BMJ Open

Impact of public health insurance coverage of novel anticancer medication on medical expenditure and patient affordability in a provincial medical centre of China: a propensity score-matching analysis with the quasi-experimental design

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To cite: Diao Y, Lin M, Xu K, *et al*. Impact of public health insurance coverage of novel anticancer medication on medical expenditure and patient affordability in a provincial medical centre of China: a propensity score-matching analysis with the quasi-experimental design. *BMJ Open* 2022;**12**:e054713. doi:10.1136/bmjopen-2021-054713

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-054713).

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Received 22 June 2021
Accepted 28 January 2022

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ABSTRACT

Introduction Little is known about the impact of the government's efforts in having novel anticancer medicines covered by the public health insurance system in China. This study targeted the above policy implemented in Fujian province in 2017, analysed the policy impact on the medical expenditure of cancer treatment and patient affordability based on the clinical data of Fujian provincial medical centre.

Methods The study included 253 human epidermal growth factor receptor 2-positive patients with breast cancer who completed at least one course of trastuzumab treatment extracted from the hospital health information system of the provincial medical centre of Fujian. We adopted the propensity score-matching method to mimic a quasi-experimental design to estimate the impact of the public health insurance coverage policy on all the indicated patients with a before–after comparison of the total breast cancer-associated direct medical expenditures for a standard course of treatment or maintenance treatment and the proportionate patient out-of-pocket (OOP) expenditure based on the real clinical data.

Results We found evidence of an association between the public health insurance coverage of novel breast cancer medication and the reductions of the medical expenditure by US$18661.02 (95% CI 13 836.57 to 28 201.45), and the proportionate patient OOP expenditure by 24% (95% CI0.20 to 0.27). The medical expenditure and the proportionate patient OOP expenditure might be generally reduced.

Conclusions The coverage of innovative antibreast cancer medicines by the public health insurance was found to be associated with a reduction of the medical expenditure and share of patient OOP expenditure for cancer treatment of the indicated patients. Patients with lower ability-to-pay did not benefit well from the coverage policy. To maximise the welfare of the public health insurance coverage of novel anticancer medication, the study called for strengthened health insurance benefit packages of the rural patient and the patient enrolled in the urban and rural resident health insurance programme, who might have lower ability-to-pay and need more support from the public security system.

Strengths and limitations of this study

- This study was based on the clinical data extracted from the electronic medical records, which filled the gap of real-world study of the public health insurance coverage of novel anticancer medications in China.
- The quasi-experimental study design contributed to the generation of robust evidence about the impact of the above policy.
- This is a single-centre study with limited sample size, future multicentre studies may help to reduce the potentially biased sampling.
- Collecting patients' income and linking medical expenditure with patient ability-to-pay may be a more comprehensive measurement of patient affordability for future studies.

INTRODUCTION

Novel anticancer medicines provide hope of life for patients, while presents economic challenges to households and healthcare systems because of the high cost. Like many upper middle-income countries, China started to improve patient financial access to innovative high-cost anticancer medicines that are clinically needed since 2016. A series of novel anticancer medicines were included in the national basic health insurance reimbursement list through price negotiations between the National Healthcare

Security Administration and the Research and Development (R&D) based pharmaceutical companies.[1–4] Although the prices of these novel anticancer medicines have been reduced by more than 50% on average, there are increasing concerns that some patients may still have financial difficulties in adopting these medicines for treatment.

The current public health insurance system provides universal coverage (UC) of Chinese population. It is composed of two parallel programmes, the urban employee programme and the urban and rural resident programme, which are cofunded by the government, society and individuals. Enrollees of the employee programme pay much higher contribution and are entitled to better benefits packages (deductible, proportion and cap of insurance reimbursement) than those of the resident programme. The insured patient pay out-of-pocket (OOP) for the deductible (up to US$300) before insurance reimbursement and 30% to 50% of the subsequent expenditures before reaching the caps of insurance reimbursement for outpatient care (up to US$3000) and inpatient care (up to US$80 000). After which, each additional dollar has to be paid OOP by patient. A study estimated the OOP expenditure of a standard course of medication with the novel anticancer medicines newly covered by a local basic health insurance programme in 2015. It was found that rural patients still had to pay 1.8–4.4 times of the annual per capita disposable income for the OOP expenditure of cancer medication with the novel anticancer medicines of interest after the public health insurance coverage.[5] 2021 is the fifth year of the implementation of the national public health insurance coverage of novel anticancer medicines. Some studies reviewed the benefits packages of the newly covered novel anticancer medicines in different regions.[6–9] One non-controlled study found an increased outpatient service utilisation and a reduction of the average proportionate patient OOP expenditure per outpatient visit/per hospitalisation in a cancer hospital after the implementation of the public health insurance coverage.[10] One study found a 70.79% increase in the number of patients with breast cancer who used trastuzumab 1 year after the insurance coverage in a pioneer province in 2013.[11] Another study monitored the annual breast cancer treatment costs of 17 human epidermal growth factor receptor 2 (HER2)-positive patients with breast cancer who used trastuzumab during 2011 and 2015, and found that their annual average proportionate OOP expenditures were about 34%.[12] The limited existing evidence was either descriptive analysis or simple before and after comparison without control. Breast cancer has been the most common cancer in women globally, and the treatment of breast cancer including the targeted treatment with the health insurance newly covered trastuzumab has been rather standardised in China. This study took breast cancer as an example, based on the real-world clinical data of the medical centre of Fujian province, quantified the impact of this policy on all the indicated patients about their medical expenditure and affordability for cancer medication.

METHODS

Study design

We divided the targeted patients into ‘before’ group and ‘after’ group by the time when Fujian province started to implement the public health insurance coverage of the medicines of interest in September 2017. We adopted the propensity score-matching (PSM) method by calculating the propensity score of each patient based on their demographic, socioeconomic and clinical characteristics. We matched the patients with the most similar propensity scores between the two groups to mimic a quasi-experimental design to achieve randomisation, which helped to reduce the selection bias and control the hidden confounders of direct before and after comparison.[13–16] We also performed pooled ordinary least square (OLS) regression to estimate the difference between the two groups by including a series of covariates to control the demographic, socioeconomic and clinical characteristics of patients.

Participants and setting

Fujian province locates in southern China with a medium economic development level. This study took the provincial medical centre of Fujian as the study setting. In September 2017, two novel antibreast cancer medicines were covered by Fujian provincial basic health insurance—lapatinib and trastuzumab. The insurance covered indication of trastuzumab was advanced and progressed HER2-positive invasive breast cancer, and that of lapatinib was HER2-positive invasive breast cancer following the treatment of trastuzumab. According to the national diagnosis and treatment guidelines[17 18] and the requirement of the national health insurance programme,[2] only HER2-positive patients with breast cancer diagnosed and treated by Fujian provincial medical centre between 1 January 2015 and 30 June 2018 were included in this study. No one used lapatinib. Considered that trastuzumab was very expensive before insurance coverage, and some patients with rich HER2-positive adopted trastuzumab treatment before insurance coverage. To compare the patient affordability of the overall population of patients with HER2-positive (who were all eligible to trastuzumab treatment, but in reality, some were treated with trastuzumab, some were not) before and after the insurance coverage, we must secure that patients in the ‘before’ group and ‘after’ group were balanced in terms of under treatment of traditional chemotherapy (covered by health insurance programme for both groups) or combined with trastuzumab (trastuzumab was not covered by the health insurance programme and totally paid OOP by the patients in the ‘before’ group; trastuzumab was covered by health insurance programme for the patients in the ‘after’ group). To analyse the medical expenditure of a complete course of treatment, the study only included the patients

who completed a standard course or maintenance treatment until progression. Patients who completed such a treatment course between 1 January 2015 and 31 August 2017 were categorised in the 'before' group, and those who completed a treatment course between 1 September 2017 and 30 June 2019 were categorised in the 'after' group. The following patients were excluded:

1. The patient was diagnosed but not treated in Fujian provincial medical centre.
2. The patient undertook surgery in other hospitals.
3. The patient did not complete at least a full course of treatment as defined by the national guidelines.
4. The patient with contraindications of the medicines targeted by this study.

Patient and public involvement

The patients and the public *were not* directly involved in the design, or conduct, or reporting, or dissemination plans of this research. However, the study was initiated by academicians considering the public debates about equal access to affordable novel anti-cancer medicines.

Source of data

The study was based on the hospital information system (HIS), which included the electronic medical record database, expense settlement database for the inpatient and outpatient care, and the prescription database.

1. The demographic and social information (gender, date of birth, address of household registration, type of health insurance, venue of care) of patients were extracted from the medical record database.
2. The disposable income level of the patient household registration area was obtained from the Provincial Statistics Yearbook.[19]
3. The service utilisation (the date of each outpatient visit and dates of the hospital admissions and discharges) and the diagnosis of each visit and hospitalisation of the patient targeted by this study were extracted from the medical record database.
4. The aggregated and disaggregated expenses of each visit and hospitalisation (total expense, expenses of medicines, laboratory test and examination, surgery, etc and the expense paid by patient OOP and covered by the health insurance) were extracted from the expenditure and prescription database. Expenditures of breast reconstruction were excluded.

Measurements

The study defined medical expenditure as the total expenditures of all breast cancer-associated diagnosis, surgery, radiotherapy and endocrine therapies in combination with the traditional chemotherapy or the targeted medication during the full course of the standard treatment for stage I, II and III patients, and the maintenance treatment for stage IV patient (metastasis or recurrence). A standard course of chemotherapy ranged from 4 to 8 waves of hospitalisation (21 days per wave) for different therapy combinations, starting from initial diagnosis to the last hospitalisation within 3–6 months. A standard course of targeted medication is 1 year in total, 7 days per wave of treatment with a lower dose or 21 days per wave of treatment with a higher dose. The maintenance treatment for stage IV patients continued until progression or intolerance,[17 18] which started from the initial diagnosis of the metastasis or recurrence to the last hospitalisation before 1 September 2017 for the patient in the 'before' group, and before 30 June 2019 for the patient in the 'after' group. Considering that the actual length of treatment in the real clinical setting might not be the same as the recommendations of the national guidelines, we carefully reviewed all the medical records of each patient targeted by this study to identify the full course of actual treatment and expenditure.

Patient affordability was measured by the share of patient OOP expenditure of breast cancer-related inpatient and outpatient care during the full course of the standard treatment or the maintenance treatment, from the initial diagnosis to the last hospitalisation.

The disposable income level of the patient household registration area was divided into three categories as follows, low-income level with the annual average disposable income lower than CNY 15 000 (equivalent to US$2300, exchange rate=7); middle-income level (between CNY 15 000–35 000, equivalent to US$2300–US$5400) and high-income level (above CNY 35 000, equivalent to US$5400).

Statistical analysis

The study conducted the PSM analysis by having the multidimensional characteristics of patients transformed into a single-dimensional propensity score. Based on which, we balanced the demographic, socioeconomic and clinical characteristics as well as tumour progression stage and medication option of patients between the 'before' and 'after' groups. All of the above characteristics of the patients were included in the logistic regression model as covariates. The conditional variable was 'before' and 'after' the insurance coverage policy ('before'=1 and 'after'=0). Patients in the 'before' and 'after' groups with similar propensity scores were matched and created two new groups, which was a mimic of quasi-experimental design with randomisation. Considering that the sample size of patients was not a large one, the nearest-neighbour matching (1:1, with replacement, calliper=0.25σ) was applied. We used a t test of two independent samples as well as the % of bias to double check the balance in each subcategory of each covariate between the matched 'before' and 'after' groups (online supplemental appendix 1). The statistically significant level was set at a=0.05. Based on the matched patients, we obtained the average treatment effect of the policy on the medical expenditure and the patient affordability. We conducted the bootstrap sampling (repetition=50) to estimate the 95% CI.[13 14 20–23]

To maximise the use of the available information, we performed the non-parametric regression of Kernel

matching (epan, bandwidths=0.06). We estimated the weighted policy effect based on the differences of the outcome variables between the matched patients in the 'before' and 'after' groups.[24] We also conducted general linear regression analysis based on Ordinary Least Square (OLS) to estimate the policy impact with the coefficient of the binary category variable ('before' group=1; 'after' group=0). The statistical analyses were performed by STATA 15.

Sensitivity analysis

Sensitivity analysis of the PSM estimate to the matching method and bandwidth

To evaluate the sensitivity of the PSM estimates to the choice of matching methods and different Kernal functions and bandwidths, in addition to the default epan function and bandwidth of 0.06, we also estimated with other Kernal functions (normal, biweight, uniform, tricube), and with a range of bandwidths (0.01, 0.06, 0.1). Considering the sample size was not a large one, 1:n matchings were not performed.[25 26] The study used the same methods to test the balance of the matched patients and bootstrap sampling (repetition=50).

Sensitivity analysis with Rosenbaum bounds to test for potential hidden bias

Considered that the observed characteristics of the patients were limited to the information that could be extracted from the hospital health information system, the unobserved characteristics might be biasing estimation of the treatment effect, like the ability-to-pay for healthcare of the patients and their respective families, different preferences due to different education and other socioeconomic backgrounds, preference of the doctors and compliance of the diagnosis and treatment guidelines, etc. To test how strongly any potential unmeasured confounding variables that might undermine the causal effect estimation, we computed the Rosenbaum bounds with the command 'rbounds' for the continuous impact measurements, that is, the change in medical expenditure and the change of the proportionate patient OOP expenditure. Gamma reflected the assumption about unmeasured heterogeneity or endogeneity in treatment assignment. Estimates at Gamma=1 (no hidden bias) were included in the calculations by default. P values were the set level of hidden bias to a certain value of Gamma. At each level, we calculated a hypothetical significance level, which represented the bound on the significance level of the treatment effect in the case of endogenous self-selection into treatment status.[27 28] The significant variation range of Gammaat different values is presented in online supplemental appendix 2.

RESULTS

As presented in table 1, a total of 258 courses of treatment were included in this study. Of which, 179 courses of either standard treatment or maintenance treatment were before the implementation of the public health insurance coverage policy, and 79 courses of either standard treatment or maintenance treatment afterwards. A small number of patients had recurrence or metastasis after completing a standard course of treatment and continued with maintenance treatment. After performing the 1:1 nearest-neighbour matching, 228 patients were within the common support, of which 149 were in the 'before' group and 79 were in the 'after' group (table 2).

The balance test of the patients before and after the matching was presented in online supplemental appendix 1. The result of the t test showed no statistical difference between the matched 'before' and 'after' groups in each subcategory of each covariate. The % of bias of the sample patients after matching was all reduced and the reduction ranged between 6.5% and 100%. However, a number of the reported '% bias' values were above the commonly used threshold of 10% for some covariates, which implied potential bias for the impact estimation. Similar results were drawn for the pairs matched with other methods. We would look at the results of the calculation of the Rosenbaum bounds in the Sensitivity Analysis, to see if the potential hidden bias for the impact estimation is acceptable.

As presented in table 3, before performing the matching, the reduction of average medical expenditure after the public health insurance coverage of novel antibreast cancer medicines was US$10 173.49 (p<0.01, exchange rate: US$1=CNY 7). The PSM estimation with the 1:1 nearest-neighbour matching of the average treatment effect of the 'after' group was a reduction of US$18 661.02 (95% CI 13 836.57 to 28 201.45, p<0.01). The PSM estimation with Kernel matching of the average treatment effect was a reduction of US$19 906.64 (95% CI 14 827.78 to 29 041.33, p<0.01). Before performing the matching, the reduction of the average share of patient OOP expenditure after the public health insurance coverage of novel anti-breast-cancer medicines was 11% (p<0.01). The PSM estimation with 1:1 nearest-neighbour matching of the average treatment effect was a reduction of 24% (95% CI 0.20 to 0.27, p<0.01). The PSM estimation with Kernel matching of the average treatment effect was a reduction of 23% (95% CI 0.17 to 0.28, p=0.04).

The OLS model for the estimation of medical expenditure and proportionate patient OOP expenditure between the 'before' and 'after' groups was with accepted goodness of fit as presented in table 3. The medical expenditure after the public health insurance coverage of novel antibreast cancer medicines was US$32 452.66 (95% CI 25 144.67143 to 39 760.64, p<0.01) lower than before, and that for the share of patient OOP expenditure was 19% (95%CI 0.12 to 0.26, p<0.01) lower than before.

Simple estimates of the policy impacts were the differences of the average medical expenditures and the proportionate patient OOP expenditures of the unmatched patients between the 'before' and 'after' groups (US$10173.49% and 11%), which were much

Table 1 Distribution of the sample patient before and after performing the 1:1 nearest-neighbour matching (with replacement)

Characteristic of patients		Before performing matching (n=258)		After performing matching (n=228)	
		'Before'group n=179 (%)	'After'group n=79 (%)	'Before'group n=149 (%)	'After'group n=79 (%)
Age	<40 years old	9 (5.0)	8 (10.1)	8 (5.4)	8 (10.1)
	40–49 years old	44 (24.6)	23 (29.1)	36 (24.2)	23 (29.1)
	50–59 years old	74 (41.3)	27 (34.2)	62 (41.6)	27 (34.2)
	>60 years old	52 (29.1)	21 (26.7)	43 (28.9)	21 (26.7)
Household registration area	Urban	80 (44.7)	39 (49.4)	71 (47.7)	39 (49.4)
	Rural	99 (55.3)	40 (50.6)	78 (52.3)	40 (50.6)
Disposable income level of patient' s household registration area	Low	72 (40.2)	43 (54.4)	71 (47.7)	43 (54.4)
	Middle	60 (33.5)	21 (26.6)	41 (27.5)	21 (26.6)
	High	47 (26.3)	15 (19.0)	37 (24.8)	15 (19.0)
Type of public health insurance coverage	Urban employee programme	55 (30.7)	27 (34.2)	48 (32.2)	27 (34.2)
	Urban and rural resident programme	100 (55.9)	39 (49.4)	79 (53.0)	39 (49.4)
	Non-insured	24 (13.4)	13 (16.5)	22 (14.8)	13 (16.5)
Local/non-local patient	Local	120 (67.0)	49 (62.0)	96 (64.4)	49 (62.0)
	Non-local	59 (33.0)	30 (38.0)	53 (35.6)	30 (38.0)
Tumour progession stage	Stage I	29 (16.1)	11 (13.9)	23 (15.4)	11 (13.9)
	Stage II	94 (52.5)	44 (55.7)	85 (57.0)	44 (55.7)
	Stage III	42 (23.5)	18 (22.8)	33 (22.1)	18 (22.8)
	Stage IV	14 (7.8)	6 (7.6)	8 (5.4)	6 (7.6)
Medication choice	Not used trastuzumab	124 (69.3)	29 (36.7)	95 (63.8)	29 (36.7)
	Used trastuzumab only and no other novel medicines	53 (29.6)	47 (59.5)	52 (34.9)	47 (59.5)
	Used trastuzumab and other novel medicines	2 (1.12)	3 (3.80)	2 (1.34)	3 (3.80)

lower than PSM estimates with the 1:1 nearest-neighbour matching (US$18 661.02% and 24%) and Kernel matching (US$19 906.64% and 23%). The SEs of the simple estimates were the largest (SE=3 8640.42 for the medical expenditure estimate; SE=0.03 for the share of patient OOP expenditure estimate). The OLS estimate of the reduction of medical expenditure was the highest, and its SE (SE=3 8640.42) was larger than that of the PSM estimates (SE=2 8750.54 for 1:1 nearest-neighbour matching; SE=3 6890.46 for Kernel matching) (tables 3 and 4).

Table 2 Number of sample patients within and off the common support after performing the 1:1 nearest-neighbour matching

	Total	On support	Off support
'Before' group	179	149	30
'After' group	79	79	0
Total	258	228	30

The sensitivity analyses showed that the PSM estimates were not sensitive to the selection of matching methods and bandwidths. The PSM estimates with different bandwidths and Kernel functions were consistent with each other. The medical expenditures ranged between US$16 398.86 and US$20 698.00, and the share of patient OOP expenditures ranged between 20% and 24% (table 5). The robustness to hidden bias varies between our two policy impact estimations. The critical level of Gamma at which we would have to question our conclusion of a medical expenditure reduction effect was between 5.5 and 6, and that was between 1.55 and 1.6 for a reduction of the share of patient OOP expenditure (online supplemental appendix 2). From these findings, we would conclude that our estimations were generally robust, and we would be more confident about the medical expenditure reduction estimation than the reduction of the proportionate patient OOP expenditure.

Table 3 PSM estimates of the impact of the public health insurance coverage of the anti-breast cancer novel medicines on the treatment expenditure and the proportionate patient OOP expenditure

Measurement	Estimation method	Average policy impact			Bootstrap sampling				
		'Before' group	'After' group	Difference	SE	Z	P value	Difference	SE	Z	P value	95% CI (lower, upper)
Medical expenditure	Unmatched	31 892.66	21 719.17	10 173.49	3 864.42	2.63	<0.01					
	1:1 nearest-neighbour matching	34 118.91	14 042.15	20 076.76	2 875.54	8.92	<0.01	18 661.02	3 686.63	4.92	<0.01	13 836.57 to 28 201.45
	Kernel matching	33 187.43	12 010.39	21 177.04	3 689.46	5.72	<0.01	19 906.64	3 882.56	5.52	<0.01	14 827.78 to 29 041.33
Proportionate patient OOP expenditure	Unmatched	0.62	0.51	0.11	0.03	3.14	<0.01					
	1:1 nearest-neighbour matching	0.73	0.50	0.23	0.02	7.91	<0.01	0.24	0.02	2.49	0.01	0.20 to 0.27
	Kernel matching	0.73	0.51	0.22	0.03	6.65	<0.01	0.23	0.04	2.14	0.03	0.17 to 0.28

OOP, out-of-pocket; PSM, propensity score matching.

DISCUSSION

This study found associations between the public health insurance coverage of novel antibreast cancer medicines and the reductions of medical expenditure as well as the proportionate patient OOP expenditure of HER2-positive breast cancer treatment in Fujian provincial medical centre. There was no breast cancer treatment-related local policies issued and no clinical pathway update during the observation time of this study. We assumed that there were no significant changes in the patients and the diagnosis and treatment behaviours in Fujian provincial medical centre during the observation time of this study. Apart from the price reduction when trastuzumab was covered by health insurance, the prices of chemotherapies and endocrine therapies as well as surgeries kept stable over the study time. The differences in the medical expenditures among different combinations of chemotherapy and endocrine therapy were low and could be neglected. Therefore, we concluded that the reductions of medical expenditure and share of patient OOP expenditure for HER2-positive breast cancer treatment were attributed to the public health insurance coverage of novel antibreast-cancer medicines.

As shown in table 1, the proportion of patients who adopted trastuzumab for treatment increased from 29.9% before the public health insurance coverage to 61.8% afterwards. Nearly 40% of patients with the insurance covered indication did not choose trastuzumab for treatment. This implied that quite a large number of patients did not benefit from the public health insurance coverage of novel antibreast cancer medicines, even though strong evidence supported that trastuzumab has outstanding clinical effects compared with the other existing therapies.[29 30] One of the critical reasons might probably be patient affordability.

Although the share of patient OOP expenditure was significantly reduced generally, OLS estimates showed significant differences between different patient groups. The rural patients had a 12% higher OOP share than urban patients, the patients enrolled in urban and rural resident health insurance programme had 16% higher OOP share than patients enrolled in urban employee health insurance programme, and the non-local medical patients had a 6% higher OOP share than local medical patient. Assumed that all diagnoses and treatments complied with the national guideline, the difference of the proportionate patient OOP expenditure would be attributable to different health insurance benefits packages of different patients. Rural patients, patients enrolled in urban and rural resident health insurance programme and non-local medical patients were entitled to relatively weak health insurance benefit packages. These patients might be the ones who still had the affordability problem and, thus, might be less likely to benefit from the public health insurance coverage of novel antibreast cancer medicines. Another study[31] analysed the utilisation of trastuzumab of the patients covered by the public health insurance programme of Fuzhou city during 2016–2018.

Table 4 OLS estimates of the impact of the public health insurance coverage of the anti-breast-cancer novel medicines on the treatment expenditure and the proportionate patient OOP expenditure

	Medical expenditure						Proportionate patient OOP expenditure					
Variable	Unadjusted coefficient (95% CI)	SE	Standardised coefficient (95% CI)	SE	t	P value	Unadjusted coefficient (95% CI)	SE	Standardised coefficient (95% CI)	SE	t	P value
Implementation of the public health insurance coverage policy (Ref. Before group)												
After group	−32 452.66 (−39 760.64 to 25 144.67)	3 839.34	−0.56 (−0.72 to −0.41)	0.04	9.47	<0.01	−0.19 (−0.26 to −0.12)	0.03	−0.47 (−0.51 to −0.29)	0.06	5.84	<0.01
Age (Ref. <40 years old)												
40–49 years old	875.35 (234.73 to 1 440.31)	475.62	0.05 (−0.11 to 0.18)	0.09	0.21	0.84	0.01 (−0.07 to 0.04)	0.03	0.02 (−0.20 to 0.19)	0.10	0.48	0.63
50–59 years old	1 006.26 (247.53 to 1 640.80)	469.05	0.09 (−0.08 to 0.22)	0.08	0.58	0.56	0.02 (−0.03 to 0.06)	0.02	0.08 (0.13 to 0.30)	0.10	0.44	0.66
>60 years old	833.11 (256.03 to 1 495.07)	435.35	0.06 (−0.11 to 0.19)	0.09	0.16	0.87	0.01 (−0.05 to 0.06)	0.03	0.03 (−0.18 to 0.24)	0.11	0.14	0.89
Household registration area (Ref. Urban)												
Rural	−7496.63 (−16027.60 to 444.08)	4180.58	−0.29 (−0.38 to −0.17)	0.05	1.86	0.06	0.12 (0.06 to 0.18)	0.04	0.41 (0.21 to 0.58)	0.11	2.27	0.02
Disposable income level of patient's household registration area (Ref. Low)												
Middle	5298.60 (1625.01 to 9656.50)	3 815.29	0.19 (0.08 to 0.31)	0.07	1.28	0.20	−0.06 (−0.15 to 0.03)	0.05	0.13 (−0.03 to 0.30)	0.08	1.44	0.15
High	5672.68 (1272.10 to 10 331.74)	4 053.71	0.21 (0.04 to 0.38)	0.07	1.49	0.14	−0.09 (−0.15 to 0.03)	0.03	0.32 (0.13 to 0.45)	0.07	2.09	0.03
Type of insurance coverage (Ref. Urban employee programme)												
Urban/rural resident programme	−757.29 (−2891.36 to 2291.07)	1 830.16	−0.08 (−0.20 to 0.07)	0.09	0.23	0.82	0.16 (0.08 to 0.25)	0.04	0.28 (0.11 to 0.45)	0.08	3.93	<0.01
Non-insured	−3281.75 (−7347.25 to 498.03)	2 085.42	−0.22 (−0.32 to −0.11)	0.04	5.52	<0.01	0.69 (0.57 to 0.79)	0.05	0.45 (0.32 to 0.55)	0.06	5.37	<0.01
Venue of medical care (Ref. Local)												
Non-local	−2726.82 (−6874.81 to 564.03)	2 105.55	−0.25 (−0.33 to −0.17)	0.05	3.75	<0.01	0.06 (0.02 to 0.13)	0.03	0.17 (0.05 to 0.30)	0.05	2.09	0.03
Tumour progression stage (Ref. Stage I)												
Stage II	806.32 (−193.01 to 1670.38)	575.6	0.17 (0.06 to 0.30)	0.06	1.91	0.06	0.01 (−0.12 to 0.11)	0.05	0.02 (−0.13 to 0.15)	0.07	0.16	0.87
Stage III	6133.37 (2429.56 to 7305.67)	2 514.31	0.32 (0.22 to 0.41)	0.05	2.98	<0.01	0.001 (−0.09 to 0.10)	0.05	0.01 (−0.15 to 0.14)	0.07	0.05	0.96
Stage IV	5689.88 (2335.86 to 6670.38)	2 691.87	0.34 (0.25 to 0.42)	0.05	3.62	<0.01	0.003 (−0.09 to 0.10)	0.04	0.03 (0.09 to 0.15)	0.06	0.06	0.94
Medication choice (Ref. Not used any novel medicines)												
Used novel medicines	40 932.81 (34 608.10 to 47 257.54)	3 210.48	0.76 (0.68 to 0.84)	0.03	16.15	<0.01	0.41 (0.33 to 0.47)	0.03	0.29 (0.18 to 0.39)	0.06	8.48	<0.01
Constant	15 034.54 (−18 771.51 to 2 988.13)	4 862.74	/	/	1.64	0.10	0.16 (0.04 to 0.31)	0.06	/	/	2.57	0.01

Bold implies statistically significant; F=18.65 (p<0.001), adjusted R^2=0.613, Durbin-Watson test statistic=1.803 (medical expenditure model); F=20.07 (p<0.001), adjusted R^2=0.637, Durbin-Watson test statistic=1.792 (share of patient OOP expenditure model).
OLS, ordinary least square; OOP, out-of-pocket.

Table 5 Sensitivity analysis of the PSM estimates to the matching methods and bandwidths

		Medical expenditure					Share of patient out-of-pocket expenditure				
		Difference	SE	t	P value	95% CI (lower, upper)	Difference	SE	t	P value	95% CI (lower, upper)
1:1 nearest-neighbour matching with replacement		18 661.02	3 686.63	4.92	<0.01	13836.57 to 28201.45	0.24	0.02	2.49	0.01	0.20 to 0.27
Kernel matching(epan)	Bandwidth=0.10	20 698.00	3 541.32	5.86	<0.01	14 519.57 to 28 893.69	0.22	0.04	3.25	<0.01	0.14 to 0.29
	Bandwidth=0.06	**19 906.64**	**3 882.56**	**5.52**	**<0.01**	**14827.78 to 29041.33**	**0.23**	**0.04**	**6.65**	**<0.01**	**0.20 to 0.27**
	Bandwidth=0.01	16 702.45	3 663.75	4.49	<0.01	13 362.95 to 30 248.39	0.21	0.05	1.14	0.21	0.02 to 0.33
Kernel matching (normal)	Bandwidth=0.10	19 626.64	3 328.24	5.89	<0.01	14 630.24 to 28 383.54	0.22	0.04	3.14	<0.01	0.16 to 0.27
	Bandwidth=0.06	19 283.61	3 442.67	5.92	<0.01	14 952.28 to 28 883.52	0.22	0.03	6.55	<0.01	0.21 to 0.27
	Bandwidth=0.01	18 824.45	3 632.55	5.76	<0.01	13 960.37 to 29 251.22	0.22	0.05	2.22	0.02	0.11 to 0.29
Kernel matching (biweight)	Bandwidth=0.10	20 539.16	3 566.75	5.78	<0.01	14 131.67 to 28 282.35	0.21	0.05	3.45	0.01	0.15 to 0.29
	Bandwidth=0.06	20 890.21	3 637.28	5.76	<0.01	15 041.82 to 28 950.62	0.23	0.03	6.41	<0.01	0.20 to 0.27
	Bandwidth=0.01	16 417.86	3 642.82	4.54	<0.01	13 765.47 to 29 876.42	0.21	0.05	1.17	0.24	0.01 to 0.31
Kernel matching (tricube)	Bandwidth=0.10	20 534.24	3 562.54	5.95	<0.01	14 221.58 to 29 023.47	0.22	0.05	3.47	0.01	0.12 to 0.30
	Bandwidth=0.06	20 894.75	3 623.65	5.76	<0.01	14 960.41 to 28 851.66	0.23	0.04	6.38	<0.01	0.19 to 0.27
	Bandwidth=0.01	16 398.86	3 615.06	4.45	<0.01	12 955.78 to 29 747.86	0.21	0.05	1.18	0.24	0.02 to 0.34
Kernel matching (uniform)	Bandwidth=0.10	20 341.20	3 460.33	5.92	<0.01	14 732.56 to 28 779.48	0.21	0.04	3.11	<0.01	0.13 to 0.28
	Bandwidth=0.06	20 510.54	3 586.54	5.61	<0.01	15 118.24 to 28 661.09	0.22	0.03	6.57	<0.01	0.21 to 0.29
	Bandwidth=0.01	16 452.45	3 628.16	4.64	<0.01	13 024.65 to 31 026.36	0.20	0.05	1.07	0.28	0.01 to 0.33

PSM, propensity score matching.

Which found that only 25 patients adopted trastuzumab for treatment during January 2016–September 2017 (before insurance coverage), and this number grew to 694 during October 2017–December 2018 (after insurance coverage); 0/25 and 100/694 (14.4%) patients completed at least one full course of treatment. The patient interview might give part of the reasons behind such a low rate—14/15 interviewed patients were advised by the physicians to adopt trastuzumab treatment combined with the chemotherapy, 11/14 felt that the adverse reaction of the chemotherapy combined with trastuzumab was tolerable, 10/15 had to borrow money to cover the patient OOP expenditure.[32] This implied that those patients in financial hardship might be forced to cease the treatment. Patient affordability might still be a barrier to the adoption of the public health insurance newly covered novel anticancer medicines and the completion of a full course of treatment.

A multicentre study on breast cancer treatment in eastern China disclosed a similar fact that more patients in high-disposable income level areas adopted novel anticancer medicines for treatment than those in less developed areas (37.3% vs 13.0%).[33] Two studies in Mexico also identified a similar phenomenon. After the expensive novel anticancer medicines were coverage by the social health insurance programmes, utilisation of the newly covered medicines in developed regions was higher than that in less developed regions, and medicines utilisation of patients enrolled in better health insurance programmes (with a better benefits package, like the programmes for the oil company staff, etc) was higher than that of those enrolled in a health insurance programme with weaker benefits package.[34 35] A study in the USA and other developed countries also showed that patients with different demographic, social and economic characteristics had disparities in adoption of novel anticancer medications. A cohort study of HER2-positive patients with breast cancer based on the Medicare data found that, within 1 year of being diagnosed, the proportion of the white patient treated with novel antibreast cancer medicines was significantly higher than that of the black. By controlling the other factors, the likelihood of the black choosing novel antibreast cancer medicines was only 75% of that of the white.[36] A global survey about access to first-line recommended novel treatments for metastatic melanoma in 34 countries found that access to innovative medicines was associated with both economic and healthcare system performance parameters.[37]

Thailand seemed to be an excellent example for developing countries. It started to include novel medicines in its national essential medicines list under the 'high-cost medicines E2 access programme' (E2 list) and committed universal access with no patient copayment since 2009. A study demonstrated that the average quarterly medical expenses across the country were 17.2% lower than the projected level in case that E2 list was not implemented 2 years after the implementation of E2 list. This proportion of the UC beneficiaries (the population with lower ability-to-pay) reached 34.2%. The cost reduction level of the population with lower ability-to-pay was significantly higher than that of the other populations, which implied that the E2 list well benefited the vulnerable patients. E2 programme has been associated with an increasing number of patients receiving specialty medicines, especially among the UC beneficiaries (the population with lower ability-to-pay) who constituted the majority of the Thai population. It may have improved clinical outcomes.[38–40]

Both domestic and international studies demonstrated that the effect of public health insurance coverage of novel anticancer medicines on patients depended on the patient's health insurance benefit package. To secure that the most vulnerable patients benefit from the public health insurance coverage of novel antibreast cancer medicines, it is critical to set a universal minimum benefit package for all when introducing the coverage policy like in Thailand, and abandon the financing model to have the patient with lower ability-to-pay entitled with weaker health insurance benefits package.[41]

This study was based on the clinical data collected from one hospital during a certain period. It is possible to reduce the potential sampling bias to a certain extent through multicentre studies. Larger size of sample may be helpful to have more power for extrapolation of the conclusion of the study. In addition, the size of on-support samples is an essential factor affecting the selection of matching methods and the robustness of the study.[23] If the sample size could be further expanded, especially for the sample size of the 'after' group, better common support might lead to more accurate policy impact estimation. The critical assumption of applying PSM method was that there was no critical unobserved variable. In reality, this is difficult to achieve. As discussed before, there were 'unmeasured confounding' that might be biasing estimation of the treatment effect, like the ability-to-pay of healthcare of the patients and their respective families, different preferences of the patients due to different education and other socioeconomic backgrounds, preference of the doctors and compliance of the diagnosis and treatment guidelines, etc'.

Accurate expenditure data are critical for appropriate estimation of both medical expenditure and the proportionate patient OOP expenditure. Some patients might benefit from the patient assistance programme,[42 43] which were not captured by the hospital HIS. However, the study team reviewed the electronic medical records of all the patients in the 'before' group and added the missing medicines expenditures for those who had a record of adopting trastuzumab but had no medicines expenditure record. This study also ignored the health expenditure growth and the change of the monetary inflation factor from 2015 to 2019.

This study analysed the effect of the public health insurance coverage of novel antibreast cancer medicines on the proportionate patient OOP expenditure. While linking the medical expenditures with the ability-to-pay of the patient may be a more comprehensive measurement of patient affordability. It is also valuable to collect patients' income and indirect medical expenses in future studies.

CONCLUSIONS

This study found the associations between the coverage of innovative antibreast cancer medicines by the public health insurance and a lower medical expenditure as well as a lower proportionate patient OOP expenditure for cancer treatment in the real clinical setting in Fujian provincial clinical centre. Rural patients, patients enrolled in urban and rural resident health insurance programme and non-local medical patients seemed not benefited well from this policy compared with the others. To maximise the welfare of the public health insurance coverage of the novel anticancer medication, this study called for strengthened health insurance benefits packages of rural patients and patients enrolled in urban and rural resident health insurance programmes, who might have lower ability-to-pay and need more support from the public security system.

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Acknowledgements The authors appreciated the health information system staff of Fujian Provincial Hospital who provided valuable support to extract data from various sources of databases.

Contributors YD, JS, HL contributed to the conceptualisation of the paper and study design. YD, KX, JH, XW and ML conducted the data collection, data clean and initial analyses. YD and ML performed the statistical analyses. All authors contributed to the data interpretation. YD wrote the first draft of the manuscript and visualisation of all tables and figures. JS and HL made substantial contributions to the validation, final data analysis, interpretation and critically revision of the manuscript. All authors have seen and approved the final version of the manuscript for submission. JS and HL were in charge of the overall project administration and supervision, JS was responsible for the overall content as the guarantor.

Funding This work was supported by Peking Union Medical College.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the Ethics Committee of Fujian Provincial Hospital. Not applicable/no human participants included.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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