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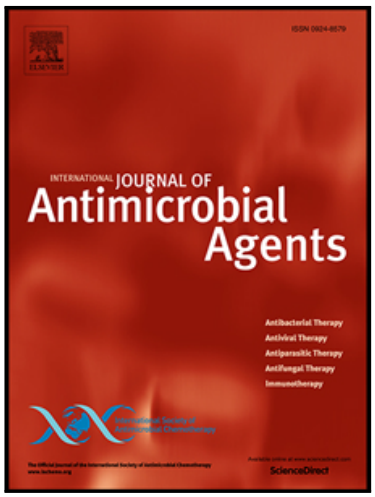

Large-scale survey of parental antibiotic use for paediatric upper respiratory tract infections in China: implications for stewardship programmes and national policy

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HIGHLIGHTS

- Caregivers account for at least 40% of outpatient antibiotic use on Chinese children.
- Parents' perception of antibiotics as efficacious for treating URTIs and easy access to antibiotics, with or without a prescription, drives antibiotic misuse in China.
- Simultaneously enhancing both prescribing guidelines, doctor-patient communication skills, and patient education targeting the family as a unit is critical.
- Patient education interventions should prioritise urban parents with low socio-economic status in less developed regions and be disseminated via medical professionals or media.

Title Page

Large-scale survey of parental antibiotic use for paediatric upper respiratory tract infections in China: implications for stewardship programmes and national policy

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ABSTRACT

BACKGROUND

Inappropriate use of antibiotics for upper respiratory tract infections among Chinese children is rampant. To identify key constructs for effective interventions targeting the public, we investigated parents' decision-making processes with respect to treatment choices and antibiotic use for paediatric URTIs.

METHODS

Data were collected between June 2017-April 2018 from a cluster random sample of 3,188 parents of children aged 0-13 across three Chinese provinces, representing different stages of economic development. Risk factors of parents' treatment choices and antibiotic use for paediatric URTIs were assessed, using binary and multinomial logistic regressions, adjusting for socio-demographic characteristics.

RESULTS

Of the 3,188 parents who self-diagnosed their children with a URTI, 46.0% children were given antibiotics, with or without prescription (n=1465). Among them, 40.5% were self-medicated with antibiotics by parents and 56.1% obtained further antibiotic prescriptions at healthcare facilities. About 70% of children with URTI symptoms sought healthcare (n=2197); of them, 54.8% obtained antibiotic prescriptions and 7.7% asked for antibiotic prescriptions with a 79.4% success rate to obtain them. Those perceiving antibiotics as effective for treating common cold and fever (aOR=1.82[1.51-2.19] and 1.77[1.47-2.13], respectively), who had access to non-prescription antibiotics (aOR=5.08[4.03-6.39]), and with greater perceived severity of infection (aOR=2.01[1.58-2.56]), were more likely to use antibiotics.

CONCLUSIONS

Context-appropriate multifaceted interventions are vital to untangle the perpetual problem of self-medication, over-prescription and ill-informed demands for antibiotics. Our findings emphasise the need to prioritise interventions enhancing clinical training, neutralising the pressure from patients for antibiotics, educating on appropriate home care, discouraging antibiotic self-medication, and improving antibiotic dispensing.

Keywords: antibiotics, child health, upper respiratory tract infections, antimicrobial resistance

INTRODUCTION (3294)

Acute, uncomplicated upper respiratory tract infections (URTIs) – often benign, self-limiting, and untreatable by antibiotics - are diagnosed on symptomatology and treatments are mainly symptomatic rather than focusing on changes in viral titres in the airway or viral shedding.[1] Considered the most common infectious disease among humans, URTIs are the most common cause of primary care visits and unnecessary use of antibiotics for children around the world, especially in China,[2-4] which has contributed to the rise of antimicrobial resistance (AMR), an imminent global health threat. Antibiotic-resistant pathogens, such as *streptococcus pneumonia*, have been reported in children across China.[5,6] Antibiotic treatment changes gut microbiota and adversely impacts the development of the immune system, making it difficult for children to recover from repeated antibiotic exposure.[7,8] Given the long-term consequences on human development and that children may experience URTIs seven to ten times on average annually,[1] misuse of antibiotics in children is particular harmful. Nevertheless, 48.2% of urban parents[9] and 62% of rural parents[10] in China reported to have self-medicated children with antibiotics outside of clinical settings within the last six months.

Understanding the underlying reasons that drive the parental decision to use antibiotics for paediatric URTIs without professional guidance is important for developing strategies to reduce antibiotic misuse. To date, most public-targeted health behaviour research and interventions on antibiotic use have centred on knowledge-attitudes-practice (KAP), with the underlying assumption that individuals would make more risk-conscious choices if informed of the risks of AMR – an approach has long been criticised for its overemphasis on personal responsibility.[11] When faced with an acute infection in themselves or a loved one, individuals may disproportionately focus on the immediate outcome of curing the illness (i.e. perceived antibiotic efficacy), and discount long term risks such as AMR.[12] As such, parents' decision-making for treating URTIs might not be as rational or informed as a KAP approach

would assume. To develop effective interventions to reduce unnecessary or inappropriate use of antibiotics for paediatric URTIs in the Chinese community, evidence is needed on parents' decision-making for care and how these decisions influence antibiotic use within or outside of clinical settings. Here, for children with self-diagnosed URTI symptoms, we investigated the extent and risk factors associated with the likelihood of (1) self-medication with non-prescription antibiotics by parents; (2) healthcare seeking; (3) parental requesting for antibiotics and unnecessary prescriptions by healthcare providers.

METHODS

Study population

We used data from a survey of parents with children aged 0-13 years between June 2017 and April 2018. Three Chinese provinces, which represent different geographical areas and stages of economic development, [13] were chosen. These included Zhejiang (East, ranked 5th out of 31 in the 2017 provincial GDP ranking of economic development), Shaanxi (Central-Northwest, ranked 12th), and Guangxi (Southwest, ranked 26th) provinces. A multistage stage random clustering sampling design was applied. The four-stage sampling units are provinces, prefecture-level cities, urban and rural areas, and local sites: primary schools (age 6-13), kindergartens (age 3-5) and community health centres (age 0-2), where most children received vaccination.[14] Parents were identified and recruited through their children from all selected sites. They were asked to complete a structured questionnaire, which was tailored to the Chinese sociocultural context informed by literature review[10,15,16] and formative/qualitative interviews with stakeholders and experts. The questionnaire was comprised of four sections: 1) parental socio-demographic information, 2) healthcare- and antibiotic-related knowledge and perceptions, 3) last episode of URTI symptoms experienced by the child within the past month, and 4) treatment and parental care-seeking process and

behaviours for the child's illness (i.e. the chemical or brand names of antibiotics obtained from clinics and retail pharmacies). To minimise the burden for the parents and ensure high quality of the response data, the survey was designed to take no more than 10 minutes and an IP address control was put in place to detect random responses or duplications. Parents could complete the questionnaire on a mobile device, online, or using a paper version and they were informed that participation was confidential, voluntary and could be terminated at any time. A consent form was presented in the first section of the questionnaire and was signed by the participants. To validate the questionnaire, we conducted a pilot study with 315 respondents to evaluate potential sources of response error and improve the instrument. The questionnaire was completed by 9,526 parents, with a response rate of 89%. Of those, 33.5% (n=3,188) reported that their children had experienced symptoms of a URTI within a month prior to the survey, including cold (cough, runny/stuffy nose), fever, sore throat, headache, and flu, either alone or in combination[1].

Outcome variables

Participating parents reported whether they (1) self-treated children with antibiotics: *did not use antibiotics, self-medication with antibiotics,* and *seeking formal care after self-medication with antibiotics at home*; (2) sought care and/or requested antibiotics: *did not seek care, sought care, and sought care and explicitly requested antibiotics for their children*. In addition, parents also reported whether clinicians' prescribed antibiotics for their child: *no antibiotic prescription, antibiotic prescriptions without being prompted,* and *inappropriate antibiotic prescriptions due to parental demands.*

Exposure variables Informed by the Health Belief Model[17,18], we included the following potential risk factors in our analyses:

(1) Whether parents had a medical background (yes/no), as it is relevant to parents' self-efficacy for making healthcare decisions for their children.

(2) Parents' ability to identify antibiotics, measured by *number of commonly available drugs correctly identified by parents as antibiotics or non-antibiotics: low (0-1), medium (2-3), high (4 or higher);*

(3) Parents' perceptions: (a) perceived benefits of antibiotic use, measured by two factual statements about antibiotics' efficacy to treat the common cold or fever; and (b) perceived severity of the infection, measured by the number of self-diagnosed URTI symptoms the child experienced*;*

(4) Cues to action: included (a) presence of fever and (b) information sources for treatment decisions: medical advice, family, and media including social media.

(5) *Parents' access to antibiotics* (with or without prescriptions), including: (a) non-prescription antibiotics: parents' habits of *keeping antibiotics at homes for children* in the past year; and (b) antibiotic prescriptions: when a child received formal care, *point of care used for treatment* was assessed, including hospitals above county level, county hospitals, township hospitals, and local clinics.

Covariates: Socio-demographic characteristics were included as potential confounders for the association between each exposure and treatment decisions, including *sex and age of the child, household income, parental education, urbanicity* and *province*.

Statistical analysis We first developed a flow diagram (Figure 1) to illustrate parental decision-making process of treatment and antibiotic use in their children for URTIs, from (non-clinical) household to (clinical) facility. We summarised the distributions of socio-demographic characteristics and factors by treatment decision/behavioural outcomes. To examine the association between each factor and outcome, we applied logistic regressions to estimate the OR (95% CI) for (1) 'self-medication with antibiotics' (vs 'no self-medication with antibiotics') and (2) 'seeking healthcare' (vs 'without seeking healthcare'). Factors considered include parental medical background, ability to identify antibiotics, perceived

antibiotic efficacy for cold or fever, self-diagnosed severity, cues to action, and access to antibiotics. We explored the associations with subgroups of antibiotic and healthcare use, and applied multinomial logistic regressions to estimate the relative risk ratio, RRR (95% CI) for (1) 'self-medication with antibiotics without seeking healthcare' and 'self-medication with antibiotics then sought healthcare' (vs 'no self-medication with antibiotics') and (2) 'sought healthcare without requesting antibiotic prescriptions' and 'sought healthcare and requested prescriptions' (vs 'no seeking healthcare'). For parents who sought healthcare for their children, we estimated RRR (95%CI) for "receiving prescriptions without patients' request' and 'receiving prescriptions due to patients' request' (vs 'without an antibiotic prescription'). For each outcome and risk factor, we first fitted an unadjusted model, and then adjusted for the potential confounders to establish whether the association was independent of these socio-demographic characteristics. Because different risk factors tend to co-occur, as sensitivity analyses, we mutually adjusted for all risk factors simultaneously.

RESULTS

Out of 3,188 parents whose children had URTI symptoms within the last month, 594 (18.6%) were self-medicated by parents without medical prescription - 56% of these children further obtained antibiotic prescriptions at healthcare facilities. Approximately 70% of children with URTI symptoms (n=2197) sought healthcare; of them, 1204 (54.8%) obtained antibiotic prescriptions – a third of which (33.9%) contained intravenous antibiotics injected directly into the bloodstream, mostly combined with oral antibiotics. Patients or caregivers - the demand-side of the healthcare system – who are engaged in self-medication and who have demanded antibiotic prescriptions were estimated to have contributed to 41% of antibiotic use for paediatric URTIs [(594+135)/(594+1204)]. (See Table 2 and Figure 1.)

Self-medication with antibiotics for paediatric URTIs (Table 2)

Perceived antibiotic efficacy for common cold or fever (aOR=1.82[1.51-2.19] and aOR=1.77[1.47-2.13], respectively), presence of fever (aOR=1.46[1.20-1.77]), high perceived severity of infection (aOR=2.01[1.58-2.56]), obtaining health information from family for treatment decisions (aOR=1.80[1.49-2.16]), and keeping antibiotics at home (aOR=5.08[4.03-6.39]) were associated with increased odds of self-medication with antibiotics use by parents for URTIs in children, after adjusting for socio-demographic characteristics**.** Parents who obtained health information from media were associated with a reduced risk (aRRR=0.46[0.24-0.89]). High levels of perceived severity of the infection and presence of fever in children were associated with increased risk of self-medication with antibiotics then seeking healthcare.

Healthcare seeking and parents request for antibiotic prescription (Table 3)

Parents who perceived antibiotics as effective for the common cold and fever, who had high levels of perceived severity of infection, or presence of fever in children were more likely to seek healthcare and request antibiotic prescriptions, compared to their respective counterparts. Parents who had a medical background, obtained health information from family, or kept antibiotics at home were less likely to seek healthcare for their children (aOR=0.65, 0.81, and 0.84, respectively). Among parents who sought healthcare for their children, keeping antibiotics at home was associated with increased risk of requesting antibiotic prescriptions (aRRR=3.63[2.54-5.17]).

Antibiotic prescriptions for the treatment of URTIs (Table 4)

Children whose parents could identify most antibiotics, perceived antibiotics as efficacious for common cold or fever, perceived higher severity in their children, and kept antibiotics at home were more likely to receive antibiotic prescriptions, with a greater risk of receiving prescriptions by request. Regarding point-of-care used, seeking healthcare from county hospitals was associated with an increased risk of antibiotic prescriptions for paediatric

URTIs and inappropriate prescriptions by parents' request (aRRR=1.48[1.11-1.96] and 2.52[1.23-5.18], respectively), compared with tertiary hospitals. Findings from sensitivity analyses showed that when all factors were mutually adjusted, most associations remained, though reduced slightly, with one exception that 'parental ability to identify antibiotics' became non-significant for all outcomes. All other factors did not change substantially (data not shown).

DISCUSSION

Main findings Of the 3,188 children experiencing URTIs, nearly half (46%) were given antibiotics either by parents or by clinicians, 69% sought care, and among them 55% were prescribed antibiotics (of these 28% had already self-treated with antibiotics at home). Caregivers account for at least 40% of outpatient antibiotic use. Antibiotic misuse for paediatric URTIs can be summarised into three forms: (1) self-medication among children by caregivers in the community; and in clinical settings from either (2) unnecessary prescriptions by doctors, or (3) inappropriate prescriptions due to parental demand. Parents' perception of antibiotics as efficacious for treating URTIs and the nearly non-existent barriers to antibiotics are key risk factors in antibiotic misuse behaviours, including self-medication children with antibiotics and the demand and receipt of antibiotic prescriptions. *Presence of fever* leads to formal care seeking and the demand and receipt of antibiotics prescriptions. Those mainly *taking advice from family members* are more likely to self-medicate children with antibiotics and less likely to seek care; when they do seek care, they are more likely to receive antibiotic prescriptions. A majority of parents (n=1,728, 54.2%) reported having kept antibiotics at home for their children for the possibility of a future cold. Pressuring doctors for antibiotic prescriptions occurred at all levels of healthcare facilities with a high success rate (79.4%).

Strengths and Limitations

This study is based on a large survey conducted in geographical areas representing various stages of economic development in China. This is the first study to comprehensively examine parental treatment decisions with respect to antibiotic use in children in both rural and urban settings across China. Though the cross-sectional study design limited us from drawing causal relationships, it helped generate causal hypotheses and offered several points for intervention. This study showed that the high childhood antibiotic consumption in China is largely driven by a combination of excessive use of formal care for URTIs, high prescription rates, and large population size. The actual antibiotic consumption in Chinese children is expected to be much more prevalent than what has been reported in this study, considering repeated infections throughout a year and non-prescription use at home.[19] We found, before the parent sought formal care, 18% of children with URTIs had already received antibiotics, without prescription.

Interpretation of our findings

Evidence generated from this study will inform intervention design to reduce unnecessary antibiotic use for paediatric URTIs in China as well as other low-/middle-income countries that share similar challenges, including rising antibiotic consumption [20] and unsupervised (e.g. use of leftover antibiotics) or inappropriate use of antibiotics (e.g. for viral infections or prevention).[21,22] First, our findings highlighted the continued need to tackle the non-clinical drivers of inappropriate prescribing behaviours (e.g. patients' or caregivers' profile and behaviours) which should be addressed along with other factors such as poor diagnostic capacity and financial incentives,[23,24] especially in primary care and rural settings[25]. More than half of paediatric patients with non-complicated URTI symptoms were prescribed with antibiotics while roughly 80% of those who demanded antibiotics were prescribed antibiotics, accounting for an estimate of 45% outpatient paediatric antibiotic use in the country. About 8% of Chinese parents admitted to having asked doctors for antibiotics for paediatric URTIs, which

is similar to what has been reported in some European countries.[26] Our study highlighted a preference for IV infusion for children that remains prevalent among Chinese parents. This phenomenon is a product of Chinese hospitals' financial incentives, as well as the expectations of consumers for rapid recovery, fueled by widespread accepting attitudes towards the use of needles in Chinese society[27] – an attitude influenced by the concept of acupuncture, an ancient traditional Chinese medical treatment. Since 2012, many Chinese hospitals have made an effort to reduce outpatient infusion treatments,[28] yet these regulations have not been adopted by most lower level hospitals and have excluded paediatric patients. Furthermore, over-prescription in rural China may be due to the lack of diagnostic knowledge among providers[29] and therefore, improving their professional capacity is necessary. Further, the influence of doctor-patient encounters on antibiotic prescriptions might be more complex than verbal communication. Our data identified a surprisingly similar set of risk factors influencing antibiotic prescription outcomes for paediatrics URTIs between parents who explicitly demand antibiotics and those who did not. If Chinese doctors' prescribing behaviours for paediatrics URTIs are mainly driven by poor diagnostic capacity or financial incentives, as suggested by previous literature,[23,24] we would have expected no association between these risk factors of parents and doctors' prescription decisions. This phenomenon might be explained by possible non-verbal cues (whether true or not) that prescribers pick up from their interactions with parents who showed certain character traits or profiles during consultation that signalled to the prescribers that an antibiotic prescription was desired. This explanation is supported by a study that identified a misalignment between parents' reported expectations, their communication messages, and physicians' perceptions of parents' expectations and their reaction to those perceptions.[26,33] These data pointed to an urgent need to enhance clinician training focusing on 1) clinical guidelines and appropriate prescribing for paediatric URTIs and 2) doctor-patient communication skills that aimed to help clinicians (a)

neutralise the perceived expectation on/pressure from parents' demand for antibiotics and (b) inquire about possible parental self-medication with antibiotics on children before reaching the facility to avoid multiple doses.

Further, compared with the estimate regarding university students,[15] parents appeared to be more cautious, but still drove 40% of antibiotic misuse in children. Overuse of medical care for self-limiting illnesses combined with a high prescription rate and the population size of the country drove the overall high antibiotic consumption in China. In our data, approximately 70% of children with common cold symptoms in the past month sought care, which was about twice as many as those in UK (34-40%).[34] The possibility of receiving an antibacterial prescription for such symptoms was around 33% in UK,[35,36] compared to 55% in our survey. As such, we estimated that an average Chinese child consumes more than three times the amount of antibiotics as their peers in UK or other European countries.[26,35,37,38] The gap is even wider for Chinese children in infancy and early childhood, as they have higher usage of medical care than older children. This estimate is alarming considering it did not account for non-prescription use antibiotics in Chinese children. Our data indicates about 18.6% of children with the common cold within the month before the survey were self-medicated with non-prescription antibiotics by parents; additionally, a previous study[39] reported about 20% were given antibiotics for prophylaxis in the past year. Therefore, we estimate non-prescription use of antibiotics for paediatric URTIs among Chinese children is at least 4-6 times higher than that of some European countries.[26,37,38,40] The true magnitude of this problem is underestimated because repeated use was not included in the calculation. This estimate is consistent with a survey conducted in 1995 and demonstrates that Chinese parental antibiotic misuse for their children has not improved over the past two decades.[41] Context-tailored patient/caregiver education interventions on appropriate home care for paediatric URTIs and prudent antibiotic use are needed. Content should prioritise correcting

perceived antibiotic efficacy for relieving or eradicating URTI symptoms and appropriate care for *self-diagnosed paediatric URTIs symptoms* and *fever*, and be delivered by medical professionals or mass media - both were identified as effective channels for health information.

In some low- and middle-income countries, especially rural areas where challenges in healthcare delivery such as inadequate access, limited medical personnel, and lack of drug regulations are prevalent, keeping medications - including antibiotics - in homes for self-medication is a common practice.[30-32] In China, we found antibiotic misuse in children was mainly associated with parents' *access to antibiotics*, within or outside of a clinical setting. Household antibiotic storage mainly came from leftover antibiotics from previous prescriptions (60.6%) and over-the-counter purchases (37.5%). *Cephalosporines*, *Amoxicillins*, and *Azithromycins* were the most commonly used antibiotics to treat paediatric URTIs, both with and without a prescription (data not shown). These antibiotics, *Cephalosporines* especially, are broad-spectrum antibiotics effective against a wide range of bacteria, which kill more normal microorganisms in children's body compared with narrow-spectrum antibiotics, and should only be used under professional supervision on patients who are sick on presentation. Furthermore, participants from all regions reported to have obtained antibiotics from retail pharmacies. Currently, antibiotic prescriptions are fulfilled and dispensed by packs, often more than the prescribed doses, leading to leftover antibiotics for unsupervised self-medication at home later on. Therefore, in addition to improving responsible prescribing practice, interventions should address the loopholes in current Chinese antibiotic dispensing system, including (1) strengthening the enforcement of Chinese government's AMR policies[42] that ban over-the-counter purchases and cap antibiotic prescriptions (e.g. at 20% for county hospitals), and (2) enabling responsible dispensing antibiotics according to prescribed doses.

Policy implications

Findings from this study suggest that context-appropriate multifaceted interventions are vital to untangle the perpetual problem of over-prescription and ill-informed demands for antibiotics. Simultaneously enhancing both prescribing guidelines, doctor-patient communication skills, and patient education targeting the family as a unit is critical. A blanket antibiotic awareness campaign in China and in other low- and middle-income countries will likely not be effective unless it is rigorously adapted to local context. Interventions enhancing parental *self-efficacy* of healthcare decision-making, especially regarding care management for paediatric URTIs, and correcting *(mis-)perceptions around antibiotic efficacy for URTI symptoms*, might reduce misuse. Education interventions should prioritise urban parents with low socio-economic status in less developed regions and be disseminated via medical professionals or media in order to effectively cue parents to a proper response. Enforcing regulations regarding the sale of antibiotics and pack-based antibiotic dispensing systems to reduce household antibiotic stockpiling could curb the main sources of non-prescription antibiotics for self-medication use in Chinese children.

CONCLUSIONS

Our data pointed to an urgent need for context-appropriate multifaceted interventions to untangle the perpetual problem of over-prescription and ill-informed demands for antibiotics. Having effective stewardship programmes that improve adherence to clinical practice guidelines for antibiotic prescribing and enhance doctor-patient communication over antibiotic use in China is vital. Risk factors influencing caregivers' antibiotic use identified in this study can inform much-needed interventions addressing the challenges posed by both the supply- and demand-side of healthcare system in China. Our findings emphasize the need to prioritise interventions enhancing clinical training, neutralising the pressure from patients for

antibiotics, educating on appropriate home care, discouraging antibiotic self-medication, and improving antibiotic dispensing.

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DECLARATIONS

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Competing Interests: The authors have declared no conflict of interests related to this study.

Ethical Approval: The study protocol and survey were reviewed and exempted by the Institutional Review Board at the Zhejiang University School of Medicine (number ZGL201706-2) and London School of Hygiene & Tropical Medicine (number 14678).

Contributors' Statement

Leesa Lin conducted the literature search, created the figures and the conceptual framework, conducted data analysis and interpretation, and drafted and revised the manuscript.

Stephan Harbarth and James Hargreaves contributed to data interpretation, and commented on the initial and following revisions of the manuscript.

Xudong Zhou conceived the study, led data collection, contributed to data interpretation, and commented on all drafts of this manuscript.

Leah Li led the study design, supervised the data analysis and interpretation, and contributed significantly to the first draft and following revisions of the manuscript.

All authors approved the final draft of this manuscript.

REFERENCES

1. Eccles R. Understanding the symptoms of the common cold and influenza. *The Lancet infectious diseases* 2005; **5**(11): 718-25.

2. Tang Q, Song P, Li J, Kong F, Sun L, Xu L. Control of antibiotic resistance in China must not be delayed: The current state of resistance and policy suggestions for the government, medical facilities, and patients. *Bioscience trends* 2016; **10**(1): 1-6.

3. Quan-Cheng K, Jian-Guo W, Xiang-Hua L, Zhen-Zhen L. Inappropriate use of antibiotics in children in China. *Lancet (London, England)* 2016; **387**(10025): 1273-4.

4. Li J, Song X, Yang T, et al. A Systematic Review of Antibiotic Prescription Associated With Upper Respiratory Tract Infections in China. *Medicine (Baltimore)* 2016; **95**(19): e3587.

5. Wang H, Wang B, Zhao Q, et al. Antibiotic body burden of Chinese school children: a multisite biomonitoring-based study. *Environ Sci Technol* 2015; **49**(8): 5070-9.

6. Zhao C, Li Z, Zhang F, et al. Serotype distribution and antibiotic resistance of Streptococcus pneumoniae isolates from 17 Chinese cities from 2011 to 2016. *BMC Infect Dis* 2017; **17**(1): 804.

7. Francino MP. Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances. *Front Microbiol* 2016; **6**: 1543-.

8. Ipci K, Altintoprak N, Muluk NB, Senturk M, Cingi C. The possible mechanisms of the human microbiome in allergic diseases. *European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery* 2017; **274**(2): 617-26.

9. Chang J, Lv B, Zhu S, et al. Non-prescription use of antibiotics among children in urban

China: a cross-sectional survey of knowledge, attitudes, and practices. *Expert review of anti-infective therapy* 2018; **16**(2): 163-72.

10. Yu M, Zhao G, Stalsby Lundborg C, Zhu Y, Zhao Q, Xu B. Knowledge, attitudes, and practices of parents in rural China on the use of antibiotics in children: a cross-sectional study. *BMC Infect Dis* 2014; **14**: 112.

11. Short SE, Mollborn S. Social Determinants and Health Behaviors: Conceptual Frames and Empirical Advances. *Current opinion in psychology* 2015; **5**: 78-84.

12. Brun KHTaW. Anticipating the future: appraising risk and uncertainty. In: Ray Crozier RR, Ola Svenson, ed. Decision Making: Cognitive Models and Explanations. 1 ed. London; : New York : Routledge; 1997.

13. China. N. National Bureau of Statistics China http://data.stats.gov.cn/english/ (Last accessed in September 2018). 2017.

14. Xinhua. China maintains high vaccination rate: official http://www.xinhuanet.com/english/2019-02/25/c_137849510.htm (Last accessed in March 2019). *Xinhua News* 2019.

15. Wang X, Peng D, Wang W, Xu Y, Zhou X, Hesketh T. Massive misuse of antibiotics by university students in all regions of China: implications for national policy. *International journal of antimicrobial agents* 2017; **50**(3): 441-6.

16. Ding L, Sun Q, Sun W, et al. Antibiotic use in rural China: a cross-sectional survey of knowledge, attitudes and self-reported practices among caregivers in Shandong province. *BMC Infect Dis* 2015; **15**: 576.

17. Ancillotti M, Eriksson S, Veldwijk J, Nihlen Fahlquist J, Andersson DI, Godskesen T. Public awareness and individual responsibility needed for judicious use of antibiotics: a qualitative study of public beliefs and perceptions. *BMC Public Health* 2018; **18**(1): 1153.

18. Janz NK, Becker MH. The Health Belief Model: a decade later. *Health education*

quarterly 1984; **11**(1): 1-47.

19. Fang Y. China should curb non-prescription use of antibiotics in the community. *Bmj* 2014; **348**: g4233.

20. Klein EY, Van Boeckel TP, Martinez EM, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A* 2018; **115**(15): E3463-e70.

21. Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide: a systematic review. *The Lancet Infectious Diseases* 2011; **11**(9): 692-701.

22. Wilkinson A, Ebata A, MacGregor H. Interventions to Reduce Antibiotic Prescribing in LMICs: A Scoping Review of Evidence from Human and Animal Health Systems. *Antibiotics (Basel)* 2018; **8**(1): 2.

23. Currie J, Lin W, Meng J. Addressing Antibiotic Abuse in China: An Experimental Audit Study. *J Dev Econ* 2014; **110**: 39-51.

24. Wei X, Zhang Z, Walley JD, et al. Effect of a training and educational intervention for physicians and caregivers on antibiotic prescribing for upper respiratory tract infections in children at primary care facilities in rural China: a cluster-randomised controlled trial. *The Lancet Global health* 2017; **5**(12): e1258-e67.

25. He P, Sun Q, Shi L, Meng Q. Rational use of antibiotics in the context of China's health system reform. *BMJ (Clinical research ed)* 2019; **365**: l4016.

26. Rousounidis A, Papaevangelou V, Hadjipanayis A, et al. Descriptive study on parents' knowledge, attitudes and practices on antibiotic use and misuse in children with upper respiratory tract infections in Cyprus. *International journal of environmental research and public health* 2011; **8**(8): 3246-62.

27. Reynolds L, McKee M. Serve the people or close the sale? Profit-driven overuse of

injections and infusions in China's market-based healthcare system. *The International journal of health planning and management* 2011; **26**(4): 449-70.

28. Wang L, Zhang X, Liang X, Bloom G. Addressing antimicrobial resistance in China: policy implementation in a complex context. *Globalization and health* 2016; **12**(1): 30.

29. Xue H, Shi Y, Huang L, et al. Diagnostic ability and inappropriate antibiotic prescriptions: a quasi-experimental study of primary care providers in rural China. *The Journal of antimicrobial chemotherapy* 2019; **74**(1): 256-63.

30. Ocan M, Bbosa GS, Waako P, Ogwal-Okeng J, Obua C. Factors predicting home storage of medicines in Northern Uganda. *BMC Public Health* 2014; **14**(1): 650.

31. Lin L, Wang X, Wang W, Zhou X, Hargreaves JR. Cleaning up China's Medical Cabinet-An Antibiotic Take-Back Programme to Reduce Household Antibiotic Storage for Unsupervised Use in Rural China: A Mixed-Methods Feasibility Study. *Antibiotics (Basel)* 2020; **9**(5): 212.

32. Lin L, Fearon E, Harbarth S, et al. Decisions to use antibiotics for upper respiratory tract infections across China: a large-scale cross-sectional survey among university students. *BMJ open* 2020; **10**(8): e039332.

33. Stivers T, Mangione-Smith R, Elliott MN, McDonald L, Heritage J. Why do physicians think parents expect antibiotics? What parents report vs what physicians believe. *The Journal of family practice* 2003; **52**(2): 140-8.

34. Hay AD, Heron J, Ness A. The prevalence of symptoms and consultations in pre-school children in the Avon Longitudinal Study of Parents and Children (ALSPAC): a prospective cohort study. *Fam Pract* 2005; **22**(4): 367-74.

35. Meropol SB, Chen Z, Metlay JP. Reduced antibiotic prescribing for acute respiratory infections in adults and children. *Br J Gen Pract* 2009; **59**(567): e321-8.

36. Easton G, Saxena S. Antibiotic prescribing for upper respiratory tract infections in

children: how can we improve? *London journal of primary care* 2010; **3**(1): 37-41.

37. Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide: a systematic review. *The Lancet Infectious diseases* 2011; **11**(9): 692-701.

38. Panagakou SG, Spyridis N, Papaevangelou V, et al. Antibiotic use for upper respiratory tract infections in children: a cross-sectional survey of knowledge, attitudes, and practices (KAP) of parents in Greece. *BMC pediatrics* 2011; **11**: 60.

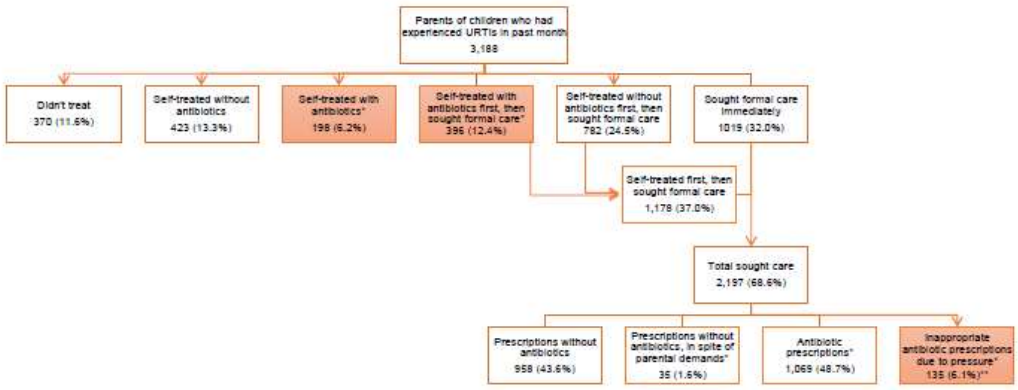
39. Sun C, Hu YJ, Wang X, Lu J, Lin L, Zhou X. Influence of leftover antibiotics on self-medication with antibiotics for children: a cross-sectional study from three Chinese provinces. *BMJ Open* 2019; **9**(12): e033679.

40. Rousounidis A, Papaevangelou V, Hadjipanayis A, et al. Descriptive study on parents' knowledge, attitudes and practices on antibiotic use and misuse in children with upper respiratory tract infections in Cyprus. *Int J Environ Res Public Health* 2011; **8**(8): 3246-62.

41. Bi P, Tong S, Parton KA. Family self-medication and antibiotics abuse for children and juveniles in a Chinese city. *Soc Sci Med* 2000; **50**(10): 1445-50.

42. PRC. National Health and Family Planning Commission of the People's Republic of China. Guiding Principles of Clinical Application of Antibacterials. Beijing, 2015:7. 2015.

Figure 1. Antibiotic use for upper respiratory tract infections (URTIs) among Chinese children



*Inappropriate antibiotic use for URTIs
**170 parents asked for antibiotic prescriptions for URTI symptoms for their children, with a success rate of 79.4%.

Table 1. Sample characteristics N (%) (N=3188)

SOCIO-DEMOGRAPHIC CHARACTERISTICS	All children N (%)	Treated with antibiotics	Self-treated with antibiotics	Children who sought care
	3188	1,465 (46.0)	594 (18.6%)	2,197(68.9%)
Sex				
Boys	1,623 (50.9)	746 (50.9)	310 (52.2)	1,125 (51.2)
Girls	1,565 (49.1)	719 (49.1)	284 (47.8)	1,072 (48.8)
Age (years)				
0-3	1,025 (32.2)	441 (30.1)	163 (27.4)	735 (33.5)
4-6	1,109 (34.8)	539 (36.8)	214 (36.0)	762 (34.7)
7-9	673 (21.1)	331 (22.6)	147 (24.8)	462 (21.0)
10-13	381 (12.0)	154 (10.5)	70 (11.8)	238 (10.8)
Average household income (RMB, monthly)				
>5,000	1,520 (47.7)	655 (44.7)	232 (39.1)	1,023 (46.6)
3,001-5,000	1,032 (32.4)	498 (34.0)	220 (37.9)	718 (32.7)
<=3,000	636 (20.0)	312 (21.3)	142 (23.9)	456 (20.8)
Parents' education level				
College or above	1,365 (42.8)	603 (41.2)	228 (38.4)	889 (40.5)
High school or below	1,823 (57.2)	862 (58.8)	366 (61.6)	1,308 (59.5)
Province				
Zhejiang	885 (27.8)	346 (23.6)	94 (15.8)	612 (27.9)
Guangxi	1,152 (36.1)	516 (35.2)	209 (35.2)	793 (36.1)
Shaanxi	1,151 (36.1)	603 (41.2)	291 (49.0)	792 (36.1)
Hometown				
Rural	1,384 (43.4)	612 (41.8)	258 (43.4)	978 (44.5)
Urban	1,804 (56.6)	853 (58.2)	336 (56.6)	1,219 (55.5)
RISK FACTORS				
Parents with medical background				
No	2,785 (87.4)	1,290 (88.1)	516 (86.9)	1,960 (89.2)
Yes	403 (12.6)	175 (12.0)	78 (13.1)	237 (10.8)
Parents ability to identify antibiotics				
Low	530 (16.6)	183 (12.5)	68 (11.5)	387 (17.6)
Medium	829 (26.0)	384 (26.2)	154 (25.9)	579 (26.4)
High	1829 (57.4)	898 (61.3)	372 (62.6)	1,231 (56.0)
Parents perceptions				
Antibiotic efficacy				
Effective for common cold				
No/Don't know	1,842 (57.8)	728 (49.7)	266 (44.8)	1,233 (56.1)
Yes	1,346 (42.2)	737 (50.3)	328 (55.2)	964 (43.9)
Effective for fever				
No/Don't know	1,767 (55.4)	670 (45.7)	254 (42.8)	1,184 (53.9)
Yes	1,421 (44.6)	795 (54.3)	340 (57.2)	1,013 (46.1)

Self-diagnosed severity				
Low (1 symptom)	940 (29.5)	330 (22.5)	143 (24.1)	545 (24.8)
Medium (2)	1354 (42.5)	604 (41.2)	236 (39.7)	918 (41.8)
High (>=3)	894 (28.0)	531 (36.3)	215 (36.2)	734 (33.4)
Cues to action				
Presence of Fever				
No	2189 (68.7)	886 (60.9)	384 (64.7)	1383 (63.0)
Yes	999 (31.3)	579 (39.5)	210 (35.4)	814 (37.1)
Information sources				
Medical advice				
No	451 (14.5)	209 (14.3)	99 (16.7)	280 (12.7)
Yes	2,737 (85.9)	1,256 (85.7)	495 (83.3)	1,917 (87.3)
Family				
No	1,672 (52.5)	737 (50.3)	254 (2.8)	1,194 (54.4)
Yes	1,516 (47.6)	728 (49.7)	340 (57.2)	1,003 (45.6)
Media				
No	2,846 (89.3)	1,313 (89.6)	545 (91.8)	1,961 (89.3)
Yes	342 (10.7)	152 (10.4)	49 (8.3)	236 (10.7)
Antibiotics access				
Keeping antibiotics at home				
No	1,460 (45.8)	471 (32.2)	105 (17.7)	1,042 (47.4)
Yes	1,728 (54.2)	994 (67.9)	489 (82.3)	1,155 (52.6)

Table 2. Estimated odds ratio (OR, 95% CI) of 'self-treated with antibiotic' for URTIs among Chinese children and relative risk ratio (RRR, 95% CI) of 'self-treated with antibiotics only' and 'self-treated then thought care' (vs 'non-self-treated') for factors affecting parental treatment decisions (N=3188)

	Self-treated with antibiotics* (594, 18.6%)			Subgroup: Self-treated with antibiotics only (198, 6.2%)			Subgroup: Self-treated with antibiotics, then sought care (396, 12.4%)		
	%	OR (95%CI)	aOR (95%CI)	%	RRR (95%CI)	aRRR (95%CI)	%	RRR (95%CI)	aRRR (95%CI)
Parents with medical background									
No	18.5	-	-	5.8	-	-	12.7	-	-
Yes	19.4	1.06 (0.81-1.38)	1.04 (0.79-1.37)	8.9	**1.55 (1.06-2.27)**	1.47 (0.99-2.19)	10.4	0.83 (0.59-1.16`)	0.83 (0.59-1.18)
Parents ability to identify antibiotics									
Low	12.8	-	-	4.5	-	-	8.3	-	-
Medium	18.6	**1.55 (1.14-2.11)**	**1.67 (1.21-2.29)**	6.3	1.48 (0.90-2.44)	1.51 (0.91-2.51)	12.3	**1.59 (1.09-2.30)**	**1.75 (1.20-2.56)**
High	20.3	**1.73 (1.31-2.29)**	**2.03 (1.51-2.72)**	6.7	**1.61 (1.03-2.53)**	**1.73 (1.08-2.77)**	13.7	**1.80 (1.29-2.52)**	**2.20 (1.55-3.13)**
Parents perceptions									
Antibiotic efficacy									
Effective for common cold									
No/Don't know	14.4)	-	-	4.9	-	-	9.6	-	-
Yes	24.4	**1.91 (1.59-2.29)**	**1.82 (1.51-2.19)**	8.0	**1.86 (1.39-2.48)**	**1.81 (1.35-2.43)**	16.3	**1.94 (1.56-2.40)**	**1.88 (1.51-2.33)**
Effective for fever									
No/Don't know	14.3	-	-	4.8	-	-	9.5	-	-
Yes	24.0	**1.89 (1.58-2.26)**	**1.77 (1.47-2.13)**	8.0	**1.86 (1.39-2.50)**	**1.69 (1.26-2.28)**	16.1	**1.90 (1.54-2.36)**	**1.81 (1.45-2.25)**
Self-diagnosed severity									
Low (1 symptom)	15.2	-	-	6.7	-	-	8.5	-	-
Medium (2)	17.4	1.18 (0.94-1.48)	1.23 (0.97-1.55)	6.1	0.94 (0.67-1.32)	0.96 (0.68-1.35)	11.3	**1.36 (1.03-1.81)**	**1.44 (1.07-1.92)**
High (>=3)	24.1	**1.76 (1.40-2.23)**	**2.01 (1.58-2.56)**	5.8	0.97 (0.66-1.42)	1.09 (0.74-1.61)	18.2	**2.39 (1.80-3.18)**	**2.73 (2.04-3.66)**
Cues to action:									
Presence of Fever									
No	17.5	-	-	6.6	-	-	10.9	-	-

Yes	21.0	**1.25 (1.04-1.51)**	**1.46 (1.20-1.77)**	5.3	0.79 (0.58-1.09)	0.99 (0.71-1.38)	15.7	**1.52 (1.23-1.88)**	**1.74 (1.39-2.17)**
Information sources									
Medical advice									
No	22.0	-	-	8.2	-	-	13.8	-	-
Yes	18.1	**0.79 (0.62-1.00)**	0.79 (0.62-1.01)	5.9	**0.68 (0.47-0.99)**	0.69 (0.47-1.01)	12.2	0.85 (0.63-1.13)	0.85 (0.63-1.14)
Family									
No	16.9	-	-	5.2	-	-	10.0	-	-
Yes	23.6	**1.61 (1.35-1.93)**	**1.80 (1.49-2.16)**	7.3	**1.54 (1.15-2.06)**	**1.72 (1.28-2.31)**	15.1	**1.65 (1.34-2.05)**	**1.84 (1.48-2.29)**
Media									
No	19.2	-	-	6.6	-	-	12.5	-	-
Yes	14.3	**0.71 (0.51-0.97)**	**0.79 (0.57-1.10)**	2.9	**0.42 (0.22-0.80)**	**0.46 (0.24-0.89)**	11.4	0.86 (0.60-1.22)	0.97 (0.68-1.39)
Keeping antibiotics at home									-
No	7.2	-	-	2.5	-	-	4.7	-	
Yes	28.3	**5.09 (4.07-6.37)**	**5.08 (4.03-6.39)**	9.4	**4.92 (3.40-7.12)**	**4.63 (3.18-6.75)**	18.9	**5.18 (3.95-6.80)**	**5.31 (4.03-7.01)**

OR, odds ratio; RRR, relative risk ratio; CI, confidence interval.
*Reference group: parents who did not self-medicated children with antibiotics (n=2,594, 81.4%)
[a]Adjusted for sex, age, household income, parents' education, urbanicity and province.

Table 3. Estimated odds ratio (OR, 95% CI) of 'healthcare seeking' for URTIs among Chinese children and relative risk ratio (RRR, 95% CI) of 'seeking formal care without requesting for antibiotics' and 'Seeking antibiotic prescriptions' (vs 'no formal care') for factors affecting parental treatment decisions (N=3188)

	Healthcare seeking* (2,197, 68.9%)			**Subgroup: Seeking formal care without requesting for antibiotics (2027, 63.6%)**			**Subgroup: Seeking antibiotic prescriptions (170, 5.3%)**		
	%	**OR (95%CI)**	**aOR (95%CI)**	%	RRR (95%CI)	**aRRR (95%CI)**	%	RRR (95%CI)	**aRRR (95%CI)**
Parents with medical background									
No	70.4	-	-	64.9	-	-	5.5	-	-
Yes	58.8	**0.60 (0.48-0.74)**	**0.65 (0.52-0.81)**	54.3	**0.60 (0.48-0.75)**	**0.79 (0.67-0.93)**	4.5	**0.59 (0.35-0.99)**	0.91 (0.55-1.51)
Parents ability to identify antibiotics									
Low	73.0	-	-	68.7	-	-	4.3	-	-
Medium	69.8	0.86 (0.67-1.10)	0.92 (0.72-1.18)	63.6	0.83 (0.65-1.06)	1.12 (0.96-1.31)	6.3	1.29 (0.76-2.20)	**1.86 (1.14-3.10)**
High	67.3	**0.76 (0.61-0.94)**	0.87 (0.69-1.09)	62.1	**0.75 (0.60-0.93)**	**1.25 (1.08-1.44)**	5.2	0.99 (0.60-1.61)	**1.81 (1.12-2.91)**
Parents perceptions									
Antibiotic efficacy									
Effective for common cold									
No/Don't know	66.9	-	-	63.8	-	-	3.2	-	-
Yes	71.6	**1.25 (1.07-1.45)**	**1.27 (1.09-1.49)**	63.3	1.16 (0.99-1.35)	**1.22 (1.10-1.35)**	8.3	**3.08 (2.19-4.33)**	**3.10 (2.25-4.28)**
Effective for fever									
No/Don't know	67.0	-	-	63.4	-	-	3.6	-	-
Yes	71.3	**1.22 (1.05-1.42)**	**1.23 (1.06-1.44)**	63.8	1.16 (0.99-1.35)	**1.18 (1.07-1.31)**	7.5	**2.37 (1.69-3.31)**	**2.32 (1.69-3.18)**
Self-diagnosed severity									
Low (1symptom)	58.0	-	-	54.9	-	-	3.1	-	-
Medium (2 symptoms)	67.8	**1.53 (1.28-1.81)**	**1.60 (1.35-1.91)**	63.0	**1.50 (1.26-1.78)**	**1.58 (1.32-1.89)**	4.8	**2.03 (1.28-3.21)**	**2.04 (1.29-3.25)**
High (>=3 symptoms)	82.1	**3.32 (2.68-4.12)**	**3.43 (2.76-4.26)**	73.6	**3.15 (2.53-3.91)**	**3.25 (2.60-4.05)**	8.5	**6.47 (4.06-10.31)**	**6.63 (4.14-10.61)**
Cues to action:									
Presence of									

Fever									
No	63.2	-	-	59.3	-	-	3.9	-	-
Yes	81.5	**2.56 (2.14-3.08)**	**2.55 (2.12-3.07)**	73.1	**2.45 (2.04-2.95)**	**2.43 (2.02-2.93)**	8.4	**4.26 (3.03-5.98)**	**4.44 (3.14-6.28)**
Information sources									
Medical advice									
No	62.1	-	-	57.7	-	-	4.4	-	-
Yes	70.0	**1.43 (1.16-1.76)**	**1.43 (1.16-1.77)**	64.6	**1.42 (1.15-1.75)**	**0.82 (0.70-0.96)**	5.5	1.56 (0.95-2.57)	0.88 (0.55-1.41)
Family									
No	71.4	-	-	65.7	-	-	5.7	-	-
Yes	66.2	**0.78 (0.67-0.91)**	**0.81 (0.70-0.94)**	61.3	**0.79 (0.68-0.92)**	**1.22 (1.10-1.35)**	4.9	**0.72 (0.52-1.00)**	1.18 (0.86-1.61)
Media									
No	68.9	-	-	63.7	-	-		-	-
Yes	69.0	1.00 (0.79-1.28)	1.05 (0.82-1.34)	62.9	0.99 (0.77-1.27)	1.10 (0.93-1.30)	6.1	1.18 (0.71-1.94)	1.45 (0.91-2.33)
Keeping antibiotics at home									
No	71.4	-	-	68.4	-	-	3.0	-	-
Yes	66.8	**0.81 (0.70-0.94)**	**0.84 (0.72-0.98)**	59.5	**0.75 (0.64-0.87)**	**1.18 (1.07-1.31)**	7.4	**2.15 (1.49-3.11)**	**3.63 (2.54-5.17)**

OR, odds ratio; RRR, relative risk ratio; CI, confidence interval.
*Reference group: Parents who did not seek formal care for their children (n=991, 31.1%)
[a]Adjusted for sex, age, household income, parents' education, urbanicity and province.

Table 4. Clinicians' antibiotic prescriptions for URTIs for among Chinese children (N= 2,197): estimated relative risk ratio (RRR, 95% CI) of 'antibiotic prescriptions' and 'Inappropriate antibiotic prescriptions due to patients' demand' (vs 'no antibiotic prescription') for factors affecting parental treatment decisions

	Antibiotic prescriptions (1,069, 48.7%)			Inappropriate antibiotic prescriptions due to patients' demand (135, 6.1%)		
	%	RRR (95%CI)	**aRRR (95%CI)**	%	RRR (95%CI)	**aRRR (95%CI)**
Parents with medical background						
No	48.7	-	-	6.2	-	-
Yes	48.5	0.99 (0.75-1.30)	0.92 (0.69-1.22)	5.9	0.95 (0.53-1.71)	1.04 (0.57-1.91)
Parents ability to identify antibiotics						
Low	37.0	-	-	3.4	-	-
Medium	46.5	**1.62 (1.24-2.12)**	**1.66 (1.26-2.18)**	7.3	**2.72 (1.45-5.09)**	**3.16 (1.64-6.09)**
High	53.4	**2.15 (1.69-2.73)**	**2.25 (1.74-2.91)**	6.5	**2.82 (1.57-5.07)**	**3.37 (1.79-6.35)**
Parents perceptions:						
Antibiotic efficacy						
Effective for common cold						
No/Don't know	46.4	-	-	3.0	-	-
Yes	51.6	**1.47 (1.23-1.75)**	**1.49 (1.24-1.78)**	10.2	**4.48 (3.00-6.68)**	**4.17 (2.78-6.25)**
Effective for fever						
No/Don't know	43.1	-	-	3.7	-	-
Yes	55.2	**1.90 (1.59-2.27)**	**1.91 (1.60-2.29)**	9.0	**3.59 (2.45-5.26)**	**3.57 (2.43-5.26)**
Self-diagnosed severity						
Low (1 symptom)	42.8	-	-	3.7	-	-
Medium (2)	47.5	**1.29 (1.04-1.61)**	**1.34 (1.08-1.68)**	6.4	**2.78 (1.46-5.32)**	**1.99 (1.17-3.40)**
High (>=3)	54.5	**1.80 (1.43-2.27)**	**2.00 (1.58-2.54)**	7.6	**2.88 (1.57-5.28)**	**3.12 (1.81-5.38)**
Cues to action:						
Presence of Fever						
No	46.0	-	-	4.8	-	-
Yes	53.2	**1.48 (1.23-1.77)**	**1.64 (1.36-1.98)**	8.4	**2.20 (1.53-3.17)**	**2.44 (1.68-3.53)**
Information sources						
Medical advice						
No	51.4	-	-	5.4	-	-
Yes	48.3	0.89 (0.69-1.15)	0.88 (0.68-1.15)	6.3	1.11 (0.63-1.96)	1.07 (0.60-1.90)
Family						
No	45.4	-	-	6.5	-	-
Yes	52.5	**1.34 (1.12-1.59)**	**1.36 (1.14-1.63)**	5.8	1.04 (0.72-1.49)	1.11 (0.77-1.60)
Media						
No	48.5	-	-	6.0	-	-
Yes	50.0	1.10 (0.83-1.45)	1.12 (0.84-1.49)	7.2	1.27 (0.74-2.20)	1.44 (0.83-2.52)
Access to antibiotics						
No	38.1	-	-	2.1	-	-
Yes	58.2	**2.85 (2.38-3.41)**	**2.84 (2.36-3.41)**	9.8	**8.65 (5.38-13.90)**	**9.81 (6.04-15.94)**
Healthcare system used						
Tertiary hospital	45.5	-	-	3.3	-	-
Secondary/County hospital	50.5	**1.34 (1.03-1.75)**	**1.48 (1.11-1.96)**	7.0	**2.55 (1.28-5.09)**	**2.52 (1.23-5.18)**
Community Health Centres/Township hospital	45.9	1.08 (0.82-1.43)	1.16 (0.87-1.56)	6.6	**2.15 (1.05-4.39)**	1.89 (0.90-3.96)
Private Clinics/	52.2	1.37	1.27	5.1	1.83	1.42

Village clinics		(0.99-1.91)	(0.90-1.80)		(0.80-4.22)	(0.60-3.37)
ANTIBIOTIC USE						
No	38.6	-	-	2.2	-	-
Yes	70.0	**6.74 (4.95-9.19)**	**6.70 (4.89-9.23)**	14.1	**24.21 (13.24-44.25)**	**25.50 (13.62-47.74)**

OR, odds ratio; RRR, relative risk ratio; CI, confidence interval.
* Reference group: No antibiotic prescription (n=993, 45.2%)
[a]Adjusted for sex, age, household income, parents' education, urbanicity, province, and point-of-care used.