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Impact of '4+7' volume-based drug procurement on the use of policy-related original and generic drugs: a natural experimental study in China

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ABSTRACT

Objective To evaluate the impact of the first round of the National Centralized Drug Procurement pilot (so-called '4+7' policy) on the use of policy-related original and generic drugs.

Methods A retrospective natural experimental design was adopted. Drug procurement data from the China Drug Supply Information Platform database were used, involving 9 '4+7' pilot cities in intervention group and 12 non-pilot provinces in control group. '4+7' policy-related drugs were selected as study samples, including 25 drugs in the '4+7' procurement list and their alternative drugs that have not yet been covered by the policy. '4+7' List drugs were divided into bid-winning and non-winning products according to the bidding results. Included drugs were sorted into original and generic products. Difference-in-difference method was employed to estimate the net effect of policy impact.

Results After policy intervention, the DDDs (defined daily doses) of '4+7' List original drugs significantly reduced (β=−39.10, p<0.001), while generic drugs increased (β=40.43, p<0.01). 17.08% of the original drugs in DDDs were substituted by generic drugs. Prominent reduction was observed in the monthly expenditure of '4+7' List drugs (¥726.40 million) and overall policy-related drugs (¥654.47 million). The defined daily drug cost (DDDc) of bid-winning original and generic drugs, as well as non-winning original drugs, decreased by 44.44%, 79.00% and 15.10% (all p<0.01), while the DDDc of non-winning generic drugs increased by 64.81% (p<0.001). The use proportion of higher-quality drugs raised prominently from 39.66% to 91.93%.

Conclusions '4+7' policy is conducive to generic substitution, drug price reduction and pharmaceutical cost-containment in China. The overall quality level of drug use of the Chinese population increased after policy intervention, especially in primary healthcare settings. However, the increased DDDc of non-winning generic drugs and alternative drugs should draw the importance of further policy monitoring.

Strengths and limitations of this study

- ► The '4+7' policy is the first policy attempt of volume-based drug procurement work at the national level in China, and is a pioneering work in the reform of Drug Supply and Guarantee System in China. This study aimed to explored the effect of this policy on original and generic drug use in China.
- ► This study used data of a national database—the China Drug Supply Information Platform. The monthly drug purchase data of 9 pilot cities and 12 non-pilot provinces in mainland China were analysed.
- ► This study adopted a natural experimental design with difference-in-difference method to evaluate the policy effect.
- ► The findings based on drug purchase data rather than drug use data in the present study might limit the interpretation and extrapolation of research results.

INTRODUCTION

In China, rising pharmaceutical expenditure has attracted a great deal of policy attention over the past decade. The costs of drugs accounted for 30%–40% of the nation's total health expenditures in 2018,[1] and this figure is much higher than the Organization for Economic Cooperation and Development countries' average (16%).[2] Causes were attributed to the absence of effective pricing strategies and distorted financial incentives by healthcare providers in overprescribing high-priced drugs.[3 4]

In the past three decades, tides of pharmaceutical policies had been implemented in China, with limited evidence for their success.[3 5] Since the early 1990s, the Chinese government implemented the price cap policy, and over 30 mandatory regulations were announced that directly set the price ceiling for each individual brand of drug.[6] These efforts seemed not as effective as anticipated, which might be attributed to the government's inability to measure real manufacturing costs, or to healthcare providers' reliance on the 15% markups from drug sales.[3 6] Eventually, the National Development

and Reform Commission (NDRC) abolished the price cap policy in 2015. Since 2009, centralised tendering and procurement of drugs became the nationwide province-based governmental practice, which started with Essential Medicine List drugs for primary care and gradually extended to the procurement of all drugs for public hospitals. Concurrently, a zero markup drug policy was gradually put forward to regulate retail prices, where all public hospitals were prohibited to add additional retail markups from the procuring price, which used to be officially set as 15%. Despite the overall drop in prices under the provincial centralised procurement practices, the procurement system was criticised for its lack of capacity to link price with volumes of purchased drugs.[7 8]

China has a complex and dynamic pharmaceutical system undergoing significant reforms as part of a broader effort to improve healthcare. After years of reforms attempting to lower drug prices, a novel pooled procurement, the National Centralized Drug Procurement (NCDP) policy, was launched in November 2018 with the primary aim of reducing drug prices and improving the affordability of effective and safe medicines.[9] The first round of the NCDP pilot was implemented in four municipalities (Beijing, Tianjin, Shanghai and Chongqing) and seven subprovincial cities (Shenyang, Dalian, Xiamen, Guangzhou, Shenzhen, Chengdu and Xi'an) in mainland China, thus known as the '4+7' policy. Unlike previous procurement pilots, the NCDP policy, organised by the central government, received an unprecedented high political commitment. The highlight of this policy lies in the implementation of 'volume-based procurement'. Volume-based drug procurement, also known as 'group purchasing', by integrating the procurement needs of all pilot cities, enhanced the negotiation power of hospitals and payers to maximise the price reduction of drugs.[10] Volume–price linkage was achieved under this procurement mechanism.[11]

In the NCDP policy, only generic drugs that had previously passed the Generic Consistency Evaluation (GCE) and original branded drugs were eligible to be listed for procurement.[9] Historically, in China, generic drugs were needed only for demonstrating comparable quality with the other marketed generic drugs, and the interchangeability between generic and brand-name drugs was unknown.[10 12] Since 2012, the GCE work was conducted and promoted by the National Medical Products Administration (NMPA) to ensure that generic drugs became equivalent to their corresponding original brand-name drugs,[13 14] and has made great strides.[15] The NMPA required that the 90% CI of the geometric mean ratio for main pharmacokinetic parameters, the peak concentration and the area under concentration time curve of the product fall entirely within the range of 80.00%–125.00% in order to be bioequivalent.[16] Under the GCE's criterion of 'essential similarity' in this policy, however, generic drugs became equivalent to their corresponding original drugs, thus original drugs as well as generic drugs certified by GCE are considered to be of higher quality when compared with generic drugs that did not pass the GCE. In the policy, unique measures, such as 'ensuring drug quality', 'achieving volume–price linkage' and 'encouraging generic substitution and rational use', were applied to achieve price cuts and improve medicine affordability with higher quality.[9–11] Twenty-five drugs in the '4+7' procurement list were successfully purchased with an average price reduction of 52%, of which 22 were generic drugs that passed the GCE and 3 were original drugs.[17]

Worldwide, tendering for off-patent medicines and promoting generic substitution are effective ways to enhance market competition, which contribute to drug cost-containment.[18 19] According to Cameron *et al*'s statistics,[20] due to the large volumes of medications consumed in public hospitals and a substantial price differential between the originator brand and lowest-priced generic products, US$370 million could be saved by switching only four drugs, saving patients an average of 65%. In China, previous studies made explorations regarding the impact of the '4+7' policy on generic substitution and the consumption of generic and original drugs. Qu *et al*[12] reported that Chinese pharmacists had a fairly good knowledge of generic drugs used in the '4+7' policy and generally have positive attitudes towards generic substitution. Wang *et al*[21] found that the price ratio of generic drugs against brand-name drugs dropped from 0.87 to 0.39 after the '4+7' policy intervention. Several relevant studies consistently reported the effect of the '4+7' policy on promoting generic substitution, and the consumption proportion of generic drugs improved after the policy intervention.[21–24] Empirical studies also reported inconsistent findings. For example, Yang *et al*[25] found that, after the '4+7' policy, the quantity and expenditures of generic products consumed in the antipsychotics had little change (less that 5%); Xie *et al*[26] reported that the generic substitution rate of some drug substances decreased after the intervention. Empirical studies confirmed the effect of the '4+7' policy on promoting the consumption of bid-winning generic drugs; however, the representativeness of relevant evidence might be insufficient, due to the small sample size and the descriptive methods. Besides, several issues were still unclear regarding the implementation of the '4+7' policy, for example, the use of original and generic drugs in different healthcare settings, the utilisation of policy-uncovered drugs, and the potential impacts on drug quality level and medication burden. Thus, we conducted this natural experimental study to quantitatively evaluate the impact of the '4+7' policy on the use of policy-related original and generic drugs in China's public medical institutions.

METHODS

Study design and data sources

This study adopted a natural experimental design with the difference-in-difference (DID) approach, given that the first round of NCDP pilot, that is, '4+7' policy, was only implemented in 11 pilot cities in mainland China. The

'4+7' policy was initially implemented in 11 pilot cities from 9 provinces, after that, 2 provinces spontaneously followed the bidding results and joined the '4+7' volume-based procurement in May 2019 (Fujian province) and July 2019 (Hebei province). To perform the DID, we assigned '4+7' pilot cities as the policy intervention object (pilot group), and set the provinces in mainland China that were not covered by the '4+7' policy but also did not spontaneously follow and implement the '4+7' bidding results as the control group. We set up the timing of the policy initiation to March 2019, when the '4+7' policy started in 11 pilot cities. Under the '4+7' policy rules, all public medical institutions in pilot cities should participate in volume-based procurement while private medical institutions can participate voluntarily; thus, this study compared the procurement records of public medical institutions in the two groups before and after the policy intervention.

Data used in this study were obtained from the China Drug Supply Information Platform (CDSIP),[27] which is a comprehensive information platform for national drug procurement data. The CDSIP was constructed and operated by the National Health Commission of the People's Republic of China, and was officially launched on 22 October 2015. The CDSIP covered drug procurement order data of all provincial drug-centralised procurement platforms from 31 provinces (autonomous regions and municipalities) in mainland China. Since 2015, the Chinese government required that all public medical institutions purchase all drugs to be used through the provincial-level drug-centralised procurement platform,[28] which to a great extent ensured the integrity and accuracy of the CDSIP procurement data. In the CDSIP database, each drug procurement order record included the name of medical institution, purchase date, drug 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.

Sample selection

We extracted procurement data from the CDSIP database with the following criteria:

a. The drug scope: the '4+7' policy-related drugs were selected as the study sample,[11 29 30] which was defined as the 25 drug substances included in the '4+7' procurement list (ie, '4+7' List drugs) and their alternative drugs that have not yet been covered by the policy (online supplemental appendix A). This study followed the definition of alternative drugs by the National Healthcare Security Administration (NHSA),[31] which refers to the clinically substitutable drugs of the same kind with '4+7' List drugs. We extracted alternative drugs according to the 'reference range of substitutable drug substances of the bid-winning drugs' given in the *Monitoring Plan for the Pilot Work of National Centralized Drug Procurement and Use*.[31] The '4+7' List drugs were then divided into bid-winning products and non-winning products based on the '4+7' city procurement bid-winning results.[17] Bid-winning products refer to products that won the tender in the '4+7' policy, otherwise they were deemed to be non-winning products. Furthermore, included drugs were sorted into original branded products that have come off-patent (ie, original drugs) and generic products.
b. The time period: this study covered 23 months from January 2018 to November 2019.
c. The scope of regions: according to the criteria of the pilot group and control group mentioned above, this study included all the regions with complete procurement data in the CDSIP database during the study period. As a result, the pilot group involved 9 '4+7' pilot cities, including Beijing, Shanghai, Chongqing, Tianjin, Chengdu, Xi'an, Shenyang, Dalian and Xiamen; while the control group involved 12 provinces, including Hubei, Hunan, Guizhou, Inner Mongolia, Jilin, Heilongjiang, Anhui, Hainan, Gansu, Qinghai, Ningxia and Xinjiang.
d. The scope of medical institutions: this study included all the public medical institutions in the pilot group and the control group. Public medical institutions were then divided into tertiary hospitals, secondary hospitals and primary healthcare centres (PHCs).

Finally, a total of 116 policy-related drugs (by generic name) were included in this study, including 25 '4+7' List drugs and 91 alternative drugs. The flow chart of the sample selection process is shown in figure 1.

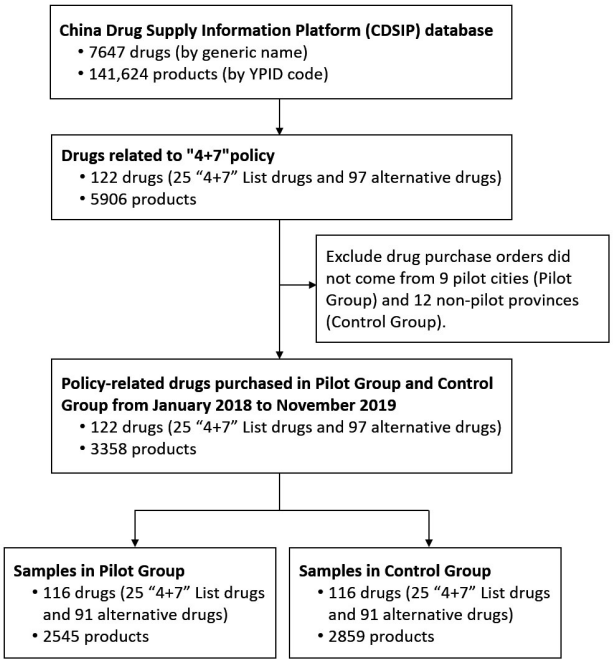

Figure 1 Flow chart of sample screening. YPID, Yao Pin Identifier.

Outcome variables

Three outcome variables were measured in this study: purchase volume, purchase expenditures and daily drug costs. Purchase expenditure data were reported

in Chinese yuan. Purchase volume was measured using defined daily dose (DDD), which is a measurement for comparing drug consumptions developed by the WHO Collaborating Centre for Drug Statistics Methodology.[32] In this study, the DDD value of each medication was determined according to the Guidelines for Anatomical Therapeutic Chemical (ATC) classification and DDD assignment 2021.[33] Daily costs of drugs were assessed by defined daily drug cost (DDDc), which was calculated by the ratio of expenditures and DDDs.

Statistical analysis

Descriptive statistics were used. We first described the change of purchase volume, purchase expenditures and DDDc of the included original and generic drugs in the corresponding period before (March–November 2018) and after (March–November 2019) the implementation of the '4+7' policy. Besides, we described the change of composition ratio between original and generic drugs in the volume and expenditures before and after the '4+7' policy.

This study employed the DID method. DID is a method commonly used for the quantitative effect evaluation of public policies or projects. By effectively combining 'the difference before and after intervention' with 'the difference with or without intervention', this method to a certain extent can control the influence of some factors other than intervention, so as to estimate the net impacts of the intervention on the outcome variable.[34–36] In this study, we constructed DID models by using the time series data in the pilot group and control group, to eliminate the net effect of the '4+7' policy on the use of original and generic drugs. The DID model is expressed as follows:

$$Y = \beta_0 + \beta_1 T_t + \beta_2 G_t + \beta_3 \left(T_t \times G_t\right) + \varepsilon_t$$

Where, Y refers to the outcome variables in this study. T_t refers to the '4+7' policy intervention with the values of 0 and 1, which 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). G_t represents groups with the values of 0 and 1, which 0 represents the control group and 1 represents the pilot group. ε_t is the error term, representing random errors that cannot be explained by variables in the model. β_0 represents the constant term. β_1 estimates the change of the outcome variable in the post-'4+7' policy period compared with the pre-'4+7' policy period. β_2 estimates the change of the outcome variable in the pilot group compared with the control group. β_3 is the interaction item between intervention measures and groups, which represents the net effect of the '4+7' policy. In this study, we observed the monthly trends of each outcome variable between the pilot group and control group before the policy intervention, to verify if the DID model met the parallel trend conditions, that is to ensure the comparability between the pilot group and the control group (online supplemental appendix B).[37] STATA V.16.0 (Stata Corp, College Station, Texas, USA) was used to perform the analyses above. A p value of <0.05 was considered statistically significant.

Patient and public involvement

In this research, we only included the drug procurement data and all the information was anonymous. Neither patients nor the public were involved in this research.

RESULTS

The change of volume, expenditures and DDDc

Table 1 shows the procurement change of policy-related drugs in pilot cities. Among the bid-winning drugs, the volume of original and generic products increased by 79.04% and 583.76%, the expenditure of generic products increased by 43.61%, the DDDc of original and generic products decreased by 44.44% and 79.00% after the policy intervention. Among the non-winning drugs, the decline of 37.77% and 81.12% in volume and 47.17% and 68.88% in expenditures were observed for original and generic products. The DDDc of non-winning original drugs decreased by 15.10%, while generic drugs increased by 64.81%. As for the alternative drugs, both original and generic products increased in volume (7.10% and 19.09%), expenditures (23.49% and 20.68%) and DDDc (15.30% and 1.33%). In terms of the overall '4+7' policy-related drugs, the volume of original products declined by 9.95%, while generic products increased by 33.24%; both original and generic products decreased in expenditures (16.83% and 13.97%) and DDDc (7.64% and 35.43%).

The change of composition ratio between original and generic drugs

After policy intervention, the volume proportion of generic products among bid-winning drugs slightly increased from 92.98% to 98.06%, generic products among non-winning drugs significantly decreased from 56.08% to 27.93%. Among the '4+7' List drugs, the volume proportion of generic drugs increased from 60.73% to 77.80%, and the expenditure proportion increased from 49.45% to 52.30% (figure 2).

As shown in figure 3, after policy intervention, the volume proportion of generic products among '4+7' List drugs increased in all of the nine pilot cities, with the increasing value ranging from 10.88% (Shanghai) to 47.18% (Xiamen). In the post-'4+7' period, with the exception of Beijing (61.67%), the volume proportion of generic products in the remaining eight cities exceeded 80%.

We calculated the proportion of generic products in each '4+7' List drug (table 2). For 20 of the 25 '4+7' List drugs, the volume proportion of generic drugs increased after policy intervention, with the increased value ranging from 0.64% (pemetrexed disodium) to 27.42% (montelukast). Three drugs appeared to have decreased volume proportion of generic drugs: olanzapine (−2.33%),

Table 1 Changes in the volume, expenditures, and DDDc of original and generic drugs in the pilot cities

Categories	n	Volume (million DDD)			Expenditures (million CNY)			DDDc (CNY)		
		Pre	Post	GR (%)	Pre	Post	GR (%)	Pre	Post	GR (%)
Bid-winning drugs										
Original	3	15.94	28.54	79.04	159.24	158.41	−0.52	9.99	5.55	−44.44
Generic	22	211.04	1442.98	583.76	1530.40	2197.85	43.61	7.25	1.52	−79.00
Subtotal	25	226.98	1471.53	548.31	1689.63	2356.25	39.45	7.44	1.60	−78.49
Non-winning drugs										
Original	22	692.14	430.72	−37.77	5805.84	3067.46	−47.17	8.39	7.12	−15.10
Generic	25	883.90	166.92	−81.12	4304.79	1339.77	−68.88	4.87	8.03	64.81
Subtotal	25	1576.04	597.64	−62.08	10110.63	4407.23	−56.41	6.42	7.37	14.95
'4+7' List drugs										
Original	23	708.08	459.26	−35.14	5965.07	3225.86	−45.92	8.42	7.02	−16.62
Generic	25	1094.93	1609.90	47.03	5835.19	3537.62	−39.37	5.33	2.20	−58.77
Subtotal	25	1803.02	2069.16	14.76	11800.26	6763.48	−42.68	6.54	3.27	−50.06
Alternative drugs										
Original	60	1046.39	1120.73	7.10	4303.76	5314.90	23.49	4.11	4.74	15.30
Generic	79	1067.53	1271.34	19.09	4278.78	5163.61	20.68	4.01	4.06	1.33
Subtotal	91	2113.93	2392.07	13.16	8582.54	10478.51	22.09	4.06	4.38	7.89
Overall policy-related drugs										
Original	81	1754.48	1579.99	−9.95	10268.83	8540.77	−16.83	5.85	5.41	−7.64
Generic	101	2162.47	2881.24	33.24	10113.97	8701.22	−13.97	4.68	3.02	−35.43
Subtotal	116	3916.94	4461.24	13.90	20382.80	17241.99	−15.41	5.20	3.86	−25.73

Pre refers to March–November 2018; post refers to March–November 2019; n refers to the number of drug substances covered in each subgroup.
CNY, Chinese yuan; DDD, defined daily dose; DDDc, defined daily drug cost; GR, growth rate.

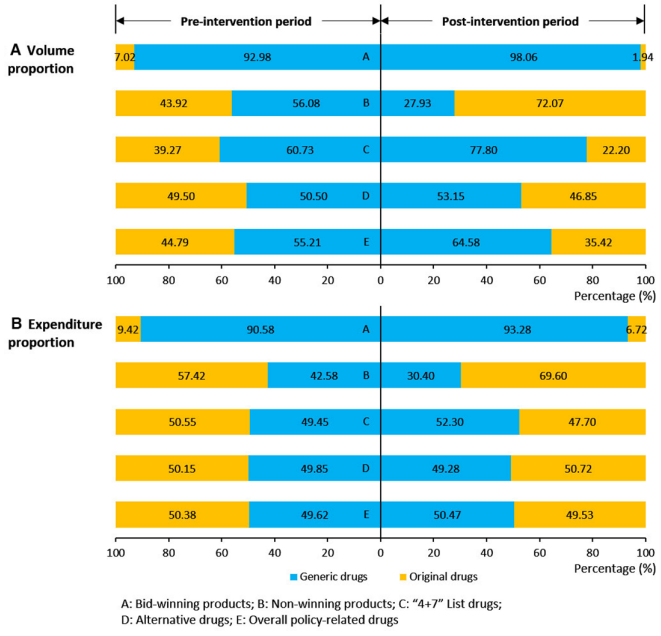

Figure 2 Changes in the (A) volume proportion and (B) expenditure proportion of original drugs and generic drugs in the pilot cities. Pre-intervention period refers to March–November 2018; post-intervention period refers to March–November 2019.

fosinopril (−26.57%) and gefitinib (−10.39%). In the post-'4+7' policy period, the overall volume proportion of generic drugs among '4+7' List drugs was 77.80%. Besides, we calculated the overall proportion of bid-winning drugs and non-winning original drugs since they represent a relatively higher-quality level, this figure increased from 39.66% to 91.93% for volume proportion and increased from 63.52% to 80.19% for expenditure proportion after the policy intervention.

The results of DID analysis

Table 3 shows the DID results of original and generic drugs in volume, expenditures and DDDc. After the '4+7' policy, the volume of both bid-winning original (coefficient=0.95 million DDD, p<0.001) and generic drugs (coefficient=134.01 million DDD, p<0.001) significantly increased. The volume of non-winning original (coefficient=−40.06 million DDD, p<0.001) and generic drugs (coefficient=−93.58 million DDD, p<0.001) significantly decreased. Among the '4+7' List drugs, the volume of original drugs decreased prominently (coefficient=−39.10 million DDD, p<0.001), while generic drugs increased (coefficient=40.43 million DDD, p<0.01). DID analysis showed that the volume change of original and generic

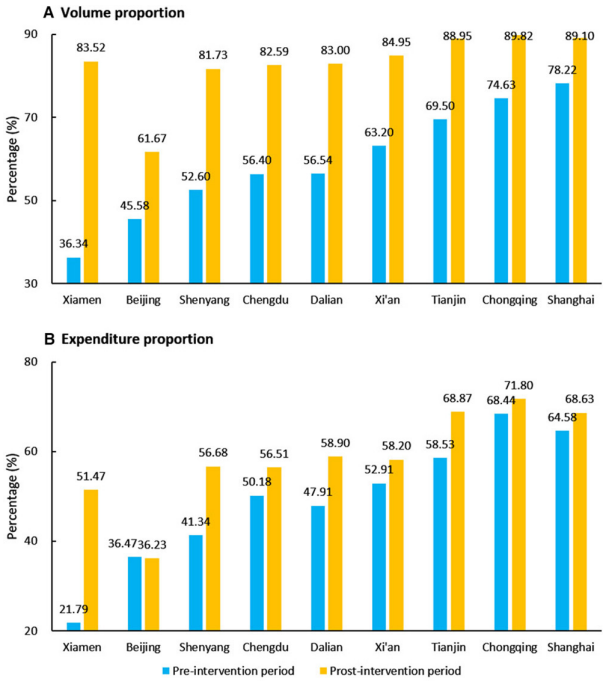

Figure 3 The (A) volume and (B) expenditure proportion of generic drugs among '4+7' List drugs in nine '4+7' pilot cities. Pre-intervention period refers to March–November 2018; post-intervention period refers to March–November 2019.

drugs in the alternative drugs had no significance (all p>0.05). Among the overall policy-related drugs, the volume of original drugs significantly decreased (coefficient=−37.43 million DDD, p<0.001), while generic drugs increased (coefficient=44.79 million DDD, p<0.05).

As for purchase expenditures, after policy intervention, the expenditure of bid-winning original drugs decreased prominently (coefficient=−¥12.14 million, p<0.01), and bid-winning generic drugs increased (coefficient=¥57.11 million, p<0.01). Among the non-winning products, the prominent decline was observed in the expenditure of original drugs (coefficient=−¥380.87 million, p<0.001) and generic drugs (coefficient=−¥390.50 million, p<0.001). Among the '4+7' List drugs, the expenditures of original drugs (coefficient=−¥393.01 million, p<0.001) and generic drugs (coefficient=−¥333.39 million, p<0.01) significantly decreased. DID analysis showed that the expenditure change of original and generic drugs in the alternative drugs had no significance (all p>0.05). Among the overall policy-related drugs, the expenditure of both original drugs (coefficient=−¥352.98 million, p<0.001) and generic drugs (coefficient=−¥301.49 million, p<0.001) declined.

In terms of the DDDc, after policy intervention, the DDDc of bid-winning original drugs (coefficient=−¥6.85, p<0.001) and bid-winning generic drugs (coefficient=−¥5.49, p<0.001) significantly declined compared with the pre-'4+7' period. The DDDc of non-winning original drugs significantly decreased (coefficient=−¥0.54, p<0.01), and non-winning generic drugs significantly increased (coefficient=¥3.64, p<0.001). In terms of the DDDc of '4+7' List drugs, both original drugs (coefficient=−¥0.78, p<0.001) and generic drugs (coefficient=−¥3.00, p<0.001) significantly declined. DID analysis showed that the DDDc change of original and generic drugs in the alternative drugs had no significance (all p>0.05). For the DDDc of the overall policy-related drugs, both original drugs (coefficient=−¥0.92, p<0.001) and generic drugs (coefficient=−¥1.69, p<0.001) significantly declined.

Subgroup analysis

Subgroup analysis was conducted towards different healthcare settings. As expressed in table 4, after '4+7' policy, the volume proportion of generic drugs among '4+7' List drugs increased by 25.27%, 15.08%, and 12.00% in tertiary hospitals, secondary hospitals, and PHCs. Among the overall policy-related drugs, the volume proportion of generic drugs increased by 13.84%, 8.84%, and 6.64% in tertiary hospitals, secondary hospitals, and PHCs. In addition, we calculated the use proportion of bid-winning drugs and non-winning original products in different healthcare settings: tertiary hospitals increased from 67.29% to 93.21%, secondary hospitals increased from 43.44% to 91.43%, and PHCs increased from 41.57% to 91.09%.

The results of DID analysis for subgroup analysis (table 5, online supplemental appendix C) indicated that, after the policy intervention, the volume of non-winning original drugs dropped significantly in tertiary hospitals (coefficient=−19.51 million DDD, p<0.001), secondary hospitals (coefficient=−8.63 million DDD, p<0.001) and PHCs (coefficient=−11.92 million DDD, p<0.001). Similarly, the volume of non-winning generic drugs significantly declined in tertiary hospitals (coefficient=−21.31, p<0.001), secondary hospitals (coefficient=−17.99, p<0.001) and PHCs (coefficient=−54.27, p<0.001). Among the '4+7' List drugs, the volume of original drugs prominently decreased in all three healthcare settings (all p<0.001), and the volume of generic drugs significantly increased in tertiary hospitals and PHCs (all p<0.05). In terms of the overall policy-related drugs, the volume of original drugs significantly decreased in all three healthcare settings (all p<0.05), and the volume of generic drugs markedly increased in tertiary hospitals (p<0.001). The expenditure of both original and generic products among '4+7' List drugs significantly decreased in different healthcare settings (all p<0.001). As for the DDDc of non-winning drugs, original products decreased in tertiary hospitals (coefficient=−¥0.50, p<0.001) and secondary hospitals (coefficient=−¥0.88, p<0.001); generic products increased in PHCs (coefficient=−¥0.34, p<0.01), while increased in tertiary hospitals (coefficient=¥8.75, p<0.001) and secondary hospitals (coefficient=¥2.65, p<0.001).

DISCUSSION

The present study examined the impact of the '4+7' policy on the use of policy-related original and generic

Table 2 Changes in the volume proportion and expenditure proportion of generic drugs among 25 '4+7' List drugs in the pilot cities

	Volume proportion (%)			Expenditure proportion (%)		
Drug name	Pre	Post	Δ	Pre	Post	Δ
Atorvastatin	42.07	68.41	26.34	35.65	28.48	−7.17
Escitalopram	96.93	98.61	1.68	98.03	97.85	−0.18
Amlodipine	56.51	75.84	19.33	26.86	20.61	−6.25
Olanzapine	93.72	91.39	−2.33	86.88	81.57	−5.31
Irbesartan	65.23	79.01	13.78	49.81	36.58	−13.22
Irbesartan hydrochlorothiazide	80.87	89.41	8.54	73.72	74.40	0.68
Entecavir	81.85	92.22	10.37	64.36	38.63	−25.74
Flurbiprofen	2.34	6.55	4.21	0.48	5.18	4.70
Fosinopril	29.91	3.34	−26.57	23.99	6.00	−18.00
Gefitinib	29.44	19.05	−10.39	21.26	18.92	−2.34
Lisinopril	100.00	100.00	0.00	100.00	100.00	0.00
Risperidone	64.59	80.00	15.41	44.73	47.52	2.79
Clopidogrel	58.97	77.19	18.22	45.25	49.58	4.33
Losartan	58.16	80.12	21.95	53.20	53.75	0.55
Montmorillonite	75.51	93.12	17.60	33.34	82.43	49.08
Montelukast	44.86	72.28	27.42	40.87	58.28	17.41
Paroxetine	77.61	90.82	13.22	60.00	71.54	11.54
Pemetrexed disodium	93.15	93.78	0.64	83.94	85.53	1.60
Rosuvastatin	69.16	83.32	14.15	59.38	53.99	−5.39
Tenofovir disoproxil	83.90	96.69	12.79	83.59	89.85	6.26
Cefuroxime	98.09	99.11	1.01	97.31	97.83	0.53
Imatinib	78.68	84.70	6.03	26.73	31.88	5.15
Enalapril	99.01	99.73	0.72	98.51	99.47	0.96
Dexmedetomidine	100.00	100.00	0.00	100.00	100.00	0.00
Levetiracetam	4.69	29.95	25.27	3.39	23.05	19.65
Total	**60.73**	**77.80**	**17.08**	**49.45**	**52.30**	**2.86**

Pre refers to March–November 2018; post refers to March–November 2019; Δ refers to the difference between pre-intervention and post-intervention periods.

drugs through a natural experimental design involving 9 pilot cities and 12 non-pilot provinces over a 23-month period. Overall, we found that '4+7' policy significantly promoted the consumption of bid-winning generic and original drugs in all healthcare settings, and was conducive to cutting down drug prices, improving overall drug quality level and achieving cost-containment.

In this study, a significant drop of 44.44% and 79.00% was observed in the DDDc of bid-winning original and generic drugs, which supported the price reduction effect of the '4+7' policy.[30 38] A significant reduction was detected for the DDDc of non-winning original drugs, which fit well with Xie *et al*'s finding[26] that many non-winning original products initiatively reduced their price under the '4+7' policy. By establishing volume–price linkage and enhancing competition, the '4+7' policy might be conducive to the shaping of the market mechanism of drug price.[39 40] However, we observed a prominent increase in the DDDc of non-winning generic drugs, especially in the healthcare settings of tertiary and secondary hospitals. More importantly, this study included the clinically substitutable drugs of '4+7' List drugs that have not yet been covered by the NCDP policy, and found that the DDDc of alternative drugs, both original and generic products, significantly increased, especially in primary healthcare settings. These results support our earlier finding in policy-related antihypertensive drugs.[11] We supposed there is possibility that the price of drugs without the bound of volume–price contract increased after policy implementation, which might be related to the unreasonable prescription behaviour, such as overprescribing of medicines.[29 41] In the future, it is recommended to strengthen the policy monitoring regarding the prices and prescription of policy-related drugs in all healthcare settings, as well as to improve medical insurance payment standards and advance the reform of medical insurance payment mode.

Table 3 DID analysis for the change of original and generic drugs in purchase volume, expenditures and DDDc

	Volume			Expenditure			DDDc		
Items	Overall	Original	Generic	Overall	Original	Generic	Overall	Original	Generic
Bid-winning products									
Constant, β_0	15.80***	0.93***	14.87***	126.29***	19.08***	107.22***	8.04***	20.62***	7.25***
Treat, β_1	3.82*	0.39**	3.44**	31.36**	10.24***	21.13*	0.003	1.75	−0.25*
Group, β_2	8.92 ***	0.90***	8.02***	59.18***	0.42	58.76***	−0.51***	−9.97***	0.01
Treat×group, β_3	134.96***	0.95***	134.01***	44.97*	−12.14**	57.11**	−5.93***	−6.85***	−5.49***
R^2	0.980	0.812	0.981	0.738	0.333	0.795	0.989	0.914	0.993
Non-winning products									
Constant, β_0	93.17***	30.45***	62.71***	610.64***	303.89***	306.75***	6.60***	10.00***	4.95***
Treat, β_1	22.58**	10.71***	11.87*	139.10**	80.25***	58.85*	−0.13	−0.67***	−0.05
Group, β_2	84.28***	46.75***	37.53***	511.32***	337.56***	173.76***	−0.28*	−1.69***	−0.15
Treat×group, β_3	−133.63***	−40.06***	−93.58***	−771.37***	−380.87***	−390.50***	1.18***	−0.54**	3.64***
R^2	0.823	0.889	0.813	0.808	0.853	0.774	0.692	0.940	0.920
'4+7' List drugs									
Constant, β_0	108.97***	31.38***	77.58***	736.94***	322.97***	413.97***	6.81***	10.30***	5.39***
Treat, β_1	26.41**	11.10***	15.31*	170.46**	90.48***	79.98*	−0.11	−0.57***	−0.07
Group, β_2	93.20***	47.65***	45.55***	570.50***	337.98***	232.51***	−0.34**	−1.94***	−0.13
Treat×group, β_3	1.33	−39.10***	40.43**	−726.40***	−393.01***	−333.39***	−3.10***	−0.78***	−3.00***
R^2	0.795	0.885	0.793	0.739	0.835	0.601	0.970	0.963	0.964
Alternative drugs									
Constant, β_0	175.89***	54.74***	121.14***	476.48***	194.23***	282.25***	2.73***	3.58***	2.34***
Treat, β_1	19.10	5.88	13.22	100.14**	61.94***	38.20	0.23***	0.65***	0.04
Group, β_2	64.77***	62.24***	2.54	515.74***	294.36***	221.39***	1.39***	0.60***	1.72***
Treat×group, β_3	6.03	1.67	4.36	71.92	40.02	31.90	0.03	−0.08	−0.04
R^2	0.529	0.880	0.109	0.866	0.926	0.758	0.976	0.817	0.989
Overall policy-related drugs									
Constant, β_0	284.85***	86.13***	198.73***	1213.41***	517.20***	696.22***	4.30***	6.04***	3.54***
Treat, β_1	45.51*	16.98**	28.53	270.60**	152.42***	118.18*	0.19*	0.46***	0.05
Group, β_2	157.97***	109.88***	48.09*	1086.24***	632.34***	453.90***	0.90***	−0.17*	1.12***
Treat×group, β_3	7.36	−37.43***	44.79*	−654.47***	−352.98***	−301.49***	−1.52***	−0.92***	−1.69***
R^2	0.691	0.879	0.540	0.766	0.863	0.614	0.911	0.807	0.950

*P<0.05, **p<0.01, ***p<0.001.
The data presented are the regression coefficients.
DDDc, defined daily drug cost; DID, difference-in-difference.

Among the 25 '4+7' List drugs, 3 were original brands from a pharmaceutical company that won the bid.[17] After policy implementation, we found that the use proportion of generic products among '4+7' List drugs increased from 60.73% to 77.80%; in other words, 17.08% of the original brand-name products were replaced by generic products in pilot cities. This was generally in line with the previous finding of 16.68% (from 49.44% to 66.12%) in four pilot municipalities.[26] This evidence supported the idea that the '4+7' policy effectively contributed to the substitution use of generic products, worth noting that these generic drugs have passed the GCE. DID analysis revealed a significant decline in the expenditure of '4+7' List drugs (¥726.40 million per month), as well as the overall policy-related drugs (¥654.47 million per month), indicating the prominent policy effect of drug cost-saving. Internationally, it is feasible policy practice for developing countries to achieve pharmaceutical cost-containment through generic substitution,[18–20] and the similar effect was presented in China under the implementation of the '4+7' policy.

Nine pilot cities were involved in this study, and they varied in the changes of use structure between original and generic products under the policy intervention. For example, in Xiamen and Shenyang, 47.2% and 29.1% of the original drugs were substituted by generic drugs, while this figure was only 10.9% and 15.2% in Shanghai and Chongqing. Such differences among pilot cities might be related to the initiative and effectiveness of local government in implementing the national bidding

Table 4 Changes in the volume proportion and expenditure proportion of generic drugs among different healthcare settings in the pilot cities

	Tertiary			Secondary			PHCs		
Categories	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ
Volume proportion									
Bid-winning products	94.93	97.77	2.84	94.75	98.29	3.54	89.98	98.19	8.21
Non-winning products	38.77	20.91	−17.86	65.81	38.45	−27.36	64.88	31.56	−33.32
'4+7' List drugs	47.54	72.81	25.27	69.88	84.96	15.08	67.38	79.37	12.00
Alternative drugs	37.24	39.75	2.51	55.04	58.12	3.08	57.97	60.49	2.52
Overall policy-related drugs	42.10	55.95	13.84	61.79	70.62	8.84	62.24	68.88	6.64
Expenditure proportion									
Bid-winning products	87.46	90.50	3.04	96.31	94.70	−1.62	92.98	97.54	4.56
Non-winning products	39.04	34.89	−4.15	54.66	40.82	−13.84	43.09	17.25	−25.84
'4+7' List drugs	46.01	53.04	7.03	61.30	64.66	3.36	49.81	45.22	−4.59
Alternative drugs	39.75	37.43	−2.32	59.77	61.16	1.39	58.55	60.42	1.87
Overall policy-related drugs	43.54	44.15	0.60	60.60	62.40	1.79	53.71	55.12	1.41

Pre refers to March–November 2018; post refers to March–November 2019; Δ refers to the difference between pre-intervention and post-intervention periods.
PHCs, primary healthcare centres.

results. What is more, the baseline drug use structure of a certain city should be considered,[42–45] for the cities with a higher use proportion of original drugs prior to policy implementation, there is naturally more space for generic substitution.

In different healthcare settings, this study found different changes in the use structure between original and generic drugs. After the '4+7' policy, the growth rate of '4+7' List generic drugs showed a trend of tertiary hospitals (84.95%)>secondary hospitals (42.62%)>PHCs (29.17%); consistently, the increased value in the use proportion of generic drugs presented the same trend of tertiary hospitals (25.27%)>secondary hospitals (15.08%)>PHCs (12.00%). These results indicated that the generic substitution effect induced by the '4+7' policy was more widespread in large hospitals, which might be closely related to the higher baseline use proportion of original drugs in China's public hospitals, [43–46] thus had greater space for generic substitution.

According to the NHSA's statistics,[46] after the implementation of the '4+7' policy, the use proportion of higher-quality drugs, that is, generic drugs certified by GCE and original drugs, increased from 50% to more than 90% in 11 '4+7' pilot cities. This study showed similar results that the overall consume proportion of bid-winning drugs and non-winning original drugs increased from 39.66% to 91.93% in nine pilot cities, which illustrates that the '4+7' policy is conducive to improving the overall quality level of drug use of the Chinese population. In the future, with the advancement of the NCDP policy, generic drugs that fail to pass the GCE will be phased out of the Chinese market, and the drug use of Chinese patients will gradually concentrate on higher-quality medicines.[8] In addition, the increased value for the use proportion of higher-quality drugs showed a trend of tertiary hospitals (25.92 percentage points)<secondary hospitals (47.99 percentage points)<PHCs (49.52 percentage points), which indicated that the '4+7' policy greatly improved the accessibility of higher-quality drugs at the primary healthcare setting.

Limitations

This study had several limitations. First, in the present study, we used non-randomised processing method in building counterfactual. It should be mentioned that the '4+7' pilot cities are China's top developed areas, thus it is difficult to assign a control group in mainland China that completely matched the pilot group in population size, economic development, medical resources, etc. Luckily, however, the common trends support the model specifications of the DID, thus to some extent ensured the comparability between two groups. We believe that this study might have a certain imperfection regarding the building of control group, thus is confronted with the risk of bias of our findings. Second, this study used 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, there is still a possibility that the two data sources may not exactly match, so there are certain limitations. Therefore, in the future, further in-depth analysis by using clinical use data of policy-related drugs might make more sense. Third, this study followed the definition of 'alternative drugs' by the NHSA, and extracted alternative drugs based on the reference list provided by the NHSA's *Monitoring Plan for the Pilot Work of National Centralized Drug Procurement and Use*.[31] While the actual clinical prescribing varies by many potential factors, such as patients' disease condition,

Table 5 DID analysis for the change of original and generic drugs in purchase volume among different healthcare settings

	Original drugs			Generic drugs		
Items	Tertiary	Secondary	PHCs	Tertiary	Secondary	PHCs
Winning products						
Constant, β_0	0.34***	0.43***	0.16***	9.01***	4.69***	1.18***
Treat, β_1	0.17**	0.14*	0.07***	1.70*	1.34*	0.40***
Group, β_2	0.30***	−0.18**	0.77***	1.32	−0.63	7.34***
Treat×group, β_3	0.48***	0.08	0.39***	44.61***	22.23***	67.16***
R^2	0.758	0.490	0.909	0.965	0.957	0.991
Non-winning products						
Constant, β_0	20.08***	8.78***	1.59***	20.67***	19.57***	22.47***
Treat, β_1	4.97***	4.43***	1.30***	3.67*	3.28	4.92*
Group, β_2	16.47***	0.38	29.90***	2.79	−1.76	36.50***
Treat×group, β_3	−19.51***	−8.63***	−11.92***	−21.31***	−17.99***	−54.27***
R^2	0.777	0.705	0.967	0.768	0.754	0.889
'4+7' List drugs						
Constant, β_0	20.43***	9.21***	1.75***	29.68***	24.25***	23.65***
Treat, β_1	5.15***	4.58***	1.38***	5.37*	4.62	5.32**
Group, β_2	16.78***	0.20	30.67***	4.10	−2.39	43.84***
Treat×group, β_3	−19.03***	−8.55***	−11.52***	23.30***	4.24	12.89*
R^2	0.767	0.686	0.970	0.782	0.308	0.908
Alternative drugs						
Constant, β_0	30.55***	17.74***	6.45***	31.65***	34.87***	54.62***
Treat, β_1	3.62	1.67	0.60	3.42	3.99	5.81
Group, β_2	19.96***	−0.77	43.04***	−0.87	−13.40***	16.80**
Treat×group, β_3	−0.31	−1.28	3.26	1.31	−1.36	4.41
R^2	0.768	0.069	0.968	0.108	0.544	0.453
Overall policy-related drugs						
Constant, β_0	50.98***	26.95***	8.20***	61.33***	59.12***	78.27***
Treat, β_1	8.76*	6.24**	1.98**	8.78	8.61	11.14
Group, β_2	36.74***	−0.56	73.71***	3.23	−15.78**	60.64***
Treat×group, β_3	−19.34***	−9.83***	−8.27*	24.61***	2.88	17.30
R^2	0.740	0.324	0.973	0.594	0.374	0.793

*P<0.05, **p<0.01, ***p<0.001.
The data presented are the regression coefficients.
DID, difference-in-difference; PHCs, primary healthcare centres.

medical history, medication habits, healthcare settings and even regions, the alternative drugs included in this study may not completely cover all drugs that the prescription of bid-winning drugs possibly shift into.

CONCLUSION

After policy intervention, the prominent effects of drug price reduction and pharmaceutical cost-containment were observed. The '4+7' policy significantly promoted the substitution use of generic drugs among '4+7' List drugs, with the substitution ratio of 17.8% in nine pilot cities. The consumption proportion of higher-quality drugs, that is, generic drugs certified by the GCE and original drugs, raised markedly, especially in primary healthcare settings, indicates the improvement of the overall quality level of drug use of the Chinese population. However, the increased DDDc of non-winning generic drugs and alternative drugs should draw the importance of further policy monitoring.

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REFERENCES

1 National Health Commission of the People's Republic of China. *China health statistics Yearbook 2020*. Beijing: Peking Union Medical College Press, 2019.
2 OECD. Health at a glance 2021: OECD indicators, 2021. Available: https://www.oecd-ilibrary.org/sites/ae3016b9-en/index.html?itemId=/content/publication/ae3016b9-en [Accessed 20 Nov 2021].
3 Hu J, Mossialos E. Pharmaceutical pricing and reimbursement in China: when the whole is less than the sum of its parts. *Health Policy* 2016;120:519–34.
4 Yip W, Fu H, Chen AT, *et al*. 10 years of health-care reform in China: progress and gaps in universal health coverage. *Lancet* 2019;394:1192–204.
5 Yip W, Hsiao W. Harnessing the privatisation of China's fragmented health-care delivery. *Lancet* 2014;384:805–18.
6 Wu B, Zhang Q, Qiao X. Effects of pharmaceutical price regulation: China's evidence between 1997 and 2008. *J Asia Pac Econ* 2015;20:290–329.
7 Fu H, Chen X, Zhang X. The analysis of key problems and countermeasure about drug centralized procurement. *Health Economics Research* 2015;09:7–9.
8 Mao Z, Yang Y, Chen L. Reform of Drug Supply and Guarantee System in China: Policy Measures and Effects. In: Wang C, Liang W, eds. *Development report on health reform in China (2020*. Beijing: Social Sciences Academic Press, 2020: 96–123.
9 State Council of the People's Republic of China. Pilot program for national centralized drug procurement and use, 2019. Available: http://www.gov.cn/zhengce/content/2019-01/17/content_5358604.htm [Accessed 09 Jan 2021].
10 Yuan J, Lu ZK, Xiong X, *et al*. Lowering drug prices and enhancing pharmaceutical affordability: an analysis of the National volume-based procurement (NVBP) effect in China. *BMJ Glob Health* 2021;6:e005519.
11 Yang Y, Tong R, Yin S, *et al*. The impact of "4+7" volume-based drug procurement on the volume, expenditures, and daily costs of antihypertensive drugs in Shenzhen, China: an interrupted time series analysis. *BMC Health Serv Res* 2021;21:1275.
12 Qu J, Zuo W, Wang S, *et al*. Knowledge, perceptions and practices of pharmacists regarding generic substitution in China: a cross-sectional study. *BMJ Open* 2021;11:e051277.
13 China Food and Drug Administration. Evaluation scheme of generic quality consistency, 2013. Available: http://www.nmpa.gov.cn/WS04/CL2196/323980.html [Accessed 20 Nov 2021].
14 State Council of the People's Republic of China. Notification on the carrying out consistency evaluation of the quality and efficacy of generic drugs, 2016. Available: http://www.gov.cn/zhengce/content/2016-03/05/content_5049364.htm [Accessed 20 Nov 2021].
15 State Council Information Office. Regular meeting on the state Council policy on 27th, November, 2019, 2019. Available: http://www.nhc.gov.cn/xcs/s7847/201911/dad7e0b2a26a4f56bd68836d33ab2fe2.shtml [Accessed 20 Nov 2021].
16 National Medical Products Administration of the People's Republic of China. Guidelines on statistical analysis in bioequivalence studies and technology in bioequivalence studies of high-variation drugs, 2018. Available: https://www.nmpa.gov.cn/yaopin/ypggtg/ypqtgg/20181029173101911.html [Accessed 20 Nov 2021].
17 Joint Procurement Office. Bid-winning results of "4+7" city centralized drug procurement, 2018. Available: http://www.smpaa.cn/gjsdcg/2018/12/17/8580.shtml [Accessed November 25, 2021].
18 Vogler S, Gombocz M, Zimmermann N. Tendering for off-patent outpatient medicines: lessons learned from experiences in Belgium, Denmark and the Netherlands. *Journal of Pharmaceutical Health Services Research* 2017;8:147–58.
19 Casanova-Juanes J, Mestre-Ferrandiz J, Espín-Balbino J. Competition in the off-patent medicine market in Spain: the National reference pricing system versus the regional system of tendering for outpatient prescription medicines in Andalusia. *Health Policy* 2018;122:1310–5.
20 Cameron A, Mantel-Teeuwisse AK, Leufkens HGM, *et al*. Switching from originator brand medicines to generic equivalents in selected developing countries: how much could be saved? *Value Health* 2012;15:664–73.
21 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;38:373–8.
22 Wang Y, Xu W, Lu N. Analysis of the effect of "4+7" centralized procurement policy implementation: Based on the drug sales data of 9 pilot regions. *Chinese Journal of Health Policy* 2021;14:36–43.
23 Zou G, Zhao J, Mei Q. 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;20:854–8.
24 Chen L, Yang Y, Luo M, *et al*. 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;17:9415.
25 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.
26 Xie J, Hu Z, Wang Y. The influences of national centralized drug procurement policy on drug price, cost and generic drug substitution: taking the four municipalities data. *Chinese Health Economics* 2021;40:24–8.

27 National Health Commission of the People's Republic of China. China drug supply information platform, 2015. Available: http://www.nhc.gov.cn/mohwsbwstjxxzx/s8555/201510/a642beea6faf415fa8bbd6563461f3be.shtml [Accessed 25 Nov 2021].
28 State Council of the People's Republic of China. Guiding Opinions on Improving the Centralized Drug Procurement in Public Hospitals (Guobanfa [2015] No. 7), 2015. Available: http://www.gov.cn/zhengce/content/2015-02/28/content_9502.htm [Accessed 06 Mar 2021].
29 Yang Y, Chen L, Ke X, *et al*. 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;21:668.
30 Wang N, Yang Y, Xu L, *et al*. Influence of Chinese national centralized drug procurement on the price of policy-related drugs: an interrupted time series analysis. *BMC Public Health* 2021;21:1–1883.
31 National Healthcare Security Administration. Monitoring plan for the pilot work of national centralized drug procurement and use, 2019. Available: http://www.nhsa.gov.cn/ [Accessed 30 Nov 2021].
32 WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD index 2021, 2021. Available: https://www.whocc.no/atc_ddd_index/ [Accessed 06 Mar 2021].
33 WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2021, 2021. Available: http://www.whocc.no [Accessed 06 Mar 2021].
34 Shen M, Hu M, Zeng N. Application of the Difference-in-difference model in medical research. *Chinese Journal of Health Statistics* 2015;32:528–31.
35 Ye F, Wang Y. Introduction and application of the Difference-in-difference model. *Chinese Journal of Health Statistics* 2013;30:131–4.
36 Wing C, Simon K, Bello-Gomez RA. Designing difference in difference studies: best practices for public health policy research. *Annu Rev Public Health* 2018;39:453–69.
37 Hu R, Lin M. Application of Difference-Difference method in public policy evaluation. *Financial Minds* 2018;84:143–4.
38 Ye S, Kang Q, Gao J. Study of Drug Price Index in Evaluating Implementation Effect of "4+7" Drug Centralized Procurement Policy in Fujian. *China Health Insurance* 2020:35–9.
39 Hursh SR. Behavioral economics of drug self-administration: an introduction. *Drug Alcohol Depend* 1993;33:165–72.
40 Hursh S, Bauman R. The behavioral analysis of demand. In: Green L, Kagel JH, eds. *Advances in behavioral economics*. Ablex, Norwood, NJ, 1987: 117–65.
41 Yu C. The practical effects and system concerns of "4+7" drug procurement. *Journal of Southwest Minzu University* 2020;41:34–9.
42 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;30:2890–4.
43 Li H, Zhu J, Chen Y. Usage of original and generic antihypertensive drugs in a special outpatient department of a hospital. *China Pharmaceuticals* 2019;28:90–3.
44 Huang Z, Liu S, Wei X. Originals and generics utilization analysis of cardiovascular medicines in 85 secondary and tertiary public hospitals in Beijing. *Chinese Journal of Pharmacoepidemiology* 2017;26:490–5.
45 Li H, Guan X, Xu L. Empirical research of price difference and market share between brand-name drugs and generics in one Province in China. *Chinese Journal of New Drugs* 2012;21:2853–6.
46 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. Available: http://www.nhsa.gov.cn/art/2020/1/17/art_38_2264.html [Accessed 29 Jan 2021].