Method for mediation analysis

We used path analysis on different financial supports with survival outcomes [including overall survival (OS) and invasive disease-free survival (iDFS)] as the dependent variable to assess the mediational relationships. Mediation model included the following 3 paths: (I) a path between the financial support status and patient's choice of trastuzumab; (II) the path between trastuzumab adjuvant therapy and survival outcomes. Both I and II were adjusted for demographic factors (including age at diagnosis: <55 or ≥55 years; menopause status: pre-menopause or post-menopause; level of education: ≤6, 7–12, >12 years), clinicopathological factors (including T stage: 0–1, 2, or 3–4; N stage:0, 1, 2, or 3; Ki-67 levels: <14%, ≥14%; hormone receptor status: negative, positive; histologic grade of tumor: I–II, III, NA), and treatment factors (including surgery: no or yes; chemotherapy: no/salvage, adjuvant/neoadjuvant; radiotherapy: no or yes; and endocrine therapy; no or yes); and (3) a direct path between financial support status and survival outcomes. The natural indirect effect, natural direct effect, and total effect were estimated based on the counterfactual approach using R package mediation.

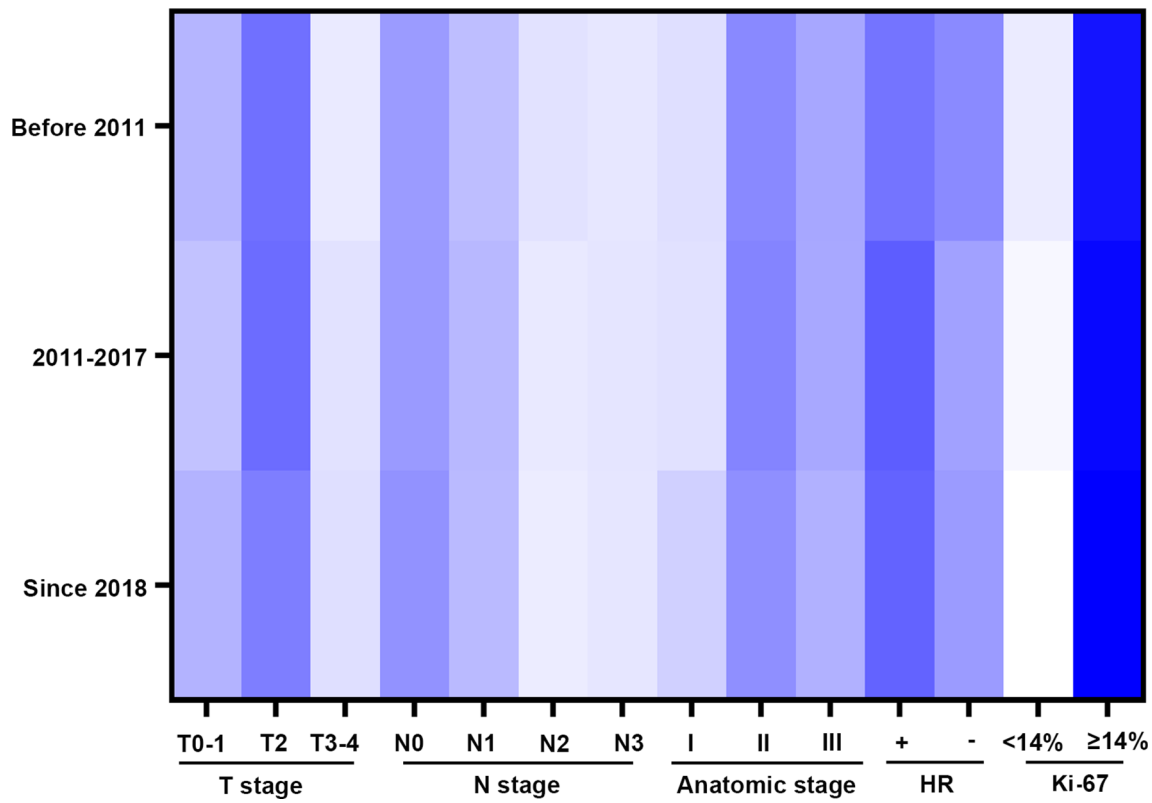

Figure S1 Distribution of clinicopathological factors in the following 3 diagnostic time periods: before 2011, 2011–2017, and from 2018. Proportions of different clinical characteristics, including T/N stage and anatomic stage, and different pathological features, including histologic grade, hazard ratio expression status, and Ki-67 status, were calculated and visualized by heatmap. Darker color indicates a higher proportion of the corresponding subset. HR, hormone receptor. +, positive; –, negative.

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Table S1 Association between insurance type, reimbursement rate, and year of diagnosis with risk of breast cancer-specific survival (BCSS)

BCSS	Cases (n=2,987)	Events, n (%)	Model A[a]		Model B[b]		Model C[c]	
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
By year of diagnosis								
Before 2011	264	37 (14.1)	1.00		1.00		1.00	
2011–2017	1657	108 (6.5)	0.70 (0.45–1.08)	0.111	0.60 (0.38–0.94)	0.026	0.58 (0.37–0.93)	0.022*
From 2018	1051	8 (0.8)	0.38 (0.17–0.88)	0.023	0.35 (0.15–0.82)	0.015	0.32 (0.14–0.76)	0.010*
By insurance type[†]								
Rural	711	58 (8.2)	1.00		1.00		1.00	
Urban	2183	87 (4.0)	0.57 (0.39–0.84)	0.004	0.63 (0.43–0.92)	0.018	0.67 (0.45–0.98)	0.041*
By reimbursement[‡]								
≤50%	752	69 (9.2)	1.00		1.00		1.00	
>50%	2149	75 (3.5)	0.63 (0.44–0.91)	0.013	0.66 (0.46–0.94)	0.023	0.68 (0.47–0.98)	0.038*

*P<0.05. [†], there were 60 patients who paid out of pocket or had commercial insurance; 18 patients without medical insurance were excluded in this analysis. [‡], 71 patients had missing information for reimbursement rate and were excluded. [a], odds ratios (ORs) were adjusted for age at diagnosis (<55 or ≥55 years), menopause status (pre-menopause or post-menopause), level of education (≤6, 7–12, >12 years). [b], ORs were additional adjusted for T stage (0–1, 2, or 3–4), N stage (0, 1, 2, or 3), Ki-67 status (<14% or ≥14%), hormone receptor status (negative, positive), and histologic grade (I–II, III, NA). [c], ORs were adjusted for surgery (no or yes), chemotherapy (no/salvage, adjuvant/neoadjuvant), radiotherapy (no or yes), and endocrine therapy (no or yes). BCSS, breast cancer-specific survival; CI, confidence interval; HR, hazard ratio.

Table S2 Association of insurance type with trastuzumab use in patients first diagnosed >2018

Insurance type[†]	Model A[a]		Model B[b]		Model C[c]	
	OR	P value	OR	P value	OR	P value
Urban scheme	1.00	–	1.00	–	1.00	–
Rural scheme	1.12 (0.74–1.66)	0.589	1.21 (0.79–1.84)	0.368	1.26 (0.79–2.00)	0.322

†, four patients who paid out of pocket or had commercial insurance and 8 patients with no insurance information were excluded in this analysis. OR, odds ratio. [a], odds ratios (ORs) were adjusted for age at diagnosis (<55 or ≥55 years), menopause status (pre-menopause or post-menopause), level of education (≤6, 7–12, >12 years). [b], ORs were additional adjusted for T stage (0–1, 2, or 3–4), N stage (0, 1, 2, or 3), Ki-67 status (<14% or ≥14%), hormone receptor status (negative, positive), and histologic grade (I–II, III, NA). [c], ORs were adjusted for surgery (no or yes), chemotherapy (no/salvage, adjuvant/neoadjuvant), radiotherapy (no or yes), and endocrine therapy (no or yes).

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Table S3 Association of insurance type with survival outcomes in patients first diagnosed >2018

Insurance type[†]	Cases (n=1,039)	Events, n (%)	Model A[a]		Model B[b]		Model C[c]	
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Overall survival								
Rural scheme	208	8 (3.8)	1.00		1.00		1.00	
Urban scheme	831	4 (0.5)	0.08 (0.02–0.41)	0.002	0.11 (0.03–0.43)	0.002	0.04 (0.01–0.14)	<0.001***
iDFS								
Rural scheme	208	17 (8.2)	1.00	–	1.00	–	1.00	–
Urban scheme	831	29 (3.5)	0.46 (0.23–0.94)	0.034	0.43 (0.21–0.89)	0.022	0.42 (0.20–0.88)	0.022*
BCSS								
Rural scheme	208	4 (1.92)	1.00		1.00		1.00	
Urban scheme	831	4 (0.48)	0.23 (0.05–1.13)	0.070	0.18 (0.03–0.98)	0.048	0.06 (0.01–0.30)	<0.001***

†, four patients who paid out of pocket or had commercial insurance and 8 patients with no insurance information were excluded in this analysis. [a], hazard ratios (HRs) were adjusted for age at diagnosis (<55 or ≥55 years), menopause status (pre-menopause or post-menopause), level of education (≤6, 7–12, >12 years). [b], HRs were adjusted for T stage (0–1, 2, or 3–4), N stage (0, 1, 2 or 3), Ki-67 levels (<14%, ≥14%), hormone receptor status (negative, positive), and histologic grade of tumor (I–II, III, NA). [c], HRs were adjusted for surgery (no or yes), chemotherapy (no/salvage, adjuvant/neoadjuvant), radiotherapy (no or yes), and endocrine therapy (no or yes), if applicable. *P<0.05, ***P<0.001. BCSS, breast cancer-specific survival; CI, confidence interval; iDFS, invasive disease-free survival.

Table S4 Mediation effect analysis of the impact of trastuzumab on breast cancer-specific survival (BCSS)

BCSS	Year of diagnosis				Insurance type	P value	Reimbursement rate	P value
	2011–2017	P value	>2018	P value				
NIE	0.60	<0.001	2.00	<0.001	9.29	0.030	0.66	<0.001
NDE	2.94	<0.001	8.65	<0.001	35.08	0.062	0.50	0.088
PM	0.18	<0.001	0.19	<0.001	0.19	0.030	0.56	<0.001

BCSS, breast cancer-specific survival; NDE, natural direct effect; NIE, natural indirect effect; PM, proportion of the total effect of financial support on patient prognosis mediated by trastuzumab.

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