Implementation and Impact of National Centralized Drug Procurement Policy in China: Evidence from the National Drug Procurement Database

Jiancheng Lu
Jilin University
Ying Yang
Wuhan University https://orcid.org/0000-0001-9252-5071
Xiaotong Wen
Wuhan University
Jing Wang
National Health Commission of the People's Republic of China
Yuan Shen
National Health Commission of the People's Republic of China
Lining Mao
Wuhan University
Dan Cui
Wuhan University
Zongfu Mao (zfmao@whu.edu.cn)
Wuhan University https://orcid.org/0000-0001-9477-4725
Jinghua Li
Jilin University

Research

Keywords: National Centralized Drug Procurement (NCDP), volume-based procurement, "4+7" policy, drug expenditures, drug use

Posted Date: August 19th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-805352/v1

Abstract

Background

Chinese government implemented the first round of National Centralized Drug Procurement pilot in 4 municipalities and 7 sub-provincial cities in 2019, so called "4 + 7" policy. This study evaluated the implementation and impact of “4 + 7” policy.

Methods

This study used drug purchase data from China Drug Supply Information Platform (CDSIP) database. “4 + 7” policy-related drugs were selected as study samples, including 25 drugs in the “4 + 7” List and 92 alternative drugs that have an alternative relationship with “4 + 7” List drugs in clinical use. “4 + 7” List drugs were divided into bid-winning and non-winning products. We applied Defined Daily Doses (DDDs), DDDs per 1000 inhabitants per day (DID), purchase expenditures, and Defined Daily Drug cost (DDDc) as outcome variables. Interrupted time-series was adopted to quantity policy effect.

Results

As of December 2019, the completion rate of overall bid-winning drugs in 9 pilot cities reached 154.40%, and the completion rate of 25 bid-winning drugs ranged between 74.77% and 477.75%. After policy intervention, the DID of bid-winning drugs, “4 + 7” List drugs, alterative drugs, as well as the overall policy-related drugs increased by 545.18%, 14.03%, 12.21%, and 13.04% in pilot cities. Bid-winning drugs significantly increased 132.84 million DDDs ($p < 0.001$) in volume and 48.95 million CNY ($p < 0.05$) in expenditures, and dropped 6.35 CNY ($p < 0.001$) in DDDc. The volume proportion of bid-winning products increased from 12.67–71.66%. The DDDc of non-winning drugs increased 0.94 CNY ($p < 0.001$). Overall, the DDDc of policy-related drugs dropped 1.38 CNY ($p < 0.001$), and the expenditures decreased 634.68 million CNY ($p < 0.001$).

Conclusion

An overall satisfying implementation progress of “4 + 7” policy was observed in pilot cities. The policy alleviated the medication burdens of patients, which is supported by the significant reduction in DDDc and costs of policy-related drugs. The accessibility and consumption of policy-related drugs improved. However, monitoring regarding the clinical use of policy-related drugs will still be necessary in the future.

Background

Worldwide, many countries are facing the challenges of ever-increasing pharmaceutical expenditures [1, 2], and the global pharmaceutical market reached $955 billion in 2019 [3]. In China, the total health expenditure increased from 145.4 billion Chinese Yuan (CNY) in 2008 to 59121.2 billion CNY in 2018, with an average compound annual growth rate of 13.4% [4]. In 2018, the total pharmaceutical expenditure was 218.3 billion CNY in China, accounting for 35.8% of the total health expenditure, which was considerably higher than the average level of 17% in the Organization for Economic Co-operation and Development (OECD) countries [5]. Of note, procurement inefficiency and transaction decoupling have been regarded as the major culprits of the ever-escalating drug price and hence the grievous burdens of medication in China [6].

Volume-based procurement is a worldwide adopted strategy for drug price and cost control [7, 8]. On January 1, 2019, the General Office of the State Council of the People's Republic of China (PRC) issued the National Centralized Drug Procurement (NCDP) policy, aiming at cutting drug prices and reducing the medication burden of patients [9]. NCDP is the first policy attempt for volume-based drug procurement at the national level in mainland China. The first round of the NCDP pilot work was carried out in 4 province-level municipalities (Beijing, Tianjin, Shanghai, and Chongqing) and 7 sub-provincial cities (Shenyang, Dalian, Xiamen, Guangzhou, Shenzhen, Chengdu, and Xi'an), known as "4 + 7" policy [10]. In the “4 + 7” policy, 25 drugs (by generic name) in the “4 + 7” List successfully purchased, adopting an exclusive bid winning method, a total of 25 products (22 generic drugs and 3 original-branded drugs) won the bid [11].

According to the National Healthcare Security Administration (NHSA) of the PRC, as of April 2020, the actual procurement volume of the 25 bid-winning drugs has reached 2.4 times higher than the volume initially committed in the enrollment of “4 + 7” pilot in 2019 [12]. It was expected to save a total amount of 5.8 billion CNY due to the initiation of the “4 + 7” pilot policy, of which 2.6 billion CNY would result from the price reduction effect and 3.2 billion CNY from drug substitution effect [13]. Despite various researches and exploratory analyses on the implementation impact of the 4 + 7 pilot, most of them were mostly restricted to single-hospital investigation [14–18] or single-city exploration [19–22]. Furthermore, a substantial body of literature has been evaluating the “4 + 7” policy impact with focal area restricted to a single-category of drugs, rather than with a comprehensive assessment by including nationwide multi-institutional multi-drug-category [23–27]. Therefore, the overall objective of this study is to quantitively evaluate the systematic effects of the “4 + 7” policy in the pilot cities, in aspects of changes in the purchase volume, purchase expenditures, and daily costs of policy-related drugs.

Methods

The policy intervention

The highlight of "4 + 7" policy lies in the implementation of "volume-based procurement", in which “Trade-for-price” and “Guarantee of use” were taken as the core policy measures [9].

(a) **“Trade-for-price”**: Under “4 + 7” policy, each public medical institution (public hospitals and government-run primary healthcare institutions) in the 11 pilot cities was required to submit the agreed procurement volume of each “4 + 7” List drug to the NHSA. The agreed procurement volume is the expected annual purchase volume of a certain “4 + 7” List drug (by generic name) estimated with reference to the use volume in the previous year. The NHSA organized competitive bidding and price negotiation based on the overall annual agreed procurement volume of 11 pilot cities. Pharmaceutical manufacturers hold original-branded drugs that beyond patent protection period or generic drugs that passed the consistency evaluation of quality and efficacy in China are eligible to participate in the bidding. The pharmaceutical manufacturer with the lowest bid price in each “4 + 7” List drug won the bid. On December 17, 2018, the bid winning results were announced, with an average price reduction of 52% for 25 bid-winning drugs [11].

(b) **“Guarantee of use”**: In “4 + 7” policy, 11 pilot cities were required to start implementing the NHSA’s bid winning results before April 1, 2019. The purchases of all the bid-winning drugs were carried out on the provincial drug bidding and procurement platform. Besides, the use volume of each bid-winning drug in each public medical institution in pilot cities was monitored and assessed by the NHSA to ensure the completion of the agreed procurement volume. In most of the pilot cities, medical institutions conducted monthly assessments on relevant clinical departments to encourage and ensure the use of bid-winning products.
From March 15 to April 1, 2019, 11 pilot cities successively implemented the “4 + 7” bidding results, starting to purchase the 25 bid-winning drugs at the winning bid prices.

Data sources

Data used in this study were retrospectively retrieved through the national drug procurement database–China Drug Supply Information Platform (CDSIP) database. The CDSIP is a national drug database constructed and operated by the Statistical Information Center of the National Health Commission of the PRC, and was officially launched on October 22, 2015. The CDSIP database covered drug purchase order data of all provincial drug bidding and procurement platforms in mainland China. In the CDSIP database, each drug purchase order record included the name of medical institution, purchase date, drug YPID (Yao Pin Identifier) code, drug generic name, dosage form, specification, conversion factor, pharmaceutical manufacturer, price per unit, purchasing unit (by box, bottle, or branch), purchase volume, purchase expenditures, etc. Details of the CDSIP database are available elsewhere [28]. A total of 7,647 drugs (by generic name) and 141,624 products (by YPID code) were contained in this national database.

Sample selection

In this study, we included samples with the following criteria: (a) The drug scope was "4 + 7" policy-related drugs, including 25 drugs (by generic name) in the “4 + 7” List and the alternative drugs that have an alternative relationship with “4 + 7” List drugs in clinical use (**APPENDIX A**). The alternative drugs were determined following the *Monitoring Plan for the Pilot Work of National Centralized Drug Procurement and Use* issued by the NHSA [29]. This study divided “4 + 7” List drugs in to bid-winning products and non-winning products according to the "4 + 7" pilot bid winning results [11]. (b) The time period was 24 months from January 2018 to December

2019. (c) The scope of regions was nine "4 + 7" pilot cities, including Beijing, Shanghai, Chongqing, Tianjin, Chengdu, Xi'an, Shenyang, Dalian, and Xiamen. Two (Guangzhou and Shenzhen) of the eleven “4 + 7” pilot cities were not included in this study, because their purchase order data in the CDSIP database was incomplete. (d) The scope of medical institutions was all the public medical institutions in the included pilot cities, for “4 + 7” pilot was only implemented in public medical institutions. In China, public medical institution consists of public hospital and government-run primary care institution. Purchase order records with incomplete information were excluded.

Finally, a total of 117 drugs (by generic name) were included in this study, consisting of 25 “4 + 7” List drugs and 92 alternative drugs. 2,562 drug products (by YPID code) were involved. The flow chart of sample screening is presented in Fig. 1.

Outcome variables

Three main outcome variables were measured in this study: purchase volume, purchase expenditures, and daily drug costs. Purchase expenditure data was reported in CNY. Purchase volume was measured using Defined Daily Doses (DDDs), which is a measurement for comparing drug consumptions developed by the WHO Collaborating Centre for Drug Statistics Methodology [30]. In this study, DDD value of each included drug was determined according to the *Guidelines for ATC classification and DDD assignment 2021* [31]. Daily drug cost was assessed using Defined Daily Drug cost (DDDc), which was calculated by the ratio of expenditures and DDDs. Besides, DDDs per 1000 inhabitants per day (DID) was calculate the measure the consumption of policy-related drugs in pilot cities.

Statistical Analysis

Descriptive statistics were used. We first calculated the completion rate of bid-winning drugs in each included pilot city based on the cumulative annual agreed procurement volume of each of the 25 bid-winning drugs announce by the Joint Procurement Office [10]. Then, we described the change of purchase volume, purchase expenditures, and DDDc of policy-related drugs in the corresponding period before (March to December 2018) and after (March to December 2019) the implementation of "4 + 7" policy.

Furthermore, a single-group interrupted time series (ITS) was designed to quantify the effect of “4 + 7” policy. ITS is a commonly employed approach for evaluating changes in longitudinal series following a quasi-experimental intervention occurring at a fixed point in time [32]. In this study, ITS analysis of each outcome variable was conducted using time series data from January 2018 to December 2019. The actual policy commencement dates in the 9 pilot cities vary between March 15 and April 1, 2019. In view of this, we set March 2019 as the cutting point of the entire timeframe and the execution time point of the policy intervention. The time unit was set to 1 month, including 14 points as pre-"4 + 7" policy period and 10 points as post-"4 + 7" policy period. The following segmented linear regression model was developed [33, 34]:

$$Yt = \beta_0 + \beta_1 \times time_t + \beta_2 \times intervention_t + \beta_3 \times time\ \ after\ \ intervention_t + \varepsilon_t$$

Where, Y_t is the independent outcome variable (volume, expenditures, or DDDc) in month *t*. *time* is a continuous variable indicating time in months at time *t* from the start of the observation period. *intervention* refers to “4 + 7” policy intervention with the value 0 and 1, and 0 represents the pre-"4 + 7" policy period (from January 2018 to February 2019) and 1 represents the post-"4 + 7" policy period (from March 2019 to November 2019). *time after intervention* is a continuous variable indicating months in the post-"4 + 7" policy period (time in the pre-"4 + 7" policy period is coded 0).

In this model, β_0 estimates the baseline level of the independent variable at the beginning of the observation period. β_1 estimates the linear trend during the pre-intervention period. β_2 estimates the level change in the outcome variable immediately following the intervention. β_3 estimates the trend change in the outcome variable in the post-intervention period compared with the pre-intervention period. ε_t is an estimate of the random error at time *t*. The relative change in level after “4 + 7” policy was expressed as β_2/β_0 [35]. Durbin-Watson test was performed to test the presence of first-order auto-correlation (a value around 2 indicates no sign of auto-correlation). If autocorrelation is detected, the Prais-Winsten method was applied to estimate the regression. Stata version 16.0 was used to perform the ITS analysis. A *p*-value < 0.05 was considered statistically significant.

Results

Completion rate of “4 + 7” policy

We calculated the completion rate of bid-winning drugs in accordance with the annual agreed procurement volume in 9 pilot cities (Fig. 2). As of December 2019, the actual purchase volume of bid-winning drugs reached 1,490.77 million DDDs, achieving an exceeding overall completion rate of 154.40%. All the 9 pilot cities have completed the cumulative annual agreed procurement volume within 9 months, among which Xi’an (1771.51%) and Xiamen (1135.87%) had the highest completion rate. Figure 3 indicates the completion rate of each of the 25 bid-winning drugs. In the 9 pilot cities included in this study, the annual agreed procurement volume of 23 drugs exceedingly achieved as of December 2019, except for Olanzapine (74.77%) and Flurbiprofen (92.22%). Among them, the actual purchase volume of Tenofovir Disoproxil (477.75%), Levetiracetam (410.12%), Gefitinib (379.36%), Irbesartan Hydrochlorothiazide (336.36%) and Entecavir (307.29%) between April and December 2019 reached more than 3 times of their agreed procurement volume.

Overall procurement of policy-related drugs in the pre- and post-“4 + 7” policy periods

Over the entire study period, the total procurement of policy-related drugs was 11243.4 million DDDs and 51606.8 million CNY in nine pilot cities. As shown in Table 1 and Fig. 4, after the implementation of “4 + 7” policy, the volume and expenditures of bid-winning drugs increased by 549.66% and 38.79%, non-winning drugs decreased by 62.74% and 57.12%. As a result, the “4 + 7” List drugs increased by 14.82% in volume, and decreased by 43.30% in expenditures. The overall DDDc of “4 + 7” List drugs decreased by 50.62%, in which bid-winning products decreased (-78.68%) and non-winning products increased (15.09%). Besides, the increment of 12.98%, 21.84%, and 7.84% were observed for the alternative drugs in volume, expenditures, and DDDc, respectively. Overall, the volume of “4 + 7” policy-related drugs increased by 13.83%, while the expenditures and DDDc decreased by 15.76% and 25.99%.

Table 1
The change of volume, expenditures, and DDDc of policy-related drugs in the pre- and post-“4 + 7” policy periods.

	Volume (million DDDs)			Expenditures (million CNY)			DDDc (CNY)		
	Pre-	Post-	GR (%)	Pre-	Post-	GR (%)	Pre-	Post-	GR (%)
Winning products	257.75	1674.50	549.66	1915.34	2658.37	38.79	7.43	1.59	-78.64
Non-winning products	1777.33	662.26	-62.74	11383.08	4881.62	-57.12	6.40	7.37	15.09
“4 + 7” List drugs	2035.08	2336.76	14.82	13298.42	7539.99	-43.30	6.53	3.23	-50.62
Alternative drugs	2395.96	2707.06	12.98	9743.69	11871.68	21.84	4.07	4.39	7.84
Overall policy-related drugs	4431.04	5043.82	13.83	23042.11	19411.67	-15.76	5.20	3.85	-25.99

DDDs, defined daily doses; CNY, Chinese Yuan; DDDc, defined daily drug cost; GR, growth rate. Pre- refers to March to December 2018; Post- refers to March to December 2019.

Specific to each of the 25 bid-winning drugs, their growth rates for purchase volume ranged from 47.11–33980.17%, of which Pemetrexed Disodium (33980.17%), Cefuroxime (19834.49%), Irbesartan (4823.92%), and Levetiracetam (4436.88%) had the greatest growth rate (Table 2). The overall volume proportion of bid-winning drugs (against all products with the same generic name) increased from 12.67–71.66% after policy intervention, the expenditure proportion mildly increased from 14.40–35.26%.

Table 2
The change of volume, expenditures, and DDDc of each “4 + 7” bid-winning drug in the pre- and post-“4 + 7” policy periods.

	Volume (million DDDs)			Expenditures (million CNY)			DDDc (CNY)		
	Pre-	Post-	GR (%)	Pre-	Post-	GR (%)	Pre-	Post-	GR (%)
Pemetrexed disodium	0.002	0.83	33980.17	1.96	242.16	12224.19	809.68	292.80	-63.84
Cefuroxime axetil	0.09	18.92	19834.49	0.47	19.52	4011.97	5.00	1.03	-79.37
Irbesartan	2.19	107.91	4823.92	2.49	43.54	1650.56	1.13	0.40	-64.45
Levetiracetam	0.05	2.39	4436.88	0.97	34.43	3436.03	18.48	14.41	-22.06
Irbesartan hydrochlorothiazide	7.07	156.53	2114.44	24.20	168.14	594.76	3.42	1.07	-68.63
Risperidone	0.47	10.04	2045.01	0.91	8.44	823.78	1.95	0.84	-56.93
montmorillonite	0.40	7.57	1775.01	1.09	15.45	1313.94	2.71	2.04	-24.59
Lisinopril	0.20	3.33	1573.38	0.23	0.77	235.29	1.16	0.23	-79.96
Entecavir	7.79	98.36	1162.27	82.19	68.57	-16.58	10.55	0.70	-93.39
Tenofovir disoproxil	2.30	18.23	691.38	29.49	19.05	-35.41	12.80	1.04	-91.84
Losartan	20.35	133.42	555.60	59.95	130.73	118.06	2.95	0.98	-66.74
Escitalopram	1.95	8.65	342.74	26.69	76.19	185.48	13.65	8.80	-35.52
Imatinib	0.14	0.56	288.45	21.48	46.60	116.92	149.85	83.68	-44.16
Atorvastatin	82.47	315.88	283.00	509.00	325.04	-36.14	6.17	1.03	-83.33
Gefitinib	0.45	1.61	256.53	105.08	93.66	-10.87	232.99	58.25	-75.00
enalapril	11.61	36.70	216.16	12.08	21.27	76.17	1.04	0.58	-44.28
Clopidogrel	80.95	165.82	104.84	803.02	630.99	-21.42	9.92	3.81	-61.64
Olanzapine	6.99	12.86	83.93	102.29	143.47	40.26	14.63	11.15	-23.75
Paroxetine	15.05	25.54	69.68	60.46	44.55	-26.32	4.02	1.74	-56.58
Fosinopril	17.20	25.30	47.11	71.28	33.82	-52.55	4.14	1.34	-67.75
Amlodipine	0.00	323.28	-	0.00	48.03	-	-	0.15	-
Rosuvastatin	0.00	164.28	-	0.00	134.11	-	-	0.82	-
Dexmedetomidine	0.00	0.38	-	0.00	137.93	-	-	358.29	-
Flurbiprofen	0.00	4.67	-	0.00	50.07	-	-	10.71	-
Montelukast	0.00	31.44	-	0.00	121.84	-	-	3.88	-
Total	257.75	1674.50	549.66	1915.34	2658.37	38.79	7.43	1.59	-78.64

DDDs, defined daily doses; CNY, Chinese Yuan; DDDc, defined daily drug cost; GR, growth rate. Pre- refers to March to December 2018; Post- refers to March to December 2019.

In nine pilot cities, the overall consumption of policy-related drugs was 105.79 DID (2018) and 118.05 DID (2019). After policy intervention, the consumption of bid-winning drugs increased from 6.27 DID to 40.43 DID (545.18% increase), non-winning drugs decreased from 43.21 DID to 15.99 DID (-63.00% decrease). The consumption of “4 + 7” List drugs (14.03% increase), alternative

drugs (12.21% increase), as well as the overall policy-related drugs (13.04% increase) increased after “4 + 7” policy. The detailed consumption changes of policy-related drugs in pilot cities are presented in Fig. 5.

ITS analysis for the change of policy-related drugs

Table 3 demonstrates the results of ITS analysis. After the implantation of “4 + 7” policy, the volume of bid-winning products significantly increased (132.84 million DDDs, 95% *CI* = 110.59 to 155.09, *p*-value < 0.0001), the volume of non-winning products significantly declined (-122.71 million DDDs, 95% *CI*= -146.03 to -99.38, *p*-value < 0.0001). While no statistically significant difference was observed for the volume of “4 + 7” List drugs, alternative drugs, and the overall policy-related drugs (all *p*-values > 0.05).

Table 3
ITS analysis for the change of policy-related drugs in volume, expenditures, and DDDc.

	Volume (million DDDs)	Expenditures (million CNY)	DDDc (CNY)
Bid-winning products			
Baseline level, β_0	23.82 (10.16, 37.48)**	168.93 (145.60, 192.26)***	7.16 (6.90, 7.43)***
Baseline trend, β_1	0.17 (-1.63, 1.96)	2.86 (-0.21, 5.93)	0.06 (0.02, 0.09)**
Level change, β_2	132.84 (110.59, 155.09)***	48.95 (10.10, 87.79)*	-6.35 (-6.75, -5.96)***
Trend change, β_3	1.61 (-1.85, 5.08)	-2.09 (-8.01, 3.84)	-0.07 (-0.14, -0.002)*
DW	1.834	2.268	1.829
R^2	0.973	0.826	0.994
Relative change (%)	557.68	28.95	-87.01
Non-winning products			
Baseline level, β_0	165.69 (151.70, 179.69)***	1031.70 (953.88, 1109.52)***	6.22 (6.00, 6.44)***
Baseline trend, β_1	1.94 (0.10, 3.79)*	14.92 (4.68, 25.15)**	0.02 (-0.01, 0.05)
Level change, β_2	-122.71 (-146.03, -99.38)***	-718.89 (-848.58, -589.20)***	0.94 (0.59, 1.29)***
Trend change, β_3	-3.34 (-6.89, 0.21)	-25.95 (-45.70, -6.20)*	-0.02 (-0.08, 0.03)
DW	2.132	2.373	1.990
R^2	0.958	0.962	0.877
Relative change (%)	-74.06	-69.68	15.11
"4 + 7" List drugs			
Baseline level, β_0	189.25 (167.29, 211.22)***	1200.25 (1103.02, 1297.49)***	6.34 (6.15, 6.53)***
Baseline trend, β_1	2.20 (-0.69, 5.09)	17.86 (5.07, 30.65)**	0.02 (-0.01, 0.05)
Level change, β_2	8.84 (-27.72, 45.40)	-671.31 (-833.36, -509.27)***	-3.10 (-3.40, -2.80)***
Trend change, β_3	-1.97 (-7.54, 3.61)	-28.08 (-52.77, -3.40)*	-0.09 (-0.13, -0.04)**
DW	2.090	2.393	1.951
R^2	0.573	0.931	0.990
Relative change (%)	4.67	-55.93	-48.90
Alternative drugs			
Baseline level, β_0	228.56 (204.73, 252.39)***	924.71 (812.64, 1036.78)***	4.04 (3.93, 4.15)***
Baseline trend, β_1	1.93 (-1.21, 5.06)	10.41 (-4.33, 25.15)	0.01 (-0.001, 0.03)
Level change, β_2	0.15 (-39.47, 39.76)	42.29 (-143.42, 227.99)	0.11 (-0.06, 0.28)

***p-value < 0.0001, **p-value < 0.001, *p-value < 0.05.

DDDs, defined daily doses; CNY, Chinese Yuan; DDDc, defined daily drug cost; DW, Durbin-Watson d statistic.

	Volume (million DDDs)	Expenditures (million CNY)	DDDc (CNY)
Trend change, β_3	0.85 (-5.20, 6.90)	4.29 (-24.15, 32.73)	-0.0001 (-0.03, 0.03)
DW	2.064	1.944	1.824
R^2	0.506	0.569	0.688
Relative change (%)	0.07	4.57	2.72
Overall policy-related drugs			
Baseline level, β_0	416.79 (375.30, 458.29)***	2118.19 (1931.43, 2304.95)***	5.09 (5.02, 5.16)***
Baseline trend, β_1	4.28 (-1.18, 9.74)	29.17 (4.59, 53.74)*	0.02 (0.01, 0.03)**
Level change, β_2	7.20 (-61.90, 76.30)	-634.68 (-945.85, -323.51)***	-1.38 (-1.49, -1.26)***
Trend change, β_3	-1.26 (-11.79, 9.28)	-25.20 (-72.61, 22.20)	-0.04 (-0.06, -0.02)***
DW	2.131	2.185	1.994
R^2	0.624	0.719	0.992
Relative change (%)	17.27	-29.96	-27.11
****p*-value < 0.0001, ***p*-value < 0.001, **p*-value < 0.05.			
DDDs, defined daily doses; CNY, Chinese Yuan; DDDc, defined daily drug cost; DW, Durbin-Watson *d* statistic.			

As for the change of expenditures, bid-winning products increased significantly (48.95 million CNY, 95% *CI* = 10.10 to 87.79, *p*-value < 0.05) and non-winning products dropped significantly (-718.89 million CNY, 95% *CI*= -848.58 to -589.20, *p*-value < 0.001) after "4 + 7" policy. As a results, the expenditures of "4 + 7" List drugs significantly decreased (-671.31 million CNY, 95% *CI*= -833.36 to -509.27, *p*-value < 0.001). The change of expenditures for alternative drugs showed no statistical difference (*p*-value > 0.05). The expenditures of the overall policy-related drugs significantly decreased (-634.68 million CNY, 95% *CI*= -945.85 to -323.51, *p*-value < 0.001).

In terms of the change of DDDc, bid-winning products significantly decreased (-6.35 CNY, 95% *CI* =-6.75 to -5.96, *p*-value < 0.0001) and non-winning products significantly increased (0.94 CNY, 95% *CI* = 0.59 to 1.29, *p*-value < 0.0001) after "4 + 7" policy. The DDDc of "4 + 7" List drugs significantly declined (-3.10 CNY, 95% *CI*= -3.40 to -2.80, *p*-value < 0.0001) while the change of alternative drugs showed no statistical significance (*p*-value > 0.05). after policy intervention, the overall DDDc of policy-related drugs significantly decreased (-1.38 CNY, 95% *CI*= -1.49 to -1.26, *p*-value < 0.001). See **APPENDIX B**.

Discussion

This study found that, after the policy was implemented for 9 months, the overall purchase volume of bid-winning drugs in the 9 pilot cities has reached up to 154.40% of the initially committed annual procurement volume. This is in accordance with the implementation progress of 183% in 11 pilot cities announced by the NHSA in December 2019 [36]. In this study, all of the 9 pilot cities completed the overall agreed procurement volume ahead of schedule, among whom Xi'an (17.7 times) and Chongqing (11.4 times) observed the fastest progress. However, the completion rate of 25 bid-winning drugs varied greatly, ranging from 75–478%. Findings in this study are in line with previous studies regarding the implementation progress of "4 + 7" policy reported in Shenzhen [22], Shenyang [21], and Chongqing [20]. Nevertheless, it is reported that some medical institutions may incline to under-report the amount of agreed procurement volume for the sake of meeting their goals of policy assessment [37]. Therefore, there may exist disparities between the reported agreed procurement volume and medical institutions' actual demands under NCDP policy, leading to a general high completion rate of the procurement of bid-winning drugs. In view of this, a standardized reporting mechanism should be established across different centralized procurement entities with refined procurement volume estimation tools, so as to further facilitate policy evaluation.

Results of this study underscored a remarkable impact of “4 + 7” policy on purchase expenditures of “4 + 7” List drugs in pilot cities, leading to a significant drop of 5.76 billion CNY (43.30%) compared to that in the pre-“4 + 7” policy period. Apart from this, when involved alternative drugs that have a substitution relationship with “4 + 7” List drugs in clinical use, the purchase expenditures of the overall policy-related drugs also largely decreased by 3.6 billion CNY (15.76%). The encouraging impact of “4 + 7” policy on drug cost mitigation found in this study is consistent with findings in a copious amount of literature [38, 13, 39, 6].

This study highlighted a stimulating impact of the “4 + 7” policy on the increased consumption/factual use of the 25 bid-winning drugs, yielding an overall increment of 549.66% in DDDs and 545.18% in DID. In some drugs, this figure even went up to 100-folds of their baseline value. The use proportion of bid-winning products has increased from 12.67–71.66%. The bid-winning drugs in “4 + 7” policy are all original-branded drugs or generic drugs that have passed the consistency evaluation, thus the increase in their consumption is conducive to the improvement of the overall quality level of drug use in China [13, 40, 36]. Under the consumption change of policy-related drugs, it is of paramount importance to strengthen the continuous monitoring of safety and effectiveness of the bid-winning drugs, as well as to carry out comprehensive clinical evaluation and re-evaluation of related drugs with real-world evidence.

In this study, we discovered that the consumption and costs of alternative drugs slightly increased, in consistent with Chen et al.’s [41] report in Shenzhen, China. In China’s contemporary medicine environment, there is a lack of motivation in public medical institutions to proactively reduce the adoption of other high-priced drugs. Following the implementation of “4 + 7” policy, there exists a negative impact on the increase in the use of non-centralized purchased drugs, which, to a degree, diminishes the welfare of the policy to the general public [37]. Yang et al. [42] reported a significant increase in overall consumption of policy-related antibiotic drugs after the implementation of “4 + 7” policy, suggesting that the risk of overuse of antibiotic drugs may increased after policy intervention. Therefore, in order to avoid such negative impacts, it is recommended to further expand the drug scope of NCDP policy and include more drugs that commonly used.

One of the goals of NCDP policy is to reduce the transaction costs of pharmaceutical companies and promote the healthy development of the pharmaceutical industry [9]. In this study, we found that the purchase expenditures of bid-winning drugs increased from 1.92 to 2.66 billion CNY (38.79% increase), and the expenditure proportion of bid-winning drugs also increased from 14.40–35.26%. This shows that “4 + 7” policy stimulated the market share of winning bidders. Moreover, most of the bid-winning drugs come from domestic pharmaceutical enterprises, indicating that the policy might be conducive to facilitate the expansion and prosperity of domestic generic drug production and distribution. Besides, we found that the purchase volume and expenditures of non-winning drugs significantly declined, corresponding to a decrease of 62.74% and 57.12%. This implicates that the market of non-winning companies has been greatly crushed, which may urge the increasing number of pharmaceutical companies to actively engage in the consistency evaluation work of generic drugs for the seek of opportunity to participate in the coming rounds of NCDP policy.

Nonetheless, the study also found that the DDDc of non-winning drugs markedly increased. This phenomenon could be partly attributed to the companies’ price-adjustment strategies that cause a rise in price for some drugs, or the sales-adjustment initiatives that lead to an increase in the proportion of high-priced drugs used in the medical institutions. In view of this, it is essential to promote relevant supporting reform measures, including a proactive exploration of a unified, scientific medical insurance payment standard, to ensure the provision of universally accessible and affordable healthcare services and drugs, as well as the establishment of equitable yet motivating incentive mechanisms in medical institutions [9].

Several potential limitations should be mentioned regarding the present study. First, “4 + 7” policy was implemented in 11 pilot cities, while this study only included 9 pilot cities for analysis due to the incomplete data of two pilot cities (Guangzhou and Shenzhen) in the CDSIP database. Besides, this study used data from January 2018 to December 2019, while the policy implementation was less than one complete procurement cycle during this period. Thus, in terms of the sample cities and the study periods, this study failed to conduct a comprehensive assessment of the final effect of the policy. Second, in terms of evaluating policy effect, the two groups of ITS has more advantages than the single group ITS by setting a control group. However, we failed to set a control group, thus it is difficult to observe and control the potential confounding factors that may affect the results. Third, the results of this study were based on drug purchase data, rather than drug use data (such as prescriptions). Although there is strong consistency between purchase data and use data under a series of policies. However, there is still a possibility that the two data sources may not exactly match, so there are certain limitations. Despite the aforementioned limitations, this study is the first of its kind in adopting nation-

wide authoritative data to conduct a thorough empirical evaluation of the “4 + 7” policy in the 9 pilot cities. The results of this study will provide a valuable empirical reference for subsequent policy adjustments and improvements.

Conclusion

This study assessed the implementation effect of “4 + 7” policy in 9 pilot cities in mainland China. An overall satisfying effect was observed for the agreed procurement volume of each drug was generally completed beyond expectations. “4 + 7” policy has played a chief role in alleviating medication burdens of patients, which is supported by the remarkable reduction in DDDc and expenditures of policy-related drugs. After policy intervention, the accessibility and consumption of policy-related drugs improved. However, the noticeable increase in the DDDc of non-winning drugs, as well as the slightly increased consumption of alternative drugs indicated the necessity and importance of policy monitoring regarding the clinical use of policy-related drugs in the future.

Abbreviations

CNY: Chinese Yuan; OECD: Organization for Economic Co-operation and Development; PRC: People's Republic of China; NCDP: National Centralized Drug Procurement; NHSA: National Healthcare Security Administration; CDSIP: China Drug Supply Information Platform; YPID: Yao Pin Identifier; DDD: Defined Daily Dose; DDDc: Defined Daily Drug cost; DID: DDDs per 1000 inhabitants per day; ITS: Interrupted Time Series.

Declarations

Ethics approval and consent to participate

The study was considered not human subjects research by the Institutional Review Board of Wuhan University. No informed consent was required for this study did not involving humans or animals.

Consent for publication

Not applicable.

Availability of data and materials

The data used in this study is not publicly available. The dataset (CDSIP database) used and analyzed during the current study is available from the corresponding author on reasonable request. In this study, no additional data is used.

Conflicting interests

The authors declared no conflict of interest.

Funding

This research was funded by the National Health Commission of the People's Republic of China Project (Grant No. 09202004); The funder had no role in the question design, analysis or interpretation.

Author’s contributions

Conceptualization, JCL, ZFM, and JHL; methodology, YY, XTW, DC, and ZFM; validation, JCL, ZFM, and JHL; formal analysis, YY, XTW, and LNM; investigation, YY, XTW, and LNM; data curation, JCL, JW, and YS; writing — original draft preparation, JCL, YY, XTW, LNM and DC; writing — review and editing, JW, YS, DC, ZFM, JHL; supervision and funding acquisition, ZFM and JHL; All authors have read and agreed to the published version of the manuscript.

Acknowledgements

The authors wish to acknowledge Prof. Lu Xiao (Science and Technology Development Center, Chinese Pharmaceutical Association), Prof. Wanyu Feng (Department of Pharmacy, Peking University People’s Hospital), and Prof. Li Yang (School of Public Health, Peking University), for their help in study design.

Authors’ information

[1]School of Public Health, Jilin University, Changchun 130021, China. [2]Editorial Department of China Health Human Resources, Beijing 100032, China. [3]Department of Drug Information Management, Statistical Information Center, National Health Commission of

the People's Republic of China, Beijing 100044, China. [4]School of Health Sciences, Wuhan University, Wuhan 430071, China. [5]Global Health Institute, Wuhan University, Wuhan 430072, China.

References

1 Parkinson B, Sermet C, Clement F, Crausaz S, Godman B, Garner S et al. Disinvestment and Value-Based Purchasing Strategies for Pharmaceuticals: An International Review. PHARMACOECONOMICS. 2015;33(9):905-24. doi:10.1007/s40273-015-0293-8.

2 Smith C. Retail Prescription Drug Spending In The National Health Accounts. HEALTH AFFAIR. 2004;23(1):160-7. doi:10.1377/hlthaff.23.1.160.

3 The IQVIA Institute. Global Medicine Spending and Usage Trends Outlook to 2024. 2020.https://www.iqvia.com/insights/the-iqvia-institute/reports/global-medicine-spending-and-usage-trends.

4 The Central People's Government of the People's Republic of China. 2019 Statistical Bulletin of China's Health Development. 2020.http://www.gov.cn/guoqing/2021-04/09/content_5598657.htm.

5 National Health Development Research Center of the National Health Commission. 2018 China Total Health Expenditure Research Report. Beijing: Institute of health and economy press; 2018.

6 Mao Z, Yang Y, Chen L. Reform of Drug Supply and Guarantee System in China: Policy Measures and Effects. In: Wang C, Liang W, "editors'. Development Report on Health Reform in China (2020): Beijing: Social Sciences Academic Press; 2020. p. 96-123.

7 Dylst P, Vulto A, Simoens S. Tendering for outpatient prescription pharmaceuticals: what can be learned from current practices in Europe? HEALTH POLICY. 2011;101(2):146-52. doi:10.1016/j.healthpol.2011.03.004.

8 Seidman G, Atun R. Do changes to supply chains and procurement processes yield cost savings and improve availability of pharmaceuticals, vaccines or health products? A systematic review of evidence from low-income and middle-income countries. BMJ Glob Health. 2017;2(2):e243. doi:10.1136/bmjgh-2016-000243.

9 General Office of the State Council of the People's Republic of China. Pilot Program for National Centralized Drug Procurement and Use. 2019.http://www.gov.cn/zhengce/content/2019-01/17/content_5358604.htm.

10 Joint Procurement Office. 4+7 City Drug Centralized Procurement Documents (No. GY-YD2018-1). 2018.http://www.smpaa.cn/gjsdcg/2018/11/15/8511.shtml.

11 Joint Procurement Office. The results of 4+7 city drug centralized procurement. 2018.http://www.smpaa.cn/gjsdcg/2018/12/07/8531.shtml.

12 , National Healthcare Security Administration. Letter from the National Health Security Administration on the Reply to Proposal No. 4733 (Economic Development No. 260) of the Third Meeting of the Thirteenth National Committee of the Chinese People's Political Consultative Conference. 2020.http://www.nhsa.gov.cn/art/2020/12/23/art_26_4167.html.

13 Zhang M. Trends in the development of centralized drug procurement in China. The 5th Wuhan University Luojia Cherry Blossom Forum2021.

14 Huang X, Li C, Pan Z. Analysis on the Effect of Drug Centralized Procurement Organized by the State in A Tertiary-grade Class A Hospital. Pharmacy Today. 2020;30(12):854-7. doi:10.12048/j.issn.1674-229X.2020.12.015.

15 Zou G, Zhao J, Mei Q, Ye H, Zhou H, Zhu X et al. Analysis of Application of Original Drugs and Generic Drugs after the Implementation of "4+7 Cities" Group Procurement of Drugs in Guangdong Second Provincial Central Hospital. Evaluation and analysis of drug-use in hospitals of China. 2020;20(07):854-8. doi:10.14009/j.issn.1672-2124.2020.07.022.

16 Chen H, Liu Y, Yu X, Zhang D, Zhou H, Feng W et al. Data Analysis on Pilot Reform of Drug Centralized Procurement and Use—Taking Beijing Chaoyang Hospital as an Example. China Health Insurance. 2019(08):51-3. doi:10.19546/j.issn.1674-3830.2019.8.012.

17 Wang Q, Liu D, Yuan W, Huang J, Wang Q, Zhang R. An Annual Effect Analysis on the First Batch of Pilot Project of National Organized Centralized Drug Procurement and Application in A Certain Grade Level A General Hospital in Chongqing. Evaluation and analysis of drug-use in hospitals of China. 2021;21(02):237-9. doi:10.14009/j.issn.1672-2124.2021.02.026.

18 Xu X, Tang J, Zhang X, Zhang T. Analysis on the Influencing Factors of Patients Using National Centralized Purchasing Drugs—Taking a Tertiary Hospital in Beijing as an Example. China Health Insurance. 2020(07):61-4. doi:10.19546/j.issn.1674-3830.2020.7.013.

19 Chen J, Tian Y, Shi LW. The Impact of Generic Drug Entry on Market Shares and Prices of Brand-Name Drugs– Evidence from Chinese Pharmaceutical Market. VALUE HEALTH. 2018;21:S9. doi:https://doi.org/10.1016/j.jval.2018.07.065.

20 Mu A. Preliminary Analysis on the Pilot Project of Drug Centralized Procurement and Use in Chongqing. China Health Insurance. 2019(08):24-7. doi:10.19546/j.issn.1674-3830.2019.8.006.

21 Meng L. Analysis on the Pilot Operation of Drug Centralized Procurement and Use in Shenyang. China Health Insurance. 2019(08):28-31. doi:10.19546/j.issn.1674-3830.2019.8.007.

22 Shenzhen Healthcare Security Bureau. Pilot Analysis on Drug Centralized Procurement and Use Organized by the State in Shenzhen. China Health Insurance. 2019(08):32-7. doi:10.19546/j.issn.1674-3830.2019.8.008.

23 Cao G, Li P, Wang Y, Liu Y, Guo Z. Analysis of the first quantity purchase of antihypertensive drugs in our hospital. Chinese Community Doctors. 2021;37(03):14-6. doi:10.3969/j.issn.1007-614x.2021.03.006.

24 Li Q, Liu Y, Zhuo S. A Hospital's "4+7" Drug Quantity Procurement Model. China Health Standard Management. 2020;11(23):41-3. doi:10.3969/j.issn.1674-9316.2020.23.014.

25 Wang H, Li X, Chen J. Impact of "4+7" City Drug Centralized Procurement Program on the utilization of original and generic cardiovascular drugs in a tertiary hospital. Journal of Pharmaceutical Practice. 2020;38(04):373-8. doi:10.12206/j.issn.1006-0111.202001054.

26 Yang Q, Guo W, Liu S. Effects of procuring with target quantity on using antipsychotics at a hospital. Chinese Journal of Hospital Pharmacy. 2020:1-6. doi:10.13286/j.1001-5213.2021.04.13.

27 Tang Y, Chen J, Li X. Utilization Analysis of the Original and Generic Drugs for Hypertension and Diabetes in a Tertiary Public Hospital in Jiangsu Province. China Pharmacy. 2019;30(21):2890-4. doi:10.6039/j.issn.1001-0408.2019.21.03.

28 Wang J, Yang Y, Xu L, Shen Y, Wen X, Mao L et al. The impact of National Centralized Drug Procurement policy on the use of policy-related original and generic drugs in public medical institutions in China: A difference-in-difference analysis based on national database. medRxiv 2021.06.21.21256568. 2021. doi:https://doi.org/10.1101/2021.06.21.21256568.

29 Wang Y, Wu Z. Keypoint Analysis of Monitoring Plan for Centralized Drug Purchase and Use Project Pilot Launched Organized by State. China Pharmacy. 2019;30(17):2317-22. doi:10.6039/j.issn.1001-0408.2019.17.03.

30 WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2021. 2021.https://www.whocc.no/atc_ddd_index/.

31 WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2021, Norway. 2021.http://www.whocc.no.

32 Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J CLIN PHARM THER. 2002;27(4):299-309. doi:10.1046/j.1365-2710.2002.00430.x.

33 Jandoc R, Burden AM, Mamdani M, Lévesque LE, Cadarette SM. Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. J CLIN EPIDEMIOL. 2015;68(8):950-6. doi:10.1016/j.jclinepi.2014.12.018.

34 Lagarde M. How to do (or not to do) ... Assessing the impact of a policy change with routine longitudinal data. HEALTH POLICY PLANN. 2011;27(1):76-83. doi:10.1093/heapol/czr004.

35 Zhang F, Wagner AK, Soumerai SB, Ross-Degnan D. Methods for estimating confidence intervals in interrupted time series analyses of health interventions. J CLIN EPIDEMIOL. 2009;62(2):143-8. doi:10.1016/j.jclinepi.2008.08.007.

36 National Healthcare Security Administration of the People's Republic of China. Answer to Reporters' Request about the Second Round of National Centralized Drug Procurement and Use. 2020.http://www.nhsa.gov.cn/art/2020/1/17/art_38_2264.html.

37 Yu C. The practical effects and system concerns of "4+7" drug procurement. Journal of Southwest Minzu University (Humanities and Social Science). 2020;41(04):34-9

38 An Y, Tang J, Mao C, Ai C. Pharmacoeconomic evaluation on the influence of national centralized drug procurement on medical insurance patients. Clinical Medication Journal. 2020;18(11):10-3. doi:10.3969/j.issn.1672-3384.2020.11.003.

39 Hu S. The Health Economics Theoretical Basis and Improvement Suggestions for the National Centralized Drug Procurement. Chinese Health Resources. 2021:1-4. doi:10.13688/j.cnki.chr.2021.200942.

40 The Central People's Government of the People's Republic of China. China's centralized drug procurement is steadily advancing. 2020.http://www.gov.cn/xinwen/2020-10/14/content_5551115.htm.

41 Chen L, Yang Y, Luo M, Hu B, Yin S, Mao Z. The Impacts of National Centralized Drug Procurement Policy on Drug Utilization and Drug Expenditures: The Case of Shenzhen, China. Int J Environ Res Public Health. 2020;17(24). doi:10.3390/ijerph17249415.

42 Yang Y, Chen L, Ke X, Mao Z, Zheng B. The impacts of Chinese drug volume-based procurement policy on the use of policy-related antibiotic drugs in Shenzhen, 2018-2019: an interrupted time-series analysis. BMC HEALTH SERV RES. 2021;21(1):668. doi:10.1186/s12913-021-06698-5.

43 He J, Tang M, Cong L, Xu Y, Song J, Chen M et al. The impact of National Centralized Drug Procurement on the clinical management and drug use. Chinese Health Resources. 2021:1-3. doi:10.13688/j.cnki.chr.2021.200802.

Figures

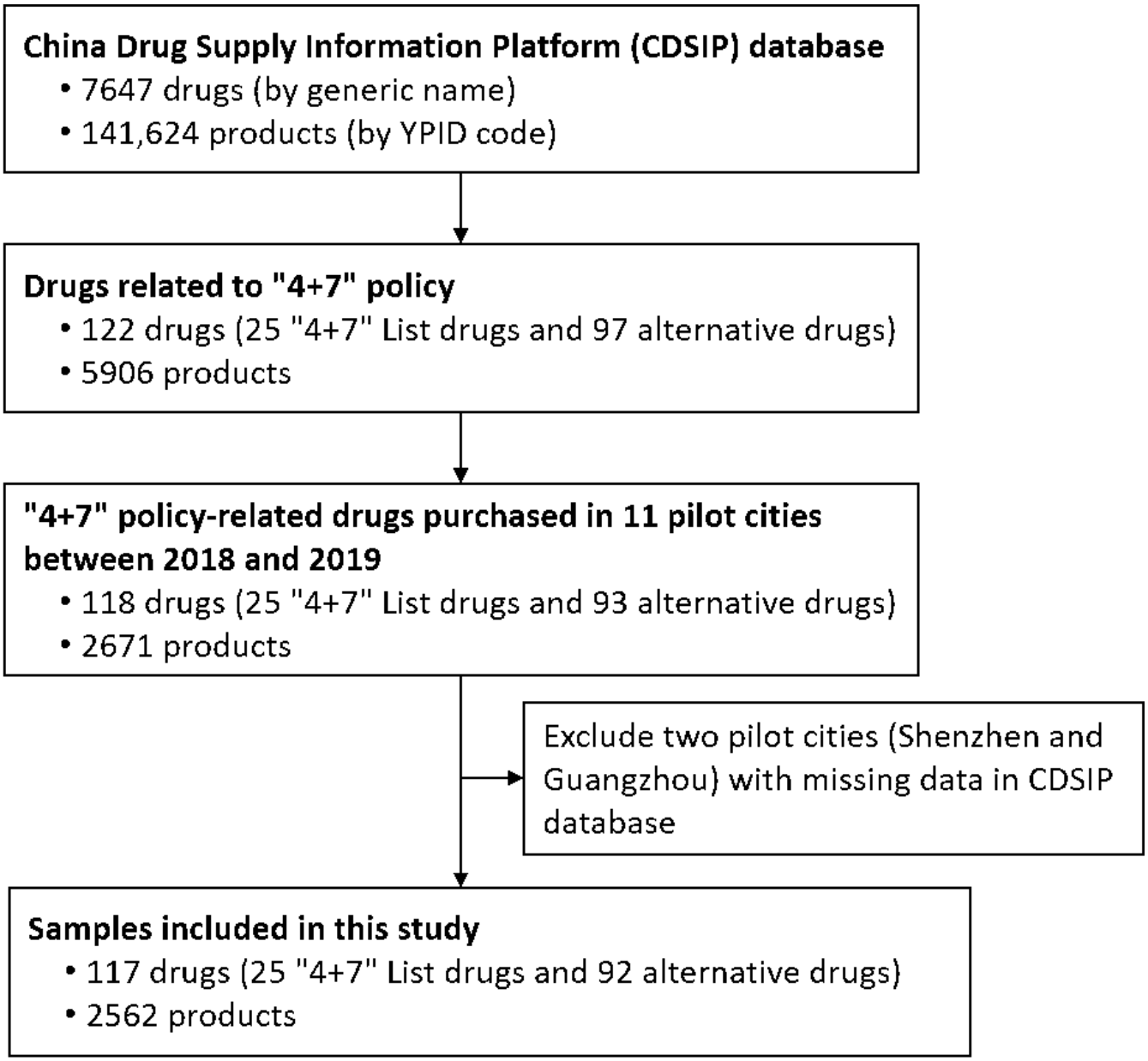

Figure 1

Flow chart of sample screening.

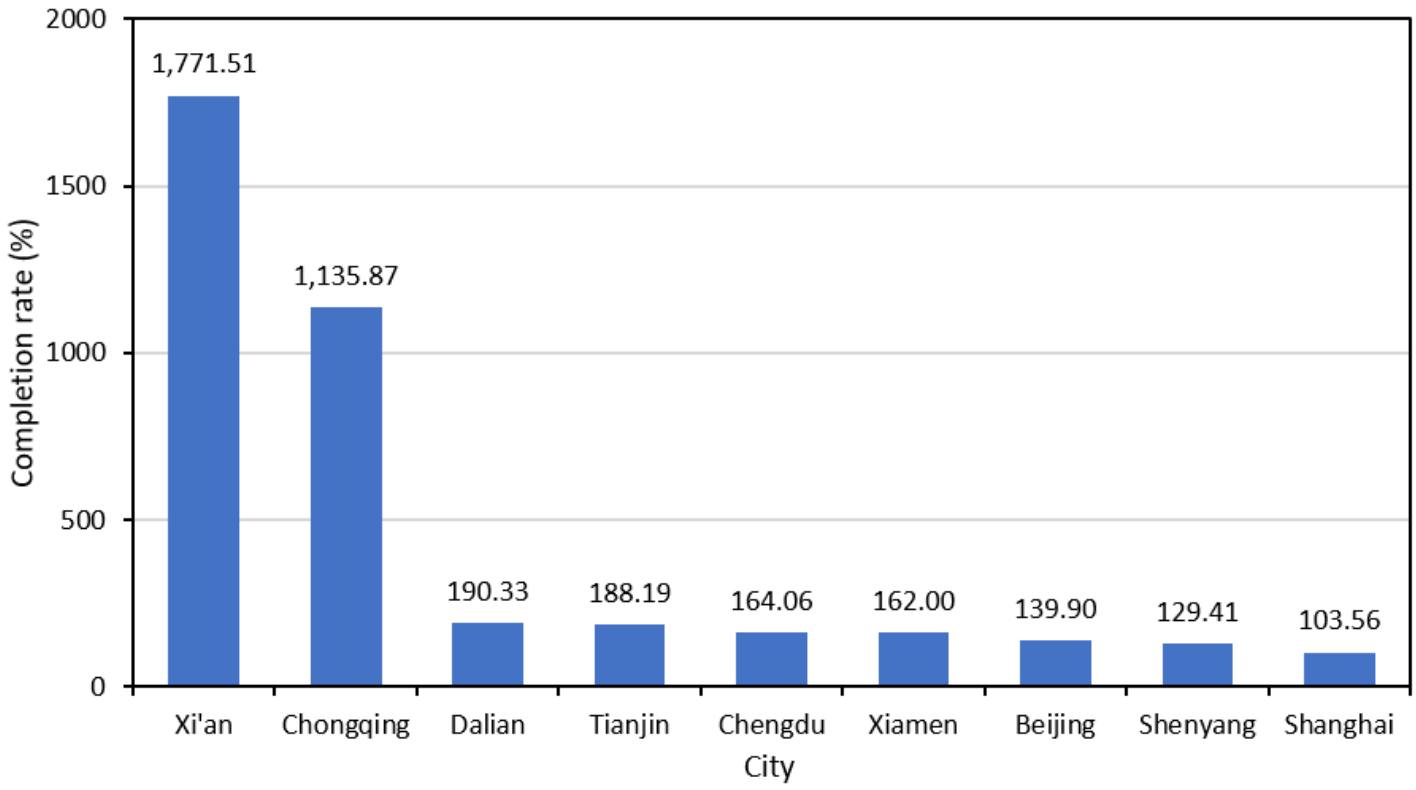

Figure 2

Completion rate of the agreed purchase volume of bid-winning products in each pilot city during April to December 2019.

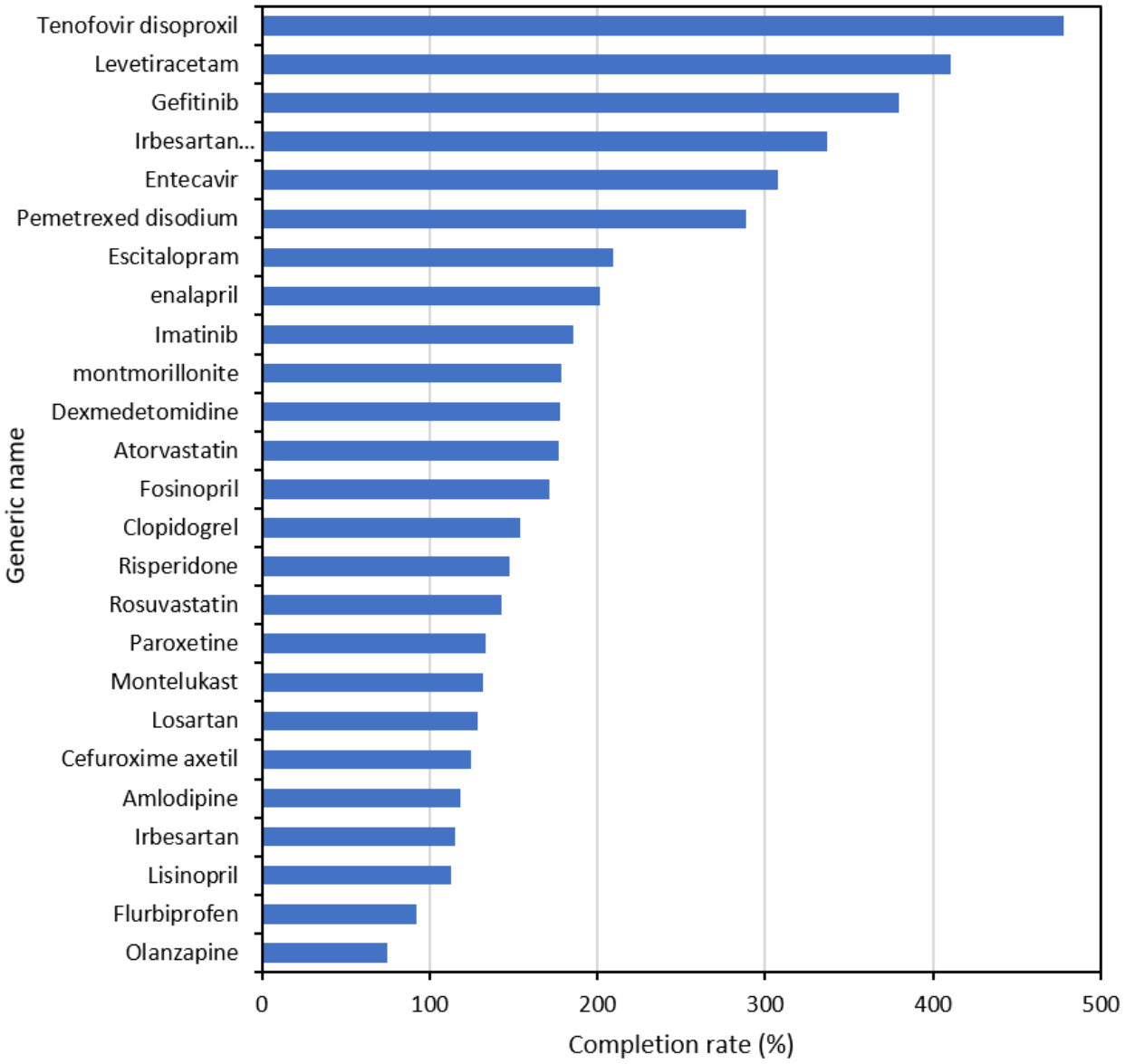

Figure 3

Completion rate of the agreed purchase volume of each bid-winning product in 9 pilot cities during April to December 2019.

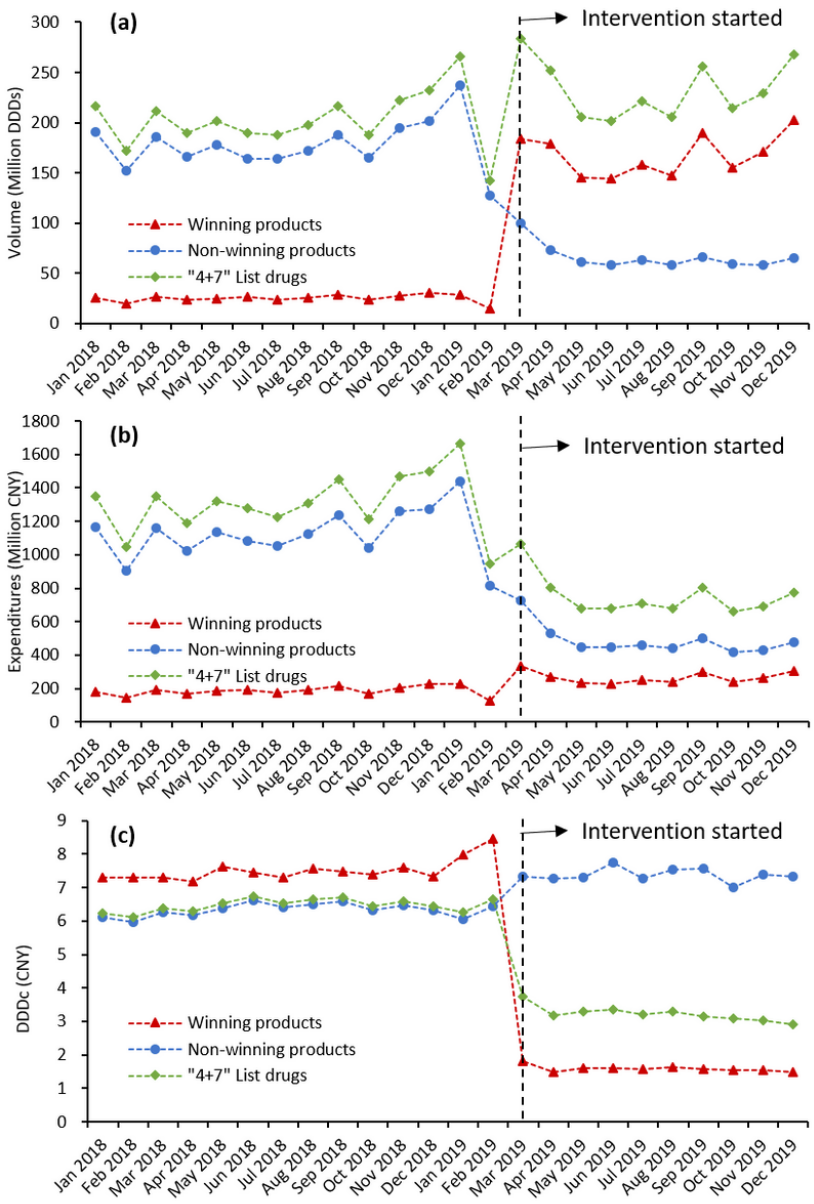

Figure 4

The procurement of “4+7” List drugs from January 2018 to December 2019: (a) purchase volume, (b) purchase expenditures, (c) DDDc. Note. DDDs, defined daily doses; CNY, Chinese Yuan; DDDc, defined daily drug cost.

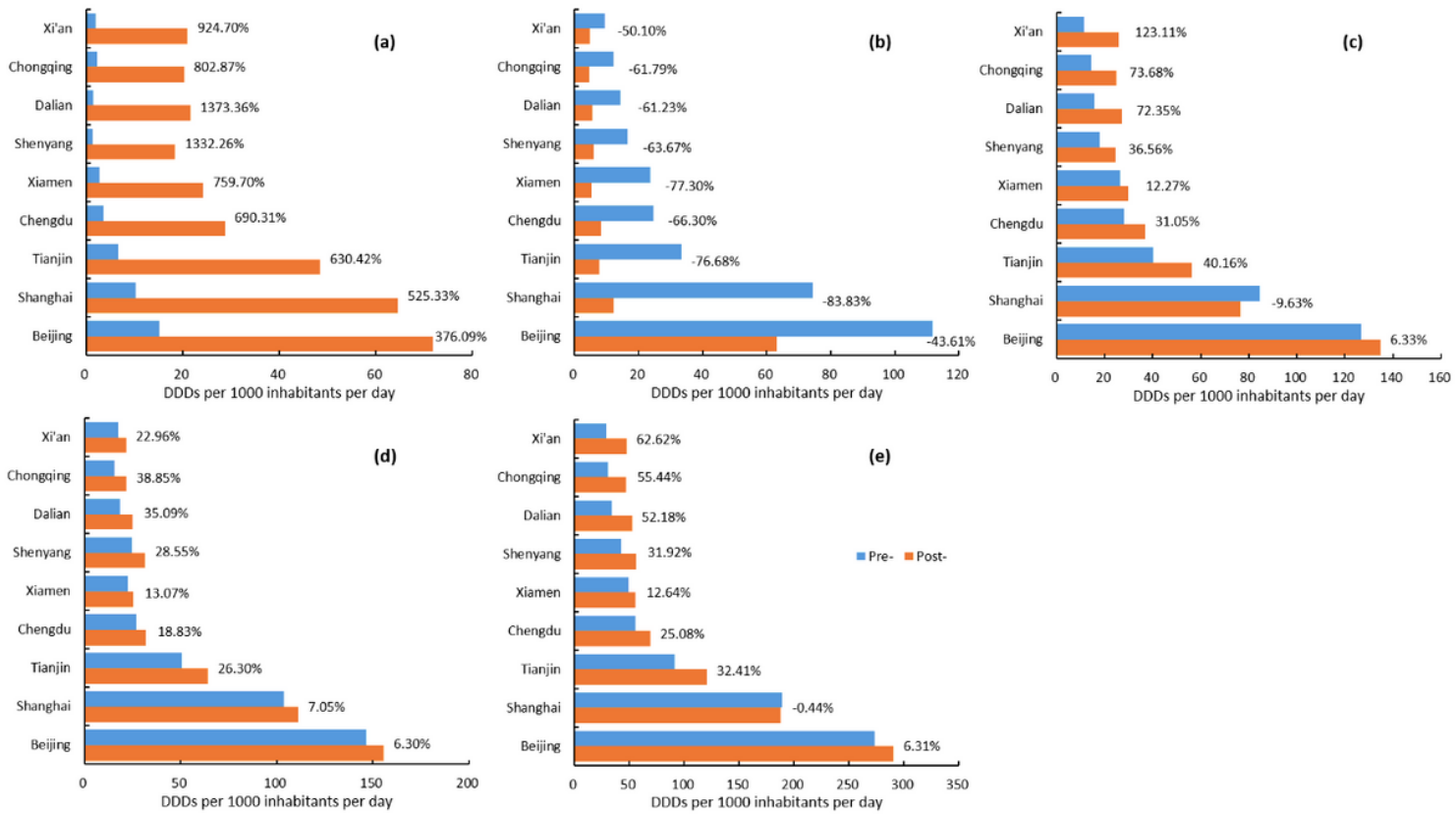

Figure 5

The consumption of policy-related drugs in the pre- and post-“4+7” policy periods: (a) bid-winning drugs, (b) non-winning drugs, (c) “4+7” List drugs, (d) alternative drugs, (e) overall policy-related drugs. Note. DDDs, defined daily doses; Pre- refers to March to December 2018; Post- refers to March to December 2019.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 0810supplementaryfile.docx