



# Differences in Breast Cancer Costs by Cancer Stage and Biomarker Subtype in New Zealand

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## Abstract

**Background** Breast cancer requires the greatest expenditure among all cancer types, and the costs vary by cancer stage and biomarker status.

**Objective** This study aimed to examine the differences in public healthcare costs of breast cancer in New Zealand by stage and subtype.

**Method** This study included patients diagnosed with invasive breast cancer between 1 July 2010 and 30 June 2018 and receiving services in public hospitals. These patients were identified from the National Breast Cancer Register and/or New Zealand Cancer Registry. Linking with the Pharmaceutical Collection, National Minimum Dataset, National Non-Admitted Patient Collection, and Mortality Collection, we estimated the median public healthcare costs of breast cancer by cancer stage and biomarker subtype.

**Results** We identified 22,948 eligible patients. The median costs of breast cancer increased with stage of disease, from \$NZ26,930 for stage I disease to \$NZ50,388 for stage IV disease. The median costs for human epidermal growth factor receptor 2-positive (HER2+) disease were three times those for HER2-negative (HER2-) disease: \$NZ106,428 for HER2+ cancers compared with \$NZ28,481 for oestrogen receptor-positive (ER+)/HER2- cancers and \$NZ31,722 for triple negative disease. Over 55% of the costs for HER2+ breast cancers were targeted therapy costs. For HER2- cancers, surgery incurred the biggest cost, followed by radiotherapy.

**Conclusions** Treating patients with early-stage breast cancer is less costly than treating those with metastatic disease. The costs vary considerably between the subtypes. Patients with HER2+ cancer incurred three times the costs of those with HER2- cancers. These results provide baseline costing data for clinicians and policy makers when considering new targeted treatments.

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### Key Points for Decision Makers

Treating patients with early-stage breast cancer is less costly than treating those with metastatic disease.

Patients with human epidermal growth factor receptor 2-positive (HER2+) cancer had three times the costs of those with HER2– cancers.

## 1 Introduction

Breast cancer is the most common cancer in New Zealand women [1]. Every year, around 3000 new cases are diagnosed in New Zealand, and around 600 deaths are specific to breast cancer [2]. Breast cancer is also one of the cancers that requires the greatest expenditure [3–5]. A New Zealand study by Blakely et al. [5] showed that breast cancer was the second-most expensive cancer (following colorectal cancer), costing New Zealand dollars (\$NZ)126.7 million per year and accounting for 14% of total cancer costs [5].

Breast cancer stage and biomarker status (oestrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor 2 positivity [HER2+]) are important predictive and prognostic indicators for breast cancer and affect treatment decision making [6, 7]. Patients diagnosed with stage I breast cancer are more likely to have breast-conserving surgery than mastectomy compared with those with stage II or III breast cancer [8]. Patients with metastatic breast cancer are most likely to have systemic treatments as the main treatment [9]. Surgery remains a mainstay of treatment for stage I–III breast cancer; however, adjuvant systemic treatments, including targeted therapy, and adjuvant radiation therapy lower the risk of recurrence and have been responsible for major improvements in survival over the last 40 years [10, 11]. For patients with hormone receptor-positive (ER+ and/or PR+) breast cancer, tamoxifen or aromatase inhibitors are usually recommended for at least 5 years [12]. HER2 targeted treatments, including trastuzumab, have been reported to be beneficial for improving the survival of patients with HER2+ disease [11, 13].

Breast cancer costs also vary by cancer stage and biomarker status. A recent systematic review showed that the mean costs of breast cancer at stage II, III, and IV were 32, 95, and 109% higher than at stage I, and the mean costs of regional and distant breast cancer were 41 and 165% higher than for local breast cancer [6]. Some systemic treatments that are specific to biomarker subtypes are expensive, which results in great variations in treatment costs by biomarker

subtype [11]. We conducted this study to examine the differences in public healthcare costs of breast cancer in New Zealand by stage and subtype.

## 2 Methods

### 2.1 Data Sources

Patients diagnosed with invasive (stage I–IV) breast cancer between 1 July 2010 and 30 June 2018 were identified from the National Breast Cancer Register and the New Zealand Cancer Registry (NZCR). We excluded patients who only received treatments for breast cancer in private hospitals and included those who received healthcare services in public hospitals (with or without private treatments). Eligible patients were linked with the Pharmaceutical Collection (PHARMS, including all publicly funded pharmaceuticals prescribed in both public and private hospitals), National Minimum Dataset (NMDS, including all publicly funded inpatient records), National Non-Admitted Patients Collection (NNAPC, including all publicly funded outpatient records), and the Mortality Collection (MORT, coded mortality information), datasets and death certificates (uncoded mortality information) using the national health index number, which is a unique identifier for people using publicly funded health and disability services in New Zealand.

Based on their prognosis and treatment pattern, breast cancer subtypes were categorised into three groups according to biomarker status: ER+/HER2–, HER2+, and triple negative. In this study, HER2+ was defined as fluorescence in situ hybridization-amplified or 3+ staining on immunohistochemistry according to the 2013 American Society of Clinical Oncology Guideline [14]. As recommended in the 2001 St. Gallen Consensus, ER+ or PR+ was assessed as any degree of immunohistochemistry positivity (at least 1+ intensity and 1% staining of nuclei) [15].

### 2.2 Cancer Care Pathway

We divided the cancer care pathway into two phases: (1) the initial treatment phase (TP, 3 months preceding and 12 months following diagnosis of breast cancer) and (2) the follow-up phase (second to fifth year following diagnosis). We further broke down the follow-up phase into the second (FU2), third (FU3), fourth (FU4), and fifth (FU5) year. The 5-year follow-up time was because eligible patients were often recommended for 5–10 years of endocrine therapy. We considered the earliest of date of death or the latest date of service (31 December 2019) available in the NNAPC, NMDS, and PHARMS as the censor date. The estimation of costs for each phase only included patients who had follow-up time for that phase. To calculate the total cost of all

phases combined, we only included patients who had follow-up time for all phases.

### 2.3 Cost Estimation

The cost estimation was from the perspective of the New Zealand Ministry of Health and only included public medical costs: public outpatient services, public inpatient services, and funded pharmaceuticals (prescribed by either public or private hospitals). Our clinical advisers (RL, MKH, and IC) checked the definitions of purchase unit codes for outpatient services (in NNAPC), the definitions of surgery codes for inpatient services (in NMDS), and pharmaceuticals, and this study only included the inpatient, outpatient, and pharmaceutical records relevant to breast cancer. Costs of diagnostic services such as radiology and pathology and of treatment response assessment tools were also included in the inpatient or outpatient costs. For pharmaceuticals, only relevant endocrine therapy, chemotherapy, and HER2-targeted therapies were included. Other medications such as pain killers were not included, because we could not identify whether these medications were breast cancer related. Including all these medications would overestimate the costs. All cost estimations were based on \$NZ, year 2019/2020 values. In terms of the purchasing power, \$NZ1 was equal to £0.484 and \$US0.692 in 2020. Appendixes 1–3 in the electronic supplementary material include the lists of included outpatient events, inpatient events, and pharmaceuticals, respectively.

Outpatient costs were estimated by multiplying the number of relevant outpatient visits recorded in the NNAPC with the unit cost of outpatient visits. The unit costs for outpatient visits were based on district health board-contracted purchase unit prices [16]. Inpatient costs were estimated by multiplying the accumulated cost weights for all relevant events by the purchase unit price as set by the national pricing programme [16]. The Ministry of Health calculates the cost weights, which provide resource utilisation information, for each diagnosis-related group code using the weighted inlier equivalent separation method, and sets a purchase unit price for each year. The 2019/2020 cost-weight unit price was \$NZ5216.21 [17]. The costs of publicly funded pharmaceuticals were estimated by multiplying the quantity of the pharmaceuticals dispensed by the unit prices for each pharmaceutical that appears in the pharmaceutical schedule [18].

Because costs are right-skewed data, we estimated the median and interquartile range (IQR) of the public medical costs of breast cancer during the initial TP and the follow-up phase. The costs were also computed by tumour anatomic stage (stage I, II, III, and IV) [19] and by biomarker subtype. The difference in median costs by tumour anatomic stage and by biomarker subtype were examined using the median test, and the subgroup difference was considered significant if the  $p$  value was  $< 0.05$ . We also calculated the proportion

of different cost components in total costs: surgery costs; costs of diagnostic tests, scans, or biopsies; radiotherapy costs; costs of medical oncology visits; chemotherapy costs; targeted therapy cost; endocrine therapy costs; and other costs.

### 3 Results

Between 1 July 2010 and 30 June 2018, a total of 22,948 patients were diagnosed with invasive breast cancer and received treatments for breast cancer in public hospitals (Table 1), including 6405 patients with stage I cancers, 6744 with stage II, 3828 with stage III, 1093 with stage IV, and 4878 with an unknown cancer stage. The majority of the cancer cases were ER+/HER2– (15,615 [74%]); 3384 (16%) were HER2+ and 1963 (9%) were triple negative. The proportion of ER+/HER2 disease decreased with increasing cancer stage, from 80% for stage I cancers to 62% for stage IV cancers. In contrast, the percentage of HER2+ cancers increased with cancer stage, from 7% for stage I disease to 27% for stage IV. The number of eligible patients in each phase decreased with time because some patients died or were censored because of loss of follow-up.

The median costs of breast cancer for the whole study period (TP–FU5) were \$NZ26,930 (IQR 12,479–41,512) for stage I disease, \$NZ31,372 (IQR 18,563–50,933) for stage II disease, \$NZ42,273 (IQR 25,681–75,162) for stage III disease, and \$NZ50,388 (IQR 20,685–116,161) for stage IV disease (median test  $p < 0.001$ ; Table 2). Stage III cancers had the highest costs during the TP, and stage IV cancers had the lowest costs during the TP. The costs in FU2–FU5 for stage IV cancers were consistently higher than the costs for other cancer stages.

The median costs for HER2+ disease were three times those for HER2– disease (Table 2): \$NZ106,428 (IQR 54,350–139,103) for HER2+ cancers compared with \$NZ28,481 (IQR 17,333–42,601) for ER+/HER2– cancers and \$NZ31,722 (IQR 17,714–47,283) for triple negative disease ( $p < 0.001$ ). HER2+ cancers had higher costs during all phases than HER2– cancers. For cancers of the same subtype, the costs increased with cancer stage. For example, the median costs increased from \$NZ25,485 (IQR 11,257–37,248) for ER+/HER2– stage I cancers to \$NZ38,855 (IQR 18,826–61,429) for stage IV cancers ( $p < 0.001$ ), and the median costs increased from \$NZ74,290 (27,117–115,479) for HER2+ stage I cancers to \$NZ279,644 (188,778–381,531) for HER2+ stage IV cancers ( $p < 0.001$ ).

Generally, the proportions of total costs accounted for by surgery and diagnostic tests, scans, or biopsies decreased with increasing cancer stage in all phases (Table 3). During the TP, the proportion of costs applicable to surgery ranged

**Table 1** Number of eligible patients by cancer stage and by subtype

Subgroup	TP, n (%)	FU2	FU3	FU4	FU5	All years
Overall	22,948	22,204	19,918	16,527	13,312	13,312
By stage						
Stage I	6405 (35)	6373	5733	4564	3539	3539
Stage II	6744 (37)	6676	6101	5129	4200	4200
Stage III	3828 (21)	3737	3377	2845	2365	2365
Stage IV	1093 (6)	753	524	359	254	254
Unknown	4878	4665	4183	3630	2954	2954
By subtype						
ER+/HER2–	15,615 (74)	15,320	13,911	11,652	9438	9438
HER2+	3384 (16)	3289	2954	2427	1907	1907
Triple negative	1963 (9)	1852	1571	1263	996	996
Unknown	1986	1743	1482	1185	971	971
Stage I						
ER+/HER2–	4796 (80)	4775	4304	3417	2643	2643
HER2+	787 (13)	784	697	560	418	418
Triple negative	428 (7)	422	372	282	223	223
Unknown	394	392	360	305	255	255
Stage II						
ER+/HER2–	4807 (75)	4768	4379	3720	3075	3075
HER2+	1012 (16)	1003	918	754	593	593
Triple negative	610 (9)	598	532	439	347	347
Unknown	315	307	272	216	185	185
Stage III						
ER+/HER2–	2452 (67)	2412	2191	1878	1562	1562
HER2+	777 (21)	763	708	603	507	507
Triple negative	444 (12)	424	363	284	225	225
Unknown	155	138	115	80	71	71
Stage IV						
ER+/HER2–	511 (62)	395	286	202	138	138
HER2+	218 (27)	169	117	77	53	53
Triple negative	91 (11)	44	21	17	13	13
Unknown	273	145	100	63	50	50

ER oestrogen receptor, FU2 second follow-up year, FU3 third follow-up year, FU4 fourth follow-up year, FU5 fifth follow-up year, HER2+/- human epidermal growth factor receptor 2 positive/negative, TP initial treatment phase

from 37% for stage I cancers to 26% for stage IV cancers, and the proportion of the costs accounted for by diagnostic tests, scans, or biopsies ranged from 21 to 12%. Conversely, the percentage of total costs incurred by medical oncology visits, targeted therapy costs, and chemotherapy costs increased with cancer stage. During the TP, the percentage of total costs from medical oncology visits ranged from 3% for stage I cancers to 7% for stage IV cancers, the percentage for targeted therapy costs ranged from 14 to 31%, and the percentage for chemotherapy ranged from 4 to 9%.

For HER2+ cancers, targeted therapy costs accounted for more than half of the total costs during the TP and 72% during the FU2 (Table 4). For ER+/HER2– cancers, surgery incurred the highest costs (44% during the TP) followed by radiotherapy (22% during the TP). Chemotherapy costs only

accounted for 5% of the total costs for ER+/HER2– disease during the TP and 11% for triple negative cancers.

## 4 Discussion

The main findings from this study were that the costs of breast cancer varied substantially by stage and subtype. The median costs of stage II, III, and IV cancers were 16, 57, and 87% higher than the costs of stage I cancers, and the costs of HER2+ disease were more than three times the costs of the HER2– cancers. These are consistent with the results from previous studies that have also demonstrated a higher cost with increasing stage and/or a higher cost for HER2+ tumours than HER2– disease [6, 20, 21]. The results from

**Table 2** Median costs (\$NZ) and interquartile range

Stage	TP	FU2	FU3	FU4	FU5	All years
Overall	25,855 (12,401–39,719)	483 (43–2529)	161 (15–856)	94 (0–595)	64 (0–542)	30,823 (17,952–51,823)
By stage						
Stage I	22,588 (10,098–34,027)	393 (30–959)	64 (0–495)	61 (0–436)	56 (0–408)	26,930 (12,479–41,512)
Stage II	26,504 (15,242–40,242)	505 (43–1915)	189 (14–814)	95 (10–580)	64 (0–537)	31,372 (18,563–50,933)
Stage III	32,226 (19,016–49,771)	1074 (393–9416)	542 (56–1547)	457 (42–1104)	407 (28–922)	42,273 (25,681–75,162)
Stage IV	17,737 (4,294–43,291)	5617 (1213–21,864)	3835 (899–19,897)	3561 (565–16,996)	3070 (462–13,410)	50,388 (20,685–116,161)
<i>p</i> value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
By subtype						
ER+/HER2–	23,467 (11,560–34,777)	437 (40–1146)	149 (30–800)	95 (16–561)	64 (11–528)	28,481 (17,333–42,601)
HER2+	71,081 (29,273–93,070)	20,261 (1218–34,411)	457 (30–1554)	393 (14–1049)	126 (0–898)	106,428 (54,350–139,103)
Triple negative	26,275 (14,050–37,461)	393 (0–1843)	64 (0–800)	3 (0–457)	0 (0–407)	31,722 (17,714–47,283)
<i>p</i> value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Stage I						
ER+/HER2–	20,826 (9778–30,204)	254 (30–809)	64 (0–467)	60 (0–423)	56 (0–407)	25,485 (11,257–37,248)
HER2+	54,704 (19,629–85,053)	11,816 (393–25,463)	125 (0–722)	74 (0–551)	60 (0–546)	74,290 (27,117–115,479)
Triple negative	22,908 (8343–34,614)	129 (0–814)	0 (0–457)	64 (0–413)	0 (0–407)	25,581 (8296–42,950)
<i>p</i> value	< 0.001	< 0.001	< 0.001	0.059	0.360	< 0.001
Stage II						
ER+/HER2–	24,341 (13,128–35,396)	449 (40–1065)	174 (20–707)	104 (23–569)	64 (10–533)	28,621 (17,647–42,261)
HER2+	69,679 (29,004–91,176)	20,684 (1064–33,333)	467 (29–1316)	393 (0–890)	104 (0–610)	101,870 (51,568–131,688)
Triple negative	26,032 (14,552–37,220)	407 (0–1501)	24 (0–786)	0 (0–407)	0 (0–407)	32,525 (17,926–47,269)
<i>p</i> value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Stage III						
ER+/HER2–	28,662 (18,061–40,816)	990 (407–2492)	547 (64–1381)	505 (56–1094)	433 (42–946)	35,748 (22,810–53,275)
HER2+	77,510 (43,501–95,584)	26,858 (8416–40,991)	554 (56–2132)	505 (40–1513)	407 (10–1051)	118,172 (80,016–150,747)
Triple negative	29,488 (17,723–39,716)	505 (0–2951)	393 (0–1860)	20 (0–545)	0 (0–449)	34,628 (22,628–49,827)
<i>p</i> value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Stage IV						
ER+/HER2–	14,607 (4874–29,520)	3072 (1065–10,717)	2767 (534–9246)	2528 (467–9230)	2697 (498–8723)	38,855 (18,826–61,429)
HER2+	80,738 (30,499–106,337)	39,593 (11,625–82,200)	35,035 (3589–82,168)	28,028 (6594–76,709)	23,123 (1815–67,262)	279,644 (188,778–381,531)
Triple negative	29,168 (12,757–43,940)	7860 (1133–23,349)	5769 (1009–13,033)	1300 (229–6633)	2737 (449–19,144)	65,380 (31,744–89,291)
<i>p</i> value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

ER oestrogen receptor, FU2 second follow-up year, FU3 third follow-up year, FU4 fourth follow-up year, FU5 fifth follow-up year, HER2+/- human epidermal growth factor receptor 2 positive/negative, TP initial treatment phase

**Table 3** Proportion (%) of each cost component in different phases by cancer stage

Cancer stage	Stage I	Stage II	Stage III	Stage IV	Overall
TP					
Surgery	37	37	33	26	35
Diagnostic test, scan or biopsy	21	18	11	12	16
Radiotherapy	18	16	17	12	17
Medical oncology	3	4	7	7	4
Targeted therapy	14	16	20	31	18
Chemotherapy	4	6	10	9	7
Endocrine therapy	0	0	0	0	0
Others	3	3	2	2	2
FU2					
Surgery	26	24	21	17	22
Diagnostic test, scan or biopsy	10	7	5	6	7
Radiotherapy	5	5	6	8	6
Medical oncology	6	7	8	11	8
Targeted therapy	42	47	49	47	47
Chemotherapy	7	7	8	10	8
Endocrine therapy	1	1	0	0	0
Others	5	3	2	1	3
FU3					
Surgery	48	43	44	16	39
Diagnostic test, scan or biopsy	15	14	8	7	11
Radiotherapy	11	8	7	9	9
Medical oncology	7	10	12	11	10
Targeted therapy	7	13	18	45	20
Chemotherapy	4	5	6	11	6
Endocrine therapy	1	1	1	0	1
Others	7	5	3	1	4
FU4					
Surgery	50	39	40	16	38
Diagnostic test, scan or biopsy	17	15	8	6	11
Radiotherapy	9	8	7	6	8
Medical oncology	6	10	11	13	10
Targeted therapy	7	16	24	44	22
Chemotherapy	3	6	7	13	7
Endocrine therapy	1	1	1	0	1
Others	6	5	2	2	3
FU5					
Surgery	39	36	37	18	34
Diagnostic test, scan or biopsy	17	14	6	3	10
Radiotherapy	12	9	9	8	9
Medical oncology	6	10	12	13	10
Targeted therapy	15	20	25	43	25
Chemotherapy	5	6	7	13	8
Endocrine therapy	1	1	1	0	1
Others	4	4	3	2	3

*ER* oestrogen receptor, *FU2* second follow-up year, *FU3* third follow-up year, *FU4* fourth follow-up year, *FU5* fifth follow-up year, *HER2+/-* human epidermal growth factor receptor 2 positive/negative, *TP* initial treatment phase

**Table 4** Proportion (%) of each cost component in different phases by cancer subtype

Cancer subtype	ER+/HER2–	HER2+	Triple negative	Overall
<b>TP</b>				
Surgery	44	18	39	35
Diagnostic test, scan or biopsy	22	7	17	16
Radiotherapy	21	9	21	17
Medical oncology	4	5	7	4
Targeted therapy	1	51	1	18
Chemotherapy	5	10	11	7
Endocrine therapy	0	0	0	0
Others	3	2	3	2
<b>FU2</b>				
Surgery	46	8	44	22
Diagnostic test, scan or biopsy	14	3	13	7
Radiotherapy	11	2	15	6
Medical oncology	12	5	10	8
Targeted therapy	7	72	7	47
Chemotherapy	5	9	5	8
Endocrine therapy	1	0	0	0
Others	5	1	5	3
<b>FU3</b>				
Surgery	50	22	46	39
Diagnostic test, scan or biopsy	14	6	13	11
Radiotherapy	10	5	11	9
Medical oncology	11	8	11	10
Targeted therapy	3	48	7	20
Chemotherapy	5	8	8	6
Endocrine therapy	1	0	0	1
Others	5	2	4	4
<b>FU4</b>				
Surgery	47	22	53	38
Diagnostic test, scan or biopsy	15	5	15	11
Radiotherapy	10	3	9	8
Medical oncology	12	8	9	10
Targeted therapy	3	52	5	22
Chemotherapy	6	8	5	7
Endocrine therapy	2	0	0	1
Others	5	2	3	3
<b>FU5</b>				
Surgery	42	15	53	34
Diagnostic test, scan or biopsy	15	2	15	10
Radiotherapy	12	4	10	9
Medical oncology	13	8	7	10
Targeted therapy	5	61	6	25
Chemotherapy	8	8	5	8
Endocrine therapy	2	0	0	1
Others	4	2	3	3

ER oestrogen receptor, FU2 second follow-up year, FU3 third follow-up year, FU4 fourth follow-up year, FU5 fifth follow-up year, HER2+/- human epidermal growth factor receptor 2 positive/negative, TP initial treatment phase



this study are important for healthcare planning, including decisions around medical resource distribution, as well as budget impact analysis for funding a new medication that is targeted for a subtype.

The differences in costs by cancer stage and subtype can be attributed to the differences in treatments and risk of cancer progression of different subgroups. For example, patients with metastatic breast cancer are less likely to receive surgical treatments than those with other cancer stages, which explains the lower surgery costs during the TP. The mainstay of treatments for stage IV cancers—systemic treatments—are included in the pharmaceutical costs [22]. Patients with stage II and III breast cancers are at higher risk of developing metastatic disease than are those with stage I cancers [23] and are therefore more likely to incur healthcare costs in subsequent years. Breast cancer screening also affects the distribution of cancer subtype at diagnosis. Screening-detected patients are more likely to have ER+/HER2– cancers [24]. These would result in lower mean costs per case for screen-detected cancers. However, screening is also associated with overdiagnosis and overtreatment and thus would increase total costs [25].

HER2+ cancers incurred higher costs primarily because of expensive targeted therapy, mainly HER2-targeted therapies. Over half of the costs for HER2+ disease were targeted therapy costs. During the study period of 1 July 2010 and 31 December 2019, trastuzumab, pertuzumab, and ado-trastuzumab emtansine (DM-1) were funded by PHARMAC to treat HER2+ breast cancer in New Zealand. Trastuzumab has been funded for HER2+ metastatic breast cancer since 2002 and for HER2+ stage I–III breast cancer since 2007 [26].

Some treatments, such as endocrine therapy (e.g. tamoxifen, aromatase inhibitors) are taken for a long time but have relatively low costs. Other targeted treatments, such as HER2-targeted therapies, have been shown to improve survival [11] but are expensive. The cost of a 12-month sequential treatment of trastuzumab continuing after initial taxane-based concurrent therapy with trastuzumab is \$NZ71,000 per patient per annum [27]. With the increasing incidence of breast cancer, the economic burden of targeted treatments is expected to increase [28]. To control the increasing costs, the funder would either need to have a better price for targeted treatments or to move to generic drugs after the patent expires.

The cost of breast cancer is a changing landscape, with new treatments becoming available and funded in New Zealand. Pertuzumab (funded since January 2017) and ado-trastuzumab emtansine (since 1 December 2019) were only recently approved by PHARMAC for HER2+ advanced breast cancer [29]. Therefore, the costs of these two medications did not account for a large proportion of the total costs in our study but may further increase the costs of treating

these patients in the future. Palbociclib, a targeting cyclin-dependent kinase 4/6 inhibitor, has been funded in New Zealand since April 2020. Some biosimilars for targeted therapies are now available for breast cancer, which may reduce future treatment costs [30]. Further studies will be needed to estimate the impact of newly funded medications on the costs of breast cancer.

One of the strengths of this study is that we combined the National Breast Cancer Register data with the NZCR, PHARMS, NMDS, NNAPC, and MORT datasets, and death certificates, so we had comprehensive data on all patients with breast cancer. This provided a large cohort of patients with detailed information on cancer stage and subtype. One limitation of this study was that, to calculate the pharmaceutical costs, we used the unit costs of drugs available in the pharmaceutical schedule. Using these unit costs might lead to an overestimation of the costs of cancer, because we did not know whether any confidential rebates existed for these drugs [31]. Over 20% of patients had cancer of an unknown stage. Most were identified from the NZCR, which mainly applies the Surveillance Epidemiology and End Results programme cancer staging definitions. While we reported the costs each year following diagnosis, we censored patients who died or reached their censor date, which means the number of patients reduced in the later years (especially in FU4 and FU5). Another limitation is that we included only endocrine therapy, chemotherapy, and HER2-targeted therapy but no other drugs that might have been used for breast cancer, e.g. anti-emetic drugs, growth factors, pain killers, and bisphosphonates, because we could not identify whether these drugs were used for breast cancer or other diseases, e.g. arthritis and osteoporosis. This study only estimated public healthcare costs. More research is needed on private and patient costs. Access to systemic treatments in New Zealand is more limited than in other developed countries. The cost differences by tumour anatomic stage and by biomarker subtype may be greater in countries with more liberal access to new targeted therapies.

## 5 Conclusions

Treating patients with early-stage breast cancer is less costly than treating those with metastatic disease. The costs vary considerably between different subtypes. Patients with HER2+ cancer had three times the costs of those with HER2– disease. These results provide baseline costing data for clinicians and policy makers considering new targeted treatments.

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## Declarations

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**Conflict of interest** Chunhuan Lao, Mohana Mondal, Marion Kuper-Hommel, Ian Campbell, and Ross Lawrenson have no conflicts of interest that are directly relevant to the content of this article.

**Availability of data and material** The data used for this study are not publicly available because of the ethics for patient information. They can be accessed through the National Breast Cancer Register and the Ministry of Health with appropriate ethics approval.

**Code availability** Not applicable.

**Author contributions** All authors contributed to the study conception and design. Material was prepared and data acquired by CL. Data were cleaned and analysed by MM and CL. The first draft of the manuscript was written by CL, MM, and RL, and all authors commented on subsequent versions of the manuscript. All authors read and approved the final manuscript.

**Ethics approval** Ethics approval for the study was granted through the Northern B Health and Disability Ethics Committee, reference: 19/NTB/188.

**Consent** Not applicable.

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