Public health insurance and cancer-specific mortality risk among patients with breast cancer: a prospective cohort study in China

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Abstract

Background Little is known about how health insurance policies, particularly in developing countries, may influence breast cancer prognosis. We aimed to examine the association between individual health insurance plans and breast cancer-specific mortality among patients in China.

Methods We included 7,436 women diagnosed with invasive breast cancer between January 1 st , 2009, and December 31 st , 2016, at West China Hospital, Sichuan University. The health insurance plan of each patient was classified as either urban or rural schemes and was also categorized as reimbursement rate (i.e., the covered/ total charge) below or above the median. Breast cancer-specific mortality was the primary outcome. Using Cox proportional hazards models, we calculated hazard ratios (HRs) for cancer-specific mortality, contrasting rates among patients with a rural insurance scheme or low reimbursement rate to that of those with an urban insurance scheme or high reimbursement rate, respectively.

Results During the median follow-up of 3.1 years, we identified 326 deaths due to breast cancer. Compared with patients covered by urban insurance schemes, patients covered by rural insurance schemes had a 29% increased cancer-specific mortality (95% CI 0% to 65%, P=0.046) after adjusting for demographics, tumor characteristics, and treatment modes. Reimbursement rate below the median was associated with a 42% increased rate of cancer-specific mortality (95% CI 11% to 82%). Every 10% increase in the reimbursement rate is associated with a 7% (95% CI, 2% to 12%) reduction in cancer-specific mortality risk, particularly in patients covered by rural insurance schemes (26%, 95% CI 9% to 39%).

Conclusions Our findings suggest that under-insured patients with breast cancer in China face increased breast cancer-specific mortality, which may provide fresh insights into the role of reimbursement rate in cancer health disparities.

Background

Battling cancer is a crushing burden for all patients, but particularly so for those who are vulnerable to financial stress. It is common that cancer patients experience severe financial stress throughout their survivorship [1], especially in developing countries where the health system is not ready to ease the burden for everyone. Cancer patients have higher out-of-pocket costs and may be absent from work for quite a while, which further lowers the ability to pay for medical care [1, 2]. As an avalanche of “financial toxicity” – the damaging economic side effects of illness, cancer patients are at tremendous risk for debt, bankruptcy and impaired psychological wellbeing [3, 4].

The presence of a public health insurance system seems essential for a country to achieve universal health-care coverage and health equity [5]. Improved health insurance coverage can reduce sociodemographic disparities in cancer care, including breast cancer, through early diagnosis and optimal treatment [6, 7].Fewer studies have paid attention to the impact of health insurance on cancer prognosis. So far, four US studies [7–10], support the hypothesis that under-insured patients have a worse breast

cancer prognosis, but two other studies from Australia and Brazil reported no clear differences related to the level of health insurance [11–12]. However, it is largely unclear whether the health insurance policies particularly in developing countries, where the patients may face higher financial toxicity, influence breast cancer prognosis. Moreover, all reports have focused on insurance status or types, while no studies have addressed the out-of-pocket cost as an important barrier to cancer care [7–12]. It is, therefore, of critical importance to understand how different insurance plans, featured by varying reimbursement rates (i.e., the covered/ total charge) within specific insurance type, further contribute to the disparities in diagnosis, treatment, and prognosis of breast cancer.

Leveraging a prospective large-scale cohort of patients with invasive breast cancer in China diagnosed during 2009–2016, we aimed to examine the associations of health insurance types and reimbursement rates with the risks of breast cancer-specific mortality.

Methods

Study population

We identified 7,623 female patients who were diagnosed with invasive breast cancer at West China Hospital (WCH), Sichuan University from January 1st, 2009, to December 31st, 2016, based on the Breast Cancer Information Management System (BCIMS). The BCIMS covers virtually all patients with breast cancer diagnosed at WCH since 2008 and prospectively collects information on demographic and clinical characteristics, laboratory examinations, treatment, and follow-up visits [13]. We excluded 37 male patients, three patients due to loss to follow-up and 147 patients without the information on both type of health insurance and reimbursement rate, leaving 7,436 patients in the final cohort.

This study is approved by the Clinical Test and Biomedical Ethics Committee at West China Hospital, Sichuan University (reference number 2012-130). Consent forms have been obtained from all participants.

Health insurance

There are three major state-run schemes of public health insurance, including the new rural cooperative medical scheme (NRCMS, covering the residents of rural households and launched in 2003), urban resident-based basic medical insurance scheme (URBMI, covering the unemployed, children, and elderly and launched in 2007), and urban employee-based basic medical insurance scheme (UEBMI, covering employees and launched in 1998) [13]. The reimbursement rate is defined as the amount of medical expense covered by insurance divided by the total expense. As the insurance is partly funded by local governments, the reimbursement rates may vary widely across counties, even under the same insurance scheme. Moreover, the rate is individual-based, affected and calculated by age, years of employment, hospital level, and treatment modes.

The information on insurance types and reimbursement rates (for the primary treatment) is routinely documented in BCIMS. Specifically, the information on the type of insurance is provided by patients at the registration to BCIMS, while the rate of reimbursement is collected for the primary treatment during follow-up. Given the different administrations and insurance plans (see details in Additional file 1), we classified insurance types into urban (i.e., URBMI, UEBMI, and/or commercial insurances) and rural (i.e., NRCMS) schemes, respectively. In the analysis of insurance type, 139 patients without any insurance and eight patients of unknown insurance status were excluded. Our data showed that the reimbursement rate was different among patients insured by urban or rural schemes (see Additional file 2). We also classified patients by reimbursement rate below (0-69%) or above (70%-100%) the median. Patients without insurance were coded as 0 reimbursement rate. 569 patients (192 insured by rural schemes) were excluded from this analysis due to unknown reimbursement rate.

Breast cancer-specific and overall mortality

All patients were actively followed through telephone contact and medical visits until death or May 17st, 2017, whichever came first. The underlying cause of death was ascertained from the medical records, whenever possible, or informed by the immediate family members. We studied breast cancer-specific mortality as the primary outcome and overall mortality as the secondary outcome.

Statistical Analysis

First, we described the demographic and clinical characteristics among patients with different insurance types and reimbursement rates. Demographic and clinical characteristics were obtained from BCIMS and classified as showed in Table 1. We examined the associations of health insurance type and reimbursement rate with different treatment modes, using logistic regression with adjustment for demographic and clinical characteristics.

Next, we calculated and plotted the cumulative rates and 95% confidence intervals (CIs) of breast cancer-specific and overall mortality by insurance type and reimbursement rate up to five years after cancer diagnosis using a competing risk model [14]. Hazard ratios (HRs) and 95% CIs of breast cancer-specific and overall mortality were then estimated from Cox regression by contrasting patients insured by the rural scheme to patients insured by the urban scheme, as well as patients with low reimbursement rate to those with high. The proportional hazards assumption, tested based on Schoenfeld residuals, was not violated. To illustrate the joint effect of insurance type and reimbursement rate, we further examined the association of every 10% increase in reimbursement rate with mortality risks by insurance type.

In Model A, we adjusted for demographic factors, including age, calendar year at diagnosis, ethnic group, educational level (as a proxy for socioeconomic status, SES), and marital status. In Model B, we additionally adjusted for clinical characteristics (as potential mediators), including comorbidity, histological type, tumor stage, hormone receptor status (including both estrogen and progesterone receptors), HER2 status, and Ki-67 level. In Model C, we additionally controlled for treatment modes,

namely surgery, chemotherapy, radiotherapy, hormonal therapy, and trastuzumab therapy. Age was treated as continuous variables, whereas other covariates were categorized as showed in Table 1.

Because BMI would be neither the cause nor consequence of different insurances, we did not adjust for it in the primary analysis. We, however, noted that patients with different insurance were characterized by different BMI. We, therefore, performed an additional analysis by adjusting for BMI at diagnosis. SES and accessibility to medical service are highly correlated with individual insurance plans. To further disentangle the potential influence of SES and accessibility to health-care, we performed a sensitivity analysis by clustering patients residing in the same community/county through the zip code of residence.

All analyses were performed in STATA statistical software (version 14; STATA, College Station, TX). P value <0.05 indicated statistical significance.

Results

Patients' characteristics

1,962 (26.9% of 7,289 patients with known insurance type) were insured by rural schemes, and 3,279 (47.8% of 6,867 patients with known reimbursement rate) were reimbursed £69% of their healthcare cost. Patients insured by rural schemes were younger and diagnosed more recently. They were less likely to be Han people, less well-educated, non-married, and postmenopausal, as well as with lower BMI and fewer comorbidities at diagnosis (all P<0.05; Table 1). Their tumors were more likely to be HER2-positive, highly proliferative (Ki-67 ³14%), poorly differentiated, and to have an advanced stage and ductal origin. These patients were less treated by all kinds except for chemotherapy, even after accounting for tumor characteristics (Table 2). Similar patterns were found for patients with reimbursement rate £69%.

Health insurance and breast cancer-specific mortality

During follow-up (median 3.1 years, interquartile range 1.4-5.1 years), 372 deaths were observed and 326 of them were due to breast cancer. The cumulative rates of breast cancer-specific mortality were higher among patients insured within rural insurance schemes and with reimbursement rates £69 %, compared with patients with urban insurance schemes and higher reimbursement rates, respectively (Fig. 1). Similar patterns were noticed for overall mortality.

When adjusting for demographic characteristics, patients insured by rural insurance schemes had a 46% increased risk of cancer-specific mortality (95% CI 14% to 87%) compared with patients within urban insurance schemes (Table 3). With additional control for clinical characteristics and treatment modes, the association was attenuated somewhat yet remained significant (HR 1.29, 95% CI 1.00 to 1.65). Similarly, patients with low reimbursement rate had a 42% increased risk of cancer-specific mortality (95% CI 11% to 82%) compared with patients within high reimbursement rate. Similar patterns were found for overall mortality (Table 3).

Largely similar results were yielded for both insurance type and reimbursement rate after additional control for BMI (see Additional file 3). Comparable but less significant associations were observed by conditioning on residence areas to further address SES and accessibility to care (see Additional file 4).

Joint effect of insurance type and reimbursement rate

We showed that every 10% increase in the reimbursement rate was associated with a 7% reduced risk of cancer-specific mortality (95% CI 2% to 12% after full adjustment; Table 4). Particularly, every 10% increase of reimbursement rate in rural insurance schemes was associated with remarkable risk reduction of cancer-specific mortality (HR 0.74, 95% CI 0.61 to 0.91), compared with that in urban insurance schemes (HR 0.94, 95% CI 0.86 to 1.03, P-for-difference=0.039). Similar results were found in overall mortality (Table 4).

Discussion

To the best of our knowledge, this is the first study to demonstrate that under-insured patients with invasive breast cancer are at increased risk of cancer-specific mortality in a country with less-developed health insurance system. Importantly, our findings strongly suggest that a higher reimbursement rate, particularly in rural scheme insurance, is associated with a remarkable risk reduction of breast cancer-specific mortality. These associations are partly but not entirely explained by known prognostic indicators, including tumor characteristics and cancer treatment.

Findings from several studies in developed countries, mostly from the US, have shown that under-insured patients with breast cancer are more likely to suffer an increased risk of cancer-specific mortality, compared with those with adequate insurance [7–10]. Only one study from developing countries showed that breast cancer prognosis is comparable between patients insured by public and private health insurances [12]. Our data further illustrated the impact of public health insurance status on breast cancer prognosis in developing countries independent of clinical factors. Most importantly, in addition to insurance status or type, we are the first to reveal that the low reimbursement rate is associated with an excess risk of breast cancer-specific mortality. In many developed countries, insurance plans usually come with a fixed coinsurance or reimbursement rate. Our setting therefore provides a unique opportunity to understand the potential mechanisms underlying the relationship between insurance and cancer prognosis, which highlights the urgent need of promoting reimbursement rate in rural insurance schemes, to significantly improve breast cancer prognosis and reduce health disparities at large.

Several mechanisms may contribute to the observed association of suboptimal health insurance and compromised prognosis after a breast cancer diagnosis. It is plausible that under-insured patients have limited access to medical service, which may lead to delayed diagnosis and suboptimal treatment [15]. This is also supported by our data that patients insured by rural schemes or with low reimbursement rate were more likely to have an advanced tumor stage and were less treated in all kinds of care options except for chemotherapy. In general, primary care is less established in rural areas, and no organized screening program for breast cancer is in place in Sichuan, which may result in delayed cancer diagnosis

among rural living women [15, 16]. Moreover, under-insured patients face greater financial burden and are less likely to afford out-of-pocket medical expenses for advanced therapy [17]. For instance, trastuzumab was not covered by the insurances during the study period, and the high out-of-pocket medical cost may prevent financially vulnerable patients from such therapy.

However, the increased risk of mortality among under-insured patients with breast cancer is not entirely explained by the differential tumor characteristics and treatment modes. In the present study, the elevated risks of cancer-specific mortality remained robust, although slightly attenuated, among patients insured by rural insurance schemes or with low reimbursement rate, after exhaustive adjustment for clinical factors. It is known that cancer diagnosis and treatment induce enormous psychological stress in cancer patients [18]. The financial hardship, as a result of inadequate insurance, may add extra emotional turmoil to cancer patients. A growing body of evidence from animal studies suggests that psychological stress might modulate cancer progression through facilitating tumor growth and invasion as well as inhibiting host immune responses, operated by the hypothalamic pituitary adrenal axis [19]. It is not implausible that the lack of financial support may impact breast cancer prognosis through psychological stress.

Our findings may partly reflect the difference of SES across rural and urban regions as well as between individuals. Of note, SES is highly correlated with, and to some extent reflected by, health insurance status. As health insurance is likely underlying the causal pathway between SES and cancer prognosis, we did not consider it as a confounder in the studied association. However, we have adequately addressed educational attainment (as a proxy for SES) in all analyses. To further separate the influence of SES, we performed a sensitivity analysis by conditioning on 88 residence areas to better control for SES and accessibility to health-care. Increased risks of cancer-specific and overall mortality are still suggested, although some are not significant likely due to power issue. This largely refutes the possibility that our findings are completely explained by the differential socioeconomic status.

One major merit of our study is the large-scale prospective cohort design with virtually complete follow-up, largely limiting the common sources of bias. The rich information on demographic and clinical characteristics helped to disentangle the direct influence of health insurance on cancer-specific mortality, from the influence through tumor characteristics and treatment modes. Our study also has several limitations to consider. First, some deaths due to other causes may be misclassified as breast cancer-specific mortality. However, in our data, 297 out of 326 cancer-specific deaths (91.1%) entailed a clinically detected local recurrence or distant metastasis, which largely alleviates such concerns. Furthermore, we have little information regarding extra insurances beyond the basic/public insurance. However, there were only 11 patients with commercial insurances included in our study and it is less likely to impact our results. As this cohort is based on a regional medical center, the findings may not be generalized to the entire population. The major selection forces include urban and well-educated residents, as well as advanced disease due to referrals from other hospitals. We, however, observed similar associations across regions of residence, educational levels, and tumor stages (data not shown). We may also miss the patients that are most financially vulnerable, because of the nature of our study setting. Reassuringly,

we noted the strongest association in the youngest patients (aged 18–39 years), where we should have a smaller selection force because young patients with breast cancer were more likely to seek health-care in a tertiary hospital.

Conclusions

In summary, our findings suggest that under-insured patients face a higher risk of breast cancer-specific mortality in China. The compromised survival of under-insured patients seems to some extent, but not entirely, explained by suboptimal prognostic indicators at diagnosis as well as cancer treatment. Increasing public health insurance coverage of breast cancer patients in developing countries, particularly in rural areas of China, may not only increase access to medical service but also favorably influence breast cancer prognosis.

Abbreviations

HR: Hazard ratios; CIs: Confidence intervals; OR, Odds ratio; WCH: West China Hospital; BCIMS: Breast Cancer Information Management System; NRCMS: New rural cooperative medical scheme; URBMI: Urban resident-based basic medical insurance scheme; UEBMI: Urban employee-based basic medical insurance scheme; SES: Socioeconomic status; HER2: Human epidermal growth factor receptor 2; BMI: Body mass index.

Declarations

Ethics approval and consent to participate

This study is approved by the Clinical Test and Biomedical Ethics Committee at West China Hospital, Sichuan University (reference number 2012-130). Consent forms have been obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yuxin Xie, Unnur A. Valdimarsdóttir, Ting Luo, and Donghao Lu conceived the study concept and design. Xiaorong Zhong, Hong Zheng, Ping He, and Kejia Hu collected data. Yuxin Xie and Chengshi Wang performed statistical analysis. Yuxin Xie and Donghao Lu drafted the manuscript, and all authors significantly contributed to the critical revision of the manuscript, data interpretation, and approved the submission.

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Additional information

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Tables

Table 1 Characteristics of patients with invasive breast cancer by insurance type and reimbursement rate.

	All (n=7,436)	By insurance type			By reimbursement rate		
		Urban schemes (n=5,327)	Rural schemes (n=1,962)		70%-100% (n=3,588)	0-69% (n=3,279)	
	No. (%)	No. (%)	No. (%)	*P*	No. (%)	No. (%)	*P*
Age at diagnosis, years				*			*
18 to 39	1,276（17.2）	876 (16.4)	365 (18.6)		581 (16.2)	580 (17.7)	
40 to 49	3,145（42.3）	2,102 (39.5)	975 (49.7)		1,414 (39.4)	1,517 (46.3)	
≥50	3,015（40.6）	2,349 (44.1)	622 (32)		1,593 (44.4)	1,182 (36.0)	
Calendar year at diagnosis				*			*
2009-2012	3,419（46.0）	2,485 (46.7)	853 (43.5)		1,514 (42.2)	1,588 (48.4)	
2013-2016	4,017（54.0）	2,842 (53.3)	1,109 (56.5)		2,074 (57.8)	1,691 (51.6)	
Ethnic groups				*			
Han	7,278（97.9）	5,228 (98.1)	1,909 (97.3)		3,527 (98.3)	3,197 (97.5)	
Minority	155（2.1）	97 (1.8)	53 (2.7)		60 (1.6)	81 (2.4)	
Unknown	3（0.1）	2 (0.1)	0 (0.0)		1 (0.1)	1 (0.1)	
Education (years)				*			*
≤6	1,326（17.8）	587 (11.0)	707 (36.0)		389 (10.8)	799 (24.4)	
7-9	2,739（36.8）	1,689 (31.7)	986 (50.2)		1,091 (30.4)	1,428 (43.6)	
10-12	1,583（21.3）	1,359 (25.5)	200 (10.2)		878 (24.5)	594 (18.1)	
>12	1,763（23.7）	1,671 (31.4)	68 (3.5)		1,219 (34.0)	450 (13.7)	
Unknown	25（0.4）	21 (0.4)	1 (0.1)		11 (0.3)	8 (0.2)	
Marital status				*			
Married	7,253（97.5）	5,168 (97.0)	1,942 (98.9)		3,490 (97.3)	3,208 (97.8)	
Non-married	183（2.5）	159 (3.0)	20 (1.1)		98 (2.7)	71 (2.2)	
BMI, kg/m^2				*			*
<23	3,806（51.2）	2,869 (53.9)	870 (44.3)		1,943 (54.2)	1,591 (48.5)	
≥23	3,602（48.4）	2,440 (45.8)	1,085 (55.3)		1,633 (45.5)	1,680 (51.3)	
Unknown	28（0.4）	18 (0.3)	7 (0.4)		12 (0.3)	8 (0.2)	
Menopausal status				*			*
Premenopausal	4,523（60.8）	3,054 (57.3)	1,361 (69.4)		2,028 (56.5)	2,146 (65.5)	
Postmenopausal	2,893（38.9）	2,258 (42.4)	597 (30.4)		1,554 (43.3)	1,126 (34.3)	
Unknown	20（0.3）	15 (0.3)	4 (0.2)		6 (0.2)	7 (0.2)	
Comorbidity				*			*
No	6,719（90.4）	4,786 (89.8)	1803 (91.9)		3,220 (89.7)	2,985 (91.0)	
Yes	717（9.6）	541 (10.2)	159 (8.1)		368 (10.3)	294 (9.0)	
Hormone receptor status							*
Negative	1,867（25.1）	1,323 (24.8)	516 (26.3)		835 (23.3)	887 (27.1)	
Positive	5,229（70.3）	3,747 (70.3)	1,372 (69.9)		2,608 (72.7)	2,257 (68.8)	
Unknown	340（4.6）	257 (4.9)	74 (3.8)		145 (4.0)	135 (4.1)	
HER2 status				*			*
Negative	4,155（55.9）	3,033 (56.9)	1,047 (53.4)		2,060 (57.4)	1,793 (54.7)	
Positive	1,680（22.6）	1,183 (22.2)	460 (23.4)		811 (22.6)	762 (23.2)	
Unknown	1,601（21.5）	1,111 (20.9)	455 (23.2)		717 (20.0)	724 (22.1)	
Ki-67 level				*			*
<14%	1,301（17.5）	975 (18.3)	296 (15.1)		665 (18.5)	541 (16.5)	
≥14%	5,507（74.1）	3,906 (73.3)	1,501 (76.5)		2,673 (74.5)	2457 (74.9)	
Unknown	628（8.5）	446 (8.4)	165 (8.4)		250 (7.0)	281 (8.6)	
Molecular subtype							*
Luminal A	603（8.1）	456 (8.6)	129 (6.6)		325 (9.1)	239 (7.3)	
Luminal B	3,968（53.4）	2,817 (52.9)	1,071 (54.6)		1,985 (55.3)	1,725 (52.6)	
HER2 positive	728（9.8）	514 (9.7)	200 (10.2)		343 (9.6)	334 (10.2)	
Triple-negative	863（11.6）	623 (11.7)	230 (11.7)		391 (10.9)	410 (12.5)	
Unknown	1,274（17.1）	917 (17.2)	332 (16.9)		544 (15.1)	571 (17.4)	
Tumor stage				*			*
I	1,406（18.9）	1,107 (20.8)	271 (13.8)		753 (21.0)	572 (17.4)	
II	3,182（42.8）	2,300 (43.2)	820 (41.8)		1,565 (43.5)	1,385 (42.2)	
III	1,713（23.1）	1,147 (21.5)	531 (27.1)		791 (22.1)	771 (23.6)	
IV	180（2.4）	119 (2.2)	56 (2.9)		89 (2.5)	90 (2.7)	
Unknown	955（12.8）	654 (12.3)	284 (14.4)		390 (10.9)	461 (14.1)	
Histological type				*			

	All (n=7,436)	By insurance type			By reimbursement rate		
		Urban schemes (n=5,327)	Rural schemes (n=1,962)		70%-100% (n=3,588)	0-69% (n=3,279)	
	No. (%)	No. (%)	No. (%)	P	No. (%)	No. (%)	P
Ductal	6,897（92.8）	4,910 (92.2)	1,849 (94.2)		3,321 (92.6)	3,076 (93.8)	
Others	308（4.1）	228 (4.3)	75 (3.9)		158 (4.4)	125 (3.8)	
Unknown	231（3.1）	189 (3.5)	38 (1.9)		109 (3.0)	78 (2.4)	
Histological grade				*			*
I	194（2.6）	152 (2.9)	34 (1.7)		96 (2.7)	87 (2.7)	
II	2,216（29.8）	1,628 (30.6)	549 (28.0)		1,154 (32.2)	933 (28.4)	
III	3,134（42.2）	2,212 (41.5)	868 (44.2)		1,492 (41.5)	1,412 (43.1)	
Unknown	1,892（25.4）	1,335 (25.0)	511 (26.1)		846 (23.6)	847 (25.8)	
Surgery				*			*
No	323（4.3）	197 (3.7)	116 (5.9)		117 (3.3)	163 (5.0)	
Yes	7,113（95.7）	5,130 (96.3)	1,846 (94.1)		3,471 (96.7)	3,116 (95.0)	
Chemotherapy				*			
No	520（7.0）	414 (7.8)	97 (4.9)		253 (7.1)	188 (5.7)	
Yes	6,916（93.0）	4,913 (92.2)	1,865 (95.1)		3,335 (93.0)	3,091 (94.3)	
Radiotherapy				*			*
No	5,141（69.1）	3,633 (68.2)	1,402 (71.5)		2,395 (66.8)	2,295 (70.0)	
Yes	2,295（30.9）	1,694 (31.8)	560 (28.5)		1,193 (33.3)	984 (30.0)	
Hormonal therapy				*			*
No	2,645（35.6）	1,781 (33.4)	808 (41.2)		1,124 (31.3)	1,238 (37.8)	
Yes	4,791（64.4）	3,546 (66.6)	1,154 (58.8)		2,464 (68.7)	2,041 (62.2)	
Use of trastuzumab							
No	6,824（91.8）	4,804 (90.2)	1,882 (95.9)		3,214 (89.6)	3,058 (93.3)	
Yes	612（8.2）	523 (9.8)	80 (4.1)		374 (10.4)	221 (6.7)	

NOTE. Patients with missing information on insurance type (N=147, 1.98%) or reimbursement rate (N=569, 7.65%) were not included for the corresponding analysis. Body mass index (BMI) was classified into < 23 kg/m^2 (non-overweight) and ≥ 23 kg/m^2 (overweight). Tumor stage was categorized as localized (no nodal or metastatic disease), regional (nodal disease), or distant (any metastatic disease). Pearson's χ^2 statistic was used to assess significance of the difference between proportions in assessment of univariable associations.

* P value <0.05.

Abbreviations: HER2, human epidermal growth factor receptor 2.

Table 2 Associations of insurance type and reimbursement rate with treatment type.

Treatment type	By insurance type OR (95% CI)				By reimbursement rate OR (95% CI)			
	Model A†		Model B‡		Model A†		Model B‡	
	Urban schemes	Rural schemes	Urban schemes	Rural schemes	70%-100%	0-69%	70%-100%	0-69%
Surgery	1.00	0.65 (0.50-0.83)	1.00	0.71 (0.54-0.92)	1.00	0.62 (0.49-0.80)	1.00	0.67 (0.51-0.87)
Chemotherapy	1.00	1.56 (1.22-1.98)	1.00	1.36 (1.04-1.78)	1.00	1.16 (0.95-1.42)	1.00	1.14 (0.91-1.42)
Radiotherapy	1.00	0.87 (0.77-0.98)	1.00	0.72 (0.63-0.83)	1.00	0.84 (0.76-0.94)	1.00	0.78 (0.69-0.88)
Hormonal therapy	1.00	0.71 (0.63-0.80)	1.00	0.62 (0.53-0.72)	1.00	0.74 (0.67-0.82)	1.00	0.74 (0.63-0.86)
Use of trastuzumab	1.00	0.44 (0.34-0.56)	1.00	0.33 (0.25-0.43)	1.00	0.70 (0.59-0.83)	1.00	0.57 (0.47-0.70)

NOTE. Patients with missing information on insurance type (N=147, 1.98%) or reimbursement rate (N=569, 7.65%) were not included for the corresponding analysis.

Abbreviations: OR, odds ratio; CI, confidence interval.

† ORs were adjusted for age at diagnosis, calendar year at diagnosis (2009-2012 or 2013-2016), ethnic group (majority or minority/unknown), education (>6 years, or ≤6 years/unknown), and marital status (married or non-married).

‡ ORs were additionally adjusted for comorbidity (no or yes), hormone receptor status (negative, positive, or unknown), HER2 status (negative, positive, or unknown), Ki-67 level (<14%, ≥14%, or unknown), histological type (ductal or other types/unknown), tumor stage (I, II, III, IV, or unknown).

Table 3 Associations of insurance type and reimbursement rate with risks of breast cancer-specific and overall mortality.

	N of patients	N of events	Rate	Model A†		Model B‡		Model C§	
				HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Breast cancer-specific mortality									
By insurance type					0.003		0.028		0.046
Urban schemes	5,327	211	1.16	1.00		1.00		1.00	
Rural schemes	1,962	109	1.84	1.46 (1.14-1.87)		1.32 (1.03-1.69)		1.29 (1.00-1.65)	
By reimbursement rate					<0.001		<0.001		<0.005
70%-100%	3,588	115	0.97	1.00		1.00		1.00	
0-69%	3,279	172	1.52	1.60 (1.25-2.04)		1.56 (1.22-1.99)		1.42 (1.11-1.2)	
Overall mortality									
By insurance type					0.004		0.028		0.045
Urban schemes	5,327	248	1.37	1.00		1.00		1.00	
Rural schemes	1,962	118	1.99	1.41 (1.11-1.78)		1.30 (1.03-1.64)		1.27 (1.01-1.61)	
By reimbursement rate					<0.001		<0.001		<0.001
70%-100%	3,588	124	1.04	1.00		1.00		1.00	
0-69%	3,279	192	1.70	1.68 (1.33-2.12)		1.66 (1.32-2.10)		1.52 (1.20-1.93)	

NOTE. Patients with missing information on insurance type (N=147, 1.98%) or reimbursement rate (N=569, 7.65%) were not included for the corresponding analysis.

Abbreviations: N, number; Rate, mortality rate (per 100 person-years); HR, hazard ratio; CI, confidence interval.

† HRs were adjusted for age at diagnosis, calendar year at diagnosis, ethnic group (majority or minority/unknown), education (>6 years, or ≤6 years/unknown), and marital status (married or non-married).

‡ HRs were additionally adjusted for comorbidity (no or yes), hormone receptor status (negative, positive, or unknown), HER2 status (negative, positive, or unknown), Ki-67 level (<14%, ≥14%, or unknown), histological type (ductal or other types/unknown), tumor stage (I, II, III, IV, or unknown).

§ HRs were additionally adjusted for surgery (yes or no), chemotherapy (yes or no), radiotherapy (yes or no), hormonal therapy (yes or no), and trastuzumab therapy (yes or no).

Table 4 Association of every 10% insurance reimbursement rate increase with risks of cancer-specific and overall mortality.

	N of patients	N of events	Rate	Model A†		Model B‡		Model C§	
				HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Breast cancer-specific mortality									
Any insurance type					<0.001		0.001		0.008
Per 10% increase	6,867	287	1.33	0.90 (0.86-0.95)		0.91(0.87-0.96)		0.93 (0.88-0.98)	
Within urban schemes					0.078		0.052		0.215
Per 10% increase	4,993	191	1.16	0.92 (0.84-1.00)		0.91 (0.83-1.00)		0.94 (0.86-1.03)	
Within rural schemes					<0.001		0.002		0.004
Per 10% increase	1,743	92	1.84	0.70 (0.58-0.84)		0.73(0.60-0.89)		0.74 (0.61-0.91)	
*P for difference**				0.007		0.039		0.039	
Overall mortality									
Any insurance type					<0.001		<0.001		0.002
Per 10% increase	6,867	316	1.52	0.90 (0.86-0.95)		0.91 (0.86-0.95)		0.92 (0.88-0.97)	
Within urban schemes					0.014		0.008		0.051
Per 10% increase	4,993	214	1.37	0.89 (0.83-0.98)		0.89 (0.82-0.97)		0.92 (0.84-1.00)	
Within rural schemes					<0.001		0.002		0.005
Per 10% increase	1,743	98	1.99	0.72 (0.60-0.85)		0.75 (0.62-0.90)		0.76 (0.63-0.92)	
*P for difference**				0.016		0.087		0.087	

NOTE. Patients with missing information on insurance type (N=147, 1.98%) or reimbursement rate (N=569, 7.65%) were not included for the corresponding analysis.

Abbreviations: N, number; Rate, mortality rate (per 100 person-years); HR, hazard ratio; CI, confidence interval.

† HRs were adjusted for age at diagnosis, calendar year at diagnosis, ethnic group (majority or minority/unknown), education (>6 years, or ≤6 years/unknown), and marital status (married or non-married).

‡ HRs were additionally adjusted for comorbidity (no or yes), hormone receptor status (negative, positive, or unknown), HER2 status (negative, positive, or unknown), Ki-67 level (<14%, ≥14%, or unknown), histological type (ductal or other types/unknown), tumor stage (I, II, III, IV, or unknown).

§ HRs were additionally adjusted for surgery (yes or no), chemotherapy (yes or no), radiotherapy (yes or no), hormonal therapy (yes or no), and trastuzumab therapy (yes or no).

* We added an interaction term between insurance type and reimbursement rate (as continuous variable) in the model, and reported the P value of the interaction term as a significance test of the difference between HRs.

Supplementary Information

Additional file 1. Supplementary Material.

Additional file 2. Fig. S1 Distribution of reimbursement rates among breast cancer patients covered by urban and rural insurance schemes. NOTE. Patients with missing information on either insurances type (N=147, 1.98%) or reimbursement rate (N=569, 7.65%) were not included in analysis.

Additional file 3. Table S1 Associations of health insurance type and reimbursement rate with the risks of breast cancer-specific mortality and overall mortality among patients with invasive breast cancer, with additional adjustment for calendar year and BMI at diagnosis.

Additional file 4. Table S2 Associations of health insurance type and reimbursement rate with the risks of breast cancer-specific mortality and overall mortality among patients with invasive breast cancer, with additionally adjustment for residence area.

Figures

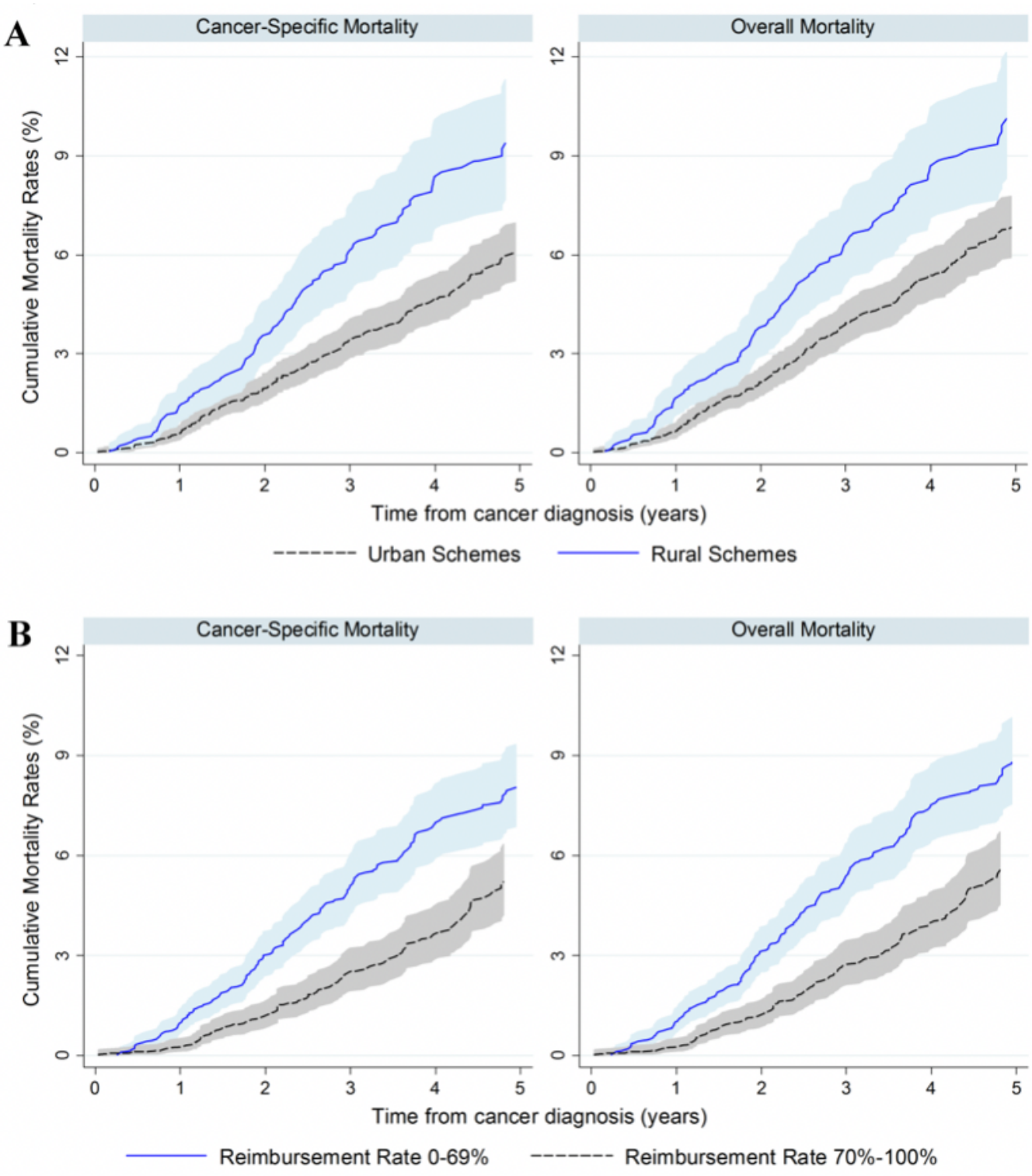

Figure 1

Cumulative mortality rates of cancer-specific or overall mortality by insurance type (A) and reimbursement rate (B). Patients with missing information on insurances type (N=147, 1.98%) were not included in the analysis A. Patients with missing information on reimbursement rate (N=569, 7.65%) were not included in analysis B.

Supplementary Files

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

- Additionalfile4.docx
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