

# Non-Prescription Antibiotic Use for Cough Among Chinese Children Aged Under 5 Years: A Community-Based Cross-Sectional Study

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## Research Article

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# Abstract

**Background:** Cough is a common symptom in childhood and is an important circumstance of inappropriate antibiotic use. This study aimed to investigate the non-prescription use of antibiotics for cough among children aged under 5 years.

**Methods:** We conducted a community-based survey of under-5 children in Yiwu, China from October to November 2019. The subjects were enrolled from 14 townships using a two-stage stratified sampling procedure. Detailed information was collected through a face-to-face interview based on a standard questionnaire, and the children's caregivers answered as agents. Univariable and multivariable logistic regression analyses were performed to explore the factors associated with nonprescription use of antibiotics for cough in children.

**Results:** A total of 3102 children were included in the study, and 1211 children were reported to have a cough in the past month. Among them, 40.2% (487/1211) were medicated with antibiotics, and 18.7% (91/487) of these were unprescribed. Cephalosporins were the most frequently used antibiotic (52.8%), and community pharmacies were the main source (53.7%). Children who coughed for 1–2 weeks (OR=1.73, 95% CI=1.03-2.90) or 3–4 weeks (OR=2.39, 95%CI=1.08-4.97), with 2 or more accompanying symptoms (OR=2.44, 95% CI=1.14-5.72), or with a family annual income between 50000 and 100000 RMB (OR=4.14, 95% CI=1.41-17.69) had a higher risk of non-prescription use of antibiotics than those coughing for <1 week, without accompanying symptoms, or with family annual income <50000 RMB.

**Conclusions:** Our findings indicated that a high proportion of infants and young children had been treated with antibiotics for cough, and nearly 1/5 of them were used without prescription. More public health campaigns and further health teaching on the appropriate use of antibiotics are needed to ensure the rational treatment of cough in children.

## Background

Cough is a common symptom of childhood respiratory illness[1], of which uncomplicated viral acute respiratory tract infections (ARTIs) account for the majority[2, 3]. Children typically experience between 2 and 7 ARTI episodes annually[4-7]. As cough is easily detectable and parents are often concerned and anxious about it, inappropriate antibiotic use is common in this condition. Inappropriate use of antibiotics can result in serious consequences, such as aggravated antimicrobial resistance[8], masked underlying infectious processes[9] and wasted scarce resources[10]. The non-prescription use of antibiotics, as a main form of misuse of antibiotics, is a public health concern worldwide[11-14] and is particularly prevalent in China[15, 16]. A global systematic review estimated a 36% frequency of non-prescription use of antimicrobials in the Chinese general population [17]. A mixed cross-sectional and longitudinal study with simulated client method in China showed that non-prescription antibiotic was dispensed for 1690 (70.1%) of 2411 adult URTI interactions[18].

Children are more vulnerable to inappropriate use of antibiotics due to their particular physiologic and clinical characteristics, and non-prescription use of antibiotics is also serious in this population. A cross-sectional study of 4200 caregivers of children aged under 7 years conducted in urban China showed that 48.2% of respondents experienced self-medicating the children with antibiotics in the past 6 months[19]. Another survey of 854 people in rural China found that 62% of parents had given their children antibiotics in the previous year without the advice of a physician[20].

Although previous studies have reported the prevalence of non-prescription use of antibiotics in Chinese children[19, 21-23], few studies have focused on their use for cough, especially in young children aged under 5 years. Given the commonness and possible dangers of coughing, we put forward the hypothesis that children have a certain proportion of antibiotics after coughing in China. Addressing the frequency and the corresponding factors of non-prescription use of antibiotics after the onset of cough in children is important for antibiotic abuse prevention and control. Therefore, the aim of this study was to investigate the prevalence and associated factors of non-prescription use of antimicrobials in children under 5 years after cough.

## **Methods**

### **Study design and participants**

We performed a cross-sectional survey in Yiwu, a county-level city of about 2,000,000 people situated in the central Zhejiang Province of China. The survey targeted children aged under 5 years within October to December 2019. The subjects were enrolled from 14 townships in Yiwu using a two-stage stratified sampling procedure. First, probability proportionate to size sampling (PPS) method was used to adopt 50 groups from 14 townships. Then, a quota sampling method based on age and sex was used to select a fixed number of participants from each survey point for the questionnaire survey.

A face-to-face interview was conducted by trained interviewers using a standardized questionnaire, and the children's parents, grandparents, or other caregivers who made routine decisions on children's medication answered as agents. Data were collected into the panel computer. We selected only one child as a participant from every household, without replacement. Impermanent residents from the sampled village (residential community) who lived in Yiwu for less than 6 months were excluded. Children who had a cough in the past month were included in the final analysis of non-prescription use of antibiotics.

### **Study questionnaire**

The questionnaire consisted of three parts. The first part collected basic information of the participants, including age, sex, ethnic group of children, occupation, educational level, and annual family income of parents (caregivers). The second part was about the experience of cough, including whether the child had experienced a cough during the past month, the cough duration, cough characteristics, accompanying symptoms, and health-seeking behaviors. Health-seeking behaviors included whether they went to a doctor because of the last cough, which health facilities they chose for treatment, and whether the

antibiotics were administered to the children after the onset of the cough. If respondents reported that antibiotics had been administered to the children, the source and type would be asked in detail with multiple responses. The third part included the knowledge of antibiotics, which was measured by ten questions related to the rational use of antibiotics. Each question was answered with a 5-point Likert-type scale (strongly disagree, disagree, uncertain, agree, strongly agree).

## **Definitions of variables**

### ***Cough***

In the current study, cough was assessed by asking the respondents “Have your child had a cough during the past month?” The duration of cough was categorized into less than 1 week, 1-2 weeks, 3-4 weeks, and >4 weeks. Accompanying symptoms included fever, expectoration, sore throat, runny nose, dyspnea, headache, fatigue, and lethargy. The number of accompanying symptoms was categorized into three as 0 (reference), 1, and 2 or more.

### ***Non-prescription use of antibiotics***

Non-prescription use of antibiotics was defined as intermittent or continuous use of antimicrobial agents in the treatment of self-diagnosed diseases or symptoms without medical guidance. It was assessed by asking participants the source of antibiotics (if they had been used). The respondents would be regarded as using antibiotics without prescription if they reported any of the following approaches for antibiotics: self-purchase from pharmacies in community, remainder from a previous course of treatment, domestic stock, or given by friends.

### ***Other covariates***

Demographic and socioeconomic characteristics included age, sex, residential area (rural or urban) of the children, education level (primary school or below, middle/high school, college or above) and annual family income (<50,000, 50,000~, 100,000~, 200,000~, and  $\geq$ 500,000 RMB) of the children’s caregivers.

## **Statistical analysis**

The participants’ characteristics were described as frequencies and percentage for categorical variables. The source of antibiotics and type of antibiotics were evaluated based on multiple response questions, and all responses were calculated as multiple response frequencies (percentages). The 5-point Likert-type scale responses to the 10 questions related to the rational use of antibiotics were reclassified into 3 levels and depicted in the bar chart, among which strongly disagree and disagree were combined to disagree, strongly agree and agree were combined to agree, and another response was uncertain. We used both univariate and multivariate logistic regressions to estimate the associations of socio-demographic characteristics and features of cough with non-prescription use of antibiotics. All analyses were conducted using R software 3.5.1. A two-sided P value of <0.05 was considered statistically significant.

# Results

A total of 3,123 caregivers of under-5 children participated in the interviews. After eliminating invalid questionnaires from 21 caregivers, data from 3102 respondents were analyzed. Of the 3102 respondents, 1211 reported that their children had experienced cough during the past month and were included in the final analysis. Majority of the respondents were children's mothers (65.6%), followed by their fathers (18.2%) and grandparents (15.5%). Overall, 690 (57.0%) and 521 (43.0%) of the children were boys and girls, respectively. The characteristics of the total participants and children who had cough in the last month are shown in Table 1.

## Non-prescription use of antibiotics

Among the 1211 children who had a cough in the last month, 487 (40.2%) children were medicated with antibiotics, and 91/487 (18.7%) of them received these without prescription. The most common source of the non-prescription antibiotics was community pharmacies (53.7%), followed by domestic stock (30.5%) and leftover from a previous course of treatment (15.7%).

Figure 1(a) shows the types of antibiotics used without a prescription for the treatment of cough. Cephalosporins were used most frequently (52.8%), followed by penicillins (amoxicillin, ampicillin, amoxicillin, and clavulanate potassium) (30.3%) and macrolides (16.8%). Figure 1(b) shows the types of antibiotics prescribed by doctors. There was no significant difference in the types of antibiotics between those prescribed by doctors and those used without prescription by the caregivers ( $\chi^2=0.934$ ,  $P=0.627$ ).

## Cognition of rational use of antibiotics

Figure 2 shows the respondents' knowledge and attitudes toward the use of antibiotics. In total, 31.6% to 80.1% of the respondents had correct knowledge about antibiotics. Of the respondents, 14.7% believed that antibiotics should be used as soon as possible for coughs. More than 60% of the respondents failed to distinguish between antibiotics and anti-inflammatories. In total, 12.5% of respondents believed that patients have the right to decide on antibiotic use and that the patients can request the doctor to prescribe antibiotics. Further, 12.9% of them believed that the more expensive the antibiotics, the better the effect. In addition, 11.7% agreed that intravenous antibiotics are more effective than oral antibiotics. However, 82.3% of respondents agreed that antibiotics are a prescribed drug and should thus be used with prescription.

## Factors associated with non-prescription use of antibiotics

The association of sociodemographic and cough-related characteristics with non-prescription use of antibiotics after the onset of cough is presented in Table 2. In univariable analysis, the caregiver's relationship with the children and annual family income were associated with non-prescription use of antibiotics. In multivariable analysis, family annual income, cough duration, and number of accompanying symptoms were associated with non-prescription use of antibiotics. Children whose

annual family income was between 50000 and 100000 RMB (OR=4.14, 95% CI=1.41-17.69) had a higher risk of non-prescription use of antibiotics than those whose family annual income was less than 50000 RMB. Further, compared with children who coughed for less than 1 week, those who coughed for 1-2 weeks (OR=1.73, 95% CI=1.03-2.90) and 2-3 weeks (OR=2.39, 95% CI=1.08-4.97) had a higher risk of non-prescription use of antibiotics. However, there was no significant difference between those who coughed more than 4 weeks and less than 1 week. Moreover, compared with children who had no accompanying symptoms, those with accompanying symptoms were more likely to be administered non-prescribed antibiotics, particularly those with at least two accompanying symptoms (OR=2.44, 95% CI: 1.14-5.72). In addition, hospital visits were associated with a lower risk of non-prescription use of antibiotics in both univariate and multivariate analyses.

## Discussion

Our study corroborated a high frequency of cough and a high proportion of antibiotic use among under-5 children. Acute and chronic cough caused by URIs are prevalent in 9%-64% and in 7.2%-33% of the general population, respectively[3]. In the current study, 30.9% (1211/3102) of the children had experienced a cough in the past month, and 40.2% of them had been medicated with antibiotics. Cough is mainly caused by uncomplicated viral respiratory tract infections[2] and thus antibiotics are ineffective for etiologic or symptomatic relief[3, 24]. The diagnostic and treatment guidelines for cough recommend that antibiotics should not be prioritized or can only be used after adequate assessment[25-27]. Parents self-medicating their children with antibiotics for cough may be even more dangerous and harmful. In our study, the prevalence of nonprescription antibiotic use was 7.5% (about one-fifth of antibiotic users for cough). This was relatively lower than that reported in previous studies conducted in children[19-22, 28] and could be explained by the difference in populations, specific scenarios, and time interval as our study focused on children under 5 years and restricted the condition to cough in the past month. However, despite the lower proportion, non-prescription antibiotic use was still concerning because most of the caregivers lacked knowledge on rational antibiotic use. We found that only 31.60%-80.08% of the caregivers had adequate knowledge on appropriate antibiotic use. This indicates the need for further public health campaigns and education on the rational use of antibiotics.

The main source of non-prescribed antibiotics in this study was community pharmacies, consistent with previous studies[17]. Although the purchase of antibiotics from retail pharmacies without a prescription has been forbidden by China's Food and Drug Administration regulations since 2004, several studies using the simulated client method (SCM) demonstrated that customers can still easily obtain antibiotics in retail shops or in private pharmacies. A survey of 2423 community pharmacies from 221 districts or counties across China reported that non-prescription antibiotic dispensing (NPAD) was observed during 70.1% of adult URTI interactions[18]. A multi-center cross-sectional study conducted in Zhejiang, Hubei, and Sichuan reported that 73.3% of the SCM interactions generated NPAD[29]. Another cross-sectional study in northeast China yielded a similar high rate (79.5%)[22]. This may explain our result of the main source of self-medication.

Our finding of cephalosporins as the most frequent type of self-medicated antibiotics was different from a previous study based on simulated scenarios of adult acute cough that reported macrolides to be the most frequent antibiotic dispensed without prescription [22]. However, a dissertation evaluating antibiotic use in children with acute upper respiratory infections also reported that cephalosporins were used more frequently than macrolides in China[30]. The inconsistent results may be explained by the age of the subjects, as cephalosporins have fewer side effects or adverse reactions in young children.

We also found that the duration of cough and the number of accompanying symptoms were associated with non-prescription antibiotic use. Children who coughed for 1-2 weeks and 3-4 weeks had a higher risk of non-prescription use of antibiotics than those coughed for less than 1 week. Meanwhile, those who coughed for more than 4 weeks did not. In general, cough lasting >4 weeks in children is defined as chronic cough, while cough lasting 2–4 weeks is defined as protracted acute[25]. Our results indicated that a cough duration of 4 weeks alarmed the parents to seek medical attention from doctors, while protracted acute cough was a potential risk for non-prescription antibiotic use. A previous study of 1596 children aged 2-18 years showed that non-prescription antibiotic use increased with children's age<sup>[21]</sup>. However, we did not observe a similar association, which might be because of the less obvious hierarchy of age in our study.

Our study has several strengths, including the community-based population and the adoption of the PPS method for representative samples. However, our study also has some limitations. First, this cross-sectional study cannot exclude potential recall and report bias, even though we enquired information within the past month to reduce such biases. Second, a certain proportion of the respondents (18.5%) were the children's grandparents, which may have affected our results. Third, the subjects in our study were enrolled from only one district, and thus the generalizability of our findings to other Chinese populations may be limited.

## Conclusions

A high proportion of infants and young children had been treated with antibiotics for cough in China, and nearly 1/5 of these antibiotics were used without prescription. Cough duration, number of accompanying symptoms, and annual family income were the influencing factors. More public health campaigns and further education on the appropriate use of antibiotics should be implemented to ensure the rational treatment of cough in children.

## List Of Abbreviations

*ARTIs* acute respiratory tract infections

*NPAD* non-prescription antibiotic dispensing

*PPS* proportionate to size sampling

## Declarations

**Ethics approval and consent to participate:** This cross-sectional survey was approved by the institutional review board of Zhejiang provincial center for disease control and prevention and was conducted according to the tenets of the Declaration of Helsinki. Written informed consent to participate was obtained from the parents and/or legal guardians of children. Written informed consent was also obtained from adult participants themselves.

**Consent for publication:** Not applicable

**Availability of data and materials:** The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests" in this section.

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**Authors' contributions:** The study as conceptualized by all the authors. ZY, HH, and XT designed the study. YZ and SL performed the statistical analyses and wrote the manuscript. DX and RY participated in the data collection. HH and YZ revised the manuscript. All authors have read and approved the final manuscript.

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## Tables

Table 1. Children and caregiver characteristics

	Total	Cough in the last month
<b>Characteristics</b>	<b>n=3102</b>	<b>n=1211</b>
<b>Child's sex</b>		
Male	1740 (56.09%)	690 (56.98%)
Female	1362 (43.91%)	521 (43.02%)
<b>Child's age, months</b>		
0-11	756 (24.37%)	183 (15.11%)
12-23	623 (20.08%)	197 (16.27%)
24-35	613 (19.76%)	236 (19.49%)
36-47	558 (17.99%)	307 (25.35%)
48-59	552 (17.79%)	288 (23.78%)
<b>Child's residence</b>		
Urban	1870 (60.28%)	714 (58.96%)
Rural	1232 (39.72%)	497 (41.04%)
<b>Caregiver's relationship with children</b>		
Mother	1975 (63.67%)	794 (65.57%)
Father	552 (17.79%)	221 (18.25%)
Grandparents	560 (18.05%)	188 (15.52%)
Else	15 (0.48%)	8 (0.66%)
<b>Caregiver's education level</b>		
Primary school and lower	446 (14.38%)	154 (12.72%)
Middle school	1053 (33.95%)	356 (29.40%)
High school	680 (21.92%)	289 (23.86%)
College and higher	923 (29.75%)	412 (34.02%)
<b>Family annual income (RMB)</b>		
<50000	356 (11.48%)	127 (10.48%)
50000~	890 (28.69%)	339 (27.99%)
100000~	1222 (39.39%)	476 (39.31%)
200000~	488 (15.73%)	212 (17.51%)

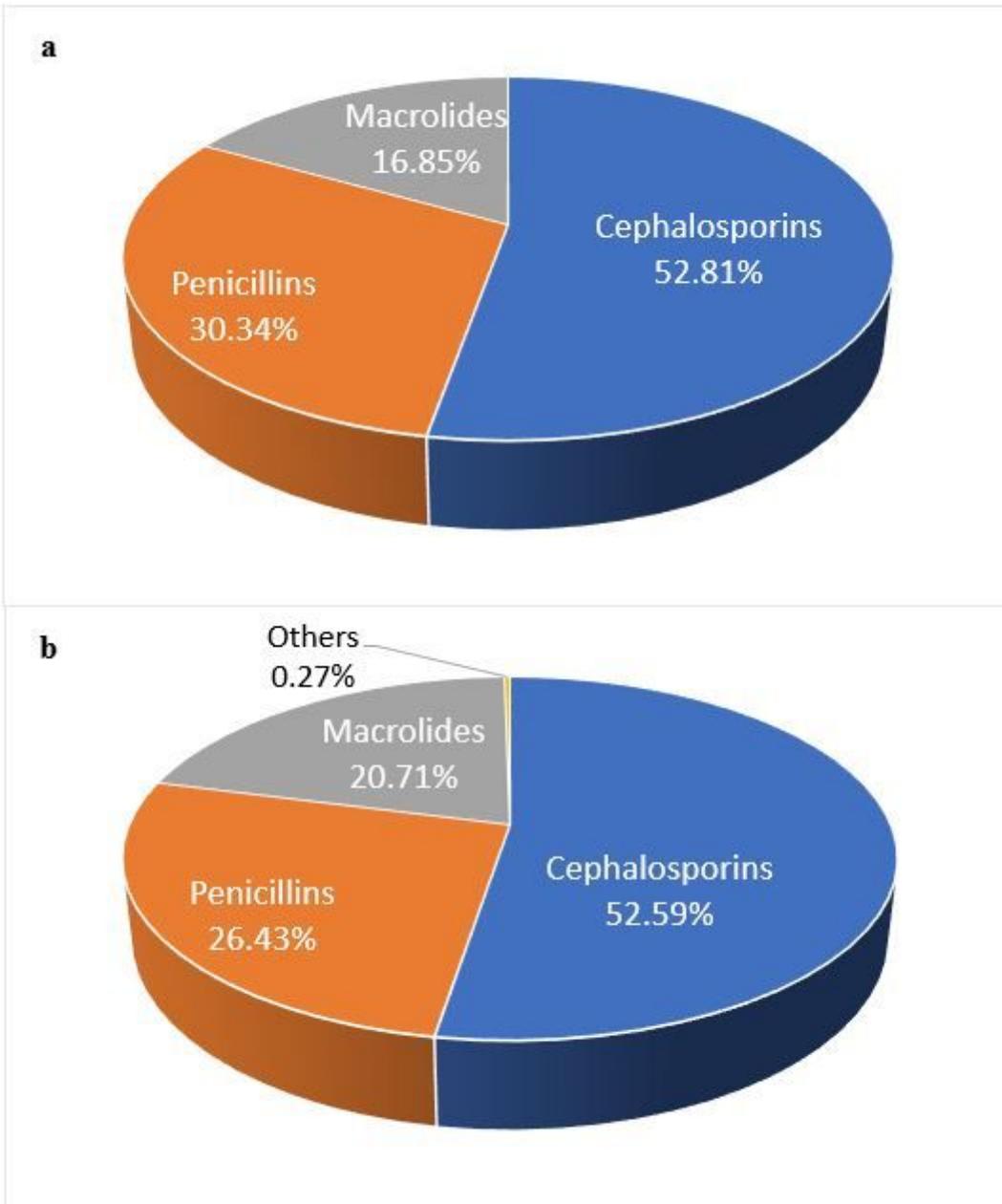
500000~	120 (3.87%)	48 (3.96%)
Unknown	26 (0.84%)	9 (0.74%)
<b>Child's cough duration, weeks</b>		
<1		732 (60.44%)
1-2		347 (28.65%)
3-4		99 (8.17%)
5-8		19 (1.57%)
>8		14 (1.15%)
<b>Nonprescription use</b>		91 (7.51%)

**Table 2. Univariable and multivariable analyses of the influencing factors of non-prescription use of antibiotics for cough**

	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
<b>Child's sex</b>				
Male	1.00 (ref)		1.00 (ref)	
Female	0.95 (0.61-1.45)	0.360	0.93 (0.59-1.46)	0.756
<b>Child's age, months</b>				
0-11	1.00 (ref)		1.00(ref)	
12-23	1.63 (0.74-3.77)	0.239	1.52 (0.67-3.66)	0.327
24-35	1.25 (0.56-2.93)	0.586	1.14 (0.49-2.74)	0.770
36-47	2.02 (0.99-4.42)	0.061	1.81 (0.86-4.09)	0.133
48-59	1.02 (0.46-2.38)	0.955	0.83 (0.36-2.00)	0.671
<b>Child's residence</b>				
Rural	1.00 (ref)		1.00 (ref)	
Urban	1.24 (0.80-1.96)	0.336	1.22 (0.77-1.96)	0.408
<b>Caregiver's relationship with the children</b>				
Mother	1.00 (ref)		1.00 (ref)	
Father	<b>0.52 (0.26-0.96)</b>	<b>0.049</b>	0.59 (0.28-1.11)	0.123
Others	<b>0.43 (0.19-0.85)</b>	<b>0.026</b>	0.57 (0.23-1.26)	0.192
<b>Caregiver's education level</b>				
Primary school and lower	1.00 (ref)		1.00 (ref)	
Middle school	2.11 (0.86-5.19)	0.106	1.61 (0.65-4.64)	0.333
High school	2.03 (0.81-5.12)	0.133	1.58 (0.59-4.79)	0.385
College and higher	2.29 (0.94-5.55)	0.067	1.98 (0.75-5.97)	0.191
<b>Annual family income, RMB</b>				
<50000	1.00 (ref)		1.00 (ref)	
50000~	<b>2.69 (1.43-5.62)</b>	<b>0.004</b>	<b>4.14 (1.41-17.69)</b>	<b>0.023</b>
100000~	<b>2.31 (1.24-4.79)</b>	<b>0.015</b>	2.42 (0.80-10.48)	0.164
200000~	<b>2.19 (1.09-4.79)</b>	<b>0.036</b>	1.39 (0.39-6.58)	0.633
500000~	1.51 (0.46-4.34)	0.461	1.19 (0.14-7.93)	0.861

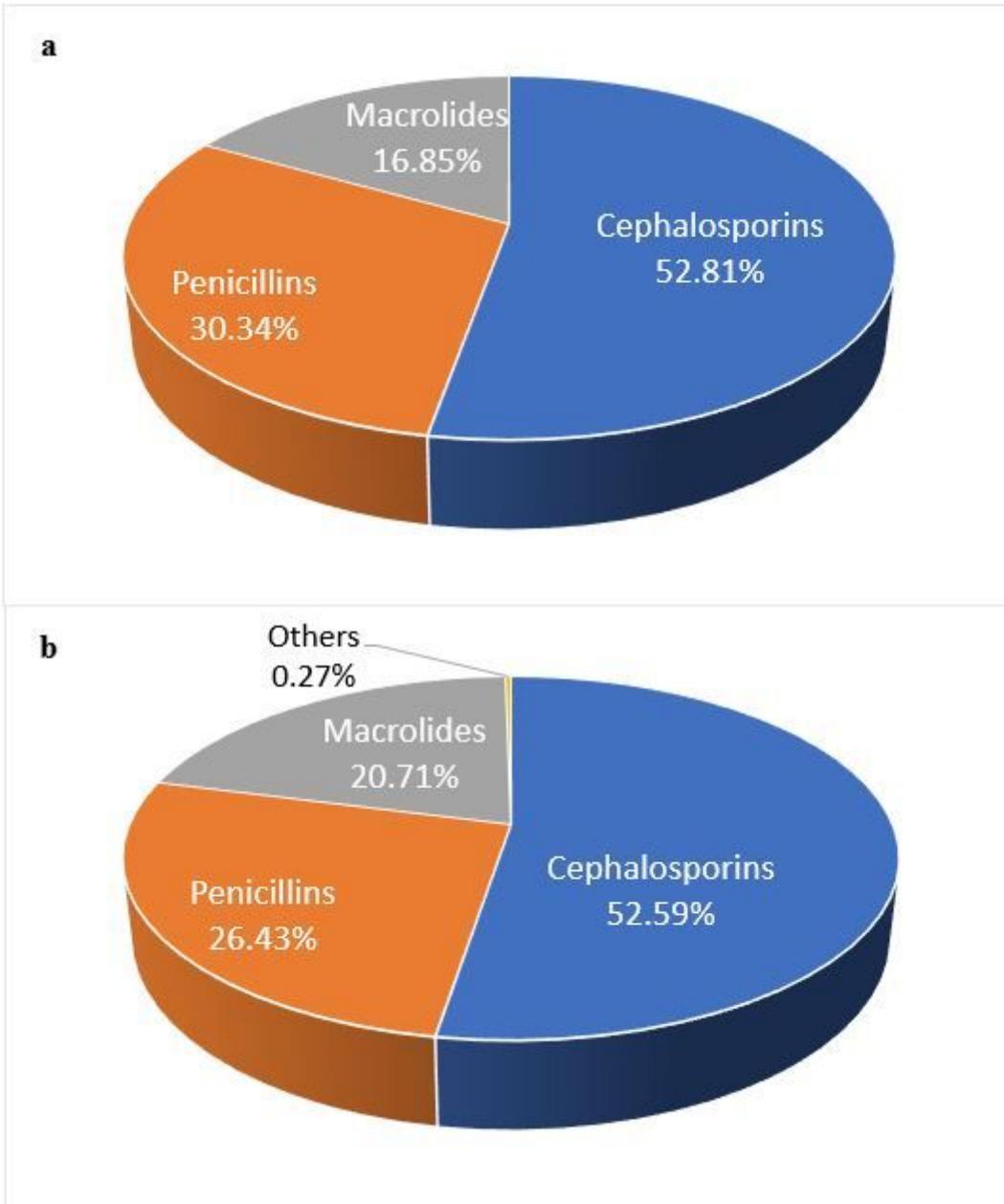
Unknown	1.39 (0.07-7.69)	0.759	2.67 (0.12-26.34)	0.437
<b>Cough duration, weeks</b>				
<1	1.00 (ref)		1.00 (ref)	
1-2	1.57 (0.98-2.49)	0.059	<b>1.73 (1.03-2.90)</b>	<b>0.037</b>
3-4	1.86 (0.89-3.61)	0.079	<b>2.39 (1.08-4.97)</b>	<b>0.024</b>
>4	0.47 (0.03-2.25)	0.457	0.54 (0.03-2.85)	0.559
<b>Number of accompanying symptoms</b>				
0	1.00 (ref)		1.00 (ref)	
1	1.57 (0.78-3.52)	0.238	1.66 (0.79-3.81)	0.204
≥2	1.91 (0.95-4.24)	0.086	<b>2.44 (1.14-5.72)</b>	<b>0.029</b>
Hospital visit	<b>0.41 (0.26-0.62)</b>	<b>&lt;0.01</b>	<b>0.29 (0.18-0.47)</b>	<b>&lt;0.01</b>

## Figures



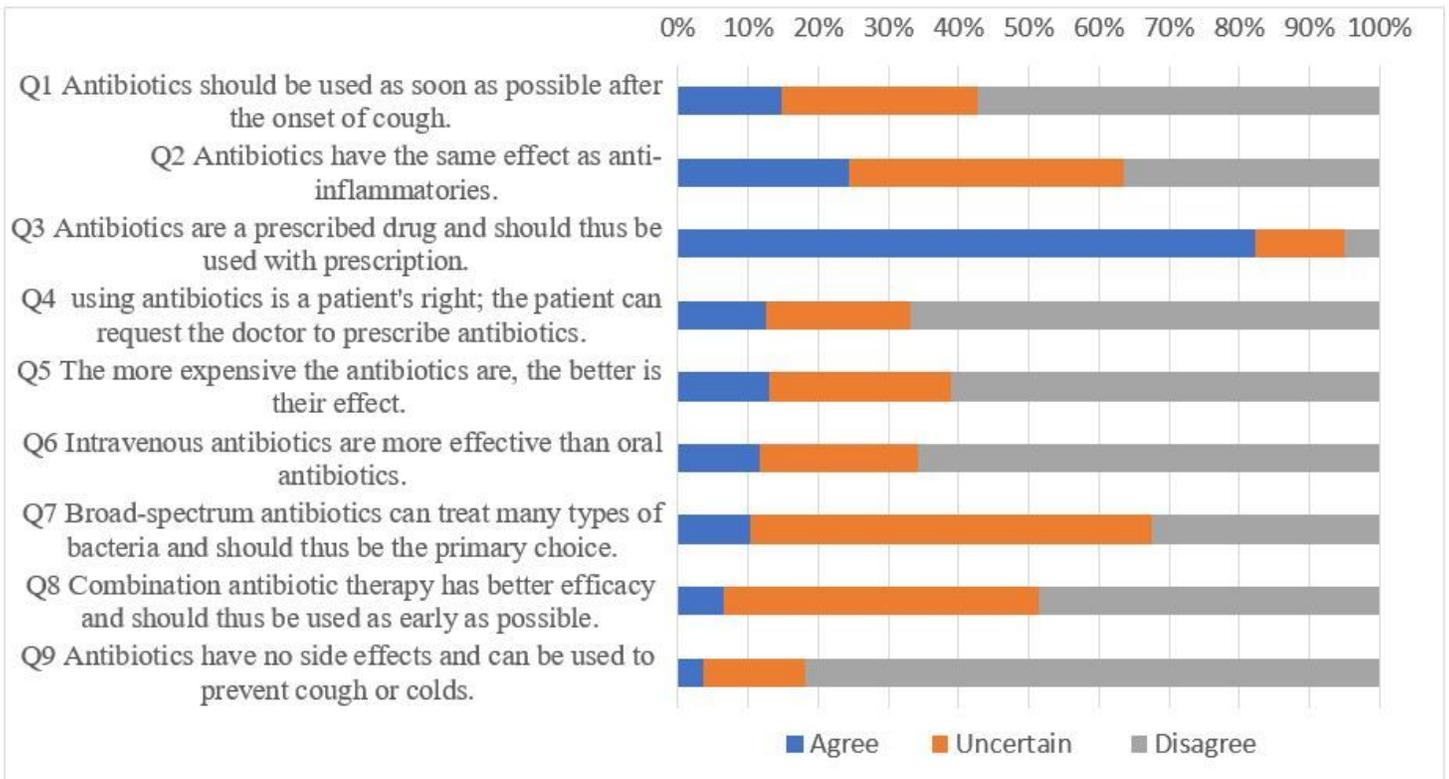
**Figure 1**

Types of antibiotics prescribed by doctors and those used without prescription (a). The types of antibiotics used without a prescription. (b) the types of antibiotics prescribed by doctors. \*Penicillins include amoxicillin, ampicillin, amoxicillin, and clavulanate potassium. Cephalosporins include cephalexin, cefuroxime, cefminox, cefepime, and other cephalosporins. Macrolides include azithromycin, erythromycin, roxithromycin, and clarithromycin.



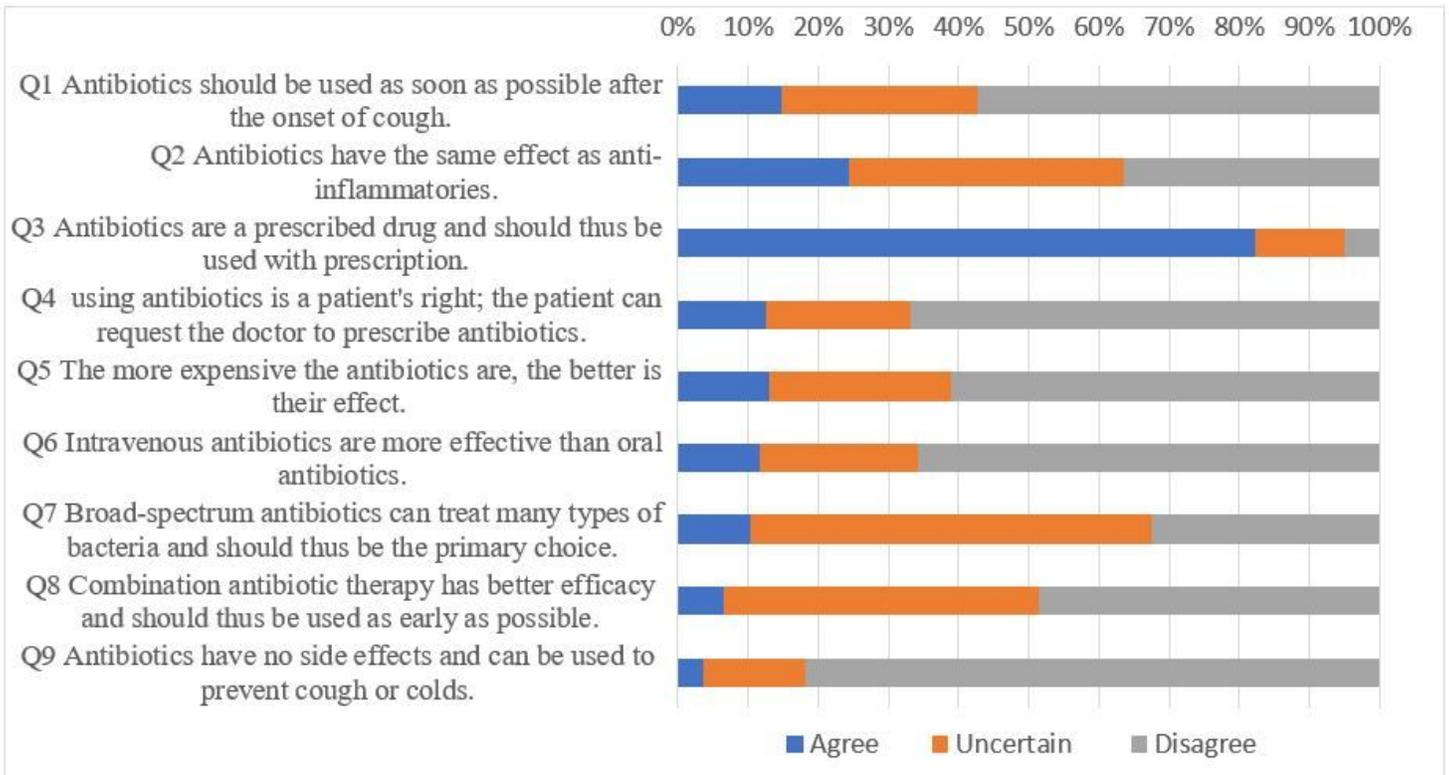
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**Figure 2**

Knowledge on the use of antibiotics



## Figure 2

Knowledge on the use of antibiotics