced their communication with parents during consultations and, in turn, their antibiotic-related care of children. Providers in CHIs noted how this hierarchical relationship influenced how they managed demands from parents for antibiotics for their child. This systems-level perspective ran across the interviews.

'Many patients will go directly to the hospital rather than visit a CHI first. Yes, I think the majority of our patients are like that [who will go to the hospital directly]. ... In the busiest period, we can see 50-60 children in one morning. So it will take 3-4 minutes to see one ill child. Yes, as you see 60 children within 4 hours, it takes 4 minutes for each child.' [Paediatrician 6]

'For some parents who insist and require us to use antibiotics for their ill child, as we seldom use antibiotics here, I will say like 'you need to do a test if you strongly require the use of antibiotics'. ...So in this situation, we actually transfer this type of patients to the hospital. Moreover, some parents prefer to use better [more expensive or imported] antibiotics for their child. For this type of parents, I will also ask them to go to the hospital...'

[GP 1]

'As you come here and ask me to diagnose your child's disease, I will make my decision on your child about whether antibiotics are needed; but if you insist on demanding antibiotics, you can choose to go to the higher level hospital.' [GP 2]

Providers considered that the more tightly regulated use of antibiotics in hospitals had worsened antibiotic use in retail pharmacies. For example, some interviewees noted that paediatricians would ask patients to purchase unnecessary antibiotics from retail pharmacies, as prescriptions issued within the hospitals were restricted by regulations. For these interviewees, including some paediatricians and hospital pharmacists, retail pharmacies were regarded as a solution when faced with parents who made strong demands for antibiotics.

'On one hand, these physicians understand antibiotics should not be used for particular diseases and they are afraid of the checks and punishment from the hospital; on the other hand, they still feel it is too risky to not prescribe antibiotics even though antibiotics are not needed. Therefore, they choose to prescribe antibiotics and ask patients to buy them out of the hospital, so the hospital cannot find out about their inappropriate antibiotic prescribing behaviour.' [Hospital Pharmacist 1]

'Exactly, [antibiotic use is regulated less strictly in the retail pharmacies.] [This situation has become worse] after antibiotic use became strictly regulated in the hospital. As there is the standard of antibiotic use frequency in the hospital, [some doctors] will even recommend to patients that they buy antibiotics in the retail pharmacies.' [Hospital Pharmacist 2]

At the same time, most providers in retail pharmacies regarded hospitals and CHIs as the primary source of inappropriate antibiotic-related behaviour. As most consumers did not

have medical-related knowledge, they would strictly follow doctors' prescriptions when purchasing antibiotics in retail pharmacies.

'Therefore, the doctor is the key. As most families only have one child, parents usually bring their child to the hospital [when they are unwell], and most of them will comply with the doctors' suggestions. They will purchase drugs strictly based on the prescriptions no matter what kinds of drugs are prescribed by doctors.' [Licensed Pharmacist 1]

5.3.2 National policies and guidelines

All of the 26 providers referred to national policies when discussing the use of antibiotics for children. Within this broad theme, two sub-themes were evident, relating to guidelines and regulations connected to the use of antibiotics and to the enforcement of regulations. These sub-themes were discussed respectively, by 26 and 25 providers.

5.3.2.1 Guidelines and regulations related to the use of antibiotics

Accounts from providers suggested that they were deeply influenced by the guidelines and protocols launched with the three-year strategy – *'National Special Campaign for the Clinical Use of Antibiotics'*. The guidelines highlighted by this strategy, which relate to prescribing antibiotics based on laboratory test results, were noted by all hospital- and CHI-based providers, as well as one of four licensed pharmacists when describing how they diagnosed disease and made antibiotic prescribing decisions for children.

'Yes, the national government issued some documents for the strategy – such as the 'Principles of Clinical Use of Antibiotics' that particularly focus

on the abuse of antibiotics – to reduce the amount of antibiotics used. ... Yes, I think all these policy-related factors are able to reduce the usage of antibiotics, but this guideline [‘Principles of Clinical Use of Antibiotics’] is the most important one.’ [Hospital Pharmacist 3]

‘Antibiotics should be used when you are infected by bacteria and have [bacterial infection] indications. They [antibiotics] are prescribed drugs, and must be sold with prescriptions.’ [Licensed Pharmacist 4]

Other requirements in the protocols and guidelines, such as restrictions on the proportions of the prescriptions containing antibiotics, the priority given to oral antibiotics over other modes of treatment, and inspections of the use of antibiotics by pharmacists, were also discussed by providers.

‘Moreover, there are restrictions on prescribing antibiotics for us, such as the proportion of prescriptions containing antibiotics.’ [GP 3]

However, providers noted problems with adhering to the guidelines and how this could work against their appropriate use of antibiotics.

‘However, when it is very ambiguous, there will be no guideline for me to identify [whether it is a viral infection or bacterial infection]. ... Yes, so it [using antibiotics] cannot only rely on the guideline. Yes, and it is also related to our organisational system.’ [Paediatrician 4]

‘And sometimes the blood test has a bias. Sometimes we face a confusing situation like we send two samples collected from the same patient at the same time to two different laboratories, and the results are largely different, with one high blood test result and one low blood test result.’ [Paediatrician 5]

Providers in hospitals and CHIs referred to the influence of wider policies, such as EDL and ZMU policies, on the drug lists in their workplace.

'You [hospitals] must purchase the drugs that are covered by the 'National Essential Drug List' as a priority, and you can then choose some special drugs [that are not covered by the list], such as higher-level drugs, through the discussion among [experts in the hospital]. But you must choose drugs from the 'National Essential Drug List' first, yes, this is regulated by the national government.' [Hospital Pharmacist 4]

'All drugs we used here belong to the 'National Essential Drug List', we can only use drugs from this list.' [GP 1]

For providers in retail pharmacies, all of them mentioned the regulations in relation to the fact that pharmacists cannot prescribe drugs; however, only licensed pharmacies noted that antibiotics should only be sold with a prescription when they described how they dispensed antibiotics.

'Antibiotics must be sold with prescriptions and cannot be sold only based on your requirements. Yes, the sale of antibiotics must be based on prescriptions issued by physicians. The situation is the same in retail pharmacies, where antibiotics also must be sold with prescriptions, as it is regulated that all prescribed drugs in retail pharmacies must be sold with prescriptions.' [Licensed Pharmacist 3]

'No [pharmacists cannot prescribe antibiotics for children]. Only physicians can prescribe drugs.' [Pharmacy Staff 4]

Requirements linked to the basic medical insurance schemes (discussed in section 1.3.1) were regarded by some hospital-based providers as factors that influence their antibiotic

prescribing decisions. In contrast, these influences were not discussed by providers in CHIs and retail pharmacies.

'I think another factor [that will have impact on prescribing antibiotics] is the medical insurance schemes, as most people in China have joined a medical insurance scheme, either the social medical insurance [Urban Employee Basic Medical Insurance or Urban Resident Basic Medical Insurance] or the New Rural Cooperative Medical Scheme. They impose restrictions on the drug selection.' [Paediatrician 6]

'We will not be influenced by this factor [medical insurance schemes]. Yes, I don't care about it.' [GP 6]

5.3.2.2 The enforcement of regulations and protocols

All providers discussed the enforcement of antibiotic-related regulations and protocols in healthcare institutions, which suggest it had an influence on their use of antibiotics. From providers' accounts, it appeared that they considered that overall enforcement had improved.

'The antibiotic use standard in the hospital [influences my antibiotic prescribing behaviours]. Every hospital has the antibiotic use standard; [my antibiotic prescribing behaviour is influenced by] whether the enforcement of the standard is good.' [Paediatrician 2]

'Therefore, I think the enforcement of antibiotic use regulations will only become better and better as our government is paying more attention to the problem of abusing antibiotics. ...In fact, antibiotic use has been regulated strictly in the hospital.' [Hospital Pharmacist 2]

However, in line with views expressed with respect to diagnostic facilities (section 5.3.1.1) and financial influences (section 5.3.1.2), providers' accounts suggested that the set of policies issued since 2009 was better enforced in higher-level healthcare institutions, particularly in tertiary A hospitals, compared with CHIs.

'The [enforcement of] antibiotic use regulation is [becoming more stringent] step by step, so the use of antibiotics [in the hospital] might be more regulated than the lower level [of healthcare institutions]. Yes, the higher the level of the medical institution, such as the secondary A or tertiary A hospitals, the more regulated the use of antibiotics will be.' [Hospital Pharmacist 3]

At primary care level, compliance with antibiotic-related regulations was weaker in community health stations than community health centres.

'However, the situation in the community health stations is different [from community health centres]. Although there are also some inspections in community health stations, it is very uncommon. Moreover, the management in the community health stations is relatively...flexible. Like what I said above, as the proportion of prescriptions containing antibiotics is required to be no more than 20%, they can separate non-antibiotic drugs into several prescriptions to tackle the inspections.' [GP 4]

'To be honest, the enforcement of regulations in community health stations and retail pharmacies is still very weak, and these areas are the flaws of [antibiotic use regulations]. But it is very hard to be stringent about the enforcement of regulations in these areas.' [Community Pharmacist 2]

As policies issued by the 2009 health reforms and 2011 antibiotic-related reforms were not mainly focused on retail pharmacies, the enforcement of this set of policies in retail

pharmacies was not noted by providers. However, all providers pointed to the poor enforcement of regulations focusing on retail pharmacies, including problems of selling antibiotics without prescriptions, licensed pharmacists being absent during business hours in retail pharmacies, and the inappropriate prescription of antibiotics by doctors employed in retail pharmacies.

'There are differences [related to the use of antibiotics between different healthcare institutions]. In the hospital's pharmacy and CHI's pharmacy, you cannot buy any drugs without a prescription. ...But for the retail pharmacy... you can get any drugs you want [and you don't need a prescription].' [GP 2]

'But most retail pharmacies cannot go as far as that [selling antibiotics with the prescription], and their enforcement of regulations is relatively not stringent. So consumers can buy whatever they want [including antibiotics] in these retail pharmacies.' [Paediatrician 5]

'Some of them [retail pharmacies] don't have [licensed pharmacists]. Generally, licensed pharmacists will send their certificate to the small-scale pharmacies but not work there. For the large-scale pharmacies, they usually also have a doctor working there. But, honestly, the doctors are very unprofessional, and they dare not diagnose the disease for you.' [Licensed Pharmacy 1]

With respect to the poor compliance with regulations in retail pharmacies, financial incentives and an ineffective supervision system were noted by providers as major factors.

'This kind of situation [selling antibiotics without prescriptions] will not happen in the hospitals, but it might happen in the retail pharmacies. ...But the retail pharmacies are also concerned about their drug sales amount, so they may sell prescribed drugs without a prescription sometimes.' [Hospital Pharmacist 3]

'Moreover, it [selling antibiotics without prescriptions] is because the control and management provided by the [municipal] Food and Drug Administration is not effective, and therefore, OTC antibiotics can still be purchased from retail pharmacies.' [Licensed Pharmacist 2]

In addition, some providers talked about their concerns about the unintended consequences of over-stringent enforcement of antibiotic-related regulations, and noted that the national government should balance various factors in the policy-making process, such as the inequity of healthcare resources in China.

'So if you want to restrict the use of antibiotics strictly, you must forbid their usage in all healthcare institutions, including the private clinics. Yes, only in this way can you control the abuse of antibiotics. However...the national government needs to consider a variety of factors when making a policy. If there are no antibiotics in all clinics, for some villages only having one private clinic [and no other higher-level healthcare institutions], how could a patient be treated when his/her disease is very serious and antibiotics are indeed needed to be used? Actually, this situation is very common [in the rural areas], and our national government also feels very embarrassed about it.' [Community Pharmacist 2]

'However, if the enforcement is too stringent and all retail pharmacies have to be closed, what will the Food and Drug Administration work for? Who will they oversee as all retail pharmacies are closed? Yes, and then the officers in the Food and Drug Administration will lose their jobs too...So this is the situation.' [Licensed Pharmacist 4]

5.4 Discussion

To researcher's knowledge, this is the first city-based qualitative study in China exploring providers' perceptions of organisational influences on their behaviour, with respect to the use of antibiotics for children five years after the introduction of antibiotic-related reforms. As noted in Chapter 4, this study has limitations related to its small sample size and its focus on provider accounts, rather than their actual behaviours. Additionally, it is cross-sectional and, therefore, cannot compare provider views pre and post 2011, but relies on comparisons that providers made about practices prior to and following the reforms. However, its qualitative approach has provided insight into provider perspectives. This study indicates that, in the period after the 2009 health reforms and 2011 antibiotic-related reforms, providers considered a set of organisational influences – healthcare facilities and staffing, financial incentives, and national policies – as factors influencing their antibiotic-related behaviour for children, factors in turn situated in the wider context of China's healthcare system as a whole.

Accounts from providers suggested wide influences of national policies on their behaviour with respect to the use of antibiotics on children, which are related to both the 2009 and 2011 reforms. The three-year strategy – '*National Special Campaign for the Clinical Use of Antibiotics*' – was the most widely reported policy among providers in this study. It also appeared to be the most important organisational influence on providers' behaviour, which is supported by evidence from this study as most providers noted their concerns about this strategy, as well as evidence from another study that the high antibiotic usage in hospitals has been gradually decreasing since its implementation in 2011 (Bao *et al.*, 2015). Additionally,

the interview data from the present suggested that this three-year strategy promoted the adherence to guidelines among providers. In China, the nationwide guidelines related to the use of antibiotics, named '*Principles for Clinical Use of Antimicrobials*', was implemented as early as 2004 by the Ministry of Health; however, studies undertaken prior to the roll-out of this strategy indicated that the guidelines' effects on promoting appropriate use of antibiotics for children were limited (Zhang *et al.*, 2008A, 2008B). Reynolds & McKee's (2009) study even pointed to providers' perceptions of the lack of actual clinical guideline at any level of China's healthcare system. In contrast, as the three-year strategy highlighted this guideline, the important role of this guideline has been widely noted by providers in the present study.

Despite the important influences of the three-year strategy on providers, accounts noted that facilities within the healthcare system influenced providers' use of antibiotics and their compliance with this strategy. Similar to hospital-based providers, providers in CHIs referred to laboratory test results as an important influence on their antibiotic prescribing decisions for children. However, data suggested that the different status and resourcing levels of healthcare institutions in China's healthcare system, for example the constraints relating to the limited diagnostic facilities at the primary care level (particularly for community health stations), resulted in lower compliance with requirements related to laboratory test result among providers in CHIs and, in consequence, different behaviour with respect to the use of antibiotics.

This fits with findings from LMIC focused studies that described how the uncertainty related to the limited availability and unaffordability of diagnostic facilities influenced providers'

antibiotic-related behaviour (Nkengasong *et al.*, 2018; Wilson *et al.*, 2018). For instance, a study conducted in India indicated that GPs prescribed antibiotics when they could not distinguish whether an infection was viral or bacterial, as medical tests were not available at their public facilities and patients could not afford the test from private labs (Kotwani *et al.*, 2010). Similarly, Zhang *et al.*'s (2016) qualitative study undertaken after the reforms also pointed to a lack of diagnostic tests in village clinics in rural China and its influences on doctors' inappropriate antibiotic-prescribing behaviour. The lack of diagnostic facilities at the primary care level has also been noted by a nationwide survey (Li *et al.*, 2017).

Providers in hospitals and CHIs noted the EDL and ZMU policies influenced the institutional drug lists, but few providers noted these policies' influences on their antibiotic-prescribing decisions for children. Moreover, as noted in section 1.4.3, the EDL and ZMU policies are mainly focused on the primary care level, such as CHIs, to reduce incentives to prescribe unnecessary drugs (Li *et al.*, 2017; Xi *et al.*, 2015); however, evidence from the present study suggested financial considerations among providers in different healthcare institutions were not in line with the policies' focus. The interview data indicated that this set of policies seemed to have limited influences in CHIs, with evidence that providers still referred to making profit from prescriptions as a contribution to the use of antibiotics in CHIs, particularly community health stations. In contrast, for providers in hospitals, it appeared that financial incentives had no influence on their antibiotic use, even though the ZMU policies had not been implemented in the hospital of the study city (Taiyuan city).

The present findings relating to these financial policies and incentives' influences at CHIs are similar to studies undertaken in various provinces in China, which noted that the EDL and ZMU policies had no effect on the inappropriate use of antibiotics at the primary care level (Song *et al.*, 2014; Xiao *et al.*, 2016; Yang *et al.*, 2013), even after the introduction of antibiotic-related reforms (Jiang *et al.*, 2015; Wang *et al.*, 2014; Xi *et al.*, 2015). In China, despite increased government subsidies at the primary care level since the 2009 healthcare reforms, the CHIs are still facing problems of underutilization as well as low incomes compared with the hospital (Li *et al.*, 2017), which means that financial concerns were more evident in their decision-making about the use of antibiotics for children. Each patient encounter therefore mattered, with concerns about maximising sales and ensuring patient loyalty. These problems under the healthcare system as a whole conflicted with the aims of the EDL and ZMU policies to reduce the financial incentives. In addition, although the importance of the EDL has been highlighted as one of five pillars of the 2009 healthcare reforms, there is no national pharmaceutical policy framework in China, which strongly challenges EDL's implementation (Mossialos *et al.*, 2016). Together with provider facilities in different healthcare institutions, these findings pointed to how the structure of the healthcare system influenced policies' effects on providers' use of antibiotics.

However, with respect to financial incentives' influences in the hospital, Currie *et al.* (2014) and Sun *et al.*'s (2015) studies, undertaken in 2011-2012 and 2012, respectively, suggested that hospital-based providers' antibiotic-prescribing behaviour was influenced by financial incentives (profits), which were different from the present study. These two studies were undertaken a few years earlier than the present research, when the 2009 healthcare reforms

were at their early stage. Moreover, the complex health supervision system in China, involving horizontal fragmentation across different ministries and vertical fragmentation from central to local governments, as well as the variation in social and economic development across China, is likely to lead to non-transparency in policy-making and differences in policy implementation on the ground (Mossialos *et al.*, 2016).

In the studies of HICs, the organisational factors including high workload and limited time have been identified as factors that influence providers' antibiotic-related behaviour for children in primary care (Horwood *et al.*, 2016; Lucas *et al.*, 2015). These factors were also noted by providers in the present study; however, they appeared to combine in different ways among providers working in different parts of China's healthcare system, pointing to the structure of China's current healthcare system as an overarching factor shaping the organisational influences on providers' antibiotic-related behaviour. In China, the hospital sector has been particularly affected by the rapid increase in patient demand over the last several decades (Mossialos *et al.*, 2016). China has a long-lasting problem of overutilization of hospitals for all forms of healthcare provision; even after the 2009 healthcare reform, hospitals are still the main provider (WHO, 2015C), with higher levels of trust and resources than other primary care institutions in China (Duckett *et al.*, 2016; Li *et al.*, 2017; Mossialos *et al.*, 2016). High patient demand and the resulting pressure on the hospital paediatricians in the present study required them to maintain high levels of patient throughput, a factor that appeared to increase pressures on them to prescribe antibiotics. In contrast to the hospitals, China's primary care system is weak and faces multiple challenges, including a lack of trust from the public, being staffed with less educated workers and being under-resourced

(Li *et al.*, 2017; Mossialos *et al.*, 2016). Moreover, it was reported that patients were not switching from hospitals to the primary care system after the first few years of the 2009 reform (Mossialos *et al.*, 2016). Consistent with this picture, providers in the present study who worked at CHIs did not report the workload pressures described by the hospital paediatricians.

The retail pharmacies are a relatively independent sector in China's healthcare system, mainly supervised by the China Food and Drug Administration and controlled by regulations that are different from those for hospitals and primary care institutions (WHO, 2015C). Similar to studies focusing on the antibiotic distribution in China's retail pharmacies (Fang, 2014; Fang *et al.*, 2013; Jiang *et al.*, 2013), this study found that antibiotics were inappropriately used in retail pharmacies, with poor enforcement of regulations, a lack of licensed pharmacists, and financial incentives that were considered influential factors by providers. In addition, while the data are limited to a small-scale study, they suggest that the tighter enforcement of regulations in hospitals and CHIs as a consequence of the reforms may result in retail pharmacies with poorer enforcement of antibiotic-related regulations becoming relatively more significant as a source of unnecessary antibiotics. Consumers could purchase unnecessary antibiotics prescribed by doctors from the retail pharmacies, or, as no retailers in this study mentioned the need for a prescription, they could get OTC antibiotics from the retail pharmacies when doctors refuse their antibiotic demands. This indicated that the influences of one particular policy were linked with the healthcare system as a whole, transforming the inappropriate use of antibiotics by moving from institutions with stringent enforcement to poor enforcement. Moreover, there were some further concerns about the

adverse consequences of over-stringent enforcement in the whole system, considering the challenges of health inequity (Chan *et al*, 2008), accessibility and affordability of healthcare service for some people (Yip *et al.*, 2012), as well as a lack of health professionals in rural China (Hou & Ke, 2015).

In addition, for all policies discussed above, their enforcement and influences on providers' antibiotic-related behaviour could be relevant to their legal power and severity level. Compared with the relatively poor enforcement of pharmaceutical-related regulations in retail pharmacies, the strong effects of the three-year strategy on the use of antibiotics may be related to the fact that it is underwritten by strict regulation – '*Administrative Regulations for the Clinical Use of Antibiotics*' – which set punishment from an economic penalty to legal liability (Xiao & Li, 2013, 2015). However, the maximum penalty set for the illegal sale of antibiotics in retail pharmacies is only 1,000 CNY (152 USD)²⁸ (CFDA, 2007).

5.5 Conclusions

This study provides evidence of providers' perceptions of organisational influences on their behaviour with respect to the use of antibiotics for children in the period after the 2009 health and 2011 antibiotic-related reforms. From the providers' accounts, the three-year strategy appeared to be the most widely reported organisational factor influencing their antibiotic-related behaviour for children, along with other organisational factors, such as

²⁸ Exchange rate: 1 USD= 6.59 CNY (in 10th Oct 2017)

provider facilities and workload, that differentially influenced providers' behaviour in different institutions. The present study, therefore, points to the importance of strengthening the relatively weaker parts of China's healthcare system – the primary care sector and retail pharmacies – through an increase of government investment and subsidy and launching more effective regulations (Lancet, 2018). Additionally, it indicates the importance of understanding organisational influences in the context of China's healthcare system as a whole, as the interactions and relationships between healthcare institutions were identified as important overarching factors shaping providers' antibiotic-related behaviours.

Together with Chapter 4, this study suggests that providers believed that parental and organisational influences are the two most important factors contributing to their antibiotic-related prescribing behaviours. Having focused in Chapters 4 and 5 on providers' perspectives, Chapter 6 focuses on the other key constituency in decision-making about the use of antibiotics for children, namely parents.

Chapter 6. Parents' accounts of influences on their behaviour with respect to the use of antibiotics for children

6.1 Introduction

Studies of China have pointed to high rates of inappropriate paediatric use of antibiotics in hospitals (Li *et al.*, 2013; Zou *et al.*, 2014), primary care systems (Li *et al.*, 2012; Liang *et al.*, 2011), retail pharmacies (Jiang *et al.*, 2013; Liao *et al.*, 2013) and by parents (Yu *et al.*, 2014), and have identified this inappropriate use as a major contributor to the problem of ABR in China (Currie *et al.*, 2011; Heddinet *et al.*, 2009; Zhang *et al.*, 2006). In line with this evidence, providers and parents were highlighted in the frameworks discussed in Chapter 1 as two particularly important influences on paediatric use and inappropriate use of antibiotics in China. Additionally, drawing on data from the interviews conducted for this study, Chapter 4 suggested that providers believed that parental influences are one of the important factors contributing to their behaviour with respect to the use of antibiotics for children. Parents are the other key constituency in the use and inappropriate use of antibiotics for children, and have influence on providers' decision-making about paediatric antibiotic use, and as such this chapter describes factors influencing parents' behaviour related to the use of antibiotics for their children.

With paediatric use of antibiotics being recognised as central to the wider problem of antibiotic use (Laxminarayan *et al.*, 2013), factors influencing parents' use of antibiotics for their children have been explored by many studies in HICs. In a study of 1,247 parents of children age 0-14 in Italy, a lack of antibiotic-related knowledge was noted as being linked to parental attitudes and habits that resulted in the inappropriate use of antibiotics for children (Bert *et al.*, 2016). Communication and interactions between doctors and parents in the

consultation process have also been widely identified as influencing parents' antibiotic-related decisions (Cabral *et al.*, 2014, 2015, 2016). A systematic review of studies in HICs further noted that, during consultation, parents want antibiotic prescriptions when they believe that antibiotics would be efficacious for their children's current illness or felt pressures from daycare providers or employees, while their reluctance to accept antibiotics was mainly due to their concerns about the side effects of antibiotics (Lucas *et al.*, 2015). It also identified a divergence between the consultation needs of parents and doctors. Parents were more concerned about the medical diagnosis and decision-making process but doctors sought to shorten the consultation and, at the same time, satisfy parents (Lucas *et al.*, 2015).

Compared with HICs, very little is known about influences on parental behaviours with respect to the use of antibiotics for children in Mainland China. Very few (in total five studies) were located through literature search on both English (MEDLINE Ovid) and Chinese (CNKI) databases, and all those studies found were quantitative (Bi *et al.*, 2000; Ding *et al.*, 2015, 2015A; Wang *et al.*, 2017; Yu *et al.*, 2014). Similar to studies of HICs, the role of physicians was noted as an important influence on parents' use of antibiotics for their children in two Chinese studies, undertaken in rural areas of Jiangxi province in 2012 and rural areas of Shandong provinces in 2014, respectively (Ding *et al.*, 2015; Yu *et al.*, 2014). Studies in rural China pointed to a lack of antibiotic-related knowledge among parents (Ding *et al.*, 2015, 2015A; Yu *et al.*, 2014). Ding *et al.* (2015) also indicated a combination of over-expectation, under-expectation and a lack of antibiotic knowledge and noted how this combination of factors could result in parents inappropriately using antibiotics for children. Additionally, socio-demographic characteristics, including the age and number of children and place of

residence, as well as ease of access to antibiotics without prescriptions in retail pharmacies and storing antibiotics at home, were found to be associated with parental medicating behaviour (Yu *et al.*, 2014).

The marked differences in socio-economic development and health-related policies across China mean rural-based studies may not capture the influences on parents' behaviour in urban settings (WHO, 2015C). However, there have been only two studies conducted in urban China exploring factors relating to the parental use of antibiotics for their children. One questionnaire-based study, undertaken over two decades ago, reported that, among 1,459 parents in Hefei city in 1995, the mother's educational level and socio-economic status, the age and severity of diseases of the children, and ease of access to antibiotics from doctors and retail pharmacies all influenced parental medication of antibiotics for children (Bi *et al.*, 2000). The other more recent study of 310 parents in Changsha city similarly noted that the age of the children, parents' educational level and whether the children ever accepted antibiotic prescriptions from doctors significantly influenced the parents' use of antibiotics for their children (Wang *et al.*, 2017).

While these quantitative studies (three in rural and two in urban areas of China) have identified a range of influences on parents' use of antibiotics for children, qualitative studies can shed a unique light on the perceptions held by parents of influences on their antibiotic-related behaviour and contextual understandings (Johnson & Onwuegbuzie, 2004; Pope *et al.*, 2006; Ritchie & Lewis, 2013). However, to date, there has been no qualitative study of parents in China. Considering there are advantages to both types of study and there are very

few studies in China, this chapter seeks to add to both the quantitative and qualitative evidence. Moreover, the diversity of China, and the recent unprecedented economic growth and rapid changes in its healthcare system, underline the need for further studies (Mossialos *et al.*, 2016). Therefore, a multi-method study was conducted to explore the influences on parents' behaviour with respect to the use of antibiotics for their children in China. The aim of the quantitative study was to explore parents' knowledge of antibiotics and ABR, and antibiotic-related behaviour on children, as well as factors influencing their antibiotic-related behaviour. The aim of the qualitative study was to obtain contextual data regarding parents' perceptions of influences on their use of antibiotics for children.

This study builds on the particularly limited evidence in Chinese urban settings by being located in Taiyuan city. As noted in section 4.2.1 of Chapter 4, Taiyuan is a medium-sized city with an average GDP (Pan & Wei, 2015; Statistical Information Centre of NHFPC, 2016); it also has the highest GDP and yearly income of the public enterprise' staff among other cities within Shanxi province (Shanxi Statistics Bureau, 2017; Taiyuan Health Bureau, 2017). The multi-method design involves qualitative and quantitative components that are planned and completed independently, and then their results are brought together (Byren & Humble, 2007; Morse, 2003). By using a multi-method design to collect qualitative and quantitative data, a richer picture of influences on parental behaviour regarding the use of antibiotics for their children can be developed. The main reason to recruit participants from different populations (outpatient clinic and nurseries) relates to the access to study sites for these different components. For instance, semi-structured interviews were found to be unsuitable

for participants in the outpatient clinics due to the crowded and busy clinic setting and the time constraints on parents waiting with their children.

6.2 Qualitative study of parents' perceptions of influences on the use of antibiotics for their children

6.2.1 Research question and method

As noted in the end of section 6.1, the qualitative component aims to obtain contextual data regarding parents' perceptions of factors influencing their use of antibiotics for children, and thus to answer the research question:

- What are the influences on parents' behaviour with respect to the use of antibiotics for children in urban China?

The following sub-sections provided a detailed description of the study design and methods.

6.2.1.1 Study area and subjects

Focus groups were recruited from two of the city's major nurseries: one is a large general nursery providing day-care for children of working parents, the other is an affiliated nursery of a medical university, which provides day-care focusing mainly for children of university staff, as well as others of parents who do not work there. The study sites and participants were recruited by the gatekeepers identified through personal networks in the pilot work (the recruitment process is discussed in section 3.3.3 of Chapter 3). At the beginning of the fieldwork, it was only possible to secure the support of one general nursery through the

researcher's personal networks and only three participants were recruited for a focus group. The other nursery, a university affiliated nursery, was therefore recruited pragmatically at a slightly later stage to recruit more participants and focus groups to maximise the quality of data (Twinn, 1998).

For gaining participants, the heads of the nurseries contacted nursery children's parents through group messaging by mobile phone to elicit interest, and parents who were interested in the study then responded to participate. As the focus groups were planned to be undertaken after the day-care service finished (i.e. when parents came to pick their children), the main difficulty the heads had in gaining parental interest was problems related to the time, for instance, the focus group discussion started too late and was time-consuming. The researcher was not involved in this recruitment process and therefore had no influence on the number of parents recruited or on the social composition of the sample.

6.2.1.2 Data collection

Focus groups are a qualitative data collection method that is increasingly used in health research (Twinn, 1998). They can enable in-depth information on complex topics to be obtained within a short time (White & Thomson, 1995), as well as reduce the pressures and anxiety that participants may experience in one to one interviews (Twinn, 1998). It is a method that has been successfully used in China; Twinn (1988) found that Chinese populations were willing to discuss issues, including sensitive and controversial topics, in groups. This was supported by the finding during the pilot work for this study where parents

would talk more openly in a group with other parents, compared with in an individual interview. Therefore, the focus group method was undertaken with parents in this study.

A topic guide (see a summary of topic guide in Table 10 and the full version in Appendix K) was used for focus group discussion. This was informed by evidence from earlier studies and revised in light of pilot work, and included open questions, such as introductory and probing questions, and a vignette, a short piece of writing about a fictional character or scenario designed for this research (O'Dell *et al.*, 2012). The vignette questions can be helpful in grounding participants' views and accounts of behaviour in particular situations with a more concrete context, and allow participants to discuss issues from a non-personal and less risky perspective (Bryman, 2008; Hughes, 1998). Therefore, the vignette and open questions were used together to examine parents' behaviour regarding their use of antibiotics for children and to explore factors influencing this behaviour. The topic guide was translated into Chinese before the focus groups were run.

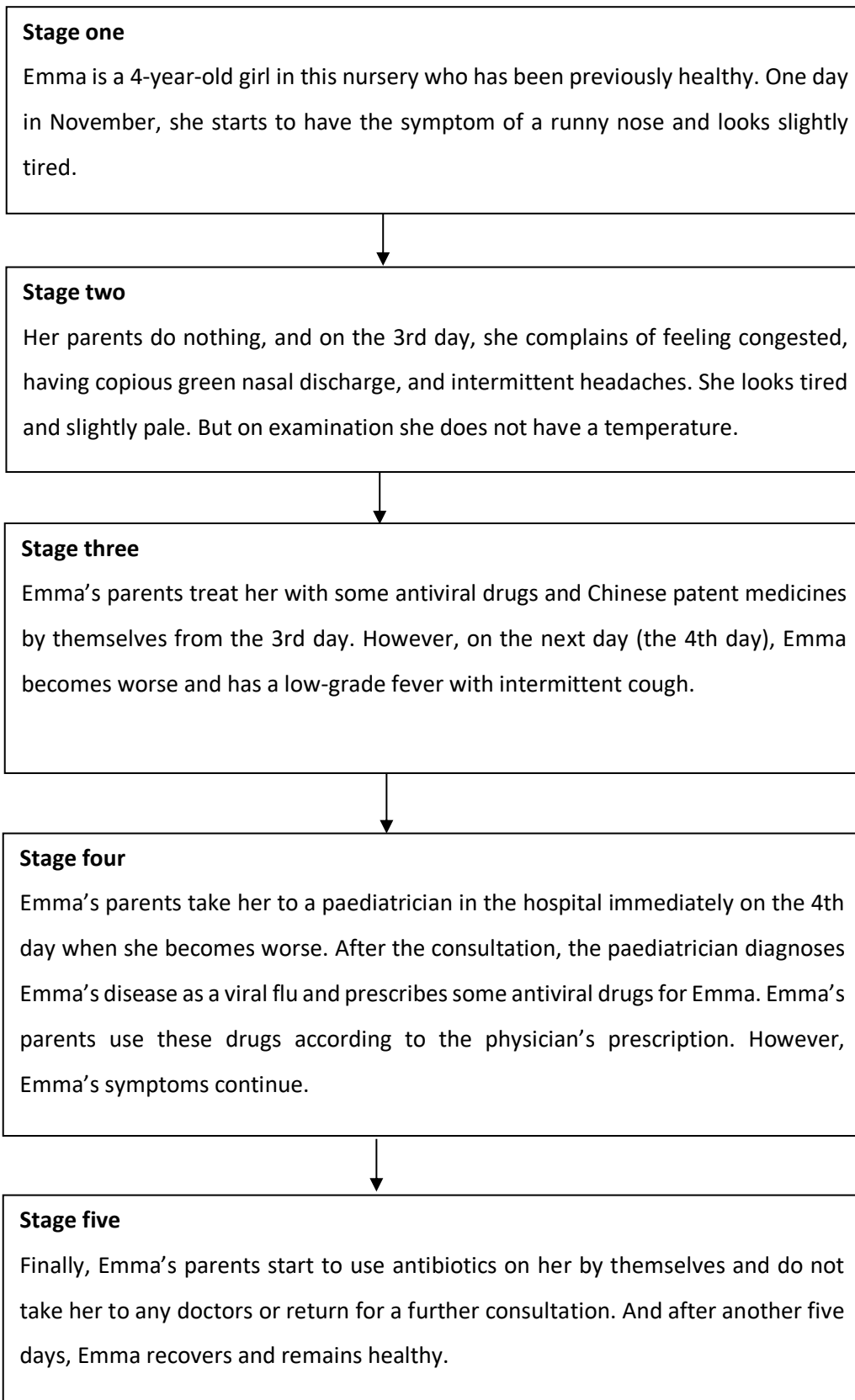
As presented in Table 10, focus group discussions began with a brief introduction to the study, followed by the vignette and open questions. The vignette was a short story about a 4 year-old girl becoming ill and how her parents responded. It included five stages, designed to describe the development of the girl's illness and the symptoms step by step (Figure 8). For the first four stages, participants were asked (i) what the girl's parents should do and (ii) why they thought the girl's parents should respond that way; for the last stage, participants were asked to discuss if they believed that antibiotics cured the 4 year-old girl's illness. For both nurseries, focus groups were carried out in the nursery's classroom. The discussions ranged

in duration from 30 to 120 minutes. All focus group discussions were conducted face-to-face by the researcher and recorded by audio-recorder in June 2016. Field notes were completed after each focus group to record the settings.

Table 10 Summary of focus group topic guide

Main topic areas	Specific Approaches
Introductions	Explain rationale for the study
An overview of parents' behaviour when their children are unwell	Using open questions to ask parents to recall what they did when their children were unwell, including whether antibiotics were used, and why
	Using a vignette to explore parents' understandings and their management of an unwell nursery-aged girl and the factors influencing their behaviour, including their use of antibiotics
Seeking professional care for their children	Showing parents a list of childhood symptoms and exploring parents' expectations of antibiotic prescriptions from doctors
	Using open questions to examine parents' antibiotic-related behaviour during the consultation and the influencing factors, mainly including: Demanding or being reluctant to accept an antibiotic prescription for their children; Communicating with the provider and their satisfaction; Compliance with the antibiotic prescription for their children
Parental medication of antibiotics for their children	Using open questions to seek information on parents' behaviour related to their parental use of antibiotics for their children and the factors affecting this, and the main source of the OTC antibiotics
Antibiotics and ABR	Showing a list of antibiotics' side-effects to parents and exploring their understandings of antibiotics
	Exploring parents' understandings of ABR through open questions
Participant profile and wrap-up	Collecting participants' information through questionnaire and providing an opportunity for parents to ask questions

Figure 8 The vignette used to explore parents' responses to their child's illness



6.2.1.3 Ethics statement

As discussed in Chapter 4 (section 4.2.3), ethical approval was granted by the Research Governance Committee of the Department of Health Sciences at the University of York. Parents who were introduced by the heads of nurseries were informed that taking part in the study was entirely voluntary and they were free to withdraw at any time before they agreed to take part. No incentives were offered to parents and informed consent was obtained from all participants.

6.2.1.4 Data management and analysis

Audio-recorded data were transcribed and then translated from Chinese to English; translations were checked for ambiguities in meaning (e.g. Chinese concepts without an English equivalent) by Professor Hilary Graham and Professor Piran White prior to data analysis. Transcripts were analysed together using framework analysis to identify influences on parents' behaviour with respect to the use of antibiotics for children. The process of data analysis was the same as in the work undertaken for the interviews with providers (discussed section 4.2.4). However, as participants were recruited from two different groups – the affiliated nursery and general nursery – checks were also performed to find whether themes or sub-themes were drawn disproportionately from one group or another during this data analysis process. Reporting this qualitative component adhered to the COREQ guidelines (Tong *et al.*, 2007), and a COREQ Checklist was included in the appendix (Appendix L).

6.2.2 Results

The final sample consisted of three focus groups of 12 parents in total. Two focus groups (focus group 1 and focus group 2 included four and five participants, respectively) were recruited from the medical university affiliated nursery and one (focus group 3 with three participants) from the general nursery. Most participants (n=10) were mothers. Participants all lived in Taiyuan city and were aged 30-39 years. Participants were not asked directly how many children they had, but the response to questions indicated that most parents had one child, although two parents noted that they had two children. Most of their children (13 out of 14) were aged 3-7 years (preschool age). Other participant characteristics are presented in Table 11. This indicates that the sample was well-educated, and more advantaged than the general population in Shanxi province, as well as the nationwide population (Shanxi Statistics Bureau, 2011; State Council Population Census Office & Population and Employment Statistics Division of National Statistics Bureau, 2012), and none lived in a household with an income less than 25,000 CNY. Additionally, as the affiliated nursery delivers day-care services mainly focusing on the university's staff, participants recruited from this nursery had a higher potential to undertake health-related jobs. Among the nine participants within focus groups 1 and 2, three were involved in health-related jobs, with one in focus group 2 working as a doctor and two (one participant in focus group 1 and one participant in focus group 2) working as nurses.

Table 11 Participant profile of focus group study

Participants		Affiliated nursery		General nursery
		FG 1	FG 2	FG 3
Sex	Male	0	2	0
	Female	4	3	3
Educational level	High school/secondary technical college	0	1	0
	College/university	3	2	3
	Postgraduate or above	1	2	0
Occupation	Health-related job	1	2	0
	Non-health related job	3	3	3
Yearly income of household	Below 10,000 CNY	0	0	0
	10,000-24,999 CNY	0	0	0
	25,000-49,999 CNY	1	1	1
	50,000 CNY and above	3	4	2

As the qualitative and quantitative studies were undertaken simultaneously, analysis of the qualitative data was influenced by the analysis of quantitative data. The coding work also drew on the coding framework in Chapter 4 related to providers' perceptions of parental influences on their use of antibiotics for children. All study participants spoke about influences on their behaviour with respect to the use of antibiotics for children. These influences clustered into two broad themes on how parents' use of antibiotics was influenced: firstly, by their understandings of children's disease and treatment and, secondly, by their perceptions of different providers (hospitals, CHIs, retail pharmacies)²⁹. The focus group

²⁹ There were no participants who discussed online sources of antibiotics.

excerpts include comments made by a single participant as part of the focus group discussion as well as capturing short exchanges between focus group members.

6.2.2.1 Parents' understandings of their children's diseases and treatments

All parents referred to their understandings of children's diseases and treatments when describing whether and how they used antibiotics for their children. Here, three sub-themes were evident, relating to (i) their dual use of TCM and Western medicine perspectives, (ii) their understanding of antibiotics and antibiotic treatment, and (iii) their personal experience and understandings of their particular child. These were discussed respectively by 10, 12 and 12 study participants across the three focus groups.

(i) Dual use of TCM and Western medicine perspectives among parents

Parents' accounts indicated their understanding of diseases and treatments is informed by a TCM perspective. In answering the questions in stage one and stage two of the vignette (Figure 8) parents described early symptoms and the causes of diseases using TCM understandings, for example, the retention of food, catching cold or having excessive internal heat. Most parents continued their discussions using TCM-related methods, such as Chinese patent medicines, to treat children's diseases at these early stages.

'The green nasal discharge will be caused by excessive internal heat, and it may combine with catching cold. I will definitely use some drugs that can treat both excessive internal heat and cold. In general, I use the drug called 'Children Cough and Cold Cleaner'. It is a type of oral liquid and can treat

both cold and excessive internal heat. I usually rely more on TCMs and use antibiotics as a supplement when treating children's diseases.' [Affiliated nursery, P4]

'Generally, I will not use anti-inflammatory drugs at the start. I will use some Chinese patent medicines, or ...as she has runny nose which can be connected to the cold, I will use the Paediatric Paracetamol Artificial Cow-bezoar and Chlorphenamine [Western medicine]. Yes, these kinds of drugs are more commonly used by me.' [General nursery, P12]

In response to a vignette question about what they should do if a child's symptoms still persisted after taking drugs (stage four of the vignette in Figure 8), some parents noted that the treatment was a process and the effectiveness of drugs took time. They also said that some diseases were self-limiting and could resolve spontaneously without specific treatment.

'As it is a process when drugs become effective, it is almost impossible that the drugs become effective as soon as you take them.' [Affiliated nursery, P7]

'Yes, in general, the course of flu is around 7 days, and it can be cured by itself.' [Affiliated nursery, P9]

Parents drew on TCM and Western medicine perspectives at the same time; parents integrated both into their understanding and management of child ailments. For example, most parents appeared able to accept both systems; they used TCM treatment for minor diseases or at the early stage of the disease, while turning to Western medicine treatment when the TCM was not effective.

'For instance, when you use TCMs for your children and find they [the

traditional Chinese medicines] do not work very well, you will definitely use antibiotics on your children then.’ [Affiliated nursery, P4]

The accounts also suggested some parents’ degrees of trust in one system was influenced by their views of the other system. For instance, their trust in TCM was related to their concerns about Western medicine, including their resistance to using Western medicine for childhood illnesses. Additionally, parents noted that they decided on the use of TCM or Western medicine³⁰ based on whether their children found the respective drugs easy to use. Overall, the TCM perspective was found to be more prominent among parents from the general nursery and these parents appeared to have a greater degree of trust in TCM.

‘P10: The TCM practitioner said Western medicine can only press the symptoms into your body, which makes you look like you are recovering; however, the actual causes of the disease are still in your body and cannot be cured. For infant massage, you will find your child becomes even worse for the first few days after the treatment; but, actually, it is because the root of the disease is going outside of your body.

P11: Exactly. The TCM practitioner is trying to pull the root of the disease out.

P10: After my child was cured by TCM, I brought him to that clinic every time when he had a cough or retention of food, and I have seldom gone back to the hospital again.’ [General nursery, P10 & P11]

‘I will use TCMs for my children when they are able to swallow them. After

³⁰ In China, the formulation types of TCM are usually liquid while Western medicine’s formulation types are typically capsules, tablets and pills, etc.

all, [unlike the Western medicines that have been shaped as pills], the TCMs are usually hard to take, particularly for children. However, you know, they are all related to some general diseases.’ [General nursery, P10]

(ii) The parents’ understandings of antibiotics and antibiotic treatment

Parental misunderstandings of antibiotics and antibiotic treatment were related to inflammation and anti-inflammatory drugs. Accounts indicated that some parents considered antibiotics and anti-inflammatory drugs the same; antibiotics could and should, therefore, be used to treat any kind of inflammation.

‘But the only cause of fever is inflammation. If the inflammation cannot be controlled, how can the fever be released? ... Yes, [that’s why most parents want to use anti-inflammatory drugs once their child has a fever. Anyway, there is inflammation.’ [General nursery, P10]

Parents’ concerns about antibiotics were found to be mainly related to the side effects; however, most only described these concerns in general terms, for example, that antibiotics are not good for children’s bodies, rather than identifying the specific harms. This, in turn, appeared to be linked to a lack of antibiotic-related knowledge among parents.

‘P5: Nowadays, people only know antibiotics are not good, but they do not know why.

P6: Yes, exactly. For instance, when it refers to the disadvantages of smoking, we all know that smoking is harmful to our lungs. However, we are not clear about which parts of the body antibiotics are harmful to.’ [Affiliated nursery, P5 & P6]

'The side effects of antibiotics are too strong, so I do not want my children to rely on antibiotics too much. Moreover, antibiotics are harmful to the brain, aren't they? I avoid using antibiotics in case they cause any harm in my children, although I understand the probability is extremely low.'
[General nursery, P10]

It was clear that antibiotics were located within Western medicine and, while concerns were expressed about their use (see accounts above), parents believed that antibiotics provided the only effective cure for potentially-serious childhood conditions, particularly those associated with a high temperature fever. In consequence, they would only use antibiotics for serious childhood ailments. Some parents also noted that antibiotics could cure disease more quickly than TCM methods.

'P1: Antibiotics will be used for serious fever, the high temperature fever.'

P2: Yes, that's true.' [Affiliated nursery, P1&P2]

'I will not use anti-inflammatory drugs if she does not have a fever.' [General nursery, P10]

'The Western medicine doctors rely more on antibiotics because the antibiotics' effects come very quickly.' [General nursery, P 11]

With respect to parents' expectations of antibiotic treatment, fever, sore throat and cough were childhood symptoms that most parents considered to lead doctors to prescribing antibiotics; moreover, parents, particularly those with a health-related background,

considered that antibiotics should be prescribed based on the severity of the symptoms or on the results of a blood test. For instance, they noted the need for prescribing antibiotics only when the fever exceeded 38.5 degrees.

'P3: In general, it is fever [that doctors might prescribe antibiotics for children].

P4: Yes, only fever. For other symptoms doctors will not prescribe antibiotics...but if the cough is very serious, the doctors will also suggest using antibiotics.

P3: Exactly. ...For pneumonia, generally, the doctors will prescribe antibiotics for bronchial pneumonia.' [Affiliated nursery, P3 & P4]

'Generally, it is sore throat. For fever, it depends on the particular temperature. Well, [prescribing antibiotics for sore throat] also depends on the degree of swelling of the tonsils, and antibiotics should be used when the tonsils are purulent. With respect to fever, antibiotics are probably used when the temperature exceeds 38.5 degrees. Other symptoms will not [contribute to an antibiotic prescribing decision].' [Affiliated nursery, P8]

Over half the parents pointed to the importance of the blood test in doctors' antibiotic-prescribing decisions and, therefore, their acceptance of this for their children.

'Antibiotics will be used for sore throat when the infection has worsened or the blood test result is high. However, antibiotics will not be used for aches and pains, vomiting or diarrhoea, generally.' [Affiliated nursery, P9]

'P12: I think paediatricians in the Children Hospital, I am not sure other kinds of hospitals' doctors, will ask your child to do a blood test firstly, and they

will decide whether or not to prescribe antibiotics based on the result of the blood test.

P10: Yes, exactly! [General nursery, P10 & P12]

ABR was only discussed in focus groups one and two, where participants were recruited from the affiliated nursery, and, within these two focus groups, mainly by parents with health-related backgrounds. They noted that antibiotics should be used appropriately, for example, completing the full course, to prevent ABR. However, rather than a characteristic of particular bacteria, ABR was perceived to occur in the human body when the individual's responsiveness to antibiotics was lost, a compromised immune function associated with consistently using antibiotics. The response to questions related to ABR also indicated that most parents appeared not to be concerned about this issue.

'I think we should try our best to use antibiotics based on their treatment course, otherwise it will contribute to antibiotic resistance.' [Affiliated nursery, P5]

'I am not familiar with antibiotic resistance with the respect to pharmaceutical areas; however, I think it is like that you will lose the immune function after consistently using a kind of drug. ...Some of them [parents] believe that that frequently using antibiotics does not matter, and they do not know the terrible influences on the human body caused by antibiotic resistance at all.' [Affiliated nursery, P7]

'P12: I have not found any influence [of ABR] on me and my child's daily life. ...antibiotic resistance? They [parents] are not concerned about it very much.'

P10: Yes, yes. [General nursery, P10&P12]

(iii) Parents' personal experience and understandings of their particular child[ren]

Parents, both those with one child and those with two, described how their understandings of children's diseases became better as their children aged. With the accumulation of experience, parents said that they were more likely to parentally-medicate their children with drugs, rather than bring them to visit a provider.

'My child went to the paediatric emergency once when he was six months. We brought him to the hospital because it was the first time he got a fever and we did not have any experience. ...Yes. We definitely chose to go to hospital when [our] child got a fever for the first time.' [Affiliated nursery, P1]

'As I did not have any experience when my children were young, particularly for my first child, I always visited the hospital if she felt a little bit uncomfortable. But now, as they have grown up and their immune systems have become better, I will parentally medicate them with drugs and seldom go to the hospital.' [General nursery, P 11]

Most parents believed the severity of the child's disease was one of the factors that led them to seek professional help. They only visited a provider when their children were seriously ill, such as having a long-lasting high temperature fever; otherwise, they would self-treat their children. Fever, particularly one exceeding 38.5 degrees, as well as serious cough, were the symptoms that were most commonly associated with serious diseases by parents.

'For some minor diseases [we do not need to bring our child to visit a doctor]. We have become a kind of 'family doctor'. ... Yes. It is almost impossible that we go to hospital every time the child feel a little uncomfortable, isn't it?'
[Affiliated nursery, P6]

'It will be based on his/her (particular situation). For instance, if the temperature of his/her fever has reached 38.5 degrees or above, I will choose to bring him/her to visit a healthcare provider; otherwise, I will treat him/her by myself.' [Affiliated nursery, P5]

In addition, some parents noted that their understandings of children's diseases took into account their child's particular characteristics, which differed between children.

'P10: So different children have different situations. Some children may get used to drinking more water, so their symptoms are very likely to be related to a lack of water. For my children, they always drink only a little water every day, so they never suffered from any disease caused by a lack of water.'

P11: Different children have different patterns.' [General nursery, P10 & P11]

6.2.2.2 Providers' influence on parents' use of antibiotics for children

Most parents discussed how (i) familiarity and trust in providers and (ii) the accessibility of treatment influenced their use of antibiotics for children. Therefore, within this broad theme, these two sub-themes were evident, discussed respectively by 12 and 8 parents.

(i) Familiarity and trust in providers as an influence on parents' antibiotic using behaviour

Accounts from all focus groups suggested that trust and familiarity were major factors determining parents' choices in healthcare institutions and providers to visit. Most parents reported that they would bring their children to the hospital when they needed to visit a provider; however, other parents would choose the CHIs or clinics that they were particularly familiar with and regarded as trustworthy.

'I usually visit some trustworthy doctors in the CHIs, and they would give you a satisfactory answer as long as you ask them.' [Affiliated nursery, P1]

'But for me, I prefer to go to some well-known small clinics, such as the one I often visit, as it is familiar with my children's situations, or some other clinics that have a good reputation among the public. I will go to these kinds of clinics first rather than directly go to the hospital under the situation you mentioned above [in stage three of the vignette in Figure 8]. ...Unlike my cousin who trusts the large hospital, I usually go to the clinics if my children's diseases are not serious. I think the most important thing is the sense of trust.' [General nursery, P10]

Parents also noted that they would choose hospitals for serious childhood diseases while visiting the CHIs for minor diseases.

'For some not serious diseases, we just visit some average level doctors [in the private clinics or CHIs] who are familiar with my child's condition. Like the minor cold, we will not go to the hospital. For some very serious diseases that cannot be controlled, such as fever with very high temperature and purulent tonsils, we will consider going to the hospitals.' [Affiliated nursery, P4]

Parents also pointed to the influence of providers on their use of antibiotics for children. Their accounts indicated that all parents complied with the providers during the consultation, including neither demanding, nor being reluctant to accept, antibiotic prescriptions. They noted that they trusted the providers, and the trust in providers was also referenced as a factor that influenced their compliance with antibiotic prescriptions for children.

'P8: Yes, I think I trust the doctor. At least, they will not inappropriately prescribe drugs. ...

P5: Yes. Moreover, as we trust the doctor, we will strictly comply with their prescriptions.' [Affiliated nursery, P5 & P8]

'I think the trust is a very important thing. ...For these trustworthy places [small clinics], I will fully comply with their suggestions and prescriptions, even for taking an injection [that I am normally reluctant to], and they will do the skin test as well before taking an injection.' [General nursery, P10]

(ii) The accessibility of different types of providers

In all focus groups, parents described how their ability to access different sources of treatment – hospitals, CHIs, and OTC antibiotics from retail pharmacies – influenced their behaviour, including treating their children themselves. Parents reported feeling hospitals were overused by patients, with too many waiting for consultations and outpatient clinic environments perceived to expose their children to high infection risks. In consequence, they would medicate their children themselves. In addition, they pointed to retail pharmacies as their main sources of antibiotics for parentally-medicating.

'P8: The environment in the hospital is also not good and safe, and hospital acquired infections are very common and serious. Therefore, we will not go to the hospital as long as we can deal with the diseases.

P6: Yes. They may be infected with other diseases when going to the hospital.' [Affiliated nursery, P6 & P8]

'Because it is very convenient to purchase [OTC] antibiotics from retail pharmacies. We do not need to request antibiotics strongly from doctors.' [Affiliated nursery, P3]

6.2.3 Discussion on qualitative findings

The qualitative data indicated a co-existence of TCM and Western medicine perspectives among parents regarding their children's diseases and treatments, which confirmed findings of providers' perceptions on the public's dual use of two medicine systems in Chapter 4, as well as findings related to a complementary use of TCM and Western medicine in other studies (Chan, 2002; Simpson, 2003). With respect to antibiotics, in line with providers' perceptions noted in Chapter 4, parents clearly located them within Western medicine. Also, according to parents' opposing understandings of TCM and the Western medicine system, antibiotics were particularly expected by parents for potentially-serious childhood diseases such as fever, sore throat and cough. This is similar to findings in other studies that noted that the public's perceptions of the TCM system was a portal opposite of their perception of the Western medicine system (Bishop *et al.*, 2009; Lew-Ting, 2005; Xu *et al.*, 2006). Along with a lack of antibiotic and ABR-related knowledge, such as the association between antibiotics and anti-inflammatory drugs, the qualitative study pointed to how important the way that parents

understand diseases and treatment influenced their behaviour of the use of antibiotics for children.

This qualitative study also indicated that parents' understandings of the severity of children's diseases influenced their antibiotic-related behaviour, including the decisions about parentally-medicating their children or seeking professional help, and their expectation of being prescribed antibiotics as a result of the consultation. For instance, parents' understandings of TCM and Western medicine meant that antibiotics were often regarded as essential for serious diseases and they were particularly expected for conditions that were perceived as potentially serious, such as fever. These symptoms were also identified as childhood conditions associated with an over-expectation for antibiotic prescriptions by rural parents in Ding *et al.*'s (2015) study. Further, through describing how parents became more likely to parentally-medicate antibiotics as their children got older and they understood their children's diseases better, these qualitative data suggested that parents' antibiotic-related behaviour was related to increased personal experience of caring for children. This could also possibly explain the findings from the other two quantitative studies in China where the age and number of children were positively associated with parents' self-medicating children with antibiotics (Bi *et al.*, 2000; Yu *et al.*, 2014), and that parents' antibiotic-related behaviour is driven by their accumulated experience of their children, but not by the experience of antibiotics.

Additionally, the qualitative study indicated that trust and familiarity were key factors regarding providers' influences on parents, including parents' selection of providers and their

compliance with their advice. This is similar to Kerse *et al.*'s (2004) GP waiting room survey of 370 patients, which pointed to familiarity as the significant factor relating to patient compliance. Specifically, in line with Duckett *et al.*'s (2016) study and providers' perceptions of parental trust and familiarity in Chapter 4, parents' accounts suggested that they have higher levels of trust in hospitals, as most parents chose to visit the hospital when their children were ill and for serious diseases. In contrast, familiarity was highly valued by parents when they chose to visit the CHIs, and they only regarded as trustworthy those CHIs and providers with whom they were familiar. The focus group data also pointed to the direct effects of trust on providers' influences on parents, as parents noted that trust was important for their acceptance of providers' decisions, including antibiotic prescriptions, which was also noted in studies in HICs and rural China (Bosley *et al.*, 2018; Brookes-Howell *et al.*, 2013; Jin *et al.*, 2011; Ridd *et al.*, 2009). With the strengthening of primary care highlighted as a key goal in China's annual government work report in 2018, as well as the Health China 2030 plan (CPC Central Committee & State Council, 2016; Lancet, 2018), further research could explore how these organisational changes among China's healthcare system may be influencing parents' use of antibiotics for their children.

6.3 Quantitative study of parents' knowledge of antibiotics and antibiotic resistance and influences on the use of antibiotics for their children

6.3.1 Research question and method

As mentioned above, the aim of the quantitative component was to provide a broader picture of parents' antibiotic-related knowledge and behaviour with their children, as well as to

explore influences on parental behaviour regarding the use of antibiotics for children. The research questions were:

- What are parents' understandings of antibiotics and ABR and how do they use antibiotics with their children? Do parents' knowledge of antibiotics and ABR and their socio-demographic characteristics influence their antibiotic-related behaviours?

Therefore, the objectives of this quantitative part include:

- Describing the profile of participants, which related to their socio-demographic characteristics;
- Accessing parents' knowledge related to antibiotics and ABR based on a series of knowledge-related questions, and then identifying if there were significant differences between the total knowledge score of parents with different socio-demographic characteristics;
- Describing parental behaviour regarding the use of antibiotics for children, with the focus on (i) parents' use of prescribed antibiotics for their children at the most recent occasion (hereafter 'prescribed use of antibiotics', and (ii) whether parents ever used antibiotics without prescriptions for their children (hereafter 'non-prescribed use of antibiotics'); and
- Exploring the influences of parents' knowledge of antibiotics and ABR, and socio-demographic characteristics on parental behaviour regarding the use of antibiotics for children, including (i) prescribed use of antibiotics, and (ii) non-prescribed use of antibiotics.

6.3.1.1 Study area and subjects

As discussed in section 1.3.1.1 of Chapter 1, within hospitals' 3-tier system (Mossialos *et al.*, 2016), the highest tier hospital in China is the tertiary A hospitals, which are commonly large public hospitals serving large populations. Hospitals still deliver most inpatient services and a substantial portion of outpatient services in China, with the general tertiary hospitals being reported as the main provider among all hospitals (Mossialos *et al.*, 2016; WHO, 2015C). Moreover, as this study focused on parents of children, two of the city's major tertiary A hospitals – one general hospital and one children's hospital– were identified as study sites. They were also the study sites for the two qualitative studies discussed above in Chapter 4 and Chapter 5, respectively.

Parents of ill children at the paediatric clinic of those two hospitals were defined as potential participants, in order to obtain a broader sample of parents than was the case in the focus group study (section 6.2) and to more systematically collect parents' knowledge and behaviour related to the use of antibiotics. However, the number of parents recruited in the study was relatively low and the recruiting process was difficult, which related to the time constraints for inviting parents and for parents to complete the questionnaire, as well as the limited resources of the project. Therefore, along with parents of ill children in the paediatric clinics, another group of parents – clinic staff – was pragmatically included to supplement this study. Another reason of including clinic staff in this quantitative survey is that the participants of the qualitative component are recruited from two kinds of nurseries – the medical university affiliated nursery and the general nursery, and some parents from

affiliated university are undertaking health-related jobs. Therefore, like the focus group study that included some parents with health-related background, the clinic staff were the part of questionnaire survey participants that were commonly highly educated with a health-related background, which made the participant composition of the two aspects of the study more similar, and facilitate the comparison and discussion of the aspects together.

Study sites were enrolled via personal connections and networks (discussed in section 3.3.3 of Chapter 3). Specifically, the study sites were accessed through the gatekeepers identified through personal networks in the pilot work for this study. They were senior-level staff or administrators in the paediatric department of these two hospitals. To recruit parents of ill children, after getting access to the paediatric clinic and being allowed to recruit parents of ill children there, the researcher was presented at the outpatient sessions of the paediatric clinics and approached parents waiting for their child to be seen by a doctor. The researcher started the recruiting process with a brief introduction of herself and the study, after being introduced to parents by the senior-level staff, and then invited them to take part. Potential participants who were willing to participate were then recruited in the study. If both parents of an ill child, or more than one family member, were present at the clinics, the mother was invited to take part because, in China, she is the one usually responsible for taking care of family members and is, therefore, likely to have the most detailed information on the child (discussed in section 1.3.2.1). For the other parent group of clinic staff, potential participants were the staff in the outpatient department of the two hospitals and they were made aware of the project by the senior-level staff in the outpatient department.

6.3.1.2 Data collection

A 37-item structured questionnaire was developed based on evidence from earlier studies and revised in light of the pilot work, in order to collect parents' knowledge of and views on antibiotics and ABR, parental behaviour regarding the use of antibiotics for their children, and their socio-demographic characteristics (see a summary of the questionnaire in Table 12 and the full version in Appendix M). In summary, the questions accessing parents' knowledge and views mainly drew on the studies of Yu *et al.* (2014), Lv *et al.* (2014), and Huang *et al.* (2013), which include a number of questions on knowledge of and attitudes toward antibiotics and ABR among parents and Chinese students, respectively. For behaviour-related questions, the present questionnaire also drew on the three above studies, together with another two studies focusing on self-medication with antibiotics among Chinese students (Pan *et al.*, 2012; Zhu *et al.*, 2015). The questionnaire was translated into Chinese before use.

Table 12 Summary of the questionnaire to explore parents' antibiotic-related knowledge, views and behaviour

Main topic areas	Specific approaches
1. Introductions	1.1 Explain rationale for the study and how to complete the questionnaire
2. Parents' knowledge of and views on antibiotics and ABR	2.1 Closed-ended questions Q1-Q8, such as multiple choice questions and Likert-type scales, relating to parents' knowledge of and attitude toward antibiotics and ABR
3. Parents' behaviour when their	3.1 Closed-ended questions (Q9-Q23) relating to parents' behaviour in seeking professional help for their unwell children, including:

<p>children are unwell and using antibiotics</p>	<p>Bringing their children to visit a doctor and the reasons (Q9-Q10); Expecting to or being reluctant to accept antibiotic prescriptions for their children, as well as communication and satisfaction with the doctor during the consultation (Q11-Q19); Parents' compliance with the antibiotic prescriptions for their children (Q20-Q23);</p> <p>3.2 Closed-ended questions (Q24-Q29) relating to parents' behaviour of parental medication of antibiotics on children and the sources of parentally used antibiotics</p>
<p>4. Background information of parents</p>	<p>4.1 Closed-ended questions (Q30-Q37) relating to socio-demographic characteristics of parents, including their gender and age, educational level, occupation, insurance situation, the age of their child, yearly household income, and place of residence</p>

The planned sample size was 100, taking into account the limited access to participants and the length of the questionnaire, which took approximately 25 minutes for parents to complete. A similar sample size has been used in the quantitative component of other health-related multi-method studies (Giblin *et al.*, 2004; Norris *et al.*, 2009; Tofighi *et al.*, 2017). The invitation and recruitment of participants for the questionnaire-based study therefore continued until the sample size reached 100, including both parents at the paediatric clinics and clinic staff. The questionnaire survey was undertaken from April to June 2016. All questionnaires were self-completed by participants immediately after they agreed to take part. Generally, for both hospitals, parents of ill children completed the questionnaire in the waiting areas of the paediatric clinic, while the hospital staff completed it in their offices.

6.3.1.3 Ethics statement

As noted in section 4.2.3 of Chapter 4, ethical approval was granted by the Research Governance Committee of the Department of Health Sciences at the University of York. Both groups of parents (parents at the paediatric clinic and the clinic staff) were made aware that participating in the study was entirely voluntary and they were free to withdraw at any time before they agreed to take part. No incentives were offered to participants and informed consent was obtained.

6.3.1.4 Data management and analysis

Blank questionnaires (n=2), with no answers to any questions, were excluded. Data from the remaining questionnaires (n=98) were entered into Microsoft Excel and SPSS for Windows, version 24.0 for further analysis. Excel was used to describe the patterns of response in each question, and the analysis was then undertaken using SPSS.

Parents' knowledge related to antibiotics and ABR (part 2.1 in Table 12), as well as prescribed use of antibiotics (part 3.1 in Table 12) were further assessed by a scoring scheme, which gave a score of 1 for the correct knowledge or behaviour and 0 for the incorrect/uncertain/missed responses. As shown in Table 13, questions Q2, Q3, and Q6 were used to assess parents' knowledge with a total score ranging from 0 to 11; to analyse prescribed use of antibiotics, a total score (ranging from 0 to 4) was given based on parents' responses to Questions Q20-Q23.

Table 13 Scoring scheme relating parents' knowledge of antibiotics and ABR and prescribed use of antibiotics

Questions used to access the total score of parents' knowledge of antibiotics and ABR	
Questions	Correct response
<p>Q2. Do you think antibiotics are the same as anti-inflammatories?</p> <p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Don't know</p>	No (1 point)
<p>Q3. In your opinion, what kind of diseases are antibiotics used for?</p> <p>(Check more than one if applicable)</p> <p><input type="checkbox"/> Bacterial infections</p> <p><input type="checkbox"/> Viral infections</p> <p><input type="checkbox"/> Others (specify) _____</p> <p><input type="checkbox"/> Don't know</p>	Bacterial infections only (1 point)
Q6 (i). Higher doses of antibiotics result in faster recovery	False (1 point)
Q6 (ii). Lower doses of antibiotics result in fewer adverse effects	False (1 point)
Q6 (iii). Antibiotic treatment should be stopped as soon as symptoms have disappeared	False (1 point)
Q6 (iv). Continuing antibiotic use after the full treatment course will consolidate the effectiveness of the treatment	False (1 point)
Q6 (v). Stopping the antibiotic treatment before the course is completed will increase the risk of antibiotic resistance	True (1 point)
Q6 (vi). The more expensive antibiotics are, the better and more effective they are	False (1 point)
Q6 (vii). Broad-spectrum antibiotics (e.g. Amoxicillin) are more effective because they can kill a variety of bacteria	False (1 point)
Q6 (viii). Antibiotics can only be prescribed by doctors	True (1 point)
Q6 (ix). Antibiotics must be obtained (purchased) with a doctor's prescription	True (1 point)
Questions used to access the total score of prescribed use of antibiotics	
Questions	Correct response

Q20. I used antibiotics on my child in line with the dosage instructions that came with the antibiotics. <input type="checkbox"/> Yes <input type="checkbox"/> No	Yes (1 point)
Q21. My child took the full course of antibiotics. <input type="checkbox"/> Yes <input type="checkbox"/> No	Yes (1 point)
Q22. I needed to give my child antibiotics at dosages higher than instructed. <input type="checkbox"/> Yes <input type="checkbox"/> No	No (1 point)
Q23. I kept unused antibiotics for future use on my child. <input type="checkbox"/> Yes <input type="checkbox"/> No	No (1 point)

Continuous variables were summarised using the median values and quartiles, and categorical variables were reported by the percentage. Differences in total score of knowledge between parent groups with different socio-demographic characteristics were examined by the Mann-Whitney or Kruskal-Wallis tests. Other differences between the group of ill children’s parents and the clinic staff parent group were evaluated by the Mann-Whitney test and chi-square test; Fisher’s exact test was used where the sample size was too small for the chi square test. With respect to influences on parental behaviour regarding the use of antibiotics for their children (including prescribed use of antibiotics and non-prescribed use of antibiotics), Spearman rank correlations were used to examine the association between the total score of prescribed use of antibiotics and total score of parents’ knowledge, and binary logistic regression was used to test the association between whether parents ever use

antibiotics without prescriptions and the total score of parents' knowledge. Binary logistic regression models were also used to examine the associations between whether parents achieved a full score regarding their use of prescribed antibiotics and their socio-demographic characteristics, and between whether parents ever use antibiotics without prescriptions and their socio-demographic characteristics. The reference for regression models was the category of response with the largest number. Missing data were excluded in the analysis. A value of $p < 0.05$ was considered as statistically significant.

6.3.2 Results

A total of 100 questionnaires were collected from 78 parents of ill children and 22 clinic staff, respectively, with a response rate of 82.6% (100 responded from 121 handed out). After excluding two blank questionnaires, the final sample of this quantitative study consisted of 98 participants; most of them (76 out of 98 participants) were parents of ill children at the paediatric clinic of the recruited hospitals during the clinic time, and 22 participants were the clinic staff were parents.

The participant profile is shown in Table 14 with information on missing data presented in Table 15. The majority of participants in the ill children's parent group and all participants in the clinic staff group lived in Taiyuan city. For both groups, most parents were aged 30-39 years. Data also indicated that the samples of both groups, particularly the clinic staff, were well-educated, and were more advantaged than the general population in Shanxi province, as well as nationwide (Shanxi Statistics Bureau, 2011; State Council Population Census Office & Population and Employment Statistics Division of National Statistics Bureau, 2012). In

addition, most participants of both groups lived in a household with an income of more than 25,000 CNY.

Table 14 Participant profile of the questionnaire study

Participants		Number of parents (%)	Number of Clinic staff (%)
Sex	Male	13 (18.1)	11 (50.0)
	Female	59 (81.9)	11 (50.0)
Age	Under 30 years old	12 (16.0)	1 (4.5)
	30-39 years old	21 (68.0)	15 (68.2)
	40 years old and above	12 (16.0)	6 (27.3)
Educational level	Secondary school	9 (12.0)	1 (4.5)
	High school/secondary technical college	14 (18.7)	0 (0.0)
	College/university	42 (56.0)	10 (45.5)
	Postgraduate or above	10 (13.3)	11 (50.0)
Insurance	Only basic medical insurance scheme	63 (86.3)	22 (100.0)
	Only commercial insurance	4 (5.5)	0 (0.0)
	Both basic and commercial insurances	4 (5.5)	0 (0.0)
	None	2 (2.7)	0 (0.0)
Age of child	<3 (pre-nursery)	15 (21.7)	3 (16.7)
	3≤child age<7 (preschool)	31 (44.9)	10 (55.6)
	7≤child age<13 (primary school)	23 (33.3)	5 (27.8)
Yearly income of household	Below 10,000 CNY	8 (11.4)	2 (9.1)
	10,000-24,999 CNY	8 (11.4)	2 (9.1)
	25,000-49,999 CNY	21 (30.0)	6 (27.3)
	50,000 CNY and above	33 (47.1)	12 (54.5)
Place of residence	Taiyuan city	59 (79.7)	22 (100.0)
	Other cities in Shanxi province	8 (10.8)	0 (0.0)
	Rural areas in Shanxi province	6 (8.1)	0 (0.0)
	Other provinces	1 (1.4)	0 (0.0)

Table 15 Missing data across the 98 participants

Socio-demographic characteristics	The number of incomplete answers	
	Parents	Clinic staff
Sex	4	0
Age	1	0
Educational level	1	0
Insurance	3	0
Age of child	7	4
Yearly income of household	6	0
Place of residence	2	0

6.3.2.1 Parents' knowledge of antibiotics and antibiotic resistance

Most participants, including 90.8% of parents in the clinic and 100% of clinic staff, agreed that parents should be given more information related to the use of antibiotics for children. The doctor and pharmacy staff were identified as two major information sources among both parent groups, while the internet and professional training were noted as another important information source. With respect to concerns about ABR-related knowledge, 86.8% of parents in paediatric clinics were worried that their ABR-related knowledge is not sufficient; among clinic staff, 77.3% reported these concerns.

Table 16 shows how parents understand antibiotics as well as their understandings related to the use of antibiotics and ABR, which indicates some widespread misunderstandings. For instance, there were widespread perceptions that antibiotics are the same as anti-inflammatory drugs among both parents of ill children (72.4%) and clinic staff (63.6%).

Approximately half of parents of ill children as well as clinic staff believed that the effectiveness of antibiotic treatment will be consolidated when continuing antibiotic use after the full course; similarly, relatively high proportions of parents of ill children (46.1%) and clinic staff (40.9%) believed that lower doses of antibiotics result in fewer adverse effects. Additionally, among parents of ill children, 86.8% reported that they knew what antibiotics are while less than one-third correctly understood that antibiotics can only be used for bacterial infections (30.3%). Although clinic staff have a significantly higher correct response rate (72.7%) (Chi-square, $\chi^2(1, N = 98^{31}) = 12.84, p < 0.01$) on this question, 27.3% had perceptions that antibiotics can be used for non-bacterial infections.

Table 16 The number and proportion of parents who correctly answered questions related to antibiotics and ABR

Questions	Correct response no. (%)	
	Parents*	Clinical staff*
Q2. Are antibiotics the same as anti-inflammatory drugs?	21 (27.6)	8 (36.4)
Q3. Are antibiotics only used for bacterial infections?	23 (30.3)	16 (72.7)
Q6 (i) Do high doses of antibiotics result in faster recovery?	59 (77.6)	20 (90.9)
Q6 (ii) Do lower doses of antibiotics result in fewer adverse effects?	41 (53.9)	13 (59.1)
Q6 (iii) Should antibiotics treatment be stopped as soon as symptoms have disappeared?	51 (67.1)	21 (95.5)
Q6 (iv) Will continuing antibiotic use after the full treatment course consolidate the effectiveness of the treatment?	39 (51.3)	12 (54.5)

31 There was one missing case, and it was interpreted as an incorrect response on whether antibiotics only treat bacterial infections.

Q6 (v) Will stopping the antibiotic treatment before the course is completed increase the risk of ABR?	41 (53.9)	15 (68.2)
Q6 (vi) The more expensive antibiotics are, the better and more effective they are, is it true?	69 (90.8)	19 (86.4)
Q6 (vii) Are broad-spectrum antibiotic more effective because they can kill a variety of bacteria?	56 (73.7)	18 (81.8)
Q6 (viii) Can antibiotics only be prescribed by doctors?	50 (65.8)	18 (81.8)
Q6 (ix) Can antibiotics only be obtained with a doctors' prescription?	52 (68.4)	19 (86.4)

*Note: *There were 1, 2, 2, 2, 3, 6, 1, 4, 3 and 2 participants missing Q3 to Q6 (ix), respectively, among parents of ill children, and no missing data among clinic staff.*

The median total scores of parents' knowledge related to antibiotics and ABR (calculated based on Table 13) was 6 for the group of ill children's parents and 8 for clinic staff. Moreover, for the group of ill children's parents, the 25th and 75th percentile were 5.25 and 8.00, respectively, and for clinic staff parent group, the 25th percentile was 7.00 and the 75th was 9.00.

For analyses that examined socio-demographic factors associated with differences in parents' knowledge scores, considering the small numbers involved in this quantitative study and the lack of variation on some of the socio-demographic characteristics for the group of clinic staff (e.g. insurance scheme), the two groups were examined together, and a new variable relating to whether the participant is a clinic staff or not was added. There was a significant difference between total scores of knowledge of antibiotics and ABR between clinic staff and parents of ill children (Mann-Whitney, $U = 480.00$, $n_1 = 76$, $n_2 = 22$, $p < 0.01$). Moreover, there was an overall significant difference in total scores of knowledge between parent groups with different educational levels (Kruskal-Wallis, $H = 10.36$, $df = 3$, $p < 0.05$) (Table 17); further

pairwise analysis indicated that there was a significant difference between total scores of knowledge of parents with secondary school educational level and parents with a postgraduate qualification or above (Dunn’s pairwise test, $p < 0.05$).

Table 17 Mann-Whitney and Kruskal-Wallis analysis on the differences between the total scores of knowledge of antibiotics and ABR in parents with different socio-demographic characteristics.

Socio-demographic characteristics	No. of parents	No. of groups	Mann-Whitney U	Kruskal-Wallis H	p value
Gender	94	2	731.50	N/A	0.34
Age of parents	97	3	N/A	2.90	0.24
Education of parents	97	4	N/A	10.36	0.02
Occupations (health-related or not)	98	2	480.00	N/A	<0.01
Insurance scheme (have or not)	95	2	231.50	N/A	0.58
Age of children	87	3	N/A	0.89	0.64
Income of parents	92	4	N/A	7.80	0.05
Place of residence (Taiyuan or other places)	96	2	465.50	N/A	0.15

Mann-Whitney or Kruskal-Wallis test was applied depending on the numbers of groups being compared.

6.3.2.2 Parents’ behaviour regarding the use of antibiotics for their children

Most parents, including 72.4% of parents of ill children and 77.3% of clinic staff, respectively, acknowledged that whether parents seek professional help for their ill children depends on the severity of their condition. During the consultation, potentially-serious childhood conditions – fever (56.6% of parents of ill children and 45.5% of clinic staff) and sore throat (36.8% of parents of ill children and 45.5% of clinic staff) – were widely reported as conditions

that made them expect the doctor to prescribe antibiotics, while antibiotics were less commonly demanded for minor conditions, such as a runny nose (2.6% of parents of ill children and 9.1% of clinic staff). However, despite being keen on antibiotics, only 21.1% of parents of ill children reported that they would demand antibiotics from the doctor for their children. In contrast, 53.9% of them recalled that they had on occasion been reluctant to accept an antibiotic prescription for their children, with their main concerns being ABR (75%) and the side effects of antibiotics (75%). This situation is similar among the clinic staff, in that 31.8% of them reported they would make clear to the doctor their desire for antibiotics to be prescribed, while 63.6% of them have sometimes been reluctant to accept antibiotic prescriptions.

The questions related to prescribed use of antibiotics are shown in Table 18. Most parents in both groups reported using antibiotics at the right dosage and for the full course for their children; however, nearly half (47.4%) of parents of ill children and an even higher proportion (68.2%) in the parent group of clinic staff answered that they kept unused antibiotics for future use on their children. Data analysis indicated that there were no significant differences in prescribed use of antibiotics between the ill children's group and the clinic staff group (Table 19). With respect to the total score of prescribed use of antibiotics (calculated based on Table 13), most parents in both groups had a high score with either 3 or the full score of 4. Specifically, in the group of ill children's parents, there were 48.7% and 32.9% of parents earning a score of 3 and 4, respectively; while 63.6% of clinic staff obtained a score of 3 and 18.2% obtained a score of 4. In addition, the median was 3 for both groups, and this total

score was found to be not significantly different between them (Mann-Whitney, $U = 741.00$, $n_1 = 76$, $n_2 = 22$, $p > 0.05$).

Table 18 The proportion of parents who answered yes in questions related to prescribed use of antibiotics

Questions	The proportion of participants who answered 'Yes' (%)	
	Parents*	Clinic staff*
Q20. I used antibiotics on my child in line with the dosage instructions with antibiotics.	85.5	90.9
Q21. My child took the full course of antibiotics.	86.8	81.8
Q22. I needed to give my child antibiotics at dosages higher than instructed.	6.6	4.5
Q23. I kept unused antibiotics for future use on my child.	47.4	68.2

*Note: *There were 10, 9, 11, 10 participants missing Q20, Q21, Q22 and Q23, respectively, among parents of ill children; there were 2 participants missing Q20-Q23 among clinic staff.*

Table 19 Chi-square tests on differences in prescribed use of antibiotics between parents of ill children and clinic staff

Variables	df	N	χ^2	p value
*Q20. I used antibiotics on my child in line with the dosage instructions with antibiotics	1	86	N/A	>0.99
*Q21. My child took the full course of antibiotics	1	87	N/A	0.13
*Q22. I needed to give my child antibiotics at dosages higher than instructed	1	85	N/A	>0.99
Q23. I kept unused antibiotics for future use on my child.	1	86	2.66	0.13

*Note: *Fisher's exact test was used as there were more than 20% of expected frequency being less than 5 and/or the minimum expected frequency was less than 1 (Field, 2005)*

While the appropriate use of prescribed antibiotics among parents in both groups (see Table 18), data suggested that a majority acknowledged that they have used antibiotics without

prescriptions for their children, which accounted for 73.7% of parents of ill children and 68.2% of clinic staff, and there was no significant difference between parents of ill children and clinic staff (Chi square, $\chi^2 (1, N = 95^{32}) = 0.65, p = 0.42$). The median number of occasions that parents used antibiotics without prescriptions for their children in the last 12 months was 2 and 1 for parents of ill children and clinic staff, respectively. In addition, the majority of parents (65.8% of ill children's parents and 68.2% of clinic staff) had purchased antibiotics without prescriptions, with the retail pharmacies reported to be the main source by both groups.

6.3.2.3 Factors influencing parents' behaviour regarding the use of antibiotics for their children

Based on the objectives of this quantitative study, this section explores the influences of parents' knowledge of antibiotics and ABR and socio-demographic characteristics on their parental behaviours, including (i) prescribed use of antibiotics and (ii) non-prescribed use of antibiotics. Clinic staff and ill children's parents were again grouped together for the following analyses, and a new variable relating to whether the participant is clinic staff or not was added. This was for reason of the small sample size and the lack of variation on socio-demographic factors, as well as the similar patterns of use of antibiotics among the two groups discussed in section 6.3.2.2.

³² There were three missing cases.

(i) Influences of parents' knowledge of antibiotics and antibiotic resistance and their socio-demographic characteristics on prescribed use of antibiotics

The total score of prescribed use of antibiotics (discussed in section 6.3.2.2) and total score of parents' knowledge of antibiotics and ABR (discussed in section 6.3.2.1) were used to assess the association between prescribed use of antibiotics and parents' knowledge. For the total score of prescribed use of antibiotics, among 98 participants, the median was 3. However, no parent obtained a score of 1 and very few parents obtained scores of 0 or 2; on the contrary, 52.0% (51) and 29.6% (29) of parents obtained scores of 3 and 4, respectively. For the knowledge of antibiotics and ABR, the majority obtained scores between 6 to 9, with a median of 7. It was found that there was no significant association between total score of prescribed use of antibiotics and total score of parents' knowledge (Spearman rank correlation, $r_s = 0.03$, $N = 98$, $p = 0.75$).

Additionally, the association between prescribed use of antibiotics and parents' socio-demographic characteristics was analysed by logistic regression. Because of distribution of scores relating to the prescribed use of antibiotics (discussed in section 6.3.2.2, pp.240), this variable, which originally contained five categories, was reduced to two binary categories: parents obtaining a score of 4 and parents obtaining a score of less than 4. There was no relationship between whether or not parents obtained the full score and their socio-demographic characteristics (Table 20).

Table 20 Logistic regression analysis on the association between whether or not parents obtained the full score of prescribed use of antibiotics and their socio-demographic characteristics

Factors	Parents*	
	B (SE)	p value
Gender (male)	-0.27 (0.77)	0.73
Age of parents (years)		
< 30	0.66 (1.06)	0.53
30-39	Reference	
≥ 40	0.03 (0.90)	0.98
Education of parents		
Secondary school	-1.02 (1.41)	0.47
High school/Secondary technical college	0.17 (0.89)	0.85
College/University	Reference	
Postgraduate or above	-2.71 (1.16)	0.02
Occupations (health-related)	-0.49 (0.79)	0.54
Insurance (without insurance schemes)	-1.06 (1.28)	0.41
Age of children (years)		
< 3	-0.25 (0.90)	0.79
3-7	Reference	
7-12	0.08 (0.68)	0.90
Income of parents		
< 10,000 CNY	0.86 (0.97)	0.37
10,000 CNY -24,999CNY	-0.44 (0.91)	0.63
25,000 CNY – 49,999CNY	-0.99 (0.70)	0.16
≥ 50,000 CNY	Reference	
Place of residence (other places than Taiyuan city)	-1.05 (0.86)	0.22

*Note: *There were 18 missing cases*

(ii) Influences of parents' knowledge of antibiotics and antibiotic resistance and their socio-demographic characteristics on non-prescribed use of antibiotics

The binary variable of whether or not parents ever use antibiotics without prescriptions for their children (discussed in section 6.3.2.2) was used to describe non-prescribed use of antibiotics, and to assess associations between non-prescribed use of antibiotics and parent' knowledge and between non-prescribed use of antibiotics and parents' socio-demographic characteristics. The median values of total score of knowledge in groups of parents who never use antibiotics without prescriptions and parents who ever use antibiotics without prescriptions were both 7. The 25th percentile and 75th percentile of the total score of knowledge were 6 and 8 in the group of parents who ever use antibiotics without prescriptions, while they were 6 and 9 of the group of parents who never use antibiotics without prescriptions. In the logistic regression analysis, whether or not parents ever use antibiotics without prescriptions for their children was not associated with their total score of knowledge of antibiotics and ABR (Table 21), nor their socio-demographic characteristics (Table 22).

Table 21 Logistic regression analysis on the association between whether or not parents ever use antibiotics without prescriptions for their children and their knowledge of antibiotics and ABR

Factors	Parents*	
	B (SE)	p value
Knowledge of ABs	-0.12 (0.12)	0.32

*Note: *there were 3 missing cases*

Table 22 Logistic regression analysis on the association between whether or not parents ever use antibiotics without prescriptions for their children and their socio-demographic characteristics

Factors	Parents*	
	B (SE)	p value
Gender (male)	0.93 (0.75)	0.22
Age of parents (years)		
< 30	0.55 (1.09)	0.61
30-39	Reference	
≥ 40	0.20 (0.95)	0.83
Education of parents		
Secondary school	1.62 (1.45)	0.27
High school/Secondary technical college	-1.10(0.92)	0.23
College/University	Reference	
Postgraduate or above	-0.75 (0.77)	0.33
Occupations (health-related)	-0.62 (0.73)	0.40
Insurance (without insurance schemes)	0.20 (1.42)	0.89
Age of children (years)		
< 3	-0.80 (0.84)	0.34
3-7	Reference	
7-12	0.97 (0.74)	0.19
Income of parents		
< 10,000 CNY	-1.09 (0.94)	0.24
10,000 CNY -24,999CNY	0.92 (1.28)	0.47
25,000 CNY – 49,999CNY	-0.16 (0.72)	0.82
≥ 50,000 CNY	Reference	
Place of residence (other places than Taiyuan city)	-0.44 (0.84)	0.60

*Note: *There were 19 missing cases*

6.3.3 Summary

The quantitative study indicated a general lack of knowledge of antibiotics and ABR among parents of ill children and clinic staff. It also pointed to their behaviour regarding the appropriate use of prescribed antibiotics, including the use of antibiotics at the right dosage and the full course for their children, as well as the widespread use of non-prescribed antibiotics with the retail pharmacies being regarded as a main source of OTC antibiotics. In addition, the study identified that parents' prescribed and non-prescribed use of antibiotics were not associated with either their knowledge of antibiotics and ABR, or their socio-demographic characteristics. These findings are discussed together with findings from the qualitative study in the following section.

6.4 Discussion

To the knowledge of the researcher, this is the first multi-method study, as well as the first qualitative study, in China exploring influences on parents' behaviour with respect to the use of antibiotics for their children. The multi-method design, in which the qualitative and quantitative components are undertaken separately and then the results are brought together, draws on the strengths of each method and provides a fuller picture of the study area (Byrne & Humble, 2007; Morse, 2003). Therefore, in this study, the qualitative section described how their understandings of children's diseases and treatment, and of providers influenced their use of antibiotics for their children; the quantitative component further assessed their knowledge related to antibiotics and ABR, and identified that parental use of

antibiotics for their children was not associated with parents' antibiotic and ABR knowledge and their socio-demographic characteristics, such as educational level.

Previous studies focusing on China noted the lack of antibiotic and ABR-related knowledge among parents (Ding *et al.*, 2015, 2015A; Yu *et al.*, 2014). They also discussed the influences of providers, the ease of access to antibiotics, and socio-demographic characteristics, such as the age and number of children as well as the severity of conditions, on parental behaviour regarding the use of antibiotics for children (Bi *et al.*, 2000; Ding *et al.*, 2015, 2015A; Wang *et al.*, 2017; Yu *et al.*, 2014). In line with previous studies' findings, this multi-method study pointed to a lack of knowledge and incorrect beliefs about antibiotics and ABR among parents; it also shed light on the influences of knowledge on parents' antibiotic-related behaviour through both qualitative and quantitative data. Moreover, this study described how parental use of antibiotics for their children was influenced by parents' understandings of their children and trust, and the accessibility of different providers, which is consistent with previous studies and gives deeper discussion based on the insights provided by qualitative data.

The data from the focus groups and the questionnaire suggested that there was a lack of antibiotics and ABR-related knowledge among parents. As noted by studies focusing on rural parents in China (Ding *et al.*, 2015, 2015A; Yu *et al.*, 2014), this quantitative study reported a relatively low correct response rate on antibiotics and ABR-related questions, such as the

difference between antibiotics and anti-inflammatory drugs³³, among parents. The qualitative information further provided detailed information on parents' misunderstandings of antibiotics and ABR. For instance, some of the beliefs held by parents were not based on scientific facts (e.g. that antibiotics are not good for children without being able to identify specific harms), which may result in their expectations or resistance to the use of antibiotics for their children. Also, there were only a few parents who were aware of ABR and were concerned about it, and, consistent with qualitative studies of the general population in rural China (Jin *et al.*, 2011; Reynold & McKee, 2009), these parents believed ABR was the development of resistance to antibiotics in the human body rather than in bacteria. Similar misunderstandings have also been noted by providers in their perceptions on parents' understanding of antibiotics and ABR in Chapter 4.

Similar to the studies of Yu *et al.* (2014) and Ding *et al.* (2015A), this quantitative study indicated that there were no associations between parental use of antibiotics for their children and parents' knowledge of antibiotics and ABR. Additionally, among the two parent groups in the quantitative study, although their antibiotics and ABR knowledge scores were significantly different, there were no differences in their behaviour regarding the use of antibiotics, including parental use of prescribed antibiotics and parentally-medicating with antibiotics for their children.

³³ In China, anti-inflammatory drugs actually include antipyretic-analgesic, anti-inflammatory drugs, and steroid hormones. (Jin *et al.*, 2011)

The lack of an association between parents' knowledge and behaviour may reflect the composition of the study samples as the researcher was sampling just one end of a distribution; there may be found a correlation if this present study samples a broader distribution of educational level . Moreover, based on this qualitative data, this may also be related to parents' understandings of disease and treatment, which influenced their use of antibiotics for children being grounded in both TCM and Western medicine perspectives. Among Chinese populations, the use of TCM theory in interpreting illnesses is widespread (Chung *et al.*, 2014), and, in line with the present findings, a concurrent use of TCM and Western medicine in understanding of diseases and treatment was highlighted (Chan, 2002; Simpson, 2003). However, among Chinese populations, antibiotics were only located conceptually within Western medicine. Therefore, exploring parents' knowledge of antibiotics and ABR, which simply evaluates parents' understandings of disease and treatment through a Western medicine perspective, may be too simplistic an approach to reveal the various influences on their use of antibiotics for children. Further research that takes an integrated TCM and Western medicine perspective into account could be helpful in investigating potential understandings of disease and treatment, including antibiotics, and exploring how these understandings influence parents' antibiotic-related behaviour for their children. Along with Chapter 4 that noted how public's understanding of disease and treatment built around TCM and Western medicine influenced providers' paediatric use of antibiotics , this thesis thus pointed to the important influences of the dual use of TCM and Western medicine perspectives on providers' and parents' behaviour with respect to the use of antibiotics for children in China, which is detailed discussed in the next chapter.

Studies of parents' use of antibiotics focusing on HICs and rural China have pointed to the important influence of providers on parental behaviour (Cabral *et al.*, 2014, 2015, 2016; Ding *et al.*, 2015; Yu *et al.*, 2014). This point was also supported by both the present qualitative and quantitative parental studies, with evidence of high parental compliance with providers' antibiotic-prescribing decisions in the consultation as well as parental compliance in the use of prescribed antibiotics for their children. As Chapter 4 highlighted the parental influences on providers, this thesis described how the interaction between providers and parents influenced their use of antibiotics for children in China (discussed in next chapter).

These qualitative and quantitative parental studies both found that the retail pharmacy was the main source for parents to purchase antibiotics without a prescription, even though this practice has been officially forbidden since 2004 (Fang, 2014). Parents purchasing OTC antibiotics is a long-standing problem in China that has been identified in studies undertaken before prescription requirements were enforced in retail pharmacies (Bi *et al.*, 2000), as well as after the introduction of regulations (Yu *et al.*, 2014). Similar to previous studies (Bi *et al.*, 2000; Jin *et al.*, 2011; Yu *et al.*, 2014), the present data pointed to how ease of access to OTC antibiotics influenced parents' use of them for their children, and therefore the importance of reinforcing the supervision and administration of regulations on dispensing prescribed drugs in retail pharmacies. Additionally, along with the qualitative evidence that described how difficult it could be to get access to professional care in the hospital and the ease of obtaining OTC antibiotics from the retail pharmacy, this study indicated that parents' behaviour of the use of antibiotics was influenced by the healthcare system as a whole. This kind of organisational influences was also noted by providers, which was related to how the

interactions between different healthcare institutions influenced their paediatric use of antibiotics, in the present provider study in Chapter 5.

Finally, the present results suggested that there was a similar lack of knowledge related to antibiotics and ABR in this advantaged group as in the general population (Ding *et al.*, 2015; Jin *et al.*, 2011; Yu *et al.*, 2014). In response to the questions about whether antibiotics and anti-inflammatory drugs are the same, for example, the proportion of parents giving the correct response was 27.6% and 36.4% of the ill children's parents and clinic staff, respectively, similar to the findings of a study conducted with rural parents (34.8%) (Yu *et al.*, 2014). Some of the same types of influences on parents' antibiotic-related behaviour, such as providers, were also found both among general populations and this advantaged group (Ding *et al.*, 2015; Yu *et al.*, 2014). Further, the qualitative part of the present study suggested a co-existence of TCM and Western medicine perspectives in understanding children's diseases and treatment among parents with higher educational backgrounds and incomes. This is consistent with findings from other Chinese populations studies, which found that double (TCM and Western medicine) consulters were more likely to have higher socioeconomic backgrounds (Chung *et al.*, 2007; Chung *et al.*, 2009).

Within the present qualitative study, although all participants were more advantaged than the general population, there were still some differences between participants recruited from the general nursery and from the university affiliated nursery. The differences were similarly found in the quantitative study among parents of ill children and clinic staff. For the qualitative part, parents were recruited from two groups (a general nursery and a medical

university affiliated nursery) with the majority from the affiliated nursery. This led to some sub-themes being drawn disproportionately from one group's accounts. For instance, parents from the general nursery appeared to have greater trust in the TCM, even though the TCM perspective was noted by both groups of parents, while concerns about antibiotic treatment and ABR arose disproportionately from the affiliated (more advantaged) group, particularly for parents with a health-related background. Similarly, within the quantitative study, knowledge of antibiotics and ABR was significantly different between participants from the ill children's parent group and the clinic staff group. A possible explanation for these differences is that participants from the affiliated nursery in the qualitative study and from the clinic staff group in the quantitative study typically had Western medicine-related backgrounds. They may, therefore, be more likely to understand diseases and treatment through a Western medicine perspective, and, because antibiotics are a type of western medicine, to have greater antibiotic-related knowledge. However, as the main aim of this study is to explore factors influencing parents' use of antibiotics for their children, and the sample sizes of both qualitative and quantitative studies were small, it would not be appropriate to draw strong conclusions from these differences. Further research focusing on a larger sample and providing a broader picture would be helpful to investigate these differences in more detail.

Methodological limitations

When interpreting the results, some limitations of the study need to be borne in mind. First, the sample size was small for both the qualitative and quantitative studies. For the qualitative study, the number of focus groups and focus group sizes were small – there were only three focus groups included and the smallest focus group only had three participants. However,

analysis based on the comments of single participants as well as short exchanges between parents indicated that all themes reached saturation, meaning that including more participants would have been unlikely to increase the breadth of qualitative findings. When the findings of the present study were compared with those of other studies focusing on influences on parental use of antibiotics, it was found that the key influences identified in other studies were also noted in present study. There is a risk that in a small focus group, the discussion is dominated by one member and this influences the quality of data (Twinn, 1998). However, Twinn's (1998) study also noted problems in large focus groups related to the potential failure to capture full discussion, as well as the inability to go into greater depth on different topics (Twinn, 1998). Moreover, while there was a more dominant member in one focus group (FG 3), the impact was positive; the dominant member helped to create a friendly atmosphere and guide the discussion.

For the quantitative study, participants were recruited from two groups, and both parent groups, particularly the clinic staff, were based on small samples. This was principally due to the inherent difficulties in recruiting participants and the time constraints imposed by clinic schedules; these restricted the time available to invite parents to be involved in the study and for study participants to complete the questionnaire. Therefore, similar to other mixed method studies with a small sample in the quantitative component (Norris *et al.*, 2009; Tofighi *et al.*, 2017), the sample size of this study was determined by practical constraints rather than by a power calculation. For quantitative studies, a small sample size can lead to problems in interpreting the results, because it does not normally generate reliable or precise estimates (Field, 2005; Hackshaw, 2008). Nonetheless, the quantitative component did meet the study's

aim of describing parents' antibiotic knowledge and their antibiotic-using patterns for children in a broader group. Moreover, being an exploratory study, findings from the present study mainly focused on informing larger studies rather than generating firm conclusions. Therefore, in the analysis of the statistical results, such as associations between parents' antibiotic and ABR-related knowledge and their antibiotic-use behaviours, no strong conclusions were based on the results; instead, the potential reasons of yielding certain results were discussed and suggestions for further research were provided.

Additionally, there are limitations related to pragmatically recruiting the group of clinic staff alongside parents of ill children in the sample. As the socio-demographic characteristics, such as educational level and insurance, between clinic staff and ill children's parents were very different, this study's analysis was based on two different kinds of parent groups rather than parents of ill children only, which is different from the initial goal of the study. Moreover, although, for most part, these two groups were analysed separately, they were examined together in regression models because of the small sample size of both groups and the lack of variation on some predictors (Field, 2005), which would also decrease the reliability of the regression results.

Secondly, rather than representing the general population of parents in China, the study is based on data from relatively socio-economically advantaged parents. This is a consequence of the selection of study sites and potential participants. First, as mentioned above in section 4.1, the study city is more advantaged than the wider Shanxi province with respect to residents' incomes. Moreover, in China, the common situation is that parents with higher

incomes would send their children to the nursery while poorer parents may take care of their children at home. As the study sites for the qualitative study were two major nurseries in the city, including one university-affiliated nursery, potential participants are very likely to have higher educational levels and, therefore, higher incomes than the general population. For the quantitative study, clinic staff working at the paediatric department in the hospital, who usually have a higher educational level than the general population of parents, were recruited. In consequence, the sample of this study was relatively advantaged and many participants in both components of the study also worked in the healthcare sector and had a health-related background, including three of the 12 focus group participants and 22 of the 98 survey respondents. Along with the small sample size, these factors therefore limit the wide generalisation of the findings. For instance, among the advantaged groups, this study pointed to some types of understandings and behaviour related to the appropriate use of antibiotics, such as parents' understandings of compliance with the antibiotic prescription, which have not been commonly identified in other studies in China. Nevertheless, similar to the general population, there was evidence of a considerable lack of knowledge around what antibiotics and ABR are. In addition, some wider issues, such as the use of TCM perspectives in understanding diseases and treatment or the use of OTC antibiotics, are very likely to be found in the wider population of parents, given that they were evident in the more advantaged people recruited to this study. These dimensions will be discussed further below.

Considering these limitations of the present study, a further mixed-method study that focused on a larger sample, particularly in the quantitative part, and relied on a random sampling method, would be helpful to obtain more widely representative data and reveal the

influences on parental use of antibiotics in more detail. A further study should also encompass a more general population, such as including parents from less advantaged communities who are more likely to care for their children at home.

6.5 Conclusions

This multi-method study has provided insights into influences on the use of antibiotics for children among parents in a city with a profile typical of Mainland China. While both components of the study included a relatively advantaged group of parents, they illuminate a set of influences on parental behaviour of broader relevance. First, the evidence from the study indicates that, rather than being based solely on antibiotic and ABR-related knowledge from a Western medicine perspective, parents' decisions about the use of antibiotics for their children are influenced by their understanding of disease and treatment that is built on a combination of TCM and Western medicine perspectives, as well as their personal experience of taking care of their children. Additionally, the study has shown that providers are another important influence on parents' behaviour with respect to the use of antibiotics for their children, and that trust and familiarity, as well as accessibility, are important factors in determining their influence. These findings therefore suggest that interventions to reduce the use of antibiotics need to include a focus on parents, since even for parents with a high educational level and a high income, relatively low levels of understanding of antibiotics and ABR were found. In addition, any interventions need to take into account cultural factors, in particular the co-existence of TCM and Western medicine perspectives, among Chinese populations. Interventions also need to address parents' trust in and use of the primary care

system. This is in line with the Health China 2030 plan that the government has focused on strengthening the primary care system and the retail pharmacy sector in China (CPC Central Committee & State Council, 2016).

Chapter 7. Discussion and conclusions

7.1 Introduction

As noted in earlier chapters, high rates of antibiotic use are the key contributors of ABR in China, where the prevalence of many antibiotic resistant strains ranks amongst the highest in the world (Heddini *et al.*, 2009; Xiao *et al.*, 2011). The paediatric use of antibiotics by providers and parents has been identified as a particular challenge (Jiang *et al.*, 2013; Yu *et al.*, 2014; Zou *et al.*, 2014; Yang *et al.*, 2010). However, the present literature searches and reviews, including both English- and Chinese-language records, found a major gap in research, and qualitative research in particular, relating to influences on providers' and parents' antibiotic-related behaviours for children in China. This is the gap that this project has helped to address. A qualitative study and a multi-method study were undertaken of providers and parents, respectively, in a major city of China. They pointed to a variety of influences on the use of antibiotics for children. Building on all previous chapters, this final chapter provides an overview of the thesis and highlights insights as well as issues arising from this research.

There are three main parts of this chapter. The first part (section 7.2) summaries key findings from the primary studies and discusses the limitations. The second part (section 7.3) then discusses empirical chapters together and locates the insights within the SEF and, specifically, within the individual, interpersonal and organisational levels. The final part (section 7.4) provides conclusions, along with implications related to the use of antibiotics drawing on different levels of the SEF, as well as suggestions for further research.

7.2 Results and limitations

This doctoral research is an urban-based study conducted with providers and parents who are resident in a major city in China. As a consequence, the study setting is advantaged with respect to basic medical insurance benefits and residents' health conditions due to inequities in coverage between rural and urban areas (discussed in section 1.3.1, pp.42). Moreover, it was found in both the present and Gao *et al.*'s (2018) studies that urban residents have a higher household income and education than the average level. Gao *et al.* (2018) further indicated that those urban residents with stable, better jobs were better protected by social benefits. As the large population of parents in the present study had professional jobs (some of the jobs were health-related), they are likely to be more secure and better paid, as confirmed by their answers to questions on household income. In consequence, the present study is based in advantaged groups in an advantaged setting. This also influenced the questions used in questionnaire survey and focus groups of parents; for example, problems with affording antibiotics were not asked.

The qualitative study of providers pointed to two key influences on their antibiotic-related behaviour. Firstly, they described how parents influenced their antibiotic prescribing, with influences clustering under three themes: the importance of (i) public understandings of disease and treatment within traditional Chinese medicine and Western medicine, (ii) parental trust, and (iii) good relationships with patients (discussed in Chapter 4). Secondly, they described the influence of the organisational context. Providers noted that their behaviour with respect to the use of antibiotics for children was influenced by China's

healthcare system and national policies, which could be located within domains identified in the SEF relating to the organisational level and policy level (discussed in Chapter 5). The multi-method study, undertaken with an advantaged group of parents, indicated that, rather than solely derived from their knowledge of Western medicine, parents' decisions about the use of antibiotics for their children were influenced by understandings of disease and treatment that drew on both TCM and Western medicine perspectives, as well as their personal experience of taking care of their children. It additionally noted that trust and familiarity, as well as the accessibility to providers, were important influences on parents' behaviour with respect to the use of antibiotics for their children (discussed in Chapter 6).

This doctoral thesis provides insight into factors influencing providers' and parents' antibiotic-related behaviours through small-scale studies conducted in a single urban study location. The provider study included 26 providers, and the parental study included three focus groups (in total 12 parents of nursery children) together with 98 parents in the questionnaire survey. Furthermore, as noted above, the analysis was based on evidence from parents in more advantaged groups, and concerns about medical insurance and other economic-related influences, such as the cost of medicines, were not reported. Therefore, caution needs to be exercised in generalising these findings to broader populations or settings.

Generalisability is a widely recognised issue for qualitative studies. Because qualitative studies are characterised by rich data from small samples (Hart *et al.*, 2006; Mustafa *et al.*, 2014; Petursson, 2005), the application of criteria commonly used to determine the

generalisability of quantitative studies can fail to do justice to these strengths and contributions (Lewis & Ritchie, 2003). As noted by Lewis and Ritchie (2003), generalisability in the context of qualitative studies is more related to the quality and appropriate use of original data, and the clear description of the research and study setting, than to sample size (Lewis & Ritchie, 2003). As noted in Chapters 4 to 6, the interviews and focus groups were conducted in Chinese and data were then translated, verbatim, into English, with any ambiguities discussed with the researcher's supervisors (both of whom were UK researchers) in order to identify English words that retained the original meaning of concepts and terms for the analysis and interpretation, such as the term 'quality' (discussed in section 4.3.2.2, pp.157). The content related to participants, such as the background setting and the features participants displayed, were also collected by audio-recording and field notes. Furthermore, as noted in empirical chapters, in reporting the findings of the qualitative studies, the COREQ guidelines were followed (Tong *et al.*, 2007). In addition, although the present research was conducted in one city, the study city – Taiyuan city – is medium-sized with average wealth and health expenditure (Pan & Wei, 2015; Statistical Information Centre of NHFPC, 2016), and therefore represented the profile of a typical city in China.

The present study was based on providers' and parents' accounts; beyond my field notes, there was no direct observation of participants' behaviour. Participant accounts of their behaviour and the influences on it may not accord with their actual practices and influences. For instance, a study focusing on doctors in Shandong province, China indicated that, although 87% of the doctors reported in a questionnaire survey that they would refuse to

prescribe antibiotics to patients with a common cold, more than half of prescriptions for common cold collected from the healthcare institutions in which the doctors were working included antibiotics (Sun *et al.*, 2015).

Mindful of this issue, the researcher sought to safeguard the validity of this data by relying on culturally appropriate processes of study site selection and participant recruitment, as well as data collection. As discussed in section 3.3, personal contacts were relied on to gain entry to study sites and participants; personal networks and ‘familiarity’ are recognised to facilitate recruitment, participant trust and, therefore, data validity in Confucian-based cultures (Huang & Pan, 2009; Liu, 2007; Park & Lunt, 2015). The researcher also used verbal consent processes and chose the location and record method of interviews in accordance with participants’ preference to address negative concerns, such as fear and suspicion, and to further protect the validity of the data (Huang & Pan, 2009; Liu, 2006). Alongside, one group’s accounts on their behaviours were compared with the descriptions of their behaviours from other groups, as well as field notes of the researcher’s observations, to see the validity and credibility of their views.

7.3 Key influences on providers’ and parents’ antibiotic-related behaviours

These empirical studies (Chapters 4 to 6) have identified three overarching factors influencing providers’ and parents’ antibiotic-related behaviours, which could be located within the individual level, interpersonal level and organisational level, respectively, of the SEF.

7.3.1 Influences located at the individual level of SEF – the dual use of TCM and Western medicine perspectives among providers and parents

Providers described how their perceptions of parents' use of TCM and Western medicine perspectives influenced their antibiotic-prescribing decisions. Similarly, parents' accounts pointed to the dual use of TCM and Western medicine perspectives and their influences on their use of antibiotics for children. Taken together, this study points to how understandings of disease and treatment drawing on both TCM and Western medicine were shared between providers and parents and, therefore, influenced their use of antibiotics for children.

Growing out of Chinese culture, TCM, rather than being only a medical system, is a type of philosophy and an art of healing (Liu, 1998; Qiu, 2007; Qiu, 2015; Yin & Zhang, 2006). As noted in section 1.3.2.2 of Chapter 1, the dual use of TCM and Western medicine is part of China's healthcare system and health-related education, as well being evident among Chinese populations. For instance, Chung *et al.*'s (2014) systematic review of Chinese populations' views on TCM highlighted the faith in, and lay understanding of, TCM among people in Mainland China as well as overseas Chinese populations, and linked their beliefs in TCM to Chinese culture and heritage. In line with Chung *et al.*'s findings, as noted in Chapter 4 and Chapter 6, the present study suggested that the TCM is an underlying belief system, along with Western medicine theories, and this dual use of TCM and Western medicine influences their use of antibiotics for children.

What has not been widely reported by previous studies is how antibiotic-related behaviour was related to understandings of disease and treatment drawing on both TCM and Western medicine. In HICs, Harbarth *et al.* (2002) explored the cultural perspective's influences on antibiotic treatment in Germany and France and, identified that the wide acceptance of alternative medicine – homeopathy – among German parents was related to their much lower outpatient antibiotic utilization than French parents (Harbarth *et al.*, 2002). In contrast, an observational study focusing on pre-school children in the UK found the use of homeopathy was not associated with reduced antibiotic consumption (Wye *et al.*, 2008). With respect to China, only one study was located through the literature searches, which compared the knowledge, attitudes and practices of antibiotic use between Hong Kong residents who usually attend TCM practitioners and those who usually visit Western medicine doctors (Wun *et al.*, 2014). Therefore, the present study provides a particularly important information to this field.

With respect to the influence of the dual use of TCM and Western medicine on antibiotic-related behaviour, evidence from this study indicates that providers and parents shared an understanding of the strengths and weaknesses of these two systems and located antibiotics within Western medicine. As noted in Chapter 4 and Chapter 6, TCM treatments were regarded as more suitable for chronic or minor diseases and the early stage of treatment; in contrast, Western medicine, including antibiotics, was seen as more effective for diseases, particular potentially serious conditions, and for curing diseases more quickly than TCM methods. Therefore, providers and parents chose to use TCM or Western medicine based on

different conditions and they understood that antibiotics should not be used for some milder conditions. Although no previous studies have linked perceptions of the strengths and weaknesses of the two systems to antibiotic-related behaviour, understandings of the strengths and weaknesses of the two systems among Chinese populations have been widely noted. Harmsworth and Lewith's (2001) survey found a clear consensus among Western trained doctors in Mainland China that TCM was useful for chronic illness, while life-threatening diseases should be treated with Western medicine (Harmsworth & Lewith, 2001). A study focusing on Western medical students in Hong Kong similarly noted that TCM was considered to be good for milder ailments and chronic diseases (Wong *et al.*, 2006). Among the public, TCM and Western medicine were considered as both having strengths and weakness by Chinese populations in China as well as overseas; they choose TCM or Western medicine based on the specific types of illness (Green *et al.*, 2006; Lam, 2001; Xu *et al.*, 2006).

Previous research noted that Chinese populations regarded TCM as safer and causing less adverse effects, and described, based on the dual medical systems, how their perceptions of adverse effects made them reluctant to use Western medicine (Bishop *et al.*, 2009; Green *et al.*, 2006; Lew-Ting, 2005; Xu *et al.*, 2006; Zhang & Verhoef, 2002). Consistent with this evidence, the present study further pointed to similar adverse effect-related concerns regarding antibiotic use compared with TCM, which influenced providers' and parents' use of antibiotics. Wun *et al.* (2014) described that Hong Kong people who usually attended TCM practitioners were more likely to agree that antibiotics had side effects and to refuse antibiotic prescriptions than people who usually visited Western medicine practitioners (Wun

et al., 2014). As with the present study, they noted how the trust in TCM system was associated with resistance to Western medicine-based healthcare and to antibiotics.

In conclusion, while small-scale, the present study addresses an important gap relating to understanding of disease and treatment drawing on TCM and Western medicines. Providers' and parents' understandings of strengths and weaknesses, as well as the adverse effects, of these two medical systems influenced their use of antibiotics for children.

7.3.2 Influences located at the interpersonal level of SEF – trust and familiarity in the provider-parent relationship

In Chapter 4, providers pointed to parental influences on providers' antibiotic-prescribing decisions for children; the multi-method study (Chapter 6) of parents also highlighted providers as an influence on their use of antibiotics for their children. Together, these findings pointed to the importance of the interpersonal level of the SEF, and the interrelationship between providers and parents in particular. As noted in Chapter 4 and Chapter 6, the importance of relationships between providers and parents in HICs has been discussed in a recent systematic review (Lucas *et al.*, 2015); China-based studies focusing on village doctors and parents also referred to parents and doctors, respectively, as important influences (Ding *et al.*, 2015; Yu *et al.*, 2014; Zhang *et al.*, 2016). However, the present literature review located no China-based study that looked at both providers and parents to explore them with respect to their use of antibiotics.

Two systematic reviews based on HIC studies have pointed to the importance of trust in the doctor-patient relationship (Bosley *et al.*, 2018; Ridd *et al.*, 2009). Studies focusing on China also noted the key role of trust, particularly in the deterioration of the doctor-patient relationship when trust was lost (Jing *et al.*, 2013; Yin, 2017). In line with these findings related to the importance of trust, this study further pointed to trust being clearly understood by providers and parents as a key influence on their use of antibiotics, which was not reported by other studies focusing on China. For instance, providers discussed their concerns about maintaining parental trust, as well as avoiding undermining trust by refusing parents' demands on antibiotics. Parents noted that trust was an important factor influencing their choice of providers to visit and their compliance with their advice.

With respect to building a trusted doctor-patient relationship and its influences on antibiotic use, Bosley *et al.*'s (2018) systematic review pointed to the importance of good communication. Similarly, in Chapter 4 of the present study, providers noted the essential role of clearly explaining why antibiotics were not prescribed to parents in order to maintain their trust. They also described how they would ultimately prescribe unnecessary antibiotics to children when their explanation did not work. Along with the role of communication, this study further pointed to the organisational differences that influenced trust within provider and parent relationships. As with this study, Duckett *et al.* (2016) and Li *et al.*'s (2017) nationwide surveys found huge differences in public trust in different healthcare institutions, with much higher levels of distrust in the primary care system, such as CHIs, compared with

hospitals (Duckett *et al.*, 2016; Li *et al.*, 2017). What this study added was the similar concerns about the varied trust levels held by providers; CHI and retail pharmacy based providers acknowledged that the public's trust in their institutions was lower than in hospitals.

As this suggests, providers' and parents' shared understandings of the varied levels of trust in different healthcare institutions were a factor influencing their antibiotic-related behaviours; this kind of influence on antibiotic use has not been reported by previous studies. Duckett *et al.*'s (2016) and Li *et al.*'s (2017) studies referred to the trust level as one of the major reasons relating to patients' choice of healthcare institutions, as lower trust levels in primary care institutions led patients to go to hospitals directly for healthcare services. This trust-related influence on the choice of healthcare institutions is similar to the present study where parents noted that they preferred to first visit hospitals, as they were more trusted than other institutions. This study further suggested that the trust was positively related to parents' adherence to hospital-based providers' antibiotic-related decisions. With respect to providers, this study found that providers in hospitals were concerned about maintaining parental trust to reduce pressures to prescribe unnecessary antibiotics to meet parents' demands, while providers in CHIs and retail pharmacies noted the importance of familiarity to compensate for the low public trust level, which will be discussed below. Additionally, this study identified some differences between providers' and parents' accounts of trust, with parents having a higher level of trust in hospitals than hospital-based providers expected; however, given the small sample sizes, it would not be appropriate to draw strong conclusions from these differences.

Familiarity was emphasized by both providers and parents with respect to provider-parent interactions in CHIs and retail pharmacies, where public trust was lower. Previous studies (discussed in Chapters 4 and 6) have noted the benefits of familiarity between providers and patients, including helping GPs in making diagnostic and therapeutic decisions (Hjortdahl, 1992; Hjortdahl & Borchgrevink, 1991), as well as improving patients' medication compliance (Kerse *et al.*, 2004), satisfaction (Schers *et al.*, 2005) and enablement (Freeman *et al.*, 2002). This study further added evidence that familiarity was used to counter the distrust between providers and parents in low-trust healthcare institutions and influenced their antibiotic-use behaviour, particularly in CHIs. As noted in Chapter 6, parents only referred to familiar CHIs as trustworthy, and trust was highly related to their compliance with providers' decisions and antibiotic prescriptions. This fits with an earlier study that found that patients' compliance with short-term antibiotic prescriptions was strongly associated with knowing the doctor well (Ettlinger & Freeman, 1981). With respect to providers, most CHI-based providers in this study noted that they would be more prudent in prescribing unnecessary antibiotics for familiar parents because these parents were more easily persuaded against antibiotic use when demanding antibiotics. Brookes-Howell *et al.*'s (2012) study in EU countries discussed familiarity as an influence on providers' antibiotic-related behaviour with respect to their greater knowledge of the patient's medical history and continuity of care (Brookes-Howell *et al.*, 2012); however, this aspect of familiarity was rarely noted by providers in the present study (discussed in Chapter 4).

Differences in the relative importance of familiarity can be related to the structure of China's healthcare system and the status of healthcare institutions (i.e. to factors related to the organisational and policy levels of SEFs influencing factors located in the interpersonal level). For instance, it was noted in Chapter 4 that, compared with providers in CHIs and retail pharmacies, hospital-based providers had fewer opportunities to develop 'familiarity' with parents, as well as fewer financial concerns (Beam, 2014; Li *et al.*, 2017; Mossialos *et al.*, 2016; Woodhead, 2014; Yin, 2017). This is likely to be related to inequities in health-related funding and facilities between hospitals and other healthcare institutions (Fang, 2014; Li *et al.*, 2017; Yip *et al.*, 2012), which also led to the higher level of public trust in hospitals (discussed in section 1.3.1 of Chapter 1). Furthermore, as noted in Chapter 4, the financial pressures on CHIs have increased since the implementation of EDL and ZUM policies, which made CHI-based providers rely more on good doctor-patient relationships and patient retention to increase their income.

In summary, this thesis added novel evidence on antibiotic use in China by describing how trust and familiarity among providers and parents influenced their behaviours related to antibiotic use for children. The results of this study pointed to the importance of trust in providers' and parents' use of antibiotics. Within CHIs and retail pharmacies where the trust levels were relatively low, familiarity was used to counter the broader public distrust and, therefore, emerged as an influence on providers' and parents' antibiotic-related behaviour in these healthcare institutions.

7.3.3 Influences located at the organisational and policy levels – China’s healthcare system and antibiotic-related reforms

The present qualitative studies (Chapter 5 and Chapter 6) described the influences of provider facilities, staffing and financial considerations within China’s healthcare system on the use of antibiotics for children, particularly by providers, and how these influences are related to the China’s whole healthcare system.

As noted in Chapter 5, studies focusing on HICs have widely reported how uncertainty during the diagnostic process can contribute to providers’ inappropriate use of antibiotics (Horwood *et al.*, 2016; Tonkin-Crine *et al.*, 2011). In LMICs’ studies, including two qualitative studies of China, the uncertainty that influenced providers’ antibiotic-related behaviour was always related to limited availability and the unaffordability of diagnostic facilities; as these studies have noted, problems relating to diagnostic facilities are a key challenge to accurate diagnosis and prognosis, and therefore to effective treatment, in LMICs (Kotwani *et al.*, 2010; Nkengasong *et al.*, 2018; Reynolds & McKee, 2009; Wilson *et al.*, 2018; Zhang *et al.*, 2016). Similar to these studies, this study noted the key role of diagnostic facilities, such as the laboratory-based blood tests, in providers’ antibiotic-prescribing decisions, with some providers regarding them as the most important factor.

However, different from previous studies that noted the limited accessibility of diagnostic tests (Reynolds & McKee, 2009; Zhang *et al.*, 2016), in this study such concerns were only discussed by providers in community health stations, which they compared with what they

saw to be the wide availability in hospitals. This fits with a national survey that noted the lack of quality-assured diagnostic facilities at the primary care level in China (Li *et al.*, 2017). The inequitable distribution of resources between healthcare institutions was found to be an influence on providers' antibiotic prescribing decisions in this study. Previous studies also discussed the issues of inadequate training and low incomes among providers in China's primary care system (Gao *et al.*, 2012; Li *et al.*, 2017). In line with these findings, this study additionally noted how the lack of well-qualified doctors and the greater financial pressures on CHIs compared with hospitals influenced CHI providers' use of antibiotics. For instance, as noted in Chapter 5, while no providers in hospitals spoke about financial considerations in the context of their antibiotic-related behaviour, these concerns were widely noted as influences on CHI-based providers' antibiotic-prescribing decisions, which is similar to Zhang *et al.*'s (2016) study focusing on village doctors in China's primary care system. Zhang *et al.*'s (2016) and the present findings all point to influences stemming from the differential development of China's healthcare institutions on providers' use of antibiotics.

With respect to parents, data from the focus groups with parents (discussed in Chapter 6) also pointed to the unbalanced development of China's healthcare institutions as a factor in their use of antibiotics. As discussed in Chapter 1 and in section 7.3.2 above, hospitals are heavily used by patients in China where waiting times are often long and consultation times are short (Woodhead, 2014; Mossialos *et al.*, 2016; Yin, 2017). As a consequence, parents in this study noted that access to retail pharmacies was easier than hospitals, an availability that led them to parentally-medicate antibiotics for their children. This has also been reported in

previous studies focusing on parents as well as other populations in China (Lv *et al.*, 2014; Yu *et al.*, 2014).

As discussed in Chapter 1 (section 1.4.2), China's major antibiotic-related policies were established in the 2011 antibiotic-related reforms, including the three-year strategy named '*National Special Campaign for the Clinical Use of Antibiotics*' and the much stricter administrative regulations, which have a particular focus on hospitals. Previous studies have indicated the effectiveness of these policies with respect to the use of antibiotics in both general and specialised hospitals, with evidence of the decreased antibiotic use frequency and antibiotic use intensity (see Box 3 and Box 4 for their definitions) in selected hospitals after the issue of the policies (Bao *et al.*, 2015; Zou *et al.*, 2014). Similarly, results from Chapter 5 pointed to these policies as important influences on the use of antibiotics in hospitals as well as CHIs. However, providers' accounts also noted some unexpected consequences, such as how the regulated use of antibiotics in hospitals appeared to have worsened antibiotic use in retail pharmacies, and how the limitations of diagnostic facilities, particularly in CHIs, influenced adherence to antibiotic-related guidelines. These phenomena have not been reported by previous studies focusing on the effectiveness of antibiotic-related policies. Therefore, along with evidence of antibiotic-related policies promoting the appropriate use of antibiotics, the present study additionally pointed to some adverse unintended consequences of antibiotic-related policies, which were related to differences in provider facilities in different healthcare institutions, as well as the structure of the whole healthcare system in China.

Wider policies were also intended to promote the appropriate use of antibiotics. For instance, the EDL and ZMU policies are designed to remove financial incentives from drug prescriptions, and regulations focus on retail pharmacies to stop the sale of OTC drugs (discussed in section 1.4.3). However, both previous studies and the present findings (discussed in Chapter 5) pointed to the limited effectiveness of EDL and ZMU in promoting the appropriate use of antibiotics (Gong *et al.*, 2016; Jiang *et al.*, 2013; Song *et al.*, 2014; Yang *et al.*, 2013), as well as of regulations with respect to selling the OTC antibiotics (Fang, 2014;). Furthermore, this study identified an economic basis to CHI-based providers prescribing unnecessary antibiotics to maintain good relationships with parents and ensure parent retention. It therefore suggested that, in contrast to their original aims, the EDL and ZMU policies may contribute to the inappropriate use of antibiotics among providers in CHIs, because of the financial pressures from reduced remuneration from drug sales following their implementation, as well as the inadequate compensation provided via government subsidies for the already-low incomes in CHIs. This phenomenon was similarly noted by Chen *et al.* (2014) and Xiao *et al.* (2016), which described how the unbalanced economic status of healthcare institutions represented policy-level factors that worked against providers' appropriate use of antibiotics. Additionally, it was noted by Xiao *et al.* (2016) that patients' expectations of antibiotics had been further raised by the low price of essential drugs.

In conclusion, present thesis described how facilities, financial considerations and policies influenced providers' and parents' antibiotic-related behaviours for children. It provided

evidence on organisational influences within the whole healthcare system in China after 2009 health reforms and 2011 antibiotic-related reforms, which has not been widely reported by previous studies.

7.3.4 Principal novel contributions of this thesis

Although this thesis is a small-scale study focusing on one city, it provides three novel contributions related to antibiotic use and ABR in China, including (i) the influences of the dual use of TCM and Western medicine in understanding diseases and treatment on providers' and parents' behaviours with respect to the use of antibiotics for children in China; (ii) the trust and familiarity in provider-parent relationship that influence their antibiotic-use behaviours for children in China; (iii) the broader health contexts and policies' influences on providers' and parents' antibiotic-use behaviours for children after China's recent health reforms and antibiotic reforms.

As the SEF is a framework that takes into account reciprocal relationships between individuals and their environments, the concentric layers of factors influencing the outcome of interest (the use of antibiotics) also inter-relate (Schneider & Stokols, 2009). Evidence from the present study indicated that, firstly, the broader layers of organisational and cultural factors influenced factors located at the inner layers, which together influenced providers' and parents' use of antibiotics for children. For example, providers' and parents' dual use of TCM and western medicine was a factor operating at the individual level, but was also shaped by factors operating at broader layers, including the interpersonal (provider-parent

relationships), organisational (China's healthcare system in which TCM and Western medicine are practised alongside each other at every level) and cultural/societal levels. China's healthcare system, with its unequal development of hospital and community-based institutions, influenced providers' and parents' concerns about trust and familiarity, which were factors operating at the interpersonal level. Furthermore, the factors located at broader levels were also interactive. One example was the finding that positive impacts of antibiotic-related policies on hospital use of antibiotics offset by increased pressures on other parts of the healthcare system (CHIs and retail pharmacies) to provide antibiotics to compensate for the loss of income.

7.4 Conclusions

7.4.1 Implications and recommendations

Two broad implications can be drawn from the present study, both leading to recommendations for future research. The first implication relates to the SEF and its contribution to understanding the complicated and reciprocal relationships between factors influencing behaviour. A SEF was used in this study to guide both the review of literature and the interpretation of results, an approach which has not been used in other research focusing on impacts of antibiotic use. By using the SEF, it was able to locate results (influences on the use of antibiotics) at the individual level, interpersonal level, and the wider organisational level of the SEF, and can therefore draw out implications and recommendations at these different SEF levels.

At the individual level of the SEF, the use of both TCM and Western medicine in parental and providers' understandings and communication around disease and treatment suggests that policy-makers need to develop strategies based on the two medical systems, in order to promote the appropriate use of antibiotics. Antibiotic-related education programmes, as noted in section 2.3.2.3, pp.103-104, have been used as an important strategy in antibiotic stewardship to promote the appropriate use of antibiotics by providers in hospitals and the primary care level in China. These programmes have trained providers in relation to antibiotic-related policies launched by MoH (NHFPC from 2013) (Hou *et al.*, 2014), clinical use and management of antibiotics (Bao *et al.*, 2015), and other control methods like prescribing antibiotics with different restriction levels (Lin *et al.*, 2013). The present study suggests that TCM knowledge relevant to understanding diseases and antibiotic treatments would also be important to include in this training. Policy-makers could also take note of the importance of TCM perspectives when they draft guidelines or policy documents on the use of antibiotics. Practical guidelines were widely applied to eliminate the inappropriate use of antibiotics in hospitals in China, such as the use of procalcitonin for guiding antibiotic use (Ding *et al.*, 2013; Long *et al.*, 2011; Qu *et al.*, 2012; Tang *et al.*, 2013), and the use of guidelines of '*Principles for Clinical Use of Antimicrobials (2015 edition)*' since the 2011 antibiotic-related reforms (Bao *et al.*, 2015; Sun *et al.*, 2015A). The '*Principles for Clinical Use of Antimicrobials*' guides how to prescribed antibiotics for different kinds of diseases, though only in Western medicine terms; thus, this study suggests that it might be more helpful to provide the corresponding TCM terms and explanations of these diseases in the guidelines.

The Chinese government also introduced a public information week (13th November – 19th November) in 2017 to promote the appropriate use of antibiotics (NHFPC, 2017C), as part of a series of public information campaigns used to reduce the public's misunderstandings of and promote more appropriate use of antibiotics (Cross *et al.*, 2017; Shehadeh *et al.*, 2015; Trepka *et al.*, 2001). The present study suggested that, along with providing more information about antibiotics themselves and explaining common misconceptions about the conditions for which antibiotics are appropriate (NHFPC, 2017C), it could be helpful to align and compare TCM-related conditions, such as excessive heat (*shanghuo*), with Western medicine conceptions of similar symptoms (e.g. inflammation and fever) in the information campaign for the Chinese public.

The results relating to the doctor-patient level suggest that the inappropriate use of antibiotics could be addressed by improving trust and familiarity in the doctor-patient relationship. Information campaigns could provide more detailed information on China's healthcare system. For instance, they could note the primary care system is under rapid development, citing the large amount of outpatient care services it provided, to reduce public misunderstandings and to boost their trust in the primary care system. For hospital-based providers, as suggested by a systematic review of HICs (Cabral *et al.*, 2016), guidelines and trainings could focus more on how to develop effective communication between providers and patients, for example, to help hospital-based providers give essential and understandable information to patients within the limited time period (3 – 5 minutes) available for the

consultation. Similar training for providers in the primary care system and retail pharmacies could focus on communication skills to build patient trust.

Furthermore, differences in the trust level and in the relative importance of familiarity in hospitals and CHIs reflect the different development of these healthcare institutions, including inequities in, for example, health staff. Together with results located at the organisational level, the present study, therefore, would support a further strengthening of primary care, such as improving diagnostic facilities, the compensation for income losses related to ZMU and EDL policies, as well as greater investment in staff training and support. This suggestion is in line with Chinese government's policy goal that emphasizes primary care as a key aspect of its national plan (Lancet, 2018). This study further suggests that policy makers could widen the focus of current antibiotic-related policies to include the primary care level and retail pharmacies, and could develop new antibiotic-related strategies particularly for these healthcare institutions. Finally, as well as developing strategies, this study also suggested the importance of improving mechanisms to ensure implementation of existing and new policies, such as the effectively implementing the existing regulations on the sale of antibiotics in retail pharmacies

The second implication relates to research governance procedures. The dominant approach is one developed in Western societies such as the UK and, as other researchers have noted (Liu, 2006, 2007; Park & Lunt, 2015), it requires adaptation if it is to be sensitive to the organisational contexts and cultural backgrounds of study participants in China. Together

with other studies, the present study has implications for how research ethics are understood and implemented in study settings other than Western high-income countries, where, in addition, there is a lack of familiarity with 'standard' (Western) research ethics. It suggests that culturally appropriate processes are required to ensure participant trust in the study and thus secure access to and approval from study sites as well as informed consent from participants. As discussed in section 3.3, such processes offer benefits with respect to data validity, particularly in Confucian-based cultures.

7.4.2 Suggestions for further research

Focusing on both English- and Chinese-language records in the literature review, this study pointed to the importance of searching and reviewing literature published in languages other than English. Therefore, it is valuable for further studies, particularly when the study setting is not an English-speaking area, to review records published in English and the other languages used in journals of the country under study, in order to increase comprehensiveness. In addition, the quality of records published in other languages should be assessed if they are not indexed in international databases.

As mentioned in the section 7.2, insights from this doctoral research are derived from a set of small-scale studies based in one major city. It is therefore important to explore these findings in studies with larger and more representative samples across multiple settings in China. Additionally, this study has pointed to the importance of both TCM and Western medicine use in the public's understanding of disease and treatment. This influence is worthy

of further study beyond China in other countries with well-established TCM practices are competing with Western medicine, as well as among Chinese population living in other countries. Understanding these influences in greater depth and breadth would be the next step in developing interventions and policies, and in evaluating their effectiveness.

Furthermore, while there were differences in the themes in provider and parent accounts, this study found some common themes, such as the public's understanding of disease and treatment (including antibiotics), and trust and familiarity. However, small sample sizes meant that these similar themes could not be examined in depth. Therefore, in further studies with large sample sizes, it would be interesting to undertake systematic comparisons of themes from providers and parents. Confirmation of similar themes would provide a stronger empirical basis for informing the design of interventions and policies to promote appropriate antibiotic use.

Finally, the development and strengthening of the primary care system means that new policies focusing on the primary care level are likely to be launched in the future. Future research could, therefore, review and evaluate how new policies and interventions launched by the Chinese government affect the use of antibiotics. For instance, studies could compare provider and public views on antibiotic use in the primary care system pre and post new policies, as well as analyse antibiotic use frequency in the primary care level pre and post new policies, to evaluate these policies' effects on appropriate use of antibiotics.

7.4.3 Conclusions

This doctoral research sheds light on influences on providers' and parents' use of antibiotics for children, which has been identified as a major factor in ABR in China. Results from the qualitative and multi-method studies pointed to factors operating at different levels of the SEF as influencing providers' and parents' antibiotic-related behaviours. The key insights included the influence of (i) both TCM and Western medicine in parental and providers' understandings and communication around disease and treatment, (ii) trust and familiarity in the doctor-patient relationship, and (iii) the healthcare system and antibiotic-related reforms. These factors were interactive and can be located at the individual level, interpersonal level, and organisational and policy level, respectively, of the SEF. Through using the SEF to identify influences on the use of antibiotics for children, this study suggests that public knowledge, the provider-patient relationship and the healthcare system are important determinants of antibiotic use in China. It also argues for studies based on representative samples in multiple settings to explore these influences in greater depth.

Appendices

Appendix A – Search strategy for human ABR and antibiotic use in China

1. The searching strategy for section 1.2.4.1 (human antibiotic resistance in China)

MEDLINE Ovid (3rd Mar 2016)

1. Bacterial Infections/ or Anti-Bacterial Agents/ or Drug Resistance, Bacterial/ or antimicrobial resistance.mp. or Drug Resistance, Microbial/ or Drug Resistance, Multiple, Bacterial/
2. limit 1 to (abstracts and English language)
3. China.mp. or China/
4. limit 3 to (English language and full text)
5. 2 and 4
6. limit 5 to humans
7. limit 6 to yr="1949 -Current"(in total 394 published papers)

Wanfang Data (万方数据)(3rd Mar 2016)

The term of 'CHINET 日期 (*date*):2010-2016' and 'Mohnarin' were used to identify the national surveillance data of antibiotic resistance in China published in Chinese.

2. The searching strategy for section 1.3.3.1 (antibiotic use and inappropriate use in hospitals and primary care institutions)

MEDLINE Ovid (5th Mar 2016)

1. antibiotic.mp.
2. China.mp. or China/
3. Drug Prescriptions/ or Prescription Drugs/ or Prescriptions/ or Practice Patterns, Physicians'/ or prescri*.mp. or Prescription Drug Misuse/
4. 1 and 2 and 3

5. hospital*.mp.
6. Public Health/ or Community Health Services/ or community health institution*.mp.
7. physicians/ or general practitioners/ or hospitalists/ or physicians, primary care/
8. doctor*.mp.
9. prescriber*.mp.
10. Pediatrics/ or pediatrician*.mp.
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 and 11(in total 41 published papers)
13. rural .mp.
14. 12 and 13 (in total 6 published papers)

Wanfang Data (万方数据)(5th Mar 2016)

The term of ‘医院 (*hospital*)’, ‘住院 (*inpatients*)’, ‘门诊 (*outpatients*)’, ‘急诊 (*emergency*)’, ‘乡镇 (*rural areas*)’, ‘社区 (*community*)’, ‘抗生素 (*antibiotic*)’, ‘使用率 (*use frequency*)’ and ‘使用强度 (*use intensity*)’ were used to identify studies published in Chinese related to antibiotic use for inpatients, outpatient and emergency in hospitals and in community health institutions of urban areas in China, as well as antibiotic use in the rural areas of China.

3. The searching strategy for section 1.3.3.3 (antibiotic use and inappropriate use by the general public)

MEDLINE Ovid (8th Mar 2016)

1. antibiotic.mp.
2. China.mp. or China/
3. Hong Kong/
4. Macao.mp.
5. the public.mp.
6. Adult/ or general population.mp.
7. 2 or 3 or 4
8. 1 and 5 and 6 and 7(in total 14 published papers)

9. 1 and 2 and 5 and 6(in total 5 published papers)
10. Patient Compliance/ or parental medication.mp. or Self Medication/
11. Medication Adherence/ or Guideline Adherence/ or adherence.mp.
12. 10 or 11
13. 1 and 2 and 12 (in total 14 published papers)

Wanfang Data (万方数据)(8th Mar 2016)

The terms of ‘抗生素 (*antibiotic*)’, ‘居民 (*resident*)’, ‘使用率 (*usage frequency*)’, ‘使用情况 (*usage situation*)’ and ‘滥用(*abuse*)’ were used to identify related evidence of in Chinese published studies.

4. The searching strategy for section 1.3.3.2 (antibiotic use and inappropriate use in pharmacies)

MEDLINE Ovid (12th Mar 2016)

1. antibiotic.mp.
2. China.mp. or China/
3. Pharmacy Service, Hospital/ or dispense.mp. or Drug Prescriptions/
4. Pharmacy/
5. Pharmacists/ or pharmacists.mp.
6. 3 or 4 or 5
7. 1 and 2 and 6(in total 18 published papers)

Wanfang Data (万方数据)(12th Mar 2016)

The terms of ‘抗生素 (*antibiotic*)’, ‘药店 (*retail pharmacy*)’, ‘药剂师 (*pharmacist*)’ and ‘销售 (*dispense or sale*)’ were used to identify related evidence in Chinese published studies.

Appendix B – Information on the health supervision system and the health financing system

Health Supervision System

In China, the National People's Congress (NPC) is the highest decision-making body, responsible for issuing China's laws. Apart from the NPC, the People's Congress at provincial and capital city level, as well as the governments from the national level (the State Council) to the capital city level, also have the power to issue laws and regulations. Therefore, the legislative system in China is composed of administrative laws and regulations issued by the NPC and State Council, and the local laws, regulations and rules issued by local People's Congress and local governments (WHO, 2015C). The legislation for the healthcare system is produced by the same process as above.

Under the guidance of the health-related legislation and regulations, the health supervision system can provide management and administration to China's healthcare system. The main Chinese health administration has four levels, from NHFPC, at the national level, to local health authorities at provincial, city and county levels (Chan *et al.*, 2008; WHO, 2015C). The NHFPC was transformed by the MOH in 2013 due to a public reform initiated by the State Council (WHO, 2015B). It provides central guidance for China's healthcare system, such as health regulations and major public health programmes (Chan *et al.*, 2008). Each level's health administration is the member of the same level's government and overseen by it; the health administration can provide management and guidance to healthcare providers at the same level and the lower-level health administration (e.g. the provincial health

administration can manage provincial-level healthcare providers and the municipal-level health administration) (Bloom & Tang, 2004; Liu, 2004; Yip *et al.*, 2012). Therefore, the NHFPC, State Council and their local authorities are the central body of China's health supervision system.

Health Financing System

The main sources of health funding are the government, insurers (through the basic medical insurance schemes) and individuals, and payment methods³⁴ are mixed (Meng, 2005). China has a long history of paying for medical services by health insurance schemes and individuals through fee for service (FFS) methods, and the government provides subsidies to the medical service delivery system by through its global budget³⁵ (Meng, 2005); public health services are mainly funded by government subsidies (WHO, 2015C).

The basic medical security system is mainly responsible for providing social finance to the medical service delivery system, and the basic medical insurance schemes, including Urban Employee Basic Medical Insurance (UEBMI), Urban Resident Basic Medical Insurance (URBMI), and New Rural Cooperative Medical Scheme (NRCMS) are the main part of China's basic medical security system. Beginning in 1998 they have been carried out by the Chinese government to cover specific groups of urban employees, unemployed urban residents, and

34 The payment method is defined as 'methods of pricing of healthcare services, paying of healthcare providers, and arrangement of payment including supplementary measures and contractual relationship between payers and providers' (Meng, 2005).

35 The global budget means an overall spending target or limit determined by a government agency that constrains the price and the quality of the services provided (Dredge, 2004). For instance, every year, a fixed amount of funding is distributed by the government annually to hospitals to pay for all hospital-based services (Sutherland, 2011).

rural residents, respectively, in order to achieve comprehensive universal health coverage by 2020 (Barber & Yao, 2010). The overview of three main medical insurance schemes is shown in Table 1. For financing methods of basic medical insurance schemes, the UEBMI is paid by employers and individuals (employees), while URBMI and NRCMS are paid by the government and individuals (residents) (Yip *et al.*, 2012). In addition, employees in urban areas are compulsorily covered by UEBMI while residents are voluntarily enrolled into URBMI and NRCMS (Yip *et al.*, 2012).

Table. Summary of three basic medical insurance schemes

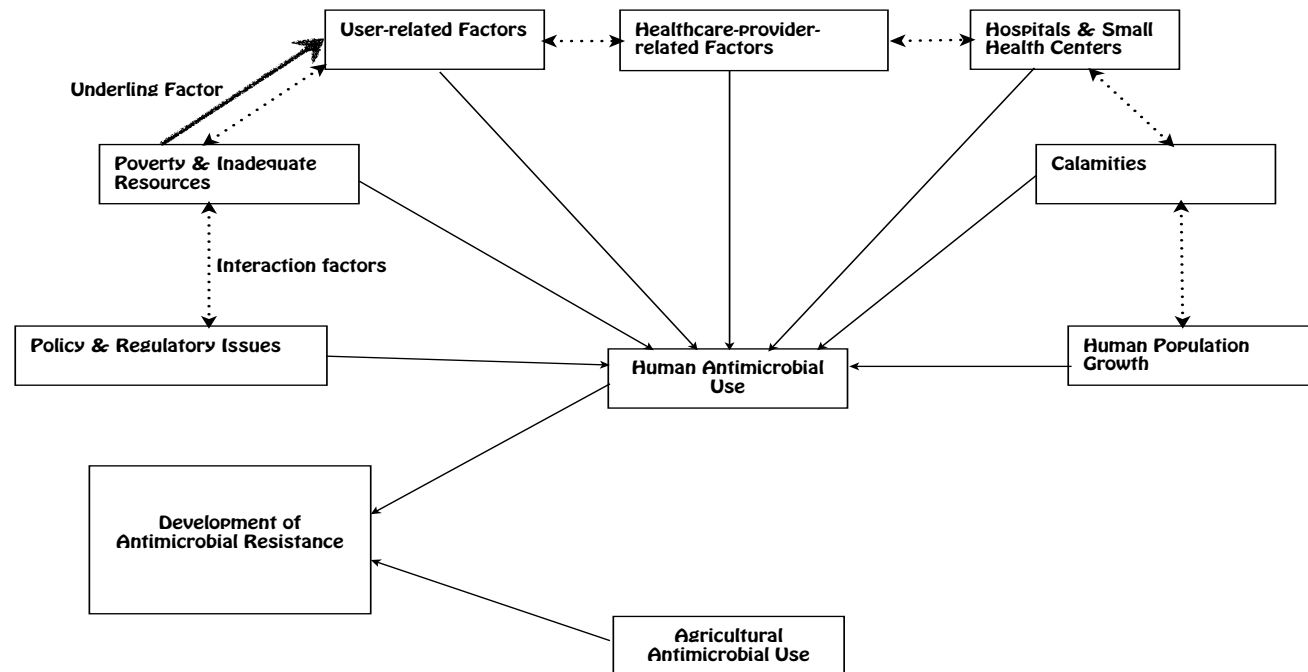
Characteristic	NRCMS	UEBMI	URBMI
Administration	County level	Municipal level	Municipal level
Start date	2003	1998	2007
Participation	Voluntary	Mandatory	Voluntary
Populations	Rural residents	Urban employed	Children, students, elderly, disabled, other non-working urban residents
Current coverage	98.7% (end 2013)	92.4% (2010)	92.9 (2010)
Enrolment (million people)	802 (end 2013)	274.43 (end 2013)	296.29 (end 2013)
Revenues	297.25 billion CNY (47.85 billion US\$) (2013)	706.16 billion CNY (113.67 billion US\$) (2013)	118.66 billion CNY (19.10 billion US\$) (2013)
Expenditures	290.92 billion CNY (46.83 billion US\$) (2013)	582.99 billion CNY (93.84 billion US\$) (2013)	97.11 billion CNY (15.63 billion US\$) (2013)
Source of revenues	Government (at central and local levels) and individuals (2013)	Employers and employees	Government (at central and local levels) and individuals (2013)
Central government (/person/year)	120 CNY (same in 2014)	0 CNY	120 CNY (same in 2014, 2015)

Local government (/person/year)	160CNY (200 in 2014) The central government pays 80% (128 CNY) of 160 CNY for western areas' local governments and 60% (96 CNY) of 160 CNY for central areas' local governments. Central government subsidies for eastern areas' local governments tend to be lower.	0 CNY	160 CNY (200 in 2014, 260 in 2015) The central government pays 80% (128 CNY) of 160 CNY for western areas' local governments and 60% (96 CNY) of 160 CNY for central areas' local governments. Central government subsidies for eastern areas' local governments tend to be lower.
Employers (/person/year)	0 (No employer)	5%-7% of employee's salary	0 (No employer)
Individuals (/person/year)	70 CNY (90 in 2014)	2% of employee's salary	70 CNY (90 in 2014, 120 in 2015)
Total revenues per person per year	370.59 CNY (59.65 US\$) (2013) ¹	About 2573.19 CNY (414.20 US\$) (2013) ²	About 400.49 CNY (64.47 US\$) (2013) ²
<p>1. For NCMS, the total revenues /person /year (370.59 CNY) was greater than the sum of government and individual contributions /person /year (350 CNY) because local governments can contribute more than the minimally required amount. The URBMI has the same situation.</p> <p>2. For UEBMI and URBMI, the total revenues /person /year were not published. The data were obtained through using 'Revenues' divided by 'Enrolment'.</p>			

Source: adapted from Yip et al., 2012; Barber & Yao, 2010. NHFPC, 2014; NBSC, 2015; MoHRSS & MoF, 2015; MoF, NHFPC & MoHRSS, 2014

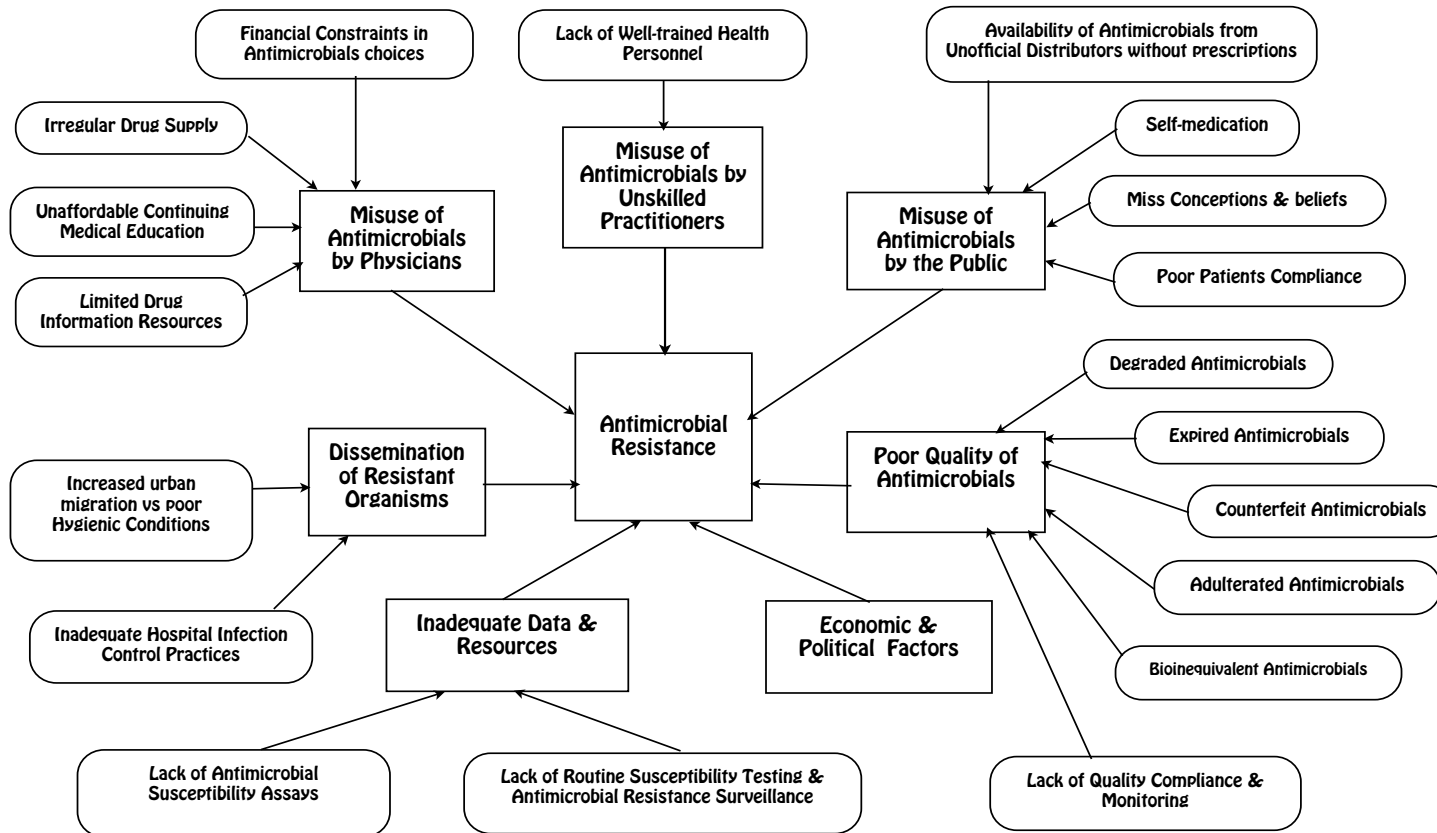
Appendix C – Framework derived from three papers

Paper one



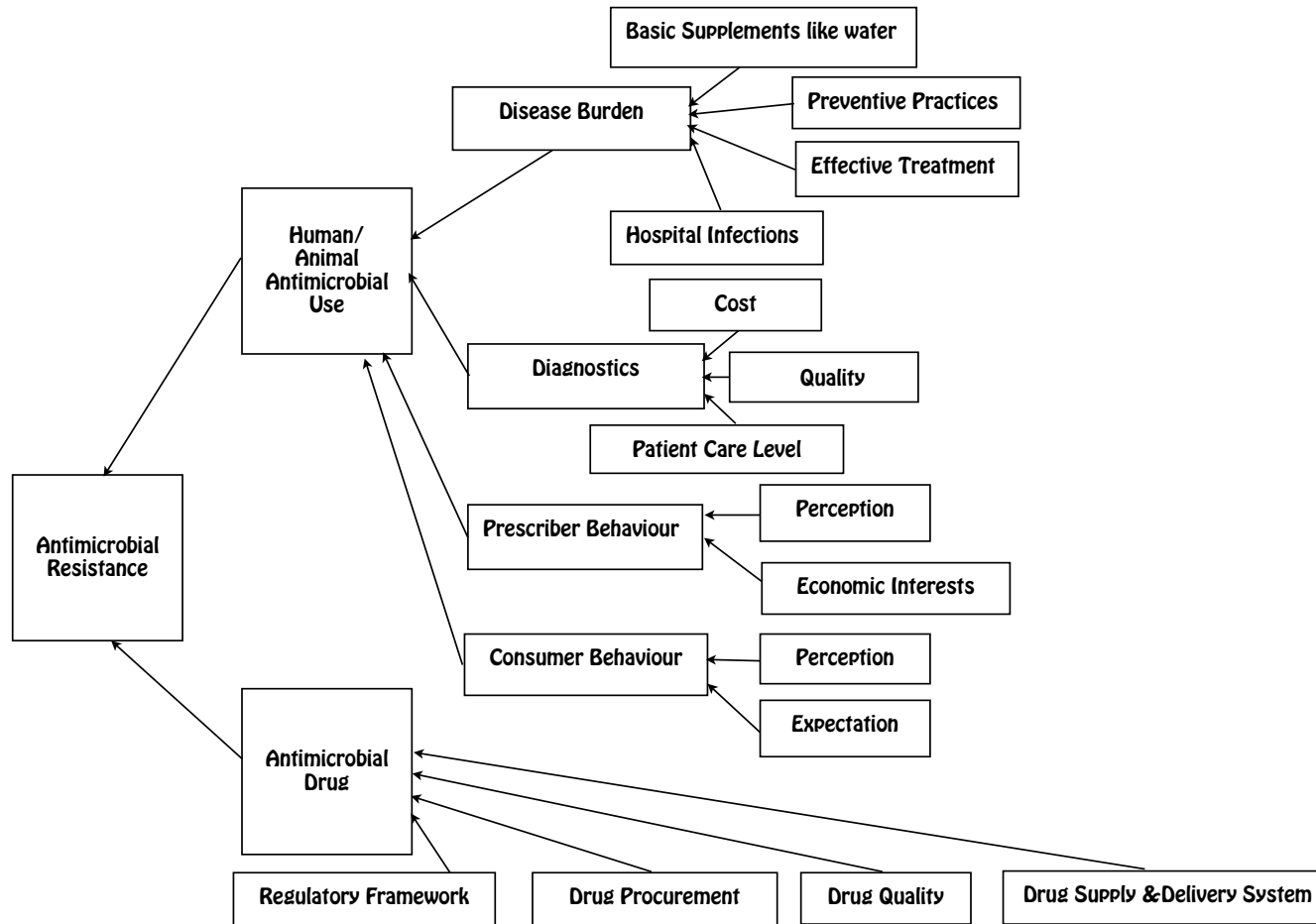
Framework of risk factors responsible for antimicrobial resistance in low and middle-income countries

Paper two



Socioeconomic & Behavioral Factors Contribute to Antimicrobial Resistance in Low and Middle-income Countries

Paper three



Framework of risk factors responsible for antimicrobial resistance

Appendix D – Search strategy for factors influencing providers’ and parents’ use of antibiotics in China

1. The searching strategy for section 2.3 (factors influencing healthcare providers’ behaviour with respect to the use of antibiotics in China)

MEDLINE Ovid (29th May 2017)

Advanced search: keyword

1. antibiotic*.mp. or Anti-Bacterial Agents/
2. antimicrobial*.mp.
3. Physicians, Family/ or Primary Health Care/ or Practice Patterns, Physicians'/ or general practitioner*.mp.
4. Pharmacy Service, Hospital/ or Pharmacists/ or pharmacist*.mp.
5. Health Personnel/ or healthcare provider*.mp.
6. physician*.mp.
7. pediatrician*.mp. or Pediatrics/ or Pediatricians/
8. China.mp. or China/
9. Hong Kong.mp. or Hong Kong/
10. Macao.mp. or Macau/
11. Taiwan.mp. or Taiwan/
12. 1 or 2
13. 3 or 4 or 5 or 6 or 7
14. 8 or 9 or 10 or 11
15. 12 and 13 and 14 (in total 217 papers were found)

中国知网 (CNKI) 2016 年 7 月 6 日

选择学科领域: 医药卫生科技, 社会科学 I 辑, 社会科学 II 辑

高级检索: 关键词

检索 1: [关键词 ‘抗生素’ 或含 ‘抗菌药物’ 精确]

并且[关键词 ‘医生’ 或含 ‘药店’ 精确]

中英文扩展 共检索出文章 47 篇

检索 2: [关键词 ‘抗生素’ 或含 ‘抗菌药物’ 精确]

并且[关键词 ‘药师’ 精确]

中英文扩展 共检索出文章 749 篇

Translation

Chinese database: CNKI (6th Jul 2016)

Research areas: Medicine and health sciences, Social science I and Social science II

Advanced search: Keyword

Advanced search 1: [Keyword ‘antibiotic’ or Keyword ‘antibacterial drug’ exact terms]

And [Keyword ‘doctor’ or Keyword ‘pharmacy’ exact terms]

Including papers in English and papers in Chinese (in total 47 papers were founded)

Advanced search 2: [Keyword ‘antibiotic’ or Keyword ‘antibacterial drug’ exact terms]

And [Keyword ‘pharmacist’ exact terms]

Including papers in English and papers in Chinese (in total 749 papers were founded)

2. The Searching strategy for section 2.4 (factors influencing public's and parents' behaviour with respect to the use of antibiotics in China

MEDLINE Ovid (27th Jul 2017)

Advanced search: keyword

1. Anti-Bacterial Agents/ or antibiotic*.mp.
2. Antimicrobial*.mp.
3. China.mp. or China/
4. Hong Kong.mp. or Hong Kong/
5. Macao.mp. or Macau/
6. Taiwan.mp. or Taiwan/
7. Knowledge*.mp. or Health Knowledge, Attitudes, Practice/
8. Behavio*.mp. or Behavior/
9. Patient Compliance/ or Compliance/ or compliance*.mp.
10. Drug Prescriptions/ or Self Medication/ or Pharmacists/ or self-medicat*.mp.
11. Patient Satisfaction/ or expectation.mp.
12. Middle Aged/ or Adult/ or Adolescent/ or general population.mp. or Aged/
13. Parent*.mp.
14. Child*.mp. or Child/ or Child Health/ or Child, Hospitalized/
15. Public*.mp
16. 1 or 2
17. 3 or 4 or 5 or 6
18. 7 or 8 or 9 or 10 or 11

19. 12 or 13 or 14 or 15

20. 16 and 17 and 18 and 19 (in total 222 papers were found)

中国知网 (CNKI) 2017 年 7 月 27 日

选择学科领域: 医药卫生科技, 社会科学 I 辑, 社会科学 II 辑

高级检索: 关键词

检索 1: [关键词 ‘抗生素’ 或含 ‘抗菌药物’ 精确]

并且[关键词 ‘家长’ 或含 ‘居民’ 模糊]

并且[关键词 ‘行为’ 或含 ‘认知’ 模糊]

中英文扩展 共检索出文章 44 篇

Translation

Chinese database: CNKI (27th Jul 2017)

Research areas: Medicine and health sciences, Social science I and Social science II

Advanced search: Keyword

[Keyword ‘antibiotic’ or Keyword ‘antibacterial drug’ exact terms]

And [Keyword ‘parent’ or Keyword ‘resident/the public’ blurred terms]

And [Keyword ‘behaviour/practice’ or Keyword ‘knowledge/cognition’ blurred terms]

Including papers in English and papers in Chinese (in total 44 papers were founded)

Appendix E – Quality appraisal for the 29 Chinese language papers included in the review of literature

The quality appraisal tool in Hawker *et al.*'s (2002) study was used to appraise the quality of 29 Chinese language papers located via Chinese portal of CNKI in this literature review. This tool assesses the quality of papers from nine aspects through clear criteria, and ranks the quality of papers in each aspect as 'good', 'fair', 'poor' and 'very poor'. The nine aspects are related to the clear description of abstract and title (Q1), introduction and aims (Q2), method and data (Q3), sampling (Q4), analysis (Q5), ethics and bias (Q6), results (Q7), transferability or generalisability (Q8), and implications and usefulness (Q9), respectively. Based on Hawker *et al.*'s (2002) study, a score of four, three, two, and one to the level of 'good', 'fair', 'poor' and 'very poor' was given, respectively, to each aspect. Then a summed score of each paper was calculated and 29 Chinese-language papers were divided into four levels (1-9 very poor; 10-18 poor; 19-27 fair; 28-36 good) in line with their quality. Table below provided more specific information related to the quality of 29 Chinese language papers; among them, 10 Chinese language papers were defined as fair quality while the other 19 Chinese language papers were poor quality.

Table. The quality appraisal for 29 Chinese language papers

Authors	Title	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total score
Chen & Wang, 2014	住院患者对预防性使用抗菌药物相关信息认知情况的调查分析	3	2	2	3	3	1	3	1	2	20
Ding <i>et al.</i> , 2015	农村儿童家长抗生素认知态度与使用行为分析	3	3	3	2	2	2	4	2	2	23
Ding <i>et al.</i> , 2016	农村儿童家长抗生素认识现状及影响因素分析	3	3	2	2	2	1	4	2	2	21
Ding <i>et al.</i> , 2014	湖北省三级医疗机构医务人员抗菌药物合理使用认识现状调查	3	2	3	2	2	1	3	2	3	21
Du <i>et al.</i> , 2009	某三甲医院外科医师抗菌药认知调查	2	2	2	1	2	1	3	1	2	16
Fan, 2010	泰安市儿童家长对小儿应用抗生素认知情况的调查	2	3	3	2	2	1	2	1	2	18
Huang <i>et al.</i> , 2013	兰州市上呼吸道感染患者院外抗生素使用和认知状况调查研究	2	2	2	2	2	1	3	1	2	17
Li & Tong, 2013	住院手术患者对预防性使用抗菌药物相关信息认知情况的调查分析	3	2	2	2	2	1	3	1	2	18

Lin <i>et al.</i> , 2015	社区居民对抗菌药物的认知和态度以及使用情况分析	3	3	3	1	2	1	4	1	2	20
Liu <i>et al.</i> , 2013	2012年宜昌地区大学生抗生素认识与使用知识调查	3	1	1	2	1	1	3	1	2	15
Ma <i>et al.</i> , 2014	国家基本药物制度背景下山东居民抗菌药物认知与使用现状的调查分析	3	3	1	2	2	1	3	1	2	18
Rahmanjan <i>et al.</i> , 2013	喀什市社区医生合理使用抗生素的现状影响因素分析	3	2	1	1	1	1	3	1	2	15
Su <i>et al.</i> , 2012	我国各级医院医师对普通感冒认知与认知现状的调查	3	2	3	1	2	1	3	1	2	18
Tan <i>et al.</i> , 2016	居民对抗生素的认知及滥用现状的调查分析	3	1	1	1	2	1	3	1	2	15
Tan <i>et al.</i> , 2014	川东北地区乡镇居民抗生素认知和使用情况调查	3	2	1	1	2	1	3	1	2	16
Tian <i>et al.</i> , 2015	某高校大学生对抗生素认知状况的调查	2	2	1	2	2	1	2	1	2	15
Tian <i>et al.</i> , 2014	保定市南市区居民对抗生素的认知状况调查	3	2	2	2	2	1	3	1	2	18

Wang & Wang, 2013	居民抗菌药物认知和用药行为现状的评估及影响因素实证研究	3	3	3	2	3	1	4	1	2	22
Wang <i>et al.</i> , 2017	长沙市家长儿童上呼吸道感染抗生素使用知识与行为调查	3	3	3	3	2	1	3	1	3	22
Wang, 2013	我院患儿家长抗生素使用认知调查分析	2	2	2	2	2	1	2	1	2	16
Wang <i>et al.</i> , 2013	患者及家属对抗菌药物应用认识度的调查	3	2	2	2	2	1	3	1	2	18
Wang <i>et al.</i> , 2013	社区医生抗菌药物认知及使用情况调查分析	3	2	2	2	2	1	3	1	2	18
Wu, 2009	乡村医生抗生素的认知及应用情况调查	2	2	2	1	2	1	3	1	2	16
Xie & Zhang, 2014	泰安市儿科医生抗生素使用认知状况调查分析	3	3	2	1	2	1	3	1	2	18
Xiong <i>et al.</i> , 2015	居民对抗生素类药物的认知及自主使用现状分析	3	3	2	2	2	1	3	1	2	19
Ye <i>et al.</i> , 2014	东莞地区居民抗菌药物认知和用药行为现状的评估及影响因素实证研究	3	2	2	1	2	1	2	1	1	15

Zhang, 2015	社区医生应用抗生素的调查与分析	3	2	3	2	2	1	3	1	2	19
Zhao <i>et al.</i> , 2013	山东省农村居民抗生素认知与使用行为	3	3	3	4	2	1	4	1	2	23
Zheng, 2012	患儿家长109名抗生素认知水平调查分析	2	2	3	2	2	1	2	1	2	17

Appendix F – Information sheets and consent form for primary studies



[Knowledge, attitudes and behaviour relevant to antibiotic use among physicians, pharmacists and parents in Taiyuan City of Shanxi Province, China]

Participant Information Sheet

A qualitative study of antibiotic use among physicians in Taiyuan City

Dear Physicians,

I would like to invite you to take part in the above named study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information. Please feel free to ask the researcher if there is anything that is not clear or if you would like more information.

What is the purpose of this study?

Antimicrobial resistance (AMR), especially the development of bacteria resistant to antibiotics, is increasing rapidly all over the world. Compared with western countries, China has a higher rate of antibiotic use for the treatment of human illnesses, including among children. Also, China consistently ranks close to the top of global rankings for the prevalence of multiple antibiotic resistant strains, and the reported number of ineffective antibiotics is increasing. The causes of antibiotic use and resistance are multifactorial. This study aims to shed light on one aspect of this complex problem by learning about the views and experiences of physicians. The study will also include pharmacists and parents. Therefore, this part of the study would like to explore your views and experiences relevant to antibiotic use and resistance.

Who is doing the study?

This study is a part of a wider programme of research at the University of York in the UK concerned with human health and the natural environment. The study is funded by the University of York as part of a PhD Studentship. The chief researcher is Tingting Zhang, who is a PhD student in the Department of Health Sciences of the University of York, and is supervised by Professor Hilary Graham and Professor Piran White.

Who is being asked to participate?

I am inviting physicians who work at different health care institutions to reflect their views and experiences relevant to antibiotic use and resistance. Therefore, 6 paediatricians working at city hospitals and 6 general practitioners working at community health institutions will be invited.

What will be involved if I take part in this study?

If you are willing, I would invite you to participate in an interview to explore your views and experiences relevant to antibiotics use and resistance. The interview will be face-to-face, conducted on your worksite, and last approximately 30-45 minutes. The interview will be audio-recorded, with your permission. The audio-files from interviews will then be transcribed (listened to and written down in full) and analysed by the researcher.

Do I have to take part?

No. Taking part in the research is entirely voluntary. Whether you choose to take part or not, will not affect your work in any way. If you decide to take part, you will be given this information sheet to keep, and I will explain the consent process and confirm that you are willing to take part in the study. I will also allow time before the start of the interview to answer any further questions or clarify details, as required.

What are the advantages/benefits and disadvantages/risks of taking part?

Advantages/benefits: There are no incentives or payments for taking part. Taking part may help you to reflect on your views and experiences relevant to antibiotic use. In addition, a summary of study findings (in Chinese and English) will be sent to participants who wish to

receive it. You may benefit from an understanding of the views and experiences of other physicians as well as pharmacists, and parents in Taiyuan City.

Disadvantages/risks: The interview will take some of your time. You may be aware of some inappropriate prescribing behaviour relevant to antibiotics in hospitals or community health centres/stations. No information collected will allow you to be identified and all data will be kept securely.

Can I withdraw from the study at any time?

If you decide to take part, you are free to withdraw from this study at any time and you do not have to give a reason. Withdrawing from this study will not affect anything of your work. Data collected from participants who decided to withdraw from this study will not be used.

Will the information obtained in the study be confidential?

All the information is confidential. No information will be held that allows you to be identified, and all data will be kept securely. All audio-files, transcripts and analysis notes will be given a number to safeguard confidentiality and will be stored electronically on an encrypted storage device in a locked bag and at the University of York using its secure data systems (VPN - Virtual Private Network). Only the researcher and supervisors will have access to the data. At the end of the research the audio-files will be deleted securely and all electronic data will be stored for a maximum of five years. All data will be treated in accordance with the UK Data Protection Act (1998) and the University of York Department of Health Sciences' Data Security Policy.

What will happen to the results of the study?

The results will be reported in the PhD dissertation and in papers in scientific and professional journals, as well as in conference presentations. We will also provide a summary of findings to participants who wish to receive it.

Who has reviewed this study?

Two supervisors (Professor Hilary Graham and Professor Piran White) and Research Governance Committee of Department of Health Sciences, University of York reviewed this study for ethical compliance.

Who do I contact in the event of a complaint?

Please raise any difficulties or questions with the study supervisors:

Professor Hilary Graham (Department of Health Sciences, University of York) on email hilary.graham@york.ac.uk

Professor Piran White (Deputy Head of Department for Research, Environment Department, University of York) on email piran.white@york.ac.uk

If you agree to take part, would like more information or have any questions or concerns about the study please contact:

Name: Tingting Zhang

Position: PhD student in the Department of Health Sciences, University of York

Contact details: tz746@york.ac.uk

If you would like to receive a summary of study findings, please provide the contact details you prefer in the card of 'Participant Contact Details for Receiving the Study Summary'. I will send a summary to you and then destroy the contact details. (Please note that you don't need to provide your name in the contact details)

Thank you for taking the time to read this information sheet.

**[Knowledge, attitudes and behaviour relevant to antibiotic use among physicians,
pharmacists and parents in Taiyuan City of Shanxi Province, China]**

Participant Information Sheet

A qualitative study of antibiotic use among pharmacists in Taiyuan City

I would like to invite you to take part in the above named study. This leaflet explains why the study is being done and what it will involve. Please take time to read it. Please feel free to ask the researcher if there is anything that is not clear or if you would like more information.

What is the purpose of this study?

Antimicrobial resistance (AMR), especially the development of bacteria resistant to antibiotics, is increasing rapidly all over the world. Compared with western countries, China has a higher rate of antibiotic use for the treatment of human illnesses, including among children. Also, China consistently ranks close to the top of global rankings for the prevalence of multiple antibiotic resistant strains, and the reported number of ineffective antibiotics is increasing. The causes of antibiotic use and resistance are multifactorial. This study is aiming to learn about the views of pharmacists, as well as parents and physicians. Therefore, this study would like to explore your views and experiences relevant to antibiotic use and resistance.

Who is doing the study?

This study is a part of a wider programme of research at the University of York in the UK concerned with human health and the natural environment. The study is funded by the University of York as part of a PhD Studentship. The chief researcher is Tingting Zhang, who is a PhD student in the Department of Health Sciences of the University of York, and is supervised by Professor Hilary Graham and Professor Piran White.

Who is being asked to participate?

I am inviting pharmacists who work at different kind of pharmacies. Therefore, 16 participants will be invited to talk about antibiotic use and resistance, including 4 pharmacists working at city hospitals, 4 pharmacists in community health institutions, 4 pharmacists in retail pharmacies and 4 untrained staff in retail pharmacies.

What will be involved if I take part in this study?

If you are willing, we would invite you to participate in an interview to explore your knowledge, views and experiences relevant to antibiotics use and resistance. The interview will be face-to-face, conducted on your worksite and last approximately 30-45 minutes. The interview will be audio-recorded, with your permission. The audio-files from interviews will then be transcribed (listened to and written down in full) and analysed by the researcher.

Do I have to take part?

No. Taking part in the research is entirely voluntary. Whether you choose to take part or not, will not affect your work in any way. If you decide to take part, you will be given this information sheet to keep, and I explain what is involved and confirm that you are willing to take part in the study. I will also allow time before the start of the interview to answer any further questions or clarify details as required.

What are the advantages/benefits and disadvantages/risks of taking part?

Advantages/benefits: There are no incentives or payments for taking part. Taking part may help you to reflect on your views and experiences relevant to antibiotic use. In addition, a summary of study findings (in Chinese) will be sent to participants who wish to receive it. You may benefit from an understanding of the views and experiences of other pharmacists as well as physicians, and parents in Taiyuan City.

Disadvantages/risks: The interview will take some of your time. You may be aware of some inappropriate behaviour relevant to antibiotics (such as the sale of over-the-counter antibiotics) in pharmacies. No information collected will allow you to be identified and all data will be kept securely.

Can I withdraw from the study at any time?

If you decide to take part, you are free to withdraw from this study at any time and you do not have to give a reason. Withdrawing from this study will not affect anything of your work. Data collected from participants who decide to withdraw from this study will not be used.

Will the information obtained in the study be confidential?

All the information is confidential. No information will be held that allows you to be identified, and all data will be kept securely. All audio-files, transcripts and analysis notes will be given a number to safeguard confidentiality and stored electronically on an encrypted storage device in a locked bag and at the University of York using its secure data systems (VPN - Virtual Private Network). Only the researcher and supervisors will have access to the data. At the end of the research the audio-files will be deleted securely and all electronic data will be stored for a maximum of five years. All data will be treated in accordance with the UK Data Protection Act (1998) and the University of York Department of Health Sciences' Data Security Policy.

What will happen to the results of the study?

The results will be reported in the PhD dissertation and in papers in scientific and professional journals, as well as in conference presentations. We will also provide a summary of findings to participants who wish to receive it.

Who has reviewed this study?

Two supervisors (Professor Hilary Graham and Professor Piran White) and Research Governance Committee of Department of Health Sciences, University of York reviewed this study for ethical compliance.

Who do I contact in the event of a complaint?

Please raise any difficulties or questions with the study supervisors:

Professor Hilary Graham (Department of Health Sciences, University of York) on email hilary.graham@york.ac.uk

Professor Piran White (Deputy Head of Department for Research, Environment Department, University of York) on email piran.white@york.ac.uk

If you agree to take part, would like more information or have any questions or concerns about the study please contact:

Name: Tingting Zhang

Position: PhD student in the Department of Health Sciences, the University of York

Contact details: tz746@york.ac.uk

If you would like to receive a summary of study findings, please provide the contact details you prefer in the card of 'Participant Contact Details for Receiving the Study Summary'. I will send a summary to you and then destroy the contact details. (Please note that you don't need to provide your name in the contact details)

Thank you for taking the time to read this information sheet.

Participant Information Sheet

Giving antibiotics to children: understanding parents' views and experiences in Taiyuan City

I would like to invite you to take part in the above named study. This leaflet explains why the study is being done and what it will involve. Please take time to read it. Please feel free to ask the researcher if there is anything that is not clear or if you would like more information.

What is the purpose of this study?

Children consume considerable amounts of antibiotics worldwide because they are susceptible to infections, particularly upper respiratory tract infections (such as cold). In China, children are more likely to be given antibiotics than in other countries. Therefore, this study aims to explore parents' views and experiences relevant to antibiotic use for their child, as well as pharmacists and physicians.

Who is doing the study?

This study is a part of a wider programme of research at the University of York in the UK concerned with human health and the natural environment. The study is funded by the University of York as part of a PhD Studentship. The chief researcher is Tingting Zhang, who is a PhD student in the Department of Health Sciences of the University of York, and is supervised by Professor Hilary Graham and Professor Piran White.

Who is being asked to participate?

During the study about 100 parents of child patients in the paediatric department of two city hospitals (First Hospital of Shanxi Medical University and Taiyuan Hospital Health Centre for Women and Children) like yourself will be invited to answer a self-completion questionnaire about antibiotic use on their children.

What will be involved if I take part in this study?

You will not be asked to give your name, your child's name or your address. I will invite you to complete a questionnaire about your views and experiences of antibiotic use for your child. It will take about 20-25 minutes to complete within your waiting time at the paediatric clinic. Each questionnaire will then be given a number and the information from the questionnaires will be analysed by the researcher using a statistical analysis software on the computer.

Do I have to take part?

No. Taking part in the research is entirely voluntary. Whether you choose to take part or not, will not affect you and your child's health care in any way. If you decide to take part, you will be given this information sheet to keep, and I will explain what is involved and confirm that you are willing to take part in the study. I will also allow time when I give you the questionnaire to answer any further questions or clarify details as required.

What are the advantages/benefits and disadvantages/risks of taking part?

Advantages/benefits: There are no incentives or payments for taking part. Taking part may help you to reflect on your views and experiences regarding using antibiotics for your child. In addition, a summary of study findings (in Chinese) will be sent to participants who wish to receive it.

Disadvantages/risks: You might become more anxious about using antibiotics on your child. You do not need to answer any questions you do not want to and you will be given a summary of parents' views and experiences of antibiotic use.

Can I withdraw from the study at any time?

If you decide to take part, you are free to withdraw from the study at any time and you do not have to give a reason. Withdrawing from this study will not affect you and your child's health care.

Will the information obtained in the study be confidential?

All the information is confidential. No information will be held that allows you to be identified, and all data will be kept securely. All questionnaires will be given a number to safeguard

confidentiality and stored electronically on an encrypted storage device in a locked bag and at the University of York using its secure data systems (VPN - Virtual Private Network). Only the researcher and supervisors will have access to the data. The paper-based questionnaires will be destroyed by a shredder as soon as the information has been stored electronically and all electronic data will be stored for a maximum of five years. All data will be treated in accordance with the UK Data Protection Act (1998) and the University of York Department of Health Sciences' Data Security Policy.

What will happen to the results of the study?

The results will be reported in the PhD dissertation and in papers in scientific and professional journals, as well as in conference presentations. We will also provide a summary of findings to participants who wish to receive it.

Who has reviewed this study?

Two supervisors (Professor Hilary Graham and Professor Piran White) and Research Governance Committee of Department of Health Sciences, University of York have reviewed this study for ethical compliance.

Who do I contact in the event of a complaint?

Please raise any difficulties or questions with the study supervisors:

Professor Hilary Graham (Department of Health Sciences, University of York) on email hilary.graham@york.ac.uk

Professor Piran White (Deputy Head of Department for Research, Environment Department, University of York) on email piran.white@york.ac.uk

If you agree to take part, would like more information or have any questions or concerns about the study please contact:

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What is the purpose of this study?

Children consume considerable amounts of antibiotics worldwide because they are susceptible to infections, particularly upper respiratory tract infections (such as cold). In China, children are more likely to be given antibiotics than in other countries. Therefore, this study aims to explore parents' views and experiences relevant to antibiotics use for their child, as well as pharmacists and physicians.

Who is doing the study?

This study is a part of a wider programme of research at the University of York in the UK concerned with human health and the natural environment. The study is funded by the University of York as part of a PhD Studentship. The chief researcher is Tingting Zhang, who is a PhD student in the Department of Health Sciences of the University of York, and is supervised by Professor Hilary Graham and Professor Piran White.

Who is being asked to participate?

During the study period, about 30 parents of children, like yourself in this nursery, will be invited to participate in this study. You will then be divided into different groups (there are in total 6 groups with 5-6 parents in each group) to talk about antibiotic use on your child with researcher and other parents within your group.

What will be involved if I take part in this study?

You will not be asked to give your name, your child's name or your address. I will invite you to talk about your views and experiences of antibiotic use on your child with the researcher and another 4-5 parents. The discussion will be face-to-face, conducted in this nursery, and last approximately 45-60 minutes. It will be audio-recorded, with your permission. The audio-files will then be transcribed (listened to and written down in full) and analysed by the researcher.

Do I have to take part?

No. Taking part in the research is entirely voluntary. Whether you choose to take part or not, will not affect you and your child's anything in this nursery. If you decide to take part, you will be given this information sheet to keep, and I will explain what is involved and confirm that you are willing to take part in the study. I will also allow time before the start of focus group to answer any further questions or clarify details as required.

What are the advantages/benefits and disadvantages/risks of taking part?

Advantages/benefits: There are no incentives or payments for taking part. Taking part may help you to reflect on your views and experiences regarding using antibiotics for your child. In addition, a summary of study findings (in Chinese) will be sent to participants who wish to receive it.

Disadvantages/risks: You might become more anxious about using antibiotics on your child. You do not need to answer any questions you do not want to and you will be given a summary of parents' views and experiences of antibiotic use.

Can I withdraw from the study at any time?

If you decide to take part, you are free to withdraw from the study at any time and you do not have to give a reason. Withdrawing from this study will not affect anything of you and your child in this nursery.

Will the information obtained in the study be confidential?

All the information is confidential. No information will be held that allows you to be identified, and all data will be kept securely. The pseudonyms will be used in the transcripts to distinguish different speakers. All audio-files, transcripts and analysis notes will be given a number to safeguard confidentiality and stored electronically on an encrypted storage device in a locked bag and at the University of York using its secure data systems (VPN - Virtual Private Network). Only the researcher and supervisors will have access to the data UK. At the end of the research the audio-files will be deleted securely and all electronic data will be stored for a maximum of five years. All data will be treated in accordance with the UK Data Protection Act (1998) and the University of York Department of Health Sciences' Data Security Policy.

What will happen to the results of the study?

The results will be reported in the PhD dissertation and in papers in scientific and professional journals, as well as in conference presentations. We will also provide a summary of findings to participants who wish to receive it.

Who has reviewed this study?

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Name: Tingting Zhang

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Contact details: tz746@york.ac.uk

If you would like to receive a summary of study findings, please provide the contact details you prefer in the card of 'Participant Contact Details for Receiving the Study Summary'. I will send a summary to you and then destroy the contact details. (Please note that you don't need to provide your name in the contact details)

Thank you for taking the time to read this information sheet.

Record of verbal participant consent

Title of Study: Understanding antibiotic use in Taiyuan City of Shanxi Province, China

Name of researcher: Tingting Zhang (tz746@york.ac.uk)

	I have confirmed the statements by putting my initials in the boxes below
The participant has been given the information sheet which they have read/asked me to go through with them, and has had the opportunity to ask questions.	
I have explained that participation in the study is voluntary, the participant is free to withdraw from the study without giving any reason and that data provided prior to withdrawal will not be used	
I have explained that all the information is confidential and the participant will not be able to be identified	
I have explained that I may publish the results of this research and explained that I will not use any names or personal information.	
The participant has agreed to take part in this study	
Investigator Signature	Date
Participant number:	

Appendix G – The paper based on Chapter 2



HERALD

Community Medicine and Public Health Care

Zhang T, et al., J Community Med Public Health Care 2018, 5: 036
DOI: 10.24966/CMPH-1978/100036

HSOA Journal of
Community Medicine and Public Health Care

Research Article

Healthcare Providers' Accounts of Parental Influence on Their Behavior With Respect to the Use of Antibiotics for Children: A Qualitative Study in China

Tingting Zhang^{1,2*}, Hilary Graham² and Piran CL White¹

¹Environment Department, University of York, York, UK

²Department of Health Sciences, University of York, York, UK

Abstract

Background

High rates of paediatric use of antibiotics by healthcare providers are a key driver of antibiotic resistance in China. Qualitative studies are increasingly used to capture provider perceptions of influences on their antibiotic-related behavior; however, very few studies have been conducted in China. We undertook a qualitative study of providers in paediatric outpatient departments, primary care and retail pharmacies to examine their perceptions of influences on their antibiotic-related behavior.

Methods

Qualitative semi-structured interviews were conducted with 20 providers in a Chinese city of average wealth and health expenditure: 6 hospital-based paediatricians; 6 general practitioners in community health institutions; and 8 providers in retail pharmacies. Interviews were transcribed verbatim, translated from Chinese to English, and analysed using framework analysis.

Results

Parents were the most frequently-mentioned influence on providers' antibiotic-related behavior. Parental influences clustered under

three themes: the importance of public understandings of disease and treatment within Traditional Chinese Medicine and Western medicine; parental trust; and good relationships with patients.

Conclusion

To our knowledge, this is the first city-based qualitative study in China of providers' perceptions of influences on their antibiotic-related behavior, which points to the importance of cultural and system-level contexts: Public understandings of the human body grounded in Traditional Chinese Medicine and the role of trust and familiarity in provider-parent interactions. It suggests that information campaigns to promote appropriate antibiotic use should take account of these public understandings and be supported by a further strengthening of primary care, including remuneration systems that reward the quality of clinical decision-making.

Keywords: Antibiotic resistance; Familiarity; Traditional Chinese Medicine; Trust; Shanxi province

Introduction

High rates of paediatric use of antibiotics by healthcare providers (hereafter 'providers') are a key driver of antibiotic resistance in China [1,2], where rates of antibiotic resistance to most common bacteria are particularly high [3]. Prescription rates for paediatric patients using primary healthcare and hospital outpatient clinics range from 57.7% to 80.3% [4-7], well above the 30% rate recommended by World Health Organisation [8]. Additionally, while antibiotics are officially available on prescription only [9], retail pharmacies are a major source of over-the-counter (OTC) antibiotics for children [10].

Hospitals remain the cornerstone of China's healthcare system [11] but community health institutions (CHIs), which include community health centres and smaller community health stations, and retail pharmacies are rapidly-growing sectors [12]. All providers support both Western medicine and Traditional Chinese Medicine (TCM) [12,13], a holistic knowledge system used for 2000 years to prevent, diagnose and treat ill-health [14-16]. In the context of TCM, disease indicates unbalanced *yin-yang*, caused by bodily excesses (*liuyin*) and emotions (*qiqing*) [16]. Excess bodily heat can result in inflammatory conditions, along with fever, sore throat and other symptoms. TCM treatment methods include herbal medicines and diets, while surgical procedures are seldom used [13,14].

Qualitative studies are increasingly used to capture provider perspectives on factors influencing their behavior [17,18]; in high-income countries (HICs), studies of antibiotic-related behavior (ARB) have identified parental pressure as a key influence [19]. However, few studies have been conducted in China [2,20-22]. Our search of English-language (MEDLINE Ovid) and Chinese (Chinese National Knowledge Infrastructure) databases located two qualitative studies reporting providers' perceptions of influences on their ARB, both based in rural China [23,24]. Here we present the results of a qualitative study which aimed to examine the perceptions of providers in

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Citation: Zhang T, Graham H, White PCL (2018) Healthcare Providers' Accounts of Parental Influence on Their Behavior With Respect to the Use of Antibiotics for Children: A Qualitative Study in China. J Community Med Public Health Care 5: 036.

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Appendix H – COREQ checklist for study of parental influences on providers' use of antibiotics for children in China

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Topic and Item No.	Guide questions/description	Reported on Page No.
Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	pp.144
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	pp.20
3. Occupation	What was their occupation at the time of the study?	pp.20
4. Gender	Was the researcher male or female?	pp.144
5. Experience and training	What experience or training did the researcher have?	N/A
<i>Relationship with participants</i>		
6. Relationship established	Was a relationship established prior to study commencement?	pp.142
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	pp.142
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	pp.161-162
Domain 2: study design		
<i>Theoretical framework</i>		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	pp.86-89
<i>Participant selection</i>		

10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	pp.142
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	pp.144
12. Sample size	How many participants were in the study?	pp.141
13. Non-participation	How many people refused to participate or dropped out? Reasons?	pp.141
<i>Setting</i>		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	pp.144-145
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	N/A
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	pp.142
<i>Data collection</i>		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	pp.143-144
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	N/A
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	pp.144-145
20. Field notes	Were field notes made during and/or after the interview or focus group?	pp.145
21. Duration	What was the duration of the inter views or focus group?	pp.145
22. Data saturation	Was data saturation discussed?	pp.146
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	N/A
Domain 3: analysis and findings		
<i>Data analysis</i>		
24. Number of data coders	How many data coders coded the data?	pp.145-146
25. Description of the coding tree	Did authors provide a description of the coding tree?	pp.146-147
26. Derivation of themes	Were themes identified in advance or derived from the data?	pp.146
27. Software	What software, if applicable, was used to manage the data?	N/A
28. Participant checking	Did participants provide feedback on the findings?	N/A

<i>Reporting</i>		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	pp.147-161
30. Data and findings consistent	Was there consistency between the data presented and the findings?	pp.147-161
31. Clarity of major themes	Were major themes clearly presented in the findings?	pp.147-161
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	pp.147-161

Appendix I – The paper based on Chapter 3



Public Health Open Access

Healthcare Providers' Accounts of Influences of Antibiotic-Related Reforms on their Behavior with Respect to the Use of Antibiotics for Children: A Qualitative Study in China

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²Department of Health Sciences, University of York, UK

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Research Article

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Published Date: May 04, 2018

Abstract

Purpose: High and inappropriate pediatric use of antibiotics by healthcare providers is a key driver of antibiotic resistance in China. The Chinese government initiated a programme of antibiotic-related reforms in 2011 after a wider healthcare reform in 2009. However, very few studies shed light on the influence of these reforms on providers' antibiotic-related behavior; only one qualitative study of providers' perspectives and experiences has been undertaken. Therefore, our qualitative study aims to explore the influence of the 2009 and 2011 reforms on providers' pediatric antibiotic use.

Methods: Qualitative interviews were conducted with 26 providers in Taiyuan city, a typical Chinese city in central China in 2016. Interviews were transcribed verbatim, translated from Chinese to English, and analyzed using framework analysis.

Results: Healthcare providers described how their behavior was influenced by the availability of diagnostic testing. They also pointed to financial considerations and pressures, as well as other healthcare institutions within China's healthcare system that influence their antibiotic-related behavior.

Conclusions: As far as we are aware, this is the first city-based qualitative study in China providing evidence of the influences of the 2009 and 2011 reforms on providers' antibiotic-related behavior. It points to issues around the enforcement of antibiotic-related reforms in community health institutions and retail pharmacies, and highlights the importance of understanding the reforms' influences on provider behavior within China's healthcare system as a whole.

Keywords: Diagnostic facilities; Financial considerations; Essential Drug List; Zero mark-up; China's healthcare system

Appendix J – COREQ checklist for study of organisational influences on providers' use of antibiotics for children in China

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Topic and Item No.	Guide questions/description	Reported on Page No.
Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	pp.144
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	pp.20
3. Occupation	What was their occupation at the time of the study?	pp.20
4. Gender	Was the researcher male or female?	pp.144
5. Experience and training	What experience or training did the researcher have?	N/A
<i>Relationship with participants</i>		
6. Relationship established	Was a relationship established prior to study commencement?	pp.142
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	pp.142
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	pp.191
Domain 2: study design		
<i>Theoretical framework</i>		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	pp.86-89
<i>Participant selection</i>		

10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	pp.142
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	pp.144
12. Sample size	How many participants were in the study?	pp.173
13. Non-participation	How many people refused to participate or dropped out? Reasons?	pp.172-173
<i>Setting</i>		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	pp.144-145
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	N/A
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	pp.142, 172-174
<i>Data collection</i>		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	pp.143-144,174
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	N/A
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	pp.144-145
20. Field notes	Were field notes made during and/or after the interview or focus group?	pp.145
21. Duration	What was the duration of the interviews or focus group?	pp.145
22. Data saturation	Was data saturation discussed?	pp.146
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	N/A
Domain 3: analysis and findings		
<i>Data analysis</i>		
24. Number of data coders	How many data coders coded the data?	pp.145-146
25. Description of the coding tree	Did authors provide a description of the coding tree?	pp.175-176
26. Derivation of themes	Were themes identified in advance or derived from the data?	pp.175-176
27. Software	What software, if applicable, was used to manage the data?	N/A

28. Participant checking	Did participants provide feedback on the findings?	N/A
<i>Reporting</i>		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	pp.176-190
30. Data and findings consistent	Was there consistency between the data presented and the findings?	pp.176-190
31. Clarity of major themes	Were major themes clearly presented in the findings?	pp.176-190
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	pp.176-190

Appendix K – A topic guide used for focus groups in parental study

Giving antibiotics to children: understanding parents' views and experiences in Taiyuan city

Dear Parents,

Good day. I am a PhD student at the University of York in the UK. My study is exploring antibiotic use by parents, doctors and pharmacists. In China, parents may not always be sure what is wrong with their children when they are not well and may wonder if antibiotics would be helpful. This focus group will help me gain a better understanding of the views and experiences of parents in Taiyuan City regarding the use of antibiotics for their children. I would really appreciate it if you could share your opinions and experiences on antibiotic use. Thanks again for your time and cooperation. Now, let's start!

Topics:

1. Could you please recall what you did when your children were ill in the last 12 months? (Visit a doctor? Parental medication? To do nothing?) Could you please give me some examples?
2. Did your children use antibiotics in the last 12 months?
3. Case study

Emma is a 4-year-old girl in this nursery who has been previously healthy. On one day of November, she starts to have the symptom of a runny nose and looks slightly tired.

- a) What do you think Emma's parents should do? (Do nothing, seek professional health care, self-treat)

Her parents do nothing for her, and on the 3rd day, she complains of feeling congested, having copious green nasal discharge, and intermittent headaches. She looks tired and slightly pale. But on examination she does not have a temperature.

- b) What should Emma's parents do?
Should they bring her to visit a doctor? If yes, should they go to hospitals or community health institutions?
Should they treat her by themselves? If yes, what kind of treatments should they give?

Should they still do nothing on her?

Why should they do that?

In fact, Emma's parents use some antiviral drugs and Chinese patent medicines on her by themselves from the 3rd day. However, on the next day (the 4th day), Emma becomes worse and has a low-grade fever with intermittent cough.

c) What should Emma's parents do?

Should they bring her to visit a doctor? If yes, go to hospitals or community health institutions?

Should they use some antibiotics on Emma by themselves instead of antiviral drugs and Chinese patent medicines?

Why should they do that?

Actually, Emma's parents take her to a paediatrician in the hospital immediately on the 4th day when Emma becomes worse. After the consultation, the paediatrician diagnoses Emma's disease as viral flu and prescribes some antiviral drugs to Emma. Emma's parents use these drugs according to the physician's prescription. However Emma's symptoms still continue.

d) What should Emma's parents do?

Should they still use the drugs according to the prescription and then return for further consultation?

Should they take her to another doctor? If yes, hospitals or community health institutions?

Should they start to use some antibiotics on Emma by themselves?

Why should they do that?

Finally, Emma's parents start to use antibiotics on Emma by themselves and do not take her to any doctors or return for a further consultation. And after another five days, Emma recovers and remains healthy.

e) Do you think that the antibiotics cured Emma's disease?

4. When you bring your children to visit a doctor, for which of the following symptom(s) do you think a doctor might prescribe antibiotics?

A. Runny nose

- B. Nasal congestion
- C. Cough
- D. Sore throat
- E. Fever
- F. Ache and Pains
- G. Vomiting
- H. Diarrhoea
- I. Skin wounds
- J. None
- K. Other (please specify)

5. During the consultation, when you are keen that your child receive antibiotics, do you directly make clear your wish to the doctor to prescribe antibiotics?

Please think about the last time you made clear you wished a doctor prescribe antibiotics for your child, did the doctor refuse your request?

If No, did you have to persuade the doctor to give your child a prescription for antibiotics, before they did so? Could you please try to describe what you said?

If Yes, did you try to persuade the doctor to give your child a prescription for antibiotics, after he/she told you he/she is not going to prescribe your child any? Could you please try to describe what you said?

Do you still think the doctor should have prescribed your child antibiotics? Why do you think so?

Do you feel dissatisfied if he/she refuses your request for antibiotics?

6. When a doctor prescribes antibiotics for your child, have you ever refused or been reluctant to accept the prescription?

If yes, could you please give some examples (For instance, refuse any antibiotics, or refuse to use expensive or new generation antibiotics, or prefer oral antibiotics to the treatment of intravenous infusion, before or after the prescription)?

What do you think are reasons that you refused the antibiotics?

7. Do you think the communication about prescribing antibiotics to your children between you and doctors during the consultation is sufficient?

Does the doctor explain to you the reasons that he/she prescribes antibiotics to your child during the consultation?

When the doctor does not explain, do you ask for the reasons for prescribing antibiotics?

8. Do you usually use antibiotics on your child according to the prescription?

For example, does your child take a full course of antibiotics?

Does your child take the right dosage of antibiotics at the right time?

Do you ever use a higher dose on your child?

Do you keep unused antibiotics for future use?

If No, could you please give me some reasons or examples?

9. Do you ever visit a doctor without your child when he/she is ill? Do you ever not bring your child for a further consultation even though it is required by a doctor?

10. Do you ever treat your child with antibiotics by yourself when he/she is ill or symptomatic? When you treat your child with antibiotics by yourself, what are the main sources where you get antibiotics?

Where did you usually purchase the over-the-counter antibiotics?

11. What kinds of side effects of antibiotics sometimes happen in your child?

- A. Nausea
- B. Vomiting
- C. Diarrhoea
- D. Rash
- E. Vaginal thrush
- F. Antibiotic resistance
- G. Others (Please specify)
- H. Never experienced any adverse effects

11.1 a). Have you ever heard of antibiotic resistance? (If antibiotic resistance is not mentioned in Topic 11)

If No, the focus group will finish.

If yes, what do you know about antibiotic resistance?

b). As you mentioned antibiotic resistance above, what do you know about antibiotic resistance? (If antibiotic resistance is mentioned in Topic 9)

11.2 Do you think antibiotic resistance is a problem?

If yes, what do you think is the most important cause of the resistance of antibiotics? (e.g. consumer behaviour, behaviour of retail pharmacies, physicians' prescribing behaviour)

Do you have any ideas to tackle the problems of antibiotic resistance?

11.3 Where do parents usually get the information about antibiotics and antibiotic resistance?

11.4 Who do you think should provide information about antibiotics and antibiotic resistance to parents?

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Research Date:

Research Place:

1. Your gender: <input type="checkbox"/> Male <input type="checkbox"/> Female
2. Your age: <input type="checkbox"/> under 30 years old <input type="checkbox"/> 30-39 years old <input type="checkbox"/> 40-49 years old <input type="checkbox"/> 50 or over years old
3. Your highest educational level: <input type="checkbox"/> Primary school or below <input type="checkbox"/> Secondary school <input type="checkbox"/> High School/ Secondary technical college <input type="checkbox"/> College/ University <input type="checkbox"/> Postgraduate studies or above
4. Your occupation: _____
5. What kind(s) of health insurance(s) do you have now? (Check more than one if applicable) <input type="checkbox"/> Urban Employee Basic Medical Insurance <input type="checkbox"/> Urban Resident Basic Medical Insurance <input type="checkbox"/> New Rural Cooperative Medical Insurance <input type="checkbox"/> Commercial health insurance

None

Others (please specify) _____

6. Would you describe the yearly income of your household in 2015 as: (the yearly income should be the total gross income of all residents in your household, including salary, bonus, business and agricultural income, pension, dividend, interest, rent and any other income)

Below 10,000 RMB

10,000-24,999RMB

25,000-49,999RMB

50,000 RMB and above

7. Where did you live?

Taiyuan City

Other cities in Shanxi Province

Rural areas in Shanxi Province

Other Province

That is all. Thank you very much for your cooperation and I wish you and your family all the best!

Appendix L – COREQ checklist for the focus group of parental study

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Topic and Item No.	Guide questions/description	Reported on Page No.
Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	pp.207
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	pp.20
3. Occupation	What was their occupation at the time of the study?	pp.20
4. Gender	Was the researcher male or female?	pp.144
5. Experience and training	What experience or training did the researcher have?	N/A
<i>Relationship with participants</i>		
6. Relationship established	Was a relationship established prior to study commencement?	pp.205
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	pp.205
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	pp.246-247, 253-257
Domain 2: study design		
<i>Theoretical framework</i>		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	pp.86-89
<i>Participant selection</i>		

10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	pp.205
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	pp.206-207
12. Sample size	How many participants were in the study?	pp.209
13. Non-participation	How many people refused to participate or dropped out? Reasons?	pp.205-206
<i>Setting</i>		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	pp.206
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	N/A
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	pp.209-210
<i>Data collection</i>		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	pp.206-208
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	N/A
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	pp.207
20. Field notes	Were field notes made during and/or after the interview or focus group?	pp.207
21. Duration	What was the duration of the inter views or focus group?	pp.207
22. Data saturation	Was data saturation discussed?	pp.146,209
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	N/A
Domain 3: analysis and findings		
<i>Data analysis</i>		
24. Number of data coders	How many data coders coded the data?	pp.209
25. Description of the coding tree	Did authors provide a description of the coding tree?	pp.211-212
26. Derivation of themes	Were themes identified in advance or derived from the data?	pp.209, 211-212
27. Software	What software, if applicable, was used to manage the data?	N/A
28. Participant checking	Did participants provide feedback on the findings?	N/A

<i>Reporting</i>		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	pp.212-223
30. Data and findings consistent	Was there consistency between the data presented and the findings?	pp.212-223
31. Clarity of major themes	Were major themes clearly presented in the findings?	pp.212-223
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	pp.212-223

Appendix M – A questionnaire for the survey of parental study

Code

Giving antibiotics to children: understanding parents' views and experiences in Taiyuan city

Dear Parents,

Good day. I am a PhD student at the University of York in the UK. My study is exploring antibiotic use by parents, doctors and pharmacists in China. Parents may not always be sure what is wrong with their children when they are not well and may wonder if antibiotics would be helpful. This questionnaire will help me gain a better understanding of the views and experiences of parents in Taiyuan City regarding the use of antibiotics for their children. I would really appreciate it if you could share your opinions and experiences of antibiotic use. In this research, all the information is confidential. No information will be held that allows participants to be identified, and all data will be kept securely. In addition, a summary of findings about this research will be sent to participants who wish to receive it. Thanks again for your time and cooperation.

Completing the questionnaire

- Please answer questions by ticking the box before the answer, as in the example below.

Example Question: Did you have breakfast this morning? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

- Please answer questions according to the instructions and guidelines. Please tick only one box when there is no instruction. Please tick more than one answer if instructions saying '**please check more than one if applicable**' or '**please tick any that apply to you**' are marked. Please follow the specific instructions of particular questions.
- For some particular questions, instructions will show which question to answer next. If there are no instructions, please just answer the next question.
- Important information will be in **bold** and (or) underlined, please pay more attention to this information.

Now please go to Q1 and start filling in your answers.

Section 1. These questions are about your views on antibiotic use

1. Do you know what antibiotics are?
 Yes
 No
 Not sure

2. Do you think antibiotics are the same as anti-inflammatories?
- Yes
 - No
 - Don't know
3. In your opinion, what kind of diseases are antibiotics used for? **(Check more than one if applicable)**
- Bacterial infections
 - Viral infections
 - Others (specify) _____
 - Don't know
4. Do you think that children may suffer from any of the following side-effects as a result of taking antibiotics? **(Check more than one if applicable)**
- Nausea
 - Vomiting
 - Diarrhoea
 - Rash
 - Vaginal thrush
 - Antibiotic resistance
 - None of the above
 - Others (please specify) _____
 - Don't know
5. Do you know what antibiotic resistance is?
- Yes
 - No
 - Not sure
6. Which of the following statements do you think is (are) correct? **(Please write True (T)/False (F) against each statement)**
- Higher doses of antibiotics result in faster recovery
 - Lower doses of antibiotics result in fewer adverse effects
 - Antibiotic treatment should be stopped as soon as symptoms have disappeared
 - Continuing antibiotic use after the full treatment course will consolidate the effectiveness of the treatment
 - Stopping the antibiotic treatment before the course is complete will increase the risk of antibiotic resistance
 - The more expensive antibiotics are, the better and more effective they are
 - Broad-spectrum antibiotics (e.g. Amoxicillin) are more effective because they can kill a variety of bacteria
 - Antibiotics can only be prescribed by doctors
 - Antibiotics must be obtained (purchased) with a doctor's prescription

7. Which of the following sources of information have you found helpful when thinking about using antibiotics for your child? **(Please tick the 3 most helpful)**

- Doctors
- Staff in retail pharmacies
- Friends and family
- Internet
- Television
- Radio
- Newspaper
- Professional training
- Public lectures held in the community
- None of these
- Others (please specify) _____

8. Please indicate whether you agree or disagree with each following statements by ticking the box that applies to you.

	Disagree	Uncertain	Agree
Antibiotics are used too much on children in our country.			
When my child suffers from a cough, she/he would be cured more quickly if she/he received antibiotics as early as possible.			
Antibiotics should be the first choice when my child has a fever.			
Parents should be given more information about how to use antibiotics to help their child.			
Scientists can produce new varieties of antibiotics without difficulty when these are needed.			
The resistance of antibiotics among children is a serious problem.			
I worry that my knowledge of resistance of antibiotics is not sufficient.			

Section 2. These questions are about times when your child is unwell and using antibiotics

9. Could you please recall the number of times you brought this child to visit a doctor **in the last 12 months?** _____

10. Here are some reasons why a parent may not take their child to the doctor when they are not well. Thinking back **over the last 12 months** to times when your child has not been well, **please tick any that apply to you.**

- I did not have enough time to visit a doctor.
- I thought that my child's condition was not serious enough.
- Some drugs previously prescribed by doctor for the similar symptoms were left over at home.

- It is convenient to purchase drugs like antibiotics without prescriptions.
- I did not have enough money to pay for the hospital visit.
- Others (please specify)_____

11. Could you please recall whether your child has used antibiotics **in the last 12 months?**

- Yes
- No
- Not sure

12. For which of the following symptom(s) would you expect the doctor to prescribe antibiotics for your child? **(Check more than one if applicable)**

- Runny nose
- Nasal congestion
- Cough
- Sore throat
- Fever
- Ache and Pains
- Vomiting
- Diarrhoea
- Skin wounds
- None
- Others (please specify)_____

13. When you see a doctor with your child and you are keen that your child receives antibiotics, would you make clear your wish to the doctor to prescribe antibiotics?

- Yes
- No **(Please go directly to Q16)**

14. Please thinking about **the last time** that you make clear your wish to a doctor to prescribe antibiotics to your child, did the doctor refuse your request?

- Yes
- No **(Please go directly to Q16)**

15. Would you feel dissatisfaction with the doctor when he (she) refused your request for antibiotics?

- Yes
- No

16. Have you ever been reluctant to accept a prescription from a doctor for antibiotics for your child?

- Yes
- No **(Please go directly to Q18)**

17. For what reasons would you be reluctant to accept the prescription of antibiotics for your child? **(Please tick any that are apply to you)**

- I worry about the side-effects caused by antibiotics

- I worry about the antibiotic resistance (ABR) caused by antibiotics
- I do not want my child to use new generation antibiotics
- I think there may be some financial interests between the antibiotics prescribed and doctors
- The antibiotics prescribed are too expensive
- Others (Please specify)_____

Thinking about **the last time** that your child was prescribed antibiotics by doctors, please could you answer each question below by ticking in the box that applies to you.

	Yes	No
18. I was satisfied with the communication between the doctor and me about the reasons for prescribing antibiotics to my child during the consultation.		
19. My child came with me to see a doctor.		
20. I used antibiotics on my child in line with the dosage instructions with came with the antibiotics.		
21. My child took the full course of antibiotics.		
22. I needed to give my child antibiotics at dosages higher than instructed.		
23. I kept unused antibiotics for future use on my child.		

Sometimes when a child is not well, parents may give their child some antibiotics rather than take their child to a doctor. Thinking about your child.

24. Have you ever treated your child with antibiotics yourself?

- Yes, always
- Yes, sometimes
- No (**Please go directly to Q27**)

25. If yes, thinking about **the last time** you treated your child with antibiotics by yourself, did your child get better?

- Yes
- No
- Not sure

26. Could you please recall the number of times you treated your child with antibiotics by yourself **in the last 12 months?** _____

27. Apart from the antibiotics prescribed by the doctor, what is (are) source(s) that you get antibiotics from? (**Check more than one if applicable**)

- Unused antibiotics from previous prescription
- Antibiotics purchased without a doctor's prescription

- Antibiotics received from others (family, friends)
- Others (please specify)_____

28. Have you purchased antibiotics without a doctor's prescription?

- Yes
- No **(Please go directly to section 3)**

29. Where would you usually purchase antibiotics without a doctor's prescription? **(Check more than one if applicable)**

- Community health centres (stations)
- Retail pharmacy
- Online pharmacy
- Bazaar
- Others (please specify)_____

Section 3. Background information

<p>30. Your gender:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Male <input type="checkbox"/> Female
<p>31. Your age:</p> <ul style="list-style-type: none"> <input type="checkbox"/> under 30 years old <input type="checkbox"/> 30-39 years old <input type="checkbox"/> 40-49 years old <input type="checkbox"/> 50 and over years old
<p>32. Your highest educational level:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Primary school or below <input type="checkbox"/> Secondary school <input type="checkbox"/> High School/ Secondary technical college <input type="checkbox"/> College/ University <input type="checkbox"/> Postgraduate studies or above
<p>33. Your occupation: _____</p>
<p>34. What kind(s) of health insurance(s) do you have now? (Check more than one if applicable)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Urban Employee Basic Medical Insurance <input type="checkbox"/> Urban Resident Basic Medical Insurance <input type="checkbox"/> New Rural Cooperative Medical Insurance <input type="checkbox"/> Commercial health insurance <input type="checkbox"/> None <input type="checkbox"/> Not sure <input type="checkbox"/> Others (please specify)_____
<p>35. The age of your child in today's visit: _____ years (please give months if under 1 year)</p>

36. Would you describe the yearly income of your household (the total gross income of all adults in your household, including earnings and income from other sources) **in 2015** as:

- Below 10,000 RMB
- 10,000-24,999RMB
- 25,000-49,000RMB
- 50,000 RMB and above

37. Where did you live?

- Taiyuan City
- Other cities in Shanxi Province
- Rural areas in Shanxi Province
- Other Province

The end. Please give the questionnaire to the interviewer.

Thank you very much for your cooperation and I wish you and your family all the best!

List of abbreviations

ABR	Antibiotic resistance
AIDS	Acquired immune deficiency syndrome
AMR	Antimicrobial resistance
CFDA	China Food and Drug Administration
CHIs	Community health institutions
CNKI	Chinese National Knowledge Infrastructure
COREQ	Consolidated criteria for REporting Qualitative research
DDDs	Defined daily doses
EDL	Essential drug list
ESBLs	Extended-spectrum β -lactamases
FFS	Fee-for-service
GDP	Gross Domestic Product
GPs	General practitioners
HICs	High-income countries
ICUs	Intensive care units
LMICs	Low and middle-income countries
MoH	Ministry of Health
MoHRSS	Ministry of Human Resources and Social Security
MRCNS	Methicillin-resistant coagulase negative <i>Staphylococcus</i>
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
NHFPC	National Health and Family Planning Commission
NRCMS	New Rural Cooperative Medical Scheme
OTC	Over-the-counter
SATCM	State Administrations of Traditional Chinese Medicine
SEF	Social ecological framework
TB	Tuberculosis
TCM	Traditional Chinese medicine
THE	Total health expenditure

UEBMI	Urban Employee Basic Medical Insurance
URBMI	Urban Resident Basic Medical Insurance
VISA	Vancomycin-intermediate <i>Staphylococcus aureus</i>
WHO	World Health Organisation
WTO	World Trade Organisation
ZMU	Zero mark-up

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