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ORIGINAL RESEARCH

New Evidence of the Impact of the National Drug Price Negotiation Policy on the Availability, Utilization, and Cost of Anticancer Medicines in China: An Interrupted Time Series Study

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Purpose: The increasing global burden of cancer has become a significant challenge for public health. The Chinese government introduced the National Drug Price Negotiation (NDPN) policy with the goal of lowering the prices of innovative drugs and enhancing their accessibility. This study aims to evaluate the impact of the 2021 NDPN policy on the availability, utilization, and cost of anticancer medicines in China.

Methods: Data was gathered from 1519 hospitals between April 2021 and December 2022, with a focus on eight anticancer drugs affected by the 2021 NDPN policy. The availability, Defined Daily Doses (DDDs), and cost per Defined Daily Dose (DDDc) before and after the intervention were evaluated through interrupted time series analysis.

Results: The NDPN policy resulted in a substantial 5.10% increase in the availability of anticancer drugs ($p < 0.001$). Utilization also experienced a significant surge, with an immediate increase of 11,254.36 DDDs ($p < 0.001$) and a monthly increase of 1208.28 DDDs ($p < 0.001$) following policy implementation. The DDDc decreased by US$ 111.00 ($p < 0.001$) immediately after the policy. Disparities in regional drug utilization were evident, with higher usage in the eastern region.

Conclusion: The 2021 NDPN policy has notably enhanced the availability and utilization of anticancer medications in China while reducing their cost, in line with the policy's objectives. However, continuous monitoring is essential to ensure sustained access and to tackle regional disparities in drug utilization.

Keywords: anticancer medicines, national drug price negotiation, China, availability, utilization, cost, interrupted time series analysis

Introduction

The increasing global incidence of cancer presents a significant challenge to public health systems worldwide. In 2022, an estimated 20 million new cases and 9.7 million deaths were recorded.[1] In China, cancer also become a leading public health concern, with approximately 4,824,700 new cases and 2,574,200 deaths in 2022.[2] Access to effective anticancer drugs is crucial for improving patient outcomes and reducing the burden of the disease. Unfortunately, the financial cost of cancer treatment often proves to be insurmountable for many patients in China.[3] A staggering half of these patients have resorted to borrowing money or incurring debt to cover medical expenses, and about 10% of cancer patients have forgone essential care solely due to cost-related barriers.[4] High-priced targeted anticancer drugs, which form the cornerstone of modern cancer therapy, remain out of reach for a significant portion of the patient population.[5]

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In response to these challenges, the Chinese government introduced the National Drug Price Negotiation (NDPN) policy in 2017, aiming to curb soaring drug prices and enhance accessibility to life-saving drugs. The NDPN policy encompasses negotiations between the state and pharmaceutical companies to determine the pricing of innovative drugs for inclusion in the National Reimbursement Drug List (NRDL).[6] These drugs are known as "national negotiated drugs". Manufacturers view inclusion in the NRDL as an opportunity for rapid market expansion, thus spurring their engagement in the NDPN. This policy represents a pivotal stride towards ensuring fair access to critical anticancer therapies, aiming to alleviate the economic strain on patients and their families and simultaneously bolstering the sustainability of the healthcare system.

Nevertheless, the accessibility of these negotiated anticancer drugs is hindered by several systemic factors. Chinese public hospitals often lack the motivation to dispense negotiated drugs due to constraints on drug expenditure ratios, the global budget payment system, and the drug zero mark-up policy, casting doubt on the policy's efficacy. To refine and assess the NDPN policy, it is imperative for policymakers to gather empirical evidence on the utilization of medicines. Although prior studies have delved into the policy's impact on anticancer drugs,[7–12] there is a lack of analysis specifically focusing on the NDPN in 2021. Interrupted time series (ITS) analysis was frequently used to assess the impact of policy changes on the continuous outcome variable over time, thereby helping to determine whether the policy has had a significant effect on the outcome variable.[13,14]

Therefore, this study employs an ITS approach to thoroughly assess the impact of the 2021 NDPN on the availability, utilization, and cost of anticancer medicines. Understanding the impact of the NDPN on anticancer drugs is essential for informing evidence-based policy decisions and ensuring that patients have equitable access to essential treatments.

Methods

Study Design

We used an ITS design to analyze the changes in availability, utilization, and cost per Defined Daily Dose (DDDc) of anticancer drugs from April 2021 to December 2022. These drugs were incorporated into the NRDL in January 2022. Specifically, we examined the data over a 9-month period before and a 12-month period after the policy's introduction. Additionally, we specifically selected the availability figures for November 2021 and December 2022 to provide a descriptive comparison of availability before and after implementation. No ethical statement is required, as there is no need for patient recruitment and personal data collection.

Data Collection

Among the anticancer drugs negotiated in 2021,[15] we excluded those with less than eight months between launch and inclusion in the NRDL, as they did not meet the criteria for ITS analysis. Additionally, we excluded anticancer drugs used for rare diseases due to significant differences in prices and volumes compared to other anticancer drugs. The final selection for our study comprised eight drugs: ensartinib, surufatinib, eribulin, fluzoparib, dacomitinib, pomalidomide, apalutamide, and orelabrutinib.

We collected continuous monthly purchasing data for eight selected anticancer drugs from the Chinese Medicine Economic Information (CMEI) database. The database consolidates procurement data from 1519 hospitals, representing 29.04% and 3.32% of tertiary and secondary hospitals nationwide. It offers a comprehensive overview of healthcare facilities in 31 provincial-level administrative regions, encompassing the eastern, central, and western zones. The basic drug information was obtained from the National Healthcare Security Administration (NHSA) of China,[16] and the defined daily doses (DDD) were directly derived from the drug labels. All cost-related data were meticulously converted to US dollars using the prevailing exchange rate of US$ 1 = 6.7328 Chinese yuan (CNY).[17]

Outcome Measures

Our evaluation focused on four pivotal outcomes: availability, utilization, and DDDc. To ascertain the outcome, we adhered to the standardized survey methodology established by the World Health Organization and Health Action International (WHO/HAI).[18] The availability of a medicine was calculated using the following formula:

$$Availability = \frac{Number\ of\ hospitals\ that\ procured\ the\ medicine}{Total\ number\ of\ hospitals} * 100\%$$

The utilization was measured using Defined Daily Doses (DDDs), a metric that standardizes the dosage of a drug.[19] This approach allows for a direct comparison across different drugs, irrespective of the actual quantities procured. The calculation for DDDs is as follows:

$$DDDs = \frac{Total\ volume\ procured}{Defined\ daily\ dose\ (DDD)}$$

Additionally, the cost of each medicine was expressed through the DDDc. This measure was calculated using the following formula:

$$DDDc = \frac{Procurement\ spending}{DDDs}$$

Statistical Analysis

Descriptive statistics were employed to provide an overview of the availability of anticancer drugs both prior to and following the intervention. To quantitatively assess the impact of the NDPN on these drugs, we conducted a single-group ITS analysis. The ITS analysis was grounded in the following regression model:

$$Y_t = \beta_0 + \beta_1 T_t + \beta_2 X_t + \beta_3 X_t T_t + \varepsilon_t$$

In this model, Y_t represents the aggregated outcome variable, measured at each equally spaced time point t. The term β_0 is the intercept, β_1 signifies the pre-intervention slope, β_2 represents the the immediate change in level subsequent to the intervention's introduction, and β_3 reflects the difference in slopes between the pre- and post-intervention periods. A significant p-value for β_2 indicates an immediate effect of the treatment, while significance in β_3 suggests an ongoing treatment effect over time.[20]

For the estimation of coefficients, we applied the Newey model through ordinary least squares (OLS) regression. This approach was complemented by the computation of Newey-West standard errors to effectively manage issues of autocorrelation and potential heteroskedasticity.[21,22] All statistical analyses were performed using Stata/MP V.16.0 software (StataCorp).

Results

Characteristics of Anticancer Medicines

Out of the eight anticancer drugs, only one was administered through injection, while the others were in oral dosage forms. Three of these drugs were introduced to the Chinese market in 2019, and five in 2020 (Table 1). In terms of their therapeutic indications, two of the drugs are meant for non-small cell lung cancer (NSCLC), namely ensartinib and dacomitinib. Both dacomitinib and apalutamide target the EGFR pathway.

Impact of the NDPN on Availability

After the implementation of the NDPN policy, the availability of anticancer drugs increased by an average of 6.72%, representing a significant 13.55-fold improvement over pre-policy levels (Table 2). The average availability of these drugs after the NDPN was 7.27%. Among them, ensartinib, apalutamide, and pomalidomide emerged as the top three in terms of availability, with 13.69%, 10.63% and 7.96%, respectively. In contrast, fluzoparib had the lowest availability at 4.19%. Surufatinib had the largest increase in availability with a 27.17-fold increase, while fluzoparib had the smallest increase with a 7.73-fold increase.

The availability of negotiated anticancer drugs increased by 5.10% ($p < 0.001$) immediately after the policy was implemented, as depicted in Figure 1 and Table 3. Subsequently, after the implementation of the NDPN policy, the trend exhibited a monthly increase of 0.18% ($p = 0.052$) compared to the pre-intervention period.

Table 1 Characteristics of Anticancer Medicine in the NDPN Policy

Generic Name	Dosage Form	Launch in China	Marketing Authorization Holder	Indication	Target
Ensartinib	Capsule	November 2020	Betta	Non-small cell lung cancer	ALK
Surufatinib	Capsule	December 2020	Hutchison Whampoa	Neuroendocrine tumors	VEGFR
Eribulin	Injection	July 2019	Eisai	Breast cancer	Microtubule proteins
Fluzoparib	Capsule	December 2020	Hengrui	Epithelial ovarian, fallopian tube, or peritoneal cancer	BRCA
Dacomitinib	Tablet	May 2019	Pfizer	Non-small cell lung cancer	EGFR
Pomalidomide	Capsule	November 2020	Chia Tai Tianqing	Myeloma	CRBN
Apalutamide	Tablet	September 2019	Janssen-cilag	Prostate cancer	EGFR
Orelabrutinib	Tablet	December 2020	Innocare	Lymphoma	BTK

Table 2 Availability of Anticancer Medicines Before and After the NDPN Policy

Generic Name	Availability Before NDPN (%)	Availability After NDPN (%)	Absolute Change in Availability (%)	Relative Change in Availability
Ensartinib	1.12	13.69	12.57	11.22
Surufatinib	0.18	5.07	4.89	27.17
Eribulin	0.64	6.50	5.86	9.16
Fluzoparib	0.48	4.19	3.71	7.73
Dacomitinib	0.31	4.59	4.28	13.81
Pomalidomide	0.62	7.96	7.34	11.84
Apalutamide	0.60	10.63	10.03	16.72
Orelabrutinib	0.47	5.51	5.04	10.72
Mean (SD)	0.55 (0.28)	7.27 (3.34)	6.72 (3.11)	13.55 (6.15)

Impact of the NDPN on Utilization

Figure 2 and Table 3 reflect the changes in utilization after the implementation of the NDPN. Both the immediate intervention effect and the long-term effect were significant after the implementation of the NDPN policy. The initial level of utilization was estimated at 317.35 DDDs and appeared to increase by 66.12 DDDs per month before the intervention. The average utilization increased rapidly by 11254.36 DDDs in the first month of the intervention. The difference between the post-intervention trend and the pre-intervention trend was also significant ($\beta3=1208.28$, $p < 0.001$). The monthly utilization of anticancer drugs was graphed at both national and regional levels, revealing variations across different regions (Figure S1). The eastern region exhibited the highest utilization, whereas the western region showed the lowest.

Impact of the NDPN on Cost

The initial DDDc level was estimated at US$ 171.52, and there were no significant changes in DDDc before the intervention ($P = 0.364$). Subsequently, the DDDc of the negotiated anticancer medicines decreased by US$ 111.00 ($p < 0.001$) immediately after the policy implementation. Post-intervention trends did not differ significantly from pre-intervention trends ($p = 0.320$), and the post-intervention DDDc remained stable (Figure 3 and Table 3).

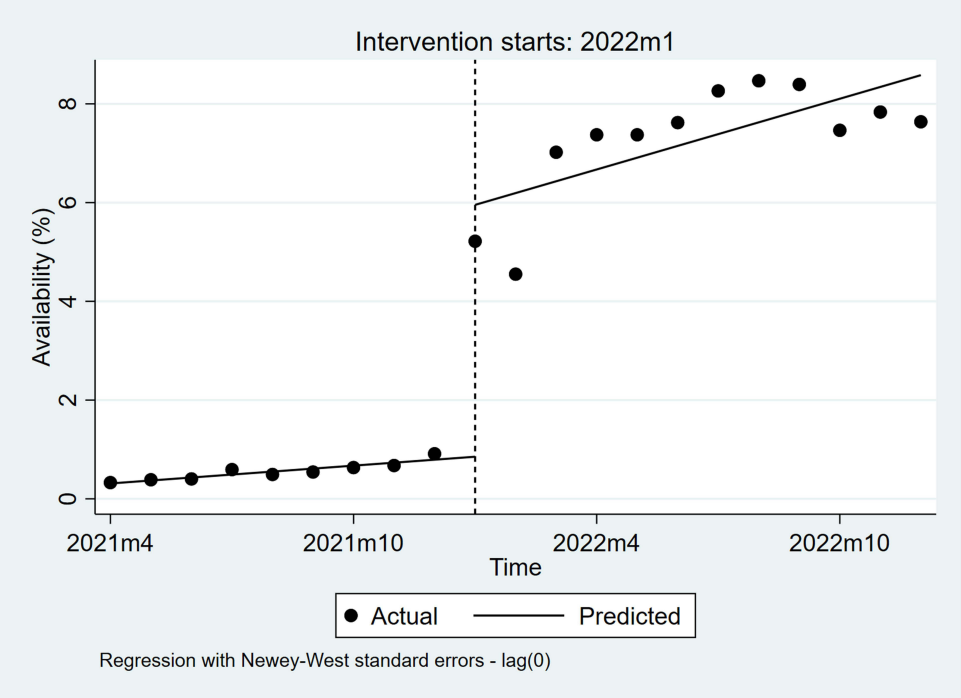

Figure 1 Observed and predicted availability of negotiated anticancer drugs.

Discussion

The findings of this study provide a comprehensive analysis of the impact of the 2021 NDPN policy on the availability, utilization, and cost of anticancer medicines in China. The results show a notable rise in availability and utilization, as well as a decrease in the cost of anticancer drugs.

Table 3 Changes in Levels and Trends of Availability, Utilization, and Cost

Availability (%)	**Coefficient**	**P value**	**95% CI**
Baseline level (β0)	0.31	< 0.001	0.24 to 0.38
Baseline trend (β1)	0.06	< 0.001	0.04 to 0.08
Level change immediately after intervention (β2)	5.10	< 0.001	3.84 to 6.36
Trend change after intervention (β3)	0.18	0.052	0.00 to 0.36
Utilization (DDDs)			
Baseline level (β0)	317.35	< 0.001	218.23 to 416.48
Baseline trend (β1)	66.12	< 0.001	46.65 to 85.59
Level change immediately after intervention (β2)	11,254.36	< 0.001	7621.98 to 14886.75
Trend change after intervention (β3)	1208.28	< 0.001	629.15 to 1787.42
Cost per DDD (US$)			
Baseline level (β0)	171.52	< 0.001	163.3 to 179.74
Baseline trend (β1)	−1.24	0.364	−4.06 to 1.57
Level change immediately after intervention (β2)	−111.00	< 0.001	−129.42 to −92.59
Trend change after intervention (β3)	1.37	0.320	−1.45 to 4.18

Abbreviation: DDD, Defined Daily Dose.

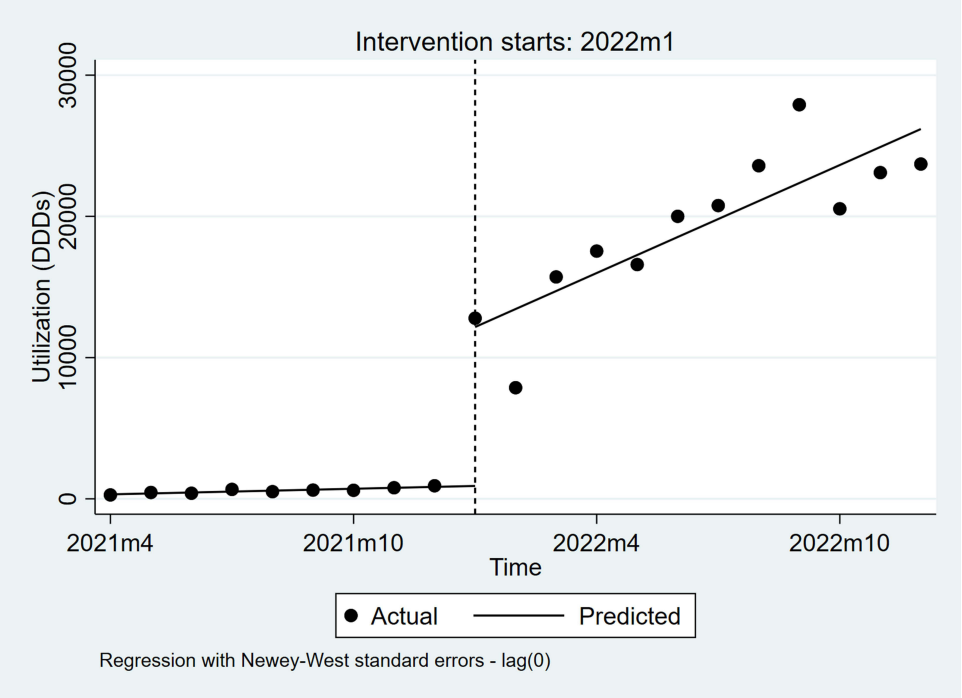

Figure 2 Observed and predicted utilization of negotiated anticancer drugs.

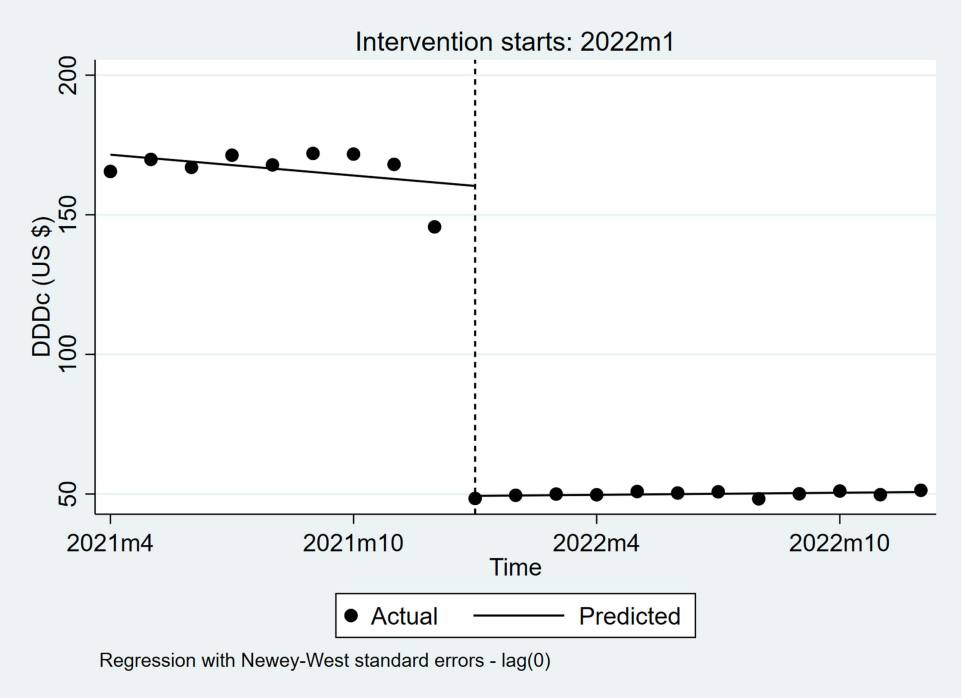

Figure 3 Observed and predicted DDDc of negotiated anticancer drugsP.

Policymakers are concerned about controlling the cost and improving the accessibility of medicines. The Chinese government has sought to address this issue through the NDPN policy. Negotiations on the price of innovative cancer drugs are not limited to China, but are also prevalent in Europe. Several European countries have begun negotiating the prices of new drugs with pharmaceutical manufacturers to obtain rebates.[23] Previous research has shown that the NDPN

policy resulted in substantial increases in procured volumes and notable reductions in DDDc of anticancer drugs,[9,12] which aligns with our findings.

After the policy's implementation, there was an immediate increase in availability. However, our observed availability of only 7.27% one year after NDPN was lower than the mean availability of 28.78% for negotiated anticancer medicines in 2018.[12] This difference may be due to several factors. Firstly, the specific drugs negotiated in 2018 may have had different clinical demands compared to those negotiated in 2021. Secondly, the period from market launch to inclusion in the NRDL for the anticancer drugs in our study was shorter than for the negotiated anticancer medicines in 2018. Newly launched drugs require time for physicians and patients to become acquainted with them and for their incorporation into clinical guidelines. Thirdly, in 2021, the government implemented a "dual-channel" management policy for negotiated medicine to further improve availability.[24] Patients can now obtain negotiated anticancer medicines at community pharmacies in addition to hospitals. Nevertheless, continuous monitoring and enhancement of anticancer drug availability are still needed.

The NDPN policy had a positive short-term and ongoing impact on the utilization of these anticancer drugs in the ITS analysis, indicating its success in increasing drug usage over time. This increase is likely due to reduced financial burden on patients, making the drugs more affordable and thus more widely used. It is important to consider regional disparities in anticancer drug utilization, as evidenced by higher usage in the eastern region compared to the western region. These disparities may be linked to socioeconomic factors, regional healthcare infrastructure, and differences in healthcare-seeking behaviors.[25] Policymakers should address these disparities to ensure equitable access to anticancer treatments across all regions.

The cost analysis revealed a substantial immediate decrease after the policy, and the DDDc remained stable one year after the intervention. This decrease in cost validates the negotiation's effectiveness in reducing the price of anticancer drugs, thereby improving affordability. This trend indicates the policy's success in not only making these drugs more affordable but also in maintaining their affordability over time.

There are a couple of limitations in the research. Firstly, in this ITS analysis, we did not include a control group because it was challenging to identify anticancer drugs with the same targets and indications that were unaffected by the policy. Secondly, due to the absence of procurement data from community pharmacies, this study only analyzed data of these drugs from hospitals. Thirdly, we did not analyze the reasons behind the regional disparities in anticancer drug utilization, which could be an area for further investigation in future studies.

Conclusion

The 2021 NDPN policy has demonstrated a positive impact on the availability, utilization, and cost of anticancer medicines in China. Although the policy has achieved significant improvement, continuous monitoring and evaluation are still needed to enhance the accessibility of anticancer drugs to the Chinese population.

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Disclosure

The authors report no conflicts of interest in this work.

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