Breast cancer outcomes in different ethnic groups in New Zealand patients detected through breast screening

Short title: Ethnic differences through breast screening

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Abstract

Objectives

This study aims to compare the characteristics and survival of New Zealand European, Māori and Pacific women detected through breast screening with women with non-screen detected breast cancer.

Methods

Women aged 45-69 years diagnosed with invasive breast cancer between January 2005 and May 2013 were identified from the Waikato and Auckland Breast Cancer Registries. Patient demographics and tumour characteristics were described by mode of detection and by ethnic group. Kaplan-Meier method was used to estimate the 5-year breast cancer-specific survival of women with stage I-III breast cancer by ethnicity and by mode of detection.

Results

Screen detected women were older, had smaller tumours, had fewer stage IV (0.8% vs 7.6%), fewer high grade (16.8% vs 39.0%) and fewer lymph node positive diseases (26.3% vs 51.5%) compared to non-screen detected women. There were more Luminal A cases (70.0% vs 54.0%), fewer HER2+ non-Luminal (4.4% vs 8.8%) and fewer triple negative disease (7.0% vs 13.8%) in the screen detected cancers than non-screen detected cancers. If not screen detected 22.7% of Pacific women were diagnosed with stage IV breast cancer compared to 2.4% if screen detected. If not screen detected, the 5-year breast cancer-specific survival was 91.1% for NZ European women, 84.2% for Māori women and 80.2% for Pacific women (p-value <0.001). If screen detected, the survival between different ethnic groups was similar.

Conclusions

Women detected through breast screening are diagnosed at an earlier stage and have a greater proportion of subtypes with better outcome. Variations in survival for Māori and Pacific women are only found in non-screen detected women.

Key words: Breast screening, breast cancer, ethnicity, survival

Introduction

It is known that outcomes of breast cancer in Māori and Pacific women are poor compared with New Zealand (NZ) European women.[1-4] One of the main reasons for this is the late stage at diagnosis in Māori and Pacific women.[4] We also know that Māori and Pacific women are less likely to have screen-detected breast cancer.[4,5] Patients identified through breast screening have better outcomes mainly due to being diagnosed at an earlier stage.[6] In addition, breast cancers detected through screening may be less aggressive than those diagnosed symptomatically. There are differences in the type of breast cancer found in Māori and Pacific women compared with NZ European women.[2,7] Māori and Pacific women are less likely to have triple negative disease compared to other women, while Pacific women are more likely to have human epidermal growth factor receptor 2 positive (HER2+) non-Luminal disease than others.[2,7] We wanted to know what influence breast screening has on the outcomes for Māori and Pacific women compared with NZ European women and how this is influenced by cancer stage at diagnosis and biomarker subtype.

Breast screening became universally available in New Zealand in 1998 for women aged 50 to 64 years and in 2004 the age was widened to include all women aged 45 to 69 years. Screening has been reasonably well accepted by NZ European women but uptake in Māori women has been slower,[8,9] although the gap is narrowing.[10] This study is based on data from two large population based registers of newly diagnosed breast cancer in the Auckland and Waikato regions. These registers are derived from a baseline population from approximately 1.7 million residents and include about 1000 new breast cancer cases per year. This study aims to compare the characteristics and survival of NZ European, Māori and Pacific women detected through breast screening with women of similar age with non-screen detected breast cancer.

Methods

Data for this study were obtained from the Waikato (WBCR) and Auckland (ABCR) Breast Cancer Registries. The WBCR is a prospectively maintained regional cancer registry that includes all in-situ and invasive breast cancers diagnosed in the Waikato District Health Board area since 1999. The ABCR was established in 2000 by the Auckland Breast Cancer Study Group and includes all breast cancers diagnosed within the Auckland, Waitemata and Counties Manukau District Health Boards, including those from private Breast Centres within the region. The WBCR and ABCR data covers an area with a population of approximately 1.7

million, of which 29% of women are in the targeted screening age groups (45-69 years). Waikato DHB area have a larger proportion of Māori (23%) than Auckland DHB (8%), Waitemata DHB (10%) and Counties Manukau DHB (16%), but have a smaller proportion of Pacific (3%) than the other three DHBs (11%, 7% and 21%, respectively).

This study only included women aged 45 to 69 years diagnosed with invasive breast cancer between January 2005 and May 2013. Data extracted for the study include: age, stage at diagnosis, tumour size, lymph nodes, year of diagnosis, method of diagnosis (screen detected, not screen detected), biomarker type (Luminal A, Luminal B1, Luminal B2, HER2+ non-Luminal, triple negative disease),[2,7] and mortality data (date of death and cause of death). The Mortality Collection was also linked to the Combined Register through the National Health Index (NHI) number to identify data on mortality to ensure the accuracy and completeness of these data.

Patient demographics and tumour characteristics were described by mode of detection and by ethnic group. Survival analyses were performed in women with stage I-III breast cancer only. Patients were considered to be censored on the date of death or the last updated date of Mortality Collection, which was 31 December 2014. Kaplan-Meier method was used to estimate the 5-year breast cancer-specific survival by ethnicity and by mode of detection. All data analyses were performed in IBM SPSS statistics 25 (New York, United States).

The study is covered under ethics approval from the Health and Disability Ethics Committee (HDEC) – Approval Number: 12/NTA/42/AM01.

Results

The number of breast cancer cases detected by screening increased per year over the study period, and the number of non-screen detected cases decreased (Table 1). The characteristics of screen detected women varied compared with non-screen detected women. Screen detected women were slightly older (mean age 57.3 years compared to 55.3 for non-screen detected women), had smaller tumours, were less likely to have stage IV (0.8% vs 7.6%) and high grade diseases (16.8% vs 39.0%), and were less likely to be lymph node positive (26.3% vs 51.5%) compared to non-screen detected breast cancers. There were more Luminal A cases (70.0% vs 54.0%), fewer HER2+ non-Luminal (4.4% vs 8.8%) and fewer triple negative disease (7.0% vs 13.8%) in the screen detected cancers than non-screen detected cancers.

Māori and Pacific women were more likely to have advanced breast cancer stage, positive lymph node, bigger tumour size and HER2+ disease, but less likely to have triple negative disease than NZ European women (Table 2). These differences were identified in both the non-screen detected group and in the screen detected group. If not screen detected, 22.7% of Pacific women were diagnosed with stage IV breast cancer compared to 2.4% if they were screen detected.

Overall, survival was better in screen detected women than non-screen detected women (Figure 1, Figure 2 and Table 3). The 5-year breast cancer-specific survival was 89.8% for not screen detected patients and 97.2% for screen detected patients. If not screen detected, the 5-year breast cancer-specific survival was 91.1% for NZ European women, 84.2% for Māori women and 80.2% for Pacific women (log-rank test p-value <0.001). If screen detected, the breast cancer-specific survival between different ethnic groups became similar (log-rank test p-value =0.075).

Discussion

Previous studies have demonstrated that some screen detected breast cancers have a unique natural history and biology compared to symptomatic breast cancer.[11,12] Our results show, as expected, screen detected women had less aggressive disease with 70% Luminal A breast cancers compared to 54% in non-screen detected women. Screen detected women were diagnosed at an earlier stage (66.8% stage I disease and 26.3% lymph node positive). This is consistent with other studies[13-17] showing that most screen detected patients had Luminal A cancer and stage I disease, and only 1% of patients had stage IV cancer.

There were also differences between Māori, Pacific and NZ European women. The greatest difference was found in Pacific patients. That corresponded to the greatest 5-year survival difference (13.9%) between screen detected Pacific patients (94.1%) and non-screen detected Pacific patients (80.2%). Adherence to the screening programme and improvements in access to earlier diagnosis for Pacific women have the potential to make a substantial difference in breast cancer outcomes for Pacific women.[3]

Five year survival outcomes, are short term for breast cancer, yet even at this early stage, there are major differences in survival by ethnicity for women diagnosed through a non-screen pathway. These differences are expected to grow in magnitude with longer follow up. We have previously published on some of the reasons behind this.[18] When women are diagnosed

through a screen detected pathway, these differences almost disappear, and the 5-year survival outcomes for all ethnic groups are very high. In part, these higher survival rates are explained by lead-time bias and length-time bias.[13-17,19] Screening advances the date of diagnosis, with a longer survival time expected even without treatment, and identifies more slow growing tumours, e.g. more Luminal A diseases in the screen detected group.

However there are real survival benefits for women as a result of breast cancer screening. Multiple previous studies, have demonstrated a 20-30% reduction in breast cancer mortality, as a result of population based screening.[20-22] This is the kind of benefit seen when screening is applied to an average population. When screening is made available to populations that have much higher than average death rates for breast cancer, there is the potential for a much greater mortality benefit, if high population coverage can be achieved. In New Zealand, a major effort has been made to improve coverage amongst Māori and Pacific women, which were initially poor. Currently, coverage for these ethnic groups is now approaching 70% of eligible women.[23]

Our study, strongly supports this initiative, and the message that Māori and Pacific women diagnosed through breast cancer screening do just as well as any ethnic group, is a really important one to promulgate. Not only may this result in further improvements in screening coverage, it enhances breast awareness, and the need for early diagnosis – later stage at diagnosis having previously been demonstrated to be the single most important reason for worse outcomes in our Māori and Pacific populations. This study suggests that when population based screening is applied successfully to disadvantaged ethnic groups, mortality benefits may be significantly better than for more advantaged populations.

On the other hand, the Breast Screen Aotearoa Programme has strict protocol with regards the management of women post diagnosis while there is more variation in the management of non-screen detected women. This also suggests that standard management can reduce the inequity in outcomes in Māori and Pacific women.

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.[24] We have large numbers of patients in different ethnic groups for comparison analyses, and have comprehensive data on patient characteristics, mode of diagnosis and

outcomes. One weakness is that the follow-up time for some patients (701, 29.3% of patients diagnosed in 2011-13) was short and may not be enough to identify ethnic differences in survival in screen detected breast cancers.

Conclusion

We have shown that in our population in New Zealand an increasing proportion of breast cancers are being diagnosed through breast screening. Women detected through breast screening are diagnosed at an earlier stage of disease and have a greater proportion of subtypes that have a more favourable outcome. We have also shown that there are differences in the characteristics of Māori and Pacific women especially those who are not screen detected. It appears that the variations in survival for Māori and Pacific women are only found in those who are non-screen detected.

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Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest

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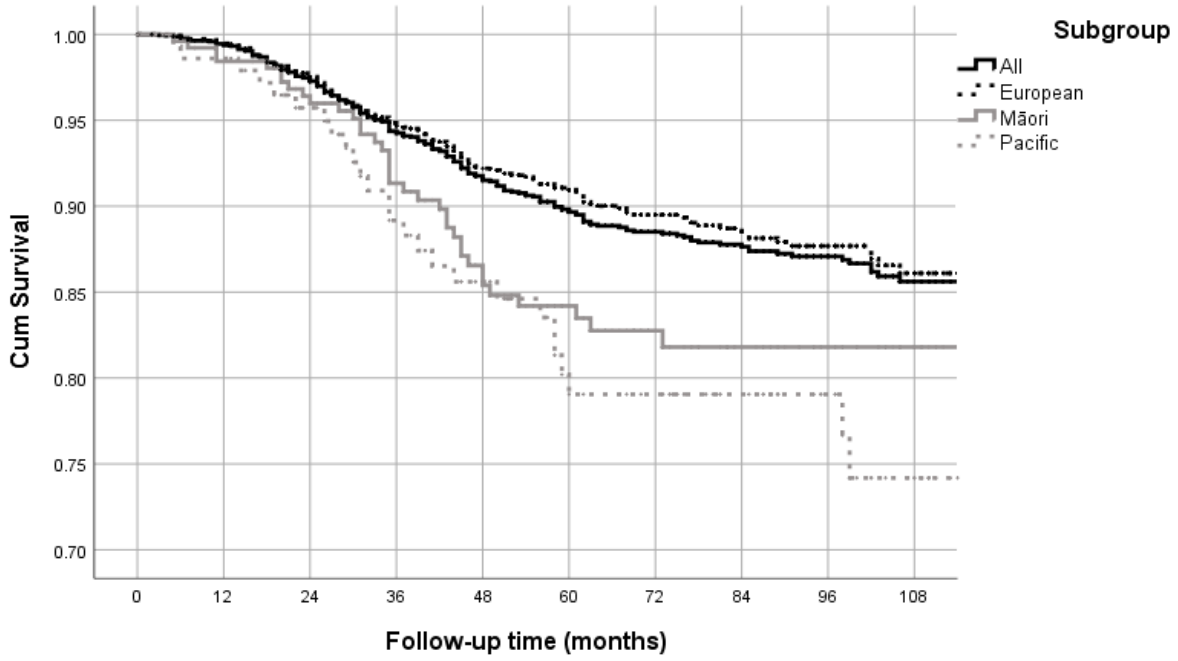
Table 1. Characteristics of breast cancer patients by mode of detection

Factors	Screen detected		Not Screen detected		Odds ratio	95% Confidence interval
Mean age (years)	57.3		55.3			
Year of diagnosis						
2005-2007	855	27.2%	898	37.5%	0.62	0.56 - 0.70
2008-2010	1195	38.0%	796	33.2%	1.23	1.10 - 1.38
2011-2013 (till May)	1095	34.8%	701	29.3%	1.29	1.15 - 1.45
Cancer stage						
Stage I	2102	66.8%	685	28.6%	5.03	4.48 - 5.65
Stage II	825	26.2%	995	41.5%	0.50	0.45 - 0.56
Stage III	193	6.1%	532	22.2%	0.23	0.19 - 0.27
Stage IV	25	0.8%	183	7.6%	0.10	0.06 - 0.15
Cancer grade						
1	1160	37.6%	376	16.5%	3.06	2.68 - 3.50
2	1404	45.6%	1018	44.6%	1.04	0.93 – 1.16
3	518	16.8%	890	39.0%	0.32	0.28 – 0.36
Unknown	63		111			
Lymph node						
No positive lymph node	2262	73.7%	1071	48.5%	2.98	2.65 - 3.34
Have positive lymph nodes	807	26.3%	1138	51.5%	0.34	0.30 - 0.38
Unknown	76		186			
Biomarker subtype						
Luminal A	2076	70.0%	1232	54.0%	1.99	1.78 - 2.23
Luminal B HER2-	333	11.2%	289	12.7%	0.87	0.74 - 1.03
Luminal B HER2+	220	7.4%	246	10.8%	0.66	0.55 - 0.80
HER2+ non-Luminal	129	4.4%	202	8.8%	0.47	0.37 - 0.59
Triple Negative	207	7.0%	314	13.8%	0.41	0.34 - 0.49
Unknown	180		112			
Tumour size (mm)						
0~10	894	28.7%	150	6.6%	5.65	4.71 - 6.79
10~20	1378	44.2%	639	28.3%	2.01	1.79 - 2.26
20~30	524	16.8%	649	28.8%	0.50	0.44 - 0.57
30+	319	10.2%	819	36.3%	0.20	0.17 - 0.23
Unknown	30		138			
Total	3145		2395			

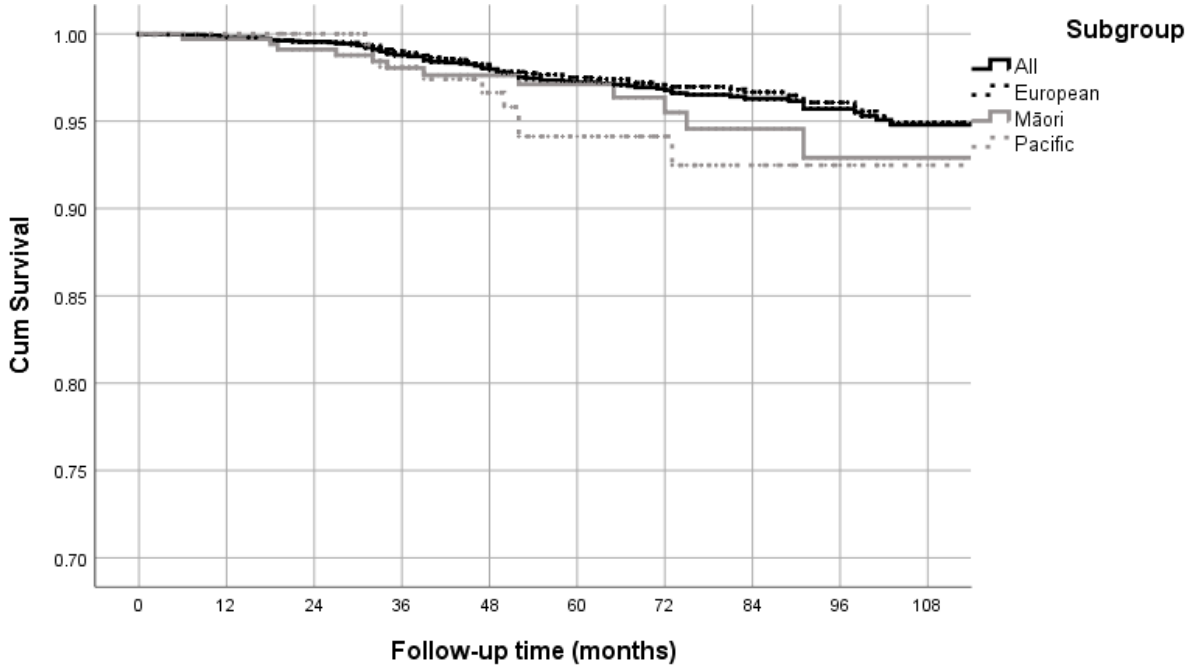
Table 2. Characteristics of breast cancer patients by ethnicity

Mode of detection	Characteristics	NZ European		Māori		Pacific	
Not Screen detected	**Mean age (years)**	55.7		55.1		54.7	
	Year of diagnosis						
	2005-2007	593	36.7%	102	35.8%	83	44.9%
	2008-2010	546	33.8%	101	35.4%	54	29.2%
	2011-2013 (till May)	478	29.6%	82	28.8%	48	25.9%
	Cancer stage						
	Stage I	491	30.4%	58	20.4%	28	15.1%
	Stage II	670	41.4%	127	44.6%	69	37.3%
	Stage III	362	22.4%	74	26.0%	46	24.9%
	Stage IV	94	5.8%	26	9.1%	42	22.7%
	Cancer grade						
	1	275	17.7%	37	13.7%	22	13.0%
	2	697	45.0%	138	51.1%	69	40.8%
	3	578	37.3%	95	35.2%	78	46.2%
	Unknown	67		15		16	
	Lymph node						
	No positive lymph node	744	48.8%	107	42.3%	60	42.6%
	Have positive lymph nodes	782	51.2%	146	57.7%	81	57.4%
	Unknown	91		32		44	
	Biomarker subtype						
	Luminal A	832	54.0%	146	53.9%	93	54.7%
	Luminal B HER2-	193	12.5%	37	13.7%	15	8.8%
	Luminal B HER2+	160	10.4%	36	13.3%	27	15.9%
	HER2+ non-Luminal	122	7.9%	24	8.9%	21	12.4%
	Triple Negative	235	15.2%	28	10.3%	14	8.2%
	Unknown	75		14		15	
	Tumour size (mm)						
	0~10	116	7.5%	8	3.1%	14	8.6%
	10~20	466	30.3%	55	21.3%	23	14.1%
	20~30	437	28.4%	83	32.2%	37	22.7%
	30+	521	33.8%	112	43.4%	89	54.5%
	Unknown	77		27		22	
Screen detected	**Mean age (years)**	57.8		56.6		56.1	
	Year of diagnosis						
	2005-2007	638	28.9%	72	20.9%	36	17.4%
	2008-2010	820	37.2%	147	42.7%	94	45.4%
	2011-2013 (till May)	748	33.9%	125	36.3%	77	37.2%
	Cancer stage						
	Stage I	1488	67.5%	225	65.4%	120	58.0%
	Stage II	571	25.9%	98	28.5%	65	31.4%
	Stage III	134	6.1%	16	4.7%	17	8.2%
	Stage IV	13	0.6%	5	1.5%	5	2.4%
	Cancer grade						
	1	832	38.4%	122	36.0%	68	33.8%
	2	979	45.2%	160	47.2%	95	47.3%
	3	356	16.4%	57	16.8%	38	18.9%
	Unknown	39		5		6	
	Lymph node						
	No positive lymph node	1611	74.2%	237	71.2%	129	69.0%
	Have positive lymph nodes	561	25.8%	96	28.8%	58	31.0%
	Unknown	34		11		20	
	Biomarker subtype						
	Luminal A	1442	69.2%	242	73.8%	147	78.2%
	Luminal B HER2-	255	12.2%	33	10.1%	7	3.7%
	Luminal B HER2+	152	7.3%	29	8.8%	10	5.3%
	HER2+ non-Luminal	85	4.1%	10	3.0%	14	7.4%
	Triple Negative	151	7.2%	14	4.3%	10	5.3%
	Unknown	121		16		19	
	Tumour size (mm)						
	0~10	660	30.1%	82	24.0%	47	23.7%
	10~20	974	44.5%	154	45.2%	79	39.9%
	20~30	355	16.2%	61	17.9%	41	20.7%
	30+	202	9.3%	44	12.9%	31	15.7%
	Unknown	15		3		9	
	Total	**3823**		**629**		**392**	



Follow-up time (months)		0	12	24	36	48	60	72	84	96
Number of women at risk	All women	2212	2185	2014	1687	1400	1158	934	690	471
	European	1523	1508	1397	1173	963	804	645	473	316
	Māori	259	250	229	189	150	120	88	65	48
	Pacific	143	141	125	102	90	70	64	49	35

Figure 1. Kaplan-Meier breast cancer-specific survival curve for not screen detected women



Follow-up time (months)		0	12	24	36	48	60	72	84	96
Number of women at risk	All women	3120	3107	2914	2410	1978	1557	1160	798	533
	European	2193	2186	2057	1727	1412	1115	839	595	410
	Māori	339	333	309	249	206	153	112	66	46
	Pacific	202	202	182	145	123	93	63	30	14

Figure 2. Kaplan-Meier breast cancer-specific survival curve for screen detected women

Table 3. 5-year breast cancer-specific survival of women with stage I-III breast cancer

Mode of detection	NZ European	Māori	Pacific	All[†]
Not screen detected	91.1% (89.5% - 92.7%)	84.2% (79.2% - 89.2%)	80.2% (72.8% - 87.6%)	89.8% (88.4% - 91.2%)
Screen detected	97.5% (96.7% - 98.3%)	97.1% (95.1% - 99.1%)	94.1% (90.1% - 98.1%)	97.2% (96.6% - 97.9%)

[†] Including NZ European, Māori, Pacific and others.