Effects of County Public Hospital Reform on Procurement Costs and Volume of Antibiotics: A Quasi-Natural Experiment in Hubei Province, China

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Abstract
Background The overuse of antibiotics has become a major public health challenge worldwide, especially in low- and middle-income countries, including China. In 2009, the Chinese government launched a series of measures to de-incentivise over-prescription in public health facilities, including decoupling the link between facility income and the sale of medicines.

Objectives We evaluated the effects of these measures on procurement costs and the volume of antibiotics in county public hospitals.

Methods The study was undertaken in the Hubei province of China, where 64 county public hospitals implemented the reform in sequence at three different stages. A quasi-natural experiment design was employed. We performed generalised linear regressions with a difference-in-differences approach using 22,713 procurement records of antibiotics from November 2014 to December 2016.

Results The regression results showed that the reform contributed to a 14.79% increase in total costs for antibiotics (p = 0.013), particularly costs for injectable antibiotics (p = 0.022) and first-line antibiotics (p = 0.030). The procurement prices for antibiotics remained largely comparable to those in the control group, but the reform led to a 17.30% increase in the procurement volume (expressed as defined daily doses) of second-line antibiotics (p = 0.032).

Conclusions County public hospitals procured more antibiotics and greater numbers of expensive antibiotics, such as those administered via injection, to compensate for the loss of income from the sale of medicines, leading to an increased total cost of antibiotics.

Key Points
Public hospital reform in China’s Hubei province includes a zero markup (from wholesale to retail) policy for medicines (to reduce the cost of medicines) and increased fee levels for consultations and services (to compensate for the loss of revenue from the sale of medicines).

This reform has had some unintended consequences, with county public hospitals procuring more antibiotics and greater numbers of expensive antibiotics, such as those administered via injection, leading to an increased total cost of antibiotics.

Piecemeal remedies in hospital reform rarely fix a problem without unintended consequences if health organisations can easily find a way to take advantage of the reform for their own financial gain.

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1 Introduction

The irrational over-use of antibiotics has been identified as a key driver for the rapid development and spread of antibiotic resistance, an alarming global public health threat [1]. Concern about a potential shortage of effective antibiotics is increasing [2]. It is estimated that about 700,000 deaths worldwide are attributable to drug-resistant infections every year. This figure could surpass 10 million by 2050 if the rising trend of antibiotic resistance does not slow, resulting in an estimated $US100 trillion loss in global economic output [3–5].

The overuse of antibiotics is a serious problem in China [6]. A growing body of literature reveals very high numbers of antibiotic prescriptions in both outpatient and inpatient settings in China: 41–60% of patient encounters involve an antibiotic prescription; antibiotic injections are used in 21–60% of patient encounters [7–9]. A recent study showed that the use of antibiotics per capita (including cephalosporins, quinolones, macrolides, and all antibiotics combined) in Shanghai is higher than that in most European countries [10]. Indications are clear that irrational antibiotic prescriptions are common across all health facilities in China. For example, antibiotics are commonly prescribed for upper respiratory tract infections: 77% in tertiary hospitals, 85% in secondary hospitals, and 91% in primary hospitals [11]. The direct cost associated with the overuse of antibiotics in China is estimated to be around 2.91–13.93 billion yuan ($US0.42–2.02 billion) per year [12].

It is widely believed that the over-prescription of medicines in China has its roots in the distorted pricing system introduced when China transitioned from a planned economy to a market economy in the 1980s. The government previously contributed to > 50% of the total revenues of public hospitals, but this fell to merely 10% within a few years [13, 14]. The government developed two strategies to maintain the affordability of medical care and the operational viability of public hospitals. First, government-subsidised social health insurance programs were developed to reduce the financial burden on consumers. Second, a fee-for-service schedule was imposed on hospital services, keeping consultation fees low while allowing hospitals to charge more for high-tech diagnostic services and maintain a 15% profit margin on the sale of medicines. As a result, public hospitals were incentivised to increase revenues through enhancing service capacities and shifting priorities from consultation services to high-tech diagnostic services and prescriptions. In hospitals, bonus payments linked closely to hospital revenues became the most important instrument for employee motivation, with bonus payments accounting for an average of about half the total salary of hospital employees [15]. Such financial arrangements, combined with the increasingly autonomous clinical decision making of medical workers, translated into a strong incentive for medical workers to overprescribe medicines, particularly more expensive ones [16]. Pharmaceutical suppliers also took advantage of the distorted pricing schedule, inflating prices, promoting more expensive products, and encouraging over-prescription through volume-based commissions. The professional integrity of medical practice was seriously jeopardised, with physicians even receiving under-the-table kickbacks from pharmaceutical salespeople [17, 18]. Antibiotics became one of the most commonly abused pharmaceutical products [19, 20].

To curb the inflated prices and the overuse of medicines, the Chinese government instituted several policy interventions, including enforcing a price ceiling on some targeted products such as antibiotics [21, 22], issuing antibiotic guidelines, and imposing a target on the sale of medicines as a percentage of the total revenue of hospitals [2, 23, 24]. Unfortunately, the outcome was unexpected. Prescribers responded by switching prescriptions to products that were exempted from a price ceiling and/or increasing the volume of lower priced products [25, 26]. By 2007, sales of medicines still accounted for more than 41% of hospital revenues, and the overuse of antibiotics remained prevalent [27].

In 2009, the Chinese government launched a comprehensive package of health system reforms. Key measures included boosting government spending on health, establishing universal health insurance coverage, implementing a national essential medicines list policy for primary care, and ensuring equal access to basic public health services for all. A regional government tendering platform was set up for the procurement of medicines. Meanwhile, a zero-markup policy on the sale of medicines was introduced in primary care facilities [28, 29]. Empirical evidence indicates that revenues from the sale of medicines in primary care facilities dropped, as intended [30–32].

The zero-markup policy on the sale of medicines was later gradually extended to public hospitals, with the intention of completely eradicating the perverse incentives for the overuse of medicines. However, unlike their primary care counterparts, public hospitals did not obtain full budgetary support from the government. They had to depend on adjusted (increased) fee levels on other items, such as consultations, physical examinations, injections and other services requiring high-level professional skills to compensate for the loss of revenue from the sale of medicines [33]. This increased the chance of cost shifts. There are concerns that cost shifts may involve changing prescription patterns, which can be detrimental to overall policy goals (e.g. containing total expenditure on medicines).
In this study, we evaluated the impact of the reform on procurement volume and cost of antibiotics in county public hospitals. County public hospitals account for 50% of patient admissions in China and 40% of the total expenses of all medical institutions [34, 35]. Evidence on the effects of county public hospital reform has been mixed. A study in Zhejiang revealed a reduction in total expenses and expenses for prescribed medicines for both outpatient and inpatient care despite increased service-related charges [36], but a study in Hubei showed a prolonged length of stay and increased spending for inpatient care [37]. Studies on the effects of the reform on prescribing patterns (as indicated in procurement volume and costs) are limited.

2 Methods

2.1 Settings

This study was conducted in Hubei province, central China, which has a population of over 58 million (in 2014) across a geographic area of 185,900 km². The annual average income per capita in Hubei ranks in the middle range of all provinces: 10,849.1 yuan ($US1647) versus a country average of 10,488.9 ($US1593) for rural residents, and 24,852.3 yuan ($US3773) versus a country average of 28,843.9 ($US4380) for urban residents (year 2014 values) [38]. The total health expenditure in Hubei accounted for 4.45% of its gross domestic product (GDP). Approximately 2.17 registered physicians, 2.48 nurses, and 5.46 hospital beds per 1000 people were available in Hubei in 2014 [39].

2.2 Design

We employed a quasi-natural experiment design with a difference-in-differences (DID) approach in this study. Our primary concern was the impact of the public hospital reform on procurement volume and costs of antibiotics in county hospitals.

Hubei has 64 counties, each with one general public hospital and several other hospitals specialising in traditional medicine, maternal healthcare, child healthcare and others. Our study was restricted to the 64 general public hospitals because they were mandated to implement the hospital reform measures, whereas the other hospitals voluntarily participated in the reform.

The 64 county hospitals commenced the reform in sequence over four stages: 20 started in June 2012, three started in October 2013, 15 joined in November 2014; and the remaining 26 hospitals implemented the reform in November 2015.

Key measures in the hospital reform included removing the markup on the sale of medicines in county public hospitals and increasing fees for consultations and skilled services. County public hospitals follow the fee schedules established by the provincial government. In the reformed fee schedule, 50% of items relating to medical examinations, 80% related to nursing, and < 25% relating to diagnostic and surgical procedures were subject to a 15–80% fee increase [40]. It is important to note that the reform was implemented and expanded incrementally. While the participating county hospitals selected by the government had to implement the new fee schedule, the non-participating hospitals continued to use the old fee schedule. Although the government also issued an ambitious plan to reform payment mechanisms and human resource management in public hospitals, no detailed guidelines were provided. Little, if any, action was put into practice [37].

2.3 Data Source

We used the procurement records from the Hubei Medical Procurement Administrative Procurement System (HMPAPS) for this study. We only had access to procurement data from November 2014 onwards. At the time, 38 hospitals had already implemented the reform. As data on these hospitals before the reform were lacking, we changed our test hypothesis to “whether not implementing the reform would influence the procurement of antibiotics”. In so doing, the pre–post reform changes made by the 26 hospitals (test group) that implemented the reform in December 2015 were compared with those of the 38 county hospitals (control group) that implemented the reform throughout the entire study period (November 2014 to December 2016). The DID results reflect the differences between the two groups of hospitals between November 2014 and November 2015.
recommended usage (first, second and third line). This resulted in 22,713 procurement records for the 64 county hospitals over the 25-month period from November 2014 to December 2016.

2.4 Statistical Analysis

Three outcome indicators (volume, cost and price) were calculated to examine the impact of the reform on the procurement of all antibiotics and the subgroups. These indicators have been commonly used in previous studies [41]. The volume of procured medicines was estimated using defined daily dose (DDD), a measurement developed by the World Health Organization (WHO). The cost of procured medicines was expressed in absolute monetary terms (Chinese Yuan, CNY) without adjustment for inflation. The price of the procured medicines was calculated as unit price per DDD.

We performed DID analyses using generalised linear regressions since the outcome indicators did not follow a normal distribution.

$$Y_{ijt} = \alpha_0 + \beta \times \text{Reform}_{ijt} + \gamma \times X_{jt} + \alpha_j + \delta_t + \varepsilon_{ijt},$$

where $i$ indicates the specific antibiotic product, $j$ indicates the county hospital, and $t$ indicates the month. $X_{jt}$ is a set of fixed effects of individual hospitals that control for the unobserved time-invariant individual heterogeneity across hospitals. $\delta_t$ represents month dummies used for controlling for the flexible month effects. $\varepsilon_{ijt}$ refers to the error term. The key variable of interest is Reform$_{ijt}$, which is a dummy variable, with 1 indicating the 26 hospitals before implementation of the reform (November 2015) and 0 otherwise. The coefficient $\beta$ captures the average effects of the reform on the outcome indicators. $X_{jt}$ is a set of time-varying county covariates, including year-end population, GDP per capita, fiscal revenue as a percentage of GDP, per capita disposable income of urban residents, and urban–rural ratio of per capita disposable income. Standard errors are clustered at the level of antibiotic products.

The hospitals that implemented the policy first tended to be in counties with a higher GDP per capita, a higher share of new technology outputs as a percentage of GDP, per capita disposable income of urban residents, and urban–rural ratio of per capita disposable income than the other counties (Table 1).

We used modified Park tests to estimate family distribution and Box–Cox tests to estimate link function [37]. More specifically, we used log link and Gamma distribution for volume (DDDs) and cost; log link and Poisson distribution for the unit price of all antibiotics, injectable antibiotics, and first- and second-line antibiotics; log link and Gamma distribution for the unit price of oral antibiotics; and identity link and Gaussian distribution for the unit price of third-line antibiotics (Table 2). We used the Benjamini–Hochberg procedure [42] to adjust the $p$ values in the multiple comparisons by setting up the false discovery rate at 0.15.

3 Results

On average, 907,380 CNY were spent on procuring antibiotics per hospital per month over the study period: 489,848 CNY in the test group for 13,668 DDDs compared with 961,958 CNY in the control group for 23,339 DDDs (average monthly value × number of hospitals × number of months). Regardless of the groups, the cost for injectable antibiotics accounted for about 90% of the overall cost (range 88.86–92.07). The majority of procured antibiotics were first-line (67% of DDDs) and second-line (31% of DDDs) antibiotics. In both groups, the volume and costs of the procured antibiotics increased after December 2015 when all the hospitals had implemented the reform (Table 3).

The average unit price per DDD of procured antibiotics varied considerably: oral (15–21 CNY) and first-line (29–38 CNY) antibiotics were much cheaper than injectable (109–122 CNY) and second-/third-line (124–327 CNY) antibiotics (Table 3).

Over the study period, procurement volumes and spending on antibiotics increased in county hospitals: an increase of 11.17 thousand DDDs and 450.62 CNY thousand in each hospital in the test group compared with an increase of 13.63 thousand DDDs and 650.90 CNY thousand in each hospital in the control group each month. However, the average procurement price of antibiotics remained largely unchanged in both groups: a decrease of 2.95 CNY (3.53%) in control hospitals compared with 0.98 CNY (1.02%) in test hospitals.

The DID results revealed that non-reform was associated with a 14.79% reduction in the total cost of antibiotics ($p = 0.013$), a 14.79% reduction in the cost of injectable antibiotics ($p = 0.022$) and a 17.30% reduction in the cost of first-line antibiotics ($p = 0.030$). Non-reform was also associated with a 17.30% reduction in the total volume of second-line antibiotics ($p = 0.013$). No significant associations between the reform and the price of the procured antibiotics were found (Table 4).

3.1 Robustness Test

Quasi-natural experiment studies may incur concern about selection bias. We performed time series analyses and compared the secular trends of the two groups of hospitals after November 2015 when all the hospitals had implemented the reform (Fig. 1). There was no indication of any
differences between the two groups in secular trends ($p = 0.514$, $p = 0.889$, and $p = 0.706$, respectively, for trends in volume, cost and unit price per DDD).

To test the robustness of our findings, we performed DID analyses on the truncated sample of data from November 2015 to December 2016. We assumed that the reform occurred in June 2016 instead of the actual November 2015. The rationale of the test is that if the differences between the test and control groups prior to November 2015 were driven by selection bias due to some unobserved, time-varying heterogeneities, then these heterogeneities would lead to a placebo result in the truncated sample, similar to the early findings [43, 44]. The results showed that estimates of the placebo tests were either insignificant or had conflicting signs (Table 5). This suggests that our primary findings were unlikely to be caused by selection bias.

Table 1 Baseline characteristics of counties in which the participating hospitals are located

| County characteristics (as at 2014) | Control group ($n = 38$) | Test group ($n = 26$) | t     | p value |
|-----------------------------------|--------------------------|----------------------|-------|---------|
| Population (10,000)               | 60.93 ± 27.75            | 52.25 ± 23.27        | 1.303 | 0.197   |
| GDP per capita (CNY)              | 39,705.08 ± 23,687.79    | 26,503.19 ± 11,602.95| 2.625 | 0.011   |
| Fiscal revenue as a percentage of GDP (%) | 8.32 ± 2.65              | 8.12 ± 2.94          | 0.292 | 0.771   |
| Share of new technology outputs as a percentage of GDP (%) | 9.22 ± 6.33              | 5.86 ± 3.89          | 2.399 | 0.020   |
| Per capita disposable income of urban residents (CNY) | 21,855.92 ± 2264.12      | 20,317.23 ± 1574.67  | 2.99  | 0.004   |
| Urban–rural ratio of per capita disposable income | 2.05 ± 0.42              | 2.26 ± 0.43          | −1.89 | 0.063   |

Mean ± standard division were calculated and presented for each indicator.
The t value was derived from independent sample T test.
CNY Chinese yuan, GDP gross domestic product.

Table 2 Results of modified Park tests and Box–Cox tests to identify family distribution and link function of outcome indicators in the generalised linear regression models

| Outcome variables | Modified Park test for family distribution | Box–Cox test for link function |
|-------------------|--------------------------------------------|-------------------------------|
| Cost              |                                            |                               |
| All antibiotics   | 2.37 Gamma                                  | 0.13 Log                      |
| Oral antibiotics  | 2.00 Gamma                                  | 0.17 Log                      |
| Injectable antibiotics | 2.41 Gamma               | 0.16 Log                      |
| First-line antibiotics | 2.09 Gamma                 | 0.10 Log                      |
| Second-line antibiotics | 2.77 Gamma            | 0.10 Log                      |
| Third-line antibiotics | 2.46 Gamma              | 0.047 Log                     |
| DDD               |                                            |                               |
| All antibiotics   | 2.71 Gamma                                  | 0.068 Log                     |
| Oral antibiotics  | 2.61 Gamma                                  | 0.087 Log                     |
| Injectable antibiotics | 2.74 Gamma               | 0.064 Log                     |
| First-line antibiotics | 2.83 Gamma            | 0.083 Log                     |
| Second-line antibiotics | 2.56 Gamma           | 0.010 Log                     |
| Third-line antibiotics | 2.44 Gamma             | −0.082 Log                    |
| Unit price per DDD |                                            |                               |
| All antibiotics   | 1.36 Poisson                               | 0.13 Log                      |
| Oral antibiotics  | 2.10 Poisson                               | 0.068 Log                     |
| Injectable antibiotics | 1.38 Poisson           | 0.22 Log                      |
| First-line antibiotics | 1.01 Poisson             | 0.11 Log                      |
| Second-line antibiotics | 1.92 Poisson         | 0.28 Log                      |
| Third-line antibiotics | 0.18 Gaussian       | 0.73 Identity                 |

Coefficients derived from the modified Park tests were used to determine family distribution in the generalised linear regression models: 0 indicates Gaussian distribution with the variance unrelated to the mean; 1 indicates Poisson distribution with the variance equal to the mean; 2 indicates Gamma distribution with the variance exceeding the mean. Coefficients derived from the Box–Cox tests were used to determine link function: 0 for log link; 0.5 for square root link; 1 for identity link.

DDD defined daily dose.
4 Discussion

This study assessed the impact of hospital reforms on the procurement of antibiotics in county public hospitals in Hubei, China. Overall, there was an increasing trend in procurement volumes and spending on antibiotics in all county public hospitals after the reform, even though the procurement price of antibiotics remained largely unchanged. The DID results suggest the reform was associated with an increase in the cost of procured antibiotics, particularly those administered via injection and first-line antibiotics, and an increase in the volume of second-line antibiotics.

Several underlying reasons exist for the increased cost of procured antibiotics. First, county public hospitals in China continue to face serious financial challenges despite increased government investment [45]. The incomes of hospital employees are linked to hospital revenues, which are mainly determined by the volume of services. The government budget for secondary hospitals (mostly county hospitals) as a share of hospital revenues increased only slightly from 9.39% in 2012 to 12.81% in 2016 [46]. Although the zero-markup policy means county hospitals can no longer profit from the sale of medicines, they can still charge a fee for medicine-associated services, such as injections.

Second, the reform measures have little, if any, effect on the promotional activities of pharmaceutical suppliers. It is commonly believed that pharmaceutical suppliers may have continued to offer volume-based commissions to prescribers ‘under the table’. Many large pharmaceutical companies also sponsor doctors and/or their professional bodies for academic activities. Some doctors use their low government-defined salary to justify these commissions [18].

Third, the loss of profit from the sale of medicines may have inadvertently encouraged more hospital admissions. Arguably, some admissions may be unnecessary, but they can contribute to profitable revenues, such as accommodation services in county hospitals. Hospital admissions also increase the chance of the parenteral administration of medicines, for which a consumables and services fee can be charged [33]. A recent study observed increasing inpatient activities, including increased expenses in intravenous infusion, electrotherapy, acupuncture, and nursing-related activities.

\[ \text{CNY Chinese Yuan, DDD defined daily dose} \]

| Table 3 | Volume (defined daily dose), cost and unit price of procured antibiotics in county hospitals |
|---------|------------------------------------------------------------------------------------------------|
| Outcome indicators | Overall November 2014–November 2015 | December 2015–December 2016 |
| | Test group (pre-reform) | Control group | Test group (post-reform) | Control group |
| Average cost (CNY in thousands) of procured antibiotics per hospital per month (% as a share in total) |
| Total | 907.38 | 519.29 | 674.12 | 969.91 | 1325.02 |
| Injectable | 826.14 (91.05) | 465.83 (89.71) | 599.01 (88.86) | 889.67 (91.73) | 1219.90 (92.07) |
| Oral | 81.24 (8.95) | 53.46 (10.29) | 75.11 (11.14) | 80.24 (8.27) | 105.13 (7.93) |
| First-line | 319.91 (35.26) | 202.02 (38.90) | 257.35 (38.18) | 343.05 (35.37) | 436.28 (32.93) |
| Second-line | 542.45 (59.78) | 287.69 (55.40) | 392.94 (58.29) | 565.74 (58.33) | 825.43 (62.30) |
| Third-line | 45.02 (4.96) | 29.58 (5.70) | 23.84 (3.54) | 61.09 (6.30) | 63.33 (4.78) |
| Average volume (DDDs in thousands) of procured antibiotics per hospital per month (% as a share in total) |
| Total | 23.13 | 15.22 | 17.48 | 26.39 | 31.11 |
| Injectable | 14.00 (60.53) | 8.49 (55.78) | 11.18 (63.96) | 15.68 (59.42) | 18.93 (60.85) |
| Oral | 9.13 (39.47) | 6.73 (44.22) | 6.29 (35.98) | 10.71 (40.58) | 12.19 (39.18) |
| First-line | 15.53 (67.14) | 10.87 (71.42) | 11.45 (65.50) | 17.90 (67.83) | 20.59 (66.18) |
| Second-line | 7.23 (31.26) | 3.94 (25.89) | 5.79 (33.12) | 8.11 (30.73) | 10.00 (32.14) |
| Third-line | 0.38 (1.64) | 0.38 (2.50) | 0.24 (1.37) | 0.41 (1.55) | 0.51 (1.64) |
| Average unit price per DDD of procured antibiotics (CNY) |
| Total | 91.62 | 86.49 | 95.47 | 83.54 | 96.45 |
| Injectable | 116.94 | 113.81 | 118.77 | 108.97 | 121.66 |
| Oral | 17.77 | 14.64 | 20.64 | 16.60 | 18.49 |
| First-line | 33.02 | 29.38 | 37.58 | 29.85 | 34.56 |
| Second-line | 130.90 | 132.40 | 127.28 | 123.81 | 135.50 |
| Third-line | 307.40 | 295.36 | 326.78 | 295.68 | 310.98 |
services in county public hospitals as a result of the reform [37].

Finally, zero markup on the sale of medicines may have improved the affordability of medicines. Consequently, consumers may request more prescriptions with perceived greater efficacy. There is a common belief in China that intravenous infusion is more effective than oral pills [23, 47]. It is also not unusual for patients to demand antibiotics without proper indications [48, 49]. A qualitative study revealed that patients with a common cold in

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**Table 4** DID Results from generalised linear regression analyses

| Outcome indicators | N   | Coefficient | p value | Benjamini–Hochberg significance | 95% CI        | Robust SE | AIC          | BIC          | Chi-squared |
|--------------------|-----|-------------|---------|---------------------------------|---------------|-----------|--------------|--------------|-------------|
| **Cost of procured antibiotics** |     |             |         |                                 |               |           |              |              |             |
| Total              | 22,713 | -0.16       | 0.013   | S                               | -0.29 to -0.034 | 0.064     | 23.79        | 173,507.8    | 81,107.20*** |
| Oral               | 5800  | -0.062      | 0.460   | NS                              | -0.23 to 0.10  | 0.085     | 21.50        | 40,068.02    | 10,419.89*** |
| Injectable         | 16,913 | -0.16       | 0.022   | S                               | -0.29 to -0.023 | 0.069     | 24.21        | 126,109.99   | 50,487.46*** |
| First-line         | 11,973 | -0.19       | 0.030   | S                               | -0.37 to -0.019 | 0.090     | 22.90        | 79,471.19    | 35,355.20*** |
| Second-line        | 9156  | -0.13       | 0.163   | NS                              | -0.32 to 0.054 | 0.096     | 24.56        | 68,396.78    | 22,757.94*** |
| Third-line         | 1584  | -0.11       | 0.547   | NS                              | -0.48 to 0.25  | 0.19      | 22.99        | 9357.73      | 2487.68***   |
| **Volume (DDDs) of procured antibiotics** |     |             |         |                                 |               |           |              |              |             |
| Total              | 22,713 | -0.048      | 0.444   | NS                              | -0.17 to 0.074 | 0.062     | 16.54        | 182,440.8    | 83,574.35*** |
| Oral               | 5800  | 0.063       | 0.402   | NS                              | -0.084 to 0.21 | 0.075     | 17.40        | 40,418.51    | 11,507.98*** |
| Injectable         | 16,913 | -0.14       | 0.069   | NS                              | -0.30 to 0.011 | 0.079     | 16.07        | 131,604.8    | 63,016.08*** |
| First-line         | 11,973 | 0.028       | 0.736   | NS                              | -0.13 to 0.19  | 0.082     | 17.01        | 88,620.58    | 37,112.34*** |
| Second-line        | 9156  | -0.19       | 0.032   | S                               | -0.37 to -0.017 | 0.091     | 15.97        | 70,147.39    | 22,776.77*** |
| Third-line         | 1584  | -0.0051     | 0.98    | NS                              | -0.41 to 0.40  | 0.21      | 12.59        | 8605.61      | 3595.26***   |
| **Average price per DDD of procured antibiotics (CNY)** |     |             |         |                                 |               |           |              |              |             |
| Total              | 22,713 | 0.036       | 0.486   | NS                              | -0.066 to 0.14 | 0.052     | 53.22        | 885,415.7    | 2,509,287.49*** |
| Oral               | 5800  | -0.10       | 0.239   | NS                              | -0.28 to 0.070 | 0.089     | 27.05        | 79,277.97    | 143,170.44*** |
| Injectable         | 16,913 | 0.050       | 0.342   | NS                              | -0.053 to 0.15 | 0.052     | 59.33        | 770,543.7    | 2,287,719.04*** |
| First-line         | 11,973 | -0.10       | 0.088   | NS                              | -0.22 to 0.015 | 0.059     | 26.47        | 156,510.2    | 398,925.10*** |
| Second-line        | 9156  | 0.075       | 0.239   | NS                              | -0.05 to 0.20  | 0.064     | 63.66        | 463,126.9    | 1,055,398.45*** |
| Third-line         | 1584  | 8.70        | 0.695   | NS                              | 52.20 to 34.80 | 22.19     | 58.48        | 72,766.75    | 105,739.38*** |

Bold values indicate significance of p value (p < 0.05)

AIC Akaike information criterion, BIC Bayesian information criterion, CI confidence interval, DDD defined daily doses, DID difference in differences, NS not significant, S significant, SE standard error

***p<0.001

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Fig. 1 Average volume, cost and unit price of procured antibiotics per hospital by month. CNY Chinese Yuan, DDD defined daily dose
China usually sought self-medication first but turned to injectable treatments if symptoms persisted simply because "pills have failed" [23]. This distorted perception and consumer demand may put additional pressure on prescribers [9], exacerbating overprovision and the irrational use of injections.

Our findings have some policy implications. Hospitals operate within a very complex system. Many of the problems are shaped by multiple policy arrangements involving various stakeholders. A systems approach to health reform is critical. Piecemeal remedies rarely fix a problem without leading to unintended consequences if health organisations can easily find a way to take advantage of the reform for their own financial gains. It is essential that strategies that can align policy goals with the financial incentives of health providers are developed, at both individual and organisational levels [45]. These often require changes in governance structure, accountability, payment mechanisms and autonomy of decision making [50–52].

To our knowledge, this is the first study of its kind to examine the impact of hospital reform on the procurement of antibiotics. Our findings complement existing evidence from the literature, which points to the potential risk of cost shifting from outpatient to inpatient care [37] and from supplier-induced sale of medicines to supplier-induced demand for services due to the reform [36]. This study has several strengths over previous studies. We used a large sample and also used institutionalised data, which avoids much of the bias of sampling. We also examined the robustness of the findings.

| Table 5 | Placebo tests (DID analyses) using the truncated sample of data from November 2015 to December 2016 |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Outcome indicators | N | Modified Park test | Box–Cox test | Coefficient | p value | Benjamini–Hochberg significance | 95% CI | Robust SE |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Cost of procured antibiotics | | | | | | | | |
| Total | 16,488 | 2.37 | 0.13 | 0.034 | 0.54 | NS | – 0.075 to 0.14 | 0.056 |
| Oral | 4222 | 2.00 | 0.17 | 0.18 | 0.008 | S | 0.050 to 0.31 | 0.068 |
| Injectable | 12,266 | 2.41 | 0.16 | 0.0084 | 0.886 | NS | – 0.11 to 0.12 | 0.059 |
| First-line | 8681 | 2.09 | 0.10 | 0.14 | 0.034 | S | 0.01 to 0.27 | 0.067 |
| Second-line | 6655 | 2.77 | 0.10 | – 0.054 | 0.451 | NS | – 0.19 to 0.086 | 0.072 |
| Third-line | 1152 | 2.46 | 0.047 | – 0.018 | 0.904 | NS | – 0.304 to 0.27 | 0.15 |
| Volume of procured antibiotics (DDDs) | | | | | | | | |
| Total | 16,488 | 2.48 | 0.079 | 0.11 | 0.034 | S | 0.0083 to 0.21 | 0.053 |
| Oral | 4222 | 2.52 | 0.107 | 0.16 | 0.016 | S | 0.030 to 0.29 | 0.067 |
| Injectable | 12,266 | 2.63 | 0.077 | 0.066 | 0.294 | NS | – 0.057 to 0.19 | 0.063 |
| First-line | 8681 | 2.52 | 0.095 | 0.13 | 0.070 | S | – 0.010 to 0.26 | 0.80 |
| Second-line | 6655 | 2.59 | 0.029 | 0.063 | 0.333 | NS | – 0.065 to 0.19 | 0.066 |
| Third-line | 1152 | 2.33 | – 0.068 | – 0.045 | 0.758 | NS | – 0.33 to 0.24 | 0.15 |
| Unit price per DDD of procured antibiotics | | | | | | | | |
| Total | 16,488 | 1.37 | 0.11 | 0.027 | 0.487 | NS | – 0.049 to 0.10 | 0.039 |
| Oral | 4222 | 2.17 | 0.037 | 0.014 | 0.794 | NS | – 0.092 to 0.12 | 0.054 |
| Injectable | 12,266 | 1.39 | 0.22 | 0.018 | 0.653 | NS | – 0.060 to 0.095 | 0.040 |
| First-line | 8681 | 1.06 | 0.075 | 0.061 | 0.192 | NS | – 0.031 to 0.15 | 0.047 |
| Second-line | 6655 | 1.98 | 0.27 | 0.0025 | 0.961 | NS | – 0.099 to 0.10 | 0.052 |
| Third-line | 1152 | 0.21 | 0.76 | – 9.46 | 0.444 | NS | – 33.71 to 14.78 | 12.37 |

CI confidence interval, DDD defined daily dose, NS not significant, S significant, SE standard error
This study has several limitations. First, data were drawn from procurement records, which do not directly reflect the actual use of medicines. We were unable to evaluate the appropriateness of antibiotic use at the individual patient level. Second, medicines used for outpatient and inpatient care were not separated in the procurement records. This prevented us from exploring the effects of the reform on outpatient and inpatient care separately.

5 Conclusion

The public hospital reform in China diminished the profit margin on sales of medicines in public hospitals, but the entire funding structure for hospitals remained largely unchanged, which negated the potential of the reform to contain the excessive procurement of antibiotics. On the contrary, county public hospitals procure more antibiotics and a greater number of expensive antibiotics, such as those administered via injection, to compensate for the loss of income from the sale of medicines, leading to increased total costs of antibiotics. A systems approach to health reform is critical and will require coordinated changes in funding, governance, management and payment mechanisms.

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Compliance with Ethical Standards

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Conflict of interest Yuqing Tang, Chaojie Liu, Junjie Liu, Xunping Zhang and Keyuan Zuo have no conflicts of interest.

Data availability statement The datasets analysed for the current study are available from the corresponding authors on reasonable request.

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