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cross-sectional study from three

et al. Influence of leftover

BMJ Open Influence of leftover antibiotics on selfmedication with antibiotics for children: a cross-sectional study from three Chinese provinces

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ABSTRACT

Objectives To investigate leftover antibiotics and their influence on self-medication with antibiotics (SMA) for Chinese children, and further explore the different influences of leftovers from two main sources: previous prescriptions and pharmaceutical purchases.

Design A cross-sectional questionnaire study. **Setting** The participants were approached through kindergartens and primary schools as well as in vaccination clinics.

Participants A total of 9526 parents from three Chinese provinces whose children were aged 0–13 years completed the survey.

Outcome measures The prevalence of keeping antibiotics at home for children and the proportion of leftover antibiotics from two main sources were measured by a self-administrated questionnaire. Logistic regression models were established to examine the association between keeping antibiotics at home and SMA for children, specifically the risks of leftovers from two main sources. Results Overall, 4580 (48,1%) reported keeping antibiotics at home for children. Among those who had leftovers, 2891 (63.1%) reported that their leftovers came from previous prescriptions and 1619 (35.3%) reported that their leftovers came from pharmaceutical purchases. Mothers, older age of child, higher household income, higher education level and medical background were significantly associated with keeping antibiotics at home. Keeping antibiotics at home was significantly associated with SMA for children (adjusted OR=4.91, 95% CI 3.84 to 6.28). Particularly, compared with parents who did not keep antibiotics at home, parents who kept leftover antibiotics from previous prescriptions and those whose leftovers came from pharmaceutical purchases were 3.80 (95% CI 2.89 to 5.00) and 6.45 (95% CI 4.89 to 8.51) times more likely to engage in SMA for children, respectively. Conclusions Keeping antibiotics at home for children was pervasive in China. Most leftovers came from previous prescriptions, while those from pharmacies had a higher risk of SMA for children.

INTRODUCTION

Antimicrobial resistance (AMR) is a growing health concern which the WHO lists as one of the top ten threats to public health

Strengths and limitations of this study

- This survey had a large sample size which spanned three Chinese provinces with differing economic development levels and included urban as well as rural areas.
- Our study first explored the different influences of the leftover antibiotics from two main sources (previous prescriptions and pharmaceutical purchases) on self-medication with antibiotics for children.
- Only parents were recruited as respondents for our study, contexts in which grandparents or others acted as children's caregivers were not included.
- Other sources of leftover antibiotics (1.6%) aside from previous prescriptions and pharmaceutical purchases were not investigated in this study.

worldwide.^{1 2} Widespread antibiotic misuse increases selection pressure for mutated strains of microbes, thereby accelerating the development of AMR.³ The spread of AMR renders routine treatments for infectious diseases, such as pneumonia, ineffective,⁴⁵ thereby increasing mortality rates from common diseases and deepening the financial burden of public health systems as they struggle to find new and more effective treatment options.¹

Human antibiotic misuse plays a leading role in the development of AMR.³⁶ Self-medication with antibiotics (SMA) is a common form of antibiotic misuse which leads to a plethora of nefarious outcomes, including AMR.^{7–9} SMA occurs worldwide; with a rate of 3.1% among European adults in the past 12 months¹⁰ and 85.5% among Nigerian undergraduates within the past 2–3 months.¹¹ In China, the prevalence of SMA was reported to be 40% among undergraduates¹² and 38% among urban children¹³ in the past 6 months.

Keeping antibiotics at home increases the likelihood of SMA.¹⁴ One study reported

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that 50% of antibiotics used in self-medication were leftovers.¹⁵ In developed countries, leftover antibiotics originate almost entirely from previous prescriptions due to strict regulations on the retail sale of antibiotics,^{16 17} while leftovers in developing countries also include nonprescription antibiotics purchased from pharmacies.^{12 18} It is assumed that leftover antibiotics from the above two sources might have different influences on SMA.¹⁹

Antibiotic misuse in children is especially pervasive²⁰; 10% of Greek parents²¹ and 60% of Mongolian parents admitted to having self-medicated their children with antibiotics in the past 2weeks.²² The rate of SMA for children over the past year in Chinese rural areas reached as high as 62%.²³ Keeping antibiotics at home can facilitate SMA for children.²² Two studies in China found that parents who kept antibiotics at home were 2.8²³ and 6.3¹³ times more likely to engage in SMA for children than parents who did not. However, no study thus far has investigated the different influences of leftovers from previous prescriptions and pharmacies, which have further implications for intervention strategies. Moreover, existing studies were limited by the relatively long recall periods of their questionnaires, their small sample sizes and their limited geographical locations. Additionally, little attention has been paid to SMA for children for prophylaxis in China; this practice is widespread in developing countries.²⁴ Therefore, our study aims to (1) assess the situation of keeping antibiotics at home for children and the influencing factors of this behaviour and (2) explore the association between keeping antibiotics at home and SMA for children (remedial and prophylactic), as well as the influences of leftover antibiotics from two different sources.

METHODS

Study design and participants

Data for this study came from a cross-sectional survey conducted in three provinces in China between June 2017 and April 2018. These three provinces were selected according to their geographical locations and gross domestic product per capita to encompass eastern (Zhejiang, ranked 5th), central-northwestern (Shaanxi, ranked 12th) and southwestern (Guangxi, ranked 26th) regions with significant differences in socioeconomic development levels.²⁵

To ensure an adequate sample size for the subgroup analyses, we aimed to survey ca. 3000 parents per province with an even distribution in urban and rural areas. Multistage stratified cluster random sampling was adopted to ensure the representativeness of data from diverse Chinese parents whose children were aged between 0 and 13 years. In each province, a prefecture-level city was randomly selected and within each city, an urban and a rural district were randomly chosen as sampling sites. At each site, a certain number of kindergartens, primary schools and vaccination clinics were randomly selected as clusters according to their size or daily flow to meet the target sample size. All parents of children aged 4–13 years who attended those kindergartens and primary schools, and all parents who took their children aged under 3 years to those vaccination clinics during working days were sampled. In China, children are required to be fully vaccinated for school enrolment and up to 99% of children aged under 3 years were covered by government subsidised vaccinations.^{26 27}

Study measurement

A self-administered questionnaire (see online supplementary file) which consisted of two main sections was used: (1) sociodemographic characteristics, including the parents' sex, education level, average monthly household income, location of residence, medical background, as well as their children's age and sex, and (2) whether the respondents (i) engaged in SMA when children fell ill in the past month, (ii) engaged in SMA for children for prophylaxis in the past year and (iii) kept leftover antibiotics (not for current use) at home for children at the time of survey, and if so, where the leftovers came from. The questionnaire was based on literature review,²³ ²⁸⁻³⁰ modified by qualitative interviews and finalised after a pilot test.

Data collection

The questionnaire was easily accessed through a smartphone by scanning a QR code (quick response code) which led to a survey on WenJuanXing (the Chinese version of SurveyMonkey).³¹ The first page of the questionnaire provided a brief introduction assuring the anonymity of respondents as well as their right to withdraw from the study at any time. Additionally, it is explained during the introduction that the questions only involve the child who was receiving vaccination or attending the kindergarten/primary school if the participant had more than one child.

The parents who acted as the main caregiver and health decision-maker for the child were invited to fill out the questionnaire. Parents whose children aged 0–3 years were surveyed in vaccination clinics during their waiting time. Our research assistants (1) distributed informative leaflets about the survey, (2) introduced the survey and (3) obtained signed consent forms from participants. Parents scanned the QR code with smartphones and completed the survey after vaccination. Parents whose children aged 4–13 years were surveyed in kindergartens and primary schools with the help of teachers. Teachers distributed the QR code and sent consent forms to children's parents. Parents who agreed to participate signed the consent form and completed the questionnaire.

Statistical analyses

Data were analysed using the SPSS V.24.0. χ^2 and t tests were conducted to compare the sociodemographic characteristics and prevalence of SMA for children between parents who kept antibiotics at home for children and those who did not. Logistic regression was used to identify factors associated with keeping antibiotics at home for children. Two other logistic regression models were established to further explore associations between keeping antibiotics at home and SMA for children (when they were sick and for prophylaxis). In model 1, responses to *keeping antibiotics at home for children* were simply divided into yes or no, while in model 2, responses were divided into three subgroups according to the sources of leftover antibiotics: group 1=no; group 2=yes, previously prescribed by doctors; and group 3=yes, previously purchased from pharmacies. A statistical significance level of p<0.05 was applied.

Patient and public involvement

Members of the public were involved in the development of our survey by participating in qualitative interviews as stakeholders, which helped to tailor the questionnaire to the local Chinese context. In addition, 315 respondents contributed to the pilot study to improve the instrument and enhance better validity. All respondents were informed that their answers would be valuable to scientific research and policy decisions which, in turn, benefit their children.

RESULTS

Basic information of the sample

A total of 9526 questionnaires were collected with a response rate of 88.7%. The number of respondents in three provinces (Zhejiang, Shaanxi and Guangxi) were 2924, 3355 and 3247, respectively (30.7% vs 35.2% vs 34.1%). Mothers accounted for the majority of respondents (7283, 76.5%). There were slightly more male children than females (4943, 51.9%, vs 4583, 48.1%), and the mean age of children was 5.8 years (SD=3.6 years). Slightly less than half of the respondents had college and above levels of education (4242, 44.5%). More than half of the respondents had an average household income of 5000 RMB (US\$769) or less per month (4991, 52.4%), and more than half were urban residents (5265, 55.3%). A small proportion (1122, 11.8%) of the respondents had a medical background.

Almost half of the respondents (4580, 48.1%) kept antibiotics at home for children. A total of 2891 (63.1%) reported that their leftover antibiotics came from previous medical prescriptions, while 1619 (35.3%) reported that their leftovers had been purchased from pharmacies. Among all the respondents, 3579 (37.6%) reported their children fell ill within the month before the survey. The most commonly reported illnesses were cold (2938, 82.1%), sore throat (1707, 47.7%) and fever (1108, 31.0%). To manage these illnesses, 1944 (54.3%) self-treated their children, of whom 621 (31.9%) used antibiotics. Moreover, 1983 (20.8%) of all respondents reported that they had engaged in SMA for children for prophylaxis in the past year.

Sociodemographic characteristics and antibiotic use behaviours of parents

As presented in table 1, significant differences were found regarding sex, highest education level, average household income per month, province, residence and medical background between respondents who kept antibiotics at home for children and those who did not (p<0.001). The rates of SMA for children when they were sick and for prophylaxis were both significantly higher in the respondents who kept antibiotics at home for children (p<0.001).

Factors associated with keeping antibiotics at home for children

As table 2 presents, mothers (adjusted OR (aOR)=1.17, 95% CI 1.06 to 1.29) and respondents with higher education levels (aOR=1.34, 95% CI 1.20 to 1.51; aOR=1.50, 95% CI 1.33 to 1.70) were more likely to keep antibiotics at home for children. Respondents from Shaanxi (aOR=1.96, 95% CI 1.75 to 2.20) and respondents with medical backgrounds (aOR=1.54, 95% CI 1.35 to 1.75) had greater odds of keeping antibiotics at home for children.

The association between keeping antibiotics at home and SMA for children

Among 1927 parents who self-medicated their children in the last month (model 1), those who kept antibiotics at home for children were nearly five times (aOR=4.91, 95% CI 3.84 to 6.28) more likely to engage in SMA for children than those who did not. Model 2 illustrates that parents who had leftover antibiotics which came from previous prescriptions and which were purchased from pharmacies were 3.80 (95% CI 2.89 to 5.00) and 6.45 (95% CI 4.89 to 8.51) times more likely to engage in SMA for children, respectively, than those who did not keep antibiotics at home (table 3).

The association between keeping antibiotics at home and SMA for children for prophylaxis

Among 9456 respondents (model 1), those who kept antibiotics at home for children were 3.16 times (95% CI 2.83 to 3.53) more likely to prophylactically engage in SMA for children than those who did not keep antibiotics at home. Model 2 illustrates that parents who had leftover antibiotics which came from previous prescriptions and which were purchased from pharmacies were 2.96 (95% CI 2.62 to 3.34) and 3.53 (95% CI 3.07 to 4.05) times more likely to engage in SMA for children for prophylaxis, respectively, than those who did not keep antibiotics at home (table 4).

DISCUSSION

To the best of our knowledge, this is the first study covering both rural and urban Chinese populations to investigate parental behaviours of keeping antibiotics at home for children and its association with SMA for sick children and prophylaxis. This is also the first study to identify the two main sources of leftover antibiotics for children: previous prescriptions and pharmaceutical purchases. We found that keeping antibiotics at home

		Ke	ep antibi	otics at home				
		No	o (n=4946)	, n (%)		Yes (n=4580), n (%)	χ²/t	P valu
Sex of caregiver							17.04	<0.00
Male		12	50 (25.3)			993 (21.7)		
Female		36	96 (74.7)			3587 (78.3)		
Sex of child							1.784	0.18
Male		25	99 (52.5)			2344 (51.2)		
Female		2347 (47.5)			2236 (48.8)			
Age of child, years,	mean (SD)		5.6 (0.5)			6.0 (0.5)	5.454	< 0.00
Parents' highest leve	el of education						77.43	<0.00
Middle school and	d below	14	93 (30.2)			1026 (22.4)		
High school		14	1400 (28.3)			1365 (29.8)		
College and abov	e	20	53 (41.5)			2189 (47.8)		
Average household	income (RMB, mo	nthly)					47.62	<0.00
<3000 (US\$461)		12	28 (24.8)			874 (19.1)		
3000–5000 (US\$4	62–769)	14	55 (29.4)			1434 (31.3)		
5001–10 000 (US	\$770–1538)	13	94 (28.2)			1355 (29.6)		
>10000 (US\$1538	3)	8	69 (17.6)			917 (20.0)		
Province							228.9	< 0.00
Zhejiang		15	91 (32.2)			1333 (29.1)		
Shaanxi		14	05 (28.4)			1950 (42.6)		
Guangxi		19	50 (39.4)			1297 (28.3)		
Residence							31.76	< 0.00
Rural		23	49 (47.5)			1912 (41.7)		
Urban		25	97 (52.5)			2668 (58.3)		
Parents with medica	al background						65.85	< 0.00
No		44	91 (90.8)			3913 (85.4)		
Yes		4	55 (9.2)			667 (14.6)		
	SMA for childre	n			SMA for child for prophyla			
	Yes (n (%))	χ²/t		P value	Yes (n (%))	χ²/t	P value	
Keeping antibiotics for children at home		187.5		<0.001		481.9	<0.001	
No	108 (17.4)				595 (30.0)			
Yes	513 (82.6)				1388 (70.0)			

SMA, self-medication with antibiotics.

for children is a widespread practice in China, which increases the chances of parents engaging in SMA for their children. In this study, leftover antibiotics from previous prescriptions accounted for a larger proportion of total in-home antibiotics; however, leftovers which originated from pharmaceutical purchase had a higher risk of SMA for children. These findings indicate an urgent need for intervention programmes on reducing leftover antibiotics and enhancing appropriate antibiotic use for children.

The prevalence of keeping antibiotics for children varies greatly across China. Rates of antibiotics kept at home by parents or caregivers in central rural, eastern rural and urban China were reported as 75%,²³32%²⁹ and 25%,¹³ respectively, and in our study as 48.1%. Unlike previous studies, our results are based on data from disparate locations, thereby providing a broader picture of the prevalence of leftover antibiotics in China. Compared with similar studies conducted overseas, the rate in China is higher than that reported in Trinidad and Tobago (21.8%)³² but lower than that in Mongolia (58.4%).²²

As is consistent with our results, previous studies have proven that keeping antibiotics at home could increase the likelihood of parents engaging in SMA for children.^{13 22 23} It has been found that people tend to use

Table 2Factors associated with keeping antibiotics at home for children (n=9526)			
Independent variables	aOR (95% CI)		
Sex of caregiver			
Male	Ref		
Female	1.17 (1.06 to 1.29)**		
Sex of child			
Male	Ref		
Female	1.04 (0.96 to 1.13)		
Age of child	1.05 (1.04 to 1.07)***		
Parents' highest level of education			
Middle school and below	Ref		
High school	1.34 (1.20 to 1.51)***		
College and above	1.50 (1.33 to 1.70)***		
Average household income (RMB, monthly)			
<3000 (US\$461)	Ref		
3000–5000 (US\$462–769)	1.22 (1.08 to 1.38)**		
5001–10 000 (US\$770–1538)	1.17 (1.02 to 1.33)*		
>10000 (US\$1538)	1.36 (1.16 to 1.60)***		
Province			
Zhejiang	Ref		
Guangxi	1.00 (0.89 to 1.13)		
Shaanxi	1.96 (1.75 to 2.20)***		
Residence			
Rural	Ref		
Urban	1.03 (0.94 to 1.13)		
Parents with medical background			
No	Ref		
Yes	1.54 (1.35 to 1.75)***		

*p<0.05, **p<0.01 and ***p<0.001.

aOR, adjusted odds ratio; Ref, reference group.

the same drug when they confronted similar symptoms based on their experiences.³³ Recent evidence also shows that parents who keep antibiotics at home prefer to selfmedicate their children rather than directly seeking advice from a medical professional.¹³ Therefore, leftover antibiotics at home facilitate parents' deleterious practice of SMA for children by referring to previous practices. One survey in China even reported that among parents who kept antibiotics at home, 97% used the leftovers for their children on a second occasion.²⁹

Overall, we found that 63.1% of leftover antibiotics came from previous prescriptions. This result differs from a study of Chinese university students which identified nonprescription pharmaceutical purchases as the main source of leftover antibiotics.¹⁹ In this study, there were 69.2% of parents who engaged in hospital visits (not shown in tables), while the rate among university students was only 27.4%.²⁷ In addition, medications are dispensed in fixed packages rather than exact doses in China.¹⁴ High consultation rates and inadequate dispensing systems explain the origin of most leftover antibiotics for children—previous
 Table 3
 The association between keeping antibiotics at

 home and SMA for children when they fell sick (n=1927)†

Independent variables	Model 1 aOR (95% CI)	Model 2 aOR (95% CI)		
Sex of caregiver				
Male	Ref	Ref		
Female	1.23 (0.93 to 1.62)	1.28 (0.97 to 1.69)		
Sex of child				
Male	Ref	Ref		
Female	0.95 (0.77 to 1.18)	0.95 (0.77 to 1.17)		
Age of child	1.03 (0.99 to 1.06)	1.02 (0.99 to 1.06)		
Parents' highest level of education				
Middle school and below	Ref	Ref		
High school	0.81 (0.60 to 1.11)	0.79 (0.58 to 1.08)		
College and above	0.72 (0.52 to 0.99)*	0.71 (0.52 to 0.98)*		
Average household income (RMB, monthly)				
<3000 (US\$461)	Ref	Ref		
3000–5000 (US\$462– 769)	0.92 (0.68 to 1.24)	0.94 (0.69 to 1.27)		
5001–10 000 (US\$770– 1538)	0.65 (0.46 to 0.91)*	0.66 (0.47 to 0.94)*		
>10000 (US\$1538)	0.76 (0.50 to 1.16)	0.78 (0.51 to 1.20)		
Province				
Zhejiang	Ref	Ref		
Guangxi	1.91 (1.38 to 2.65)***	1.69 (1.21 to 2.35)**		
Shaanxi	2.63 (1.91 to 3.60)***	2.41 (1.75 to 3.31)***		
Residence				
Rural	Ref	Ref		
Urban	0.97 (0.77 to 1.23)	0.96 (0.76 to 1.21)		
Parents with medical background				
No	Ref	Ref		
Yes	0.71 (0.52 to 0.97)*	0.71 (0.52 to 0.98)*		
Keeping antibiotics at home for children				
No	Ref	-		
Yes	4.91 (3.84 to 6.28)***	-		
Keeping antibiotics at home for children				
No	-	Ref		
Yes, previously prescribed by doctors	-	3.80 (2.89 to 5.00)***		
Yes, previously purchased from pharmacies	-	6.45 (4.89 to 8.51)***		

*p<0.05, **p<0.01 and ***p<0.001.

†A total of 17 of 1944 respondents who self-treated their children in the past month kept antibiotics from other sources except for the two main ones (previous prescriptions or pharmacies), leaving 1927 for analysis in the regression models. aOR, adjusted odds ratio; Ref, reference group; SMA, self-medication with antibiotics.

prescriptions. Moreover, non-compliance could also be responsible for a large portion of leftovers²⁸ since many children fail to complete the course of treatment because their parents incorrectly accuse antibiotics for the side effects of other drugs taken at the same time.³⁴

Table 4	The association between keeping antibiotics at
home and	prophylactic SMA for children (n=9456)†

	Model 1 aOR (95% CI)	Model 2 aOR (95% CI)
Independent variables		
Sex of caregiver	Dof	Dof
Male	Ref 0.83 (0.74 to 0.94)**	Ref
	0.83 (0.74 to 0.94)***	0.83 (0.74 to 0.94)**
Sex of child	Def	Def
Male	Ref	Ref
Female	1.06 (0.96 to 1.18)	1.06 (0.96 to 1.18)
Age of child	1.01 (1.00 to 1.03)	1.01 (1.00 to 1.03)
Parents' highest level of education		
Middle school and below	Ref	Ref
High school	0.97 (0.84 to 1.12)	0.97 (0.84 to 1.11)
College and above	0.85 (0.73 to 0.99)*	0.84 (0.72 to 0.98)*
Average household income (RMB, monthly)		
<3000 (US\$461)	Ref	Ref
3000–5000 (US\$462– 769)	0.93 (0.80 to 1.08)	0.93 (0.80 to 1.08)
5001–10 000 (US\$770– 1538)	0.90 (0.76 to 1.06)	0.90 (0.76 to 1.06)
>10000 (US\$1538)	0.84 (0.68 to 1.03)	0.84 (0.69 to 1.04)
Province		
Zhejiang	Ref	Ref
Shaanxi	1.59 (1.38 to 1.84)***	1.56 (1.35 to 1.80)***
Guangxi	1.00 (0.86 to 1.17)	0.97 (0.83 to 1.13)
Residence		
Rural	Ref	Ref
Urban	0.94 (0.84 to 1.06)	0.94 (0.84 to 1.06)
Parents with medical background		
No	Ref	Ref
Yes	0.62 (0.52 to 0.75)***	0.62 (0.52 to 0.75)***
Keeping antibiotics at home for children		
No	Ref	-
Yes	3.16 (2.83 to 3.53)***	-
Keeping antibiotics at home for children		
No	-	Ref
Yes, previously prescribed by doctors	-	2.96 (2.62 to 3.34)***
Yes, previously purchased from pharmacies	-	3.53 (3.07 to 4.05)***

*p<0.05, **p<0.01 and ***p<0.001.

†A total of 70 of 9526 respondents kept antibiotics from other sources except for the two main ones (previous prescriptions or pharmacies), leaving 9456 for analysis in the regression models.

aOR, adjusted odds ratio; Ref, reference group; SMA, self-medication with antibiotics.

In this study, only one-third of leftover antibiotics for children came from pharmacies. However, one should note that this kind of leftovers shows higher risks of SMA for children. In China, although a prescription-only regulation for antibiotics at retail pharmacies has been

in place since 2004,³⁵ it still remains easy for parents to purchase antibiotics without prescriptions due to the lack of an effective monitoring system for sales of antibiotics. As one multicentre survey in urban China concluded, 55.9% pharmacies sold non-prescription antibiotics for paediatric diarrhoea.³⁶ Another nationwide study also reported that nearly 70% university students who succeeded in pharmaceutical purchases of antibiotics had no prescription at all.²⁸ It can be inferred that substantial leftover antibiotics from pharmacies in our study had been purchased without a prescription. Furthermore, previous studies found that antibiotics purchased from pharmacies without prescription strongly contributed to the problem of SMA for children,^{13 37} and most leftover antibiotics from pharmacies were kept for future use.¹⁸ In contrast, as already discussed, leftover antibiotics from previous prescriptions were usually unintentionally left and not necessarily meant to be used on a second occasion.³⁸ This finding reinforces our belief that China needs stronger regulations on prohibiting non-prescription sales of antibiotics at retail pharmacies.

In line with previous evidence,¹⁹ parents with medical backgrounds were more likely to keep antibiotics at home for children; however, they were also less likely to engage in SMA for children. A possible explanation could be that parents with medical backgrounds had easier access to antibiotics. One study found that some pharmacists helped their families to obtain non-prescription antibiotics.³⁹ On the other hand, parents with medical backgrounds might keep standby antibiotics since they believed that they have the capacity to handle some of their children's illnesses. However, most conditions in this study were self-limited diseases which did not need antibiotic therapy. Parents with medical backgrounds could be aware of that: thus, they were more likely to self-treat their children without antibiotics. Additionally, mothers were less likely to engage in SMA for children for prophylaxis in our study, which might be attributed to their role of the main caregiver and health decision-maker in the family.²² However, this predictor was not significant in remedial use, which deserves further investigation.

Our findings have several important implications for medical practitioners and policymakers. For the supply side, close supervision of sales of antibiotics at retail pharmacies is urgently needed, and the dispensing system of medication in healthcare institutions needs reformation so that patients get a precise dosage of antibiotics. For the demand side, it is essential to provide public education programmes which teach appropriate knowledge and skills to manage common self-limited juvenile diseases, which may help to reduce the rates of unnecessary hospital visits and improper antibiotic use. Furthermore, collecting and recycling programmes for leftover antibiotics could be useful in China, as these have been proven successful in reducing leftover antibiotics elsewhere.^{40,41}

Our study has several limitations. First, this study only recruited parents, which excluded situations when grandparents or others acted as children's primary caregivers. Second, the study relied on self-reports of parents, which undoubtedly reflected their misunderstanding of antibiotics.^{12 13} This means that they might have overestimated or underestimated the rates at which they use or keep antibiotics; however, we tried to minimise this bias by a brief explanation about antibiotics in the questionnaire. Third, our study cannot show the direct relation between leftover antibiotics and SMA for children, instead only a strong association has been found. Specific sources of leftover antibiotics used in SMA should be investigated in future studies. Fourth, our findings only focus on the influence of leftover antibiotics from two main sources because others represent a very small proportion (1.6%)in this study. This might not be the case in other countries so future studies are needed to convey more pictures of leftover antibiotics.

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Contributors CS analysed the data and drafted the manuscript. YJH revised the manuscript critically for important intellectual content. XZ and XW led the design of the study. XZ is the principal investigator of the study and participated in the coordination of data collection and critical review of the manuscript. XW, JL and LL participated in critical review of the manuscript. All the authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

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Data availability statement Data are available on reasonable request.

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