


Treatment and survival disparities by ethnicity in New Zealand women with stage I–III breast cancer tumour subtypes

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Abstract

Purpose This study aims to look at the distribution of different subtypes of stage I–III breast cancer in Māori and Pacific versus non-Māori/Pacific women, and to examine cancer outcomes by ethnicity within these different subtypes. **Method** This study included 9,015 women diagnosed with stage I–III breast cancer between June 2000 and May 2013, recorded in the combined Waikato and Auckland Breast Cancer Registers, who had complete data on ER, PR and HER2 status. Five ER/PR/HER2 subtypes were defined. Kaplan–Meier method and Cox proportional hazards model were used to examine ethnic disparities in breast cancer-specific survival.

Results Of the 9,015 women, 891 were Māori, 548 were Pacific and 7,576 others. Both Māori and Pacific women were less likely to have triple negative breast cancer compared to others (8.6, 8.9 vs. 13.0%). Pacific women were more than twice as likely to have ER–, PR– and HER2+ cancer than Māori and others (14.2 vs. 6.0%, 6.7%). After adjustment for age, year of diagnosis, stage, grade and treatment, the hazard ratios of breast cancer-specific mortality for Māori and Pacific women with ER+, PR+ and HER2– were 1.52 (95% CI 1.06–2.18) and 1.55 (95% CI 1.04–2.31) compared to others, respectively. Māori women with HER2+ cancer were twice more likely to die of their cancer than others.

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Conclusions Outcomes for Māori and Pacific women could be improved by better treatment regimens especially for those with HER2+ breast cancer and for women with ER+, PR+ and HER2– breast cancer.

Keywords Breast cancer · Subtypes · Ethnic disparities · Estrogen receptor · Progesterone receptor · Human epidermal growth factor receptor 2

Introduction

Biomarkers, including oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2), are important prognostic and predictive indicators for breast cancer. In New Zealand, ER and PR status have been routinely measured for the last 25 years. The measurement of HER2 status became increasingly common from the first part of this century and has been routine since 2006. Women with breast cancers that are both ER and PR positive (+) have a better prognosis than those with ER and PR negative (–) disease, while women with HER2+ cancers have a worse prognosis than those with HER2– disease [1]. A US study showed that women with ER+, PR+ and HER2– breast cancer were half as likely to die of breast cancer as those with ER–, PR– and HER2+ cancers [2]. This large study also demonstrated that women with triple negative (ER–, PR– and HER2–) breast cancer had the worst prognosis after adjustment for cancer stage [2]. This is consistent with the results in other studies [3–5].

Patients can receive personalised treatments based on the results of these biomarkers [6–8]. Women with hormone receptor-positive (ER+ and/or PR+) breast cancers are recommended to receive endocrine therapy and women with HER2+ breast cancer may benefit from chemotherapy and trastuzumab [9–12]. Trastuzumab was first funded in New Zealand for use in early stage HER2+ breast cancer in July 2007 [10].

There are great variations in the prevalence of breast cancer subtypes by ethnicity [12]. African American, Hispanic Whites, and Asian/Pacific Islanders were shown to be more likely to have HER2+ breast cancer than Non-Hispanic Whites in the US [12, 13]. African Americans were twice as likely to have triple negative breast cancer as Non-Hispanic Whites [12]. Within the same breast cancer subtype, there are ethnic disparities in survival. Asian/Pacific Islanders had a better breast cancer-specific survival in most subtypes than non-Hispanic Whites, except in the ER+, PR– and HER2+ subtype [13].

New Zealand has a population of 4.7 million, with 15% Māori and 7% Pacific people [14]. Māori is the indigenous population in New Zealand [15], while Pacific people [16] are a heterogeneous group with a long history of migration

to NZ from an array of island nations, including but not limited to Fiji, Samoa, Tonga and Cook islands. In a previous study, Māori and Pacific women were shown to be more likely to be diagnosed with HER2+ breast cancer than others (22%, 27 vs. 16%, p value < 0.05) [17]. Māori women were significantly more likely to have hormone receptor-positive cancers than others, but Pacific women were less likely [17]. There have been limited studies investigating the ethnic differences in subtypes in New Zealand [18, 19]. It is well recognised that there are differences in the treatment of Māori and Pacific women with breast cancer and that they have poorer survival [17–22]. This study aims to look at the distribution of different subtypes of stage I–III breast cancer in Māori and Pacific versus non-Māori/Pacific, and to examine the treatment and outcomes by ethnicity within different subtypes.

Methods

Data sources

This study included 9,015 women diagnosed with stage I–III breast cancer between June 2000 and May 2013, recorded in the combined Waikato and Auckland Breast Cancer Registers, who had complete data on their ER, PR and HER2 status [23]. 2,783 stage I–III breast cancer cases with incomplete information on ER, PR, and HER2 were excluded. The registers' data includes patient characteristics (age and ethnicity), tumour information (diagnosis date, cancer stage and grade) and information on treatment (surgery, endocrine therapy, chemotherapy, trastuzumab and radiation therapy). Information on comorbidities was obtained by reviewing linked data from the National Minimum dataset (NMDS) and characterising patients as having no comorbidities (C0), one comorbidity (C1) or 2 or more (C2+) using the C3 comorbidity index [24, 25].

The three biomarkers ER, PR and HER2 were designated as being either positive or negative. In this study, HER2+ was defined as FISH amplified or IHC 3+. There are eight possible groups defined by ER, PR and HER2 status. There is a small group (1%, 112) of women with breast cancer that is ER– but PR+. These women are usually treated with hormone therapy that is the same as women with ER+, PR+ cancer. We categorised women into five groups based on the clinical advice and practice in our region. The grouping is similar to published literature [26–30].

- Group 1 (ER+, PR+, and HER2–): 5,331 women
- Group 2 (Mixed ER/PR, HER2–):
 - ER+, PR–, and HER2–: 1,037 women
 - ER–, PR+, and HER2–: 88 women
- Group 3 (HER2+ not overexpressing):

- ER+, PR+, and HER2+: 573 women
- ER+, PR–, and HER2+: 261 women
- ER–, PR+, and HER2+: 24 women
- Group 4 (HER2+ overexpressing):
 - ER–, PR–, and HER2+: 589 women
- Group 5 (Triple negative):
 - ER–, PR–, and HER2–: 1,112 women

Statistical analyses

Cancer characteristics and treatments by ethnicity within the five subtypes were explored, and differences were examined by Chi-Square tests. Logistic regression models were used to estimate the odds ratios of receiving endocrine therapy, chemotherapy and trastuzumab by ethnicity within the five subtypes after adjustment for age, year of diagnosis, cancer stage, grade and C3 score [24, 25].

Mortality data for this study was derived from the National Mortality Collection and linked via the National Health Index (NHI) number to the register data. The NHI number is a unique identifier for people who use health and disability services in New Zealand. For cancer-specific survival analyses, patients who died from other causes were censored on their date of death, and patients without mortality information were considered to be censored on the last updated date for Mortality Collection which was 31 December 2014. The Kaplan Meier method was used to examine ethnic disparities in breast cancer-specific survival within the five subtypes. Cox proportional hazard models were used to estimate the hazard ratio of dying of breast cancer for Māori and Pacific women compared to others in the five subtypes after adjustment for age, year of diagnosis, stage, grade and treatments. All data analyses were performed in IBM SPSS statistics 23 (New York, United States).

Ethical approval for the study was granted through the Northern A Health and Disability Ethics Committee (reference: 12/NTA/42/AM01).

Results

Of the 9,015 women, 891 were Māori, 548 were Pacific, and 7576 were others including European and Asian (Table 1). Both Māori and Pacific women were less likely to have triple negative breast cancer compared to others (8.6% and 8.9 vs. 13.0%). Pacific women were more than twice as likely to have HER2+ overexpressing (Group 4) cancer than Māori and other women (14.2 vs. 6.7% and 6.0%), but were less than half as likely to have mixed ER/PR, HER2 (Group 2) breast cancer than Māori and others (5.5 vs. 11.2% and 13.1%). Māori and Pacific women were more likely to have stage III breast cancer than others in the five subtypes, except

for Māori women with mixed ER/PR, HER2– cancer (Group 2). Among women with ER+, PR+ and HER2– breast cancer, Pacific women were significantly more likely to have grade 3 disease than others (21.5 vs. 12.4%). However, only 67.4% of Pacific women with triple negative breast cancer (Group 5) had grade 3 cancer compared to 80.6% of others.

For women with ER+, PR+ and HER2– (Group 1) breast cancer, Māori and Pacific women received more endocrine therapy and chemotherapy (Table 2). After adjustment for age, year of diagnosis, cancer stage, grade and C3 score (Table 3), there was no difference in treatment between Māori and others, but Pacific women were less likely to receive chemotherapy (odds ratio 0.51, 95% CI 0.35–0.75) than others. Among women with triple negative or HER2+ disease, Pacific women were again less likely to be treated with chemotherapy (Table 3). After adjustment for other factors (age, year of diagnosis, cancer stage, grade and C3 score), Māori women with HER2+ breast cancer were half as likely to receive trastuzumab than others, and Pacific women with HER2+ breast cancer were only 20% as likely to receive chemotherapy and trastuzumab than others.

Kaplan–Meier method showed small but significant differences in breast cancer-specific survival for women with ER+, PR+, and HER2– cancer (Group 1) and women with HER2+ overexpressing cancer (Group 4) by ethnic group (Fig. 1). The respective 5-year breast cancer-specific survival for Māori, Pacific and others with ER+, PR+, and HER2– cancer was 94.2, 93.1 and 96.5% (p value for Log-rank test < 0.001). In women with HER2+ overexpressing breast cancer (Group 4), the 5-year breast cancer-specific survival (Fig. 2) was worst for Māori (57.8%), followed by Pacific (66.4%) compared with others (78.5%) (p value < 0.001). No significant ethnic differences in breast cancer-specific survival were found in women with mixed ER/PR, HER2– (Group 2), HER2+ not overexpressing (Group 3) or triple negative cancer (Group 5).

After adjustment for age, year of diagnosis, stage, grade and treatment (specified in Table 4), hazard ratios of breast cancer-specific mortality for Māori and Pacific women with ER+, PR+ and HER2– cancer (Group 1) were 1.52 (95% CI 1.06–2.18) and 1.55 (95% CI 1.04–2.31) compared to others. Survival differences between Pacific women and others with HER2+ breast cancer were not significant after adjustment for other factors. However, Māori women with HER2+ breast cancer (Group 3 and 4) were twice more likely to die of their cancer than others.

Discussion

Breast cancer survival inequities between ethnic groups of women in New Zealand are large and of great concern. There is an increasing understanding that cancer survival inequities

Table 1 Characteristics by ethnicity in the five subtypes

| Characteristics | Māori | | Pacific | | Others | | Total N | Chi square test (p value) |
|-------------------------------------|-------|------|---------|------|--------|------|------------|---------------------------------|
| | N | % | N | % | N | % | | |
| Subtype | | | | | | | | <0.001 |
| Group 1 (ER+, PR+, and HER2−) | 555 | 62.3 | 327 | 59.7 | 4,449 | 58.7 | 5,331 | |
| Group 2 (Mixed ER/PR, HER2−) | 100 | 11.2 | 30 | 5.5 | 995 | 13.1 | 1,125 | |
| Group 3 (HER2+, not overexpressing) | 99 | 11.1 | 64 | 11.7 | 695 | 9.2 | 858 | |
| Group 4 (HER2+ overexpressing) | 60 | 6.7 | 78 | 14.2 | 451 | 6.0 | 589 | |
| Group 5 (Triple negative) | 77 | 8.6 | 49 | 8.9 | 986 | 13.0 | 1,112 | |
| Group 1 (ER+, PR+, and HER2−) | | | | | | | | |
| Cancer stage | | | | | | | | <0.001 |
| Stage I | 248 | 44.7 | 122 | 37.3 | 2,318 | 52.1 | 2,688 | |
| Stage II | 228 | 41.1 | 129 | 39.4 | 1,570 | 35.3 | 1,927 | |
| Stage III | 79 | 14.2 | 76 | 23.2 | 561 | 12.6 | 716 | |
| Cancer grade | | | | | | | | <0.001 |
| Grade 1 | 170 | 31.1 | 91 | 27.9 | 1,536 | 35.1 | 1,797 | |
| Grade 2 | 311 | 56.9 | 165 | 50.6 | 2,300 | 52.5 | 2,776 | |
| Grade 3 | 66 | 12.1 | 70 | 21.5 | 542 | 12.4 | 678 | |
| Unknown | 8 | | 1 | | 71 | | 80 | |
| Age (years) | | | | | | | | <0.001 |
| <50 | 186 | 33.5 | 131 | 40.1 | 1,240 | 27.9 | 1,557 | |
| 50–69 | 307 | 55.3 | 166 | 50.8 | 2,293 | 51.5 | 2,766 | |
| 70+ | 62 | 11.2 | 30 | 9.2 | 916 | 20.6 | 1,008 | |
| C3 score | | | | | | | | <0.001 |
| 0 | 389 | 70.1 | 251 | 76.8 | 3,623 | 81.4 | 4,263 | |
| 1 | 48 | 8.6 | 19 | 5.8 | 348 | 7.8 | 415 | |
| 2+ | 118 | 21.3 | 57 | 17.4 | 478 | 10.7 | 653 | |
| Year of diagnosis | | | | | | | | 0.055 |
| 2000–2003 | 28 | 5.0 | 16 | 4.9 | 366 | 8.2 | 410 | |
| 2004–2006 | 115 | 20.7 | 67 | 20.5 | 948 | 21.3 | 1,130 | |
| 2007–2009 | 173 | 31.2 | 104 | 31.8 | 1,370 | 30.8 | 1,647 | |
| 2010–2013 | 239 | 43.1 | 140 | 42.8 | 1,765 | 39.7 | 2,144 | |
| Group 2 (mixed ER/PR, HER2−) | | | | | | | | |
| Cancer stage | | | | | | | | 0.004 |
| Stage I | 41 | 41.0 | 9 | 30.0 | 418 | 42.0 | 468 | |
| Stage II | 45 | 45.0 | 8 | 26.7 | 408 | 41.0 | 461 | |
| Stage III | 14 | 14.0 | 13 | 43.3 | 169 | 17.0 | 196 | |
| Cancer grade | | | | | | | | 0.071 |
| Grade 1 | 16 | 16.7 | 4 | 13.8 | 213 | 22.0 | 233 | |
| Grade 2 | 52 | 54.2 | 10 | 34.5 | 476 | 49.1 | 538 | |
| Grade 3 | 28 | 29.2 | 15 | 51.7 | 281 | 29.0 | 324 | |
| Unknown | 4 | | 1 | | 25 | | 30 | |
| Age (years) | | | | | | | | <0.001 |
| <50 | 23 | 23.0 | 14 | 46.7 | 200 | 20.1 | 237 | |
| 50–69 | 66 | 66.0 | 13 | 43.3 | 545 | 54.8 | 624 | |
| 70+ | 11 | 11.0 | 3 | 10.0 | 250 | 25.1 | 264 | |
| C3 score | | | | | | | | 0.076 |
| 0 | 69 | 69.0 | 21 | 70.0 | 783 | 78.7 | 873 | |
| 1 | 9 | 9.0 | 2 | 6.7 | 82 | 8.2 | 93 | |
| 2+ | 22 | 22.0 | 7 | 23.3 | 130 | 13.1 | 159 | |
| Year of diagnosis | | | | | | | | 0.065 |
| 2000–2003 | 7 | 7.0 | 0.0 | | 117 | 11.8 | 124 | |

Table 1 (continued)

| Characteristics | Māori | | Pacific | | Others | | Total N | Chi square test (p value) |
|-------------------------------------|-------|------|---------|------|--------|------|------------|---------------------------------|
| | N | % | N | % | N | % | | |
| 2004–2006 | 18 | 18.0 | 11 | 36.7 | 239 | 24.0 | 268 | |
| 2007–2009 | 32 | 32.0 | 11 | 36.7 | 284 | 28.5 | 327 | |
| 2010–2013 | 43 | 43.0 | 8 | 26.7 | 355 | 35.7 | 406 | |
| Group 3 (HER2+, not overexpressing) | | | | | | | | |
| Cancer stage | | | | | | | | 0.052 |
| Stage I | 29 | 29.3 | 15 | 23.4 | 247 | 35.5 | 291 | |
| Stage II | 42 | 42.4 | 24 | 37.5 | 284 | 40.9 | 350 | |
| Stage III | 28 | 28.3 | 25 | 39.1 | 164 | 23.6 | 217 | |
| Cancer grade | | | | | | | | 0.963 |
| Grade 1 | 5 | 5.2 | 2 | 3.2 | 37 | 5.4 | 44 | |
| Grade 2 | 46 | 47.4 | 31 | 50.0 | 325 | 47.8 | 402 | |
| Grade 3 | 46 | 47.4 | 29 | 46.8 | 318 | 46.8 | 393 | |
| Unknown | 2 | | 2 | | 15 | | 19 | |
| Age (years) | | | | | | | | 0.002 |
| <50 | 43 | 43.4 | 37 | 57.8 | 266 | 38.3 | 346 | |
| 50–69 | 52 | 52.5 | 24 | 37.5 | 334 | 48.1 | 410 | |
| 70+ | 4 | 4.0 | 3 | 4.7 | 95 | 13.7 | 102 | |
| C3 score | | | | | | | | 0.197 |
| 0 | 80 | 80.8 | 50 | 78.1 | 578 | 83.2 | 708 | |
| 1 | 13 | 13.1 | 6 | 9.4 | 50 | 7.2 | 69 | |
| 2+ | 6 | 6.1 | 8 | 12.5 | 67 | 9.6 | 81 | |
| Year of diagnosis | | | | | | | | 0.513 |
| 2000–2003 | 11 | 11.1 | 7 | 10.9 | 115 | 16.5 | 133 | |
| 2004–2006 | 22 | 22.2 | 11 | 17.2 | 155 | 22.3 | 188 | |
| 2007–2009 | 31 | 31.3 | 20 | 31.3 | 179 | 25.8 | 230 | |
| 2010–2013 | 35 | 35.4 | 26 | 40.6 | 246 | 35.4 | 307 | |
| Group 4 (HER2+ overexpressing) | | | | | | | | |
| Cancer stage | | | | | | | | <0.001 |
| Stage I | 9 | 15.0 | 13 | 16.7 | 146 | 32.4 | 168 | |
| Stage II | 18 | 30.0 | 36 | 46.2 | 167 | 37.0 | 221 | |
| Stage III | 33 | 55.0 | 29 | 37.2 | 138 | 30.6 | 200 | |
| Cancer grade | | | | | | | | 0.801 |
| Grade 1 | 0 | 0.0 | 0 | 0.0 | 5 | 1.1 | 5 | |
| Grade 2 | 11 | 19.0 | 16 | 21.1 | 86 | 19.8 | 113 | |
| Grade 3 | 47 | 81.0 | 60 | 78.9 | 344 | 79.1 | 451 | |
| Unknown | 2 | | 2 | | 16 | | 20 | |
| Age (years) | | | | | | | | <0.001 |
| <50 | 33 | 55.0 | 41 | 52.6 | 141 | 31.3 | 215 | |
| 50–69 | 26 | 43.3 | 27 | 34.6 | 260 | 57.6 | 313 | |
| 70+ | 1 | 1.7 | 10 | 12.8 | 50 | 11.1 | 61 | |
| C3 score | | | | | | | | 0.047 |
| 0 | 43 | 71.7 | 61 | 78.2 | 366 | 81.2 | 470 | |
| 1 | 5 | 8.3 | 4 | 5.1 | 43 | 9.5 | 52 | |
| 2+ | 12 | 20.0 | 13 | 16.7 | 42 | 9.3 | 67 | |
| Year of diagnosis | | | | | | | | 0.674 |
| 2000–2003 | 11 | 18.3 | 10 | 12.8 | 70 | 15.5 | 91 | |
| 2004–2006 | 16 | 26.7 | 20 | 25.6 | 121 | 26.8 | 157 | |
| 2007–2009 | 20 | 33.3 | 25 | 32.1 | 118 | 26.2 | 163 | |
| 2010–2013 | 13 | 21.7 | 23 | 29.5 | 142 | 31.5 | 178 | |

Table 1 (continued)

| Characteristics | Māori | | Pacific | | Others | | Total N | Chi square test (p value) |
|---------------------------|-------|------|---------|------|--------|------|------------|---------------------------------|
| | N | % | N | % | N | % | | |
| Group 5 (triple negative) | | | | | | | | |
| Cancer stage | | | | | | | | 0.035 |
| Stage I | 20 | 26.0 | 9 | 18.4 | 347 | 35.2 | 376 | |
| Stage II | 36 | 46.8 | 28 | 57.1 | 459 | 46.6 | 523 | |
| Stage III | 21 | 27.3 | 12 | 24.5 | 180 | 18.3 | 213 | |
| Cancer grade | | | | | | | | 0.037 |
| Grade 1 | 1 | 1.4 | 1 | 2.2 | 21 | 2.2 | 23 | |
| Grade 2 | 21 | 28.4 | 14 | 30.4 | 167 | 17.3 | 202 | |
| Grade 3 | 52 | 70.3 | 31 | 67.4 | 780 | 80.6 | 863 | |
| Unknown | 3 | | 3 | | 18 | | 24 | |
| Age (years) | | | | | | | | 0.065 |
| <50 | 28 | 36.4 | 17 | 34.7 | 335 | 34.0 | 380 | |
| 50–69 | 44 | 57.1 | 24 | 49.0 | 456 | 46.2 | 524 | |
| 70+ | 5 | 6.5 | 8 | 16.3 | 195 | 19.8 | 208 | |
| C3 score | | | | | | | | <0.001 |
| 0 | 51 | 66.2 | 32 | 65.3 | 814 | 82.6 | 897 | |
| 1 | 11 | 14.3 | 8 | 16.3 | 69 | 7.0 | 88 | |
| 2+ | 15 | 19.5 | 9 | 18.4 | 103 | 10.4 | 127 | |
| Year of diagnosis | | | | | | | | 0.631 |
| 2000–2003 | 14 | 18.2 | 10 | 20.4 | 151 | 15.3 | 175 | |
| 2004–2006 | 16 | 20.8 | 11 | 22.4 | 261 | 26.5 | 288 | |
| 2007–2009 | 20 | 26.0 | 14 | 28.6 | 304 | 30.8 | 338 | |
| 2010–2013 | 27 | 35.1 | 14 | 28.6 | 270 | 27.4 | 311 | |
| Total | 891 | | 548 | | 7,576 | | 9,015 | |

result from multiple, often small, but cumulative inequities which occur along the cancer treatment pathway [31]. Previous New Zealand studies have looked at the impact of commonly measured biomarkers (ER/PR and HER2) individually instead of different biomarker combinations [18, 19, 32]. This study has highlighted the differences in recognised biomarker combinations in Māori and Pacific women.

Pacific women were less likely to be diagnosed with triple negative breast cancer (Group 5) but were more likely to be diagnosed with HER2+ overexpressing cancer (Group 4) compared to others (8.9 vs. 13.0%, and 14.2 vs. 6.0%). A US study demonstrated consistent results but with a smaller difference: 10.6% of Pacific Islanders and 11.3% of Whites having triple negative breast cancer, 10.6% of Pacific Islanders and 5.6% of Whites having ER-, PR- and HER2+ breast cancer [33]. Māori were as likely to have triple negative breast cancer as Pacific women, and were as likely to have ER-, PR- and HER2+ breast cancer as others.

Differences in subtype distribution by ethnic group may be related to the genetic factors, environment, diet, obesity and hormone exposure including oral contraceptive use and hormone replacement therapy [34–38]. Triple negative subtype breast cancer is associated with specific DNA

methylation profile [37], which may explain the ethnic difference in having triple negative subtype breast cancer. Another reason may be the difference in number of pregnancies a woman has had. Māori and Pacific women in New Zealand tend to have more pregnancies than others [39]. A Norway study indicated that increasing parity was inversely associated with triple negative cancer (Group 5), though the result was not significant (OR 0.70, 95% CI 0.41–1.21) [34]. The risk of having HER2+ overexpressing cancer (Group 4) was found to increase with increasing waist size before menopause, and increased in association with metabolic syndrome in postmenopausal women [35]. The 2015/16 New Zealand Health Survey shown that 47% of Māori adults and 67% of Pacific adults were obese, [40] which may have contributed to the higher risk of having HER2+ overexpressing cancer (Group 4).

Our previous study showed that the probability of receiving trastuzumab decreased with age and comorbidities score, and increased with cancer stage and grade [41]. In this analysis, we found the discrepancy by ethnicity after adjustment for these variables (Table 3). It is worrying that the adjusted HR for Māori women with HER2+ disease is double that of others. The disparity in the use

Table 2 Treatment by ethnicity in the five subtypes

| Subtype group | Māori | | Pacific | | Others | | Chi-square test (p value) |
|-------------------------------------|-------|------|---------|------|--------|------|---------------------------|
| | N | % | N | % | N | % | |
| Group 1 (ER+, PR+, and HER2–) | | | | | | | |
| Endocrine therapy | 439 | 79.1 | 253 | 77.4 | 3,246 | 73.0 | 0.003 |
| Chemotherapy | 149 | 26.8 | 107 | 32.7 | 1,034 | 23.2 | <0.001 |
| Trastuzumab | – | – | – | – | – | – | – |
| Group 2 (mixed ER/PR, HER2–) | | | | | | | |
| Endocrine therapy | 76 | 76.0 | 21 | 70.0 | 753 | 75.7 | 0.771 |
| Chemotherapy | 36 | 36.0 | 16 | 53.3 | 311 | 31.3 | 0.027 |
| Trastuzumab | – | – | – | – | – | – | – |
| Group 3 (HER2+, not overexpressing) | | | | | | | |
| Endocrine therapy | 93 | 93.9 | 57 | 89.1 | 603 | 86.8 | 0.119 |
| Chemotherapy | 71 | 71.7 | 43 | 67.2 | 449 | 64.6 | 0.364 |
| Trastuzumab | 52 | 52.5 | 34 | 53.1 | 378 | 54.4 | 0.929 |
| Group 4 (HER2+ overexpressing) | | | | | | | |
| Endocrine therapy | – | – | – | – | – | – | – |
| Chemotherapy | 50 | 83.3 | 47 | 60.3 | 349 | 77.4 | 0.002 |
| Trastuzumab | 35 | 58.3 | 35 | 44.9 | 284 | 63.0 | 0.010 |
| Group 5 (triple negative) | | | | | | | |
| Endocrine therapy | – | – | – | – | – | – | – |
| Chemotherapy | 59 | 76.6 | 28 | 57.1 | 672 | 68.2 | 0.071 |
| Trastuzumab | – | – | – | – | – | – | – |

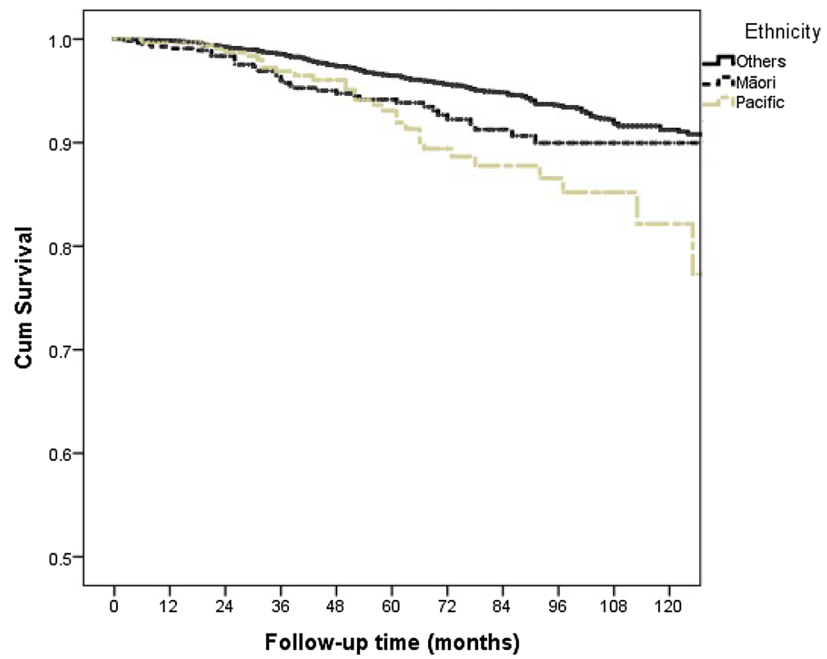
Endocrine therapy is usually provided to patients with hormone receptor-positive cancers, and trastuzumab is provided to patients with HER2 positive cancers

Table 3 Odds ratios of receiving endocrine therapy, chemotherapy and trastuzumab after adjustment for age, year of diagnosis, cancer stage, cancer grade and C3 score

| Subtype group | Māori vs. others (ref) | | Pacific vs. others (ref) | |
|-------------------------------------|------------------------|---------|--------------------------|---------|
| | Odds ratio (95% CI) | p value | Odds ratio (95% CI) | p value |
| Group 1 (ER+, PR+, and HER2–) | | | | |
| Endocrine therapy | 1.21 (0.94–1.56) | 0.147 | 0.81 (0.59–1.12) | 0.211 |
| Chemotherapy | 0.80 (0.59–1.08) | 0.150 | 0.51 (0.35–0.75) | <0.001 |
| Trastuzumab | – | – | – | – |
| Group 2 (Mixed ER/PR, HER2–) | | | | |
| Endocrine therapy | 1.15 (0.65–2.05) | 0.635 | 0.47 (0.18–1.19) | 0.111 |
| Chemotherapy | 0.86 (0.45–1.64) | 0.646 | 0.65 (0.20–2.13) | 0.480 |
| Trastuzumab | – | – | – | – |
| Group 3 (HER2+, not overexpressing) | | | | |
| Endocrine therapy | 2.44 (0.95–6.28) | 0.064 | 1.31 (0.53–3.25) | 0.559 |
| Chemotherapy | 0.80 (0.45–1.42) | 0.443 | 0.31 (0.14–0.69) | 0.004 |
| Trastuzumab | 0.48 (0.27–0.84) | 0.011 | 0.24 (0.11–0.51) | <0.001 |
| Group 4 (HER2+ overexpressing) | | | | |
| Endocrine therapy | – | – | – | – |
| Chemotherapy | 0.77 (0.32–1.85) | 0.555 | 0.19 (0.10–0.37) | <0.001 |
| Trastuzumab | 0.48 (0.23–1.00) | 0.048 | 0.19 (0.10–0.36) | <0.001 |
| Group 5 (triple negative) | | | | |
| Endocrine therapy | – | – | – | – |
| Chemotherapy | 1.33 (0.65–2.72) | 0.440 | 0.40 (0.18–0.89) | 0.024 |
| Trastuzumab | – | – | – | – |

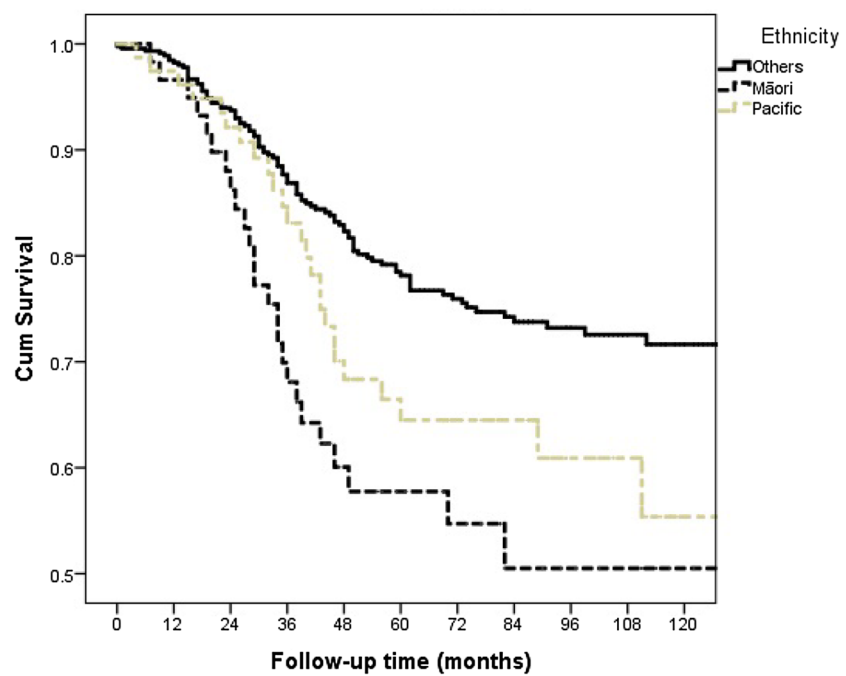
Endocrine therapy is usually provided to patients with hormone receptor-positive cancers, and trastuzumab is provided to patients with HER2 positive cancers

Fig. 1 Breast cancer-specific survival for women with ER+, PR+ and HER2– (Group 1) stage I–III breast cancer by ethnicity



| Follow-up time (months) | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 | 96 | 108 | 120 | |
|-------------------------|---------|------|------|------|------|------|------|------|------|------|-----|-----|
| Number of women at risk | Others | 4449 | 4423 | 4150 | 3554 | 2986 | 2482 | 1996 | 1527 | 1139 | 774 | 478 |
| | Māori | 555 | 545 | 499 | 414 | 353 | 288 | 217 | 151 | 115 | 77 | 37 |
| | Pacific | 327 | 324 | 295 | 246 | 213 | 164 | 124 | 84 | 66 | 37 | 20 |

Fig. 2 Breast cancer-specific survival for women with ER–, PR– and HER2+ (Group 4) stage I–III breast cancer by ethnicity



| Follow-up time (months) | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 | 96 | 108 | 120 | |
|-------------------------|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| Number of women at risk | Others | 451 | 444 | 396 | 329 | 273 | 228 | 189 | 155 | 119 | 87 | 63 |
| | Māori | 60 | 57 | 49 | 38 | 26 | 22 | 18 | 11 | 8 | 6 | 3 |
| | Pacific | 78 | 76 | 67 | 54 | 41 | 34 | 29 | 24 | 14 | 11 | 5 |

Table 4 Hazard ratio in breast cancer-specific mortality after adjustment for age, year of diagnosis, stage, grade and treatment

| Subtype group | Unadjusted hazard ratio (95% CI) | | Adjusted hazard ratio (95% CI) | | Adjusted treatments |
|-------------------------------------|----------------------------------|--------------------------|--------------------------------|--------------------------|---------------------|
| | Māori vs. others (ref) | Pacific vs. others (ref) | Māori vs. others (ref) | Pacific vs. others (ref) | |
| Group 1 (ER+, PR+, and HER2–) | 1.61 (1.13–2.28) | 2.19 (1.49–3.24) | 1.52 (1.06–2.18) | 1.55 (1.04–2.31) | E, C |
| Group 2 (Mixed ER/PR, HER2–) | 0.88 (0.47–1.62) | 1.44 (0.63–3.26) | 0.98 (0.51–1.88) | 1.11 (0.48–2.58) | E, C |
| Group 3 (HER2+, not overexpressing) | 1.59 (0.96–2.64) | 1.47 (0.78–2.75) | 2.10 (1.22–3.61) | 1.51 (0.74–3.09) | E, C, T |
| Group 4 (HER2+ overexpressing) | 2.26 (1.46–3.52) | 1.58 (1.02–2.45) | 2.06 (1.29–3.29) | 1.21 (0.74–1.99) | C, T |
| Group 5 (Triple negative) | 0.81 (0.46–1.41) | 0.95 (0.50–1.78) | 0.76 (0.43–1.34) | 0.86 (0.45–1.64) | C |

E endocrine therapy, C chemotherapy, T trastuzumab

of an effective and expensive treatment in Māori women with HER2+ disease linked to evidence of substantially poor outcomes is of concern and requires further research.

In women with ER+, PR+ and HER2– (Group 1) breast cancer, Māori and Pacific women had worse breast cancer-specific survival than others, although in the three ethnic groups overall breast cancer-specific survival is very good. Women with ER+, PR+ and HER2– breast cancer are mainly treated with endocrine therapy. While in this study Māori and Pacific women with ER+ breast cancer are just as likely to receive endocrine therapy, in a previous study we noted poorer adherence to endocrine therapy in Māori women compared to others, and this was shown to be associated with worse breast cancer outcome [9].

The strengths of this study include that this study is based on the Waikato and Auckland population-based Breast Cancer Registers that collect good quality data on all breast cancer patients [23]. We have comprehensive data on patient characteristics, patient treatment as well as outcomes. One weakness is that in earlier years not all women had their biomarkers tested, especially HER2 status. Consequently, there may be differences in the distribution of subtypes (e.g. by age and stage) in earlier years in this study. Also there may be some differences in treatment over time with increasing use of trastuzumab and changes of the regimens of chemotherapy. However, in the Cox proportional hazard models we have adjusted age, year of diagnosis, stage, grade and treatment.

Conclusion

This study does give us some indications that outcomes for Māori and Pacific women could be improved by better uptake of treatment, especially for those with HER2+ breast cancer. There are also differences in outcomes for Māori and Pacific women with ER+, PR+ and HER2– cancer. When treatment is increasingly targeted to patient characteristics including hormonal status, it is

important to ensure treatment is equally delivered to high need Māori and Pacific women.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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