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Research paper

# Effects of housing value and medical subsidy on treatment and outcomes of breast cancer patients in Singapore: A retrospective cohort study

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ABSTRACT

*Background:* Socioeconomic status (SES) is likely to affect survival in breast cancer patients. Housing value is a reasonable surrogate for SES in Singapore where most residents own their own homes, which could be public (subsidised) or private housing. We evaluated effects of housing value and enhanced medical subsidies on patients' presentation, treatment choices, compliance and survival in a setting of good access to healthcare.

*Methods:* A retrospective analysis of breast cancer patients treated in a tertiary hospital cluster from 2000 to 2016 was performed. Individual-level Housing value Index (HI) was derived from each patient's address and then grouped into 3 tiers: HI(high)(minimal subsidy), HI(med)(medium subsidy) and HI(low)(high subsidy). Cox regression was performed to evaluate the associations between overall survival (OS) and cancer-specific survival (CSS) with HI and various factors.

*Findings:* We studied a multiracial cohort of 15,532 Stage 0–IV breast cancer patients. Median age was 53.7 years and median follow-up was 7.7 years. Patients with lower HI presented with more advanced disease and had lower treatment compliance. On multivariable analysis, compared to HI(high) patients, HI(med) patients had decreased OS (HR=1.14, 95% CI 1.05–1.23) and CSS (HR=1.15, 95% CI 1.03–1.27), and HI(low) patients demonstrated reduced OS (HR=1.16, 95% CI 1.01–1.33). Ten-year non-cancer mortality was higher in lower HI-strata. Enhanced medical subsidy approximately halved treatment noncompliance rates but its receipt was not an independent prognostic factor for survival.

*Interpretation:* Despite good healthcare access, lower-HI patients have poorer survival from both cancer and non-cancer causes, possibly due to delayed health-seeking and poorer treatment compliance. Enhanced subsidies may mitigate socioeconomic disadvantages.

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Research in context

**Evidence before this study**

Socioeconomic status (SES) is likely to affect survival in breast cancer patients. We searched PubMed for research on socioeconomic status and breast cancer, not limited to English language publications up to March 2019, and identified hundreds of studies using the search terms "socioeconomic" and "breast cancer" in combination with permutations of "outcomes", "survival", "universal healthcare", "Asian". Most studies performed comparison between broad groupings of SES such as residential neighborhoods, insurance or along poverty or racial lines. Few studies were done in the setting of good access to healthcare and even fewer in an Asian context. The available studies were uniform in their conclusion that socioeconomic inequalities were associated with divergent breast cancer survival, but none examined the mitigative value of adding enhanced means-tested subsidies (MediFund).

**Added value of this study**

This study was conducted in Singapore which is an affluent country with heavily subsidized access to healthcare. The cohort of patients was representative of the cross-section of the country with high resolution individual clinical data and substantial follow-up. A robust, quasi-individualized characterisation of each patient using their Housing Index (HI) was used as a proxy for socio-economic status. We showed that MediFund can double the compliance to treatment, particularly HER-2 targeted therapy. Despite these measures, MediFund was insufficient to equalize survival between patients of different SES. The divergence in survival between SES tiers was driven by breast cancer mortality in the first decade post-diagnosis but sustained by non-breast cancer mortality in the survivorship years.

**Implications of all the available evidence**

SES exerts a pervasive lifelong influence on the health of breast cancer patients beyond the immediate impact of cancer itself. Studies like ours can guide policy development to target interventions to vulnerable populations. Enhanced means-tested subsidies are valuable tools to improve treatment compliance. However, universal access to healthcare and subsidies towards direct medical care alone are unlikely to erase inherent inequalities between patients of different SES. A more holistic approach including building awareness and educating patients on cancer and general health, enhanced screening availability, employment and economic support for family and caregivers and empowerment of underprivileged women is urgently needed.

## 1. Introduction

In Singapore, breast cancer is the most common and rapidly increasing cancer in women. Socioeconomic status (SES) is known to have a powerful influence on patients' health. Studies have demonstrated strong association between SES and the prevalence and outcomes of cardiovascular disease, respiratory disease, mental disorders and cancer [1–4].

Studies in breast cancer have associated low SES with decreased survival resulting from delayed health seeking behavior, reduced uptake of screening, treatment choices and poor compliance to treatment [5–10]. Most studies have used broad groupings of SES, often by residential neighborhood, enrolment in insurance programs, census-tract-level poverty, level of segregation or along racial divides. Many of these studies were conducted in the United States where the absence of universal health coverage and prohibitively high medical cost impede access to care and accentuate disparities in health outcomes.

Singapore is a relatively affluent country. According to the World Bank, 2018 per capita Gross Domestic Product (GDP) for Singapore was US$64,581. A well-designed health system enables Singapore residents to enjoy one of the highest life expectancies in the world with an average annual healthcare expenditure of about 4% of GDP over the last decade. Eighty percent of healthcare is delivered through highly regulated, autonomous 'Clusters' of integrated public hospitals and clinics. Healthcare costs are subsidized by up to 80% on a co-payment basis in the form of cash, private or nationalized insurance schemes, or compulsory medical savings. Patients who face financial difficulties with medical bills despite the above measures may receive additional subsidy (MediFund) from the Government [11]. Eligibility and quantum of MediFund assistance is assessed by an independent MediFund Committee based on the patient and her family's financial, health and social circumstances as well as the size of the medical bill.

The common approach of using income, education, and employment status as measurements of SES is particularly challenging in Singapore's women. Despite women becoming an increasingly important component of the workforce with Singapore's development into a modern economy, a large proportion of older breast cancer patients are in the traditional role of an unremunerated homemaker. Furthermore, household income and spousal occupation are not routinely collected medical information.

Housing value may provide a good surrogate measurement of SES in Singapore where 79% of residents live in public housing under a tiered subsidy scheme [12]. Apartments (commonly called 'flats') built by Singapore's public housing authority, Housing & Development Board (HDB) vary in size and price, with tiered household monthly income ceilings to be eligible for purchase or rent (Table 1) [13]. In addition, first-time buyers of HDB flats receive grants to subsidize their purchase. Applicants with household income below S$1500 receive the maximum subsidy of $80,000. Every S$500 income increment, up to the maximum of S$9000, reduces the grant by S$5000. Families earning S$8501 to S$9000 receive the minimum subsidy of $5000 [14]. Therefore, the average price of each room-type after subsidy ranged from S$43 000 to more than S$396 000 for 2-room and executive flats respectively (Table 1).

The extent to which SES affects breast cancer patients in Singapore and similar countries with good access to health care, and the adequacy of financial 'safety-nets' for economically challenged patients is unknown. This study aimed to assess whether housing value, as a proxy for SES, influenced breast cancer patients' presentation, treatment choices, compliance and outcomes. The secondary objective was to investigate the effects of enhanced subsidies (MediFund) on patients' receipt of treatment and survival. Evaluating disparities in outcomes between patients of different SES as a litmus test of social equity.

## 2. Methods

### 2.1. Study design

This was a retrospective study of data extracted from a registry of breast cancer patients treated in the largest public healthcare cluster in Singapore (Singapore Health Services, SingHealth), which consists of four general hospitals and various national speciality centres including National Cancer Centre Singapore. Nationwide, SingHealth sees approximately 60% of all breast cancer patients treated in the public healthcare sector. (Supplementary Table 1) The patients included in this study is meant to represent Singapore breast cancer patients.

Only female Singapore residents with breast cancer diagnosed between January 2000 and December 2016 were included in this study. Patients with unknown stage or missing follow-up informa-

**Table 1**
Comparison of size, income ceiling for eligibility to purchase, average price after subsidy of public housing and derived categories of Housing value Index (HI) by apartment types.

| Apartment type | Average size (m2) | Income ceiling (SGD / month) | Average price after subsidy (SGD) | Approximate housing value index (HI) category |
|---|---|---|---|---|
| 1–2 rooms | 33–45 | $800 before Nov 2003; $1 500 after Nov 2003 | $43 000 | HI(low) |
| 3 rooms | 65 | $4 000–$8 000 | S$132 000 | HI(med) |
| 4 rooms | 90 | $12 000–18 000 | $270 000 | |
| 5 rooms | 110 | $12 000–18 000 | $396 000 | HI(high) |
| Executive | 130 | $12 000–18 000 | >$396 000 | |
| Private apartments[a] | ~ 85 | Nil | $1 250 000 | |

Source: https://www.cbreresidential.com/uk/sites/uk-residential/files/CBRE-Global%20Living-Artwork-Phase%206-v18.pdf.
SGD: Singapore Dollars. (Mar 2020: 1 US Dollars = 1.45 SGD).
*[a] Source: https://www.cbreresidential.com/uk/sites/uk-residential/files/CBRE-Global%20Living-Artwork-Phase%206-v18.pdf.

tion were excluded. For each patient, demographics, disease, treatment, and outcomes information were retrieved from the registry. Patients with bilateral breast cancers were included based first on the higher stage (American Joint Committee on Cancer, 7th edition) and then disease grade. All patients were included for overall survival (OS) analysis, cancer specific survival (CSS) and non-cancer specific survival (NCSS).

To estimate residential housing value, the 6-digit postal code in each patient's resident address was first matched to either a unique HDB-block based on data from HDB or a private apartment or landed housing on the master plan on land use from the Singapore Land Authority. Patients with unmatched addresses were excluded. 1-room to 5-room HDB flats were assigned corresponding values of 1 to 5. Non-subsidized private apartments were assigned a room index of 6; private landed housing were assigned a value of 7 to reflect the ordinal increase in value of each category of dwellings.

The "Housing value Index" (HI) of the HDB block for each patient was then generated by the following formula: Summation (number of rooms in a flat x number of such flats per block) / total number of units in a block. Details of this method has been previously described [12]. Patients were then categorised into 3 tiered HI categories viz. HI(low)(high subsidy), HI(med)(moderate subsidy) and HI(high)(minimal or no subsidy) (Table 1).

Itemized treatment bills for all patients starting 6 months till 5 years after cancer diagnosis were examined to identify payments made by MediFund. Patients with any such occurrence were classified as "ever received" MediFund vs "never received" for the rest.

Depending on stage and disease characteristics, breast cancer management includes various treatment modalities: surgery, chemotherapy, radiotherapy, endocrine therapy and targeted therapy. Patients were assessed for compliance based on the criteria in Table 2 and classified as "Yes" or "No" according to their receipt of the needed treatment, "Not needed", or "Not assessable" if information was insufficient to determine treatment requirement or receipt. Noncompliance was defined as patient not having received a treatment deemed necessary, i.e. ["No"/("Yes"+"No")].

This study was conducted with ethics approval for waiver of consent (CIRB2019/2419).

### 2.2. Outcomes

Overall survival (OS) was defined as time from diagnosis to death from all causes. Cancer specific survival (CSS) was defined as time from diagnosis until death from breast cancer, patients who died from other causes were taken as competing risk events. Non-Cancer specific survival (NCSS) was defined as time from diagnosis until death from causes other than breast cancer, patients who died from breast cancer were taken to have competing causes of non-breast cancer deaths. For each survival outcome, alive patients were censored at their last follow-up date. Follow-up date was taken as patients' last date of contact with the health system. Death information was retrieved from Singapore Registry of Births & Deaths.

### 2.3. Statistical methods

Patients' clinicopathologic and treatment characteristics were summarized using frequency and percentage. Differences in the characteristics between HI strata were compared using the Chi-square test. Follow-up time was estimated using the reverse Kaplan–Meier method. Survival estimates were estimated using the Kaplan–Meier Method. Differences in survival between groups of patients were assessed using the log-rank test for OS and the Gray's test for CSS and NCSS in accordance with the competing risk analysis approach. Univariable and multivariable Cox/Fine and Gray regression analyses were performed to assess the association between survival outcome with clinicopathologic and treatment characteristics. Proportional hazards (PH) assumption is verified for all variables in the regression model for OS and CSS by adding a time-by-variable interaction term for each variable in each model.

Due to concern of multicollinearity, Timely surgery was excluded from multivariable analyses as all Stage IV patients were categorized as "Not needed" under Timely surgery.

Because of the retrospective nature of this study, there were several variables with missing data. The impact of missing data on the association of survival outcomes with HI and Medifund was evaluated via sensitivity analyses in which the regression models for OS and CSS were performed using variables with non-extensive missing data only, namely Age, Race, Stage, Housing Index, MediFund and Marital status. No imputation was performed.

Statistical significance was defined by two-sided p value less than 0.05. All statistical analyses were performed using R software (version 3.6.3).

### 2.4. Role of the funding source

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## 3. Results

A total of 15,532 patients met the selection criteria and were analysed. The median age at diagnosis was 53.7 years-old (range 17.3–97.2). Our study cohort was slightly over-represented by ethnic Chinese (82.1%) vs Malays (9.8%) and Indians (5.3%) compared to the actual population percentiles of 76.2%, 15.0%, and 7.4% respectively. Most patients (66.6%) lived in properties with HI of 3

**Table 2**
Criteria to determine recommendations for each modality of therapy for the individual patient based on their stage and disease characteristics.

| Treatment modality | Criteria |
|---|---|
| Surgery: | All non-metastatic cancer patients (Stage 0–III) were assumed to need surgery. Patients were deemed compliant if surgery was performed within 6 months from histological diagnosis in those without neoadjuvant chemotherapy and within 1 year for those who received neoadjuvant chemotherapy. |
| Chemotherapy: | Patients were assumed to require chemotherapy if<br>AJCC N-stage is N1–3 or<br>AJCC T-stage is T2–4 or<br>Tumour size > 10 mm and<br>Grade 3 tumour or<br>ER negative or<br>HER2 positive |
| Radiotherapy: | Patients were assumed to require radiotherapy if<br>AJCC N-stage is N1–3 or<br>AJCC T-stage is T3–4 or<br>Breast conservation surgery |
| Endocrine therapy: | Patients were assumed to require endocrine therapy if<br>ER positive or<br>PR positive |
| Targeted therapy: | Patients were assumed to require targeted therapy if<br>HER 2+ positive and<br>needs chemotherapy |

AJCC: American Joint Committee on Cancer, 7th edition, ER: estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2.

and 4, followed by 27.4% in HI of 5 or more and the remaining 6.0% in 1–2 room HDB flats (HI<3) (Table 3).

Overall, 15.8% of patients had received MediFund. Patients in HI(low) were much more likely to have received MediFund compared to HI(high) (37.6% vs 5.5%) (Table 3). Moreover, 26.5% of Stage III patients and 26.9% of Stage IV patients had received MediFund compared to 16.5% and 9.3% of stage II and I respectively, suggesting that patients with higher stage disease with higher treatment burden were more likely to receive MediFund.

Comparing across the three HI strata, patients in lower tiers were more likely to be older at presentation, not married, ethnic Malay and to present with more advanced disease (Table 3). Patients in the lower HI-tiers also appeared to present with higher grade disease (37.9% vs 41.9% vs 43.5%) but with only small differences in Estrogen Receptor (ER) and Progesterone Receptor (PR) and Human Epidermal Receptor 2 (HER2) receptor status. Patients with higher HI were more likely to undergo breast conserving surgery (BCS) (36.6% vs 28.8% vs 21.2%). Among those who had mastectomy, higher HI was associated with higher rates of postmastectomy reconstruction (20.9% vs 14.5% vs 8.7%) (Table 3).

Amongst the treatment modalities, noncompliance rates were higher for targeted therapy (35.6%) and chemotherapy (24.5%). All other treatments had noncompliance rates of less than 10%. Patients in lower HI-tiers were more likely to be noncompliant to timely surgery and radiotherapy (Table 3). Patients who received MediFund subsidies were twice as likely to be compliant to systemic therapy (Table 4). This effect was most evident for targeted therapy (noncompliance rates 42.8% vs 19.8%).

Patients were followed-up for a median of 7.6 years (IQR: 4.5–11.3years). Observed five- and ten-year survival were significantly better for patients with higher HI for each survival endpoint. Ten-year OS were 75.8%, 69.7% and 61.3% (Table 5, Fig. 1); ten-year CSS were 83.2%, 77.6% and 74.6% (Table 5, Fig. 2); ten-year NCSS were 92.6%, 92.1% and 86.6% (Table 5, Fig. 2) for HI(high), HI(med) and HI(low) respectively. Approximately 80% of deaths at 5 years were due to breast cancer which decreased to about 70% at 10 years (Table 5, Fig. 2).

In the multivariable analysis (MVA) for OS, commonly known clinical breast cancer prognostic factors including older age, higher cancer stage, higher tumour grade, ER/PR negativity were associated with higher risk of any deaths. Relative to the dominant Chinese ethnicity in Singapore, Malays had higher death risks; HR 1.40 (95% CI 1.27–1.54, $p<0.0001$). Noncompliance to treatment significantly increased the odds of deaths. In the adjuvant setting, noncompliance to treatment significantly increased risks of death with HR 1.87 (95% CI 1.63–2.14, $p<0.0001$) in patients who were noncompliant to radiotherapy to HR 2.41 (95% CI 2.01–2.90, $p<0.0001$) for those noncompliant to targeted therapy (Table 6). Compared to HI(high), both HI(med) and HI(low) have increased deaths risk with HR 1.14 (95% CI 1.05–1.23, $p = 0.0015$) and HR 1.16 (95% CI 1.01–1.33, $p = 0.030$) respectively in MVA. Despite being associated with OS in univariable analysis (HR=1.64 [95% CI 1.52–1.77], $p<0.0001$), the receipt of MediFund is no longer an independent prognostic factor for OS (HR=1.03 [95% CI 0.95–1.12], $p = 0.52$) in MVA (Table 6).

In the MVA for CSS, the same pattern of significantly increased risks of breast cancer deaths in patients with higher stage, higher grade, ER/PR negative disease as well as in ethnic Malay patients was observed. Patients at the extremes of ages also have higher risks of breast cancer deaths. Increased breast cancer death risk was associated with the noncompliance to adjuvant therapy. Compared to HI(high), patients in HI(med) were associated with higher risk of breast cancer deaths, HR 1.15 (95% CI 1.03–1.27, $p = 0.010$). The association of patients in HI(low) with breast cancer deaths in UVA (HR 1.63 (95% CI 1.39–1.92, $p<0.0001$) was not seen in the MVA, HR 1.14 (95% CI 0.95–1.37, $p = 0.17$). Similar with OS, the receipt of MediFund is not an independent prognostic factor for CSS (Table 7).

The PH assumption was violated for all the variables in the OS model other than Race and Radiotherapy, and for all the variables in the CSS model other than Race, MediFund, PR status and Radiotherapy. Adjustments to the models to account for variables which violated the PH assumption did not change the conclusions on the associations noted between HI / MediFund with OS in Table 6 and CSS in Table 7 (results not shown).

A significant proportion of the study cohort had missing data for Tumour grade, ER, PR, HER2 status and the various treatment modalities (9.6% to 33.2%). However, the missing data did not have a major impact on the results. There were no large differences between the univariate HRs of these variables in Tables 6 and 7 and those obtained when the unknowns in each of these variables were excluded. Excluding these variables from the sensitivity analysis for OS (Supplementary Table 2) and CSS (Supplementary Table 3), the HR for HI and MediFund based on the reduced models were also similar as those based on the full models in Table 6 and 7.

**Table 3**
Patients and disease characteristics, treatment, and compliance by Housing value Index (HI) categories.

| | Overall (N/%) $N = 15,532$ | HI(high) 4251 (27.3%) | HI(med) 10,343 (66.6%) | HI(low) 938 (6.0%) | *P* value |
|---|---|---|---|---|---|
| Median follow-up (Inter Quartile Range) | 7.6 years | 7.63 years (4.26–11.60) | 7.69 years (4.56–11.22) | 8.01 years (4.53–12.04) | |
| Age | | | | | |
| <40yrs | 1381 (8.9%) | 363 (8.5%) | 961 (9.3%) | 57 (6.1%) | <0.0001 |
| 40 to 50yrs | 4457 (28.7%) | 1232 (29.0%) | 3050 (29.5%) | 175 (18.7%) | |
| 50 to 60yrs | 4874 (31.4%) | 1290 (30.3%) | 3299 (31.9%) | 285 (30.4%) | |
| 60 to 70yrs | 3125 (20.1%) | 860 (20.2%) | 1998 (19.3%) | 267 (28.5%) | |
| ≥70yrs | 1695 (10.9%) | 506 (11.9%) | 1035 (10.0%) | 154 (16.4%) | |
| Race | | | | | |
| Chinese | 12,753 (82.1%) | 3638 (85.6%) | 8418 (81.4%) | 697 (74.3%) | <0.0001 |
| Indian | 816 (5.3%) | 222 (5.2%) | 534 (5.2%) | 60 (6.4%) | |
| Malay | 1519 (9.8%) | 227 (5.3%) | 1131 (10.9%) | 161 (17.2%) | |
| Others | 444 (2.9%) | 164 (3.9%) | 260 (2.5%) | 20 (2.1%) | |
| Stage | | | | | |
| 0 | 1944 (12.5%) | 652 (15.3%) | 1201 (11.6%) | 91 (9.7%) | <0.0001 |
| I | 4214 (27.1%) | 1384 (32.6%) | 2631 (25.4%) | 199 (21.2%) | |
| II | 5272 (33.9%) | 1360 (32.0%) | 3588 (34.7%) | 324 (34.5%) | |
| III | 2795 (18.0%) | 583 (13.7%) | 2002 (19.4%) | 210 (22.4%) | |
| IV | 1307 (8.4%) | 272 (6.4%) | 921 (8.9%) | 114 (12.2%) | |
| MediFund | | | | | |
| Never received | 13,074 (84.2%) | 4019 (94.5%) | 8470 (81.9%) | 585 (62.4%) | <0.0001 |
| Ever received | 2458 (15.8%) | 232 (5.5%) | 1873 (18.1%) | 353 (37.6%) | |
| Marital Status | | | | | |
| Married | 10,440 (67.2%) | 3036 (71.4%) | 6909 (66.8%) | 495 (52.8%) | <0.0001 |
| Never married | 1992 (12.8%) | 425 (10.0%) | 1412 (13.7%) | 155 (16.5%) | |
| Previously married | 1329 (8.6%) | 279 (6.6%) | 884 (8.5%) | 166 (17.7%) | |
| Unknown | 1771 (11.4%) | 511 (12.0%) | 1138 (11.0%) | 122 (13.0%) | |
| Tumour Grade | | | | | |
| Grade 1–2 | 7562 (48.7%) | 2222 (52.3%) | 4928 (47.6%) | 412 (43.9%) | <0.0001 |
| Grade 3 | 6352 (40.9%) | 1613 (37.9%) | 4331 (41.9%) | 408 (43.5%) | |
| Unknown | 1618 (10.4%) | 416 (9.8%) | 1084 (10.5%) | 118 (12.6%) | |
| ER Status | | | | | |
| Positive | 10,160 (65.4%) | 2760 (64.9%) | 6797 (65.7%) | 603 (64.3%) | <0.0001 |
| Negative | 3646 (23.5%) | 929 (21.9%) | 2469 (23.9%) | 248 (26.4%) | |
| Unknown | 1726 (11.1%) | 562 (13.2%) | 1077 (10.4%) | 87 (9.3%) | |
| PR Status | | | | | |
| Positive | 8650 (55.7%) | 2348 (55.2%) | 5788 (56.0%) | 514 (54.8%) | <0.0001 |
| Negative | 5022 (32.3%) | 1301 (30.6%) | 3393 (32.8%) | 328 (35.0%) | |
| Unknown | 1860 (12.0%) | 602 (14.2%) | 1162 (11.2%) | 96 (10.2%) | |
| HER2 Status | | | | | |
| Negative | 8377 (53.9%) | 2276 (53.5%) | 5581 (54.0%) | 520 (55.4%) | <0.0001 |
| Positive | 3528 (22.7%) | 842 (19.8%) | 2454 (23.7%) | 232 (24.7%) | |
| Unknown | 3627 (23.4%) | 1133 (26.7%) | 2308 (22.3%) | 186 (19.8%) | |
| Surgery | | | | | |
| Breast Conserving Surgery | 4731 (30.5%) | 1555 (36.6%) | 2977 (28.8%) | 199 (21.2%) | <0.0001 |
| Mastectomy | 8251 (53.1%) | 2002 (47.1%) | 5674 (54.9%) | 575 (61.3%) | |
| No Surgery | 451 (2.9%) | 85 (2.0%) | 327 (3.2%) | 39 (4.2%) | |
| Unknown | 2099 (13.5%) | 609 (14.3%) | 1365 (13.2%) | 125 (13.3%) | |
| Breast reconstruction[a] | | | | | |
| Yes | 1293 (15.7%) | 419 (20.9%) | 824 (14.5%) | 50 (8.7%) | <0.0001 |
| No | 6405 (77.6%) | 1455 (72.7%) | 4461 (78.6%) | 489 (85.0%) | |
| Unknown | 553 (6.7%) | 128 (6.4%) | 389 (6.9%) | 36 (6.3%) | |
| Timely Surgery | | | | | |
| Yes | 12,474 (80.3%) | 3434 (80.8%) | 8306 (80.3%) | 734 (78.3%) | <0.0001 |
| No | 259 (1.7%) | 65 (1.5%) | 169 (1.6%) | 25 (2.7%) | |
| Not needed | 1307 (8.4%) | 272 (6.4%) | 921 (8.9%) | 114 (12.2%) | |
| Not assessable | 1492 (9.6%) | 480 (11.3%) | 947 (9.2%) | 65 (6.9%) | |
| Non-compliance rate[b] | 2.03% | 1.86% | 1.99% | 3.29% | 0.036[c] |
| Radiotherapy | | | | | |
| Yes | 7023 (45.2%) | 1940 (45.6%) | 4705 (45.5%) | 378 (40.3%) | 0.014 |
| No | 749 (4.8%) | 183 (4.3%) | 512 (5.0%) | 54 (5.8%) | |
| Not needed | 4286 (27.6%) | 1143 (26.9%) | 2858 (27.6%) | 285 (30.4%) | |
| Not assessable | 3474 (22.4%) | 985 (23.2%) | 2268 (21.9%) | 221 (23.6%) | |
| Non-compliance rate[b] | 9.63% | 8.62% | 9.81% | 12.50% | 0.034[c] |
| Chemotherapy | | | | | |
| Yes | 6069 (39.1%) | 1457 (34.3%) | 4236 (41.0%) | 376 (40.1%) | <0.0001 |
| No | 1965 (12.7%) | 506 (11.9%) | 1297 (12.5%) | 162 (17.3%) | |
| Not needed | 2339 (15.1%) | 773 (18.2%) | 1459 (14.1%) | 107 (11.4%) | |
| Not assessable | 5159 (33.2%) | 1515 (35.6%) | 3351 (32.4%) | 293 (31.2%) | |
| Non-compliance rate[b] | 24.50% | 25.78% | 23.44% | 30.11% | 0.0008[c] |
| Endocrine therapy | | | | | |
| Yes | 8563 (55.1%) | 2260 (53.2%) | 5781 (55.9%) | 522 (55.7%) | <0.0001 |
| No | 857 (5.5%) | 250 (5.9%) | 561 (5.4%) | 46 (4.9%) | |
| Not needed | 3097 (19.9%) | 797 (18.7%) | 2095 (20.3%) | 205 (21.9%) | |
| Not assessable | 3015 (19.4%) | 944 (22.2%) | 1906 (18.4%) | 165 (17.6%) | |
| Non-compliance rate[b] | 9.10% | 9.96% | 8.85% | 8.10% | 0.18[c] |

(*continued on next page*)

**Table 3** (*continued*)

| | Overall (N/%) $N = 15,532$ | HI(high) 4251 (27.3%) | HI(med) 10,343 (66.6%) | HI(low) 938 (6.0%) | *P* value |
|---|---|---|---|---|---|
| Targeted therapy | | | | | |
| Yes | 1366 (8.8%) | 309 (7.3%) | 974 (9.4%) | 83 (8.8%) | 0.0005 |
| No | 756 (4.9%) | 187 (4.4%) | 520 (5.0%) | 49 (5.2%) | |
| Not needed | 9518 (61.3%) | 2627 (61.8%) | 6321 (61.1%) | 570 (60.8%) | |
| Not assessable | 3892 (25.1%) | 1128 (26.5%) | 2528 (24.4%) | 236 (25.2%) | |
| Non-compliance rate[b] | 35.63% | 37.70% | 34.81% | 37.12% | 0.47[c] |

[a] Receipt of reconstruction was assessed only amongst patients who received mastectomy.
[b] Non-compliance was assessed only amongst patients defined as needing the treatment, i.e. ["No"/("Yes"+"No")].
[c] The chi square test was conducted between HI-tiers for each treatment modality only amongst patients assessed to need the treatment.ER: estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2.

**Table 4**
Receipt of treatment according to MediFund status.

| | Never received Medifund ($n = 13,074$) | Ever received Medifund ($n = 2458$) | Chi square *P* value |
|---|---|---|---|
| Timely surgery | | | |
| **Yes** | 10,576 (80.9%) | 1898 (77.2%) | |
| **No** | 195 (1.5%) | 64 (2.6%) | |
| **Not needed** | 956 (7.3%) | 351 (14.3%) | |
| **Not assessable** | 1347 (10.3%) | 145 (5.9%) | |
| **Non-compliance rate[a]** | 1.81% | 3.26% | <0.0001[b] |
| Radiotherapy | | | |
| **Yes** | 5858 (44.8%) | 1165 (47.4%) | |
| **No** | 612 (4.7%) | 137 (5.6%) | |
| **Not needed** | 3704 (28.3%) | 582 (23.7%) | |
| **Not assessable** | 2900 (22.2%) | 574 (23.4%) | |
| **Non-compliance rate[a]** | 9.46% | 10.52% | 0.24[b] |
| Chemotherapy | | | |
| **Yes** | 4601 (35.2%) | 1468 (59.7%) | |
| **No** | 1725 (13.2%) | 240 (9.8%) | |
| **Not needed** | 2127 (16.3%) | 212 (8.6%) | |
| **Not assessable** | 4621 (35.3%) | 538 (21.9%) | |
| **Non-compliance rate[a]** | 27.27% | 14.05% | <0.0001[b] |
| Endocrine therapy | | | |
| **Yes** | 7050 (53.9%) | 1513 (61.6%) | |
| **No** | 785 (6.0%) | 72 (2.9%) | |
| **Not needed** | 2513 (19.2%) | 584 (23.8%) | |
| **Not assessable** | 2726 (20.9%) | 289 (11.8%) | |
| **Non-compliance rate[a]** | 10.02% | 4.54% | <0.0001[b] |
| Targeted therapy | | | |
| **Yes** | 834 (6.4%) | 532 (21.6%) | |
| **No** | 625 (4.8%) | 131 (5.3%) | |
| **Not needed** | 8127 (62.2%) | 1391 (56.6%) | |
| **Not assessable** | 3488 (26.7%) | 404 (16.4%) | |
| **Non-compliance rate[a]** | 42.84% | 19.76% | <0.0001[b] |

[a] Non-compliance was assessed only amongst patients defined as needing the treatment, i.e. ["No"/("Yes"+"No")].
[b] The chi square test was conducted between HI-tiers for each treatment modality only amongst patients assessed to need the treatment.

**Table 5**
Clinical outcomes[a] of patients by housing value index (HI) tiers.

| | **Overall** | **HI (high)** | **HI (med)** | **HI (low)** | ***P* value** |
|---|---|---|---|---|---|
| **OS** | | | | | <0.0001[b] |
| **5-year** | 82.2% (81.6%–82.9%) | 85.6% (84.4%–86.7%) | 81.5% (80.7%–82.3%) | 75.9% (72.8%–78.6%) | |
| **10-year** | 70.8% (69.9%–71.7%) | 75.8% (74.2%–77.4%) | 69.7% (68.6%–70.8%) | 61.3% (57.2%–65.1%) | |
| **CSS** | | | | | <0.0001[c] |
| **5-year** | 85.9% (85.3%–86.4%) | 88.9% (87.8%–89.9%) | 85.1% (84.4%–85.9%) | 80.8% (78.1%–83.4%) | |
| **10-year** | 79.0% (78.2%–79.7%) | 83.2% (81.8%–84.5%) | 77.6% (76.7%–78.6%) | 74.6% (71.3%–77.9%) | |
| **NCSS** | | | | | <0.0001[c] |
| **5-year** | 96.4% (96.0%–96.7%) | 96.8% (96.2%–97.3%) | 96.3% (95.9%–96.7%) | 95.1% (93.4%–96.4%) | |
| **10-year** | 91.9% (91.3%–92.4%) | 92.6% (91.5%–93.6%) | 92.1% (91.4%–92.7%) | 86.6% (83.7%–89.3%) | |

OS: Overall survival, CSS: Cancer specific survival; NCSS: Non-cancer specific survival.
[a] Unadjusted actuarial rates.
[b] Logrank test.
[c] Gray's test* *P* value calculated using wald test.

**Table 6**
Univariable and multivariable Cox regression analysis of overall survival.

| | E/N | Univariable analysis HR (95% CI) | *P* value | Multivariable analysis HR (95% CI) | *P* value |
|---|---|---|---|---|---|
| **Age** | | | | | |
| **<40yrs** | 295/1381 | 1 | | 1 | |
| **<50yrs** | 762/4457 | 0.74 (0.65–0.84) | <0.0001 | 0.81 (0.71–0.93) | 0.0029 |
| **<60yrs** | 1127/4874 | 1.09 (0.96–1.24) | 0.19 | 1.04 (0.92–1.19) | 0.51 |
| **<70yrs** | 7,97/3125 | 1.35 (1.18–1.54) | <0.0001 | 1.23 (1.07–1.41) | 0.0028 |
| **≥70yrs** | 771/1695 | 3.07 (2.69–3.52) | <0.0001 | 2.17 (1.88–2.51) | <0.0001 |
| **Race** | | | | | |
| **Chinese** | 2903/12,753 | 1 | | 1 | |
| **Indian** | 224/816 | 1.36 (1.19–1.56) | <0.0001 | 1.12 (0.98–1.29) | 0.0998 |
| **Malay** | 530/1519 | 1.81 (1.65–1.98) | <0.0001 | 1.40 (1.27–1.54) | <0.0001 |
| **Others** | 95/444 | 1.05 (0.86–1.29) | 0.64 | 1.01 (0.82–1.24) | 0.91 |
| **AJCC Stage** | | | | | |
| **0** | 113/1944 | 1 | | 1 | |
| **I** | 397/4214 | 1.60 (1.30–1.97) | <0.0001 | 1.62 (1.30–2.02) | <0.0001 |
| **II** | 1033/5272 | 3.47 (2.85–4.21) | <0.0001 | 2.72 (2.20–3.36) | <0.0001 |
| **III** | 1123/2795 | 8.97 (7.39–10.88) | <0.0001 | 7.34 (5.93–9.09) | <0.0001 |
| **IV** | 1086/1307 | 38.73 (31.86–47.09) | <0.0001 | 19.60 (15.72–24.43) | <0.0001 |
| **Housing Index** | | | | | |
| **HI (high)** | 845/4251 | 1 | | 1 | |
| **HI (med)** | 2602/10,343 | 1.30 (1.21–1.41) | <0.0001 | 1.14 (1.05–1.23) | 0.0015 |
| **HI (low)** | 305/938 | 1.76 (1.55–2.01) | <0.0001 | 1.16 (1.01–1.33) | 0.03 |
| **MediFund** | | | | | |
| **Never received** | 2942/13,074 | 1 | | 1 | |
| **Ever received** | 810/2458 | 1.64 (1.52–1.77) | <0.0001 | 1.03 (0.95–1.12) | 0.52 |
| **Marital Status** | | | | | |
| **Married** | 2417/10,440 | 1 | | 1 | |
| **Never married** | 437/1992 | 0.99 (0.89–1.09) | 0.80 | 1.04 (0.94–1.16) | 0.42 |
| **Previously married** | 412/1329 | 1.57 (1.41–1.74) | <0.0001 | 1.07 (0.96–1.19) | 0.24 |
| **Unknown** | 486/1771 | 1.45 (1.31–1.60) | <0.0001 | 1.22 (1.10–1.36) | 0.0001 |
| **Tumour grade** | | | | | |
| **Grade 1–2** | 1237/7562 | 1 | | 1 | |
| **Grade 3** | 1719/6352 | 1.84 (1.71–1.97) | <0.0001 | 1.39 (1.28–1.50) | <0.0001 |
| **Unknown** | 796/1618 | 4.02 (3.68–4.39) | <0.0001 | 1.22 (1.10–1.35) | 0.0001 |
| **ER status** | | | | | |
| **Positive** | 2088/10,160 | 1 | | 1 | |
| **Negative** | 1152/3646 | 1.63 (1.52–1.76) | <0.0001 | 1.59 (1.36–1.86) | <0.0001 |
| **Unknown** | 512/1726 | 1.18 (1.07–1.30) | 0.0008 | 0.81 (0.59–1.12) | 0.20 |
| **PR status** | | | | | |
| **Positive** | 1686/8650 | 1 | | 1 | |
| **Negative** | 1521/5022 | 1.67 (1.56–1.79) | <0.0001 | 1.41 (1.28–1.56) | <0.0001 |
| **Unknown** | 545/1860 | 1.27 (1.15–1.40) | <0.0001 | 1.16 (0.85–1.60) | 0.3537 |
| **HER2 status** | | | | | |
| **Negative** | 1953/8377 | 1 | | 1 | |
| **Positive** | 980/3528 | 1.27 (1.17–1.37) | <0.0001 | 0.99 (0.72–1.38) | 0.97 |
| **Unknown** | 819/3627 | 0.83 (0.77–0.91) | <0.0001 | 0.97 (0.69–1.36) | 0.86 |
| **Timely surgery**[a] | | | | | |
| **Yes** | 2028/12,474 | 1 | | | |
| **No** | 147/259 | 4.41 (3.73–5.21) | <0.0001 | | |
| **Not needed** | 1086/1307 | 12.98 (12.02–14.01) | <0.0001 | | |
| **Not assessable** | 491/1492 | 2.40 (2.17–2.65) | <0.0001 | | |
| **Radiotherapy** | | | | | |
| **Yes** | 1278/7023 | 1 | | 1 | |
| **No** | 307/749 | 2.71 (2.39–3.07) | <0.0001 | 1.87 (1.63–2.14) | <0.0001 |
| **Not needed** | 563/4286 | 0.75 (0.68–0.83) | <0.0001 | 1.07 (0.96–1.20) | 0.22 |
| **Not assessable** | 1604/3474 | 3.86 (3.59–4.16) | <0.0001 | 1.92 (1.73–2.13) | <0.0001 |
| **Chemotherapy** | | | | | |
| **Yes** | 1403/6069 | 1 | | 1 | |
| **No** | 550/1965 | 1.21 (1.10–1.33) | 0.0002 | 1.10 (0.99–1.23) | 0.086 |
| **Not needed** | 151/2339 | 0.27 (0.23–0.32) | <0.0001 | 0.61 (0.48–0.79) | 0.0001 |
| **Not assessable** | 1648/5159 | 1.56 (1.45–1.67) | <0.0001 | 1.22 (1.09–1.36) | 0.0004 |
| **Endocrine therapy** | | | | | |
| **Yes** | 1795/8563 | 1 | | 1 | |
| **No** | 142/857 | 0.83 (0.70–0.98) | 0.030 | 1.40 (1.17–1.67) | 0.0002 |
| **Not needed** | 966/3097 | 1.68 (1.55–1.81) | <0.0001 | 0.84 (0.69–1.02) | 0.072 |
| **Not assessable** | 849/3015 | 1.38 (1.27–1.50) | <0.0001 | 1.42 (1.26–1.61) | <0.0001 |
| **Targeted therapy** | | | | | |
| **Yes** | 201/1366 | 1 | | 1 | |
| **No** | 310/756 | 2.28 (1.91–2.73) | <0.0001 | 2.41 (2.01–2.90) | <0.0001 |
| **Not needed** | 2031/9518 | 1.33 (1.15–1.54) | 0.0001 | 2.02 (1.41–2.89) | 0.0001 |
| **Not assessable** | 1210/3892 | 1.93 (1.66–2.24) | <0.0001 | 1.81 (1.51–2.18) | <0.0001 |

[†a] Due to concern of multicollinearity, "Timely surgery" was excluded from multivariable analyses as all Stage IV patients were categorized as not needing ("No") surgery.AJCC: American Joint Committee on Cancer, 7th edition, ER: estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2.

**Table 7**
Univariable and multivariable Cox regression analysis of cancer specific survival.

| | E/N | Univariable analysis HR (95% CI) | *P* value | Multivariable analysis HR (95% CI) | *P* value |
|---|---|---|---|---|---|
| **Age** | | | | | |
| **<40yrs** | 245/1381 | 1 | | 1 | |
| **<50yrs** | 618/4457 | 0.73 (0.64–0.85) | <0.0001 | 0.86 (0.73–1.00) | 0.053 |
| **<60yrs** | 850/4874 | 0.97 (0.84–1.11) | 0.64 | 0.94 (0.81–1.10) | 0.43 |
| **<70yrs** | 522/3125 | 0.99 (0.85–1.15) | 0.89 | 0.95 (0.80–1.12) | 0.55 |
| **≥70yrs** | 444/1695 | 1.74 (1.49–2.03) | <0.0001 | 1.26 (1.05–1.51) | 0.015 |
| **Race** | | | | | |
| **Chinese** | 2045/12,753 | 1 | | 1 | |
| **Indian** | 155/816 | 1.28 (1.09–1.50) | 0.0032 | 1.00 (0.83–1.20) | 0.99 |
| **Malay** | 417/1519 | 1.94 (1.74–2.16) | <0.0001 | 1.28 (1.13–1.46) | 0.0001 |
| **Others** | 62/444 | 0.95 (0.74–1.22) | 0.69 | 0.91 (0.69–1.20) | 0.50 |
| **AJCC Stage** | | | | | |
| **0** | 24/1944 | 1 | | 1 | |
| **I** | 185/4214 | 3.46 (2.26–5.29) | <0.0001 | 4.03 (2.60–6.24) | <0.0001 |
| **II** | 639/5272 | 9.83 (6.55–14.77) | <0.0001 | 8.14 (5.30–12.49) | <0.0001 |
| **III** | 886/2795 | 29.84 (19.91–44.72) | <0.0001 | 25.19 (16.41–38.66) | <0.0001 |
| **IV** | 945/1307 | 115.26 (76.81–172.97) | <0.0001 | 65.11 (42.03–100.86) | <0.0001 |
| **Housing Index** | | | | | |
| **HI (high)** | 589/4251 | 1 | | 1 | |
| **HI (med)** | 1884/10,343 | 1.33 (1.21–1.46) | <0.0001 | 1.15 (1.03–1.27) | 0.0099 |
| **HI (low)** | 206/938 | 1.63 (1.39–1.92) | <0.0001 | 1.14 (0.95–1.37) | 0.17 |
| **MediFund** | | | | | |
| **Never received** | 2078/13,074 | 1 | | 1 | |
| **Ever received** | 601/2458 | 1.63 (1.49–1.79) | <0.0001 | 0.96 (0.86–1.07) | 0.47 |
| **Marital Status** | | | | | |
| **Married** | 1753/10,440 | 1 | | 1 | |
| **Never married** | 348/1992 | 1.08 (0.97–1.22) | 0.16 | 1.09 (0.96–1.23) | 0.17 |
| **Previously married** | 267/1329 | 1.32 (1.16–1.50) | <0.0001 | 0.93 (0.80–1.08) | 0.36 |
| **Unknown** | 311/1771 | 1.22 (1.08–1.38) | 0.0015 | 1.01 (0.87–1.17) | 0.9 |
| **Tumour grade** | | | | | |
| **Grade 1–2** | 742/7562 | 1 | | 1 | |
| **Grade 3** | 1315/6352 | 2.28 (2.09–2.49) | <0.0001 | 1.52 (1.38–1.69) | <0.0001 |
| **Unknown** | 622/1618 | 4.93 (4.42–5.50) | <0.0001 | 1.24 (1.08–1.42) | 0.0019 |
| **ER status** | | | | | |
| **Positive** | 1394/10,160 | 1 | | 1 | |
| **Negative** | 900/3646 | 1.92 (1.76–2.09) | <0.0001 | 1.87 (1.53–2.28) | <0.0001 |
| **Unknown** | 385/1726 | 1.47 (1.31–1.65) | <0.0001 | 0.88 (0.52–1.50) | 0.64 |
| **PR status** | | | | | |
| **Positive** | 1136/8650 | 1 | | 1 | |
| **Negative** | 1138/5022 | 1.84 (1.70–2.00) | <0.0001 | 1.40 (1.23–1.60) | <0.0001 |
| **Unknown** | 405/1860 | 1.53 (1.36–1.72) | <0.0001 | 1.08 (0.64–1.82) | 0.76 |
| **HER2 status** | | | | | |
| **Negative** | 1351/8377 | 1 | | 1 | |
| **Positive** | 753/3528 | 1.40 (1.28–1.54) | <0.0001 | 0.79 (0.47–1.33) | 0.38 |
| **Unknown** | 575/3627 | 0.92 (0.83–1.01) | 0.083 | 0.88 (0.52–1.50) | 0.65 |
| **Timely surgery**[a] | | | | | |
| **Yes** | 1280/12,474 | 1 | | | |
| **No** | 103/259 | 4.40 (3.60–5.39) | <0.0001 | | |
| **Not needed** | 945/1307 | 13.66 (12.49–14.94) | <0.0001 | | |
| **Not assessable** | 351/1492 | 2.71 (2.41–3.05) | <0.0001 | | |
| **Radiotherapy** | | | | | |
| **Yes** | 921/7023 | 1 | | 1 | |
| **No** | 218/749 | 2.48 (2.14–2.87) | <0.0001 | 1.84 (1.55–2.19) | <0.0001 |
| **Not needed** | 270/4286 | 0.49 (0.43–0.56) | <0.0001 | 0.87 (0.75–1.01) | 0.075 |
| **Not assessable** | 1270/3474 | 3.90 (3.58–4.25) | <0.0001 | 1.72 (1.50–1.97) | <0.0001 |
| **Chemotherapy** | | | | | |
| **Yes** | 1086/6069 | 1 | | 1 | |
| **No** | 320/1965 | 0.90 (0.79–1.01) | 0.084 | 0.99 (0.85–1.16) | 0.93 |
| **Not needed** | 61/2339 | 0.14 (0.11–0.18) | <0.0001 | 0.53 (0.37–0.76) | 0.0005 |
| **Not assessable** | 1212/5159 | 1.49 (1.37–1.61) | <0.0001 | 1.19 (1.03–1.36) | 0.016 |
| **Endocrine therapy** | | | | | |
| **Yes** | 1188/8563 | 1 | | 1 | |
| **No** | 91/857 | 0.81 (0.65–1.00) | 0.048 | 1.49 (1.17–1.91) | 0.0014 |
| **Not needed** | 752/3097 | 1.97 (1.80–2.16) | <0.0001 | 0.80 (0.62–1.02) | 0.077 |
| **Not assessable** | 648/3015 | 1.70 (1.54–1.87) | <0.0001 | 1.66 (1.42–1.94) | <0.0001 |
| **Targeted therapy** | | | | | |
| **Yes** | 160/1366 | 1 | | 1 | |
| **No** | 230/756 | 2.24 (1.83–2.73) | <0.0001 | 2.62 (2.11–3.24) | <0.0001 |
| **Not needed** | 1379/9518 | 1.17 (0.99–1.38) | 0.058 | 1.60 (0.93–2.76) | 0.087 |
| **Not assessable** | 910/3892 | 1.96 (1.66–2.32) | <0.0001 | 1.82 (1.45–2.28) | <0.0001 |

[a] Due to concern of multicollinearity, "Timely surgery" was excluded from multivariable analyses as all Stage IV patients were categorized as not needing ("No") surgery. All variables analysed in univariable analysis were used as covariates for adjustment in the multivariable analysis.AJCC: American Joint Committee on Cancer, 7th edition, ER: estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2.

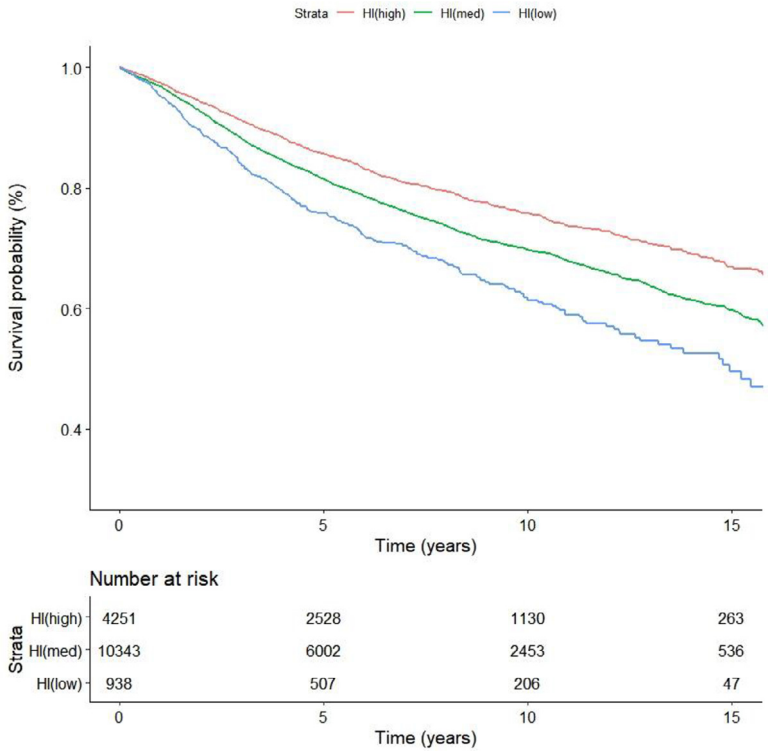


**Fig. 1.** Kaplan Meier plot of overall survival (OS) by Housing value Index (HI).
Legend: HI(high): HI≥5, HI(med): 3≤HI<5, HI(low): HI<3.

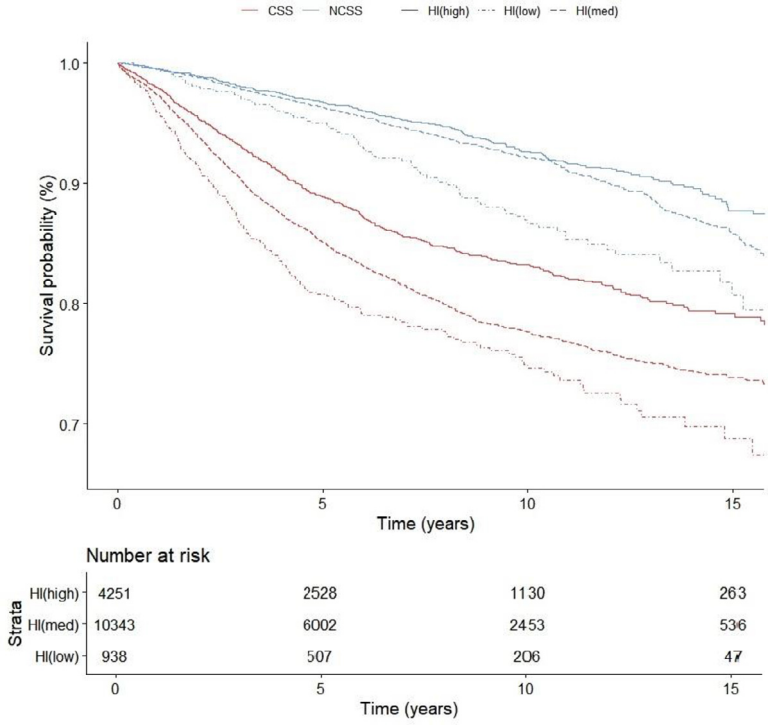


**Fig. 2.** Cancer specific survival (CSS) and Non-cancer specific survival (NCSS) by Housing value Index (HI).
Legend: HI(high): HI≥5, HI(med): 3≤HI<5, HI(low): HI<3.

## 4. Discussion

In this study, we found evidence of disparities in both cancer and non-cancer survival of breast cancer patients in Singapore. Despite having ready access to high-quality care, as well as enhanced subsidies for the financially needy, breast cancer patients who lived in lower value housing had lower CSS. Lower HI patients presented with advanced cancers more often and had higher rates of treatment non-compliance, but MediFund subsidies increased compliance, especially for targeted therapy. Furthermore, lower HI survivors suffered from higher non-cancer mortality which compounded the existing higher cancer mortality to produce a nearly

15-percentage point reduction in 10-years OS between patients at extremes of HI-tiers.

Similar to Singapore, disparities in health outcomes of patients of different SES remains a challenge in many other countries. Our findings are similar to earlier work performed using mostly district SES indicators. In Canada, using neighborhood income as estimate of SES, Kumachev and co-workers showed that higher SES breast cancer patients were diagnosed earlier and more compliant with treatment and had 5-year OS rates difference of 5.7% between extreme-most quintiles. [15] Studies from Australia and Denmark which have universal healthcare reported similar findings. [16,17] Our findings also echoed earlier local studies that associated patients staying in lower value housing with lower participation in health screening, preference for alternative medicine and poorer health outcomes in psychiatric illness, chronic disease and head and neck cancer. [12,18] Structured interviews with patients have cited costs as a major concern. [19,20]

Our methodology of using derived HI as a surrogate of SES was first used in a study of patients with head and neck cancer in Singapore. [12] Wong and co-workers found that highest SES patients have mortality risk one-third of those in the lowest tier, despite similar cancer stage. HI is a sensitive measurement of SES in Singapore where housing expenses consume a large proportion of residents' income. Using "Median Multiple" (median house price divided by the median household income) as a measurement of middle-income housing affordability as recommended by the World Bank and the United Nations, housing in Singapore (Median Multiple: 4.6) is considered "seriously unaffordable". [21] However, HI is an imperfect measurement of SES as patients may choose to live below their means hence lowering the discrimination power.

Across HI-tiers, patients had cancers with similar proportions of histological characteristics. However, patients in lower HI-tiers tended to present with more advanced cancer suggesting a lower screening uptake and delayed health-seeking behavior. Our study also revealed associations of lower HI with delays in surgery and reduced compliance to systemic treatment and radiotherapy, all of which is known to adversely affect disease control. [22,23] Patients in lower HI-tiers were also more likely to undergo mastectomy over breast conserving therapy and less likely to undergo breast reconstruction; concurring with observations noted in other studies. [24,25] We speculate that poorer patients may ill-afford the work and family disruption from a lengthy course of adjuvant radiotherapy nor the expense of reconstructive surgery.

Taken together, our study showed that stage at presentation and treatment decisions that drove the observed differences in breast cancer survival, not intrinsic disease characteristics. We speculate that patients' choices may in turn be influenced by other factors known to plague poorer patients including lower education, absence of logistics and transportation support to attend treatment, especially radiotherapy and chemotherapy, smaller family size and lack of social and psychological support, poorer nutrition and life-stresses.

In contrast to more deadly cancers such as lung and liver cancers, breast cancer is relatively curable. With treatment improvement, patients are increasingly surviving their disease. This growing proportion of cancer survivors remains vulnerable to late treatment toxicity such as cardiotoxicity and secondary cancers, and non-cancer risks of death. Compared to non-cancer patients, cancer survivors have as much as 50% increased risks of non-cancer deaths. [26,27] Beyond 10-years post diagnosis, non-breast cancer death dominates as the main cause of mortality amongst survivors, most commonly from cardiovascular and cerebrovascular disease. [28,29] We observed hints of this effect in our patients despite a short follow-up of less than 8 years. It is conceivable that the same socioeconomic factors that has influenced cancer survival persisted to further jeopardized survivors with non-cancer causes of deaths.

MediFund receipt was not an independent predictor of outcomes despite its association with patients in lower HI-strata. Partly, this may be due to the demonstrated increased compliance with treatment in patients supported by MediFund. The proportions of patient who received chemotherapy, endocrine therapy and targeted therapy were higher in those who have received MediFund. This difference is the starkest for expensive targeted therapy with trastuzumab (SGD $50 000 with partial subsidy [without MediFund] in 2011) despite being shown to be cost effective and likely to generate net societal economic benefits in Singapore. [30] We postulate that enhanced medical subsidies may have mitigated the differences in survival between HI-strata. Nonetheless, the current level of financial assistance may be inadequate as substantial differences in disease presentation, treatment compliance and outcomes were evident. Calibrating the qualification threshold of MediFund subsidy higher to support more patients, particularly those in the 'sandwiched' middle-class, may achieve more equitable clinical outcomes.

Our study is limited by its retrospective nature where bias from unmeasured confounders may not have been adequately addressed. By focusing on patients in the public healthcare system, our cohort under-represented the more affluent segment of the population who prefer unsubsidised care from private providers. (Supplementary Table 1) Our study also does not measure Quality-of-Life which is important in breast cancer where survivorship is high and long term cosmesis is important. By using only HI as a differentiating factor for SES, we may have missed the added subtlety and discrimination that a multi-dimensional SES index may have in identifying vulnerable subgroups. Despite the demonstrated association between SES and outcomes, this association may be indirect and the cause-effects relationship is not known with certainty. Treatment criteria used in this study were chosen to be reflective of practices broadly contemporaneous for patients treated during the study period. However, the often nuanced, highly individualized recommendations made for each patient based on additional considerations of fitness, presence of comorbidities and results of multigene genetic assays may result in deviations from these criteria. A significant subset of our study cohort had incomplete treatment information due to an earlier cohort which preceded availability of registry data.

Nonetheless our study cohort which included about 60% of all breast cancers diagnosed amongst Singapore residents in the similar period, along with up-to-date mortality data from the national registry, is likely an accurate representation of the country. (Supplementary Table 1) Furthermore, our findings and implications are of direct relevance to other countries with similar systems of universal health care [10]. The survival discrepancy is likely to be even more pronounced in countries with large income disparities and without universal healthcare.

In summary, we have shown that SES as measured by HI was independently associated with cancer-related and overall mortality. This effect was mostly driven by late presentation of disease and reduced compliance to treatment. We also showed that enhanced subsidy increases treatment compliance and that MediFund recipients may achieve equitable CSS.

There is an urgent need for targeted interventions to improve cancer awareness and screening access for low HI patients. Policy changes to provide employment, psychosocial and economic support to the patient to beyond include her family and caregivers may further increase compliance and improve survival.

## Contributors

Fuh Yong Wong, Ru Xin Wong and Ting Hway Wong conceptualized this research. Fuh Yong Wong, Ru Xin Wong, Siqin Zhou, Whee Sze Ong, Pin Pin Pek and Ting Hway Wong contributed to

the development of the methods and analysis of this research. Fuh Yong Wong and Ru Xin Wong drafted the manuscript. All authors reviewed, provided comments and approved the manuscript.

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## Declaration of Interests

We declare no competing interests.

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## Data sharing statement

The data that support the findings of this study are available from an institutional repository but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. De-identified patient data is available from the corresponding authors upon reasonable request following publication of this article and with permission of SingHealth, approval from an independent review committee, and signed data access agreements.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2020.100065.

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