Secular trend analysis of antibiotic consumption in China's hospitals 2011-2018, a retrospective analysis of sales data

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Abstract

Background: This study was aimed to explore the secular trends of antibiotic consumption over an 8-year period.

Methods: We retrospectively analysed aggregated monthly surveillance data on antibiotic sales to 586 hospitals from 28 provinces in China from January 2011 to December 2018. Information including generic name, sales amount, dosage form, strength, the route of administration, and geographical data were collected. Population weighted Antibiotic consumption was expressed in DDD per 1,000 inhabitants per day (DID). WHO's 'Access, Watch, Reserve' categorization was also adopted to analyse antibiotic consumption.

Results: Between 2011 and 2018, total antibiotic consumption in China's hospitals increased by 38.2% (from 4.8 DID in 2010 to 6.7 DID in 2018). Antibiotic consumption was stable or had moderately decreased in 13 provinces, while the other 15 provinces had substantially increased. Cephalosporins were the most consumed antibiotics, accounted for 26.9% of the total antibiotic consumption. In 2018, antibiotics in the Access category comprised 20.0% of total consumption, where antibiotics in the Watch category consumed the most with 72.2%. Population-weighted antibiotic consumption was larger in secondary hospitals than tertiary hospitals (7.3 DID VS 6.6 DID). The antibiotics consumption of oral form was almost two times the consumption of parenteral forms in secondary hospitals, whereas the proportion of tertiary hospitals was about the same.

Conclusions: Although efforts were made towards restricting antibiotics in the past decade by Chinese government, antibiotic consumption demonstrated an upward trend during the study period. More efforts are needed to explore the quality of antibiotic usage in terms of rationality.

Background

According to selective pressure theory, excessive antimicrobial consumption has caused an increased risk of antimicrobial resistance (AMR), which is a growing public health threat of broad concern to the world [1]. At the G20 Hangzhou Summit in 2016, AMR was one of the main topics and was included in the final communiqué. At the 71st UN General Assembly, AMR was the fourth health-related topic that was discussed in UN General Assembly in the history. It has been estimated that more than two million lives would be at risk, and up to 3.5 billion US dollars will be spent annually on average due to AMR in Europe, North America and Australia by 2050 if no action is taken [2].According to the theory of choice, the existence of an expected net benefit at individual level is one pre-requisite for collective action [3], which means that protecting the efficacy of antibacterial agents and confining AMR as a common goal needs the collective efforts of every country instead of separating oneself from the problem. Given its largest population, China is estimated to be the second largest consumer of antibiotics in the world [4]. This gives China an important role in the process of constraining the use and misuse of antibiotics.

To address this issue, China has taken many measures to strengthen antimicrobials management such as the designation of antibiotic as prescription drugs in 2003, and the introduction of guidance for clinical use of antibiotics in 2004 [5, 6].National surveillance networks for both antibiotic use and resistance were established in 2005, along with the introduction of a national formulary in 2008 [7, 8].However, due to inefficient implementation and absence of supervision and inspection these policies and strategies did not fully achieve the expectation [4]. The overuse of antimicrobials has remained a serious public health challenge. Since the 2009 health system reform, the Chinese government has been committed to tackling the irrational use of antibiotics by enhancing antimicrobial stewardship. World Health Organization (WHO) called for a combat towards drug resistance with the slogan "no action today, no cure tomorrow" in 2011. Echoing the global governance endeavors of the WHO, the National Health and Family Planning Commission (NHFPC) launched a three-year Special Antimicrobial Stewardship Campaign (SAC) nationwide to strengthen the management of clinical use antimicrobials in healthcare settings [9]. The SAC was legislated then as a ministerial decree in 2012 [10]. In addition, structured antimicrobial formulary restriction management has been established, which categorized antimicrobials into three classes (non-restricted, restricted and highly-restricted), with different prescription privileges to different level of physicians. In 2016, a national action plan to confine AMR was released responding to WHO's call for "Global Action Plan on Antimicrobial Resistance" [11]. Moreover, to respond to the increasing carbapenem-resistant bacteria, the NHFPC made specific and more restrict requirement for the clinical use of carbapenems and tigecycline in 2018 [12].

Studies have centered around the impact of SAC and short-term trends of antibiotic consumption in China [13, 14]. However, the long-term change of antibiotic consumption, especially after a decade since health system reform, was yet to explore. Hence, this study was designed to explore the secular trends of antibiotic consumption over 8-year period.

Methods

Study design

We retrospectively analyzed aggregated monthly surveillance data on antibiotic sales to 586 hospitals from 28 provinces in China from January 2011 to December 2018 (Table 1).

Table 1 Distribution of sample hospitals

Region [a]	Tertiary [b]	Secondary [c]
Eastern	256 (26.1)	73 (3.7)
Middle	132 (21.9)	36 (1.4)
Western	64 (13.2)	25 (1.7)
Total	452 (21.9)	134 (2.3)

[a]: Classification of the regions was reference to China Health Statistics Yearbook. Eastern region: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Shandong, and Guangdong; Middle region: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan; Western region: Inner Mongolia, Chongqing, Guangxi, Sichuan, Guizhou, Yunnan, Shaanxi, Gansu, Ningxia, and Xinjiang.

[b]: Percentage in the brackets was calculated by dividing the number of sampled tertiary hospitals by total number of tertiary hospitals in the region.

[c]: Percentage in the brackets was calculated by dividing the number of sampled secondary hospitals by total number of secondary hospitals in the region.

Data source

All the data was obtained from China Medicine Economic Information (CMEI), an observational database containing information of drug sales records in medical institutions from 28 provinces (out of 34) across the country (Qinghai, Tibet, Hainan, Hongkong, Macau, and Taiwan excluded). The details of the data source were described elsewhere [14]. Hospitals were selected on the basis that they each had full records of antibiotic consumption during the study period of 8 years, among which 452 tertiary hospitals accounts for 21.9% of the total tertiary hospitals and 134 secondary hospitals accounts for 2.3% of the total secondary hospitals in study regions.

Data collection and management

We extracted monthly antibiotic sales records data from the CMEI electronic database. Information including the generic name, sales amount, dosage form, strength, the route of administration, and geographical data were collected. Hospital names were concealed to protect confidentiality.

Sales data were categorized according to Anatomical Therapeutic and Chemical (ATC) classification J01 (i.e. antibacterial for systemic use) expressed in defined daily dose (DDD) as measurement unit, following the recommendation of the WHO Collaborating Center for Drug Statistic Methodology [15]. The DDD of the drugs which could not be coded in the ATC system were calculated as the recommended daily amounts for each study medication based on dosage regimen recommended in the manufacturers' instructions, as approved by China Food and Drug Administration. A total of 186 unique chemical substance names were identified in single or combination antibiotics. These antibiotics were aggregated into 32 ATC-4 classes then into 9 ATC-3 groups. Data were managed and analysed in Microsoft Excel 2013 and STATA 14.0 (StataCorp LLC, Texas, USA).

Data analysis

To make the antibiotic sales data available to provide internationally comparable information, the data were converted into DDD per 1,000 inhabitants per day (DID) at the level of the active substance. Based on the following two assumptions, equation1 was adopted to calculate the weighted population as a proxy for the population our sample hospitals had covered. First, there was no significant difference in the distribution of the sample hospitals across the provinces; second, there was no significant difference in the distribution of the population which was covered by the sample hospitals across the provinces. To avoid bias in calculating inhabitants, the inhabitants of outpatients and inpatients were calculated altogether

instead of separately calculated as we did before [14]. Coverage inhabitants for secondary hospitals and tertiary hospitals were calculated separately.

(1) [Due to technical limitations, please see supplementary files for formula.]

Y_i: Coverage inhabitants in a given year;

P_i: Total population in a given year in province i;

n_i: Number of sample hospitals in province i;

N_i: Number of total hospitals in province i;

m_i: Number of inpatients and outpatients in sample hospitals in province i;

M^i: Number of inpatients and outpatients in all hospitals in province i.

In addition to ATC classification, we adopted 'Access, Watch, Reserve' (AWaRe) categorization established by WHO as part of the update of the WHO Model List of Essential Medicines in 2017 to analyze the antibiotic consumption [16].

To derive a comparable metric of antibiotic consumption across time, we calculated the compound annual growth rate (CAGR) of antibiotic consumption.

(2) [See supp. files.]

C_{2018}: Total antibiotic consumption for year 2018 (expressed in DID).

C_{2011}: Total antibiotic consumption for year 2011 (expressed in DID).

All the relevant census data for calculating inhabitants were collected from China Health Statistics Yearbook and China Statistics Year Book [17]. Linear regression analysis was adopted to determine the trends in antibiotic use with time. A difference with $p < 0.05$ was considered to indicate statistical significance.

Results

Total antibiotic use in China's hospitals from 2011 to 2018

Between 2011 and 2018, total antibiotic consumption in China's hospitals increased by 38.2% (from 4.8 DID in 2010 to 6.7 DID in 2018). The CAGR of the total antibiotic consumption was 4.3%. In 2018, antibiotics in the Access category comprised 20.0% of total consumption, where antibiotics in the Watch category consumed the most with 72.2%. The percentage of antibiotics in the Access, Watch and Reserve categories were stable during the study period.

Cephalosporins were the most consumed antibiotics, accounted for 26.9% of the total antibiotic consumption in 2018, followed by combinations of penicillins with 22.4% and fluoroquinolones with 11.1%. The largest absolute increase in consumption between 2011 and 2018 were observed for combinations of penicillins (0.6 DID), cephalosporins (0.3 DID), and fluoroquinolones (0.2 DID). The most important relative increase from 2011 were observed for tetracyclines (102.0%), other antibacterials (fosfomycin, daptomycin, spectinomycin, linezolid, methenamine) (55.0%), combinations of penicillins (58.5%) and penicillins with extended spectrum (55.0%). Significant increase in consumption rates was also noted for one of last-resort classes of antibiotics: carbapenems (23.3%) (Figure 1, and Additional file 1).

Figure 1 Antibiotic consumption under WHO AWaRe category in China's hospitals, 2011–2018. (a) Expressed in DID. (b) Expressed in cumulative percentage.

Beijing, Jiangsu, and Shanghai were the top three largest consumers of antibiotics in 2018, with 18.3 DID, 16.7 DID, and 11.6 DID, respectively. Antibiotic consumption was stable or had moderately decreased in half of the country (13 provinces), while the other half (15 provinces) had

substantially increased between 2011 and 2018. Most of the increases in antibiotic consumption were observed in under developed regions, such as Inner Mongolia, Yunnan, Gansu, and Guizhou. Eastern coastal regions consumed more antibiotics compared with central and western regions (Figure 2).

Figure 2 Antibiotic consumption in China's hospital in 2018. (a) Expressed in DID; (b) Expressed in compound annual growth rate of antibiotic consumption between 2011 and 2018.

Antibiotic consumption in secondary and tertiary hospitals

In 2018, total antibiotic consumption in secondary and tertiary hospitals were 7.3 DID and 6.6 DID, respectively. Antibiotics in the Access category comprised 26.9% and 19.4% of total consumption in secondary and tertiary hospitals, respectively, where antibiotics in the Watch category consumed the most with 68.3% and 72.6%, respectively. Antibiotics in the Reserve category in tertiary hospitals increased from 5.6% to 6.8% from the study period (Figure 3).

Figure 3 Antibiotic consumption under WHO AWaRe category in secondary and tertiary hospitals, 2011–2018.

Antibiotic consumption in secondary hospitals fell by 5.8% from 2011 to 2015 and rose by 7.2% from 2015–2018. In tertiary hospitals, antibiotic consumption increased each year, and a 43.3% increase was observed between 2011 and 2018. The antibiotics consumption of oral form was almost two times the consumption of parenteral forms in secondary hospitals, whereas the proportion of tertiary hospitals was about the same. (Figure 4)

Figure 4 Oral and parenteral antibiotics consumed in secondary and tertiary hospitals between 2011 and 2018. (a) Oral antibiotic consumption; (b) Parenteral antibiotic consumption; (c) Total antibiotic consumption

As Figure 5 showed, the three most commonly consumed antibiotics in secondary hospitals were second-generation cephalosporins, macrolides, and third-generation cephalosporins, whereas the combinations of penicillins, which increased by 64% from 0.96 DID to 1.57 DID between 2011 and 2018, replaced second-generation cephalosporins as one of the top three in tertiary hospitals in 2018 (Figure 3).

Figure 5 Major classes of antibiotics consumed in secondary and tertiary hospitals between 2011 and 2018. (a) Secondary hospitals; (b) Tertiary hospitals

Discussion

This study, to our knowledge, is the first to estimate population-wide antibiotic consumption at the national level in China for an 8-year period, using data from a national sampling database and the accepted ATC/DDD methodology. This gives us an opportunity to analyze the antibiotic consumption in China's hospital setting and benchmark it internationally, which would be informing for healthcare providers, decision-makers, as well as the public.

In the nearly past two decades, Chinese government has endeavor to contribute for confining AMR by a series of policies and measures including confining antibiotic use. The evolution of the policy management has been well documented [10]. According to the National Health Commission, the outpatient antibiotic prescription proportion in Chinese hospitals (secondary and tertiary hospitals) has continuously declined from 16.2% in 2011 to 7.7% in 2017. Similarly, the inpatient antibiotic prescription proportion was also declined from 55.2% to 38.0% [18]. In addition, studies were conducted towards the impact on antibiotic use in secondary and tertiary hospitals in terms of the varies drug management programs to promote the proper use of antibiotics, especially after the implementation of zero mark-up policy, which led to the cut off of the economic incentives between the prescriptions and the hospital revenue [14, 19, 20]. However, our study showed that antibiotic consumption in China's hospitals increased significantly (38.2% increase between 2011 and 2018). Although the developed regions with more populations consumed more antibiotics, more increases (4 out of top 5 provinces which increased the most) were observed in underdeveloped regions although the population. Despite it is hard to explain the discrepancy with other studies that describe a decrease in antibiotic use [21–24], we found evidences that aligned with this trend from the perspective of pharmaceutical market and inpatient volume.

China's anti-infection pharmaceutical market continuously increased from 2011 to 2017, although the growth rate is decreasing; The inpatient volume at China's tertiary hospitals nearly tripled between 2010 to 2017 according to China Health Statistics Yearbook [17]. What's more, although the proportion of antibiotic prescriptions was decreasing, the median antibiotic usage intensity in 177 core members of China Antimicrobial Resistance Surveillance System was slightly increased from 2014 to 2016 from 47.21 to 47.65 DDDs/100 patient-day.

When comparing with European countries, our result showed that antibiotic consumption in China's hospitals was more than three times than the average level of antibiotic consumption in hospital setting in 24 EU/EEA countries (2.0 DID in 2017, ranged from 0.9 to 3.1 DID) [25]. One more worrying fact was that, the antibiotic consumption in China's hospitals increased by a CAGR of 4.3% while the average annual hospital setting in EU/EEA countries was 1.0% [25]. Despite the growth was significant, these results still need to be interpreted with caution, because outpatient antibiotic use accounted for 90%–94% of the total use for the countries that provided separate data in ESAC [25, 26],meaning most of the antibiotics were consumed in community setting, whilst more antibiotics were consumed in hospitals setting in China. This might explain that the consumption of antibiotics in China's hospitals was lower than antibiotics consumed in community setting in EU/EEA countries (6.31 DID VS 21.8 DID in 2017) [25]. AWaRe categories are a proposed by WHO in the context of a comprehensive review of the optimal antibiotic choices for many common infectious syndromes in adults and children. WHO set up a common global target of Access > 60% (the proportion of Access antibiotics should be more than 60% of overall antibiotic use) to reduce AMR [27]. Our study showed that the Access category proportion of sample hospitals was only 20.0%, which was lower than most of the countries that had collect this data [27].The massive use of second- and third-generation cephalosporins, macrolides, as well as combinations of penicillins contributed to the high proportion of the Watch category. Measuring antibiotic consumption by quantifying the use of antibiotics in each of the AWaRe categories allows some inference about the overall quality of antibiotic use between countries. The combination of both absolute and relative consumption by category allows simple benchmarking (e.g. an overuse of Watch antibiotics can become immediately apparent and a reduction in Watch antibiotics can be identified as a target for antibiotic stewardship interventions) and assessment of trends over time (to evaluate the impact of interventions) [2].

When looking at the pattern of antibiotic consumption, we found that cephalosporin was the most consumed antibiotics in China's hospitals, followed by combinations of penicillins, which were often defined as extended-spectrum antibiotics, and quinolones. This pattern was similar to the previous studies conducted in other regions of China [19, 20],as well as national surveillance data [18], whilst more penicillins were prescribed in Europe and United States [28–30].This might partly attribute to the different setting that antibiotics were consumed with more consumption was made to inpatient setting in China, whereas ambulatory care setting consumed more antibiotics as mentioned. Cephalosporin were recommended by national guidance for majority of the perioperative prophylaxis in China [31]. Although quinolones were noted by US FDA that should be only used for those have no other treatment options [32], physicians may prefer quinolones and cephalosporins more than penicillins due to the time-consuming skin testing requirement for penicillins prior to administration for allergy assessment in China [33],Although the consumption of carbapenems, a class of last-resort antibiotics, was similar to EU/EEA countries (0.10DID VS 0.06 DID in 2017, country range: 0.02–0.17), the significant increase of carbapenems consumption still cannot be ignored (0.03 DID in 2011 to 0.10 DID in 2018) [25]. Because carbapenems are categorized as highly restricted antibiotics by National Health Commission and requires pre-authorization before use in China, this increase could be partly due to the rise in extended-spectrum β-lactamase-producing Gram-negative bacteria, which has been identified in epidemiological surveillance studies [18, 34]. As the increase of carbapenems consumption, the resistance rate of carbapenem-resistant Enterobacteriaceae is also reported [35].

Population-weighted antibiotic consumption was larger in secondary hospitals than tertiary hospitals. As tertiary hospitals receive more severe patients than secondary hospitals, this might indicate that some increases in antibiotic consumptions, especially in secondary hospitals, are very likely caused by inappropriate use. Studies found that diseases, such as diarrheal illness, colds, pharyngitis, acute bronchitis, were likely to be prescribed antibiotics in rural and underdeveloped regions [36–38], although most of these illnesses are viral instead of bacterial. Besides, the high proportion of oral form of antibiotics consumed in secondary hospitals, though more less severe patients were received, would also support the inference that more irrational antibiotic use might took place in lower level of hospitals. This phenomenon may be severe in primary healthcare setting, especially in rural areas, not only because regulations towards primary healthcare setting in terms of antibiotic use has not been developed, but also the knowledge level of the physicians in primary healthcare setting are lower than the physicians in hospital setting [37].

The findings of this study are subject to several limitations. First, the hospital in the database was on a voluntarily basis instead of mandatory participation, especially the proportion of secondary hospitals in the study was relatively low, therefore could bring selected bias. Second, primary healthcare setting was not included which may cause bias on the pattern of antibiotic consumption since a number of antimicrobial agents was used in primary care setting. Third, the population denominator used in the study was determined under certain condition which may underestimate antibiotic consumption as it cannot include cross-provincial patient flow. Finally, as the study analyzed sales data rather than clinical usage of antibiotics, we were unable to determine the appropriateness of antibiotic use at the individual level.

Conclusions

The increase of antibiotic consumption and the increase in use of last-resort antibiotics raises serious concern for public health. The study adopted aggregated sales data to analyze the antibiotic consumption in China's hospitals over an eight-year period. Although efforts have been made towards restricting antibiotic use in the past decade by Chinese government, antibiotic consumption demonstrated an upward trend during the study period. To better facilitate the rational antibiotic use, more efforts are needed to explore the quality of antibiotic usage in terms of rationality. Besides, incorporate the primary healthcare setting into the national surveillance network should be stressed for better understanding the epidemiology of antibiotic use and AMR from a more comprehensive perspective.

List Of Abbreviations

DDD: Defined daily dose

DID: DDD per 1,000 inhabitants per day

AMR: Antimicrobial resistance

WHO: World Health Organization

NHFPC: National Health and Family Planning Commission

SAC: Special Antimicrobial Stewardship Campaign

CMEI: China Medicine Economic Information

ATC: Anatomical Therapeutic and Chemical

AwaRe: Access, Watch, Reserve

CAGR: Compound annual growth rate

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Aggregated annual consumption data used for analyses are provided as supporting information. The raw individual hospital level data used to generate these results cannot be shared publicly because of the associated legislation. Data can be made available by China Pharmacy Association (contact via tel 86 10 65660788 or fax 86 10 65661656) for researchers who meet the criteria for access to confidential data and subject to a data access fee.

Competing interests

The authors declare that they have no competing interests.

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design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

Conceptualization, XDG and LWS; methodology, HW and YZ; validation, XDG; formal analysis, HW, YZ, XZ and MYF; resources, XDG, LWS and DMF; data curation, YZ, XZ and MYF; writing—original draft preparation, HW and YZ; writing—review and editing, XDG; supervision, LWS and DMF; project administration, HW, YZ, and XZ; funding acquisition, XDG, LWS and DMF. All authors read and approved the final manuscript.

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References

1. Angebault C, Andremont A. Antimicrobial agent exposure and the emergence and spread of resistant microorganisms: issues associated with study design. Eur J Clin Microbiol Infect Dis. 2013 May;32(5):581–95.
2. OECD. Stemming the Superbug Tide: Just A Few Dollars More, OECD Health Policy Studies. Pairs; 2018. https://www.oecd-ilibrary.org/content/publication/9789264307599-en. Accessed 21 Sep 2019.
3. Smith RD, Coast J. Antimicrobial resistance: a global response. Bulletin of the World Health Organization. 2002;8.
4. van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. The Lancet Infectious Diseases. 2014 Aug;14(8):742–50.
5. National Guiding Principles for Antimicrobial. 2019. http://www.gov.cn/xinwen/2015-08/27/content_2920799.htm. Accessed 21 Sep 2019.
6. Ministry of Health of China. National Guiding Principles for Antimicrobial. http://www.sda.gov.cn/WS01/CL0055/10126.html. Accessed 21 Sep 2019.
7. Ministry of Health of China. Notification on establishing surveillance network for antibiotic use and antimicrobial resistance. http://www.nhfpc.gov.cn/zwgkzt/wsbysj/200804/18487.shtml. Accessed 21 Sep 2019.
8. Ministry of Health of China. Notification on releasing clinical guidance of national essential medicine and national essential medicine formulary. http://www.nhfpc.gov.cn/zwgkzt/wsbysj/201005/47420.shtml. Accessed 21 Sep 2019.
9. Ministry of Health of China. National special rectification activities program of clinical use of antibiotics (2011). http://www.moh.gov.cn/mohyzs/s3586/201104/51376.shtml. Accessed 21 Sep 2019.
10. Xiao Y, Li L. Legislation of clinical antibiotic use in China. The Lancet Infectious Diseases. 2013 Mar;13(3):189–91.
11. National Health Commission of People's Republic of China. Notification on releasing National Action Plan on confining AMR (2016-2020). http://www.nhfpc.gov.cn/yzygj/s3593/201608/f1ed26a0c8774e1c8fc89dd481ec84d7.shtml. Accessed 21 Sep 2019.
12. Notification on releasing 3 technical documents of expets opioins on carbapenem antibiotics. http://www.nhfpc.gov.cn/yzygj/s7659/201809/95f65ca473b44746b24590e94468b8ff.shtml. Accessed 21 Sep 2019.
13. Bao L, Peng R, Wang Y, Ma R, Ren X, Meng W, et al. Significant Reduction of Antibiotic Consumption and Patients' Costs after an Action Plan in China, 2010–2014. Singer AC, editor. PLoS ONE. 2015 Mar 13;10(3):e0118868.
14. Wushouer H, Tian Y, Guan X-D, Han S, Shi L-W. Trends and patterns of antibiotic consumption in China's tertiary hospitals: Based on a 5 year surveillance with sales records, 2011-2015. Zhou Z, editor. PLoS ONE. 2017 Dec 27;12(12):e0190314.
15. World Health Organization. Anatomical Therapeutic Chemical (ATC) Classification System: Guidelines for ATC Classification and DDD Assignment. http://www.whocc.no/atc_ddd_index/. Accessed 21 Sep 2019.
16. World Health Organization. WHO Model List of Essential Medicines (20th list). 2017. https://www.who.int/medicines/publications/essentialmedicines/20th_EML2017.pdf?%20ua=. Accessed 21 Sep 2019.
17. 17.National Bureau of Statistics. China Statistical Yearbook. http://www.stats.gov.cn/english/Statisticaldata/AnnualData/. Accessed 21 Sep 2019.
18. National Health Commission of People's Republic of China. Status report on antimicrobial administration and antimicrobial resistance in China (2018). 1st ed. Beijing: Peking Union Medical College Press; 2018.

http://www.nhc.gov.cn/yzygj/s3594/201904/1b5a42f0e326487295b260c813da9b0e/files/65d864a34e824d1abbc6807cd3c999b1.pdf. Accessed 21 Sep 2019.

19. Lin H, Dyar OJ, Rosales-Klintz S, Zhang J, Tomson G, Hao M, et al. Trends and patterns of antibiotic consumption in Shanghai municipality, China: a 6 year surveillance with sales records, 2009–14. J Antimicrob Chemother. 2016 Jun;71(6):1723–9.

20. Yin J, Li Q, Sun Q. Antibiotic consumption in Shandong Province, China: an analysis of provincial pharmaceutical centralized bidding procurement data at public healthcare institutions, 2012–16. Journal of Antimicrobial Chemotherapy. 2018 Mar 1;73(3):814–20.

21. Bhangu A, Ademuyiwa AO, Aguilera ML, Alexander P, Al-Saqqa SW, Borda-Luque G, et al. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. The Lancet Infectious Diseases. 2018 May;18(5):516–25.

22. Qu X, Yin C, Sun X, Huang S, Li C, Dong P, et al. Consumption of antibiotics in Chinese public general tertiary hospitals (2011-2014): Trends, pattern changes and regional differences. De Socio GV, editor. PLoS ONE. 2018 May 3;13(5):e0196668.

23. Li H, Yan S, Li D, Gong Y, Lu Z, Yin X. Trends and patterns of outpatient and inpatient antibiotic use in China's hospitals: data from the Center for Antibacterial Surveillance, 2012–16. Journal of Antimicrobial Chemotherapy. 2019 Jun 1;74(6):1731–40.

24. Chen J, Min R, Wang H, Zhao S, Li H, Fang P. Trends and Drivers of Inpatient Antibiotic Consumption among 89 China Tertiary General Hospitals from 2011Q1 to 2015Q4. BioMed Research International. 2018 Nov 1;2018:1–7.

25. European Centre for Disease Prevention and Control. Antimicrobial consumption. In: ECDC. Annual epidemiological report for 2017. https://ecdc.europa.eu/sites/portal/files/documents/AER_for_2017-antimicrobial-consumption.pdf. Accessed 21 Sep 2019.

26. Goossens H, Ferech M, Stichele RV, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. 2005;365:9.

27. World Health Organization. WHO Report on Surveillance of Antibiotic Consumption, 2016-2018 Early implementation. https://www.who.int/medicines/areas/rational_use/who-amr-amc-report-20181109.pdf. Accessed 21 Sep 2019.

28. van de Sande-Bruinsma N, Grundmann H, Verloo D, Tiemersma E, Monen J, Goossens H, et al. Antimicrobial Drug Use and Resistance in Europe. Emerg Infect Dis. 2008 Nov;14(11):1722–30.

29. Public Health England. English surveillance programme for antimicrobial utilization and resistance (ESPAUR) Report 2016. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/575626/ESPAUR_Report_2016.pdf. Accessed 21 Sep 2019.

30. Durkin MJ, Jafarzadeh SR, Hsueh K, Sallah YH, Munshi KD, Henderson RR, et al. Outpatient Antibiotic Prescription Trends in the United States: A National Cohort Study. Infect Control Hosp Epidemiol. 2018 May;39(5):584–9.

31. Department of Medical Administration and Committee of Experts on Rational Drug Use, National Health, and Family Planning Commission of the People's Republic of China. National Antimicrobial Therapy Guidance. 1st ed. Beijing: People's Medical Publishing House Co Ltd; 2012. https://huixue.baidu.com/book/detail?nid=e219cbc708a1284ac85043cb&isFromWenku=true. Accessed 21 Sep 2019.

32. McCarthy M. US warns against use of fluoroquinolones for uncomplicated infections. BMJ. 2016 May 16;i2755.

33. National Health and Family Planning Commission of the People's Republic of China. Notification on Implementation of Guidelines for Clinical Application of Antimicrobial Agents. http:// www.moh.gov.cn/wsb/pzcjd/200804/21154.shtml. Accessed 21 Sep 2019.

34. Quan J, Zhao D, Liu L, Chen Y, Zhou J, Jiang Y, et al. High prevalence of ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* in community-onset bloodstream infections in China. J Antimicrob Chemother. 2017 Jan;72(1):273–80.

35. Zhang Y, Wang Q, Yin Y, Chen H, Jin L, Gu B, et al. Epidemiology of Carbapenem-Resistant Enterobacteriaceae Infections: Report from the China CRE Network. Antimicrob Agents Chemother. 2017 Dec 4;62(2):e01882-17.

36. Guan X, Tian Y, Song J, Zhu D, Shi L. Effect of physicians' knowledge on antibiotics rational use in China's county hospitals. Social Science & Medicine. 2019 Mar;224:149–55.

37. Zhang Z, Hu Y, Zou G, Lin M, Zeng J, Deng S, et al. Antibiotic prescribing for upper respiratory infections among children in rural China: a cross-sectional study of outpatient prescriptions. Global Health Action. 2017 Jan;10(1):1287334.

38. Hou F-Q, Wang Y, Li J, Wang G-Q, Liu Y. Management of acute diarrhea in adults in China: a cross-sectional survey. BMC Public Health. 2013 Dec;13(1):41.
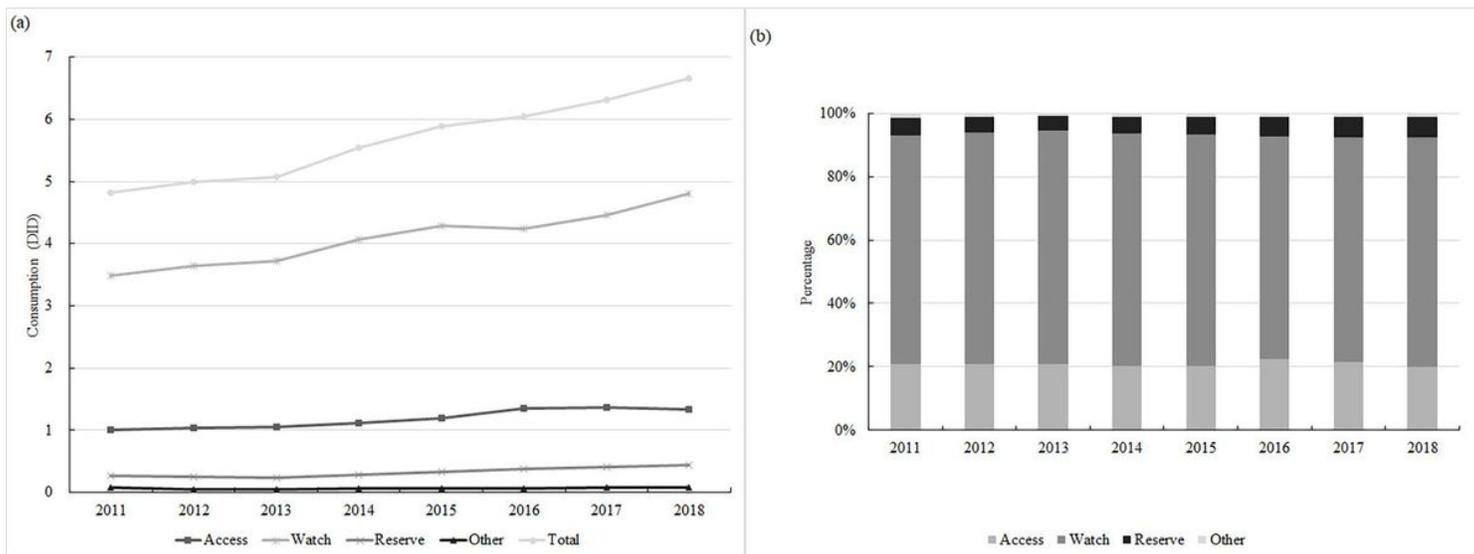
Figures

Figure 1

Antibiotic consumption under WHO AWaRe category in China's hospitals, 2011-2018. (a) Expressed in DID. (b) Expressed in cumulative percentage.
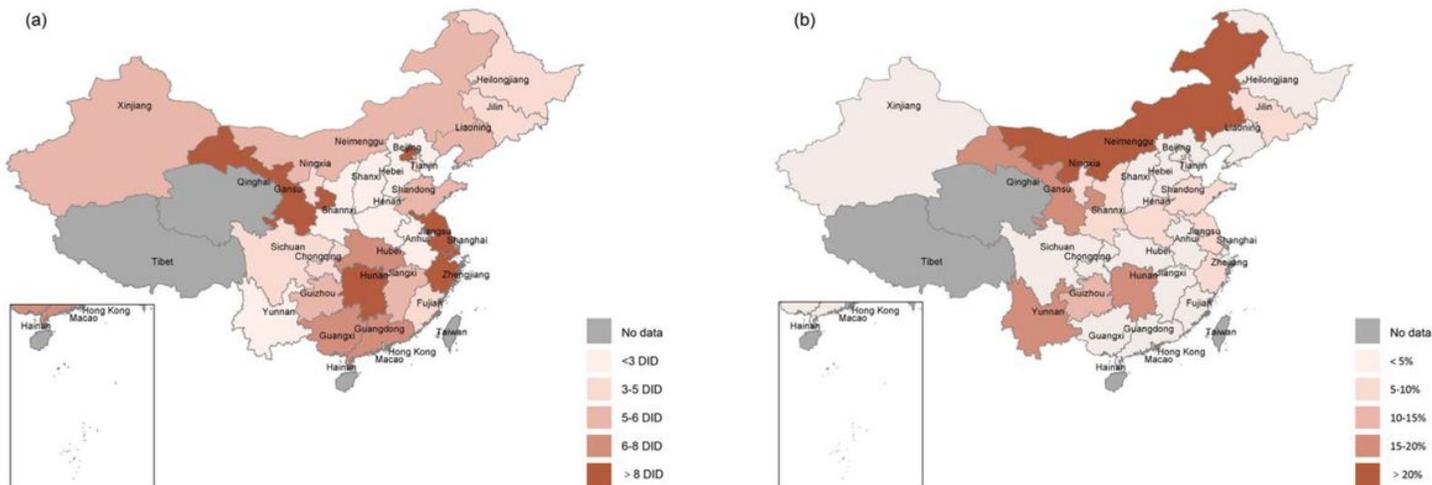

Figure 2

Antibiotic consumption in China's hospital in 2018. (a) Expressed in DID; (b) Expressed in compound annual growth rate of antibiotic consumption between 2011 and 2018. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.
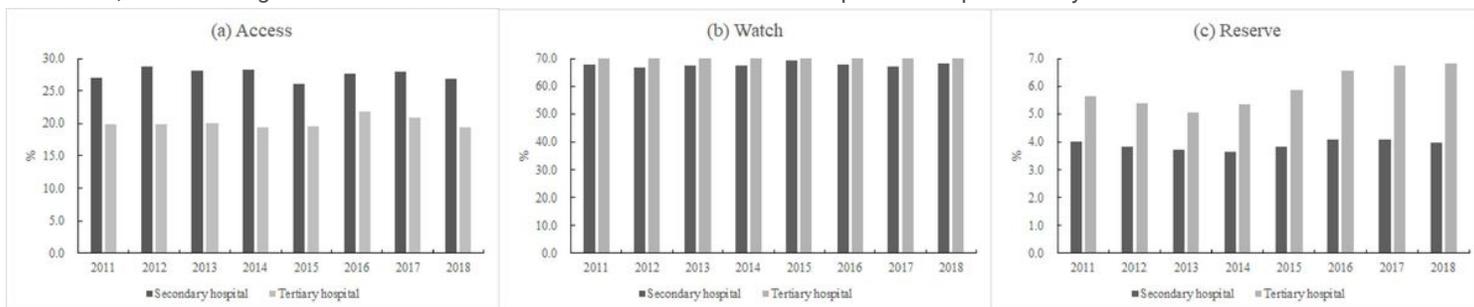

Figure 3

Antibiotic consumption under WHO AWaRe category in secondary and tertiary hospitals, 2011-2018.
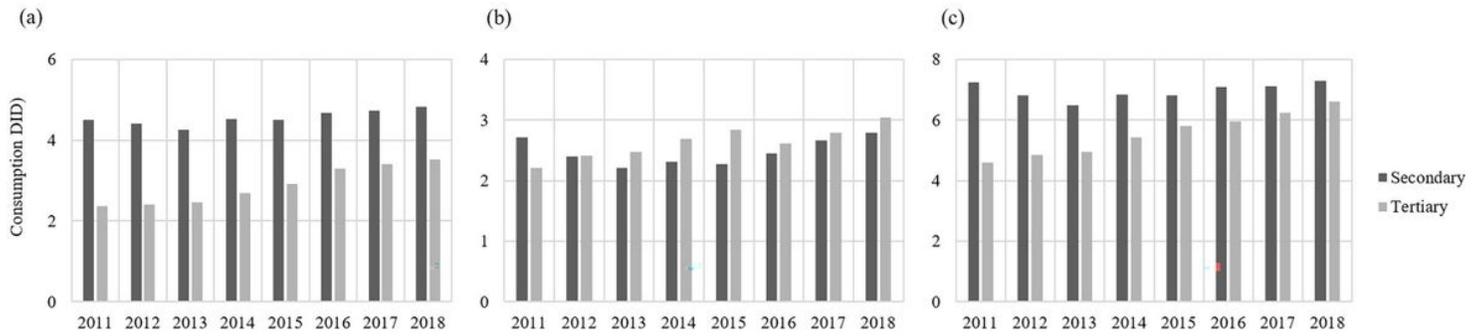

Figure 4

Oral and parenteral antibiotics consumed in secondary and tertiary hospitals between 2011 and 2018. (a) Oral antibiotic consumption; (b) Parenteral antibiotic consumption; (c) Total antibiotic consumption
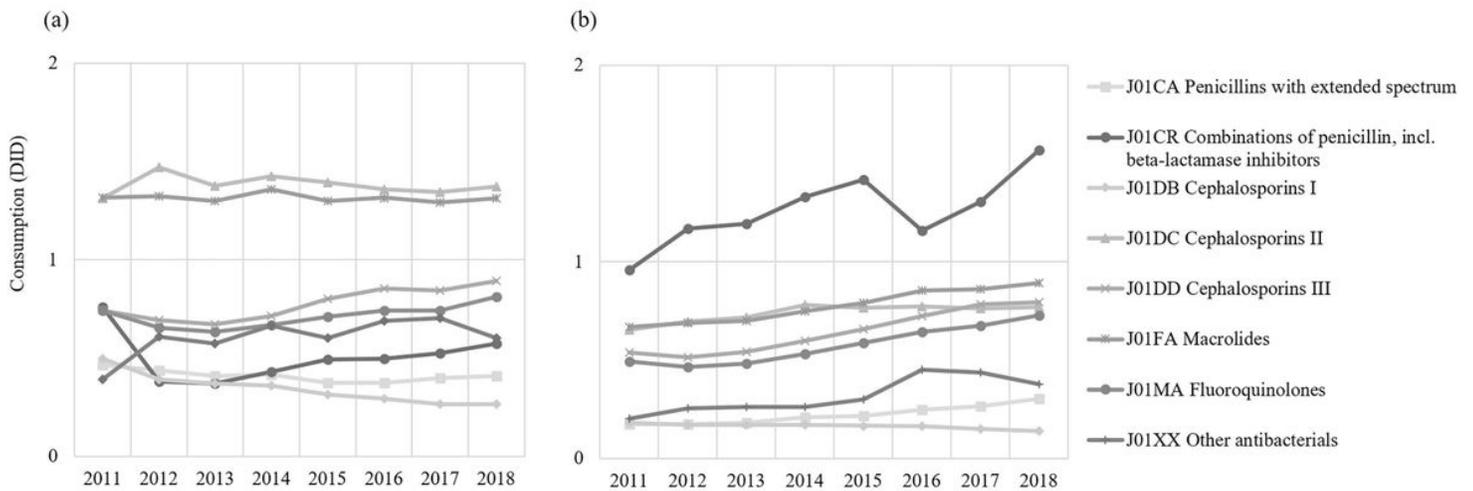

Figure 5

Major classes of antibiotics consumed in secondary and tertiary hospitals between 2011 and 2018. (a) Secondary hospitals; (b) Tertiary hospitals

Supplementary Files

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- Additionalfile1.docx
- Methodsformula.docx