Identifying antibiotic prescribing patterns through multi-level latent profile analyses: a cross-sectional survey of primary care physicians in Hubei of China

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Research article

Keywords: Primacy care, Antibiotic Prescription, Latent Profile analysis, Knowledge-Attitudes-Practices, China,

Posted Date: March 29th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-19162/v1

Abstract

Background Overuse of antibiotics significantly fuels the development of AMR, which threating the global population health. Great variations existed in antibiotic prescribing practices among physicians, indicating improvement potential for rational use of antibiotics. This study aims to identify antibiotic prescribing patterns of primary care physicians and potential determinants.

Methods A cross-sectional survey was conducted on 551 physicians from 67 primary care facilities in Hubei selected through random cluster sampling, tapping into their knowledge, attitudes and prescribing practices toward antibiotics. Prescriptions (n=501,072) made by the participants from 1 January to 31 March 2018 were extracted from the medical records system. Seven indicators were calculated for each prescriber: average number of medicines per prescription, average number of antibiotics per prescription, percentage of prescriptions containing antibiotics, percentage of antibiotic prescriptions containing broad-spectrum antibiotics, percentage of antibiotic prescriptions containing parenteral administered antibiotics, percentage of antibiotic prescriptions containing restricted antibiotics, and percentage of antibiotic prescriptions containing antibiotics included in the WHO "Watch and Reserve" list. Two-level latent profile analyses were performed to identify the antibiotic prescribing patterns of physicians based on those indicators. Multi-nominal logistic regression models were established to identify determinants with the antibiotic prescribing patterns.

Results On average, each primary care physician issued 909 (ranging from 100 to 11941 with a median of 474) prescriptions over the study period. The mean percentage of prescriptions containing antibiotics issued by the physicians reached 52.19% (SD=17.20%). Of those antibiotic prescriptions, an average of 82.29% (SD=15.83%) contained broad-spectrum antibiotics; 71.92% (SD=21.42%) contained parenteral administered antibiotics; 23.52% (SD=19.12%) contained antibiotics restricted by the regional government; and 67.74% (SD=20.98%) contained antibiotics listed in the WHO "Watch and Reserve" list. About 28.49% of the prescribers were identified as low antibiotic users, compared with 51.18% medium users and 20.33% high users. Higher use of antibiotics was associated with insufficient knowledge, indifference to changes, complacency with satisfied patients, low household income and rural location of the prescribers.

Conclusion Great variation in antibiotic prescribing patterns exists among primary care physicians in Hubei of China. High use of antibiotics is not only associated with knowledge shortfalls but also low socioeconomic status of prescribers.

Background

Antimicrobial resistance (AMR) is one of the most alarming threats to global health, which has resulted in significant human and economic loss worldwide. It was estimated that AMR led to 700,000 deaths in 2014 [1]. Without effective interventions, this figure would balloon to 10 million per year by 2050 and become the leading cause of death in the world [1].

Overuse of antibiotics is widely believed to be associated with the development of AMR [2-5]. Given that the discovery of new antibiotics has been dramatically slow over the past few decades [6], reducing irrational prescriptions of antibiotics became an urgent public health agenda. Unfortunately, irrational antibiotic prescribing has been prevalent worldwide. In the US, for example, over 50% antibiotic prescriptions are deemed inappropriate and 30% unnecessary [7].

Past studies revealed that great variations existed in antibiotic prescribing practices among physicians [8-13], which could not be fully explained by the variation in patient needs [8, 11]. The disparity of antibiotic prescription rates among prescribers could be as high as ten times after casemix adjustments for patients [12]. A recent study in Canada demonstrated that the same patient would have 1.7 times more or less chance to receive antibiotics simply by swapping to a different physician [8].

Internationally, both restrictive and persuasive measures have been attempted to curtail irrational antibiotic prescribing behaviors [14-17]. But very few interventions, if any, have tailored to the individual differences across prescribers. This could seriously jeopardise the efficiency and effectiveness of the interventions [14-16].

This study aimed to identify individual antibiotic prescribing patterns in primary care physicians through latent profile analyses, a method that categorises prescribing behaviors using multiple indicators. Our current understanding about antibiotic prescribing patterns is quite limited [18, 19]. Previous studies often adopted an over-simplified approach by examining the frequency and volume of antibiotics prescribed [8-13]. Such kind of study, although important, has failed to reveal the complex nature of antibiotic prescribing behaviors. Theoretically, irrational prescribing of antibiotics can also be reflected through the type of antibiotics (e.g. narrow- vs broad-spectrum) and the way they are administered (e.g. oral vs parenteral) [20]. This study fills the gap in the literature by employing latent profile analyses, which can help identify irrational antibiotic prescribers who would otherwise be missed in single indicators.

Methods

Setting

The study was conducted in Hubei province of central China. Hubei has a land size of 185,900 km^2 and more than 59 million populations. With a gross domestic product at $8,915 per capita in 2017, its economic status is ranked in the middle range of all provinces in China. According to the World Bank [21], Hubei is considered as a middle-high income region.

We chose primary care facilities in Hubei as the study setting. In 2017, primary care facilities in Hubei served 205.08 million patient visits, accounting for 60.24% of total outpatient visits in the province [22]. About 44.28% of the patient visits to primary care were given an antibiotic prescription [23]. It was estimated that 60% of antibiotic prescriptions in primary care in China are inappropriate [24].

Sampling and participants

A stratified cluster random sampling strategy was adopted to select study participants. Hubei has 347 urban community health centres and 1137 rural township health centres. In proportion to the urban and rural numbers, 19 community healthcare centres from 3 urban districts and 48 township health centres from 6 rural districts were randomly selected, respectively. Details of the sampling methods have been published elsewhere [23].

Primary care physicians from the selected health centres who met the following criteria were invited to participate in the study: 1) having the authority to prescribe antibiotics independently; 2) having issued at least 100 prescriptions over the three-month study period, which contained at least one antibiotic prescription.

In total, 645 physicians met the inclusion criteria and 551 (85.58%) agreed to participate in the study. Of those who agreed, 458 (71.01%) returned a valid questionnaire.

Data collection

Eight field investigators were recruited and trained to conduct data collection. Each participating facility was visited by a pair of the trained investigators. The investigators had no servicing relationships with the facilities or their employees at the time. All eligible primary care physicians were approached and invited to participate in the study. Informed written consents were obtained prior to data collection.

Prescribing records issued by the 551 study participants over a three-month period (from 1 January to 31 March 2018) were extracted from the medical records system of the participating facilities, including the name, formulation, dosage, administration route, and price of the prescribed medicines, and information about the prescribers and facilities. This was followed by a questionnaire survey of prescribers (n=458) over the period from 23 April to 6 June 2018, tapping into their socioeconomic status and professional characteristics, and their knowledge and attitudes toward antibiotic prescribing. The respondents were asked to complete the questionnaire independently, which took roughly 15 minutes. A token gift ($1.65) was given to those who returned the questionnaire to the investigators. Missing items, if any, were re-filled by the investigators through an additional interview.

Measurements

Antibiotic prescribing patterns

Seven indicators were identified for measuring antibiotic prescribing patterns through a comprehensive literature review and expert consultations:

1. average number of medicines per prescription;
2. average number of antibiotics per prescription;
3. percentage of prescriptions containing antibiotics;

4. percentage of antibiotic prescriptions containing broad-spectrum antibiotics;
5. percentage of antibiotic prescriptions containing parenteral administered antibiotics;
6. percentage of antibiotic prescriptions containing restricted antibiotics imposed by the provincial government; and
7. percentage of antibiotic prescriptions containing antibiotics included in the World Health Organisation (WHO) “Watch and Reserve List”.

The first three indicators were adapted from the prescribing indicators recommended by the WHO [25]. They measured the frequency and volume of antibiotics prescribed. Although we did not measure combined use of antibiotics directly because it was rare in primary care, the tendency of combined use of antibiotics was likely to be captured through the connection between the volume (indicator 2) and frequency (indicator 3) indicators [26]. Previous studies showed that higher number of medicines prescribed in general is also a significant predictor of higher antibiotic prescriptions [27, 28].

We added two additional indicators (indicator 4 and 5) in order to better assess irrational prescribing of antibiotics. Empirical evidence shows that broad-spectrum antibiotics is frequently used and is perhaps the most common form of antibiotic abuse in primary care [29, 30]. In addition, the high prevalence of parenteral administration of antibiotics has attracted increasing safety concerns in China. Studies showed that 36% to 60% of antibiotics were administered through parenteral injections in primary care settings in China [29-31].

Over the past two decades, China introduced some restrictive measures to reduce irrational antibiotic prescribing. These included a list of restricted antibiotics for primary care imposed by the regional governments [32]. Restricted access to certain antibiotics addresses the concerns of AMR [33-35]. The WHO also published an “Access, Watch and Reserve” (AWaRe) classification system [20]. All antibiotics were exclusively classified into three categories. The “Watch” list includes antibiotics that have higher resistance potential, while the “Reserve” list includes antibiotics that should be reserved for treatment of infections due to multi-drug-resistant organisms. We examined prescriptions of restricted antibiotics against the above two classification systems. Although the two share similar principles, they are not always consistent. In Hubei, antibiotics were classified into non-restricted, restricted, and special-restricted.

Factors associated with antibiotic prescribing patterns

Antibiotic prescribing behaviors can be influenced by the knowledge and attitudes of prescribers and their personal circumstances according to two systematic reviews [18, 19]. Prescribers with higher qualifications and better knowledge of antibiotics are less likely to prescribe antibiotics. However, their attitudes toward antibiotic prescribing are also influenced by patient expectations and collegial pressures.

This study used a 37-item questionnaire to measure the knowledge, attitudes and personal circumstances of prescribers. The questionnaire was developed based on some existing instruments [36, 37] with further consideration of the findings of the two systematic reviews [18, 19]. The reliability and validity of the questionnaire has been tested and confirmed in previous studies [36, 37].

The questionnaire respondents were asked to indicate whether they agreed to prescribe antibiotics for 11 common conditions such as upper respiratory tract infections and diarrhea [37]. A correct decision in line with the current clinical guidelines was given a score of 1, otherwise 0. The scores were summed up for each respondent.

The attitudes of the questionnaire respondents toward antibiotic prescribing were measured by 17 items, each being rated on a five-point Likert scale (0=strongly agree, 1=agree, 2=neutral, 3=disagree, 4=strongly disagree). The scores were summed up to measure the tendency of complacency to satisfied patients (0-8 measured by 4 items), fearful of adverse events (0-12 measured by 6 items), ignorance of AMR (0-16 measured by 8 items), indifference to changes (0-4 measured by 2 items), and responsibility avoidance by blaming others (0-28 measured by 7 items), respectively [36]. All item coding and summed scores were aligned into a unified direction, with a higher score indicating more positive attitudes toward reduction of irrational antibiotic prescribing.

The personal circumstances measured in this study included the demographic characteristics (age and gender) of the respondents, and their socioeconomic status (educational qualifications, and household income) and professional experiences (workplace, years of practice, sub-specialty, professional title, and continuing education on antibiotic prescribing). These factors have been proved to be significant determinants of antibiotic prescribing behaviors [18, 19].

Data analysis

Two datasets were prepared for data analyses. The first dataset contained 501,072 prescriptions made by 551 primary care physicians. For each physician, the seven prescription indicators were calculated. Antibiotics were defined based on the Anatomical Therapeutic Chemical (ATC) classification system and included only systemic use of antibiotics (ATC code J01) [38]. They were further divided into broad- and narrow-spectrum in line with the classification criteria used in the US national survey on antibiotic use [33]. Restricted antibiotics were defined based on the Hubei government's antibiotic regulation policy and the WHO AWaRe list.

To determine the antibiotic prescribing patterns, latent profile analyses (LPA) were performed using the seven prescribing indicators at the physician level. LPA belong to finite mixture modelling which can identify and describe "hidden groups" within a population. Because the 551 physicians were clustered in 67 primary care facilities, a two-level LPA model was established. Differences at the facility level were treated as random effect. Maximum likelihood parameter estimates with standard errors (MLR) were applied. The model identification was checked using 1000 initial stage starts and 1000 final stage starts [39].

We tested different models that categorised antibiotic prescribing behaviors into one, two, three, four, or five groups. The best fit model was identified using the following model index: Bayesian Information Criterion (BIC), Sample-size Adjusted BIC (SABIC), Vuong-Lo-Mendell-Rubin Adjusted Likelihood Ratio Test (VLMR-LRT), Correct Model Probability (cmP) and Entropy. A lower value of BIC and SABIC indicates better fitness of data into the estimated model. VLMR-LRT compares the model fit between two neighboring models (for example, two groups vs three groups). A non-significant *p* value (>0.05) indicates a lack of statistical significance between the two compared models. cmP provides an overall assessment of all estimated models and a larger cmP value indicates a better model fit. Entropy assesses the accuracy of classification, with a higher value indicating better classification [39]. To avoid over-stratification, the smallest group should have a minimum of 5% of participants.

The second dataset contained the 458 returned questionnaires, as well as the classification of the antibiotic prescribing patterns of the 458 respondents. A three-group model was identified in the LPA. Each questionnaire respondent was assigned into one of the antibiotic prescribing pattern groups with the highest probability.

Differences in knowledge and attitudes scores and personal circumstances among the respondents in different antibiotic prescribing pattern groups were examined using Kruskal-Wallis rank tests, one-way analysis of variance (ANOVA), or chi-square tests. Post-hoc pairwise comparisons were performed using Dunn and Bonferroni tests. Multi-nominal logistic regression models were established to determine significant factors predicting the three groups of antibiotic prescribing patterns after adjustments for variations in other factors. In the regression analyses, knowledge and attitudes scores were transformed into dichotomous variables with mean scores serving as a cut-off point. An enter approach was adopted in the modelling.

The statistical analyses were performed using STATA (version 12.0) and Mplus (version 6.0). A *p* value <0.05 was considered statistically significant.

Results

Antibiotic prescribing in primary care

On average, 909 (ranging from 100 to 11941 with a median of 474) prescriptions were issued by the 551 participating physicians over the three-month study period. Each physician prescribed an average of 2.87 (SD=0.78) medicines and 0.65 (SD=0.26) antibiotics per prescription, respectively. Of the prescribed antibiotics, cephalosporins (J01D) was the most commonly used (38.50%), followed by macrolides (J01F, 24.03%).

The mean percentage of prescriptions containing antibiotics issued by the physicians reached 52.19% (SD=17.20%). Of those antibiotic prescriptions, an average of 82.29% (SD=15.83%) contained broad-spectrum antibiotics; 71.92% (SD=21.42%) contained parenteral administered antibiotics; 23.52%

(SD=19.12%) contained restricted antibiotics imposed by the provincial government; and 67.74% (SD=20.98%) contained antibiotics listed in the WHO "Watch and Reserve" list (Table 1).

[Table 1 inserted here]

Antibiotic prescribing patterns of primary care physicians

The latent profile analyses (Appendix Table S1) identified three distinctive groups of antibiotic prescribers: 28.49% low users, 51.18% medium users and 20.33% high users (Figure 1). The low antibiotic prescribing group was characterised by the lowest values on all of the seven indicators in comparison with the other two groups, despite a lack of statistical significance in one indicator (AWaRe) between the low and medium user groups. The high antibiotic prescribing group further distinguished itself from the medium user group through higher values on these indicators except for prescriptions of restricted antibiotics imposed by the provincial government (Table 1).

The 20.33% high antibiotic prescribers contributed to 23.56% of prescribed medicines, 24.48% of prescribed antibiotics, 26.27% of broad-spectrum antibiotics, 27.84% of parenteral administered antibiotics, 23.65% of government-restricted antibiotics, and 27.36% of antibiotics in the WHO "Watch and Reserve" list.

[Figure 1 inserted here]

Factors associated with antibiotic prescribing patterns

The 458 questionnaire respondents had an average age of 43.5 years (SD=9.3) and 72% were male. Only 38.2% obtained a university degree. The vast majority worked in a rural setting (78.0%) and had an annual household income of less than 80,000 yuan (79.5%). About 48% of the respondents worked as a general practitioner. Slightly more than half (51.1%) had a junior professional title. The average knowledge score of the respondents sat in the middle range even though more than 75% reported attending continuing education on antibiotics (Table 2).

Of the questionnaire respondents, 27.07% were classified as low antibiotic users, compared with 53.06% medium users and 19.87% high users. Those who were male (p=0.003), had a lower educational qualification (p=0.018), lived with a lower household income (p<0.001), worked in rural facilities (p<0.001), had a junior professional title (p=0.017), and had a lower knowledge score (p=0.002) were more likely to be in the high user group. There were also significant differences in the antibiotic prescribing patterns across sub-specialties (*p*=0.025) (Table 2).

[Table 2 inserted here]

The multinomial logistic regression analyses confirmed that knowledge, attitudes, clinical experiences, household income and workplace settings were significant predictors of the antibiotic prescribing patterns after adjustments for variations in other variables (Table 3).

The respondents with a higher than average knowledge score were less likely to be assigned into the medium (Relative Risk Ratio (RRR)=0.440, p=0.005) or high (RRR=0.468, p=0.031) antibiotic user groups as compared with the odds of low antibiotic user group. Similarly, those who reported lower indifference to changes were also less likely to be assigned into the medium (RRR=0.416, p=0.020) or high (RRR=0.401, p=0.036) antibiotic user groups. However, the respondents with lower complacency to satisfy patients were more likely to be assigned into the medium antibiotic user group only (RRR=2.618, p=0.028) as compared with the odds of low antibiotic user group.

The respondents who worked in a rural facility were more likely than their urban counterparts to be assigned into the medium (RRR=4.275, p<0.001) or high (RRR=4.296, p=0.001) antibiotic user groups as compared with the odds of low antibiotic user group. The odds of being assigned into the medium (RRR=0.688, p=0.024) and high (RRR=0.521, p=0.003) antibiotic user groups decreased with household income. The respondents with an older age had a slightly lower odds of being assigned into the high antibiotic user group (RRR=0.942, p= 0.032). But longer years of practice slightly increased the odds of being assigned into the high antibiotic user group (RRR=1.053, p=0.015).

[Table 3 could be sited here]

Discussion

Main findings

Excessive use of antibiotics in primary care in Hubei of China is evident. The mean percentage of prescriptions containing antibiotics issued by the surveyed physicians in this study reached 52.19% (SD=17.20%), much higher than the maximal level of 30% as recommended by the WHO [40]. Of the antibiotic prescriptions, an average of 71.92% (SD=21.42%) were administered through parenteral injections. This forms a sharp contrast with the low level use (0.001% to 6.75%) of parenteral route for antibiotics in outpatient settings in Europe [35]. The high percentage (67.74%) of antibiotic prescriptions containing antibiotics listed in the WHO “Watch and Reserve” list is also concerning. The WHO AWaRe system recommends at least 60% of prescribed antibiotics in the “Access” list, instead of the “Watch and Reserve” list, to cope with the problem of antibiotic resistance [41].

About 20.33% of the prescribers in primary care were identified as high users of antibiotics in this study, compared with 51.18% medium users and 28.49% low users. This is a result of the combined effect of the seven prescribing indicators. The high user group contributed disproportionally across all the seven indicators. Previous studies usually classify high antibiotic prescribers using a single indicator [8-13].

This study shows that great variation in antibiotic prescribing patters exists in primary care in Hubei of China, which is shaped not only by the knowledge and attitudes of the prescribers, but also by their personal circumstances. High levels of antibiotic knowledge and attitudes in favor of practice changes are associated with low use of antibiotics. But lower household income and rural facilities are associated with high use of antibiotics.

Strength and limitations

Extensive studies have been undertaken to explore variations in antibiotic prescribing practices [42-47]. But very few, if any, have attempted to identify high-profile users of antibiotics. The LPA technique provides an instrument to classify antibiotic prescribers using multiple indicators. This is important because different prescribing indicators examine the issue through different angles. For example, a high antibiotic prescriber does not necessarily always use more “restricted” antibiotics or parenteral route, and vice versa.

This study identified factors associated with antibiotic prescribing patterns based on an extended knowledge-attitude-practice theory, a framework commonly used for exploring behaviors of health practitioners [18]. Validated scales were adopted to measure antibiotic knowledge and the five sub-dimensions of attitudes toward antibiotic prescribing. A lack of well-validated instruments for measuring knowledge and attitudes in previous studies was commonly criticised [48]. Contextual factors were also considered in this study. Empirical evidence shows that personal circumstances can shape the behavioral patterns of medical practitioners [18, 19].

There are several limitations in this study. The study was conducted in Hubei province using a cross-sectional design. This does not allow us to draw causal conclusions. The results should not be generalised to other regions. Instead, replications of the study in other regions using the proposed approach are advised. Further studies also need to consider risk-adjustments, in particular in hospital settings where patient conditions vary considerably. This study was not able to adjust the results for variations in patient conditions, simply because such data and risk-adjustment tools were not available.

Comparison to other studies

Antibiotic prescribing in primary care

It seems that antibiotic prescribing in primary care in Hubei declined over time. The percentage of prescriptions containing antibiotics dropped from 68% in 2011 [49] to the level of 52% in 2018 as revealed in the study.

Despite the decline, irrational antibiotic prescribing remains a serious issue of concern. The use of parenteral route for antibiotics is still very high at an average level of 71.92% as a proportion of antibiotic prescriptions, despite a slight decline in comparison with the level (84%) five years ago [50]. The high use of parenteral route is believed to be associated with the financial strategy to compensate for the loss of profit margins on sales of medicines [51].

The domination of broad-spectrum antibiotics in antibiotic prescribing in Hubei of China is comparable to findings of other studies. A study monitoring antibiotic sales in primary cares in Hubei showed that broad-spectrum antibiotics were increasingly used in recent years, rising from 74.87% as a proportion of antibiotic sales in 2012 to 85.69% in 2017 [31]. This is not unique to China. A survey on 28 European countries showed that broad-spectrum antibiotic contributed to over 80% of antibiotic use in 22 countries [52].

However, ignorance of the WHO AWaRe list in Hubei of China deserves increasing policy attention. There is serious under-use of the antibiotics in the WHO “Access” list in Hubei. The mean percentage of antibiotic prescriptions covered in the WHO “Access” list did not exceed 33% in the primary care participants in this study. This level is very low compared with the percentage of 60.17% to 63.29% of “Access” antibiotics prescribed in primary care in the UK over the period from 2011 to 2017 [53]. Although the mean percentage of government restricted antibiotics in antibiotic prescriptions is low at 23.52% in this study, it may be an outcome of the more relaxed policy of the provincial government [32]. Similar to this study, previous studies also revealed a high level of compliance with the regional government list of restricted antibiotics [54]. The effectiveness of the regional list of restricted antibiotics imposed by the government warrants further assessment.

Antibiotic prescribing patterns of primary care physicians

In this study, three distinctive groups of prescribers were identified through the LPA. Great variations in the seven indicators across the three groups were revealed. The gap in the percentage of prescriptions containing antibiotics reached 2.02 times between the high and low user groups (74.43% vs 36.76%). Despite a shortage of studies comparing individual prescribers, many existing studies point to the great variations in antibiotic prescribing across facilities and regions [8, 12, 42-47]. The European Surveillance of Antimicrobial Consumption (ESAC) project found that physicians in France used 3.20 times of antibiotics compared with those in the Netherlands [42]. In the UK, clinical guidelines were developed to reduce the use of trimethoprim for urinary tract infections. However, a nearly two-times gap was found in primary care in the use of trimethoprim as a proportion of nitrofurantoin and trimethoprim combined for urinary tract infections [55].

Factors associated with antibiotic prescribing patterns

This study found that knowledge and attitudes are significant predictors of antibiotic prescribing patterns in primary care, which is consistent with findings of previous studies [18, 19]. Good knowledge is the foundation of potential behavioral changes. But motivation is critical for translating knowledge into practice. Evidence from this study and others [56] show that higher motivation to change is associated with less antibiotic use in primary care. However, this study found that complacency to satisfy patients does not seem to fuel antibiotic prescribing as concluded in a systematic review [19]. We found that primary care physicians with lower complacency to satisfy patients are more likely to be medium antibiotic users, but not high users. This may be associated with the national culture of China: reluctance to go extremes [42, 57]. In addition, mistrust between physicians and patients is prevalent in China [58].

Prescribing behaviors can also be shaped by work and policy environments [42], as well as personal circumstances [8, 12]. This study confirms the findings of previous studies [23], showing that physicians in rural primary care facilities are more likely to be high antibiotic users than their urban counterparts. Rural patients in China are usually exposed to poorer sanitary environment and have limited education and higher expectations on antibiotics [59, 60].

Household income was found to be a significant predictor of high use of antibiotics in primary care. This is not surprising given that prescribing can bring financial gains to the prescribers in the Chinese health system. Although primary care workers are no longer able to make a profit margin on sales of medicines, a service fee and charge for disposable syringes can still be collected [51]. Perverse financial incentives have been widely believed to be the main driver of antibiotic abuse in China [57, 61]. Prescribers with low household income are particularly vulnerable to the perverse incentives.

Implications

To address AMR, many countries and institutions have established a surveillance system monitoring the use of antibiotics. The LPA adopted in this study can help identify high antibiotic prescribers. Such a strategy should only be used for targeted interventions for continuing quality improvement. It is inappropriate to punish those deemed “high users” because the major drivers of high use of antibiotics come from the system, not the individuals [23].

To curb overuse of antibiotics in primary care in China, multiple strategies need to be taken. Both restrictive and persuasive measures should emphasise on the overall reduction of antibiotic prescriptions, as well as the limited use of broad-spectrum, parenteral administrated, and the WHO “Watch and Reserve” antibiotics. In addition, the regional list of restricted antibiotics imposed by the government should be better aligned with the WHO AWaRe list. Significant increase in governmental budget support to primary care is needed to break the perverse financial incentives [62].

Conclusion

Over-use of antibiotics in primary care is prevalent in Hubei of China, in particular in relation to the prescribing of broad-spectrum, parenteral administrated and restricted antibiotics. Great individual variation in antibiotic prescribing patterns exists. Those who are deemed high users contribute disproportionally to the inappropriate use of antibiotics. Prescribers worked in a rural setting and those with insufficient knowledge, low motivations for behavioral changes, and low household income are more likely to be high users.

Abbreviations

AMR: antimicrobial resistance;

WHO: world health organization;

AWaRe: Access, Watch and Reserve;

ATC: anatomical therapeutic chemical;

LPA: latent profile analysis;

MLR: Maximum likelihood parameter estimates with standard errors;

BIC: Bayesian Information Criterion;

SABIC: Sample-size Adjusted BIC;

VLMR-LRT: Vuong-Lo-Mendell-Rubin Adjusted Likelihood Ratio Test;

cmP : Correct Model Probability

ANOVA: one-way analysis of variance;

RRR: Relative Risk Ratio;

ESAC: European Surveillance of Antimicrobial Consumption

SD: standard deviation;

Declarations

Ethics, consent and permissions

This study has been approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (NO: IORG 0003571).

Written consent was obtained before survey from each participant in the current study.

Consent for publication

Written consent for publication has been obtained from each participant before the survey.

Availability of data and material

The data of this study are derived from surveyed local institutions and restrictions apply to its availability, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of surveyed local institutions and governments.

Competing interests

The authors declare no conflict of interest.

Funding

This study was funded by the National Natural Science Foundation of China (grant no. 71373092 & 71904053).

The funding body played no part in the study design, collection, analysis and interpretation of data, writing of the manuscript or the decision to submit the manuscript for publication.

Authors' contributions

Chenxi Liu designed the project and participated in the collection and interpretation of data. Dan Wang contributed to the acquisition, analysis and interpretation of data and drafted the manuscript. Chaojie Liu participated in data analysis, interpretation of results, and writing of the manuscript. Xinping Zhang participated in the cleaning and interpretation of data. All authors have read and approved the final version of the article.

Acknowledgements

The authors would like to sincerely thank the surveyed physicians, investigators and the support from the included primary care facilities and local governments.

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Tables

Table 1: Prescribing patterns of primary care physicians

Prescribing Indicators	Mean ± Standard Deviation	Low Antibiotic User (n = 157)	Medium Antibiotic User (n = 282)	High Antibiotic User (n=112)	*p* value*			
					Low vs Medium	Low vs High	Medium vs High	Overall
Q1: Average number of medicines per prescription (N)	2.870±0.775	2.334±0.596	2.861±0.655	3.645±0.612	<0.001	<0.001	<0.001	<0.001
Q2: Average number of antibiotics per prescription (N)	0.654±0.256	0.433±0.171	0.636±0.150	1.011±0.170	<0.001	<0.001	<0.001	<0.001
Q3: Percentage of prescriptions containing antibiotics (%)	52.19±17.20	36.76±12.73	51.94±11.29	74.43±8.96	<0.001	<0.001	<0.001	<0.001
Q4: Percentage of antibiotic prescriptions containing broad-spectrum antibiotics (%)	82.29±15.83	69.14±17.77	87.09±10.41	88.66±13.41	<0.001	<0.001	0.031	<0.001
Q5: Percentage of antibiotic prescriptions containing parenteral administrated antibiotics (%)	71.92±21.42	45.83±17.35	79.7±11.50	88.89±10.48	<0.001	<0.001	<0.001	<0.001
Q6: Percentage of antibiotic prescriptions containing antibiotics in the WHO "Watch and Reserve" list (%)	67.74±20.98	63.87±20.56	66.85±19.82	75.42±22.60	0.232	<0.001	<0.001	<0.001
Q7: Percentage of antibiotic prescriptions containing restricted antibiotics (%)	23.52±19.12	18.99±16.94	25.19±18.50	25.66±22.37	0.001	0.042	0.718	0.002

*ANOVA and post-hoc pairwise Bonferroni tests for the indicators with a normal distribution; Kruskal-Wallis equality-of-populations rank tests and post-hoc pairwise Dunn's tests for the indicators without a normal distribution.

Table 2: Characteristics of questionnaire respondents with different prescribing patterns

Characteristics	Overall	Low Antibiotic User	Medium Antibiotic User	High Antibiotic User	p^*
Number of physicians (N, %)	458 (100%)	124 (27.07%)	243 (53.06%)	91 (19.87%)	-
Sociodemographic					
Age (Mean±Standard Deviation)	43.53±9.31	45.02±10.13	43.12±9.02	42.62±8.73	0.257
Gender					0.003
Male (N, %)	330 (100%)	76 (23.03%)	180 (54.55%)	74 (22.42%)	
Female (N, %)	128 (100%)	48 (37.50%)	63 (49.22%)	17 (13.28%)	
Educational qualification					0.018
High School and below (N, %)	42 (100%)	8 (19.05%)	26 (61.90%)	8 (19.05%)	
Diploma and associate degree (N, %)	241 (100%)	53 (21.99%)	135 (56.02%)	53 (21.99%)	
University degree (N, %)	175 (100%)	63 (36.00%)	82 (46.86%)	30 (17.14%)	
Annual Household Income (Chinese Yuan ¥)					<0.001
<40,000 (N, %)	132 (100%)	25 (18.94%)	74 (56.06%)	33 (25.00%)	
40,000 ~ (N, %)	232 (100%)	55 (23.71%)	130 (56.03%)	47 (20.26%)	
80,000 ~ (N, %)	70 (100%)	27 (38.57%)	33 (47.14%)	10 (14.29%)	
≥ 120,000 (N, %)	24 (100%)	17 (70.83%)	6 (25.00%)	1 (4.17%)	
Professional practice					
Facility					<0.001
Urban Community Health Centre (N, %)	101 (100%)	55 (54.46%)	33 (32.67%)	13 (12.87%)	
Rural Township Health Centre (N, %)	357 (100%)	69 (19.33%)	210 (58.82%)	78 (21.85%)	
Years of Practice (Mean±Standard Deviation)	16.54±10.01	16.01±10.30	16.52±10.14	17.31±9.17	0.520
Sub-specialty					0.025
General Practice (N, %)	219 (100%)	67 (30.59%)	101 (46.12%)	51 (23.29%)	
Internal Medicine (N, %)	117 (100%)	24 (20.51%)	73 (62.39%)	20 (17.09%)	
Surgery (N, %)	56 (100%)	10 (17.86%)	34 (60.71%)	12 (21.42%)	
Others (N, %)	66 (100%)	23 (34.85%)	35 (53.03%)	8 (12.12%)	
Professional Title					0.017
Junior (N, %)	234 (100%)	50 (21.37%)	133 (56.84%)	51 (21.79%)	
Middle (N, %)	176 (100%)	53 (30.11%)	90 (51.14%)	33 (18.75%)	
Senior (N, %)	47 (100%)	21 (44.68%)	19 (40.43%)	7 (14.89%)	
Antibiotic Training					0.622
Yes (N, %)	346 (100%)	91 (26.30%)	183 (52.89%)	72 (20.81%)	
No (N, %)	112 (100%)	33 (29.46%)	60 (53.57%)	19 (16.96%)	
Antibiotic Knowledge (Mean ± SD, Range: 0-11)	6.16±1.49	6.54±1.35	6.01±1.52	6.01±1.47	0.002
Antibiotic Attitudes (Mean ± SD)					
Complacency (Range: 0-8)	6.42±1.40	6.32±1.36	6.53±1.36	6.23±1.57	0.172
Fearful of adverse events (Range: 0-12)	7.72±2.00	7.85±1.85	7.81±2.01	7.30±2.14	0.078
Ignorance of antibiotic resistance (Range: 0-16)	11.59±1.69	11.46±1.78	11.56±1.69	11.86±1.52	0.210
Responsibility avoidance (Range: 0-28)	9.08±2.72	8.97±2.64	9.14±2.78	9.07±2.67	0.708
Indifference to changes (Range: 0-4)	2.98±0.79	3.05±0.66	2.96±0.83	2.91±0.86	0.741

*p values of Chi-square tests for categorical variables, Kruskal-Wallis equality-of-populations rank tests for continuous variables without a normal distribution, and ANOVA for continuous variables with a normal distribution.

Table 3: Multinomial logistic regression of physician's antibiotic prescribing patterns

Variable	Medium Antibiotic User		High Antibiotic Users	
	Relative Risk Ratio* (95% Confidence Interval)	p	Relative Risk Ratio* (95% Confidence Interval)	p
Sociodemographic				
Age	0.959 (0.920, 1.001)	0.055	**0.942 (0.891, 0.995)**	**0.032**
Female gender	1.217 (0.621, 2.386)	0.566	0.864 (0.37, 2.015)	0.734
Educational qualification	0.733 (0.453, 1.185)	0.204	0.749 (0.418, 1.342)	0.331
Annual household income	**0.688 (0.498, 0.952)**	**0.024**	**0.521 (0.339, 0.800)**	**0.003**
Professional Practice				
Rural facility	**4.275 (2.205, 8.285)**	**<0.001**	**4.296 (1.826, 10.105)**	**0.001**
Years of practices	1.026 (0.995, 1.059)	0.104	**1.053 (1.010, 1.097)**	**0.015**
Sub-speciality				
General practice	Ref	-	Ref	-
Interal medicine	1.339 (0.704, 2.546)	0.374	0.699 (0.319, 1.533)	0.372
Surgery	1.263 (0.528, 3.020)	0.599	0.762 (0.273, 2.123)	0.603
Others	0.600 (0.264, 1.367)	0.224	0.334 (0.111, 1.010)	0.052
Professional Title				
Junior	Ref	-	Ref	-
Middle	1.128 (0.621, 2.048)	0.694	1.149 (0.547, 2.414)	0.714
Senior	1.356 (0.501, 3.668)	0.549	1.735 (0.486, 6.192)	0.396
Antibiotic Training	0.903 (0.506, 1.611)	0.729	1.050 (0.508, 2.172)	0.894
Knowledge Score Above Mean	**0.440 (0.246, 0.785)**	**0.005**	**0.468 (0.234, 0.935)**	**0.031**
Attitudes Scores Above Mean				
Complacency with satisfied patients	**2.618 (1.107, 6.191)**	**0.028**	1.935 (0.710, 5.272)	0.197
Fearful of adverse events	1.102 (0.618, 1.965)	0.743	0.822 (0.414, 1.632)	0.575
Ignorance of antibiotic resistance	0.831 (0.212, 3.250)	0.790	3.068 (0.292, 32.195)	0.350
Responsibility avoidance	1.223 (0.214, 6.976)	0.821	1.051 (0.125, 8.817)	0.964
Indifference to changes	**0.416 (0.198, 0.873)**	**0.020**	**0.401 (0.171, 0.943)**	**0.036**

* Low antibiotic user group as reference; Bold indicates statistical significance (*p*<0.05).

Figures

Figure 1

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