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How far do we still need to go? A survey on knowledge, attitudes, practice related to antimicrobial stewardship regulations among Chinese doctors in 2012 and 2016

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How far do we still need to go? A survey on knowledge, attitudes, practice

related to antimicrobial stewardship regulations among Chinese doctors in 2012

and 2016

Ruyu Xia[1], Xiaoyang Hu[2]†, Merlin Willcox[2]†, Xinxue Li[3], Yuxiu Li[4], Jian Wang[5],

Xun Li[1], Michael Moore[2], Jianping Liu[1], Yutong Fei[1]*

[1]Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese

Medicine, Beijing, China;

[2]Primary Care and Population Sciences, University of Southampton, Southampton,

UK; [3]Department of International Liaison, World Federation of Chinese Medicine

Societies, Beijing, China;

[4]Department of endocrinology, South of Guang'anmen Hospital, China Academy of

Chinese Medical Sciences, Beijing, China;

[5]Department of neurology, The Affiliated Hospital of Changchun University of

Chinese Medicine, Changchun, China.

*Corresponding author. Tel: +86 10 6428 6757; E-mail: feiyt@bucm.edu.cn. Postal

address: No. 11, Bei San Huan Dong Road, Chaoyang District, Beijing 100029, China

†These authors contributed equally

ABSTRACT

Objectives: To explore doctors' knowledge, willingness, concerns and the countermeasures to the most stringent antimicrobial stewardship regulations of China (2012).

Design: Cross-sectional survey.

Setting: China.

Methods: A pretested 32-point structured questionnaire was distributed to doctors by sending a web link via the mobile phone application WeChat through snow-ball sampling methods and email groups of two major medical academic societies. The questionnaire inquired about the doctors' experiences, knowledge, willingness, concerns and the countermeasures to the stewardship policies. Mann-Whitney test, χ2 test and multivariate regression were applied where appropriate.

Results: 807 doctors from 29 provinces in mainland China fully completed the questionnaire. Doctors had a mean age of 39.0 years. The majority (78.9% in 2012, 89.1% in 2016) reported that they were willing or very willing to accept the regulations. Almost all respondents (93.2%) felt the stewardship regulations had the potential to adversely affect the prognosis of patients who would have been prescribed antimicrobials before they were implemented, and more than 65% (65.7% in 2012, 66.9% in 2016) of doctors were often or always concerned about the prognosis of these patients. 32% doctors prescribed restricted antimicrobials or suggested patient self-medication with restricted antimicrobials to address doctors' concerns in 2012, and this number decreased to 22.6% in 2016. Although compulsory antimicrobial stewardship training was frequent, less than half of respondents (46.8%) responded correctly to all three knowledge questions.

Conclusion: Antimicrobial stewardship regulations had some positive effect on rational antimicrobial use. Willingness and practice of doctors towards the regulations improved from 2012 to 2016. Knowledge about rational antimicrobial use was still lacking. Doctors found ways of accessing restricted antibiotics to address their concerns about the prognosis of patients, which undermined the implementation of the stewardship regulations.

Strengths and limitations of this study

- The paper is the first to comprehensively explore doctors' feelings and attitudes towards the Chinese antimicrobial stewardship regulations.
- The survey recruited participants and administered the survey via WeChat, which is a convenient, time-saving and economic method to survey a diverse population. Our respondents covered 29 of 32 administrative divisions of mainland China.
- We cannot rule out a possible selection bias as our sample was not randomly selected. Although the snowball sampling method is effective and efficient when sampling from specific populations, participants that can be reached depend on the social connections of the key respondents.
- Another limitation is the potential recall bias of information provided for year 2012 and 2016.

INTRODUCTION

The efficacy of antimicrobials is threatened by increasing levels of antimicrobial resistance.[1] [2] In 2014, it was estimated that China consumed 77,760 tons of antimicrobial agents for humans and the defined daily doses per 1000 inhabitants per day were approximately 6 times larger than in the UK, USA, Canada and Europe.[3]

During the past decade, the Chinese Government has issued a series of health care regulations.[4-7] The "Administrative regulations for the clinical use of antimicrobials", issued in August 2012, were the most stringent regulations ever (Box 1).[6] Several studies reported changes in the prescription rates of antibiotics to reflect the impact of the 2012 stewardship regulations,[8-10] but we did not find any study which investigated the attitudes of Chinese doctors towards these regulations, although they might be an important barrier to implementation of the regulations.

Our study aimed to explore knowledge, willingness, concerns and the countermeasures of doctors towards the most stringent antimicrobial stewardship regulations of China (2012) via a web-based survey. Specifically, we looked at: 1) what did they experience; 2) how good was their knowledge about prescribing antimicrobials; 3) what were their feelings (willingness/reluctance) towards the regulations (over a five-year duration of implementation) when they were practicing; 4) what were the countermeasures, if any were used.

METHODS

Study design and population

A snowball sampling strategy, focus on recruiting docors practing in mainland China, was utilized. Participants were reached by sending a link created in WenJuanXing (Changsha Ranxing Science and Technology Ltd, Shanghai, China) online survey service via the mobile phone Application (APP) WeChat and emails. WeChat is currently the most widely used social media platform in China, with more than one billion users. The invitations to participate in the survey were sent first to clinicians' WeChat groups by researchers, then they were cascaded by purposively inviting key respondents to send the link to their clinicians' WeChat groups in order to increase respondent sample size (WeChat groups details in Table S1). Email invitations were only sent to members of the World Federation of Chinese Medicine Societies. The professional occupation screening function was turned on therefore only those who identified themselves as doctors were able to proceed to the survey questions, others were directed politely to the end of the survey.

Survey questionnaire

The study was performed between March 9th to March 30th 2017 using a piloted 32-point structured questionnaire (see Table S2[11]). The structured questionnaire consisted of questions about four categories of variables: (a) demographics and practice characteristics of the doctors; (b) implementation of the antimicrobial stewardship in health care facilities; (c) attitude (willingness, concerns) and practice(impacts on prescribing antibiotic behaviour, countermeasures to concerns) of doctors towards 2012 antimicrobial stewardship regulations; (d) doctors' knowledge

of antimicrobial stewardship regulations and proper use of antimicrobials (question

30-32 originated from training examination questions for "guiding principles for

clinical application of antibacterial[4]" and "administrative regulations for the clinical

use of antimicrobials[6]"). The questionnaire was about 18 phone screens long, which

took approximately 5 minutes to complete. We consulted two doctors and one

methodologist and conducted a pilot survey with 10 doctors before starting the formal

survey.

Data were imported from the survey website into Microsoft Excel 2016, then

converted into the SPSS database. Statistical analysis was performed using IBM

SPSS Statistics for Windows, V.23.0 (IBM, Armonk, New York, USA). Descriptive

statistics, Mann-Whitney test, $\chi 2$ test and multivariate regression were applied in

description and analysis of the variables, where appropriate. Compulsory

antimicrobial stewardship training, doctor's acceptance, impact on prescribing

antibiotic behaviours, impact on prognosis of patients, concern and countermeasures

towards the antimicrobial stewardship at the beginning of the implementation (2012)

and five years after that (2016) were compared. Doctors with different educational

background, levels of seniority, practicing organizations and geographic regions were

considered as subgroups and compared. Logistic regression was used to screen factors

relevant to knowledge of clinical use of antimicrobials.

Ethical approval for this study was obtained from the Ethical committee, Beijing

University of Chinese Medicine (2017BZHYLL0201). Informed consent was

obtained from all the participants. Participants were informed at the start of the survey

about the length of time needed to complete the survey, the investigators and the

purpose of the study. Participants were free to continue the survey or to quit at any

time. Anonymous data were collected. No incentive was used to reward participants.

RESULTS

Demographics and response rates (Tables S3 and S4)

The questionnaire was sent to 19791 health professionals across 107 WeChat groups

and 3 email groups. A total of 3609 health professionals visited the web link of the

questionnaire, out of which 1194 (33.1%, 1194/3609) responded. Among the survey

respondents, 807 (67.6%, 807/1194) were doctors; others were nurses, researchers,

clinical postgraduates, or administrative staffs. Data provided by doctors were

collected and analysed. All 807 doctors fully completed the online survey. Doctors

had a mean age of 39.0 years (SD=7.4), range 22 to 68. 41.3% doctors were men. 71.2%

doctors had MSc, MD or PhD degree (n=575). Most of them were residents or

associated chief-physicians (n=336; 41.6% and n=241; 29.9% respectively).

Approximately half (n=386; 47.8%) of doctors majored in western medicine, others

majored in traditional Chinese medicine or integrative medicine. 83.7% doctors

started clinical practice before 2012. The number of outpatient services provided

weekly was diverse, ranging from none (22.8% and 15.4% in 2007-2011 and

2012-2016 respectively) to 5 days (18.7%; 17.5%). Although almost half of doctors

were from eastern China (49.2%), there was also a good number from central, western

and north-eastern China. 60.8% doctors were working in first-tier and new first-tier cities (e.g. Beijing, Shanghai and Hangzhou). Most doctors (79.8%) worked in tertiary hospitals.

Experiences of implementation of the antimicrobial stewardship regulations (Table 1)

The clear majority of practitioners reported that hospital implementation of antimicrobial stewardship regulations was stringent (45.1%) or very stringent (45.7%). Specific training sessions were frequent or intensive in 2012 (59.1%) and in 2016 (68.5%) (p< 0.001). Practitioners from tertiary western medicine hospitals in first/new first-tier cities reported more stringent requirements for the implementation of the regulations. Doctors in departments of respiratory medicine, emergency medicine, paediatrics, intensive care, haematology, and dentistry reported that they were permitted higher upper limits than the general limits of their hospitals. The largest gap in antimicrobial prescription limits was between respiratory departments (33.5%) and hospitals overall, irrespective of departments (22.4%).

Knowledge of antimicrobial stewardship regulations and proper use of antimicrobials (Table 2)

Although most doctors (65.1%) declared that they were familiar or very familiar with the 2012 stewardship regulations, less than half answered the three-question knowledge test (question 30-32) correctly (46.8%). Doctors from primary care had a lower correct rate compared to those from other hospitals (P=0.013); doctors who

majored in traditional Chinese medicine had a lower correct rate compared to those who majored in western/integrative medicine as measured in the multivariate regression equation (P=0.001). The most commonly reported criteria for prescribing antimicrobials were full blood count (94.2%), pathogen detection such as sputum or blood culture (77.0%), symptoms (72.9%), signs (71.4%), C-reactive protein level (62.9%) and the diagnosis (60.5%).

Attitudes towards implementation of the antimicrobial stewardship regulations (Table 3)

78.9% of doctors reported that they were willing or very willing to accept the regulations in 2012, and the percentage increased to 89.1% in 2016 (p=0.002). In 2012 and 2016, doctors who majored in western medicine reported lower acceptance rates (74.6%; 86.5%) than those who majored in Chinese medicine or integrative medicine (82.9%; 91.4%). 30.0% of doctors reported the antimicrobial stewardship regulations had a moderate or large impact on the prognosis of these patients "at risk" (means patients who would have been prescribed antimicrobials before the implementation of the 2012 stewardship regulations). Only 6.8% of doctors felt the stewardship regulations did not result in putting the prognosis of these patients "at risk". More than 65% of doctors (65.7% in 2012, 66.9% in 2016; p=0.367) were 'often or always concerned' about the prognosis of patients "at risk".

Doctors' practice of the antimicrobial stewardship regulations (Table 3)

41.6% of doctors reported that prescribing of antimicrobials had been very (6.1%) or

moderately (35.5%) restricted during the implementation of antimicrobial stewardship

regulations in 2012. The percentages even increased in 2016 (8.4%; 38.9%) (2016 vs

2012, p=0.019). In 2012, 32% of doctors stated that they had prescribed or suggested

patient self-medication with restricted antimicrobials (restricted by the specific

criteria for conditions in the stewardship) to address concerns for patients "at risk"

(Figure 1), but it decreased to 22.6% in 2016 (2016 vs 2012, p< 0.001). In 2012, This

prescribing behaviour was reportedly more common (42.2%) in small cities, but in

2016 there no longer seemed to be any obvious difference between city levels. This

behaviour was higher among doctors who majored in western medicine than among

those who majored in traditional Chinese medicine or integrative medicine (37.8%

and 26.5% respectively in 2012, 24.3% and 20.9% in 2016). This proportion was

higher among interns (44.6% in 2012; 30.8% in 2016) than other doctors (30.7% in

2012; 21.3 in 2016). More doctors prescribed permitted antimicrobials in 2016 than in

2012 (46.7%, 43.8%) when treatment was needed. In 2012 and 2016, 13.6% and 10.4%

prescribed alternatives to antimicrobials; 95.8% (69/72) and 96.2% (102/106) of these

prescribed traditional Chinese medicines.

DISCUSSION

Summary of findings

The distribution of geographic region, levels of cities, types of medical organizations,

education background, levels of seniority of the doctors were largely well balanced

(table S3, table S4). The common type is doctors in their 40s, with a higher educational background, comparably in mid-career stage, and have more than five years of pracitical experience. There is a good number of them from Eastern China, representing both western and traditional Chinese/integrative medicine doctors, mainly from tertiary hospitals. Regarding the location, although nearly half (49.2%) of the respondents were based in Eastern China (the population of Eastern China accounts for 37.98% of the national permanent population), there are good number of doctors from other areas (the smallest group was the ones from central China – 11% is still 89 doctors; and the respondents covered 29/32 administrative divisions of mainland China), representing the varieties of all regions in China.

The implementation of the 2012 stewardship regulations was considered stringent. The percentage of all prescriptions which are permitted to contain antimicrobials in respiratory departments was set to be high by the answers from the doctors, with an average of 33.5%. Insufficient knowledge on proper use of antimicrobials was obvious, especially in primary medical organizations. Most doctors (94.2%) used full blood count as the criterion for prescribing antimicrobials. Compulsory stewardship training and willingness to accept the stewardship regulations increased from 2012 to 2016. Due to restricted prescription of antimicrobials, doctors' concerns with prognosis of patients "at risk" remained high. It seems that the use of restricted antimicrobials has greatly reduced, but the use of permitted antimicrobials may have increased. Traditional Chinese medicine may have played a role as an alternative to

antimicrobials.

Strengths and limitations

To the best of our knowledge, this is the first survey in China to comprehensively explore doctors' feelings and attitudes toward the Chinese antimicrobial stewardship regulations. We recruited participants and administered the survey via WeChat (one of the most common social APPs in China). It is a convenient, time-saving and economic method to survey a diverse population. Our respondents covered 29 of 32 administrative divisions of mainland China. Despite this, our study has a number of limitations. Firstly, we cannot rule out a possible selection bias as our sample was not randomly selected. Although the snowball sampling method is effective and efficient when sampling from specific populations, participants that can be reached depend on the social connections of the key respondents. Also, doctors in primary care settings or private clinics are less likely to belong to any academic association or doctors' group, thus they may be less likely to be reached. Another limitation is the potential recall bias of information provided for year 2012 and 2016.

Comparisons with other studies

We did not identify any studies investigating the attitudes of doctors towards the 2012 antimicrobial stewardship regulations. Doctors' willingness and concerns might impact on their prescribing behaviors and weaken the effects of the regulations. We found in our study that the knowledge about proper use of antimicrobials of doctors from primary care clinics or private clinics seems insufficient. Similar results were

reported from three surveys (sample sizes 761, 180, 611) focusing on doctors' or trainees' knowledge and continued education.[12-14] In our study, doctors reported that they recommended self-medication of restricted antimicrobials to address concerns for patients "at risk". Another survey of 256 pharmacies in three Chinese cities[15] showed that antibiotics were obtained without a prescription from 77.7% pharmacies for adult respiratory infections. In our study, the percentage of all prescriptions which are permitted to contain antimicrobials in respiratory departments was very high. A survey of 1204 people in three Chinese cities[16] showed that cough, sore throat, and bronchitis were the most frequent reasons reported for antibiotic use. This is also consistent with the situation in the UK.[17]

In our study, full blood count (raised white blood cell counts and increased proportion of neutrophilic granulocytes) was overwhelmingly considered as the main criterion for prescribing antimicrobials. This medical behavior is in accordance with the Chinese acute bronchitis clinical practice guidelines,[18] [19] which state that oral antibiotics such as β-lactams and fluoroquinolones can be used in patients with cough before the pathogen detection results were available, if there are signs of purulent sputum or raised white cell counts (Adults usually more than 10×10^9/L). However, it has been suggested by international guidelines that doctors should not perform testing or initiate antibiotic therapy in people with acute bronchitis (pneumonia excluded).[20] Studies[21] [22] have shown that blood tests do not accurately differentiate between bacterial and viral infections. In our survey, many doctors also reported using raised

CRP as a criterion for prescribing antimicrobials. CRP may be helpful in adults and is

recommended in the NICE guidelines[23] to be considered if antibiotics are being

considered for treatment of lower respiratory tract infections. A study has shown that

use of CRP can reduce antibiotic consumption in acute respiratory tract infections.[24]

However, Lemiengre and colleagues performed a cluster-randomized trial in 2227

children showing that CRP tests did not reduce antibiotic prescribing for non-severe

acute infections in children in primary care and cannot be recommended.[25] In our

survey, doctors with a traditional Chinese medicine/integrative medicine background

felt less restricted and were more willing to accept the stewardship regulations.

Traditional Chinese medicines served as alternatives to antimicrobials for doctors.

Similarly, in the UK, a retrospective study which included 7283 General Practice

(GP) surgeries suggested that GPs additionally trained in integrative medicine or

complementary and alternative medicine had lower antibiotic prescribing rates

compared with conventional GPs.[26]

Implications for doctors and policy makers

The implementation of the antimicrobial stewardship regulations requires

administrative persistence and strengthened training of doctors on the use of

antimicrobials, especially for primary care doctors. In addition to the mandatory

administrative implementation, explanation of reasons why there is a need for proper

use of antimicrobials and how to achieve it, as well as approaches to facilitate

evidence-based clinical practicing are needed to guide clinical practice and to relieve

doctors' concerns. The common practice of prescribing antimicrobials according to elevated full blood count or CRP is controversial. Although both guidelines and the stewardship regulations mentioned this, no threshold was defined. Suggested patient self-medication with restricted antimicrobials may have diminished the effect of the antimicrobial stewardship regulations. The increase in the use of permitted antimicrobials may be associated with inappropriate use, which is also an important cause of antimicrobial resistance. More stringent measures should be applied to stop antimicrobial purchase without prescriptions from retail pharmacies. Traditional Chinese medicine can be considered for relieving symptoms, complementing or replacing antimicrobials.[27]

Future research

First, there is a need for qualitative research to explore antibiotic prescribing behaviours in China, potential concerns from doctors and pharmacists, why there were differences between doctors in different types of hospitals/regions/major, and which intervention(s) would be most acceptable in their context to reduce antimicrobial prescribing. Then, we also suggest that a large representative sample cohort study or registry study in China is warranted, to explore the possibility of delayed antimicrobials or other antimicrobial replacement therapy from the perspectives of clinical effect, safety, reducing resistance and health economics. There is a need for more evidence to back up recommendations, particularly on (i) diagnostic and prognostic accuracy of various markers e.g. white cell counts and CRP;

(ii) prognosis of infections for which antibiotics were commonly prescribed; (iii) guidelines and recommendations on when to use antibiotics. Additionally, we need to find other interventions that can relieve symptoms, complement or substitute antimicrobials, and then conduct high quality, large scale randomized controlled trials to validate their efficacy, effectiveness and safety. Traditional Chinese medicine is widely used in medical practice in China.[28] We propose more clinical or basic research to explore which traditional Chinese medicine can be recommended instead of antibiotics for different infections.

Conclusion

In summary, the 2012 antimicrobial stewardship regulations improved proper clinical use of antimicrobials in China. Attitudes and behaviours of doctors towards the stewardship regulations improved from 2012 to 2016. Concerns about the prognosis of patients "at risk" were still prevalent, and doctors found ways of accessing antibiotics which undermined the implementation of the antimicrobial stewardship regulations. There is a gap between doctors in small cities and first-tier cities in terms of implementation of antimicrobial stewardship regulations and knowledge about proper use of antimicrobials.

Contributors: RX, JL and YF conceived and designed the study. RX, XL, YL, JW and YF collected the data. RX and YF analyzed the data and prepared the manuscript. XH, MW, MM and YF contributed to the interpretation of the results and critical revision of manuscript. All authors approved the final manuscript.

Competing interests: none declared.

Ethics approval: This study was approved by the ethical committee of Beijing University of Chinese Medicine (2017BZHYLL0201).

Data sharing: No additional data are available.

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The "Administrative regulations for the clinical use of antimicrobials" was issued and implemented by the National Health and Family Planning Commission (NHFPC, the former Ministry of Health)

What are the regulations about?

In the 2012 stewardship regulations, all hospitals in China were required to set up an antimicrobial agents administrative group or identify a point person to take control of antimicrobial stewardship. Infectious diseases departments and clinical microbial laboratories were required to be set up in all tertiary and secondary hospitals. Antibacterial agents were classified according to safety, efficacy, bacterial resistance, price and other factors. Prescribers have accredited prescription rights for different categories of antimicrobials, depending on their levels of seniority. Compulsory standardized trainings on the knowledge of clinical use of antimicrobials are required for all doctors.

How was it supposed to be implemented or enforced? How was implementation monitored?

NHFPC established the Centre for Antibacterial Surveillance and the China Antimicrobial Resistance Surveillance System to monitor the use of antibiotics and antibiotic resistance in hospitals. Surveillance systems within their respective administrative areas would be developed by local health administrative departments. The rankings of total usage of antimicrobials, classification of antimicrobials, and percentage of prescriptions for antimicrobials in health facilities in their respective administrative regions are published and submitted to the higher authorities for the record. Managers of poorly performing health facilities are admonished. This is to ensure rational use of antimicrobial agents in healthcare settings.

Were there any sanctions for not implementing it?

Health facilities that fail to meet the requirements would be downgraded to a lower classification level. Doctors who fail to pass the exam of standard training or seriously violate the regulations can lose their accreditation to prescribe antibiotics, and/or have their professional qualification revoked. If doctors' actions led to serious consequences, they could be fined or prosecuted.

Who was responsible for implementing it?

NHFPC and local health administration investigate and reassign responsibility to hospital presidents or health facility management staff.

Box 1 Translated summary of "administrative regulations for the clinical use of antimicrobials" [6]

Table 1 Implementation of the antimicrobial stewardship regulations

Questions asked	Total n=807	Medical organization level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Medical organization antimicrobial stewardship implementation %										
Very stringent	45.7	50.6	33.0	11.8	47.9	36.5	44.2	47.5	50.0	41.8
Stringent	45.1	44.1	50.0	47.1	44.2	48.7	45.1	45.1	44.0	46.1
Less stringent	7.8	4.5	16.1	31.4	6.5	13.5	9.0	6.3	5.4	10.0
No	1.4	0.8	0.9	9.8	1.4	1.3	1.6	1.1	0.5	2.1
Compulsory antimicrobial stewardship training in 2012 (first year of stewardship implementation) %										
Intensive	9.7	10.9	6.3	3.9	11.4	2.7	8.3	11.4	11.1	8.4
Frequent	49.4	52.4	41.4	31.4	50.6	44.5	47.6	51.4	50.0	48.8
Less frequent	36.6	33.2	49.5	49.0	33.9	47.9	38.8	34.2	35.1	38.1
No	4.2	3.5	2.7	15.7	4.1	4.8	5.3	3.1	3.8	4.6
Not applicable	n=48									
Compulsory antimicrobial stewardship training in 2016 %										
Intensive	12.6	14.0	8.0	5.9	14.1	6.4	12.4	12.9	13.5	11.9
Frequently	55.9	58.1	50.0	41.2	55.9	55.8	53.0	59.3	56.0	55.8
Less frequency	28.6	26.4	38.4	35.3	27.0	35.3	30.5	26.4	28.0	29.2
No	2.9	1.6	3.6	17.6	2.9	2.6	4.1	1.4	2.6	3.1
% of all prescriptions which are permitted to contain antimicrobials (according to the hospital's internal policy) %										
≤20%	59.8	60.1	44.4	86.0	65.6	39.7	62.0	57.5	47.7	72.0
21-40%	32.9	33.3	43.2	9.3	29.8	43.7	31.5	34.4	43.8	22.0
41-60%	6.5	5.9	12.3	2.3	4.1	15.1	5.5	7.7	7.8	5.3
>60%	0.7	0.7	0.0	2.3%	0.5	1.6	1.0	0.4	0.7	0.7
Not reported	n=242									
% of all prescriptions which are permitted to contain antimicrobials (according to the department's internal policy) %										
≤20%	64.1	64.1	51.9	86.0	69.5	45.2	65.4	62.6	53.7	74.5
21-40%	26.5	26.6	34.2	11.6	23.5	37.3	24.3	28.9	34.3	18.8
41-60%	8.0	7.4	13.9	2.3	6.2	14.3	8.2	7.7	9.5	6.4
>60%	1.4	1.8	0.0	0.0	0.9	3.2	2.1	0.7	2.5	0.4
Not reported	n=242									

[a]Pm/Pv: Primary/ private clinic. [b]1/new1/2: First/new first/second-tier First-tier city, such as Beijing, Shanghai. New first-tier city, such as Chengdu, Hangzhou. Second -tier city, such as Shenyang, Xi'an. [c]IT/RS: intern/resident. [d]ACP/CP: Associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

Table 2 Knowledge of antimicrobial stewardship

Questions asked	Total n=807	Medical organization level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Self-reported knowledge of antimicrobial stewardship %										
Very familiar	16.1	17.1	12.5	11.8	16.9	12.8	10.6	22.8	18.9	13.5
Familiar	48.9	49.4	52.7	35.3	48.8	49.4	44.0	54.9	47.2	50.6
Know a little	31.0	30.0	32.1	41.2	30.0	35.3	39.5	20.6	30.3	31.6
Don't know	4.0	3.6	2.7	11.8	4.3	2.6	5.9	1.6	3.6	4.3
Tested results of knowledge of antimicrobial prescribing										
Which surgery should apply perioperative antimicrobial prophylaxis										
% of correct	91.9	91.6	93.8	92.2	92.5	89.7	92.3	91.5	92.2	91.7
Which antimicrobial should be used for extended-spectrum β-lactamases-producing bacterial infection										
% of correct	70.5	72.1	74.1	43.1	69.3	75.6	65.2	76.9	78.2	63.4
For how long a restricted antibiotic can be used in emergent medical situations										
% of correct	66.7	67.7	72.3	41.2	66.1	69.2	64.3	69.5	72.3	61.5
Criteria for prescribing antimicrobials (multiple choice) %										
Symptom	72.9	75.9	67.9	45.1	72.4	75.0	74.3	71.2	75.6	70.3
Sign	71.4	73.6	70.5	45.1	70.8	74.4	71.1	71.7	72.8	70.1
Full blood count	94.2	95.0	92.0	88.2	95.4	89.1	95.0	93.1	92.7	95.5
CRP [g]	62.9	64.0	59.8	56.9	62.2	66.0	61.9	64.3	61.7	64.1
PD [h]	77.0	83.2	65.2	23.5	92.0	78.2	75.4	78.8	84.2	70.3
Diagnosis	60.5	62.9	58.9	33.3	60.7	59.6	58.9	62.4	68.9	52.7
Others	18.2	19.3	14.3	13.7	18.7	16.0	17.8	18.7	21.5	15.2

[a]Pm/Pv: Primary/ private clinic. [b]1/new1/2: First/new first/second-tier First-tier city, such as Beijing, Shanghai. New first-tier city, such as Chengdu, Hangzhou. Second -tier city, such as Shenyang, Xi'an. [c]IT/RS: intern/resident. [d]ACP/CP: Associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine. [g]CRP: C-reactive protein detection. [h]PD: pathogen detection.

Table 3 Attitudes and practice of doctors towards the antimicrobial stewardship regulations in 2012 and 2016

Questions asked	Total n=807	Medical organization level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Personal willingness to accept antimicrobial stewardship regulations in 2012 (first year of implementation) %										
Very willing	26.5	26.3	18.9	45.8	28.4	18.6	27.9	25.1	24.0	28.8
Willing	52.4	52.6	52.8	47.9	53.3	48.6	49.7	55.2	50.6	54.0
Hard to accept	19.2	19.0	26.4	6.3	16.4	31.4	20.6	17.7	23.2	15.6
Unacceptable	1.9	2.1	1.9	0.0	2.0	1.4	1.8	2.0	2.3	1.6
Not applicable	n=68									
Personal willingness to accept antimicrobial stewardship regulations in 2016 %										
Very willing	27.4	28.4	17.0	37.3	27.6	26.3	24.2	31.3	25.9	28.7
Willing	61.7	60.9	69.6	54.9	61.9	60.9	64.3	58.5	60.6	62.7
Hard to accept	10.0	9.8	13.4	5.9	9.5	12.2	10.6	9.3	12.2	8.1
Unacceptable	0.9	0.9	0.0	2.0	0.9	0.6	0.9	0.8	1.3	0.5
Impact of antimicrobial stewardship on prescribing antibiotic behaviors in 2012 (first year of implementation) %										
Very restricted	6.1	6.2	5.6	6.1	6.0	6.3	7.0	5.1	7.0	5.2
Restricted	35.5	36.9	35.5	18.4	35.7	34.7	37.4	33.4	35.9	35.1
Slightly	48.3	48.0	46.7	55.1	48.2	48.6	45.5	51.4	49.0	47.6
Not restricted	10.1	8.9	12.1	20.4	10.1	10.4	10.1	10.1	8.1	12.0
Not applicable	n=66									
Impact of antimicrobial stewardship on prescribing antimicrobial behaviors in 2016 %										
Very restricted	8.4	8.5	9.8	3.9	8.0	10.3	7.4	9.6	10.6	6.4
Restricted	38.9	39.1	43.8	25.5	38.2	41.7	43.1	33.8	41.2	36.8
Slightly	43.5	43.6	40.2	49.0	44.2	40.4	41.5	45.9	40.7	46.1
Not restricted	9.2	8.7	6.3	21.6	9.5	7.7	7.9	10.7	7.5	10.7
Concerns with prognosis of patients "at risk" --who would have been given antimicrobials before the stewardship in 2012 (first year of implementation) %										
Always	16.8	17.1	19.3	8.3	13.9	29.2	18.5	15.0	19.7	14.1
Often	48.9	48.0	51.4	54.2	50.9	40.3	49.1	48.6	50.8	47.0
Sometimes	29.9	30.2	27.5	31.3	30.1	29.2	27.2	32.8	25.3	34.2
No	4.4	4.8	1.8	6.3	5.2	1.4	5.1	3.7	4.2	4.7
Not applicable	n=64									
Concerns with prognosis of patients "at risk" in 2016 %										
Always	12.6	12.7	16.1	3.9	11.5	17.3	14.7	10.2	14.5	10.9
Often	54.3	53.9	58.0	51.0	53.3	58.3	54.9	53.6	56.2	52.5
Sometimes	26.8	26.9	22.3	35.3	28.3	20.5	24.6	29.4	24.1	29.2
No	6.3	6.5	3.6	9.8	6.9	3.8	5.9	6.9	5.2	7.4
Impact of antimicrobial stewardship on prognosis of patients "at risk" %										
Strong	2.4	2.3	1.8	3.	2.5	1.9	2.3	2.5	2.6	2.1

Moderate	27.6	26.9	31.3	29.4	27.0	30.1	31.8	22.5	27.7	27.6
Slight	63.2	64.1	61.6	56.9	63.3	62.8	59.6	67.6	63.5	62.9
No	6.8	6.8	5.4	9.8	7.2	5.1	6.3	7.4	6.2	7.4
Countermeasures to concerns for prognosis of patients "at risk" in 2012 (first year of implementation) %										
AB [g]	16.8	16.9	18.3	11.1	16.4	18.3	17.9	15.5	20.3	13.4
AA [h]	43.8	43.8	41.3	48.9	46.0	34.5	47.6	39.7	41.8	45.6
OM [i]	10.4	10.8	7.7	11.1	10.2	11.3	7.5	13.5	4.0	16.4
SA [j]	15.2	14.1	22.1	13.3	13.1	23.9	15.0	15.5	17.5	13.1
No measures	13.9	14.3	10.6	15.6	14.3	12.0	12.0	15.8	16.3	11.5
Not applicable	n=85									
Countermeasures to concerns for prognoses of patients "at risk" in 2016 %										
AB	9.7	9.8	9.8	7.8	10.1	7.7	11.1	8.0	10.6	8.8
AA	46.7	46.1	50.0	47.1	46.4	48.1	50.8	41.8	48.2	45.4
OM	13.6	13.0	13.4	21.6	13.8	12.8	9.9	18.1	6.0	20.7
SA	12.9	13.4	10.7	11.8	11.7	17.9	12.2	13.7	13.7	12.1
No measures	17.1	17.7	16.1	11.8	18.0	13.5	16.0	18.4	21.5	13.1

[a]Pm/Pv: Primary/ private clinic. [b]1/new1/2: First/new first/second-tier First-tier city, such as Beijing, Shanghai. New first-tier city, such as Chengdu, Hangzhou. Second -tier city, such as Shenyang, Xi'an. [c]IT/RS: intern/resident. [d]ACP/CP: Associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine. [g]AB: Prescribe the antimicrobials as before. [h]AA: Prescribe allowable antimicrobials. [i]OM: Prescribe other medicine (except antimicrobials). [j]SA: Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations.
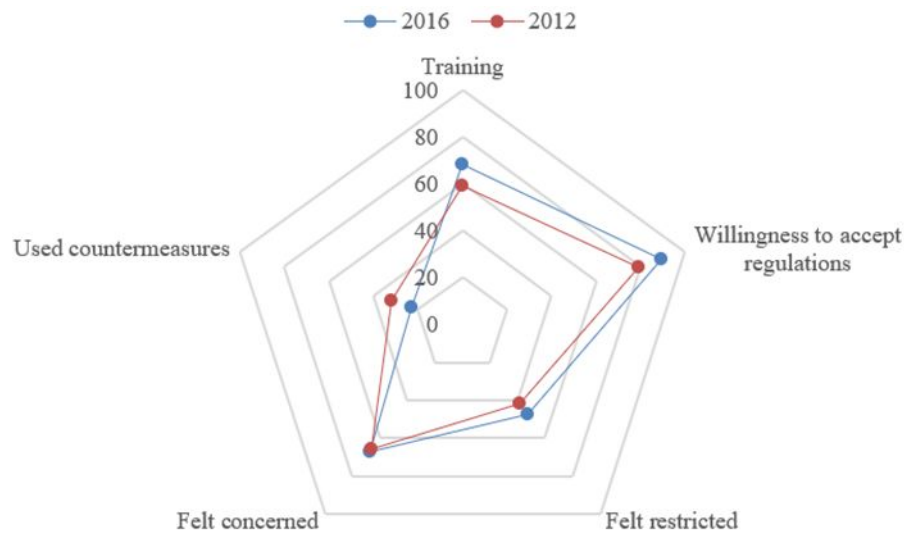
Figure 1 Attitudes and practice of doctors toward antimicrobial stewardship

Percentage of doctors who: received intensive or frequent compulsory stewardship training;

were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship;

felt often concerned or always concerned with the prognosis of patients "at risk"; prescribed

antimicrobials as before, or suggest patient-self-medication with restricted antimicrobials as

countermeasures

Table S1 Description of 107 WeChat groups and 3 Email groups

	19 WeChat groups -sent by researchers	88 WeChat groups -sent by key respondents	3 Email groups -sent by researchers
Description	Doctors currently working at departments of pediatrics, orthopaedics, diabetic, internal, oncology, endocrinology, et al.	Doctors currently working at departments of dermatologyy, oncology, respiratory medicine, paediatrics, orthopaedics, internal medicine, surgery, renal medicine, cardiology, gastroenterology, ICU, endocrinology, and general practitioners working within both urban and rural community health centers.	Members of Association of Pediatrics, Association of Diabetes, and Association of Internal Medicine in the World Federation of Chinese Medicine Societies.
Number of health professionals	2517	16640	634
Survey period	9th to 25th March 2017	22th to 30th March 2017	29th to 30th March 2017

Table S2 List of questionnaire items (translated from Chinese[a])

No	Questions	Answer categories
1	What is your occupation?	• Doctor • Nurse • Clinical postgraduate • Researcher • Administrative staff • Other
2	How old are you?	|__|__| years
3	What is your gender?	• Male • Female
4	What is your major?	• Western medicine • Traditional Chinese medicine • Integrative medicine of traditional Chinese medicine and western medicine
5	What is your highest educational level?	• College/diploma • Bachelor • MSc • MD or PhD
6	What is your level of seniority?	• Intern • Resident • Associate chief-physician • Chief-physician
7	When did your clinical work start?	• Before 2001 • 2002-2006 • 2007-2011 • From 2012 to now
8	How many days per week did you provide outpatient services between 2007 and 2011?	• 0 • 1 • 2 • 3 • 4 • 5
9	How many days per week did you provide outpatient services between 2012 and 2016?	• 0 • 1 • 2 • 3 • 4 • 5
10	Which city do you work in?	|__|__|__|__|
11	Which department do you work in?	__|__|__|__|
12	What is the level of your medical organization?	• 3-A • 3-B • 3-C

		●	2-A
		●	2-B
		●	2-C
		●	1-A
		●	1-B
		●	1-C
13	Which type of hospital are you based in?	●	Western medicine hospital
		●	Traditional Chinese medicine hospital
		●	Integrative medicine hospital of traditional Chinese medicine and western medicine
14	Is there an official requirement to restrict use of antimicrobials in your hospital?	●	No
		●	Less stringent
		●	Stringent
		●	Very stringent
15	What is/are your criteria for prescribing antimicrobials (multiple choice)?	●	Symptoms
		●	Signs
		●	Full blood count
		●	C-reactive protein detection
		●	Pathogen detection
		●	Diagnosis
		●	Others
16	Do you know the 'administrative regulations for the clinical use of antimicrobials' (hereinafter, antimicrobial stewardship regulations)?	●	Don't know
		●	Know a little
		●	Familiar
		●	Very familiar
17	Did you have any compulsory antimicrobial stewardship training in 2016?	●	No
		●	Less frequently
		●	Frequently
		●	Intensive
18	Did you have any compulsory antimicrobial stewardship training in 2012 (first year of stewardship implementation)?	●	No
		●	Less frequently
		●	Frequently
		●	Intensive
		●	Not applicable
19	How willing were you to accept the regulations in 2016?	●	Very willing
		●	Willing
		●	Hard to accept
		●	Unacceptable
20	How willing were you to accept the regulations in 2012 (first year of implementation)?	●	Very willing
		●	Willing
		●	Hard to accept
		●	Unacceptable
		●	Not applicable
21	In 2016, as a result of the potential influence of the	●	Very restricted

		antimicrobial stewardship, were there any restrictions on your antimicrobial prescription?	● Restricted ● Slightly ● Not restricted
	22	In 2012, as a result of the potential influence of the antimicrobial stewardship, were there any restrictions on your antimicrobial prescription?	● Very restricted ● Restricted ● Slightly ● Not restricted ● Not applicable
	23	Were you worried about the prognosis of patients "at risk" --who would have been given antimicrobials before the stewardship in 2016?	● Always ● Often ● Sometimes ● No
	24	If you were worried about the prognosis of patients "at risk" in the above question, what measures did you take to address your concern in 2016?	● Prescribe anyway the antimicrobials as before ● Prescribe allowable antimicrobials ● Prescribe other medicine (except antimicrobials) |_|_|_|_|_|_|_|_|_| ● Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations ● No measures
	25	Were you worried about the prognosis of patients "at risk" in 2012 (first year of implementation)?	● Always ● Often ● Sometimes ● No ● Not applicable
	26	If you were worried about the prognosis of patients "at risk" in the above question, what measures did you take to address your concern in 2012 (first year of implementation)?	● Prescribe anyway the antimicrobials as before ● Prescribe allowable antimicrobials ● Prescribe other medicine (except antimicrobials) |_|_|_|_|_|_|_|_|_| ● Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations ● No measures ● Not applicable
	27	Do you think the antimicrobial stewardship regulations have had any impact on the clinical prognosis of patients "at risk"?	● Strong ● Moderate ● Slight ● No
	28	What is the maximum permitted antimicrobial prescription rate in your medical organization?	|_|_|_|%
	29	What is the maximum permitted antimicrobial prescription rate in your department?	|_|_|_|%

30	For which operations should perioperative antimicrobial prophylaxis be used?	• Hernia repair
		• Resection of thyroid adenoma
		• Resection of mammary fibroadenoma
		• Open fractures debridement and internal fixation
31	Which antimicrobial should be used to treat extended-spectrum β-lactamase-producing bacterial infections?	• Carbapenems
		• Chloramphenicol
		• Macrolides
		• Aminoglycosides
32	For how long a restricted antibiotic can be used in emergent medical situations?	• 2 days
		• 1 day
		• 5 days
		• 30 days

[a]The English version of the questionnaire was translated from the original Chinese version by a native Chinese speaker, and then back translated into Chinese by another native Chinese speaker working in UK for 8 years.

Table S3 Demographic and practice characteristics of 807 respondents

Questions asked	Total n=807	Medical organization level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Female %	58.7	59.8	52.7	58.8	59.9	53.8	58.7	58.8	58.0	59.4
Age mean years	39.0	39.1	39.7	37.0	38.8	40.1	34.6	44.5	39.5	38.6
Education level %										
College/diploma	1.6	0.5	4.5	9.8	0.9	4.5	2.3	0.8	0.8	2.4
Bachelor	27.1	19.3	62.5	49.0	20.3	55.8	26.6	27.7	33.2	21.6
MSc	44.2	47.7	30.4	31.4	46.2	35.9	56.2	29.7	39.4	48.7
MD or PhD	27.0	32.6	2.7	9.8	32.6	3.8	14.9	41.8	26.7	27.3
Major %										
WM	47.8	48.8	51.8	27.5	43.9	64.1	47.6	48.1	NA	NA
TCM	37.7	37.4	32.1	52.9	41.9	19.9	35.9	39.8	NA	NA
IM	14.5	13.8	16.1	19.6	14.1	16.0	16.5	12.1	NA	NA
Seniority level%										
Intern	13.3	13.0	12.5	17.6	12.0	18.6	NA	NA	14.5	12.1
Resident	41.6	38.5	49.1	64.7	41.6	41.7	NA	NA	40.2	43.0
ACP	29.9	31.5	27.7	13.7	31.5	23.1	NA	NA	30.3	29.5
CP	15.2	16.9	10.7	3.9	14.9	16.7	NA	NA	15.0	15.4
Year starting to work %										
≤2001	38.9	38.7	44.6	29.4	52.5	46.2	13.1	70.3	44.3	34.0
2002-2006	22.6	21.9	19.6	37.3	22.6	22.4	23.5	21.4	24.1	21.1
2007-2011	22.2	21.9	25.0	19.6	23.5	16.7	34.1	7.7	17.9	26.1
≥2012	16.4	17.5	10.7	13.7	16.7	14.7	29.3	0.5	13.7	18.8
Outpatient service (days per week) in 2007-2011 %										
0	22.8	24.9	21.0	2.3	21.8	27.1	35.1	12.2	22.5	23.1
1	21.6	23.7	19.0	2.3	21.4	22.6	16.6	26.0	24.3	19.0
2	18.1	19.8	15.0	4.5	17.7	19.5	10.5	24.6	20.1	16.1
3	12.0	11.5	14.0	13.6	12.4	10.5	8.9	14.6	12.6	11.4
4	6.8	6.8	4.0	13.6	7.7	3.0	7.7	6.1	8.1	5.6
5	18.7	13.4	27.0	63.6	19.0	17.3	21.1	16.6	12.3	24.9
Not applicable	n=132									
Outpatient service (days per week) in 2012-2016 %										
0	15.4	16.8	13.4	2.0	14.1	20.5	25.5	3.0	15.5	15.2
1	22.6	25.3	15.2	3.9	22.0	25.0	19.9	25.8	27.2	18.3
2	21.7	22.7	18.8	15.7	21.0	24.4	14.9	29.9	23.3	20.2
3	14.3	13.5	18.8	13.7	14.9	11.5	13.3	15.4	13.5	15.0
4	8.7	8.9	5.4	13.7	10.1	2.6	7.9	9.6	8.8	8.6
5	17.5	12.9	28.6	51.0	17.8	16.0	18.5	16.2	11.7	22.8

[a]Pm/ Pv: Primary/ private clinic. [b]1/new1/2: First/new first/second–tier. First-tier city, such as Beijing, Shanghai. New first-tier city, such as Chengdu, Hangzhou. Second -tier city, such as Shenyang, Xi'an. [c]IT/RS: intern/resident. [d]ACP/CP: Associate chief-physician/chief-physician. [e]WM: western medicine.

fTCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

Table S4 Medical organization of 807 respondents

Questions asked	Total n=807	Medical organization level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/ Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/ CP [d] n=364	WM [e] n=386	TCM/ IM [f] n=421
Medical organization level %										
Tertiary	79.8	NA	NA	NA	83.4	64.7	74.9	85.7	81.3	78.4
Secondary	13.9	NA	NA	NA	9.8	30.8	15.6	11.8	15.0	12.8
Primary	5.0	NA	NA	NA	5.5	2.6	7.4	1.9	2.3	7.4
Private clinic	1.4	NA	NA	NA	1.2	1.9	2.0	0.5	1.3	1.4
Medical organization type %										
WM	51.9	51.1	61.6	41.2	47.9	68.6	51.5	52.5	84.5	22.1
TCM	34.7	37.0	30.4	15.7	38.4	19.2	31.4	38.7	5.7	61.3
Integrative	13.4	12.0	8.0	43.1	13.7	12.2	17.2	8.8	9.8	16.6
City level %										
First-tier	37.1	37.7	18.8	68.6	NA	NA	37.0	37.1	34.2	39.7
New first-tier	23.7	24.8	24.1	7.8	NA	NA	23.7	23.6	21.8	25.4
Second-tier	20.0	21.7	14.3	9.8	NA	NA	18.1	22.3	18.1	21.6
Third-tier	9.0	7.3	22.3	2.0	NA	NA	9.3	8.8	12.4	5.9
Fourth-tier	5.9	3.9	17.0	7.8	NA	NA	6.3	5.5	7.8	4.3
Fifth-tier	4.3	4.5	3.6	3.9	NA	NA	5.6	2.7	5.7	3.1
Geographic region %										
Eastern	49.2	48.6	38.4	80.4	53.6	30.8	50.6	47.5	47.2	51.1
Central	10.7	9.0	20.5	9.8	7.1	25.6	11.1	10.2	13.0	8.6
Western	21.4	20.5	33.0	7.8	17.7	37.2	21.0	22.0	34.7	9.3
Northeast	18.7	21.9	8.0	2.0	21.7	6.4	17.4	20.3	5.2	31.1

[a]Pm/ Pv: Primary/ private clinic. [b]1/new1/2: First/new first/second–tier. First-tier city, such as Beijing, Shanghai. New first-tier city, such as Chengdu, Hangzhou. Second -tier city, such as Shenyang, Xi'an. [c]IT/RS: intern/resident. [d]ACP/CP: Associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

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	2-3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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	*6*
Bias	9	Describe any efforts to address potential sources of bias	5-7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	/
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	/
		(*e*) Describe any sensitivity analyses	/
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	7
		(b) Give reasons for non-participation at each stage	/
		(c) Consider use of a flow diagram	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-8
		(b) Indicate number of participants with missing data for each variable of interest	/
Outcome data	15*	Report numbers of outcome events or summary measures	7
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	8-10

		(*b*) Report category boundaries when continuous variables were categorized	Table1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	/
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-10

Discussion

Key results	18	Summarise key results with reference to study objectives	10-11
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	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	12

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

*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.

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How far do we still need to go? A survey on knowledge, attitudes, practice related to antimicrobial stewardship regulations among Chinese doctors in 2012 and 2016

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How far do we still need to go? A survey on knowledge, attitudes, practice

related to antimicrobial stewardship regulations among Chinese doctors in 2012

and 2016

Ruyu Xia[1], Xiaoyang Hu[2]†, Merlin Willcox[2]†, Xinxue Li[3], Yuxiu Li[4], Jian Wang[5],

Xun Li[1], Michael Moore[2], Jianping Liu[1], Yutong Fei[1]*

[1]Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese

Medicine, Beijing, China;

[2]Primary Care and Population Sciences, University of Southampton, Southampton,

UK; [3]Department of International Liaison, World Federation of Chinese Medicine

Societies, Beijing, China;

[4]Department of endocrinology, South of Guang'anmen Hospital, China Academy of

Chinese Medical Sciences, Beijing, China;

[5]Department of neurology, The Affiliated Hospital of Changchun University of

Chinese Medicine, Changchun, China.

*Corresponding author. Tel: +86 10 6428 6757; E-mail: feiyt@bucm.edu.cn. Postal

address: No. 11, Bei San Huan Dong Road, Chaoyang District, Beijing 100029, China

†These authors contributed equally

ABSTRACT

Objectives: To explore doctors' knowledge, willingness, concerns and the countermeasures to the most stringent antimicrobial stewardship regulations of China (2012).

Design: Cross-sectional survey.

Setting: China.

Methods: A pretested 32-point structured questionnaire was distributed to doctors by sending a web link via the mobile phone application WeChat through snow-ball sampling methods and email groups of medical academic societies. The questionnaire inquired about the doctors' experiences, knowledge, willingness, concerns and the countermeasures to the stewardship policies. Mann-Whitney test, $\chi 2$ test and multivariate regression were applied where appropriate.

Results: There were 807 doctors from 29 provinces in mainland China fully completed the questionnaire. Doctors had a mean age of 39.0 years. The majority (78.9% in 2012, 89.1% in 2016) reported that they were willing or very willing to accept the regulations. Almost all respondents (93.2%) felt the stewardship regulations had the potential to adversely affect the prognosis of patients who would have been prescribed antimicrobials before they were implemented, and more than 65% (65.7% in 2012, 66.9% in 2016) of doctors were often or always concerned about the prognosis of these patients. In 2012, 32% of doctors prescribed restricted antimicrobials or suggested patient self-medication with restricted antimicrobials to address doctors' concerns, and this number decreased to 22.6% in 2016. Although compulsory antimicrobial stewardship training was frequent, less than half of respondents (46.8%) responded correctly to all three knowledge questions.

Conclusion: Antimicrobial stewardship regulations had some positive effect on rational antimicrobial use. Willingness and practice of doctors towards the regulations improved from 2012 to 2016. Knowledge about rational antimicrobial use was still lacking. Doctors found ways of accessing restricted antibiotics to address their concerns about the prognosis of patients, which undermined the implementation of the stewardship regulations.

Strengths and limitations of this study

- The paper is the first to comprehensively explore doctors' feelings and attitudes towards the Chinese antimicrobial stewardship regulations.
- The survey recruited participants and administered the survey via WeChat, which is a convenient, time-saving and economic method to survey a diverse population. Our respondents covered 29 of 32 administrative divisions of mainland China.
- We cannot rule out a possible selection bias as our sample was not randomly selected. Although the snowball sampling method is effective and efficient when sampling from specific populations, participants that can be reached depend on the social connections of the key respondents.
- Another limitation is the potential recall bias of information provided for year 2012 and 2016.

INTRODUCTION

The efficacy of antimicrobials is threatened by increasing levels of antimicrobial resistance.[1] [2] In 2014, it was estimated that China consumed 77,760 tons of antimicrobial agents for humans and the defined daily doses per 1000 inhabitants per day were approximately 6 times larger than in the UK, USA, Canada and Europe.[3]

During the past decade, the Chinese Government has issued a series of health care regulations.[4-7] The "Administrative regulations for the clinical use of antimicrobials", issued in August 2012, were the most stringent regulations ever (Box 1).[6] Several studies reported changes in the prescription rates of antibiotics to reflect the impact of the 2012 stewardship regulations,[8-10] but we did not find any study which investigated the attitudes of Chinese doctors towards these regulations, although they might be an important barrier to implementation of the regulations.

Our study aimed to explore knowledge, willingness, concerns and the countermeasures of doctors towards the most stringent antimicrobial stewardship regulations of China (2012) via a web-based survey. Specifically, we looked at: 1) what did they experience; 2) how good was their knowledge about prescribing antimicrobials; 3) what were their feelings (willingness/reluctance) towards the regulations (over a five-year duration of implementation) when they were practicing; 4) what were the countermeasures, if any were used.

METHODS

Survey recruitment

A snowball sampling strategy, focus on recruiting docors practing in mainland China, was utilised. Participants were reached by the mobile phone Application (APP) WeChat and emails. WeChat is currently the most widely used social media platform in China, with more than one billion users.[11] Akin to a hybrid of Twitter, Facebook and WhatsApp, WeChat combines the functions of instant messaging, a blog, and a social networking site. The invitations to participate in the survey were sent first to clinicians' WeChat groups by researchers, then they were cascaded by purposively inviting key respondents to send the link to their clinicians' WeChat groups in order to increase respondent sample size (WeChat groups details in Table S1). Email invitations were only sent to members of the World Federation of Chinese Medicine Societies. The professional occupation screening function was turned on therefore only those who identified themselves as doctors were able to proceed to the survey questions, others were directed politely to the end of the survey.

Data collection

The tool for collecting data is the questionnaire based in the WenJuanXing online survey service (English name "SurveyStar", Changsha Ranxing Science and Technology Ltd, Shanghai, China), which is a online survey platform, akin to SurveyMonkey.

Survey questionnaire

The study was performed between March 9th to March 30th 2017 using a piloted 32-point structured questionnaire (see Table S2[12]). The structured questionnaire consisted of questions about four categories of variables: (a) demographics and practice characteristics of the doctors; (b) implementation of the antimicrobial stewardship in health care facilities; (c) attitude (willingness, concerns) and practice(impacts on prescribing antibiotic behaviour, countermeasures to concerns) of doctors towards 2012 antimicrobial stewardship regulations; (d) doctors' knowledge of antimicrobial stewardship regulations and proper use of antimicrobials (question 30-32 originated from training examination questions for "guiding principles for clinical application of antibacterial" [4] and "administrative regulations for the clinical use of antimicrobials" [6]). The questionnaire was about 18 phone screens long, which took approximately 5 minutes to complete. We consulted two doctors and one methodologist and conducted a pilot survey with 10 doctors before starting the formal survey.

Data were imported from the survey website into Microsoft Excel 2016, then converted into the SPSS database. Statistical analysis was performed using IBM SPSS Statistics for Windows, V.23.0 (IBM, Armonk, New York, USA). Descriptive statistics, Mann-Whitney test, $\chi 2$ test and multivariate regression were applied in description and analysis of the variables, where appropriate. Compulsory antimicrobial stewardship training, doctor's acceptance, impact on prescribing antibiotic behaviours, impact on prognosis of patients, concern and countermeasures

towards the antimicrobial stewardship at the beginning of the implementation (2012) and five years after that (2016) were compared. Doctors with different educational background, levels of seniority, practicing organisations and geographic regions were considered as subgroups and compared. Logistic regression was used to screen factors relevant to knowledge of clinical use of antimicrobials.

Ethical approval for this study was obtained from the Ethical committee, Beijing University of Chinese Medicine (2017BZHYLL0201). Informed consent was obtained from all the participants. Participants were informed at the start of the survey about the length of time needed to complete the survey, the investigators and the purpose of the study. Participants were free to continue the survey or to quit at any time. Anonymous data were collected. No incentive was used to reward participants.

Patient and public involvement

No patient or public was involved in this study.

RESULTS

Procedures

The questionnaire was sent to 107 WeChat groups and 3 email groups that include 19791 health professionals (maximum number of potential reach). There were 3609 health professionals (actual reach) who clicked the web link of the questionnaire, out of whom 1194 completed the survey. Among the survey respondents, 807 were doctors; others were nurses, researchers, clinical postgraduates, or administrative staffs.

Demographics

Data provided by doctors were collected and analysed. All 807 doctors fully completed the online survey (Tables S3 and S4). Doctors had a mean age of 39.0 years (SD=7.4), range 22 to 68. Men account for 41.3% of the total. More than 70% of doctors（71.2%) had MSc, MD or PhD degree (n=575). Most of them were residents or associated chief-physicians (n=336; 41.6% and n=241; 29.9% respectively). Approximately half (n=386; 47.8%) of doctors majored in western medicine, others majored in traditional Chinese medicine or integrative medicine. 83.7% doctors started clinical practice before 2012. The number of outpatient services provided weekly was diverse, ranging from none (22.8% and 15.4% in 2007-2011 and 2012-2016 respectively) to 5 days (18.7%; 17.5%). Although almost half of doctors were from eastern China (49.2%), there was also a good number from central, western and north-eastern China. About three in every five (60.8%) of the doctors were working in first-tier and new first-tier cities (e.g. Beijing, Shanghai and Hangzhou). Most doctors (79.8%) worked in tertiary hospitals.

Experiences of implementation of the antimicrobial stewardship regulations

The clear majority of practitioners reported that hospital implementation of antimicrobial stewardship regulations was stringent (45.1%) or very stringent (45.7%) (Table 1). Specific training sessions were frequent or intensive in 2012 (59.1%) and in 2016 (68.5%) (p< 0.001) (Figure1). Practitioners from tertiary western medicine hospitals in first/new first-tier cities reported more stringent requirements for the

implementation of the regulations (Figure 2, Figure S1, S2 and S3). Doctors in departments of respiratory medicine, emergency medicine, paediatrics, intensive care, haematology, and dentistry reported that they were permitted higher upper limits than the general limits of their hospitals. The largest gap in antimicrobial prescription limits was between respiratory departments (33.5%) and hospitals overall, irrespective of departments (22.4%).

Knowledge of antimicrobial stewardship regulations and proper use of antimicrobials

Although most doctors (65.1%) declared that they were familiar or very familiar with the 2012 stewardship regulations, less than half answered the three-question knowledge test (question 30-32) correctly (46.8%) (Table 2). Doctors from primary care had a lower correct rate compared to those from other hospitals (P=0.013); doctors who majored in traditional Chinese medicine had a lower correct rate compared to those who majored in western/integrative medicine as measured in the multivariate regression equation (P=0.001). The most commonly reported criteria for prescribing antimicrobials were full blood count (94.2%), pathogen detection such as sputum or blood culture (77.0%), symptoms (72.9%), signs (71.4%), C-reactive protein level (62.9%) and the diagnosis (60.5%).

Attitudes towards implementation of the antimicrobial stewardship regulations

In 2012, 78.9% of doctors reported that they were willing or very willing to accept the regulations, and the percentage increased to 89.1% in 2016 (p=0.002) (Table 3). In

2012 and 2016, doctors who majored in western medicine reported lower acceptance rates (74.6%; 86.5%) than those who majored in Chinese medicine or integrative medicine (82.9%; 91.4%). 30.0% of doctors reported the antimicrobial stewardship regulations had a moderate or large impact on the prognosis of these patients "at risk" (means patients who would have been prescribed antimicrobials before the implementation of the 2012 stewardship regulations). Only 6.8% of doctors felt the stewardship regulations did not result in putting the prognosis of these patients "at risk". More than 65% of doctors (65.7% in 2012, 66.9% in 2016; p=0.367) were 'often or always concerned' about the prognosis of patients "at risk".

Doctors' practice of the antimicrobial stewardship regulations

In 2012, 41.6% of doctors reported that prescribing of antimicrobials had been very (6.1%) or moderately (35.5%) restricted during the implementation of antimicrobial stewardship regulations (Table 3). The percentages even increased in 2016 (8.4%; 38.9%) (2016 vs 2012, p=0.019). In 2012, 32% of doctors stated that they had prescribed or suggested patient self-medication with restricted antimicrobials (restricted by the specific criteria for conditions in the stewardship) to address concerns for patients "at risk" (Figure 1), but it decreased to 22.6% in 2016 (2016 vs 2012, p< 0.001). In 2012, This prescribing behaviour was reportedly more common (42.2%) in small cities, but in 2016 there no longer seemed to be any obvious difference between city levels. This behaviour was higher among doctors who majored in western medicine than among those who majored in traditional Chinese

medicine or integrative medicine (37.8% and 26.5% respectively in 2012, 24.3% and 20.9% in 2016). This proportion was higher among interns (44.6% in 2012; 30.8% in 2016) than other doctors (30.7% in 2012; 21.3 in 2016). More doctors prescribed permitted antimicrobials in 2016 than in 2012 (46.7%, 43.8%) when treatment was needed. In 2012 and 2016, 13.6% and 10.4% prescribed alternatives to antimicrobials; 95.8% (69/72) and 96.2% (102/106) of these prescribed traditional Chinese medicines.

DISCUSSION

Summary of findings

The data were collected from doctors in China with all medical education background, levels of seniority of the doctors, covering those who work in all levels of cities, types of medical organisations, and levels of medical organisations (table S3, table S4). The data covered doctors from 29/32 administrative divisions of mainland China, representing nearly all regions of China. Although about half (49.2%) of our respondents were based in Eastern China, this reflects the proportion of doctors in Eastern China, which accounts for about 43% of doctors in China.[13] Since the respondents are those with higher educational background and work in higher level hospital level than average, their knowledge, attitudes, practice related to stewardship may be overestimated.

The implementation of the 2012 stewardship regulations was considered stringent. The percentage of all prescriptions which are permitted to contain antimicrobials in

respiratory departments was set to be high by the answers from the doctors, with an average of 33.5%. Insufficient knowledge on proper use of antimicrobials was obvious, especially in primary medical organisations. Most doctors (94.2%) used full blood count as the criterion for prescribing antimicrobials. Compulsory stewardship training and willingness to accept the stewardship regulations increased from 2012 to 2016. Due to restricted prescription of antimicrobials, doctors' concerns with prognosis of patients "at risk" remained high. It seems that the use of restricted antimicrobials has greatly reduced, but the use of permitted antimicrobials may have increased. Traditional Chinese medicine may have played a role as an alternative to antimicrobials.

Strengths and limitations

To the best of our knowledge, this is the first survey in China to comprehensively explore doctors' feelings and attitudes toward the Chinese antimicrobial stewardship regulations. We recruited participants and administered the survey via WeChat (one of the most common social APPs in China). It is a convenient, time-saving and economic method to survey a diverse population. Our respondents covered 29 of 32 administrative divisions of mainland China. Despite this, our study has a number of limitations. Firstly, we cannot rule out a possible selection bias as our sample was not randomly selected. Although the snowball sampling method is effective and efficient when sampling from specific populations, participants that can be reached depend on the social connections of the key respondents. Also, doctors in primary care settings

or private clinics are less likely to belong to any academic association or doctors' group, thus they may be less likely to be reached. According to the data of the Chinese government,[13] the percentage of doctors in primary care settings and private clinics are about 4.3% and 11.4% in China in 2016 respectively. In this survey, doctors in primary care settings and private clinics accounted for 5.0% and 1.4% of respondents respectively. In addition, the use of clinician's WeChat groups by researchers for first invitations may also be one of the reasons for potential bias. Our professional connections are more likely to be similar to ourselves. In order to overcome this potential bias, we invited our first-round invitation receivers to send our links to their own clinician connections. This may have helped to correct the selection bias that relate to our first invitation receivers. We also invited members of academic associations in our first invitations and most of the members of those associations are usually academic clinicians. In China, about 80% of the clinicians work in public hospitals,[13] conducting or participating in academic research is a requirement for them. Most of the clinicians need to work both clinically and academically. Secondly, the proportion of completed questionnaires to all potential responders is low (6.0%, 1194/19791), similar to the other web-based surveys.[14] [15] 19791 is the sum of people in all the WeChat groups. This is the maximum number of people that potentially can be reached by us. There is no way to collect the number of people who saw the link but choose to ignore it. The number of people who clicked the link is an important parameter that we can achieve. 3618 people clicked the link

and 1194 completed it (33.0%, 1194/3618). Another limitation is the potential recall bias of information provided for year 2012 and 2016.

Comparisons with other studies

We did not identify any studies investigating the attitudes of doctors towards the 2012 antimicrobial stewardship regulations. Doctors' willingness and concerns might impact on their prescribing behaviors and weaken the effects of the regulations. We found in our study that the knowledge about proper use of antimicrobials of doctors from primary care clinics or private clinics seems insufficient. Similar results were reported from three surveys (sample sizes 761, 180, 611) focusing on doctors' or trainees' knowledge and continued education.[16-18] In our study, doctors reported that they recommended self-medication of restricted antimicrobials to address concerns for patients "at risk". Another survey of 256 pharmacies in three Chinese cities[19] showed that antibiotics were obtained without a prescription from 77.7% pharmacies for adult respiratory infections. In our study, the percentage of all prescriptions which are permitted to contain antimicrobials in respiratory departments was very high. A survey of 1204 people in three Chinese cities[20] showed that cough, sore throat, and bronchitis were the most frequent reasons reported for antibiotic use. This is also consistent with the situation in the UK.[21]

In our study, full blood count (raised white blood cell counts and increased proportion of neutrophilic granulocytes) was overwhelmingly considered as the main criterion for prescribing antimicrobials. This medical behavior is in accordance with

the Chinese acute bronchitis clinical practice guidelines,[22] [23] which state that oral antibiotics such as β-lactams and fluoroquinolones can be used in patients with cough before the pathogen detection results were available, if there are signs of purulent sputum or raised white cell counts (Adults usually more than 10×10^9/L). However, it has been suggested by international guidelines that doctors should not perform testing or initiate antibiotic therapy in people with acute bronchitis (pneumonia excluded).[24] Studies[25] [26] have shown that blood tests do not accurately differentiate between bacterial and viral infections. In our survey, many doctors also reported using raised CRP as a criterion for prescribing antimicrobials. CRP may be helpful in adults and is recommended in the NICE guidelines[27] to be considered if antibiotics are being considered for treatment of lower respiratory tract infections. A study has shown that use of CRP can reduce antibiotic consumption in acute respiratory tract infections.[28] However, Lemiengre and colleagues performed a cluster-randomised trial in 2227 children showing that CRP tests did not reduce antibiotic prescribing for non-severe acute infections in children in primary care and cannot be recommended.[29] In our survey, doctors with a traditional Chinese medicine/integrative medicine background felt less restricted and were more willing to accept the stewardship regulations. Traditional Chinese medicines served as alternatives to antimicrobials for doctors. Similarly, in the UK, a retrospective study which included 7283 General Practice (GP) surgeries suggested that GPs additionally trained in integrative medicine or complementary and alternative medicine had lower antibiotic prescribing rates

compared with conventional GPs.[30]

Implications for doctors and policy makers

The implementation of the antimicrobial stewardship regulations requires administrative persistence and strengthened training of doctors on the use of antimicrobials, especially for primary care doctors. In addition to the mandatory administrative implementation, explanation of reasons why there is a need for proper use of antimicrobials and how to achieve it, as well as approaches to facilitate evidence-based clinical practicing are needed to guide clinical practice and to relieve doctors' concerns. The common practice of prescribing antimicrobials according to elevated full blood count or CRP is controversial. Although both guidelines and the stewardship regulations mentioned this, no threshold was defined. Suggested patient self-medication with restricted antimicrobials may have diminished the effect of the antimicrobial stewardship regulations. The increase in the use of permitted antimicrobials may be associated with inappropriate use, which is also an important cause of antimicrobial resistance. More stringent measures should be applied to stop antimicrobial purchase without prescriptions from retail pharmacies. Traditional Chinese medicine can be considered for relieving symptoms, complementing or replacing antimicrobials.[31]

Future research

First, there is a need for qualitative research to explore antibiotic prescribing behaviours in China, potential concerns from doctors and pharmacists, why there

were differences between doctors in different types of hospitals/regions/major, and which intervention(s) would be most acceptable in their context to reduce antimicrobial prescribing. Then, we also suggest that a large representative sample cohort study or registry study in China is warranted, to explore the possibility of delayed antimicrobials or other antimicrobial replacement therapy from the perspectives of clinical effect, safety, reducing resistance and health economics. There is a need for more evidence to back up recommendations, particularly on (i) diagnostic and prognostic accuracy of various markers e.g. white cell counts and CRP; (ii) prognosis of infections for which antibiotics were commonly prescribed; (iii) guidelines and recommendations on when to use antibiotics. Additionally, we need to find other interventions that can relieve symptoms, complement or substitute antimicrobials, and then conduct high quality, large scale randomised controlled trials to validate their efficacy, effectiveness and safety. Traditional Chinese medicine is widely used in medical practice in China.[32] We propose more clinical or basic research to explore which traditional Chinese medicine can be recommended instead of antibiotics for different infections.

Conclusion

In summary, the 2012 antimicrobial stewardship regulations improved proper clinical use of antimicrobials in China. Attitudes and behaviours of doctors towards the stewardship regulations improved from 2012 to 2016. Concerns about the prognosis of patients "at risk" were still prevalent, and doctors found ways of accessing

antibiotics which undermined the implementation of the antimicrobial stewardship regulations. There is a gap between doctors in small cities and first-tier cities in terms of implementation of antimicrobial stewardship regulations and knowledge about proper use of antimicrobials.

Ethics approval: This study was approved by the ethical committee of Beijing

University of Chinese Medicine (2017BZHYLL0201).

Data sharing: No additional data are available.

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The "Administrative regulations for the clinical use of antimicrobials" was issued and implemented by the National Health and Family Planning Commission (NHFPC, the former Ministry of Health)

What are the regulations about?

In the 2012 stewardship regulations, all hospitals in China were required to set up an antimicrobial agents administrative group or identify a point person to take control of antimicrobial stewardship. Infectious diseases departments and clinical microbial laboratories were required to be set up in all tertiary and secondary hospitals. Antibacterial agents were classified according to safety, efficacy, bacterial resistance, price and other factors. Prescribers have accredited prescription rights for different categories of antimicrobials, depending on their levels of seniority. Compulsory standardised trainings on the knowledge of clinical use of antimicrobials are required for all doctors.

How was it supposed to be implemented or enforced? How was implementation monitored?

NHFPC established the Centre for Antibacterial Surveillance and the China Antimicrobial Resistance Surveillance System to monitor the use of antibiotics and antibiotic resistance in hospitals. Surveillance systems within their respective administrative areas would be developed by local health administrative departments. The rankings of total usage of antimicrobials, classification of antimicrobials, and percentage of prescriptions for antimicrobials in health facilities in their respective administrative regions are published and submitted to the higher authorities for the record. Managers of poorly performing health facilities are admonished. This is to ensure rational use of antimicrobial agents in healthcare settings.

Were there any sanctions for not implementing it?

Health facilities that fail to meet the requirements would be downgraded to a lower classification level. Doctors who fail to pass the exam of standard training or seriously violate the regulations can lose their accreditation to prescribe antibiotics, and/or have their professional qualification revoked. If doctors' actions led to serious consequences, they could be fined or prosecuted.

Who was responsible for implementing it?

NHFPC and local health administration investigate and reassign responsibility to hospital presidents or health facility management staff.

Box 1 Translated summary of "administrative regulations for the clinical use of antimicrobials" [6]

Table 1 Implementation of the antimicrobial stewardship regulations

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Medical organisation antimicrobial stewardship implementation %										
Very stringent	45.7	50.6	33.0	11.8	47.9	36.5	44.2	47.5	50.0	41.8
Stringent	45.1	44.1	50.0	47.1	44.2	48.7	45.1	45.1	44.0	46.1
Less stringent	7.8	4.5	16.1	31.4	6.5	13.5	9.0	6.3	5.4	10.0
No	1.4	0.8	0.9	9.8	1.4	1.3	1.6	1.1	0.5	2.1
Compulsory antimicrobial stewardship training in 2012 (first year of stewardship implementation) %										
Intensive	9.7	10.9	6.3	3.9	11.4	2.7	8.3	11.4	11.1	8.4
Frequent	49.4	52.4	41.4	31.4	50.6	44.5	47.6	51.4	50.0	48.8
Less frequent	36.6	33.2	49.5	49.0	33.9	47.9	38.8	34.2	35.1	38.1
No	4.2	3.5	2.7	15.7	4.1	4.8	5.3	3.1	3.8	4.6
Not applicable	n=48									
Compulsory antimicrobial stewardship training in 2016 %										
Intensive	12.6	14.0	8.0	5.9	14.1	6.4	12.4	12.9	13.5	11.9
Frequently	55.9	58.1	50.0	41.2	55.9	55.8	53.0	59.3	56.0	55.8
Less frequency	28.6	26.4	38.4	35.3	27.0	35.3	30.5	26.4	28.0	29.2
No	2.9	1.6	3.6	17.6	2.9	2.6	4.1	1.4	2.6	3.1
% of all prescriptions which are permitted to contain antimicrobials (according to the hospital's internal policy) %										
≤20%	59.8	60.1	44.4	86.0	65.6	39.7	62.0	57.5	47.7	72.0
21-40%	32.9	33.3	43.2	9.3	29.8	43.7	31.5	34.4	43.8	22.0
41-60%	6.5	5.9	12.3	2.3	4.1	15.1	5.5	7.7	7.8	5.3
>60%	0.7	0.7	0.0	2.3	0.5	1.6	1.0	0.4	0.7	0.7
Not reported	n=242									
% of all prescriptions which are permitted to contain antimicrobials (according to the department's internal policy) %										
≤20%	64.1	64.1	51.9	86.0	69.5	45.2	65.4	62.6	53.7	74.5
21-40%	26.5	26.6	34.2	11.6	23.5	37.3	24.3	28.9	34.3	18.8
41-60%	8.0	7.4	13.9	2.3	6.2	14.3	8.2	7.7	9.5	6.4
>60%	1.4	1.8	0.0	0.0	0.9	3.2	2.1	0.7	2.5	0.4
Not reported	n=242									

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second-tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second-tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

Table 2 Knowledge of antimicrobial stewardship

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Self-reported knowledge of antimicrobial stewardship %										
Very familiar	16.1	17.1	12.5	11.8	16.9	12.8	10.6	22.8	18.9	13.5
Familiar	48.9	49.4	52.7	35.3	48.8	49.4	44.0	54.9	47.2	50.6
Know a little	31.0	30.0	32.1	41.2	30.0	35.3	39.5	20.6	30.3	31.6
Don't know	4.0	3.6	2.7	11.8	4.3	2.6	5.9	1.6	3.6	4.3
Tested results of knowledge of antimicrobial prescribing										
Which surgery should apply perioperative antimicrobial prophylaxis										
% of correct	91.9	91.6	93.8	92.2	92.5	89.7	92.3	91.5	92.2	91.7
Which antimicrobial should be used for extended-spectrum β-lactamases-producing bacterial infection										
% of correct	70.5	72.1	74.1	43.1	69.3	75.6	65.2	76.9	78.2	63.4
For how long a restricted antibiotic can be used in emergent medical situations										
% of correct	66.7	67.7	72.3	41.2	66.1	69.2	64.3	69.5	72.3	61.5
Criteria for prescribing antimicrobials (multiple choice) %										
Symptom	72.9	75.9	67.9	45.1	72.4	75.0	74.3	71.2	75.6	70.3
Sign	71.4	73.6	70.5	45.1	70.8	74.4	71.1	71.7	72.8	70.1
Full blood count	94.2	95.0	92.0	88.2	95.4	89.1	95.0	93.1	92.7	95.5
CRP [g]	62.9	64.0	59.8	56.9	62.2	66.0	61.9	64.3	61.7	64.1
PD [h]	77.0	83.2	65.2	23.5	92.0	78.2	75.4	78.8	84.2	70.3
Diagnosis	60.5	62.9	58.9	33.3	60.7	59.6	58.9	62.4	68.9	52.7
Others	18.2	19.3	14.3	13.7	18.7	16.0	17.8	18.7	21.5	15.2

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second-tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second-tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine. [g]CRP: C-reactive protein detection. [h]PD: pathogen detection.

Table 3 Attitudes and practice of doctors towards the antimicrobial stewardship regulations in 2012 and 2016

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/ Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/ CP [d] n=364	WM [e] n=386	TCM/ IM [f] n=421
Personal willingness to accept antimicrobial stewardship regulations in 2012 (first year of implementation) %										
Very willing	26.5	26.3	18.9	45.8	28.4	18.6	27.9	25.1	24.0	28.8
Willing	52.4	52.6	52.8	47.9	53.3	48.6	49.7	55.2	50.6	54.0
Hard to accept	19.2	19.0	26.4	6.3	16.4	31.4	20.6	17.7	23.2	15.6
Unacceptable	1.9	2.1	1.9	0.0	2.0	1.4	1.8	2.0	2.3	1.6
Not applicable	n=68									
Personal willingness to accept antimicrobial stewardship regulations in 2016 %										
Very willing	27.4	28.4	17.0	37.3	27.6	26.3	24.2	31.3	25.9	28.7
Willing	61.7	60.9	69.6	54.9	61.9	60.9	64.3	58.5	60.6	62.7
Hard to accept	10.0	9.8	13.4	5.9	9.5	12.2	10.6	9.3	12.2	8.1
Unacceptable	0.9	0.9	0.0	2.0	0.9	0.6	0.9	0.8	1.3	0.5
Impact of antimicrobial stewardship on prescribing antibiotic behaviors in 2012 (first year of implementation) %										
Very restricted	6.1	6.2	5.6	6.1	6.0	6.3	7.0	5.1	7.0	5.2
Restricted	35.5	36.9	35.5	18.4	35.7	34.7	37.4	33.4	35.9	35.1
Slightly	48.3	48.0	46.7	55.1	48.2	48.6	45.5	51.4	49.0	47.6
Not restricted	10.1	8.9	12.1	20.4	10.1	10.4	10.1	10.1	8.1	12.0
Not applicable	n=66									
Impact of antimicrobial stewardship on prescribing antimicrobial behaviors in 2016 %										
Very restricted	8.4	8.5	9.8	3.9	8.0	10.3	7.4	9.6	10.6	6.4
Restricted	38.9	39.1	43.8	25.5	38.2	41.7	43.1	33.8	41.2	36.8
Slightly	43.5	43.6	40.2	49.0	44.2	40.4	41.5	45.9	40.7	46.1
Not restricted	9.2	8.7	6.3	21.6	9.5	7.7	7.9	10.7	7.5	10.7
Concerns with prognosis of patients "at risk" --who would have been given antimicrobials before the stewardship in 2012 (first year of implementation) %										
Always	16.8	17.1	19.3	8.3	13.9	29.2	18.5	15.0	19.7	14.1
Often	48.9	48.0	51.4	54.2	50.9	40.3	49.1	48.6	50.8	47.0
Sometimes	29.9	30.2	27.5	31.3	30.1	29.2	27.2	32.8	25.3	34.2
No	4.4	4.8	1.8	6.3	5.2	1.4	5.1	3.7	4.2	4.7
Not applicable	n=64									
Concerns with prognosis of patients "at risk" in 2016 %										
Always	12.6	12.7	16.1	3.9	11.5	17.3	14.7	10.2	14.5	10.9
Often	54.3	53.9	58.0	51.0	53.3	58.3	54.9	53.6	56.2	52.5
Sometimes	26.8	26.9	22.3	35.3	28.3	20.5	24.6	29.4	24.1	29.2
No	6.3	6.5	3.6	9.8	6.9	3.8	5.9	6.9	5.2	7.4
Impact of antimicrobial stewardship on prognosis of patients "at risk" %										
Strong	2.4	2.3	1.8	3.	2.5	1.9	2.3	2.5	2.6	2.1

Moderate	27.6	26.9	31.3	29.4	27.0	30.1	31.8	22.5	27.7	27.6
Slight	63.2	64.1	61.6	56.9	63.3	62.8	59.6	67.6	63.5	62.9
No	6.8	6.8	5.4	9.8	7.2	5.1	6.3	7.4	6.2	7.4
Countermeasures to concerns for prognosis of patients "at risk" in 2012 (first year of implementation) %										
AB [g]	16.8	16.9	18.3	11.1	16.4	18.3	17.9	15.5	20.3	13.4
AA [h]	43.8	43.8	41.3	48.9	46.0	34.5	47.6	39.7	41.8	45.6
OM [i]	10.4	10.8	7.7	11.1	10.2	11.3	7.5	13.5	4.0	16.4
SA [j]	15.2	14.1	22.1	13.3	13.1	23.9	15.0	15.5	17.5	13.1
No measures	13.9	14.3	10.6	15.6	14.3	12.0	12.0	15.8	16.3	11.5
Not applicable	n=85									
Countermeasures to concerns for prognoses of patients "at risk" in 2016 %										
AB	9.7	9.8	9.8	7.8	10.1	7.7	11.1	8.0	10.6	8.8
AA	46.7	46.1	50.0	47.1	46.4	48.1	50.8	41.8	48.2	45.4
OM	13.6	13.0	13.4	21.6	13.8	12.8	9.9	18.1	6.0	20.7
SA	12.9	13.4	10.7	11.8	11.7	17.9	12.2	13.7	13.7	12.1
No measures	17.1	17.7	16.1	11.8	18.0	13.5	16.0	18.4	21.5	13.1

[a]Pm/Pv: p/private clinic. [b]1/new1/2: first/new first/second-tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second -tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine. [g]AB: prescribe the antimicrobials as before. [h]AA: prescribe allowable antimicrobials. [i]OM: prescribe other medicine (except antimicrobials). [j]SA: suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations.

Figure 1 Attitudes and practice of doctors toward antimicrobial stewardship in 2012 and 2016

Percentage of doctors who: received intensive or frequent compulsory stewardship training; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; prescribed antimicrobials as before, or suggest patient-self-medication with restricted antimicrobials as countermeasures.

Figure 2 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different medical organisation levels in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".
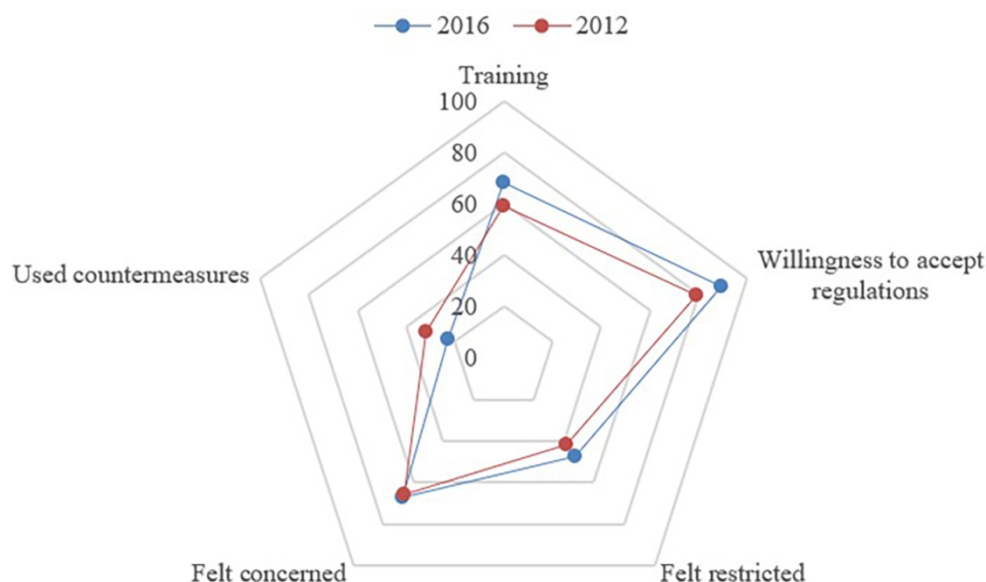
Figure 1 Attitudes and practice of doctors toward antimicrobial stewardship in 2012 and 2016
Percentage of doctors who: received intensive or frequent compulsory stewardship training; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; prescribed antimicrobials as before, or suggest patient-self-medication with restricted antimicrobials as countermeasures.
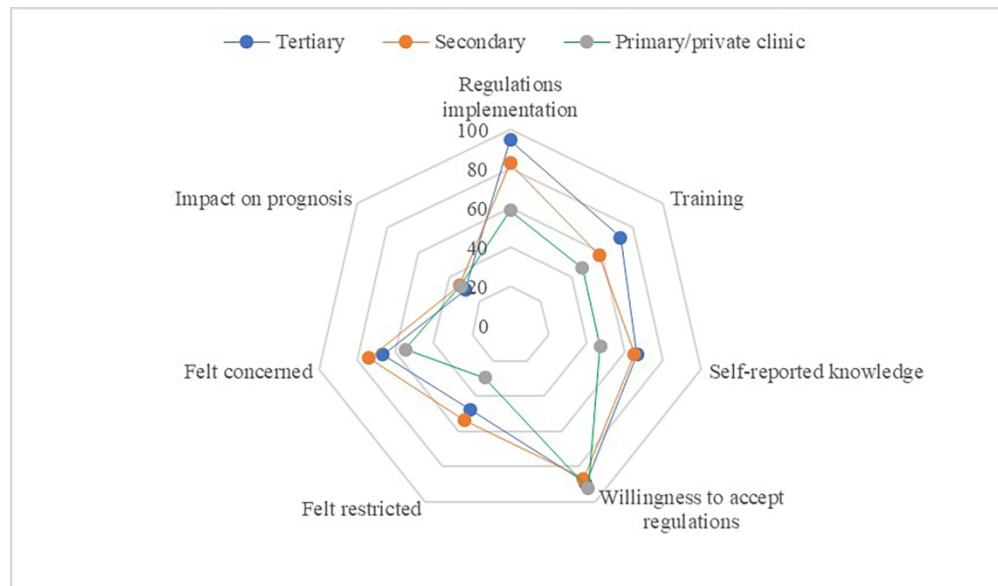
120x70mm (300 x 300 DPI)

Figure 2 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different medical organisation levels in 2016.
Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".

146x85mm (300 x 300 DPI)

Table S1 Description of 107 WeChat groups and 3 Email groups

	19 WeChat groups -sent by researchers	88 WeChat groups -sent by key respondents	3 Email groups -sent by researchers
Description	Doctors currently working at departments of pediatrics, orthopaedics, diabetic, internal, oncology, endocrinology, et al.	Doctors currently working at departments of dermatologyy, oncology, respiratory medicine, paediatrics, orthopaedics, internal medicine, surgery, renal medicine, cardiology, gastroenterology, ICU, endocrinology, and general practitioners working within both urban and rural community health centers.	Members of Association of Pediatrics, Association of Diabetes, and Association of Internal Medicine in the World Federation of Chinese Medicine Societies.
Number of health professionals	2517	16640	634
Survey period	9th to 25th March 2017	22th to 30th March 2017	29th to 30th March 2017

Table S2 List of questionnaire items (translated from Chinese[11])

No	Questions	Answer categories	
1	What is your occupation?	●	Doctor
		●	Nurse
		●	Clinical postgraduate
		●	Researcher
		●	Administrative staff
		●	Other
2	How old are you?	|___|___| years	
3	What is your gender?	●	Male
		●	Female
4	What is your major?	●	Western medicine
		●	Traditional Chinese medicine
		●	Integrative medicine of traditional Chinese medicine and western medicine
5	What is your highest educational level?	●	College/diploma
		●	Bachelor
		●	MSc
		●	MD or PhD
6	What is your level of seniority?	●	Intern
		●	Resident
		●	Associate chief-physician
		●	Chief-physician
7	When did your clinical work start?	●	Before 2001
		●	2002-2006
		●	2007-2011
		●	From 2012 to now
8	How many days per week did you provide outpatient services between 2007 and 2011?	●	0
		●	1
		●	2
		●	3
		●	4
		●	5
9	How many days per week did you provide outpatient services between 2012 and 2016?	●	0
		●	1
		●	2
		●	3
		●	4
		●	5
10	Which city do you work in?	|___|___|___|___|___|	
11	Which department do you work in?	___|___|___|___|___	
12	What is the level of your medical organisation?	●	3-A
		●	3-B
		●	3-C

		•	2-A
		•	2-B
		•	2-C
		•	1-A
		•	1-B
		•	1-C
		•	Private clinic
13	Which type of hospital are you based in?	•	Western medicine hospital
		•	Traditional Chinese medicine hospital
		•	Integrative medicine hospital of traditional Chinese medicine and western medicine
14	Is there an official requirement to restrict use of antimicrobials in your hospital?	•	No
		•	Less stringent
		•	Stringent
		•	Very stringent
15	What is/are your criteria for prescribing antimicrobials (multiple choice)?	•	Symptoms
		•	Signs
		•	Full blood count
		•	C-reactive protein detection
		•	Pathogen detection
		•	Diagnosis
		•	Others
16	Do you know the 'administrative regulations for the clinical use of antimicrobials' (hereinafter, antimicrobial stewardship regulations)?	•	Don't know
		•	Know a little
		•	Familiar
		•	Very familiar
17	Did you have any compulsory antimicrobial stewardship training in 2016?	•	No
		•	Less frequently
		•	Frequently
		•	Intensive
18	Did you have any compulsory antimicrobial stewardship training in 2012 (first year of stewardship implementation)?	•	No
		•	Less frequently
		•	Frequently
		•	Intensive
		•	Not applicable
19	How willing were you to accept the regulations in 2016?	•	Very willing
		•	Willing
		•	Hard to accept
		•	Unacceptable
20	How willing were you to accept the regulations in 2012 (first year of implementation)?	•	Very willing
		•	Willing
		•	Hard to accept
		•	Unacceptable
		•	Not applicable

21	In 2016, as a result of the potential influence of the antimicrobial stewardship, were there any restrictions on your antimicrobial prescription?	● Very restricted ● Restricted ● Slightly ● Not restricted
22	In 2012, as a result of the potential influence of the antimicrobial stewardship, were there any restrictions on your antimicrobial prescription?	● Very restricted ● Restricted ● Slightly ● Not restricted ● Not applicable
23	Were you worried about the prognosis of patients "at risk" --who would have been given antimicrobials before the stewardship in 2016?	● Always ● Often ● Sometimes ● No
24	If you were worried about the prognosis of patients "at risk" in the above question, what measures did you take to address your concern in 2016?	● Prescribe anyway the antimicrobials as before ● Prescribe allowable antimicrobials ● Prescribe other medicine (except antimicrobials) |__|__|__|__|__|__|__| ● Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations ● No measures
25	Were you worried about the prognosis of patients "at risk" in 2012 (first year of implementation)?	● Always ● Often ● Sometimes ● No ● Not applicable
26	If you were worried about the prognosis of patients "at risk" in the above question, what measures did you take to address your concern in 2012 (first year of implementation)?	● Prescribe anyway the antimicrobials as before ● Prescribe allowable antimicrobials ● Prescribe other medicine (except antimicrobials) |__|__|__|__|__|__|__| ● Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations ● No measures ● Not applicable
27	Do you think the antimicrobial stewardship regulations have had any impact on the clinical prognosis of patients "at risk"?	● Strong ● Moderate ● Slight ● No
28	What is the maximum permitted antimicrobial prescription rate in your medical organisation?	|__|__|%
29	What is the maximum permitted antimicrobial prescription	|__|__|%

		rate in your department?		
30	For which operations should perioperative antimicrobial prophylaxis be used?	●	Hernia repair	
		●	Resection of thyroid adenoma	
		●	Resection of mammary fibroadenoma	
		●	Open fractures debridement and internal fixation	
31	Which antimicrobial should be used to treat extended-spectrum β-lactamase-producing bacterial infections?	●	Carbapenems	
		●	Chloramphenicol	
		●	Macrolides	
		●	Aminoglycosides	
32	For how long a restricted antibiotic can be used in emergent medical situations?	●	2 days	
		●	1 day	
		●	5 days	
		●	30 days	

[a]The English version of the questionnaire was translated from the original Chinese version verbatim by a native Chinese speaker, and then back translated into Chinese by another native Chinese speaker working in the UK.

Table S3 Demographic and practice characteristics of 807 respondents

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Female %	58.7	59.8	52.7	58.8	59.9	53.8	58.7	58.8	58.0	59.4
Age mean years	39.0	39.1	39.7	37.0	38.8	40.1	34.6	44.5	39.5	38.6
Education level %										
College/diploma	1.6	0.5	4.5	9.8	0.9	4.5	2.3	0.8	0.8	2.4
Bachelor	27.1	19.3	62.5	49.0	20.3	55.8	26.6	27.7	33.2	21.6
MSc	44.2	47.7	30.4	31.4	46.2	35.9	56.2	29.7	39.4	48.7
MD or PhD	27.0	32.6	2.7	9.8	32.6	3.8	14.9	41.8	26.7	27.3
Major %										
WM	47.8	48.8	51.8	27.5	43.9	64.1	47.6	48.1	NA	NA
TCM	37.7	37.4	32.1	52.9	41.9	19.9	35.9	39.8	NA	NA
IM	14.5	13.8	16.1	19.6	14.1	16.0	16.5	12.1	NA	NA
Seniority level%										
Intern	13.3	13.0	12.5	17.6	12.0	18.6	NA	NA	14.5	12.1
Resident	41.6	38.5	49.1	64.7	41.6	41.7	NA	NA	40.2	43.0
ACP	29.9	31.5	27.7	13.7	31.5	23.1	NA	NA	30.3	29.5
CP	15.2	16.9	10.7	3.9	14.9	16.7	NA	NA	15.0	15.4
Year starting to work %										
≤2001	38.9	38.7	44.6	29.4	52.5	46.2	13.1	70.3	44.3	34.0
2002-2006	22.6	21.9	19.6	37.3	22.6	22.4	23.5	21.4	24.1	21.1
2007-2011	22.2	21.9	25.0	19.6	23.5	16.7	34.1	7.7	17.9	26.1
≥2012	16.4	17.5	10.7	13.7	16.7	14.7	29.3	0.5	13.7	18.8
Outpatient service (days per week) in 2007-2011 %										
0	22.8	24.9	21.0	2.3	21.8	27.1	35.1	12.2	22.5	23.1
1	21.6	23.7	19.0	2.3	21.4	22.6	16.6	26.0	24.3	19.0
2	18.1	19.8	15.0	4.5	17.7	19.5	10.5	24.6	20.1	16.1
3	12.0	11.5	14.0	13.6	12.4	10.5	8.9	14.6	12.6	11.4
4	6.8	6.8	4.0	13.6	7.7	3.0	7.7	6.1	8.1	5.6
5	18.7	13.4	27.0	63.6	19.0	17.3	21.1	16.6	12.3	24.9
Not applicable	n=132									
Outpatient service (days per week) in 2012-2016 %										
0	15.4	16.8	13.4	2.0	14.1	20.5	25.5	3.0	15.5	15.2
1	22.6	25.3	15.2	3.9	22.0	25.0	19.9	25.8	27.2	18.3
2	21.7	22.7	18.8	15.7	21.0	24.4	14.9	29.9	23.3	20.2
3	14.3	13.5	18.8	13.7	14.9	11.5	13.3	15.4	13.5	15.0
4	8.7	8.9	5.4	13.7	10.1	2.6	7.9	9.6	8.8	8.6
5	17.5	12.9	28.6	51.0	17.8	16.0	18.5	16.2	11.7	22.8

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second–tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second -tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine.

[f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

Table S4 Medical organisation of 807 respondents

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Medical organisation level %										
Tertiary	79.8	NA	NA	NA	83.4	64.7	74.9	85.7	81.3	78.4
Secondary	13.9	NA	NA	NA	9.8	30.8	15.6	11.8	15.0	12.8
Primary	5.0	NA	NA	NA	5.5	2.6	7.4	1.9	2.3	7.4
Private clinic	1.4	NA	NA	NA	1.2	1.9	2.0	0.5	1.3	1.4
Medical organisation type %										
WM	51.9	51.1	61.6	41.2	47.9	68.6	51.5	52.5	84.5	22.1
TCM	34.7	37.0	30.4	15.7	38.4	19.2	31.4	38.7	5.7	61.3
Integrative	13.4	12.0	8.0	43.1	13.7	12.2	17.2	8.8	9.8	16.6
City level %										
First-tier	37.1	37.7	18.8	68.6	NA	NA	37.0	37.1	34.2	39.7
New first-tier	23.7	24.8	24.1	7.8	NA	NA	23.7	23.6	21.8	25.4
Second-tier	20.0	21.7	14.3	9.8	NA	NA	18.1	22.3	18.1	21.6
Third-tier	9.0	7.3	22.3	2.0	NA	NA	9.3	8.8	12.4	5.9
Fourth-tier	5.9	3.9	17.0	7.8	NA	NA	6.3	5.5	7.8	4.3
Fifth-tier	4.3	4.5	3.6	3.9	NA	NA	5.6	2.7	5.7	3.1
Geographic region %										
Eastern	49.2	48.6	38.4	80.4	53.6	30.8	50.6	47.5	47.2	51.1
Central	10.7	9.0	20.5	9.8	7.1	25.6	11.1	10.2	13.0	8.6
Western	21.4	20.5	33.0	7.8	17.7	37.2	21.0	22.0	34.7	9.3
Northeast	18.7	21.9	8.0	2.0	21.7	6.4	17.4	20.3	5.2	31.1

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second–tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second -tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.
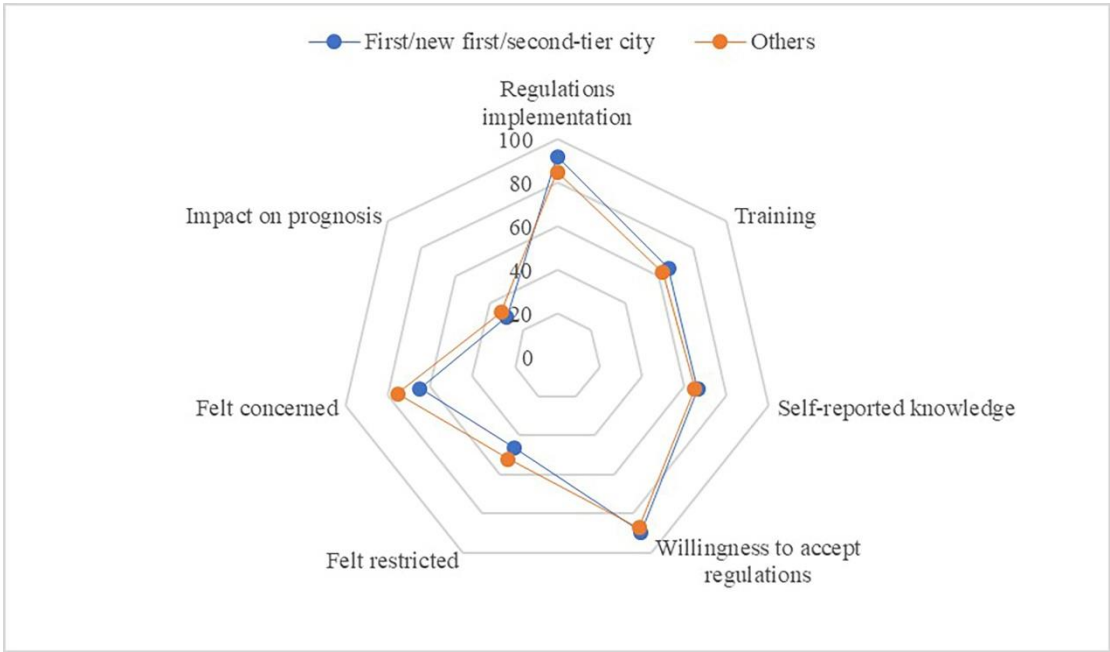
Figure S1 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different city levels in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".
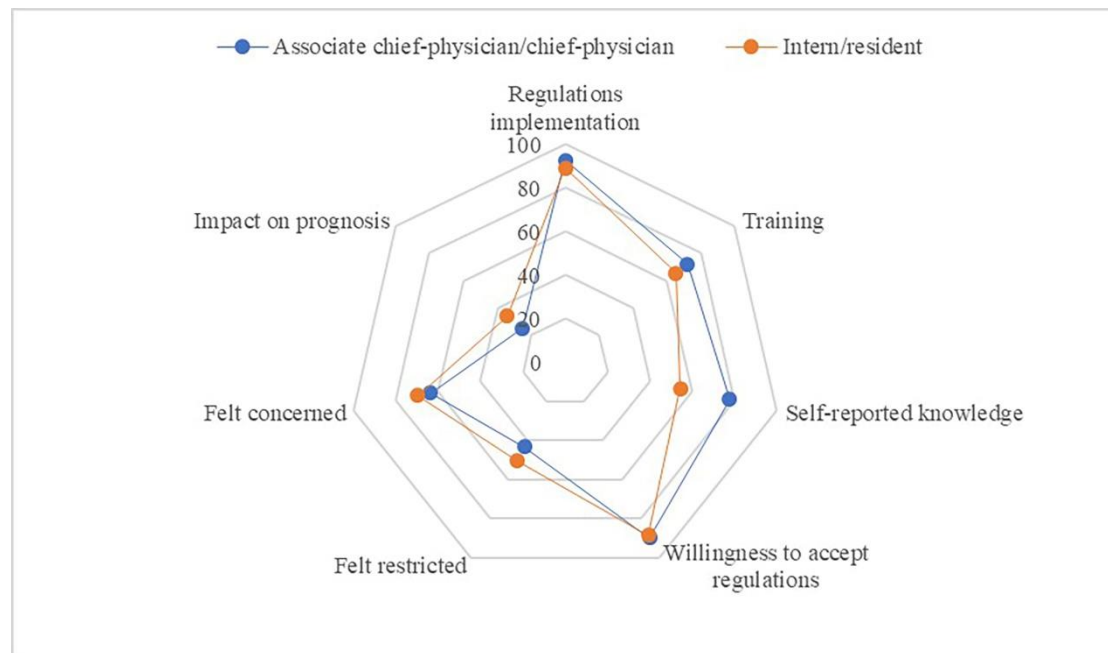
Figure S2 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different professional titles in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".
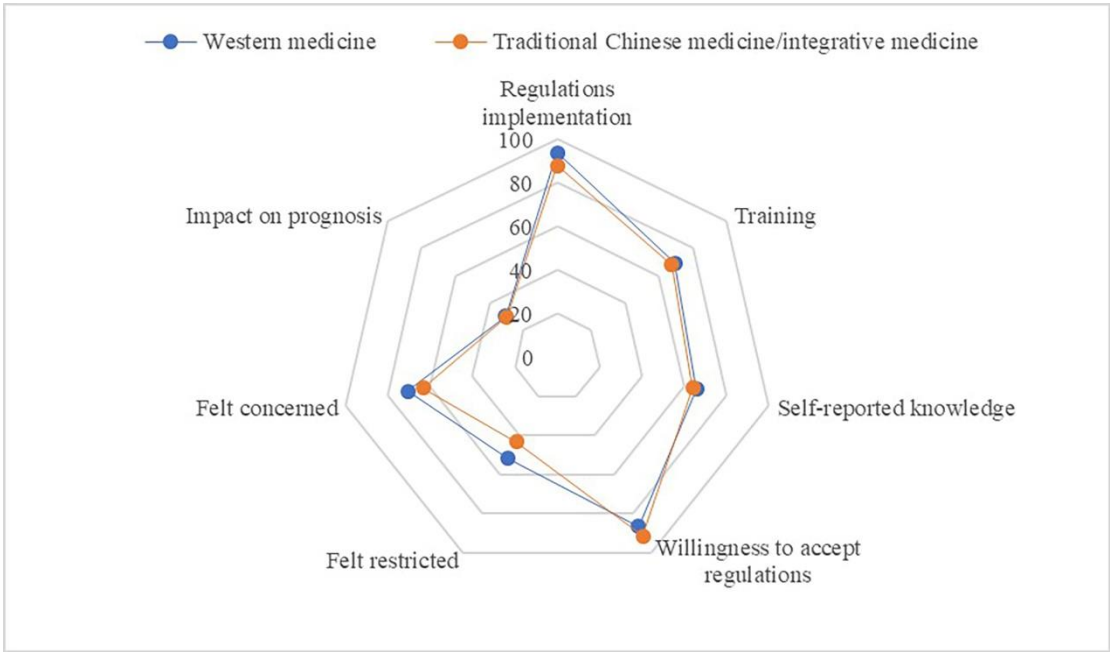
Figure S3 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different medical majors in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".

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	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
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	*5*
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	/
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	/
		(*e*) Describe any sensitivity analyses	/
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	6
		(b) Give reasons for non-participation at each stage	/
		(c) Consider use of a flow diagram	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-7
		(b) Indicate number of participants with missing data for each variable of interest	/
Outcome data	15*	Report numbers of outcome events or summary measures	6
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	7-10

		(*b*) Report category boundaries when continuous variables were categorized		Table1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		/
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		7-9

Discussion

Key results	18	Summarise key results with reference to study objectives		10-11
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		11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results		10-12

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

*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.

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How far do we still need to go? A survey on knowledge, attitudes, practice related to antimicrobial stewardship regulations among Chinese doctors in 2012 and 2016

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How far do we still need to go? A survey on knowledge, attitudes, practice related to antimicrobial stewardship regulations among Chinese doctors in 2012 and 2016

Ruyu Xia[1], Xiaoyang Hu[2]†, Merlin Willcox[2]†, Xinxue Li[3], Yuxiu Li[4], Jian Wang[5], Xun Li[1], Michael Moore[2], Jianping Liu[1], Yutong Fei[1]*

[1]Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China;

[2]Primary Care and Population Sciences, University of Southampton, Southampton, UK; [3]Department of International Liaison, World Federation of Chinese Medicine Societies, Beijing, China;

[4]Department of endocrinology, South of Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China;

[5]Department of neurology, The Affiliated Hospital of Changchun University of Chinese Medicine, Changchun, China.

*Corresponding author. Tel: +86 10 6428 6757; E-mail: feiyt@bucm.edu.cn. Postal address: No. 11, Bei San Huan Dong Road, Chaoyang District, Beijing 100029, China

†These authors contributed equally

ABSTRACT

Objectives To explore doctors' knowledge, willingness, concerns and the countermeasures to the most stringent antimicrobial stewardship regulations of China which implemented in August 2012.

Design Cross-sectional survey. A pretested 32-point structured questionnaire was distributed to doctors by sending a web link via the mobile phone application WeChat through snow-ball sampling methods and email groups of medical academic societies.

Setting China.

Participants Doctors.

Primary and secondary outcome measures The questionnaire inquired about the doctors' experiences, knowledge, willingness, concerns and the countermeasures to the stewardship policies.

Results Total of persons in the groups was 19791, among them 1194 submitted the answers, within them, 807 were doctors. Doctors had a mean age of 39.0 years. The majority (78.9% in 2012, 89.1% in 2016) reported that they were willing or very willing to accept the regulations. Almost all respondents (93.2%) felt the stewardship regulations had the potential to adversely affect the prognosis of patients who would have been prescribed antimicrobials before they were implemented, and more than 65% (65.7% in 2012, 66.9% in 2016) of doctors were often or always concerned about the prognosis of these patients. In 2012, 32% of doctors prescribed restricted antimicrobials or suggested patient self-medication with restricted antimicrobials to address doctors' concerns, and this number decreased to 22.6% in 2016. Although compulsory antimicrobial stewardship training was frequent, less than half of respondents (46.8%) responded correctly to all three knowledge questions.

Conclusion Antimicrobial stewardship regulations had some positive effect on rational antimicrobial use. Willingness and practice of doctors towards the regulations improved from 2012 to 2016. Knowledge about rational antimicrobial use was still lacking. Doctors found ways of accessing restricted antibiotics to address their concerns about the prognosis of patients, which undermined the implementation of the stewardship regulations.

Strengths and limitations of this study

- The paper is the first to comprehensively explore doctors' feelings and attitudes towards the Chinese antimicrobial stewardship regulations.
- The survey recruited participants and administered the survey via WeChat, which is a convenient, time-saving and economic method to survey a diverse population. Our respondents covered 29 of 32 administrative divisions of mainland China.
- We cannot rule out a possible selection bias as our sample was not randomly selected. Although the snowball sampling method is effective and efficient when sampling from specific populations, participants that can be reached depend on the social connections of the key respondents.
- The proportion of completed questionnaires to all potential responders is low.
- Another limitation is the potential recall bias of information provided for year

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2012 and 2016.

INTRODUCTION

The efficacy of antimicrobials is threatened by increasing levels of antimicrobial resistance.[1] [2] In 2014, it was estimated that China consumed 77,760 tons of antimicrobial agents for humans and the defined daily doses per 1000 inhabitants per day were approximately 6 times larger than in the UK, USA, Canada and Europe.[3]

During the past decade, the Chinese Government has issued a series of health care regulations.[4-7] The "Administrative regulations for the clinical use of antimicrobials", implemented in August 2012, were the most stringent regulations ever (Box 1).[6] Several studies reported changes in the prescription rates of antibiotics to reflect the impact of the 2012 stewardship regulations,[8-10] but we did not find any study which investigated the attitudes of Chinese doctors towards these regulations, although they might be an important barrier to implementation of the regulations.

Our study aimed to explore knowledge, willingness, concerns and the countermeasures of doctors towards the most stringent antimicrobial stewardship regulations of China (2012) via a web-based survey. Specifically, we looked at: 1) what did they experience; 2) how good was their knowledge about prescribing antimicrobials; 3) what were their feelings (willingness/reluctance) towards the regulations (over a five-year duration of implementation) when they were practicing; 4) what were the countermeasures, if any were used.

METHODS

Survey recruitment

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A snowball sampling strategy, focus on recruiting docors practing in mainland China, was utilised. Participants were reached by the mobile phone Application (APP) WeChat and emails. WeChat is currently the most widely used social media platform in China, with more than one billion users.[11] Akin to a hybrid of Twitter, Facebook and WhatsApp, WeChat combines the functions of instant messaging, a blog, and a social networking site. The invitations to participate in the survey were sent first to clinicians' WeChat groups by researchers, then they were cascaded by purposively inviting key respondents to send the link to their clinicians' WeChat groups in order to increase respondent sample size (WeChat groups details in Table S1). Email invitations were only sent to members of the World Federation of Chinese Medicine Societies. The professional occupation screening function was turned on therefore only those who identified themselves as doctors were able to proceed to the survey questions, others were directed politely to the end of the survey.

Data collection

The tool for collecting data is the questionnaire based in the WenJuanXing online survey service (English name "SurveyStar", Changsha Ranxing Science and Technology Ltd, Shanghai, China), which is a online survey platform, akin to SurveyMonkey.

Survey questionnaire

The study was performed between March 9th to March 30th 2017 using a piloted 32-point structured questionnaire (see Table S2[12]). The structured questionnaire consisted of questions about four categories of variables: (a) demographics and practice characteristics of the doctors; (b) implementation of the antimicrobial stewardship in health care facilities; (c) attitude (willingness, concerns) and practice(impacts on prescribing antibiotic behaviour, countermeasures to concerns) of doctors towards 2012 antimicrobial stewardship regulations; (d) doctors' knowledge of antimicrobial stewardship regulations and proper use of antimicrobials (question 30-32 originated from training examination questions for "guiding principles for clinical application of antibacterial" [4] and "administrative regulations for the clinical use of antimicrobials" [6]). The questionnaire was about 18 phone screens long, which took approximately 5 minutes to complete. We consulted two doctors and one methodologist and conducted a pilot survey with 10 doctors before starting the formal survey.

Data were imported from the survey website into Microsoft Excel 2016, then converted into the SPSS database. Statistical analysis was performed using IBM SPSS Statistics for Windows, V.23.0 (IBM, Armonk, New York, USA). Descriptive statistics, Mann-Whitney test, $\chi2$ test and multivariate regression were applied in description and analysis of the variables, where appropriate. Compulsory antimicrobial stewardship training, doctor's acceptance, impact on prescribing antibiotic behaviours, impact on prognosis of patients, concern and countermeasures

towards the antimicrobial stewardship at the beginning of the implementation (2012) and five years after that (2016) were compared. Doctors with different educational background, levels of seniority, practicing organisations and geographic regions were considered as subgroups and compared. Logistic regression was used to screen factors relevant to knowledge of clinical use of antimicrobials.

Ethical approval for this study was obtained from the Ethical committee, Beijing University of Chinese Medicine (2017BZHYLL0201). Informed consent was obtained from all the participants. Participants were informed at the start of the survey about the length of time needed to complete the survey, the investigators and the purpose of the study. Participants were free to continue the survey or to quit at any time. Anonymous data were collected. No incentive was used to reward participants.

Patient and public involvement

No patient or public was involved in the design or planning of this study.

RESULTS

Procedures

The questionnaire was sent to 107 WeChat groups and 3 email groups that include 19791 health professionals (maximum number of potential reach). There were 3609 health professionals (actual reach) who clicked the web link of the questionnaire, out of whom 1194 completed the survey. Among the survey respondents, 807 were doctors; others were nurses, researchers, clinical postgraduates, or administrative staffs.

Demographics

Data provided by doctors were collected and analysed. All 807 doctors fully completed the online survey (Tables S3 and S4). Doctors had a mean age of 39.0 years (SD=7.4), range 22 to 68. Men account for 41.3% of the total. More than 70% of doctors（71.2%) had MSc, MD or PhD degree (n=575). Most of them were residents or associated chief-physicians (n=336; 41.6% and n=241; 29.9% respectively). Approximately half (n=386; 47.8%) of doctors majored in western medicine, others majored in traditional Chinese medicine or integrative medicine. 83.7% doctors started clinical practice before 2012. The number of outpatient services provided weekly was diverse, ranging from none (22.8% and 15.4% in 2007-2011 and 2012-2016 respectively) to 5 days (18.7%; 17.5%). Although almost half of doctors were from eastern China (49.2%), there was also a good number from central, western and north-eastern China. About three in every five (60.8%) of the doctors were working in first-tier and new first-tier cities (e.g. Beijing, Shanghai and Hangzhou). Most doctors (79.8%) worked in tertiary hospitals.

Experiences of implementation of the antimicrobial stewardship regulations

The clear majority of practitioners reported that hospital implementation of antimicrobial stewardship regulations was stringent (45.1%) or very stringent (45.7%) (Table 1). Specific training sessions were frequent or intensive in 2012 (59.1%) and in 2016 (68.5%) (p< 0.001) (Figure1). Practitioners from tertiary western medicine hospitals in first/new first-tier cities reported more stringent requirements for the

implementation of the regulations (Figure 2, Figure S1, S2 and S3). Doctors in departments of respiratory medicine, emergency medicine, paediatrics, intensive care, haematology, and dentistry reported that they were permitted higher upper limits than the general limits of their hospitals. The largest gap in antimicrobial prescription limits was between respiratory departments (33.5%) and hospitals overall, irrespective of departments (22.4%).

Knowledge of antimicrobial stewardship regulations and proper use of antimicrobials

Although most doctors (65.1%) declared that they were familiar or very familiar with the 2012 stewardship regulations, less than half answered the three-question knowledge test (question 30-32) correctly (46.8%) (Table 2). Doctors from primary care had a lower correct rate compared to those from other hospitals (P=0.013); doctors who majored in traditional Chinese medicine had a lower correct rate compared to those who majored in western/integrative medicine as measured in the multivariate regression equation (P=0.001). The most commonly reported criteria for prescribing antimicrobials were full blood count (94.2%), pathogen detection such as sputum or blood culture (77.0%), symptoms (72.9%), signs (71.4%), C-reactive protein level (62.9%) and the diagnosis (60.5%).

Attitudes towards implementation of the antimicrobial stewardship regulations

In 2012, 78.9% of doctors reported that they were willing or very willing to accept the regulations, and the percentage increased to 89.1% in 2016 (p=0.002) (Table 3). In

2012 and 2016, doctors who majored in western medicine reported lower acceptance rates (74.6%; 86.5%) than those who majored in Chinese medicine or integrative medicine (82.9%; 91.4%). 30.0% of doctors reported the antimicrobial stewardship regulations had a moderate or large impact on the prognosis of these patients "at risk" (means patients who would have been prescribed antimicrobials before the implementation of the 2012 stewardship regulations). Only 6.8% of doctors felt the stewardship regulations did not result in putting the prognosis of these patients "at risk". More than 65% of doctors (65.7% in 2012, 66.9% in 2016; p=0.367) were 'often or always concerned' about the prognosis of patients "at risk".

Doctors' practice of the antimicrobial stewardship regulations

In 2012, 41.6% of doctors reported that prescribing of antimicrobials had been very (6.1%) or moderately (35.5%) restricted during the implementation of antimicrobial stewardship regulations (Table 3). The percentages even increased in 2016 (8.4%; 38.9%) (2016 vs 2012, p=0.019). In 2012, 32% of doctors stated that they had prescribed or suggested patient self-medication with restricted antimicrobials (restricted by the specific criteria for conditions in the stewardship) to address concerns for patients "at risk" (Figure 1), but it decreased to 22.6% in 2016 (2016 vs 2012, p< 0.001). In 2012, This prescribing behaviour was reportedly more common (42.2%) in small cities, but in 2016 there no longer seemed to be any obvious difference between city levels. This behaviour was higher among doctors who majored in western medicine than among those who majored in traditional Chinese

medicine or integrative medicine (37.8% and 26.5% respectively in 2012, 24.3% and

20.9% in 2016). This proportion was higher among interns (44.6% in 2012; 30.8% in

2016) than other doctors (30.7% in 2012; 21.3 in 2016). More doctors prescribed

permitted antimicrobials in 2016 than in 2012 (46.7%, 43.8%) when treatment was

needed. In 2012 and 2016, 13.6% and 10.4% prescribed alternatives to antimicrobials;

95.8% (69/72) and 96.2% (102/106) of these prescribed traditional Chinese

medicines.

DISCUSSION

Summary of findings

The data were collected from doctors in China with all medical education

background, levels of seniority of the doctors, covering those who work in all levels

of cities, types of medical organisations, and levels of medical organisations (table S3,

table S4). The data covered doctors from 29/32 administrative divisions of mainland

China, representing nearly all regions of China. Although about half (49.2%) of our

respondents were based in Eastern China, this reflects the proportion of doctors in

Eastern China, which accounts for about 43% of doctors in China.[13] Since the

respondents are those with higher educational background and work in higher level

hospital level than average, their knowledge, attitudes, practice related to stewardship

may be overestimated.

The implementation of the 2012 stewardship regulations was considered stringent.

The percentage of all prescriptions which are permitted to contain antimicrobials in

respiratory departments was set to be high by the answers from the doctors, with an average of 33.5%. Insufficient knowledge on proper use of antimicrobials was obvious, especially in primary medical organisations. Most doctors (94.2%) used full blood count as the criterion for prescribing antimicrobials. Compulsory stewardship training and willingness to accept the stewardship regulations increased from 2012 to 2016. Due to restricted prescription of antimicrobials, doctors' concerns with prognosis of patients "at risk" remained high. It seems that the use of restricted antimicrobials has greatly reduced, but the use of permitted antimicrobials may have increased. Traditional Chinese medicine may have played a role as an alternative to antimicrobials.

Strengths and limitations

To the best of our knowledge, this is the first survey in China to comprehensively explore doctors' feelings and attitudes toward the Chinese antimicrobial stewardship regulations. We recruited participants and administered the survey via WeChat (one of the most common social APPs in China). It is a convenient, time-saving and economic method to survey a diverse population. Our respondents covered 29 of 32 administrative divisions of mainland China. Despite this, our study has a number of limitations. Firstly, we cannot rule out a possible selection bias as our sample was not randomly selected. Although the snowball sampling method is effective and efficient when sampling from specific populations, participants that can be reached depend on the social connections of the key respondents. Also, doctors in primary care settings

or private clinics are less likely to belong to any academic association or doctors' group, thus they may be less likely to be reached. According to the data of the Chinese government,[13] the percentage of doctors in primary care settings and private clinics are about 4.3% and 11.4% in China in 2016 respectively. In this survey, doctors in primary care settings and private clinics accounted for 5.0% and 1.4% of respondents respectively. In addition, the use of clinician's WeChat groups by researchers for first invitations may also be one of the reasons for potential bias. Our professional connections are more likely to be similar to ourselves. In order to overcome this potential bias, we invited our first-round invitation receivers to send our links to their own clinician connections. This may have helped to correct the selection bias that relate to our first invitation receivers. We also invited members of academic associations in our first invitations and most of the members of those associations are usually academic clinicians. In China, about 80% of the clinicians work in public hospitals,[13] conducting or participating in academic research is a requirement for them. Most of the clinicians need to work both clinically and academically. Secondly, the proportion of completed questionnaires to all potential responders is low (6.0%, 1194/19791), similar to the other web-based surveys.[14] [15] 19791 is the sum of people in all the WeChat groups. This is the maximum number of people that potentially can be reached by us. There is no way to collect the number of people who saw the link but choose to ignore it. The number of people who clicked the link is an important parameter that we can achieve. 3618 people clicked the link

and 1194 completed it (33.0%, 1194/3618). Another limitation is the potential recall

bias of information provided for year 2012 and 2016.

Comparisons with other studies

We did not identify any studies investigating the attitudes of doctors towards the 2012

antimicrobial stewardship regulations. Doctors' willingness and concerns might

impact on their prescribing behaviors and weaken the effects of the regulations. We

found in our study that the knowledge about proper use of antimicrobials of doctors

from primary care clinics or private clinics seems insufficient. Similar results were

reported from three surveys (sample sizes 761, 180, 611) focusing on doctors' or

trainees' knowledge and continued education.[16-18] In our study, doctors reported that

they recommended self-medication of restricted antimicrobials to address concerns

for patients "at risk". Another survey of 256 pharmacies in three Chinese cities[19]

showed that antibiotics were obtained without a prescription from 77.7% pharmacies

for adult respiratory infections. In our study, the percentage of all prescriptions which

are permitted to contain antimicrobials in respiratory departments was very high. A

survey of 1204 people in three Chinese cities[20] showed that cough, sore throat, and

bronchitis were the most frequent reasons reported for antibiotic use. This is also

consistent with the situation in the UK.[21]

In our study, full blood count (raised white blood cell counts and increased

proportion of neutrophilic granulocytes) was overwhelmingly considered as the main

criterion for prescribing antimicrobials. This medical behavior is in accordance with

the Chinese acute bronchitis clinical practice guidelines,[22] [23] which state that oral

antibiotics such as β-lactams and fluoroquinolones can be used in patients with cough

before the pathogen detection results were available, if there are signs of purulent

sputum or raised white cell counts (Adults usually more than 10×10^9/L). However, it

has been suggested by international guidelines that doctors should not perform testing

or initiate antibiotic therapy in people with acute bronchitis (pneumonia excluded).[24]

Studies[25] [26] have shown that blood tests do not accurately differentiate between

bacterial and viral infections. In our survey, many doctors also reported using raised

CRP as a criterion for prescribing antimicrobials. CRP may be helpful in adults and is

recommended in the NICE guidelines[27] to be considered if antibiotics are being

considered for treatment of lower respiratory tract infections. A study has shown that

use of CRP can reduce antibiotic consumption in acute respiratory tract infections.[28]

However, Lemiengre and colleagues performed a cluster-randomised trial in 2227

children showing that CRP tests did not reduce antibiotic prescribing for non-severe

acute infections in children in primary care and cannot be recommended.[29] In our

survey, doctors with a traditional Chinese medicine/integrative medicine background

felt less restricted and were more willing to accept the stewardship regulations.

Traditional Chinese medicines served as alternatives to antimicrobials for doctors.

Similarly, in the UK, a retrospective study which included 7283 General Practice

(GP) surgeries suggested that GPs additionally trained in integrative medicine or

complementary and alternative medicine had lower antibiotic prescribing rates

compared with conventional GPs.[30]

Implications for doctors and policy makers

The implementation of the antimicrobial stewardship regulations requires administrative persistence and strengthened training of doctors on the use of antimicrobials, especially for primary care doctors. In addition to the mandatory administrative implementation, explanation of reasons why there is a need for proper use of antimicrobials and how to achieve it, as well as approaches to facilitate evidence-based clinical practicing are needed to guide clinical practice and to relieve doctors' concerns. The common practice of prescribing antimicrobials according to elevated full blood count or CRP is controversial. Although both guidelines and the stewardship regulations mentioned this, no threshold was defined. Suggested patient self-medication with restricted antimicrobials may have diminished the effect of the antimicrobial stewardship regulations. The increase in the use of permitted antimicrobials may be associated with inappropriate use, which is also an important cause of antimicrobial resistance. More stringent measures should be applied to stop antimicrobial purchase without prescriptions from retail pharmacies. Traditional Chinese medicine can be considered for relieving symptoms, complementing or replacing antimicrobials.[31]

Future research

First, there is a need for qualitative research to explore antibiotic prescribing behaviours in China, potential concerns from doctors and pharmacists, why there

were differences between doctors in different types of hospitals/regions/major, and which intervention(s) would be most acceptable in their context to reduce antimicrobial prescribing. Then, we also suggest that a large representative sample cohort study or registry study in China is warranted, to explore the possibility of delayed antimicrobials or other antimicrobial replacement therapy from the perspectives of clinical effect, safety, reducing resistance and health economics. There is a need for more evidence to back up recommendations, particularly on (i) diagnostic and prognostic accuracy of various markers e.g. white cell counts and CRP; (ii) prognosis of infections for which antibiotics were commonly prescribed; (iii) guidelines and recommendations on when to use antibiotics. Additionally, we need to find other interventions that can relieve symptoms, complement or substitute antimicrobials, and then conduct high quality, large scale randomised controlled trials to validate their efficacy, effectiveness and safety. Traditional Chinese medicine is widely used in medical practice in China.[32] We propose more clinical or basic research to explore which traditional Chinese medicine can be recommended instead of antibiotics for different infections.

Conclusion

In summary, the 2012 antimicrobial stewardship regulations improved proper clinical use of antimicrobials in China. Attitudes and behaviours of doctors towards the stewardship regulations improved from 2012 to 2016. Concerns about the prognosis of patients "at risk" were still prevalent, and doctors found ways of accessing

antibiotics which undermined the implementation of the antimicrobial stewardship regulations. There is a gap between doctors in small cities and first-tier cities in terms of implementation of antimicrobial stewardship regulations and knowledge about proper use of antimicrobials.

Competing interests: none declared.

Ethics approval: This study was approved by the ethical committee of Beijing

University of Chinese Medicine (2017BZHYLL0201).

Data sharing: Deidentified data are fully available upon reasonable request for

scientific research. Contact email: feiyt@bucm.edu.cn. No additional information

available.

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The "Administrative regulations for the clinical use of antimicrobials" was issued and implemented by the National Health and Family Planning Commission (NHFPC, the former Ministry of Health)

What are the regulations about?

In the 2012 stewardship regulations, all hospitals in China were required to set up an antimicrobial agents administrative group or identify a point person to take control of antimicrobial stewardship. Infectious diseases departments and clinical microbial laboratories were required to be set up in all tertiary and secondary hospitals. Antibacterial agents were classified according to safety, efficacy, bacterial resistance, price and other factors. Prescribers have accredited prescription rights for different categories of antimicrobials, depending on their levels of seniority. Compulsory standardised trainings on the knowledge of clinical use of antimicrobials are required for all doctors.

How was it supposed to be implemented or enforced? How was implementation monitored?

NHFPC established the Centre for Antibacterial Surveillance and the China Antimicrobial Resistance Surveillance System to monitor the use of antibiotics and antibiotic resistance in hospitals. Surveillance systems within their respective administrative areas would be developed by local health administrative departments. The rankings of total usage of antimicrobials, classification of antimicrobials, and percentage of prescriptions for antimicrobials in health facilities in their respective administrative regions are published and submitted to the higher authorities for the record. Managers of poorly performing health facilities are admonished. This is to ensure rational use of antimicrobial agents in healthcare settings.

Were there any sanctions for not implementing it?

Health facilities that fail to meet the requirements would be downgraded to a lower classification level. Doctors who fail to pass the exam of standard training or seriously violate the regulations can lose their accreditation to prescribe antibiotics, and/or have their professional qualification revoked. If doctors' actions led to serious consequences, they could be fined or prosecuted.

Who was responsible for implementing it?

NHFPC and local health administration investigate and reassign responsibility to hospital presidents or health facility management staff.

Box 1 Translated summary of "administrative regulations for the clinical use of antimicrobials" [6]

Table 1 Implementation of the antimicrobial stewardship regulations

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Medical organisation antimicrobial stewardship implementation %										
Very stringent	45.7	50.6	33.0	11.8	47.9	36.5	44.2	47.5	50.0	41.8
Stringent	45.1	44.1	50.0	47.1	44.2	48.7	45.1	45.1	44.0	46.1
Less stringent	7.8	4.5	16.1	31.4	6.5	13.5	9.0	6.3	5.4	10.0
No	1.4	0.8	0.9	9.8	1.4	1.3	1.6	1.1	0.5	2.1
Compulsory antimicrobial stewardship training in 2012 (first year of stewardship implementation) %										
Intensive	9.7	10.9	6.3	3.9	11.4	2.7	8.3	11.4	11.1	8.4
Frequent	49.4	52.4	41.4	31.4	50.6	44.5	47.6	51.4	50.0	48.8
Less frequent	36.6	33.2	49.5	49.0	33.9	47.9	38.8	34.2	35.1	38.1
No	4.2	3.5	2.7	15.7	4.1	4.8	5.3	3.1	3.8	4.6
Not applicable	n=48									
Compulsory antimicrobial stewardship training in 2016 %										
Intensive	12.6	14.0	8.0	5.9	14.1	6.4	12.4	12.9	13.5	11.9
Frequently	55.9	58.1	50.0	41.2	55.9	55.8	53.0	59.3	56.0	55.8
Less frequency	28.6	26.4	38.4	35.3	27.0	35.3	30.5	26.4	28.0	29.2
No	2.9	1.6	3.6	17.6	2.9	2.6	4.1	1.4	2.6	3.1
% of all prescriptions which are permitted to contain antimicrobials (according to the hospital's internal policy) %										
≤20%	59.8	60.1	44.4	86.0	65.6	39.7	62.0	57.5	47.7	72.0
21-40%	32.9	33.3	43.2	9.3	29.8	43.7	31.5	34.4	43.8	22.0
41-60%	6.5	5.9	12.3	2.3	4.1	15.1	5.5	7.7	7.8	5.3
>60%	0.7	0.7	0.0	2.3	0.5	1.6	1.0	0.4	0.7	0.7
Not reported	n=242									
% of all prescriptions which are permitted to contain antimicrobials (according to the department's internal policy) %										
≤20%	64.1	64.1	51.9	86.0	69.5	45.2	65.4	62.6	53.7	74.5
21-40%	26.5	26.6	34.2	11.6	23.5	37.3	24.3	28.9	34.3	18.8
41-60%	8.0	7.4	13.9	2.3	6.2	14.3	8.2	7.7	9.5	6.4
>60%	1.4	1.8	0.0	0.0	0.9	3.2	2.1	0.7	2.5	0.4
Not reported	n=242									

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second-tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second-tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

Table 2 Knowledge of antimicrobial stewardship

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Self-reported knowledge of antimicrobial stewardship %										
Very familiar	16.1	17.1	12.5	11.8	16.9	12.8	10.6	22.8	18.9	13.5
Familiar	48.9	49.4	52.7	35.3	48.8	49.4	44.0	54.9	47.2	50.6
Know a little	31.0	30.0	32.1	41.2	30.0	35.3	39.5	20.6	30.3	31.6
Don't know	4.0	3.6	2.7	11.8	4.3	2.6	5.9	1.6	3.6	4.3
Tested results of knowledge of antimicrobial prescribing										
Which surgery should apply perioperative antimicrobial prophylaxis										
% of correct	91.9	91.6	93.8	92.2	92.5	89.7	92.3	91.5	92.2	91.7
Which antimicrobial should be used for extended-spectrum β-lactamases-producing bacterial infection										
% of correct	70.5	72.1	74.1	43.1	69.3	75.6	65.2	76.9	78.2	63.4
For how long a restricted antibiotic can be used in emergent medical situations										
% of correct	66.7	67.7	72.3	41.2	66.1	69.2	64.3	69.5	72.3	61.5
Criteria for prescribing antimicrobials (multiple choice) %										
Symptom	72.9	75.9	67.9	45.1	72.4	75.0	74.3	71.2	75.6	70.3
Sign	71.4	73.6	70.5	45.1	70.8	74.4	71.1	71.7	72.8	70.1
Full blood count	94.2	95.0	92.0	88.2	95.4	89.1	95.0	93.1	92.7	95.5
CRP [g]	62.9	64.0	59.8	56.9	62.2	66.0	61.9	64.3	61.7	64.1
PD [h]	77.0	83.2	65.2	23.5	92.0	78.2	75.4	78.8	84.2	70.3
Diagnosis	60.5	62.9	58.9	33.3	60.7	59.6	58.9	62.4	68.9	52.7
Others	18.2	19.3	14.3	13.7	18.7	16.0	17.8	18.7	21.5	15.2

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second-tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second-tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine. [g]CRP: C-reactive protein detection. [h]PD: pathogen detection.

Table 3 Attitudes and practice of doctors towards the antimicrobial stewardship regulations in 2012 and 2016

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Personal willingness to accept antimicrobial stewardship regulations in 2012 (first year of implementation) %										
Very willing	26.5	26.3	18.9	45.8	28.4	18.6	27.9	25.1	24.0	28.8
Willing	52.4	52.6	52.8	47.9	53.3	48.6	49.7	55.2	50.6	54.0
Hard to accept	19.2	19.0	26.4	6.3	16.4	31.4	20.6	17.7	23.2	15.6
Unacceptable	1.9	2.1	1.9	0.0	2.0	1.4	1.8	2.0	2.3	1.6
Not applicable	n=68									
Personal willingness to accept antimicrobial stewardship regulations in 2016 %										
Very willing	27.4	28.4	17.0	37.3	27.6	26.3	24.2	31.3	25.9	28.7
Willing	61.7	60.9	69.6	54.9	61.9	60.9	64.3	58.5	60.6	62.7
Hard to accept	10.0	9.8	13.4	5.9	9.5	12.2	10.6	9.3	12.2	8.1
Unacceptable	0.9	0.9	0.0	2.0	0.9	0.6	0.9	0.8	1.3	0.5
Impact of antimicrobial stewardship on prescribing antibiotic behaviors in 2012 (first year of implementation) %										
Very restricted	6.1	6.2	5.6	6.1	6.0	6.3	7.0	5.1	7.0	5.2
Restricted	35.5	36.9	35.5	18.4	35.7	34.7	37.4	33.4	35.9	35.1
Slightly	48.3	48.0	46.7	55.1	48.2	48.6	45.5	51.4	49.0	47.6
Not restricted	10.1	8.9	12.1	20.4	10.1	10.4	10.1	10.1	8.1	12.0
Not applicable	n=66									
Impact of antimicrobial stewardship on prescribing antimicrobial behaviors in 2016 %										
Very restricted	8.4	8.5	9.8	3.9	8.0	10.3	7.4	9.6	10.6	6.4
Restricted	38.9	39.1	43.8	25.5	38.2	41.7	43.1	33.8	41.2	36.8
Slightly	43.5	43.6	40.2	49.0	44.2	40.4	41.5	45.9	40.7	46.1
Not restricted	9.2	8.7	6.3	21.6	9.5	7.7	7.9	10.7	7.5	10.7
Concerns with prognosis of patients "at risk" --who would have been given antimicrobials before the stewardship in 2012 (first year of implementation) %										
Always	16.8	17.1	19.3	8.3	13.9	29.2	18.5	15.0	19.7	14.1
Often	48.9	48.0	51.4	54.2	50.9	40.3	49.1	48.6	50.8	47.0
Sometimes	29.9	30.2	27.5	31.3	30.1	29.2	27.2	32.8	25.3	34.2
No	4.4	4.8	1.8	6.3	5.2	1.4	5.1	3.7	4.2	4.7
Not applicable	n=64									
Concerns with prognosis of patients "at risk" in 2016 %										
Always	12.6	12.7	16.1	3.9	11.5	17.3	14.7	10.2	14.5	10.9
Often	54.3	53.9	58.0	51.0	53.3	58.3	54.9	53.6	56.2	52.5
Sometimes	26.8	26.9	22.3	35.3	28.3	20.5	24.6	29.4	24.1	29.2
No	6.3	6.5	3.6	9.8	6.9	3.8	5.9	6.9	5.2	7.4
Impact of antimicrobial stewardship on prognosis of patients "at risk" %										
Strong	2.4	2.3	1.8	3.	2.5	1.9	2.3	2.5	2.6	2.1

Moderate	27.6	26.9	31.3	29.4	27.0	30.1	31.8	22.5	27.7	27.6
Slight	63.2	64.1	61.6	56.9	63.3	62.8	59.6	67.6	63.5	62.9
No	6.8	6.8	5.4	9.8	7.2	5.1	6.3	7.4	6.2	7.4
Countermeasures to concerns for prognosis of patients "at risk" in 2012 (first year of implementation) %										
AB [g]	16.8	16.9	18.3	11.1	16.4	18.3	17.9	15.5	20.3	13.4
AA [h]	43.8	43.8	41.3	48.9	46.0	34.5	47.6	39.7	41.8	45.6
OM [i]	10.4	10.8	7.7	11.1	10.2	11.3	7.5	13.5	4.0	16.4
SA [j]	15.2	14.1	22.1	13.3	13.1	23.9	15.0	15.5	17.5	13.1
No measures	13.9	14.3	10.6	15.6	14.3	12.0	12.0	15.8	16.3	11.5
Not applicable	n=85									
Countermeasures to concerns for prognoses of patients "at risk" in 2016 %										
AB	9.7	9.8	9.8	7.8	10.1	7.7	11.1	8.0	10.6	8.8
AA	46.7	46.1	50.0	47.1	46.4	48.1	50.8	41.8	48.2	45.4
OM	13.6	13.0	13.4	21.6	13.8	12.8	9.9	18.1	6.0	20.7
SA	12.9	13.4	10.7	11.8	11.7	17.9	12.2	13.7	13.7	12.1
No measures	17.1	17.7	16.1	11.8	18.0	13.5	16.0	18.4	21.5	13.1

[a]Pm/Pv: p/private clinic. [b]1/new1/2: first/new first/second-tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second -tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine. [g]AB: prescribe the antimicrobials as before. [h]AA: prescribe allowable antimicrobials. [i]OM: prescribe other medicine (except antimicrobials). [j]SA: suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations.

Figure 1 Attitudes and practice of doctors toward antimicrobial stewardship in 2012 and 2016
Percentage of doctors who: received intensive or frequent compulsory stewardship training; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; prescribed antimicrobials as before, or suggest patient-self-medication with restricted antimicrobials as countermeasures.

Figure 2 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different medical organisation levels in 2016.
Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".
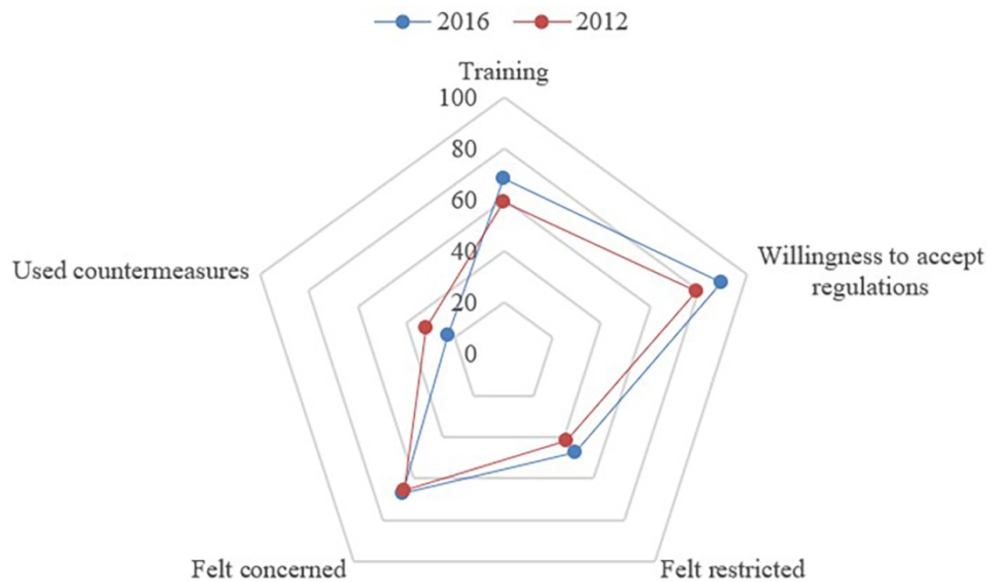
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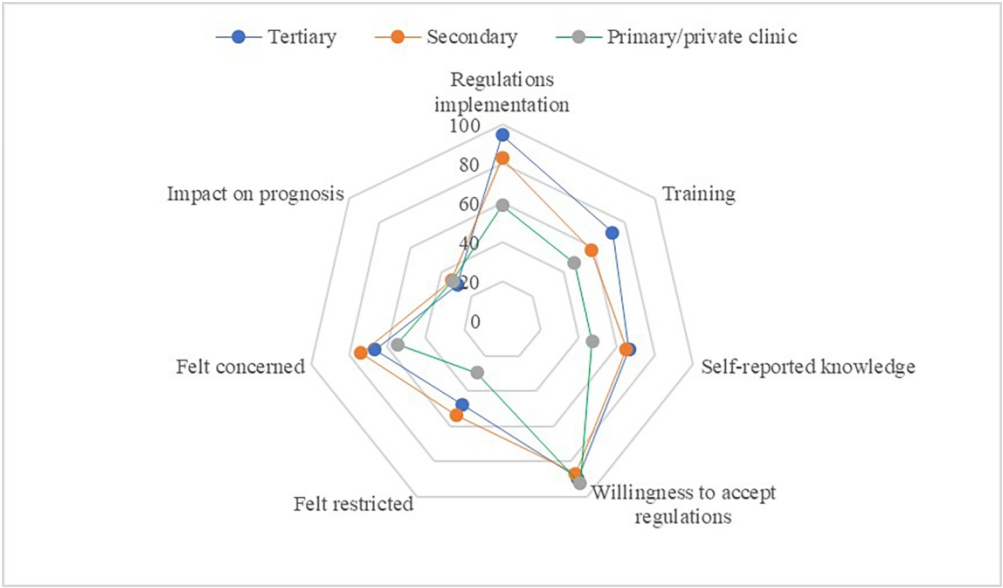
120x70mm (300 x 300 DPI)

Figure 2 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different medical organisation levels in 2016.
Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".

146x85mm (300 x 300 DPI)

Table S1 Description of 107 WeChat groups and 3 Email groups

	19 WeChat groups -sent by researchers	88 WeChat groups -sent by key respondents	3 Email groups -sent by researchers
Description	Doctors currently working at departments of pediatrics, orthopaedics, diabetic, internal, oncology, endocrinology, et al.	Doctors currently working at departments of dermatologyy, oncology, respiratory medicine, paediatrics, orthopaedics, internal medicine, surgery, renal medicine, cardiology, gastroenterology, ICU, endocrinology, and general practitioners working within both urban and rural community health centers.	Members of Association of Pediatrics, Association of Diabetes, and Association of Internal Medicine in the World Federation of Chinese Medicine Societies.
Number of health professionals	2517	16640	634
Survey period	9th to 25th March 2017	22th to 30th March 2017	29th to 30th March 2017

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Table S2 List of questionnaire items (translated from Chinese[11])

No	Questions	Answer categories
1	What is your occupation?	• Doctor • Nurse • Clinical postgraduate • Researcher • Administrative staff • Other
2	How old are you?	|__|__| years
3	What is your gender?	• Male • Female
4	What is your major?	• Western medicine • Traditional Chinese medicine • Integrative medicine of traditional Chinese medicine and western medicine
5	What is your highest educational level?	• College/diploma • Bachelor • MSc • MD or PhD
6	What is your level of seniority?	• Intern • Resident • Associate chief-physician • Chief-physician
7	When did your clinical work start?	• Before 2001 • 2002-2006 • 2007-2011 • From 2012 to now
8	How many days per week did you provide outpatient services between 2007 and 2011?	• 0 • 1 • 2 • 3 • 4 • 5
9	How many days per week did you provide outpatient services between 2012 and 2016?	• 0 • 1 • 2 • 3 • 4 • 5
10	Which city do you work in?	|__|__|__|__|
11	Which department do you work in?	|__|__|__|__|
12	What is the level of your medical organisation?	• 3-A • 3-B • 3-C

		●	2-A
		●	2-B
		●	2-C
		●	1-A
		●	1-B
		●	1-C
		●	Private clinic
13	Which type of hospital are you based in?	●	Western medicine hospital
		●	Traditional Chinese medicine hospital
		●	Integrative medicine hospital of traditional Chinese medicine and western medicine
14	Is there an official requirement to restrict use of antimicrobials in your hospital?	●	No
		●	Less stringent
		●	Stringent
		●	Very stringent
15	What is/are your criteria for prescribing antimicrobials (multiple choice)?	●	Symptoms
		●	Signs
		●	Full blood count
		●	C-reactive protein detection
		●	Pathogen detection
		●	Diagnosis
		●	Others
16	Do you know the 'administrative regulations for the clinical use of antimicrobials' (hereinafter, antimicrobial stewardship regulations)?	●	Don't know
		●	Know a little
		●	Familiar
		●	Very familiar
17	Did you have any compulsory antimicrobial stewardship training in 2016?	●	No
		●	Less frequently
		●	Frequently
		●	Intensive
18	Did you have any compulsory antimicrobial stewardship training in 2012 (first year of stewardship implementation)?	●	No
		●	Less frequently
		●	Frequently
		●	Intensive
		●	Not applicable
19	How willing were you to accept the regulations in 2016?	●	Very willing
		●	Willing
		●	Hard to accept
		●	Unacceptable
20	How willing were you to accept the regulations in 2012 (first year of implementation)?	●	Very willing
		●	Willing
		●	Hard to accept
		●	Unacceptable
		●	Not applicable

21	In 2016, as a result of the potential influence of the antimicrobial stewardship, were there any restrictions on your antimicrobial prescription?	• Very restricted • Restricted • Slightly • Not restricted
22	In 2012, as a result of the potential influence of the antimicrobial stewardship, were there any restrictions on your antimicrobial prescription?	• Very restricted • Restricted • Slightly • Not restricted • Not applicable
23	Were you worried about the prognosis of patients "at risk" --who would have been given antimicrobials before the stewardship in 2016?	• Always • Often • Sometimes • No
24	If you were worried about the prognosis of patients "at risk" in the above question, what measures did you take to address your concern in 2016?	• Prescribe anyway the antimicrobials as before • Prescribe allowable antimicrobials • Prescribe other medicine (except antimicrobials) |__|__|__|__|__|__|__| • Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations • No measures
25	Were you worried about the prognosis of patients "at risk" in 2012 (first year of implementation)?	• Always • Often • Sometimes • No • Not applicable
26	If you were worried about the prognosis of patients "at risk" in the above question, what measures did you take to address your concern in 2012 (first year of implementation)?	• Prescribe anyway the antimicrobials as before • Prescribe allowable antimicrobials • Prescribe other medicine (except antimicrobials) |__|__|__|__|__|__|__| • Suggest patient-self-medication (to buy by themselves somewhere else) with intended antimicrobials restricted by the stewardship regulations • No measures • Not applicable
27	Do you think the antimicrobial stewardship regulations have had any impact on the clinical prognosis of patients "at risk"?	• Strong • Moderate • Slight • No
28	What is the maximum permitted antimicrobial prescription rate in your medical organisation?	|__|__|%
29	What is the maximum permitted antimicrobial prescription	|__|__|%

		rate in your department?		
30	For which operations should perioperative antimicrobial prophylaxis be used?		●	Hernia repair
			●	Resection of thyroid adenoma
			●	Resection of mammary fibroadenoma
			●	Open fractures debridement and internal fixation
31	Which antimicrobial should be used to treat extended-spectrum β-lactamase-producing bacterial infections?		●	Carbapenems
			●	Chloramphenicol
			●	Macrolides
			●	Aminoglycosides
32	For how long a restricted antibiotic can be used in emergent medical situations?		●	2 days
			●	1 day
			●	5 days
			●	30 days

[a]The English version of the questionnaire was translated from the original Chinese version verbatim by a native Chinese speaker, and then back translated into Chinese by another native Chinese speaker working in the UK.

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Table S3 Demographic and practice characteristics of 807 respondents

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/Pv [a] n=51	1/new1/2 [b] n=651	Others n=156	IT/RS [e] n=443	ACP/CP [d] n=364	WM [e] n=386	TCM/IM [f] n=421
Female %	58.7	59.8	52.7	58.8	59.9	53.8	58.7	58.8	58.0	59.4
Age mean years	39.0	39.1	39.7	37.0	38.8	40.1	34.6	44.5	39.5	38.6
Education level %										
College/diploma	1.6	0.5	4.5	9.8	0.9	4.5	2.3	0.8	0.8	2.4
Bachelor	27.1	19.3	62.5	49.0	20.3	55.8	26.6	27.7	33.2	21.6
MSc	44.2	47.7	30.4	31.4	46.2	35.9	56.2	29.7	39.4	48.7
MD or PhD	27.0	32.6	2.7	9.8	32.6	3.8	14.9	41.8	26.7	27.3
Major %										
WM	47.8	48.8	51.8	27.5	43.9	64.1	47.6	48.1	NA	NA
TCM	37.7	37.4	32.1	52.9	41.9	19.9	35.9	39.8	NA	NA
IM	14.5	13.8	16.1	19.6	14.1	16.0	16.5	12.1	NA	NA
Seniority level%										
Intern	13.3	13.0	12.5	17.6	12.0	18.6	NA	NA	14.5	12.1
Resident	41.6	38.5	49.1	64.7	41.6	41.7	NA	NA	40.2	43.0
ACP	29.9	31.5	27.7	13.7	31.5	23.1	NA	NA	30.3	29.5
CP	15.2	16.9	10.7	3.9	14.9	16.7	NA	NA	15.0	15.4
Year starting to work %										
≤2001	38.9	38.7	44.6	29.4	52.5	46.2	13.1	70.3	44.3	34.0
2002-2006	22.6	21.9	19.6	37.3	22.6	22.4	23.5	21.4	24.1	21.1
2007-2011	22.2	21.9	25.0	19.6	23.5	16.7	34.1	7.7	17.9	26.1
≥2012	16.4	17.5	10.7	13.7	16.7	14.7	29.3	0.5	13.7	18.8
Outpatient service (days per week) in 2007-2011 %										
0	22.8	24.9	21.0	2.3	21.8	27.1	35.1	12.2	22.5	23.1
1	21.6	23.7	19.0	2.3	21.4	22.6	16.6	26.0	24.3	19.0
2	18.1	19.8	15.0	4.5	17.7	19.5	10.5	24.6	20.1	16.1
3	12.0	11.5	14.0	13.6	12.4	10.5	8.9	14.6	12.6	11.4
4	6.8	6.8	4.0	13.6	7.7	3.0	7.7	6.1	8.1	5.6
5	18.7	13.4	27.0	63.6	19.0	17.3	21.1	16.6	12.3	24.9
Not applicable	n=132									
Outpatient service (days per week) in 2012-2016 %										
0	15.4	16.8	13.4	2.0	14.1	20.5	25.5	3.0	15.5	15.2
1	22.6	25.3	15.2	3.9	22.0	25.0	19.9	25.8	27.2	18.3
2	21.7	22.7	18.8	15.7	21.0	24.4	14.9	29.9	23.3	20.2
3	14.3	13.5	18.8	13.7	14.9	11.5	13.3	15.4	13.5	15.0
4	8.7	8.9	5.4	13.7	10.1	2.6	7.9	9.6	8.8	8.6
5	17.5	12.9	28.6	51.8	17.8	16.0	18.5	16.2	11.7	22.8

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second–tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second -tier city, such as Shenyang, Xi'an). [e]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine.

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[f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.

Table S4 Medical organisation of 807 respondents

Questions asked	Total n=807	Medical organisation level			City level		Title		Major	
		Tertiary n=644	Secondary n=112	Pm/ Pv [a] n=51	1/new 1/2 [b] n=651	Others n=156	IT/RS [c] n=443	ACP/ CP [d] n=364	WM [e] n=386	TCM/ IM [f] n=421
Medical organisation level %										
Tertiary	79.8	NA	NA	NA	83.4	64.7	74.9	85.7	81.3	78.4
Secondary	13.9	NA	NA	NA	9.8	30.8	15.6	11.8	15.0	12.8
Primary	5.0	NA	NA	NA	5.5	2.6	7.4	1.9	2.3	7.4
Private clinic	1.4	NA	NA	NA	1.2	1.9	2.0	0.5	1.3	1.4
Medical organisation type %										
WM	51.9	51.1	61.6	41.2	47.9	68.6	51.5	52.5	84.5	22.1
TCM	34.7	37.0	30.4	15.7	38.4	19.2	31.4	38.7	5.7	61.3
Integrative	13.4	12.0	8.0	43.1	13.7	12.2	17.2	8.8	9.8	16.6
City level %										
First-tier	37.1	37.7	18.8	68.6	NA	NA	37.0	37.1	34.2	39.7
New first-tier	23.7	24.8	24.1	7.8	NA	NA	23.7	23.6	21.8	25.4
Second-tier	20.0	21.7	14.3	9.8	NA	NA	18.1	22.3	18.1	21.6
Third-tier	9.0	7.3	22.3	2.0	NA	NA	9.3	8.8	12.4	5.9
Fourth-tier	5.9	3.9	17.0	7.8	NA	NA	6.3	5.5	7.8	4.3
Fifth-tier	4.3	4.5	3.6	3.9	NA	NA	5.6	2.7	5.7	3.1
Geographic region %										
Eastern	49.2	48.6	38.4	80.4	53.6	30.8	50.6	47.5	47.2	51.1
Central	10.7	9.0	20.5	9.8	7.1	25.6	11.1	10.2	13.0	8.6
Western	21.4	20.5	33.0	7.8	17.7	37.2	21.0	22.0	34.7	9.3
Northeast	18.7	21.9	8.0	2.0	21.7	6.4	17.4	20.3	5.2	31.1

[a]Pm/Pv: primary/private clinic. [b]1/new1/2: first/new first/second–tier (first-tier city, such as Beijing, Shanghai; new first-tier city, such as Chengdu, Hangzhou; second -tier city, such as Shenyang, Xi'an). [c]IT/RS: intern/resident. [d]ACP/CP: associate chief-physician/chief-physician. [e]WM: western medicine. [f]TCM/IM: traditional Chinese medicine/integrative medicine of traditional Chinese medicine and western medicine.
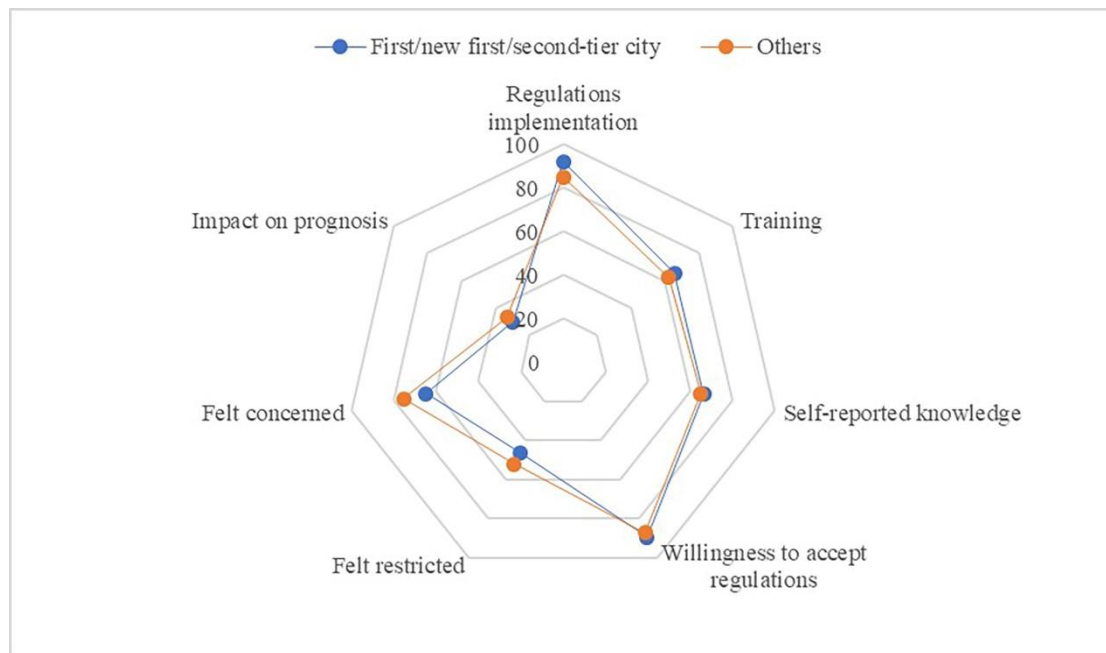
Figure S1 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different city levels in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".
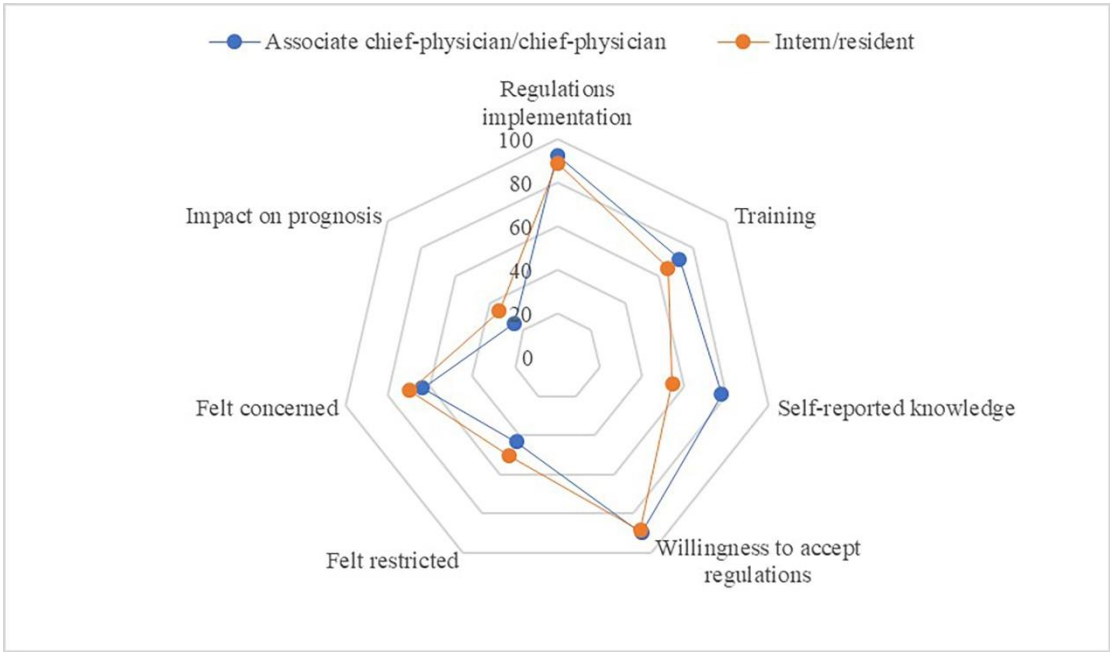
Figure S2 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different professional titles in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".
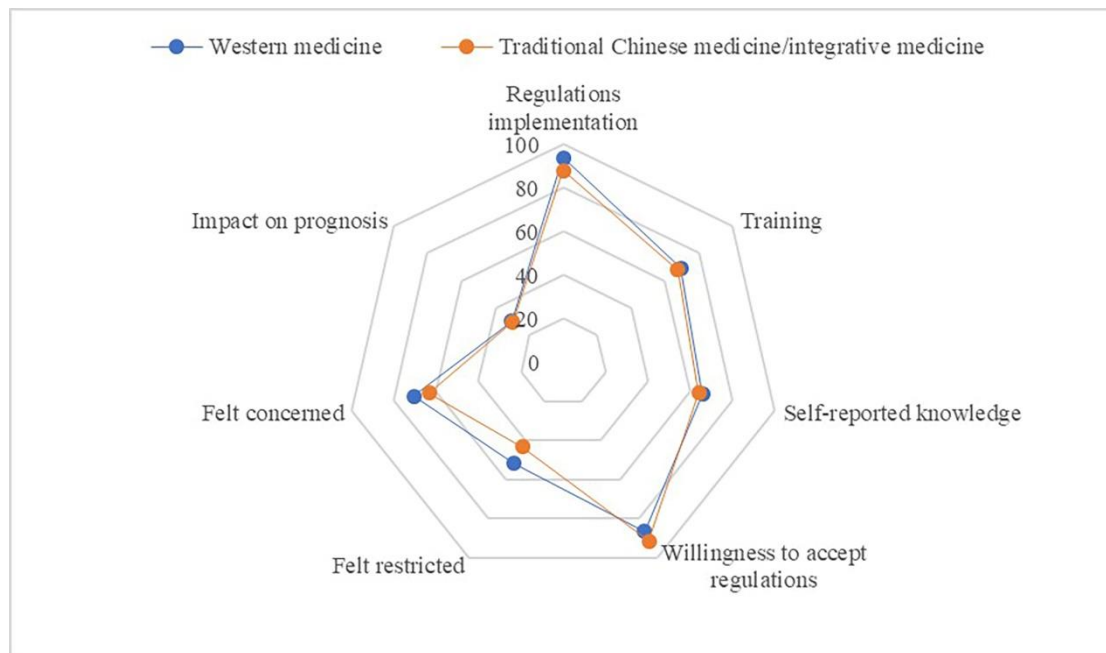
Figure S3 Knowledge, attitudes and practice of doctors toward antimicrobial stewardship in different medical majors in 2016.

Percentage of doctors who: worked in a medical organisation with stringent or very stringent stewardship regulations implementation; received intensive or frequent compulsory stewardship training; described themselves as familiar or very familiar with stewardship; were willing or very willing to accept stewardship; felt restricted or very restricted by stewardship; felt often concerned or always concerned with the prognosis of patients "at risk"; felt stewardship has a moderate or strong impact on prognosis of patients "at risk".

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	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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	*6*
Bias	9	Describe any efforts to address potential sources of bias	5-7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	/
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	/
		(*e*) Describe any sensitivity analyses	/
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	7
		(b) Give reasons for non-participation at each stage	/
		(c) Consider use of a flow diagram	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-8
		(b) Indicate number of participants with missing data for each variable of interest	/
Outcome data	15*	Report numbers of outcome events or summary measures	7
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	8-11

		(*b*) Report category boundaries when continuous variables were categorized	Table1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	/
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-10

Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
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	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-13
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	18

*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.