

Integrative Medicine Research

Use of antibiotics and other treatments in Chinese adults with acute cough: an online survey --Manuscript Draft--

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Abstract:	<p>Background: This study aimed to identify use of various treatments and their association with the use of antibiotics and patient reported clinical recovery in Chinese adults with acute cough.</p> <p>Methods: An online survey recruiting people who had recently experienced cough was conducted. Their sociodemographic, clinical characteristics, treatments received and their perceived changes in symptoms were collected. Factors influencing avoidance of antibiotics and improvement in symptoms were explored.</p> <p>Results: A total of 22,787 adults with recent acute cough completed the questionnaire, covering all 34 province-level administrative units in China. Most respondents were male (68.0%), young (89.4%, aged 18-45), with a median cough severity of 6/10 on a numerical rating scale. Nearly half of the participants (46.4%) reported using antibiotics, among which 93.1% were for presumed upper respiratory tract infections (URTIs). Fewer patients took antibiotics after taking CHM (14.9%), compared to those who started with home remedies (18.0%), allopathic non-antibiotic medication (25.0%). Antibiotics, allopathic non-antibiotic medications, CHM and home remedies were all perceived beneficial in relieving cough.</p> <p>Conclusions: Chinese adult responders report use of a considerable variety of treatments alone or in combination for acute cough. Patient-reported clinical recovery was similar regardless of treatment. There is likely a high proportion of inappropriate use of antibiotics for treatment of simple acute cough. As the majority of respondents did not use antibiotics as a first-line, and use of CHM was associated with relief of cough symptoms and reduction in the use of antibiotics, this presents an important opportunity for prudent antibiotic stewardship in China.</p>
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Opposed Reviewers:	
Response to Reviewers:	

Dear Editor and reviewers,

Many thanks for the useful comments and suggestions. We have revised the manuscript with changes tracked and responded to the two reviewers' comments point by point.

In addition to the changes made following the reviewers' suggestions, we have also updated the STROBE checklist and removed the original figure 2 as the map template used might not be an accurate representation of China.

Best wishes,
Mio on behalf of the research team

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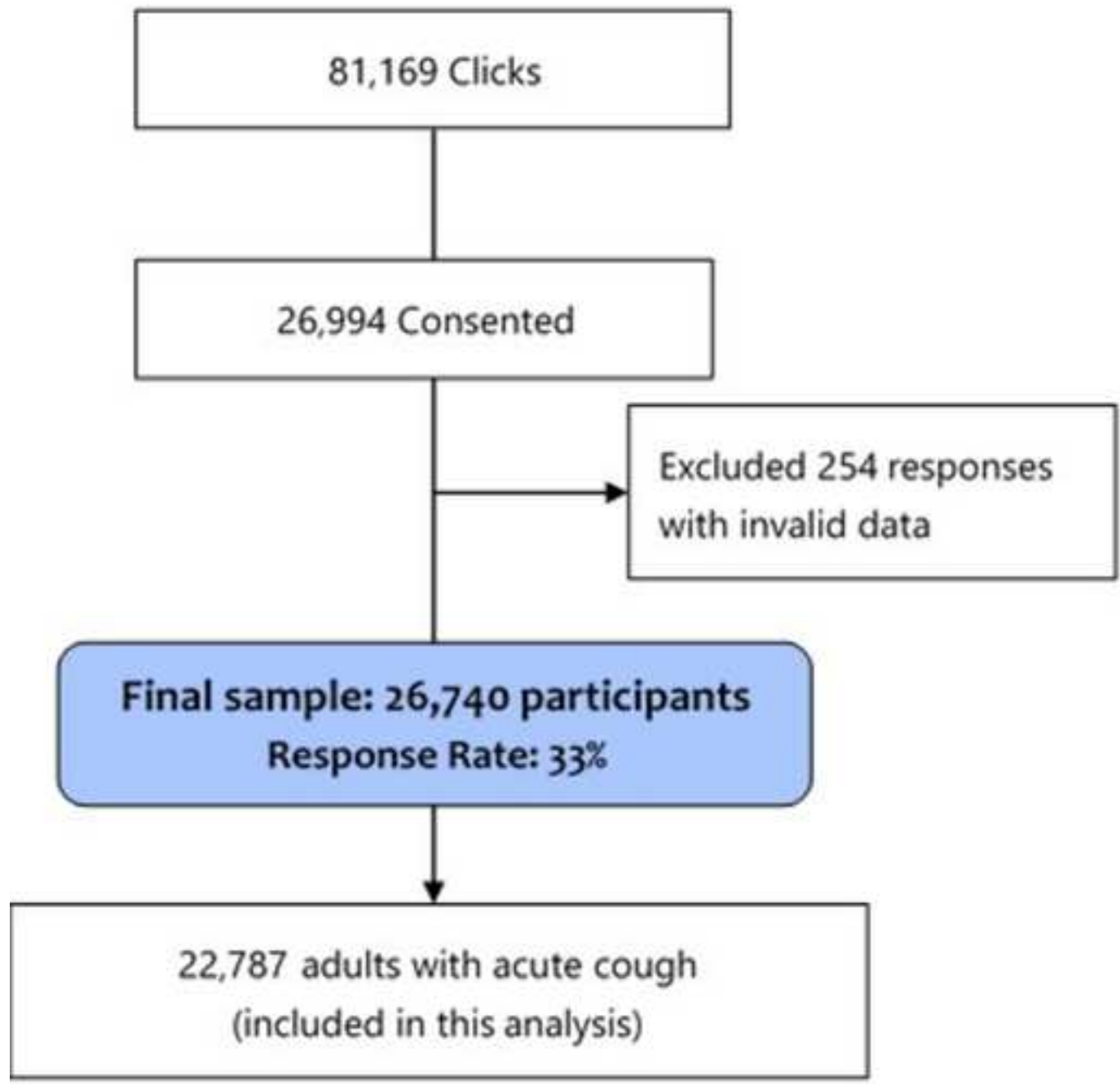
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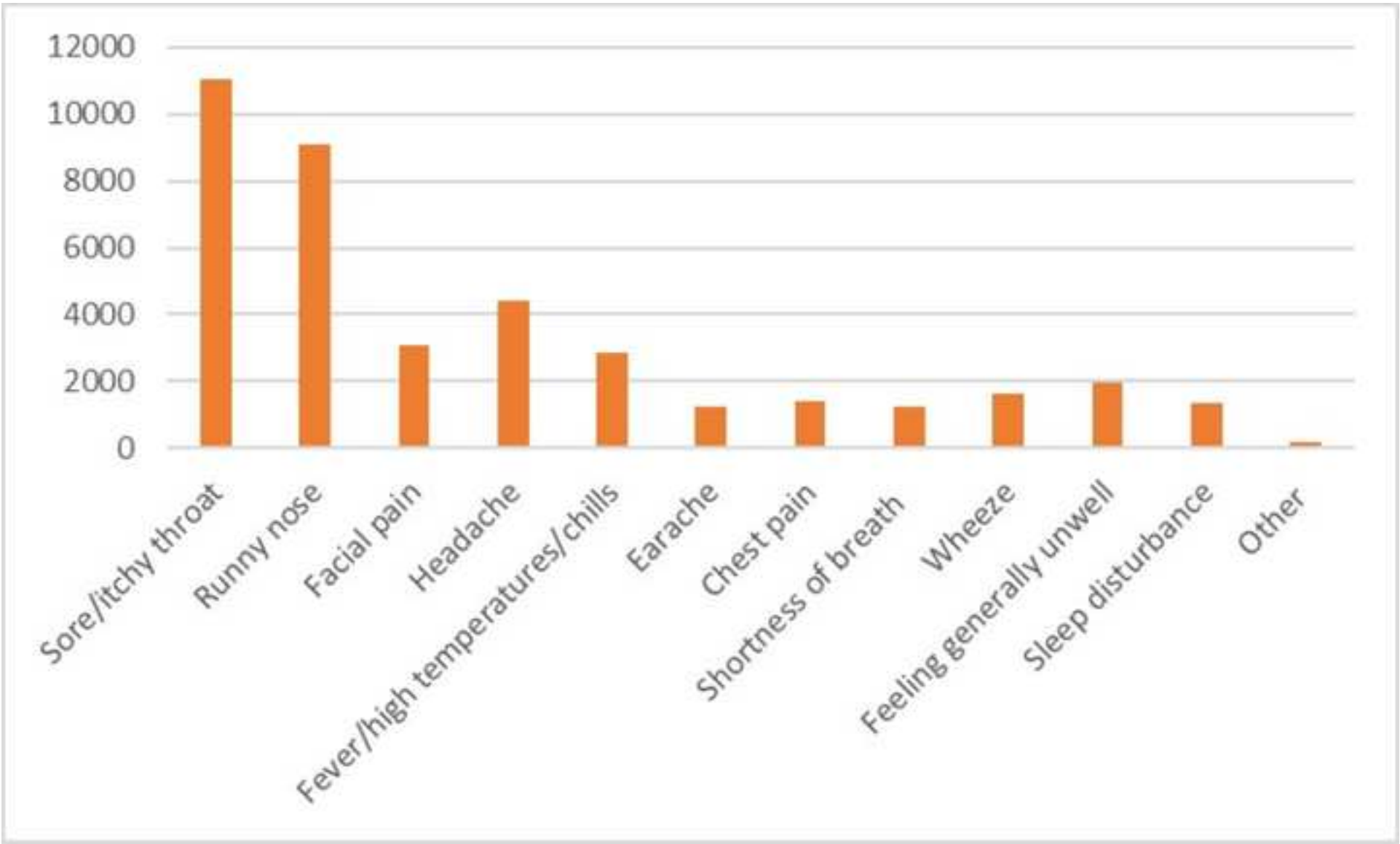
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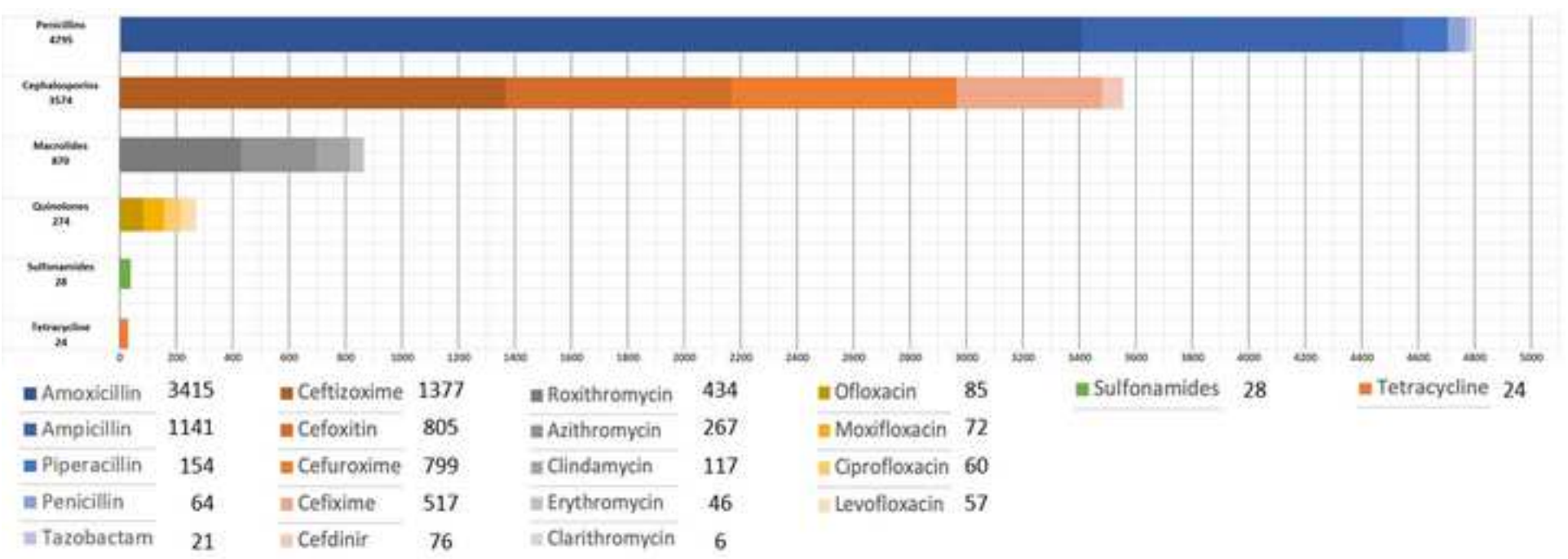
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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4 54
Objectives	3	State specific objectives, including any prespecified hypotheses	5 4
Methods			
Study design	4	Present key elements of study design early in the paper	3 45
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	3 5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 6
Bias	9	Describe any efforts to address potential sources of bias	3 46
Study size	10	Explain how the study size was arrived at	7 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4 6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	4 7
		(b) Describe any methods used to examine subgroups and interactions	4 7
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5 8
		(b) Give reasons for non-participation at each stage	5 8
		(c) Consider use of a flow diagram	5 8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5 68-12
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	12 -137

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Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A <u>12-13</u>
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	<u>9</u> 12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	4 <u>14</u>
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	4 14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-16 <u>14</u>
Generalisability	21	Discuss the generalisability (external validity) of the study results	15 <u>9</u>
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17 <u>2</u>

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*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

Responses to reviewers' comments

Submission deadline: 3rd Jan 2023

Dear Editor and reviewers,

Many thanks for the useful comments and suggestions. We have revised the manuscript with changes tracked and responded to the two reviewers' comments point by point.

In addition to the changes made following the reviewers' suggestions, we have also updated the STROBE checklist and removed the original figure 2 as the map template used might not be an accurate representation of China.

Best wishes,
Mio on behalf of the research team

Reviewer #1:

-In the methods section, the representativeness of the study participants should be described (though it is mentioned in the Discussion section for limitation).

Thanks for your suggestion. We tried to approach a representative large sample by circulating the study invites through the largest Chinese social media platform and sharing the invites to various general groups in different regions of China. We have added this information in the method section (page 6) and revised the wording in the limitation (page 15).

-Though suggested in the supplements, providing short information of the questionnaire outline would be helpful to interpret the results, such as total number of the questions, scale, total time required etc.

Thanks for your suggestions. We have briefly described the three sections of the online cough survey and provided an idea of how long it takes to complete it (page 5-6).

-Describe the full name of CHM in the footnote of the Table 2.

Revised, please see page 11.

-Why did the authors concluded that still there is 'inappropriate widespread use of antibiotics' from the results? (page 13, Discussion)

Thanks for your query. The main finding supporting this argument is that nearly half of the participants (46.4%) had used antibiotics for their cough. Among these people, 93.1% (9828/10562) used antibiotics for presumed upper respiratory tract infections. Research evidence suggests antibiotics are of very limited benefit for patients with upper RTIs such as common colds, otitis media, rhinitis, or laryngitis. We have revised the wording of the abstract results, so they link better with our conclusions (page 3, 14, 16).

-The study conclusion is still vague. Please make clear based on the survey results.

Thanks for your comments. We have clarified the study results and conclusions by linking them in the below table. As to the nature of this survey study, we have softened one of our main conclusions that there is likely overuse of antibiotics for treatment of simple acute cough. We have also ensured conclusions are consistent in the abstract and the main conclusion section.

	Results	Conclusions
Treatment pattern	-46.4% participants had used antibiotics, among which 93.1% (9828/10562) were for presumed URTIs	There is likely a high proportion of inappropriate use of antibiotics for treatment of simple acute cough.
	-28.3% participants used allopathic non-antibiotic medications to help with their acute cough, and the most used were NSAIDs. -39.2% participants used CHM to help with their acute cough. The most used patent CHM was CBPPG, followed by GML granule, KCS pill, and FFGC tablet/liquid. -21.2% participants used home remedies and the most taken one was boiled pear soup.	Chinese adult responders report use of a considerable variety of treatments alone or in combination for acute cough.
Treatment effects	-Subsequent use of antibiotics was lower in those who initially took CHM, compared to those who started with home remedies or allopathic non-antibiotic medications ($p<0.05$).	As the majority of respondents did not use antibiotics as a first line, and use of CHM was associated with relief of cough symptoms and reduction in the use of antibiotics.
	-Antibiotics, allopathic non-antibiotic medications, CHM and home remedies were considered helpful in relieving cough symptoms, with the same median of 4, with a IQR at 1 or 2 on a 1-5 Likert self-rating scale.	Patient reported clinical recovery was similar regardless of treatment.

Reviewer #2: This study reported the usage pattern of antibiotics and herbal medicines of a large number of general populations. I have several comments.

1. This survey recruited a large number of respondents, however, it seems that the questions asking to them were too simple. if there are other questions not being presented in tables, please add them.

Thanks for your comment and suggestion. In this survey, we asked three parts of questions: 1). Relating to participants socio-demographic and lifestyle characteristics, 2). Relating to their cough symptoms and other health conditions, and 3) Relating to the treatments they used to alleviate cough and participants' subsequent clinical outcomes. We have provided the questionnaire as S1 File.

We have presented all these data in text, tables and supplementary tables, except that only the top 4 commonly used patent herbal medicines are presented in this manuscript. We will present the other patent herbal medicines used with an exploration of what these remedies contain in a separate paper.

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2. Table 1 - Please describe the age distribution in a more detail.

Thanks for your suggestion. We have added ranges for age distribution, please see page 9.

3. The first shown abbreviations should be written with full-names (abbreviations). Please check in a whole manuscript. And also, it should be written the full-names in each table (e.g. URTI, LRTI).

Thanks for your suggestions. We have checked through the manuscript and added in abbreviations where appropriate.

S1 Table. Various treatments used for acute cough.

Treatment	Overall (n=22,787)	Presumed URITs* (n=20,965)	Presumed LRTIs* (n=1,822)
Antibiotics^{&}	10562 (46.4%)	9828 (46.9%)	734 (40.3 %)
Antibiotics [#]	4935 (21.7%)	4541 (21.7%)	394 (21.6%)
Antibiotics+non-antibiotic medications	1726 (7.6%)	1617 (7.7%)	109 (6.0%)
Antibiotics+CHM	1288 (5.7%)	1213 (5.8%)	75 (4.1%)
Antibiotics+Home remedies	953 (4.2%)	884 (4.2%)	69 (3.8%)
Antibiotics+CHM+Non-antibiotic medications	563 (2.5%)	544 (2.6%)	19 (1.0%)
Antibiotics+Non-antibiotic medications+Home remedies	533 (2.3%)	505 (2.4%)	28 (1.5%)
Antibiotics+CHM+Non-antibiotic medications +Home remedies	311 (1.4%)	300 (1.4%)	11 (0.6%)
Antibiotics+CHM+Home remedies	174 (0.8%)	163 (0.8%)	11 (0.6%)
CHM^{&}	8942 (39.2%)	8311 (39.6%)	631 (34.6%)
CHM [#]	5035 (22.1%)	4631 (22.1%)	404 (22.2%)
Antibiotics+CHM	1288 (5.7%)	1213 (5.8%)	75 (4.1%)
CHM+Non-antibiotic medications	688 (3.0%)	637 (3.0%)	51 (2.8%)
CHM+Home remedies	611 (2.7%)	568 (2.7%)	43 (2.4%)
Antibiotics+CHM+Non-antibiotic medications	563 (2.5%)	544 (2.6%)	19 (1.0%)
Antibiotics+CHM+Non-antibiotic medications +Home remedies	311 (1.4%)	300 (1.4%)	11 (0.6%)
CHM+Non-antibiotic medications +Home remedies	210 (0.9%)	199 (0.9%)	11 (0.6%)
Antibiotics+CHM+Home remedies	174 (0.8%)	163 (0.8%)	11 (0.6%)
Non-antibiotic medications^{&}	6441 (28.3%)	5942 (28.3%)	499 (27.4%)
Non-antibiotic medications [#]	1871 (8.2%)	1662 (7.9%)	209 (11.5%)
Antibiotics+non-antibiotic medications	1726 (7.6%)	1617 (7.7%)	109 (6.0%)
CHM+Non-antibiotic medications	688 (3.0%)	637 (3.0%)	51 (2.8%)
Antibiotics+CHM+Non-antibiotic medications	563 (2.5%)	544 (2.6%)	19 (1.0%)
Antibiotics+Non-antibiotic medications+Home remedies	533 (2.3%)	505 (2.4%)	28 (1.5%)
Non-antibiotic medications+Home remedies	488 (2.1%)	437 (2.1%)	51 (2.8%)
Antibiotics+CHM+Non-antibiotic medications +Home remedies	311 (1.4%)	300 (1.4%)	11 (0.6%)
CHM+Non-antibiotic medications +Home remedies	210 (0.9%)	199 (0.9%)	11 (0.6%)
Home remedies^{&}	4825 (21.2%)	4440 (21.2%)	385 (21.1%)
Home remedies [#]	1480 (6.5%)	1329 (6.3%)	151 (8.3%)
Antibiotics+Home remedies	953 (4.2%)	884 (4.2%)	69 (3.8%)

CHM+Home remedies	611 (2.7%)	568 (2.7%)	43 (2.4%)
Antibiotics+Non-antibiotic medications+Home remedies	533 (2.3%)	505 (2.4%)	28 (1.5%)
Non-antibiotic medications+Home remedies	488 (2.1%)	437 (2.1%)	51 (2.8%)
Antibiotics+CHM+Non-antibiotic medications +Home remedies	311 (1.4%)	300 (1.4%)	11 (0.6%)
CHM+Non-antibiotic medications +Home remedies	210 (0.9%)	199 (0.9%)	11 (0.6%)
Antibiotics+CHM+Home remedies	174 (0.8%)	163 (0.8%)	11 (0.6%)
Others^{&}	280 (1.2%)	243 (1.2%)	37 (2.0%)
Others [#]	105 (0.5%)	95 (0.5%)	10 (0.5%)
No treatment	1641 (7.2%)	1492 (7.1 %)	149 (8.2%)

*Possible LRTIs were defined as presence of "shortness of breath" OR "yellow sputum" OR "green sputum" OR "wheezing" BUT EXCLUDING "sore throat" AND "coryza". Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

&Either alone or in combinations

#Treatment used alon

S2 Table. Factors influencing subsequent use of antibiotics after various interventions.

		After CHM		Total	χ^2	P value	After non-antibiotic medication		Total	χ^2	P value	After CHM		Total	χ^2	P value
		No	Yes				No	Yes				No	Yes			
		Age	18-45				6278	1133				7411	12.317			
	46-64	665	78	743	409	98	507	311	58	369						
	≥65	135	25	160	84	15	99	72	11	83						
	Total	7078	1236	8314	4192	1394	5586	3511	769	4280						
Smoking	Smoker	2750	557	3307	16.950	<0.01	1918	642	2560	0.038	0.845	1214	274	1488	0.309	0.578
	Non-smoker	4328	679	5007			2274	752	3026			2297	495	2792		
	Total	7078	1236	8314			4192	1394	5586			3511	769	4280		
Infection	URTIs	6538	1172	7710	9.385	0.002	3812	1315	5127	16.014	<0.01	3204	721	3925	5.192	0.023
	LRTIs	540	64	604			380	79	459			307	48	355		
	Total	7078	1236	8314			4192	1394	5586			3511	769	4280		
Severity of cough	Mild	1964	211	2175	113.535	<0.01	662	169	831	25.763	<0.01	926	126	1052	38.126	<0.01
	Moderate	3056	494	3550			1711	517	2228			1422	326	1748		
	Severe	2058	531	2589			1819	708	2527			1163	317	1480		
	Total	7078	1236	8314			4192	1394	5586			3511	769	4280		
Health condition	No other disease	5161	733	5894	145.196	<0.01	2029	656	2685	24.309	<0.01	2304	455	2759	17.945	<0.01
	Lung disease	1369	428	1797			1615	615	2230			872	248	1120		
	Other health conditions	548	75	623			548	123	671			335	66	401		
	Total	7078	1236	8314			4192	1394	5586			3511	769	4280		

S3 Table. Cough relief after each type of treatment in various factors as measured by 1-5 Likert scale: median (IQR).

Treatment		Age			Smoker		Infection		Severity of cough			Comorbidity		
		18-45	46-64	≥65	Y	N	URTIs	LRTIs	Mild	Moderate	Severe	N	Lung related	Others
Antibiotics		4 (2)	4 (2)	4 (2)	4 (1)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (1)	4 (2)	4 (1)	4 (2)
Non-antibiotic		4 (2)	4 (1)	4 (1)	4 (1)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (1)	4 (2)	5 (1)	4 (1)
P	Chuan Bei Pi Pa (paste)	4 (1)	4 (2)	4 (2)	5 (1)	4 (2)	4 (1)	4 (1)	4 (2)	4 (2)	5 (1)	4 (2)	5 (1)	4 (1)
C	Gan Mao Ling (granule)	4 (2)	4 (2)	4 (2)	5 (1)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	5 (1)	4 (2)	5 (1)	4 (1)
H	Ke Chuan Shun (pill)	4 (1)	4 (2)	5 (2)	5 (1)	4 (1)	4 (1)	4 (2)	4 (2)	4 (2)	5 (1)	4 (1)	5 (1)	4 (2)
M	Fu Fang Gan Cao (table/liquid)	4 (1)	4 (2)	4 (1.5)	5 (1)	4 (2)	4 (1)	4 (1)	5 (2)	4 (2)	5 (1)	4 (1)	5 (1)	4 (2)
Individualised Chinese herbal formula		4 (1)	4.5 (1)	4 (1)	5 (1.5)	4 (1)	4 (1)	4 (2)	4 (2)	4 (1)	5 (1)	4 (1)	5 (1)	4 (1.5)
Home remedies		4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (2)	4 (1)	4 (2)	4 (1)	4 (2)

S1 File. Questionnaire for survey.

咳嗽治疗用药疗效的回顾性调查研究

本研究旨在调查您/您的家人(单人)近期的咳嗽情况,以及您采取何种措施帮助咳嗽症状。参加这个问卷是完全自愿的,您所填写的个人信息将受到严格保密。如果您决定参加,您仍可在调查结束前自由退出。研究结果将在医学会议、期刊等科学出版物上公布。问卷约5-10分钟即可完成。参与者需大于18岁,如您继续浏览答题则默认您知情同意。(现在红包已经发完,如果您仍愿意帮忙填答问卷,非常感谢!)

研究单位:英国南安普顿大学、北京中医药大学循证医学中心

联系人:费宇彤、胡晓日、夏如玉;联系方式:010-64286757,或扫描微信码



感谢您的参与!

注:请代表您本人或您的家人(单人),回答以下问题

1. 您代表以下哪种身份回答该问卷? [单选题 *]

- 您本人
- 您的配偶
- 您的父母
- 您的子女
- 您的兄弟姐妹
- 其他_____ *

2. 最近一次咳嗽是何时开始的? [单选题 *]

- 2周内
- 2-4周

- 4-6周
- 6周-3月
- 3月之前(请跳至第9卷末尾,提交答卷)

基本信息

这一部分,我们将问您的基本信息及生活习惯。

基本信息

这一部分,我们将问您代表的家人的基本信息及生活习惯。

3. 您的年龄? [填空题] *

4. 您家人的年龄? [填空题] *

5. 您的性别? [单选题] *

男

女

6. 您家人的性别? [单选题] *

男

女

7. 您的教育水平? [单选题] *

学龄前

小学

中学

专科

本科

研究生

其他_____

8. 您家人的教育水平? [单选题] *

- 学龄前
- 小学
- 中学
- 专科
- 本科
- 研究生
- 其他_____

9. 您的职业状态? [单选题] *

- 全职
- 兼职
- 退休
- 失业
- 临时工
- 因为疾病无法工作
- 家庭主妇
- 学生
- 婴幼儿
- 其他_____ *

10. 您家人的职业状态? [单选题] *

- 全职
- 兼职
- 退休
- 失业
- 临时工
- 因为疾病无法工作
- 家庭主妇
- 学生

- 婴幼儿
- 其他 _____ *

11. 您的所在地区? [填空题] *

12. 您家人的所在地区? [填空题] *

13. 您是否有抽烟习惯? [单选题] *

- 是
- 否(请跳至第18题)

14. 您家人是否有抽烟的习惯? [单选题] *

- 是
- 否(请跳至第18题)

15. 从开始抽烟到现在大约多少年? (未到一年的请填写小数) [填空题] *

16. 抽哪种烟? [多选题] *

- 普通烟
- 雪茄
- 烟管
- 电子烟
- 其他

17. 近期平均每天抽多少支烟? [填空题] *

咳嗽信息
请认真填写您所代表的家人所经历过的咳嗽症状

18. 最近这次咳嗽持续了多少天? [单选题] *

- 小于或等于28天

大于28天

19. 最近这次咳嗽是否由感冒引起? [单选题 *]

是

否

20. 最近这次咳嗽症状的严重程度如何? [单选题 *]

非常
轻微

1

2

3

4

5

6

7

8

9

非常
严重

21. 咳嗽现在是否缓解? [单选题 *]

痊愈

有所改善但仍存在症状

没有改善

症状加重

22. 咳嗽大概几天时间缓解? [填空题 *]

23. 咳嗽是否有痰? [单选题 *]

没有

有一点

有很多

24. 痰的颜色? [单选题 *]

清稀

白色

黄色

绿色

红棕色

25. 是否有其他症状 (与本次咳嗽发作相关的)? [多选题 *]

无

- 咽喉痛
- 流鼻涕
- 面部疼痛
- 头痛
- 发热恶寒
- 耳痛
- 胸痛
- 气促
- 喘息
- 疲乏
- 睡眠障碍
- 其他_____*

26. 以上哪种症状最严重? [单选题]*

- 咽喉痛
- 流鼻涕
- 面部疼痛
- 头痛
- 发热恶寒
- 耳痛
- 胸痛
- 气促
- 喘息
- 感觉不佳
- 睡眠障碍
- 其他_____

27. 是否患有其他疾病? [多选题]*

- 无

- 哮喘
- 其他肺部疾病
- 心脏疾病
- 糖尿病
- 中风
- 心理疾病
- 其他_____*

疗法

这一部分，我们将问您您代表的家人用何种疗法或健康手段，来改善咳嗽症状。

28. 请选择您采用以下哪些手段帮助咳嗽症状 [多选题] *

- 中药
- 抗生素(如阿莫西林, 头孢唑肟, 氧氟沙星等)
- 非抗生素类西药(如扑热息痛, 布洛芬, 止咳药等)
- 非药物疗法(如热水, 橙汁, 冰糖雪梨等)
- 其他_____*
- 未采用

29. 在**使用抗生素前**, 请选择您使用过的疗法措施, 并在横线处回答您是在使用该疗法第几天的时候加入抗生素 [多选题] *

- 中药_____*
- 非抗生素类西药(如扑热息痛, 布洛芬, 止咳药等) _____*
- 非药物疗法(如热水, 橙汁, 冰糖雪梨等) _____*
- 其他_____*
- 抗生素是最先采用的疗法 (或抗生素与某种疗法联合作为最先使用疗法)

30. 使用了哪种抗生素以及何种剂型, 请选择: [填空题] *

31. 服用抗生素的频率? [单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

32. 是否按处方要求服用了这些抗生素? [单选题] *

- 全疗程_____ *
请同时填写天数
- 大于或等于1/2疗程_____ *
请同时填写天数
- 小于1/2疗程_____ *
请同时填写天数
- 不清楚

33. 是从哪里获得抗生素的? [多选题] *

- 药店
- 社区医院
- 中医院
- 西医院
- 中西医结合医院
- 诊所
- 家庭自备
- 其他_____ *

34. 为什么使用抗生素? [多选题] *

- 医生推荐
- 药店人员推荐
- 家人朋友推荐
- 自己的经验
- 其他_____ *

35. 抗生素对咳嗽是否有帮助? [单选题] *

- 完全没帮助 2 3 4 非常有帮助

36. 请选择：在咳嗽时服用的非抗生素类西药的名称及其剂型？ [填空题] *

37. 服用以上非抗生素类西药的频率？ [单选题] *

- 一天一次
一天两次
一天三次
一天四次
其他_____ *

38. 非抗生素类西药服用了多少天？ [填空题] *

39. 为什么使用非抗生素西药？ [多选题] *

- 医生推荐
药店人员推荐
家人朋友推荐
自己的经验
其他_____ *

40. 非抗生素类西药对咳嗽是否有帮助？ [单选题] *

- 完全没帮助 2 3 4 非常有帮助

41. 在咳嗽改善时服用的中药的名称？ [多选题] *

- 川贝枇杷膏
感冒灵颗粒
咳喘顺丸
复方甘草(片/口服液)
小儿化痰止咳颗粒
小儿肺热咳喘口服液

- 小儿消积止咳口服液糖浆
- 通宣理肺片/丸口服液
- 蒲地蓝消炎口服液
- 肺力咳合剂
- 莲花青翘胶囊
- 急支糖浆
- 苏黄止咳胶囊
- 疏风解毒胶囊
- 金荞麦片
- 肺宁颗粒
- 百合胶囊
- 十五味龙胆花丸
- 咳特灵胶囊
- 消咳宁片
- 感冒清热(冲剂)胶囊
- 板蓝根颗粒
- 小柴胡颗粒
- 维C银翘片
- 鲜竹沥口服液
- 杏苏止咳颗粒糖浆
- 祛痰灵口服液
- 藿香正气口服液
- 小青龙颗粒合剂
- 橘红(丸/痰咳液)
- 半夏露
- 养阴清肺口服液
- 葛根芩连口服液

- 消咳喘
- 贝沥止咳口服液
- 喜炎平注射液
- 热毒宁注射液
- 痰热清注射液
- 中药方剂汤药
- 其他

42. 请选择您服用川贝枇杷膏的频率 [单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

43. 川贝枇杷膏服用了多少天? [填空题] *

44. 请选择您服用感冒灵颗粒的频率 [单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

45. 感冒灵颗粒服用了多少天? [填空题] *

46.

请选择您服用咳喘顺丸的频率
[单选题] *

- 一天一次

- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

47. 咳喘顺丸颗粒服用了多少天? [填空题] *

48.

请选择您服用复方甘草(片/口服液)的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

49. 复方甘草(片/口服液)服用了多少天? [填空题] *

50.

请选择您服用小儿化痰止咳颗粒的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

51. 小儿化痰止咳颗粒服用了多少天? [填空题] *

52.

请选择您服用小儿肺热咳喘口服液的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

53. 小儿肺热咳喘口服液服用了多少天? [填空题] *

54.

请选择您服用小儿消积止咳(口服液/糖浆)的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

55. 小儿消积止咳口服液糖浆服用了多少天? [填空题] *

56.

请选择您服用通宣理肺(片/丸/口服液)的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

57. 通宣理肺(片/丸/口服液)服用了多少天? [填空题] *

58.

请选择您服用蒲地蓝消炎口服液的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

59. 蒲地蓝消炎口服液服用了多少天? [填空题] *

60.

请选择您服用肺力咳合剂的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

61. 肺力咳合剂服用了多少天? [填空题] *

62.

请选择您服用莲花清瘟胶囊的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

63. 莲花清瘟胶囊服用了多少天? [填空题] *

64.

请选择您服用急支糖浆的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

65. 急支糖浆服用了多少天? [填空题] *

66.

请选择您服用苏黄止咳胶囊的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

67. 苏黄止咳胶囊服用了多少天? [填空题] *

68.

请选择您服用疏风解毒胶囊的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

69. 疏风解毒胶囊服用了多少天? [填空题] *

70.

请选择您服用金荞麦片的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

71. 金荞麦片服用了多少天? [填空题] *

72.

请选择您服用肺宁颗粒的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

73. 肺宁颗粒服用了多少天? [填空题] *

74.

请选择您服用百令胶囊的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

75. 百令胶囊服用了多少天? [填空题] *

76.

请选择您服用五味龙胆花丸的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他 _____ *

77. 五味龙胆花丸服用了多少天? [填空题] *

78.

请选择您服用咳特灵胶囊的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他 _____ *

79. 咳特灵胶囊服用了多少天? [填空题] *

80.

请选择您服用消咳宁片的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他 _____ *

81. 消咳宁片服用了多少天? [填空题] *

82.

请选择您服用感冒清热(冲剂/胶囊)的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____ *

83. 感冒清热(冲剂/胶囊)服用了多少天? [填空题] *

84.

请选择您服用板蓝根颗粒的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____ *

85. 板蓝根颗粒服用了多少天? [填空题] *

86.

请选择您服用小柴胡颗粒的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____ *

87. 小柴胡颗粒服用了多少天? [填空题] *

88.

请选择您服用维 C 银翘片的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

89. 维C银翘片服用了多少天? [填空题] *

90.

请选择您服用鲜竹沥口服液的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

91. 鲜竹沥口服液服用了多少天? [填空题] *

92.

请选择您服用杏苏止咳(颗粒/糖浆)的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

93. 杏苏止咳颗粒(糖粉)服用了多少天? [填空题] *

94.

请选择您用法痰灵口服液的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他 _____ *

95. 祛痰灵口服液服用了多少天? [填空题] *

96.

请选择您服用藿香正气(口服液/胶囊)的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他 _____ *

97. 藿香正气(口服液/胶囊)用了多少天? [填空题] *

98.

请选择您服用小青龙(颗粒/合剂)的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次

其他_____ *

99. 小青龙颗粒合剂用了多少天? [填空题] *

100.

请选择您服用橘红(丸/痰咳液)的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____ *

101. 橘红(丸/痰咳液)用了多少天? [填空题] *

102.

请选择您服用半夏露的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____ *

103. 半夏露用了多少天? [填空题] *

104.

请选择您服用养阴清肺口服液的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____*

105. 养阴清肺口服液用了多少天? [填空题] *

106.

请选择您服用葛根芩连口服液的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____*

107. 葛根芩连口服液用了多少天? [填空题] *

108.

请选择您服用消咳喘的频率

[单选题] *

一天一次

一天两次

一天三次

一天四次

其他_____*

109. 消咳喘用了多少天? [填空题] *

110.

请选择您服用贝沥止咳口服液的频率

[单选题] *

一天一次

一天两次

- 一天三次
- 一天四次
- 其他_____ *

111. 贝沥止咳口服液用了多少天? [填空题] *

112.

请选择您服用喜炎平注射液的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

113. 喜炎平注射液用了多少天? [填空题] *

114.

请选择您服用热毒宁注射液的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

115. 热毒宁注射液用了多少天? [填空题] *

116.

请选择您服用痰热清注射液的频率

[单选题] *

- 一天一次

- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

117. 痰热清注射液用了多少天? [填空题] *

118.

请选择您服用中药方剂的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

119. 中药方剂用了多少天? [填空题] *

120.

请选择您服用其他中药的频率

[单选题] *

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____ *

121. 其他中药用了多少天? [填空题] *

122. 为什么使用中药? [多选题] *

- 医生推荐

- 药店人员推荐
- 家人朋友推荐
- 自己的经验
- 其他_____*

123. 川贝枇杷膏对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

124. 感冒灵颗粒对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

125. 咳喘顺丸对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

126. 复方甘草片/口服液对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

127. 小儿化痰止咳颗粒对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

128. 小儿肺热咳喘口服液对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

129. 小儿消积止咳口服液糖浆对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

130. 通宣理肺片/丸/口服液对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

131. 蒲地蓝消炎口服液对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

132. 肺力咳合剂对咳嗽是否有帮助? [单选题]*

- 完全没帮助
- 2
- 3
- 4
- 非常有帮助

133. 莲花清瘟胶囊对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
134. 急支糖浆对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
135. 苏黄止咳胶囊对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
136. 疏风解毒胶囊对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
137. 金荞麦片对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
138. 肺宁颗粒对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
139. 百合胶囊对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
140. 十五味翳甘丸对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
141. 咳特灵胶囊对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
142. 消咳宁片对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
143. 感冒清热(冲剂)胶囊对咳嗽是否有帮助? [单选题] *
- 完全没帮助 2 3 4 非常有帮助
144. 板蓝根颗粒对咳嗽是否有帮助? [单选题] *

完全没帮助 2 3 4 非常有帮助

145. 小柴胡颗粒对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

146. 维C银翘片对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

147. 鲜竹沥口服液对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

148. 杏苏止咳颗粒(糖粉)对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

149. 祛痰灵口服液对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

150. 藿香正气口服液对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

151. 小青龙颗粒(合剂)对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

152. 橘红丸(痰咳液)对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

153. 半夏露对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

154. 养阴清肺口服液对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

155. 葛根芩连口服液对咳嗽是否有帮助? [单选题 *]

完全没帮助 2 3 4 非常有帮助

156. 消咳喘对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

157. 贝历止咳口服液对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

158. 喜炎平注射液对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

159. 热毒宁注射液对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

160. 痰热清注射液对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

161. 中药方剂对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

162. 其他中药对咳嗽是否有帮助? [单选题 *]

- 完全没帮助 2 3 4 非常有帮助

163. 采用的治疗咳嗽的非药物疗法名称? [多选题 *]

- 热水
 柠檬汁/橙汁
 冰糖雪梨
 猪肺汤
 苦瓜汤
 其他_____*

164. 使用此非药物疗法的频率? [单选题 *]

- 一天一次
 一天两次
 一天三次

- 一天四次
- 其他_____*

165. 非药物疗法服用了多少天? [填空题]*

166. 为什么使用非药物疗法? [多选题]*

- 医生推荐
- 药店人员推荐
- 家人朋友推荐
- 自己的经验
- 其他_____*

167. 非药物疗法对咳嗽是否有帮助? [单选题]*

- 完全没有帮助
- 2
- 3
- 4
- 非常有帮助

168. 如您使用了其他疗法上述所填, 除中药、抗生素及非抗生素类西药、非药物疗法外的其他疗法, 使用此疗法的频率? [单选题]*

- 一天一次
- 一天两次
- 一天三次
- 一天四次
- 其他_____*

169. 如您使用了其他疗法上述所填, 除中药、抗生素及非抗生素类西药、非药物疗法外的其他疗法, 此疗法服用了多少天? [填空题]*

170. 为什么使用其他疗法上述所填, 除中药、抗生素及非抗生素类西药、非药物疗法外的其他疗法? [多选题]*

- 医生推荐
- 药店人员推荐
- 家人朋友推荐

自己的经验

其他 _____ *

171. 如您使用了其他疗法上述所填，除中药、抗生素及非抗生素类西药、非药物疗法外的其他疗法，此疗法对咳嗽是否有帮助？[单选题] *

完全没帮助

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非常有帮助

慢性咳嗽

这一部分，我们将向您代表的填答人有关慢性咳嗽症状及所采取的相应治疗措施。

172. 患何种肺部疾病？[单选题] *

慢性阻塞性肺病 (COPD)

肺炎

慢性支气管炎

肺癌

肺结核

支气管扩张

肺纤维化

不清楚未诊断

其他 _____ *

173. 何时第一次诊断肺部疾病？(写到年月即可，日期如您记不清可随意选择) [填空题] *

174. 慢性咳嗽症状有多长时间？_____ 年 ____ 月 [填空题] *

如不到一年，第一空填0即可

175. 过去12个月中，是否有咳嗽加重，或出现不同颜色痰，或发热气短的症状？[单选题] *

是

否

176. 过去12个月发作次数? [填空题 *]

177. 是否服用了药物去预防发作? [单选题 *]

是

否(请跳至第182题)

178. 如果服用, 服用了何种药物? [多选题 *]

中药, 请提供名称: _____

抗生素, 请提供名称: _____

非抗生素西药, 请提供名称: _____

非药物方法(如热水), 请提供名称: _____

其他 _____

179. 服用这些药物的时间: [单选题 *]

() 天 _____ *

() 周 _____ *

() 月 _____ *

() 年 _____ *

180. 服用这些药物使用这些措施的频率? [单选题 *]

一天一次

一天两次

一天三次

一天四次

其他 _____ *

181. 对预防发作是否有帮助? [单选题 *]

完全没帮助

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非常有帮助

感谢您的参与

182. 是否还有其他想对我们说的? [填空题] *

非常感谢您的参与和配合!

请先点击‘验证’之后再提交, 本次验证不会泄露您的信息, 请您放心!

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7 **Use of antibiotics and other treatments in Chinese adults with acute cough: an online survey**

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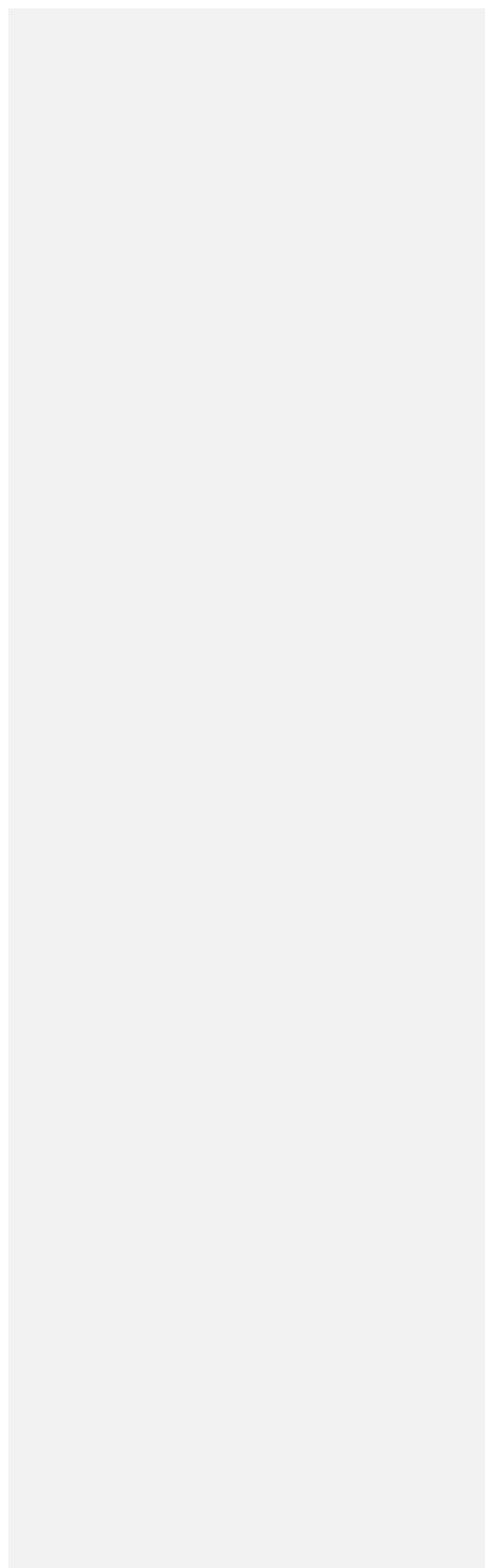
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Abstract

Background: This study aimed to identify use of various treatments and their association with the use of antibiotics and patient reported clinical recovery in Chinese adults with acute cough.

Methods: An online survey recruiting people who had recently experienced cough was conducted. Their sociodemographic, clinical characteristics, treatments received and their perceived changes in symptoms were collected. Factors influencing avoidance of antibiotics and improvement in symptoms were explored.

Results: A total of 22,787 adults with recent acute cough completed the questionnaire, covering all 34 province-level administrative units in China. Most respondents were male (68.0%), young (89.4%, aged 18-45), educated ~~at~~ to university/degree or postgraduate level (44.6%), with a median cough severity of 6/10 on a numerical rating scale. Nearly half of the participants (46.4%) reported using antibiotics, among which 93.1% were for presumed upper respiratory tract infections (URTIs). Pharmacies (48.8%) were the most common source of antibiotics. Fewer patients took antibiotics after taking CHM (14.9%), compared to those who started with home remedies (18.0%), or allopathic non-antibiotic medication (25.0%). Antibiotics, allopathic non-antibiotic medications, CHM and home remedies were all perceived beneficial in relieving cough.

Conclusions: Chinese adult responders report use of a considerable variety of treatments alone or in combination for acute cough. Patient-reported clinical recovery was similar regardless of treatment. There is likely a high proportion of inappropriate use of, ~~overuse of~~ antibiotics for treatment of simple acute cough. As the majority of respondents did not use antibiotics as a first-line, and use of CHM was associated with relief of cough symptoms and reduction in the use of antibiotics, this presents an important opportunity for prudent antibiotic stewardship in China.

Keywords: Antibiotics; acute cough; respiratory tract infection; Chinese herbal medicine; survey

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1. Introduction

Acute ~~r~~Respiratory tract infections (ARTIs) are ~~one of among~~ the most common acute complaints worldwide. They are predominantly of viral aetiology ¹ and antibiotics are of limited benefit in the majority of uncomplicated infections ^{2, 3}. Nevertheless antibiotics are widely used ^{4, 5} and this is associated with higher rates of resistance, especially with longer duration and multiple courses of antibiotics ⁶. Anti-microbial resistance is a complex and evolving global public health threat with potential serious consequences such as increased time spent in hospital, mortality, and economic constraints ⁷⁻⁹.

There has been a rapid increase in antibiotic consumption over the past decades. Globally, there was a 90.9% increase in per-capita consumption of Watch antibiotics (applied only to a limited group of well-defined syndromes) from 3.3 to 6.3 defined daily doses (DDDs) per 1000 inhabitants per day [DIDs] and an increase of 26.2% from 8.4 to 10.6 DIDs in Access antibiotics (first or second line treatments for common infections) between 2000 and 2015 ¹⁰. Three countries, namely India (6.3 billion DDDs), China (3.8 billion DDDs), and the USA (2.9 billion DDDs) ~~are with consume~~ the highest volume of antibiotics ~~consumption~~¹⁰. Since the 2009 health system reform, China has paid considerable attention to improving the use of antibiotics through strengthening national antimicrobial stewardship ¹¹. Following this, in 2011, a national campaign for the rational use of antibiotics was launched by the Ministry of Health ¹², which enacted the implementation of the most stringent decree in 2012 including comprehensive regulations on selection, procurement, prescription, and use of antibiotics ^{11, 13, 14}. Data released by the National Health Commission of the People's Republic of China suggested a decrease in the proportion of inpatients receiving antibiotics from 59.4% in 2011 to 36.4% in 2018; and in outpatients from 17.2% in 2011 to 8.9% in 2018 ¹⁵. This decrease was ~~repeatedly~~ repeatedly reported at tertiary hospitals ^{16, 17}, for both inpatients and outpatients, but less progress was observed at primary care facilities and county hospitals ¹¹. Data from Shan Dong province suggested a total of all healthcare setting antibiotic consumption increased from 16.07 DID in 2012, peaked at 17.44 DID in 2015, and decreased to 11.35 DID in 2017 with a 34.90% reduction ¹⁸.

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7 Strategies to limit unnecessary antibiotic use may include better infection prevention (e.g. hand
8 washing interventions)¹⁹, better targeting (development of clinical scores and near patient tests)²⁰,
9 and the use of ~~the~~ delayed or ‘just in case prescription’². Using a ‘just in case’ prescription appears to
10 reduce infective complications and to reduce rates of re-consultation²¹. Symptomatic relief is
11 commonly advised for self-limiting cough, focusing on reducing the effects of the infection, for
12 example with throat lozenges, decongestants, anti-pyretics (paracetamol / ibuprofen), and health
13 advice such as taking plenty of fluids and bed rest. In China, traditional herbal medicines have been
14 used for thousands of years, both to prevent and to treat RTIs.
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21 This study adopted the design from a series of successful surveys²²⁻²⁶, aiming to identify the patterns
22 of use of ~~antibiotics, allopathic non-antibiotic medications, Chinese herbal medicine, and home~~
23 ~~different treatments~~ remedies for acute cough in the adult Chinese population; and ~~to explore factors~~
24 ~~that may influence their association with~~ clinical outcomes ~~in different treatment options~~.
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29 30 **2. Methods**

31 Findings of this survey are reported following the checklist for reporting results of internet E-surveys
32 (CHERRIES) checklist²⁷.
33

34 35 **2.1 Study participants**

36 We included adult patients (≥18 years old) who (1) were experiencing or had experienced acute cough
37 (<28 days) in the last 3 months, irrespective of having chronic underlying lung diseases such as COPD
38 or asthma or not; (2) were able to read and understand Chinese, and to participate through an online
39 survey; (3) were willing to disclose information on all treatments they took for the last episode of
40 cough and their clinical outcomes. Implied consent was obtained. There was no restriction on gender
41 for this study. Participants could also answer the questionnaire on behalf of a family member.
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47 48 **2.2. Questionnaire**

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7 The survey was piloted with five Chinese-speaking lay persons, and amended according to their
8 feedback, before opening the survey to the public. All survey materials were translated and back
9 translated by two team members [RYX and XYH]²⁸.

10
11
12 ~~The online cough survey takes 5-10 minutes to complete. It contains three parts of questions:~~
13 ~~socio-demographic and lifestyle characteristics (15 questions), cough symptoms and other health~~
14 ~~conditions (10 questions), and treatments to alleviate cough. and p~~Participants' subsequent clinical
15 ~~outcomes were collected and analysed to explore potential correlations between them with the~~
16 ~~treatments taken.~~

17
18
19 ~~The survey contained questions on participants' socio-demographic characteristics, basic lifestyle~~
20 ~~information on smoking, and the cough and other health conditions. Treatments to alleviate cough and~~
21 ~~participants' subsequent clinical outcomes were collected and analysed to explore potential~~
22 ~~correlations between them.~~

23
24
25 For participants' convenience, a list of the most commonly used antibiotics, allopathic non-antibiotic
26 medications (e.g. NSAIDs), patent Chinese Herbal Medicines (PCHMs), and the most frequent home
27 remedies (including special foods, e.g. pear soup) were provided as drop-down lists. One case of
28 cough was collected from each survey response. The full questionnaire is available in S1 File.

29 30 31 32 33 34 35 36 37 **2.3 Method of recruitment**

38
39 ~~In order to approach a large representative sample, p~~Potential participants were recruited through the
40 ~~largest~~ Chinese social media platform WeChat, ~~with a~~ QR code or a link to the online survey
41 developed using Wen Juan Xing survey (<https://www.wjx.cn>) ~~was~~ ~~circulated with an invite to~~
42 ~~participate. The invites were circulated~~ through a snowballing approach starting with researchers'
43 WeChat contacts and WeChat moments, discussion groups e.g. university student groups, medical
44 associations groups, and general groups. ~~We endeavoured to approach the general population from~~
45 ~~different regions in China and have circuited~~circulated the invites to specific general groups. The
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7 participant information sheet appeared at the top as part of the survey and ~~implied consent was~~
8 ~~obtained~~ consent was implied through survey participation.
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11 12 13 **2.4 Data collection and management**

14
15 All survey data were collected and managed by researchers familiar with the use of online
16 questionnaires, on taking consent, confidentiality and data management. No identifiable data were
17 collected therefore participants could not be ~~single-identified~~ from the information collected. Each
18 record was linked with a unique ID number. Data were stored on a password-protected laptop in a
19 secure location, with data backups being made on a regular basis.
20
21
22

23 24 **2.5 Data analysis**

25
26 Participants' basic characteristics, cough and other health conditions, and the treatment used for their
27 cough were analysed descriptively. For descriptive analyses, we grouped respondents into those with
28 possible LRTIs, which were defined as: presence of at least one of "shortness of breath ~~or~~ ~~OR~~
29 "yellow sputum ~~or~~ ~~OR~~ "green sputum" ~~OR~~ " ~~or~~ wheezing, " ~~BUT EXCLUDING~~ but excluding
30 "sore throat ~~and~~ ~~AND~~ "coryza". Patients whose symptoms did not fit these criteria were presumed
31 to have had URTIs. Avoidance of antibiotics was assessed as the number and proportion of
32 participants not taking subsequent antibiotics after various treatments. Relief of symptoms was
33 ~~measured self-reported on~~ by a 0-5 Likert scale. There is no precise measure for appropriate use of
34 antibiotics following self-report of acute cough. However, European estimates for appropriate use
35 following consultation with a physician are substantially lower than those reported here. European
36 standards suggest 0-30% for acute bronchitis ²⁹, whereas more recent guidelines and expert elicitation
37 put the figure at 10%, interquartile range (IQR) (6%-16%) in patients with acute cough without
38 comorbidities ³⁰.
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49 A Chi-square test of independence was performed to examine how 5 factors, namely age, smoking,
50 presumed upper or lower RTIs, severity of cough and comorbidities, might influence outcomes on
51 subsequent antibiotic usage and relief in cough. A significance level of 0.05 with 95% CI level was
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7 utilised. Percentages were presented throughout the analysis with one decimal place. Any means,
8
9 medians and ranges/interquartile ranges were given to one decimal place. For standard deviations, two
10 decimal places were presented.

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12
13 The data analysis for this study was generated using Microsoft Excel (2016) and IBM SPSS Statistics
14 for Windows, Version 23.0. Armonk, NY: IBM Corp.

15 16 17 **2.6 Sample size calculation**

18
19 Considering ~~it is likely~~ that 70% of people ~~who are~~ surveyed would have been likely to have used
20 antibiotics ⁴, ~~then to estimate this~~ with a 95% CI around a 2% margin of error, we ~~would estimated~~
21 ~~that need~~ 2,017 participants would be required for this survey. However, we planned to continue
22
23 recruitment until February 2019 as larger numbers would be needed for the secondary outcome
24
25 measures.

Commented [LL1]: Could you clarify what 'this' is?

26 27 28 29 **2.7 Ethical considerations**

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31 Ethical approval was sought from the University of Southampton ethics committee (ERGO 31602)
32 and the Beijing University of Chinese Medicine ethics committee (2018BZHLYL0101). Participants'
33 implied consent was obtained through the online survey. Personal information from this study was
34 confidential. We guaranteed the anonymity of each participant, with any personally identifiable
35 information in questionnaires being removed. All data were handled in China and only aggregated
36 data were sent to the UK. All completed surveys were collected through online social media and
37 online surveys, with data stored in a password protected laptop. A total value of £2000 (approximately
38 16060 RMB) were circulated as incentives with a random amount of money (around 1 to 2 RMB)
39 allocated to ~~for~~ participants² upon completion of the questionnaires. ~~time taken~~
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47 48 **3. Results**

49 50 **3.1 Response rate**

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7 The online survey was circulated to researchers' WeChat contacts for cascading, which generated
8 81,169 visits between 25th January 2019 and 11th February 2019 (Fig 1). Of those who opened the
9 survey, 26,994 gave consent and completed the online questionnaire, among which 1411 provided
10 invalid data and were removed.
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14 Among the 26,740/81,169 (33.0%) valid responses, 22,787 were adult participants (or their family
15 members) with acute cough and are included in this analysis. The majority (78.5%) of the responses
16 were collected from patients themselves. Over half (52.1%) had experienced their most recent episode
17 of cough within 2 weeks and 31.3% between 2 and 4 weeks when they were completing this online
18 survey.
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24 The responses collected were across all 34 province-level regions in China, mostly from North and
25 East China, with Hebei province at the top (16.6%), followed by Shanxi (16.0%), Beijing (15.4%), and
26 Tianjin (9.2%) (Fig 2). There were 29 (0.1%) responses from overseas.
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29 **3.2 Sociodemographic, lifestyle and health condition characteristics**

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31 There were 2.1 times more male respondents than females. Most (89.4%) were young participants
32 between 18-45 years old and had a university/degree or above (44.6%). ~~Near-Almost~~ half (49.6%)
33 were employed full-time, and 40.0% were smokers (Table 1). The vast majority (92.0%) reported
34 symptoms consistent with ~~an upper respiratory tract infection (URTI)~~ a URTI.
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40 Table 1. Characteristics of respondents
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Characteristic	Overall (n=22787)	Presumed URTIs* (n=20965)	Presumed LRTIs*(n=1822)
Sex: n (%)			
Male	15502 (68.0%)	14217(67.8%)	1285 (70.5%)
Female	7285 (32.0%)	6748 (32.2%)	537 (29.5%)
Age (years): Median (IQR, range)	28 (13, 18 to 120)	28 (13, 18 to 120)	28 (17, 18 to 99)
Educational level: n (%)			
Preschool	591(2.6%)	550 (2.6%)	41 (2.3%)
Primary school	1028 (4.5%)	926 (4.4%)	102 (5.6%)
Secondary school	3880 (17.0%)	3527 (16.8%)	353 (19.4%)
College/ Diploma#	6754 (29.6%)	6227 (29.7%)	527 (28.9%)
University/ Degree	8029 (35.2%)	7445 (35.5%)	584 (32.1%)
Postgraduate	2149 (9.4%)	1974 (9.4%)	175 (9.6%)
Other	356 (1.6%)	316 (1.5%)	40 (2.2%)
Occupational status: n (%)			
Employed full time	11292 (49.6%)	10544 (50.3%)	748 (41.1%)
Employed part time	3467 (15.2%)	3196 (15.2%)	271 (14.9%)
Retired	1317 (5.8%)	1166 (5.1%)	151 (8.3%)
Unemployed	740 (3.2%)	649 (3.1%)	91 (5.0%)
Casual worker	1050 (4.6%)	922 (4.4%)	128 (7.0%)
Not working due to ill health	436 (1.9%)	377 (1.8%)	59 (3.2%)
Homemaker	917 (4.0%)	843 (4.0%)	74 (4.1%)
Student	3275 (14.4%)	3012 (14.4%)	263 (14.4%)
Infants or young children	99 (0.4%)	85 (0.4%)	14 (0.8%)
Others	194-293 (1.30-9%)	171-256 (0.81-2%)	37-23 (2.1-3%)
Smoker: n (%)	9118 (40.0%)	8300 (39.6%)	818 (44.9%)
Comorbidities: n (%)			
No underlying condition	14545 (63.8%)	13471 (64.3%)	1074 (58.9%)
Asthma or other chest diseases	6032 (26.5%)	5545 (26.4%)	487 (26.7%)
All other underlying conditions	2210 (9.7%)	1949 (9.3%)	261 (14.3%)
Severity of cough: Median (IQR)	6 (3)	6 (3)	6 (3)

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IQR: interquartile range, SD: standard deviation

URTIs: upper respiratory tract infections

LRTIs: lower respiratory tract infections

* Possible LRTIs were defined as presence of at least one of "shortness of breath" or "yellow/white sputum" or "green sputum" or "wheezing, but excluding" BUT EXCLUDING "sore throat and" AND "coryza". Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

Refers to junior college education/ professional training [专科], including technical secondary school [中专] and junior college [大专].

The cough had resolved in 34.9% of respondents when they were completing the survey. The median severity of cough was 6 (IQR 3) on a 0-10 [numerical rating scale \(NRS\)](#) (Table 1). Most participants (65.7%) had a productive cough; the sputum colour reported most was yellow (40.3%), white (33.8%), and clear (19.3%). One fifth of participants reported only a cough (21.6%), whereas others

experienced a range of symptoms, including sore/itchy throat (48.6%), runny nose (39.8%), headache (19.3%), and facial pain (13.4%) (Fig 23).

More than half (63.8%) of the participants had no underlying medical condition. Among the rest, asthma (14.9%), other chest conditions (14.9%), and heart disease (11.1%) were most frequently reported.

3.3 Use of Treatments for acute cough

Although 46.4% of adult participants with acute cough used antibiotics, only 12.7% (2886/22787) took antibiotics alone or together with another treatment as their first treatment. 39.2% used individualised or patent CHM, 28.3% and 21.2% used allopathic non-antibiotic medications and home remedies respectively; these figures include both treatments used on their own, and those used as part of a combination (Table 2). Only 7.2% of the respondents did not use any treatment. The most common combinations were antibiotics with allopathic non-antibiotic medications (7.6%), antibiotics combined with CHM (5.7%), and antibiotics combined with home remedies (4.2%) (S1 Table). Of those 19901 (87.3%) who did not initially take antibiotics, 8314 (41.8%) took CHM, 5586 (28.1%) took allopathic non-antibiotic Western medicines and 4280 (21.5%) used home remedies (Table 3).

Table 2. Various treatments used for acute cough: interventions used alone or in combination.

Treatment	Overall (n=22,787)	Presumed URTIs* (n=20,965)	Presumed LRTIs* (n=1,822)
Antibiotics	10562 (46.4%)	9828 (46.9%)	734 (40.3%)
CHM	8942 (39.2%)	8311 (39.6%)	631 (34.6%)
Allopathic non-antibiotic medications	6441 (28.3%)	5942 (28.3%)	499 (27.4%)
Home remedies	4825 (21.2%)	4440 (21.2%)	385 (21.1%)
Others	280 (1.2%)	243 (1.2%)	37 (2.0%)
No treatment	1641 (7.2%)	1492 (7.1%)	149 (8.2%)

* Possible LRTIs were defined as presence of at least one of “shortness of breath” OR “yellow sputum” OR “green sputum” OR “wheezing” BUT EXCLUDING “sore throat” AND “coryza”. Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

CHM: Chinese herbal medicine

URTIs: upper respiratory tract infections

LRTIs: lower respiratory tract infections

3.3.14 Patterns of the use of antibiotics

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7 Nearly half of the participants (46.4%) had used antibiotics, among which 93.1% (9828/10562) were
8 for presumed URTIs (Table 2). The proportions reporting antibiotic use were similar for presumed
9 LRTIs (40.3%) to those with presumed URTIs (46.9%). The most commonly used antibiotics were
10 Amoxicillin (32.5%), followed by Cefprozime (13.0%), Ampicillin (10.8%), Cefoxitin (7.6%), and
11 Cefuroxime (7.6%) (Fig 34). Under half (44.8%) of the antibiotic users used the full course of
12 antibiotics, others used more than half of the course (19.3%), less than half of the course (13.3%) or it
13 was unclear (22.5%) whether they took the full course of antibiotics.
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20 Of the participants who received antibiotics, almost half received them from a pharmacy (48.8%), and
21 a third from a public community health centre (33.1%). In our sample, more antibiotic prescriptions
22 came from TCM hospitals (28.0%) than from Western (22.1%) or integrative medicine hospitals
23 (17.6%). Respondents used antibiotics on the basis of various sources of advice (and sometimes more
24 than one), including health professionals such as doctors (52.4%), drug store staff (46.1%), family and
25 friends (29.6%) or their own experience (19.4%).
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30 **3.3.2.5 Patterns of the use of allopathic non-antibiotic medications**

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32 Of the 6441/22787 (28.3%) participants who used allopathic non-antibiotic medications to help with
33 their acute cough, non-steroidal anti-inflammatory drugs (NSAIDs, 2023, 31.4%) such as ibuprofen,
34 naproxen, and diclofenac were the most commonly used, followed by paracetamol (1312, 20.4%),
35 cough medicine (834, 12.9%) such as codeine, noscapine, pentoxyverine, and expectorants (232,
36 3.6%) such as methoxyphenamine, ambroxol and bromhexine hydrochloride.
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40 **3.3.3 Patterns of the use of Chinese herbal medicine (CHM)**

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42 Nearly half 8942/22787 (39.2%) of participants used CHM to help with their acute cough, including
43 individualised CHM (372, 4.2%) and patent CHM (8786, 98.3%). The top 8 patent CHM products
44 were each taken by more than 500 respondents. Chuan Bei Pi Pa Gao (CBPPG) was the most
45 frequently used (5019, 56.1% of all participants), followed by Gan Mao Ling granule (3316, 37.1%),
46 Ke Chuan Shun pill (1764, 19.7%), and Fu Fang Gan Cao (tablet/liquid) (1643, 18.4%).
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51 **3.3.4 Patterns of the use of home remedies**

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About one-fifth of participants used home remedies (n=4825, 21.2% of total) including boiled pear soup (2720, 56.4%), hot water (2661, 55.2%), lemon/orange juice (1729, 35.8%), pig lung soup (964, 20.0%), bitter melon soup (719, 14.9%) and others (110, 2.3%).

3.46 Treatment association with clinical recovery

3.46.1 Avoidance of antibiotics

Subsequent use of antibiotics was lower in those who initially took CHM, compared to those who started with home remedies or allopathic non-antibiotic medications (p<0.05). Other initial treatments included cupping, exercise, physically cooling down, heat therapy, hot bath, nasal wash with saline, ginger ~~water~~ tea (257, 1.3%).

Commented [LL2]: Do you mean ginger tea?

Table 3. Subsequent use of antibiotics after each type of treatment.

Initial Treatment	Overall* (n=7676)	Presumed URTIs# (n=7150)	Presumed LRTIs# (n=526)
Allopathic non-antibiotic medication	1394/5586 (25.0%)	1315/5127 (25.6%)	79/459 (17.2%)
Home remedies	769/4280 (18.0%)	721/3925 (18.4%)	48/355 (13.5%)
Chinese herbal medicine	1236/8314 (14.9%)	1172/7710 (15.2%)	64/604 (10.6%)
Other	19/257 (7.4%)	16/226 (7.1%)	3/31 (9.7%)

* Excluded those who started with antibiotics and those who had other treatment and antibiotics as the first treatment

URTIs: upper respiratory tract infections

LRTIs: lower respiratory tract infections

Possible LRTIs were defined as presence of at least one of “shortness of breath” OR “yellow sputum” OR “green sputum” OR “wheezing” BUT EXCLUDING “sore throat” AND “coryza”. Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

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A Chi-square test of independence was performed to examine the relation between various factors and subsequent use of antibiotics (S2 Table). Participants who smoked ~~ds~~ ($\chi^2 = 16.950, P < 0.01$), were aged ≥ 65 ($\chi^2 = 12.317, P = 0.002$), with severe cough ($\chi^2 = 113.535, P < 0.01$), with presumed URTIs ($\chi^2 = 9.385, P = 0.002$), and underlying lung conditions ($\chi^2 = 145.196, P < 0.01$) were the most likely to take antibiotics after taking CHM at 16.8%, 15.6%, 20.5%, 15.2%, and 23.8% respectively. Those aged 18-45 ($\chi^2 = 15.216, P < 0.01$), with severe cough ($\chi^2 = 25.763, P < 0.01$), URTIs ($\chi^2 = 16.014, P < 0.01$), and underlying lung conditions ($\chi^2 = 24.309, P < 0.01$) were the most likely to take antibiotics

after taking allopathic non-antibiotic medications; while only those with severe cough ($\chi^2 = 38.126$, $P < 0.01$), URTIs ($\chi^2 = 5.192$, $P = 0.023$), and underlying lung conditions ($\chi^2 = 17.945$, $P < 0.01$) were the most likely to take antibiotics after taking home remedies.

3.4.6.2 Relief of cough

Antibiotics, allopathic non-antibiotic medications, CHM and home remedies were considered helpful in relieving cough symptoms, with the same median of 4, with a IQR at 1 or 2 on a 1-5 Likert self-rating scale (5 represents very helpful) (Table 4).

Table 4. Cough relief after each type of treatment as measured by 1-5 Likert scale.

Treatment	Median	IQR (range)
Antibiotics	4	2 (1 to 5)
Allopathic non-antibiotic medications	4	2 (1 to 5)
Patent Chinese herbal medicines (PCHM)		
Chuan Bei Pi Pa paste	4	1 (1 to 5)
Gan Mao Ling granule	4	2 (1 to 5)
Ke Chuan Shun pill	4	1 (1 to 5)
Fu Fang Gan Cao (table/liquid)	4	1 (1 to 5)
Individualised Chinese herbal formula	4	1 (1 to 5)
Home remedies	4	2 (1 to 5)

IQR: interquartile range

Relief of cough, as assessed by Likert scale, did not differ largely between participants with varying ages, smokers or non-smokers, with presumed upper or lower RTIs, with varying severity of cough, with or without any comorbidities (S3 Table).

4. Discussion

Summary of findings and comparison with the literature

This online survey explored treatment-seeking behaviour for acute cough in Chinese adults. Although a series of antimicrobial stewardship guidelines and policies have been released in China since 2009¹¹, we found that there is likely high proportion of inappropriate use of antibiotics for the treatment of simple acute cough~~inappropriate use of antibiotics is still widespread~~, even in well-educated young adults. Antibiotics were taken by nearly half of our respondents with acute cough, of

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whom over 90% possibly had URTIs. These findings are ~~largely in line~~consistent with previous ~~study~~
~~research~~ on overuse of antibiotics by university students in China ⁴.

Both doctors and staff in pharmacies played an important role in recommending the use of antibiotics. A considerable number of patients obtained antibiotics from easily accessible pharmacies which are often less strictly regulated. Despite being illegal, it is easy to obtain antibiotics without a prescription in retail pharmacies or from online sources in China ³¹. Pharmaceutical companies tend to offer incentives for the prescribing of more expensive broad-spectrum antibiotics ³². These may be major contributors to antimicrobial resistance.

In our sample, participants reported similar levels of improvement regardless of which treatment they took, although most ~~were having~~presented with symptoms consistent with uncomplicated URTIs, the vast majority of which were most probably viral and self-limiting ^{2,3}. People used various alternatives to antibiotics to help with their acute cough. CHM was the most popular initial treatment other than antibiotics, and its initial use was associated with lower subsequent usage of antibiotics, compared to respondents who initially started with home remedies or allopathic non-antibiotic medicines. PCHMs are commonly used for uncomplicated ARTIs and most of them are readily available for patients to buy themselves over the counter, online, or in pharmacies without a prescription. In 2015, over 60% of the 1231.8 billion RMB market share in China for respiratory conditions was spent on PCHM ³³. The majority of allopathic non-antibiotic medications taken were NSAIDs. While patients with chest infections perceived benefits in symptom relief, evidence suggests they may be associated with worse prognosis ³⁴.

Strengths and limitations

Our approach enabled us to recruit a large sample within a comparably short period. We managed to collect responses from adults with acute cough across all regions of China, which increased our ability to understand the extent of antibiotic overuse ~~and misuse~~ and the alternatives to help alleviate cough and reduce the use of antibiotics. Although there is clearly an overlap, for the purposes of analysis we divided the respiratory syndromes into those consistent with LRTIs and URTIs.

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7 Our sample may not be representative of the wider Chinese population. ~~Participants were recruited~~
8 ~~through social media, and so the majority of respondents may share similarities with the researchers.~~
9 There was potentially sampling bias as some participants recruited through researchers' networks with
10 a Chinese medicine background may be systematically more likely to be selected. This may result in
11 favoured opinion bias towards the use of CHM. Those electing to use CHM first line may also have
12 been less likely to use antibiotics regardless of impact on symptoms. Among our sample, 40% were
13 smokers and 27% reported having asthma or other chest diseases. These may not be a true reflection of
14 the population as respondents were more likely to be young and actively using the internet. However,
15 they were encouraged to cascade the survey, in order to include as many people from as many
16 backgrounds as possible. A disadvantage of this method is that it is impossible to know how many
17 people received the invitation, so the presumed response rate was calculated using the number of
18 people who clicked on the survey link.

19 Although self-reported data may not accurately reflect participants' disease characteristics, lifestyle
20 characteristics or actual treatment behaviours, 83.9% of our respondents were answering questions
21 about cough within a month, therefore, the recall bias should be low. We did not capture the exact
22 order of treatments received, but recorded key information on which treatments participants took
23 before the antibiotics. The outcomes assessed were symptom relief and subsequent use of antibiotics.
24 No data on hospital admission or adverse events were collected. In such self-reported data, we are
25 unable to address residual confounding and hence more advanced statistical analysis (e.g. regression)
26 would be hard to interpret and the associations described should be treated with caution. A cross
27 sectional survey can only report on associations and causality cannot be implied.

28 **Priorities for research and clinical implications**

29 The findings are important to inform public health interventions on appropriate treatment-seeking.
30 There is a need to regulate pharmacy practices of prescribing and selling antibiotics. In-depth
31 qualitative research could help to understand the reasons for ~~the~~ inappropriate antibiotic use, especially

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in young patients with URTIs who ~~clearly typically~~ do not need them. [Complementary and alternative medicine \(CAM\)](#) treatments appeared to be acceptable to people from many different settings as a possible alternative to antibiotics, consistent with research in other countries.⁴³⁵ Future research could explore expectations of patients with cough in China, the acceptability and experiences of taking CHM, and the reasons behind decision making. These could then inform the development of future antibiotic stewardship interventions, potentially encouraging the use of CHM as an alternative to antibiotics.

Future research is needed to improve the evidence base on which specific herbal medicines should be recommended as alternatives to antibiotics. Further analyses are needed to identify the most promising PTCMs. Severity of cough, upper or lower RTIs, and underlying lung conditions may be considered as potential factors influencing how well allopathic non-antibiotic medications, CHM, or home remedies may help in reducing the use of antibiotics.

Conclusions

~~Inappropriate use of antibiotics for common respiratory infections is a serious concern in China.~~
[There is likely a high proportion of inappropriate use of antibiotics for the treatment of simple acute cough.](#) even in well-educated young adults. Many obtained antibiotics from easily accessible pharmacies which are less strictly regulated. Antibiotics, CHM, allopathic non-antibiotic medications, and home remedies were often used with similar perceived beneficial in relieving cough regardless of treatment. CHM was the most widely used alternative and has a potential role in relieving cough symptoms and reducing the use of antibiotics. Future research is needed to evaluate the effectiveness of individualised and commonly used CHM for acute cough.

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Author contributions

Conceptualization: XYH, MW, RYX, TYF; Methodology: All; Formal analysis: RYX; Investigation: RYX, TYF, XYH, ML; Resources: YTF, XYH, RYX, JPL, LZW; Data curation: RYX, YTF; Writing: XYH; Review & Editing: All; Visualization: XYH; Supervision: MW, YTF; Project administration: RYX; Funding acquisition: XYH, MW. All authors have read and agreed to the published version of the manuscript. There is no professional writer involved.

Conflict of interest

The authors declare no conflict of interest. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results

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Data availability

The data that support the findings of this study are available within the article and its supplementary material, or are available from the corresponding author upon reasonable request.

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Figure legends

Fig. 1. Recruitment flow diagram.

Fig. 2. ~~Other symptoms experienced relating to this episode of cough.~~ ~~Geographic distribution of respondents from China.~~

Fig. 3. ~~Antibiotics used by adults with acute cough.~~ ~~Other symptoms experienced relating to this episode of cough.~~

Fig. 4. ~~Antibiotics used by adults with acute cough.~~

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Use of antibiotics and other treatments in Chinese adults with acute cough: an online survey

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Abstract

1
2 Background: This study aimed to identify use of various treatments and their association with the use
3
4 of antibiotics and patient reported clinical recovery in Chinese adults with acute cough.
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6 Methods: An online survey recruiting people who had recently experienced cough was conducted.
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8 Their sociodemographic, clinical characteristics, treatments received and their perceived changes in
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10 symptoms were collected. Factors influencing avoidance of antibiotics and improvement in symptoms
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12 were explored.
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14 Results: A total of 22,787 adults with recent acute cough completed the questionnaire, covering all 34
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16 province-level administrative units in China. Most respondents were male (68.0%), young (89.4%,
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18 aged 18-45), educated to university/degree or postgraduate level (44.6%), with a median cough
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20 severity of 6/10 on a numerical rating scale. Nearly half of the participants (46.4%) reported using
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22 antibiotics, among which 93.1% were for presumed upper respiratory tract infections (URTIs).
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24 Pharmacies (48.8%) were the most common source of antibiotics. Fewer patients took antibiotics after
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26 taking CHM (14.9%), compared to those who started with home remedies (18.0%), or allopathic non-
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28 antibiotic medication (25.0%). Antibiotics, allopathic non-antibiotic medications, CHM and home
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30 remedies were all perceived beneficial in relieving cough.
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33 Conclusions: Chinese adult responders report use of a considerable variety of treatments alone or in
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35 combination for acute cough. Patient-reported clinical recovery was similar regardless of treatment.
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37 There is likely a high proportion of inappropriate use of antibiotics for treatment of simple acute cough.
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39 As the majority of respondents did not use antibiotics as a first-line, and use of CHM was associated
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41 with relief of cough symptoms and reduction in the use of antibiotics, this presents an important
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43 opportunity for prudent antibiotic stewardship in China.
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48 Keywords: Antibiotics; acute cough; respiratory tract infection; Chinese herbal medicine; survey
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1. Introduction

1 Acute respiratory tract infections (ARTIs) are among the most common acute complaints worldwide.
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3 They are predominantly of viral aetiology ¹ and antibiotics are of limited benefit in the majority of
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5 uncomplicated infections ^{2, 3}. Nevertheless antibiotics are widely used ^{4, 5} and this is associated with
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7 higher rates of resistance, especially with longer duration and multiple courses of antibiotics ⁶. Anti-
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9 microbial resistance is a complex and evolving global public health threat with potential serious
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11 consequences such as increased time spent in hospital, mortality, and economic constraints ⁷⁻⁹.
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16 There has been a rapid increase in antibiotic consumption over the past decades. Globally, there was a
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18 90.9% increase in per-capita consumption of Watch antibiotics (applied only to a limited group of
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20 well-defined syndromes) from 3.3 to 6.3 defined daily doses (DDDs) per 1000 inhabitants per day
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22 [DIDs] and an increase of 26.2% from 8.4 to 10.6 DIDs in Access antibiotics (first or second line
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24 treatments for common infections) between 2000 and 2015 ¹⁰. Three countries, namely India (6.3
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26 billion DDDs), China (3.8 billion DDDs), and the USA (2.9 billion DDDs) consume the highest
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28 volume of antibiotics ¹⁰. Since the 2009 health system reform, China has paid considerable attention to
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30 improving the use of antibiotics through strengthening national antimicrobial stewardship ¹¹.
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32 Following this, in 2011, a national campaign for the rational use of antibiotics was launched by the
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34 Ministry of Health ¹², which enacted the implementation of the most stringent decree in 2012
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36 including comprehensive regulations on selection, procurement, prescription, and use of antibiotics ¹¹.
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38 ^{13, 14}. Data released by the National Health Commission of the People's Republic of China suggested a
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40 decrease in the proportion of inpatients receiving antibiotics from 59.4% in 2011 to 36.4% in 2018;
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42 and in outpatients from 17.2% in 2011 to 8.9% in 2018 ¹⁵. This decrease was repeatedly reported at
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44 tertiary hospitals ^{16, 17}, for both inpatients and outpatients, but less progress was observed at primary
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46 care facilities and county hospitals ¹¹. Data from Shan Dong province suggested a total of all
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48 healthcare setting antibiotic consumption increased from 16.07 DID in 2012, peaked at 17.44 DID in
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50 2015, and decreased to 11.35 DID in 2017 with a 34.9% reduction ¹⁸.
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57 Strategies to limit unnecessary antibiotic use may include better infection prevention (e.g. hand
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59 washing interventions) ¹⁹, better targeting (development of clinical scores and near patient tests) ²⁰, and
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1 the use of delayed or ‘just in case prescription’². Using a ‘just in case’ prescription appears to reduce
2 infective complications and to reduce rates of re-consultation²¹. Symptomatic relief is commonly
3 advised for self-limiting cough, focusing on reducing the effects of the infection, for example with
4 throat lozenges, decongestants, anti-pyretics (paracetamol / ibuprofen), and health advice such as
5 taking plenty of fluids and bed rest. In China, traditional herbal medicines have been used for
6 thousands of years, both to prevent and to treat RTIs.
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13 This study adopted the design from a series of successful surveys²²⁻²⁶, aiming to identify the patterns
14 of use of different treatments for acute cough in the adult Chinese population and their association
15 with clinical outcomes.
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22 **2. Methods**

23 Findings of this survey are reported following the checklist for reporting results of internet E-surveys
24 (CHERRIES) checklist²⁷.
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27 **2.1 Study participants**

28 We included adult patients (≥18 years old) who (1) were experiencing or had experienced acute cough
29 (<28 days) in the last 3 months, irrespective of having chronic underlying lung diseases such as COPD
30 or asthma or not; (2) were able to read and understand Chinese, and to participate through an online
31 survey; (3) were willing to disclose information on all treatments they took for the last episode of
32 cough and their clinical outcomes. Implied consent was obtained. There was no restriction on gender
33 for this study. Participants could also answer the questionnaire on behalf of a family member.
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46 **2.2. Questionnaire**

47 The survey was piloted with five Chinese-speaking lay persons, and amended according to their
48 feedback, before opening the survey to the public. All survey materials were translated and back
49 translated by two team members [RYX and XYH]²⁸.
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57 The online cough survey takes 5-10 minutes to complete. It contains three sections: socio-
58 demographic and lifestyle characteristics (15 questions), cough symptoms and other health conditions
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(10 questions), and treatments to alleviate cough. Participants' subsequent clinical outcomes were collected and analysed to explore potential correlations with the treatments taken.

For participants' convenience, a list of the most commonly used antibiotics, allopathic non-antibiotic medications (e.g. NSAIDs), patent Chinese Herbal Medicines (PCHMs), and the most frequent home remedies (including special foods, e.g. pear soup) were provided as drop-down lists. One case of cough was collected from each survey response. The full questionnaire is available in S1 File.

2.3 Method of recruitment

In order to approach a large representative sample, potential participants were recruited through the largest Chinese social media platform WeChat. A QR code or a link to the online survey developed using Wen Juan Xing survey (<https://www.wjx.cn>) was circulated with an invite to participate through a snowballing approach starting with researchers' WeChat contacts and WeChat moments, discussion groups e.g. university student groups, medical associations groups, and general groups. We endeavoured to approach the general population from different regions in China and circulated the invites to specific general groups. The participant information sheet appeared at the top as part of the survey and consent was implied through survey participation.

2.4 Data collection and management

All survey data were collected and managed by researchers familiar with the use of online questionnaires, on taking consent, confidentiality and data management. No identifiable data were collected therefore participants could not be identified from the information collected. Each record was linked with a unique ID number. Data were stored on a password-protected laptop in a secure location, with data backups being made on a regular basis.

2.5 Data analysis

Participants' basic characteristics, cough and other health conditions, and the treatment used for their cough were analysed descriptively. For descriptive analyses, we grouped respondents into those with possible LRTIs, which were defined as: presence of at least one of shortness of breath or yellow

1 sputum or green sputum or wheezing, but excluding sore throat and coryza. Patients whose symptoms
2 did not fit these criteria were presumed to have had URTIs. Avoidance of antibiotics was assessed as
3 the number and proportion of participants not taking subsequent antibiotics after various treatments.
4 Relief of symptoms was self-reported on a 0-5 Likert scale. There is no precise measure for
5 appropriate use of antibiotics following self-report of acute cough. However, European estimates for
6 appropriate use following consultation with a physician are substantially lower than those reported
7 here. European standards suggest 0-30% for acute bronchitis ²⁹, whereas more recent guidelines and
8 expert elicitation put the figure at 10%, interquartile range (IQR) (6%-16%) in patients with acute
9 cough without comorbidities ³⁰.

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11 A Chi-square test of independence was performed to examine how 5 factors, namely age, smoking,
12 presumed upper or lower RTIs, severity of cough and comorbidities, might influence outcomes on
13 subsequent antibiotic usage and relief in cough. A significance level of 0.05 with 95% CI level was
14 utilised. Percentages were presented throughout the analysis with one decimal place. Any means,
15 medians and ranges/interquartile ranges were given to one decimal place. For standard deviations, two
16 decimal places were presented.

17
18 The data analysis for this study was generated using Microsoft Excel (2016) and IBM SPSS Statistics
19 for Windows, Version 23.0. Armonk, NY: IBM Corp.

20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 **2.6 Sample size calculation**

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43 Considering that 70% of people surveyed would have been likely to have used antibiotics ⁴, with a
44 95% CI around a 2% margin of error, we estimated that 2,017 participants would be required for this
45 survey. However, we planned to continue recruitment until February 2019 as larger numbers would be
46 needed for the secondary outcome measures.

47 48 49 50 51 52 53 54 **2.7 Ethical considerations**

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56 Ethical approval was sought from the University of Southampton ethics committee (ERGO 31602)
57 and the Beijing University of Chinese Medicine ethics committee (2018BZHYLL0101). Participants'

1 implied consent was obtained through the online survey. Personal information from this study was
2 confidential. We guaranteed the anonymity of each participant, with any personally identifiable
3 information in questionnaires being removed. All data were handled in China and only aggregated
4 data were sent to the UK. All completed surveys were collected through online social media and
5 online surveys, with data stored in a password protected laptop. A total value of £2000 (approximately
6 16060 RMB) were circulated as incentives with a random amount of money (around 1 to 2 RMB)
7 allocated to participants upon completion of the questionnaires.
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16 **3. Results**

19 **3.1 Response rate**

22 The online survey was circulated to researchers' WeChat contacts for cascading, which generated
23 81,169 visits between 25th January 2019 and 11th February 2019 (Fig 1). Of those who opened the
24 survey, 26,994 gave consent and completed the online questionnaire, among which 1411 provided
25 invalid data and were removed.
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28 Among the 26,740/81,169 (33.0%) valid responses, 22,787 were adult participants (or their family
29 members) with acute cough and are included in this analysis. The majority (78.5%) of the responses
30 were collected from patients themselves. Over half (52.1%) had experienced their most recent episode
31 of cough within 2 weeks and 31.3% between 2 and 4 weeks when they were completing this online
32 survey.
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35 The responses collected were across all 34 province-level regions in China, mostly from North and
36 East China, with Hebei province at the top (16.6%), followed by Shanxi (16.0%), Beijing (15.4%), and
37 Tianjin (9.2%). There were 29 (0.1%) responses from overseas.
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42 **3.2 Sociodemographic, lifestyle and health condition characteristics**

43 There were 2.1 times more male respondents than females. Most (89.4%) were young participants
44 between 18-45 years old and had a university/degree or above (44.6%). Almost half (49.6%) were
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employed full-time, and 40.0% were smokers (Table 1). The vast majority (92.0%) reported symptoms consistent with a URTI.

Table 1. Characteristics of respondents

Characteristic	Overall (n=22787)	Presumed URTIs* (n=20965)	Presumed LRTIs*(n=1822)
Sex: n (%)			
Male	15502 (68.0%)	14217(67.8%)	1285 (70.5%)
Female	7285 (32.0%)	6748 (32.2%)	537 (29.5%)
Age (years): Median (IQR, range)	28 (13, 18 to 120)	28 (13, 18 to 120)	28 (17, 18 to 99)
Educational level: n (%)			
Preschool	591(2.6%)	550 (2.6%)	41 (2.3%)
Primary school	1028 (4.5%)	926 (4.4%)	102 (5.6%)
Secondary school	3880 (17.0%)	3527 (16.8%)	353 (19.4%)
College/ Diploma#	6754 (29.6%)	6227 (29.7%)	527 (28.9%)
University/ Degree	8029 (35.2%)	7445 (35.5%)	584 (32.1%)
Postgraduate	2149 (9.4%)	1974 (9.4%)	175 (9.6%)
Other	356 (1.6%)	316 (1.5%)	40 (2.2%)
Occupational status: n (%)			
Employed full time	11292 (49.6%)	10544 (50.3%)	748 (41.1%)
Employed part time	3467 (15.2%)	3196 (15.2%)	271 (14.9%)
Retired	1317 (5.8%)	1166 (5.1%)	151 (8.3%)
Unemployed	740 (3.2%)	649 (3.1%)	91 (5.0%)
Casual worker	1050 (4.6%)	922 (4.4%)	128 (7.0%)
Not working due to ill health	436 (1.9%)	377 (1.8%)	59 (3.2%)
Homemaker	917 (4.0%)	843 (4.0%)	74 (4.1%)
Student	3275 (14.4%)	3012 (14.4%)	263 (14.4%)
Others	293 (1.3%)	256 (1.2%)	37 (2.1%)
Smoker: n (%)	9118 (40.0%)	8300 (39.6%)	818 (44.9%)
Comorbidities: n (%)			
No underlying condition	14545 (63.8%)	13471 (64.3%)	1074 (58.9%)
Asthma or other chest diseases	6032 (26.5%)	5545 (26.4%)	487 (26.7%)
All other underlying conditions	2210 (9.7%)	1949 (9.3%)	261 (14.3%)
Severity of cough: Median (IQR)	6 (3)	6 (3)	6 (3)

IQR: interquartile range, SD: standard deviation

URTIs: upper respiratory tract infections

LRTIs: lower respiratory tract infections

* Possible LRTIs were defined as presence of at least one of shortness of breath or yellow/ green sputum or wheezing, but excluding sore throat and coryza. Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

Refers to junior college education/ professional training [专科], including technical secondary school [中专] and junior college [大专].

The cough had resolved in 34.9% of respondents when they were completing the survey. The median severity of cough was 6 (IQR 3) on a 0-10 numerical rating scale (NRS) (Table 1). Most participants (65.7%) had a productive cough; the sputum colour reported most was yellow (40.3%), white (33.8%), and clear (19.3%). One fifth of participants reported only a cough (21.6%), whereas others experienced a range of symptoms, including sore/itchy throat (48.6%), runny nose (39.8%), headache (19.3%), and facial pain (13.4%) (Fig 2).

More than half (63.8%) of the participants had no underlying medical condition. Among the rest, asthma (14.9%), other chest conditions (14.9%), and heart disease (11.1%) were most frequently reported.

3.3 Treatments for acute cough

Although 46.4% of adult participants with acute cough used antibiotics, only 12.7% (2886/22787) took antibiotics alone or together with another treatment as their first treatment. 39.2% used individualised or patent CHM, 28.3% and 21.2% used allopathic non-antibiotic medications and home remedies respectively; these figures include both treatments used on their own, and those used as part of a combination (Table 2). Only 7.2% of the respondents did not use any treatment. The most common combinations were antibiotics with allopathic non-antibiotic medications (7.6%), antibiotics combined with CHM (5.7%), and antibiotics combined with home remedies (4.2%) (S1 Table). Of those 19901 (87.3%) who did not initially take antibiotics, 8314 (41.8%) took CHM, 5586 (28.1%) took allopathic non-antibiotic Western medicines and 4280 (21.5%) used home remedies (Table 3).

Table 2. Various treatments used for acute cough: interventions used alone or in combination.

Treatment	Overall (n=22,787)	Presumed URTIs* (n=20,965)	Presumed LRTIs* (n=1,822)
Antibiotics	10562 (46.4%)	9828 (46.9%)	734 (40.3%)
CHM	8942 (39.2%)	8311 (39.6%)	631 (34.6%)
Allopathic non-antibiotic medications	6441 (28.3%)	5942 (28.3%)	499 (27.4%)
Home remedies	4825 (21.2%)	4440 (21.2%)	385 (21.1%)
Others	280 (1.2%)	243 (1.2%)	37 (2.0%)
No treatment	1641 (7.2%)	1492 (7.1%)	149 (8.2%)

* Possible LRTIs were defined as presence of at least one of “shortness of breath” OR “yellow sputum” OR “green sputum” OR “wheezing” BUT EXCLUDING “sore throat” AND “coryza”. Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

CHM: Chinese herbal medicine

URTIs: upper respiratory tract infections

LRTIs: lower respiratory tract infections

3.3.1 Patterns of use of antibiotics

Nearly half of the participants (46.4%) had used antibiotics, among which 93.1% (9828/10562) were for presumed URTIs (Table 2). The proportions reporting antibiotic use were similar for presumed LRTIs (40.3%) to those with presumed URTIs (46.9%). The most commonly used antibiotics were Amoxicillin (32.5%), followed by Cefprozime (13.0%), Ampicillin (10.8%), Cefuroxime (7.6%), and Cefuroxime (7.6%) (Fig 3). Under half (44.8%) of the antibiotic users used the full course of antibiotics, others used more than half of the course (19.3%), less than half of the course (13.3%) or it was unclear (22.5%) whether they took the full course of antibiotics.

Of the participants who received antibiotics, almost half received them from a pharmacy (48.8%), and a third from a public community health centre (33.1%). In our sample, more antibiotic prescriptions came from TCM hospitals (28.0%) than from Western (22.1%) or integrative medicine hospitals (17.6%). Respondents used antibiotics on the basis of various sources of advice (and sometimes more than one), including health professionals such as doctors (52.4%), drug store staff (46.1%), family and friends (29.6%) or their own experience (19.4%).

3.3.2 Patterns of the use of allopathic non-antibiotic medications

Of the 6441/22787 (28.3%) participants who used allopathic non-antibiotic medications to help with their acute cough, non-steroidal anti-inflammatory drugs (NSAIDs, 2023, 31.4%) such as ibuprofen, naproxen, and diclofenac were the most commonly used, followed by paracetamol (1312, 20.4%), cough medicine (834, 12.9%) such as codeine, noscapine, pentoxyverine, and expectorants (232, 3.6%) such as methoxyphenamine, ambroxol and bromhexine hydrochloride.

3.3.3 Patterns of use of Chinese herbal medicine (CHM)

Nearly half 8942/22787 (39.2%) of participants used CHM to help with their acute cough, including individualised CHM (372, 4.2%) and patent CHM (8786, 98.3%). The top 8 patent CHM products were each taken by more than 500 respondents. Chuan Bei Pi Pa Gao (CBPPG) was the most frequently used (5019, 56.1% of all participants), followed by Gan Mao Ling granule (3316, 37.1%), Ke Chuan Shun pill (1764, 19.7%), and Fu Fang Gan Cao (tablet/liquid) (1643, 18.4%).

3.3.4 Patterns of use of home remedies

About one-fifth of participants used home remedies (n=4825, 21.2% of total) including boiled pear soup (2720, 56.4%), hot water (2661, 55.2%), lemon/orange juice (1729, 35.8%), pig lung soup (964, 20.0%), bitter melon soup (719, 14.9%) and others (110, 2.3%).

3.4 Treatment association with clinical recovery

3.4.1 Avoidance of antibiotics

Subsequent use of antibiotics was lower in those who initially took CHM, compared to those who started with home remedies or allopathic non-antibiotic medications (p<0.05). Other initial treatments included cupping, exercise, physically cooling down, heat therapy, hot bath, nasal wash with saline, ginger tea (257, 1.3%).

Table 3. Subsequent use of antibiotics after each type of treatment.

Initial Treatment	Overall* (n=7676)	Presumed URTIs# (n=7150)	Presumed LRTIs# (n=526)
Allopathic non-antibiotic medication	1394/5586 (25.0%)	1315/5127 (25.6%)	79/459 (17.2%)
Home remedies	769/4280(18.0%)	721/3925 (18.4%)	48/355 (13.5%)
Chinese herbal medicine	1236/8314 (14.9%)	1172/7710 (15.2%)	64/604 (10.6%)
Other	19/257 (7.4%)	16/226 (7.1%)	3/31 (9.7%)

* Excluded those who started with antibiotics and those who had other treatment and antibiotics as the first treatment

URTIs: upper respiratory tract infections

LRTIs: lower respiratory tract infections

Possible LRTIs were defined as presence of at least one of “shortness of breath” OR “yellow sputum” OR “green sputum” OR “wheezing” BUT EXCLUDING “sore throat” AND “coryza”.

Patients whose symptoms did not fit these criteria were presumed to have had URTIs.

A Chi-square test of independence was performed to examine the relation between various factors and subsequent use of antibiotics (S2 Table). Participants who smoked ($\chi^2 = 16.950$, $P < 0.01$), were aged ≥ 65 ($\chi^2 = 12.317$, $P = 0.002$), with severe cough ($\chi^2 = 113.535$, $P < 0.01$), with presumed URTIs ($\chi^2 = 9.385$, $P = 0.002$), and underlying lung conditions ($\chi^2 = 145.196$, $P < 0.01$) were the most likely to take antibiotics after taking CHM at 16.8%, 15.6%, 20.5%, 15.2%, and 23.8% respectively. Those aged 18-45 ($\chi^2 = 15.216$, $P < 0.01$), with severe cough ($\chi^2 = 25.763$, $P < 0.01$), URTIs ($\chi^2 = 16.014$, $P < 0.01$), and underlying lung conditions ($\chi^2 = 24.309$, $P < 0.01$) were the most likely to take antibiotics after taking allopathic non-antibiotic medications; while only those with severe cough ($\chi^2 = 38.126$, $P < 0.01$), URTIs ($\chi^2 = 5.192$, $P = 0.023$), and underlying lung conditions ($\chi^2 = 17.945$, $P < 0.01$) were the most likely to take antibiotics after taking home remedies.

3.4.2 Relief of cough

Antibiotics, allopathic non-antibiotic medications, CHM and home remedies were considered helpful in relieving cough symptoms, with the same median of 4, with a IQR at 1 or 2 on a 1-5 Likert self-rating scale (5 represents very helpful) (Table 4).

Table 4. Cough relief after each type of treatment as measured by 1-5 Likert scale.

Treatment	Median	IQR (range)
Antibiotics	4	2 (1 to 5)
Allopathic non-antibiotic medications	4	2 (1 to 5)
Patent Chinese herbal medicines (PCHM)		
Chuan Bei Pi Pa paste	4	1 (1 to 5)
Gan Mao Ling granule	4	2 (1 to 5)
Ke Chuan Shun pill	4	1 (1 to 5)
Fu Fang Gan Cao (table/liquid)	4	1 (1 to 5)
Individualised Chinese herbal formula	4	1 (1 to 5)
Home remedies	4	2 (1 to 5)

IQR: interquartile range

Relief of cough, as assessed by Likert scale, did not differ largely between participants with varying ages, smokers or non-smokers, with presumed upper or lower RTIs, with varying severity of cough, with or without any comorbidities (S3 Table).

4. Discussion

Summary of findings and comparison with the literature

1 This online survey explored treatment-seeking behaviour for acute cough in Chinese adults.
2 Although a series of antimicrobial stewardship guidelines and policies have been released in China
3 since 2009 ¹¹, we found that there is likely high proportion of inappropriate use of antibiotics for the
4 treatment of simple acute cough, even in well-educated young adults. Antibiotics were taken by nearly
5 half of our respondents with acute cough, of whom over 90% possibly had URIs. These findings are
6 consistent with previous research on overuse of antibiotics by university students in China ⁴.
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10 Both doctors and staff in pharmacies played an important role in recommending the use of antibiotics.
11 A considerable number of patients obtained antibiotics from easily accessible pharmacies which are
12 often less strictly regulated. Despite being illegal, it is easy to obtain antibiotics without a prescription
13 in retail pharmacies or from online sources in China ³¹. Pharmaceutical companies tend to offer
14 incentives for the prescribing of more expensive broad-spectrum antibiotics ³². These may be major
15 contributors to antimicrobial resistance.
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27 In our sample, participants reported similar levels of improvement regardless of which treatment they
28 took, although most presented with symptoms consistent with uncomplicated URIs, the vast majority
29 of which were most probably viral and self-limiting ^{2,3}. People used various alternatives to antibiotics
30 to help with their acute cough. CHM was the most popular initial treatment other than antibiotics, and
31 its initial use was associated with lower subsequent usage of antibiotics, compared to respondents who
32 initially started with home remedies or allopathic non-antibiotic medicines. PCHMs are commonly
33 used for uncomplicated ARTIs and most of them are readily available for patients to buy themselves
34 over the counter, online, or in pharmacies without a prescription. In 2015, over 60% of the 1231.8
35 billion RMB market share in China for respiratory conditions was spent on PCHM ³³. The majority of
36 allopathic non-antibiotic medications taken were NSAIDs. While patients with chest infections
37 perceived benefits in symptom relief, evidence suggests they may be associated with worse prognosis
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54 **Strengths and limitations**

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1 Our approach enabled us to recruit a large sample within a comparably short period. We managed to
2 collect responses from adults with acute cough across all regions of China, which increased our ability
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4 to understand the extent of antibiotic overuse and the alternatives to help alleviate cough and reduce
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6 the use of antibiotics. Although there is clearly an overlap, for the purposes of analysis we divided the
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8 respiratory syndromes into those consistent with LRTIs and URTIs.
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11 Our sample may not be representative of the wider Chinese population. There was potentially
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13 sampling bias as some participants recruited through researchers' networks with a Chinese medicine
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15 background may be systematically more likely to be selected. This may result in bias towards the use
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17 of CHM. Those electing to use CHM first line may also have been less likely to use antibiotics
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19 regardless of impact on symptoms. Among our sample, 40% were smokers and 27% reported having
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21 asthma or other chest diseases. These may not be a true reflection of the population as respondents
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23 were more likely to be young and actively using the internet. However, they were encouraged to
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25 cascade the survey, in order to include as many people from as many backgrounds as possible. A
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27 disadvantage of this method is that it is impossible to know how many people received the invitation,
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29 so the presumed response rate was calculated using the number of people who clicked on the survey
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31 link.
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37 Although self-reported data may not accurately reflect participants' disease characteristics, lifestyle
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39 characteristics or actual treatment behaviours, 83.9% of our respondents were answering questions
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41 about cough within a month, therefore, the recall bias should be low. We did not capture the exact
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43 order of treatments received, but recorded key information on which treatments participants took
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45 before the antibiotics. The outcomes assessed were symptom relief and subsequent use of antibiotics.
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47 No data on hospital admission or adverse events were collected. In such self-reported data, we are
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49 unable to address residual confounding and hence more advanced statistical analysis (e.g. regression)
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51 would be hard to interpret and the associations described should be treated with caution. A cross
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53 sectional survey can only report on associations and causality cannot be implied.
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Priorities for research and clinical implications

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3 The findings are important to inform public health interventions on appropriate treatment-seeking.
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5 There is a need to regulate pharmacy practices of prescribing and selling antibiotics. In-depth
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7 qualitative research could help to understand the reasons for inappropriate antibiotic use, especially in
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9 young patients with URTIs who typically do not need them. Complementary and alternative medicine
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11 (CAM) treatments appeared to be acceptable to people from many different settings as a possible
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13 alternative to antibiotics, consistent with research in other countries.³⁵ Future research could explore
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15 expectations of patients with cough in China, the acceptability and experiences of taking CHM, and
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17 the reasons behind decision making. These could then inform the development of future antibiotic
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19 stewardship interventions, potentially encouraging the use of CHM as an alternative to antibiotics.
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25 Future research is needed to improve the evidence base on which specific herbal medicines should be
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27 recommended as alternatives to antibiotics. Further analyses are needed to identify the most promising
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29 PTCMs. Severity of cough, upper or lower RTIs, and underlying lung conditions may be considered as
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31 potential factors influencing how well allopathic non-antibiotic medications, CHM, or home remedies
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33 may help in reducing the use of antibiotics.
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Conclusions

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39 There is likely a high proportion of inappropriate use of antibiotics for the treatment of simple acute
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41 cough, even in well-educated young adults. Many obtained antibiotics from easily accessible
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43 pharmacies which are less strictly regulated. Antibiotics, CHM, allopathic non-antibiotic medications,
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45 and home remedies were often used with similar perceived beneficial in relieving cough regardless of
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47 treatment. CHM was the most widely used alternative and has a potential role in relieving cough
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49 symptoms and reducing the use of antibiotics. Future research is needed to evaluate the effectiveness
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51 of individualised and commonly used CHM for acute cough.
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Author contributions

Conceptualization: XYH, MW, RYX, TYF; Methodology: All; Formal analysis: RYX; Investigation: RYX, TYF, XYH, ML; Resources: YTF, XYH, RYX, JPL, LZW; Data curation: RYX, YTF; Writing: XYH; Review & Editing: All; Visualization: XYH; Supervision: MW, YTF; Project administration: RYX; Funding acquisition: XYH, MW. All authors have read and agreed to the published version of the manuscript. There is no professional writer involved.

Conflict of interest

The authors declare no conflict of interest. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results

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Data availability

The data that support the findings of this study are available within the article and its supplementary material, or are available from the corresponding author upon reasonable request.

Figure legends

Fig. 1. Recruitment flow diagram.

Fig. 2. Other symptoms experienced relating to this episode of cough.

Fig. 3. Antibiotics used by adults with acute cough.

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