



Breast cancer diagnosis, patterns of care and burden of disease in Queensland, Australia (1998–2004): does being Indigenous make a difference?

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Abstract

Objectives We compared patterns of care, comorbidity, disability-adjusted life-years (DALYs) and survival in Indigenous and non-Indigenous women with breast cancer in Queensland, Australia (1998–2004).

Methods A cohort study of Indigenous ($n = 110$) and non-Indigenous women ($n = 105$), frequency matched on age and remoteness. We used Pearson's Chi-squared analysis to compare proportions, hazard models to assess survival differences and calculated disability-adjusted life years (DALYs).

Results Indigenous women were more likely to be socially disadvantaged (43 vs. 20 %, $p < 0.01$) have comorbidity (42 vs. 18 % $p < 0.01$), and have regional spread or distant metastasis (metastasis, 51 vs. 36 %, $p = 0.02$) than non-Indigenous women; there was no difference in treatment patterns. More Indigenous women died in the follow-up period ($p = 0.01$). DALY's were 469 and 665 per 100,000 for Indigenous and non-Indigenous women, respectively, with a larger proportion of the burden attributed to premature death among the former (63 vs. 59 %).

Conclusions Indigenous women with breast cancer received comparable treatment to their non-Indigenous counterparts. The higher proportion of DALYs related to early death in Indigenous women suggests higher fatality with breast cancer in this group. Later stage at diagnosis and higher comorbidity presence among Indigenous women reinforce the need for early detection and improved management of co-existing disease.

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Introduction

Cancer is the second leading cause of death for Indigenous Australians, who have higher cancer mortality and poorer survival than other Australians (Australian Institute of Health and Welfare 2014). The reasons underlying these disparities are multifactorial and include advanced cancer at diagnosis (Condon 2004; Valery et al. 2006), reduced uptake of/access to treatment (Supramaniam et al. 2014; Valery et al. 2006), treatment delays (Hall and Holman 2003), and higher rates of comorbidities amongst Indigenous patients (Valery et al. 2006). Breast cancer is the most

common cancer among Indigenous Australian women (Australian Institute of Health and Welfare and National Breast and Ovarian Cancer Centre 2009); however, diagnostic, treatment and follow-up practices in comparison to non-Indigenous women have been largely unreported. There are approximately 79,000 Indigenous women in the state of Queensland, representing 3.6 % of the state's female population (Queensland Government 2012) and their life expectancy is 10 years less than that of other Queensland women (Queensland Government 2013). Accurate information on the cause, magnitude and management of health problems such as breast cancer is essential for appropriate health services planning and resource allocation.

In Australia, incidence of breast cancer among Indigenous women is lower, breast cancer mortality similar, and 5-year crude survival worse compared to non-Indigenous women (Australian Institute of Health and Welfare and Cancer Australia 2012), similar to the profile described for Indigenous women in New Zealand, the United States and Canada (Curtis et al. 2005; Jemal et al. 2010; Sheppard et al. 2010). Studies of the reasons for breast cancer survival inequalities, including later cancer stage, greater burden of comorbidity and different patterns of care among Indigenous women are limited (Dasgupta et al. 2012; Roder et al. 2012; Supramaniam et al. 2014). Internationally, lower breast cancer survival has been attributed to economic and treatment disparities among Māori and Pacific Island women in New Zealand (McKenzie and Jeffreys 2009), late stage at diagnosis among American Indian women in Southwest America (Giuliano et al. 1998) and having a pre-existing comorbidity among First Nation women in Ontario, Canada (Sheppard et al. 2011). As Indigenous people have reportedly received less cancer treatment despite similar stage (Moore et al. 2014), and evidence of breast cancer treatment disparities between Indigenous and non-Indigenous women has not been consistent across jurisdictions (Shaw and Elston 2003; Supramaniam et al. 2014), we compared cancer treatment, along with prognostic factors and survival, among Indigenous and non-Indigenous women with breast cancer in the state of Queensland, Australia. Finally, using results of this current study, we calculated the disability-adjusted life years (DALYs), measuring loss of healthy life years among Indigenous and non-Indigenous women with breast cancer.

Methods

Subjects

The study methods have previously been described (Moore et al. 2014). Briefly, all Indigenous women residing in

Queensland and diagnosed with breast cancer during 1998–2004 were identified and matched to a random sample of non-Indigenous women with breast cancer, of corresponding age (within ± 5 years) and place of residence (in terms of degree of remoteness from a major centre). For inclusion, all cases had to have been admitted to a public hospital at least once for cancer diagnosis or treatment. Access to free public health care, including cancer treatment, is available to all Australian residents, although those with private insurance, or the means to pay, can also access treatment in the private sector; a previous study reported that only 4 % of Indigenous people with cancer were treated in private hospitals in Queensland between 1997 and 2002 (Valery et al. 2006). Hospital records were reviewed for diagnostic details such as date, histology and method of diagnosis, cancer stage, treatment and presence of comorbidities. Cancer staging was documented by treating doctors as either Tumour, Nodes and Metastasis (TNM) scores, American Joint Committee on Cancer Staging Scores (AJCC) (I–IV) (American Cancer Society 2002) or as localized cancer, regional spread or metastatic disease. For comparability, TNM and AJCC scores were converted to localized/regional/distant spread using commonly accepted cutoff points. Hormone receptor status, specifically oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER2: commonly defined as >30 % of cells with intense nuclei staining), was available through Queensland Health laboratories.

Treatment details, including surgery, radiotherapy, chemotherapy and tamoxifen use, as well as treatment intention (any treatment intent, curative intent or intention not known), and date, duration and amount of treatment were collected. A modified Charlson Comorbidity Index Score ('comorbidity score') (Charlson et al. 1987) was assigned. The scores (based on severity and number of comorbid conditions) were grouped as: No score (0), 1, 2+. A socioeconomic score was assigned using the Socio-Economic Index For Areas (SEIFA) index (based on geographical areas of residence ranked into quintiles, ranging from 1 as most disadvantage to 5 as most advantaged) (Australian Bureau of Statistics 2003). Date and cause of death were obtained from the Australian National Death Index to 31st December 2006.

Statistical methods

Pearson's Chi-squared analysis or Fisher's Exact test was used for categorical data (proportions), *t* test for normally distributed data (means) and non-parametric tests for non-normally distributed data (medians). All tests were two-tailed, and statistical significance was set at $p < 0.05$. Crude and adjusted survival analyses were conducted using

Cox proportional hazard models. Hazard ratios (HR) were adjusted for stage of cancer at diagnosis, comorbidities, socioeconomic status and cancer treatment. To calculate DALY, we used the incidence and mortality data as reported by the Queensland Cancer Registry, combined with survival and treatment data from the current project. A step-by-step analytical strategy was performed, similar to that previously done by Soerjomataram and colleagues (Soerjomataram et al. 2012). Briefly, years of life lost (YLL) and years of life lived with disability (YLD) were calculated according to Indigenous status and added to derive the DALYs. A standard life table was used to estimate YLL and disability weights to derive the YLD were drawn from previous studies. Finally, numbers of healthy life years lost were adjusted to the population size to derive rates (per 100,000) and age-adjusted to the world standard population. Specifically, the following data from 2001 was used to calculate DALYs: 24 and 2191 new breast cancer cases were reported among Indigenous and non-Indigenous women in Queensland, respectively, corresponding to age-standardized incidence rates of 60 and 89 per 100,000 women, and 9 and 465 women died from breast cancers in each of the respective group (age-standardized mortality rates of 15 and 17 per 100,000). All analyses were calculated using Statistics Package for the Social Sciences (IBM SPSS) for Windows version 18.0-20.0 or STATA for Windows version 12.

Ethical approval was obtained from the Queensland Health Department, all hospitals where data collection took place, and the QIMR Berghofer Institute of Medical Research. An Indigenous Reference Group was established to inform the study investigators about cultural matters and the translation of results to the community.

Results

The study included 110 Indigenous and 105 non-Indigenous women with breast cancer after exclusion of 28 women (11 Indigenous and 17 non-Indigenous), who did not meet the inclusion criteria. Clinical data were abstracted from records at 23 Queensland public hospitals, with additional data abstracted from secondary hospitals for 34 cases.

Patient and clinical characteristics

Mean age was the same for both Indigenous and non-Indigenous women (54 years) and matching resulted in no difference in remoteness of residence (Table 1). Indigenous women were more likely to be disadvantaged compared to their non-Indigenous counterparts (43 vs. 20 %, $p < 0.01$) and more likely to be diagnosed with

advanced cancer (regional spread or distant metastasis, 51 vs. 36 %, $p = 0.02$). The median number of days from presentation to diagnosis was similar and there was no difference in the histological types of breast tumours between the women ($p = 0.46$).

When compared to non-Indigenous women, Indigenous women were significantly ($p < 0.01$) less likely to have a comorbidity score of zero (58 % vs. 82 %), more likely to have a score of 2 or more (16 vs. 9 %) and had a higher prevalence of diabetes (26 % vs. 11 %) and serious diseases of the circulatory system (e.g. stroke, myocardial infarction, chronic heart failure) (23 % vs. 8 %) (Table 1). Indigenous women with regional spread or metastatic disease were significantly more likely to have a comorbidity score greater than zero (45 vs. 19 %, $p < 0.01$) than non-Indigenous women.

Cancer treatment (any treatment vs. no treatment) was given to 96 % Indigenous and 98 % non-Indigenous women ($p = 0.12$) (Table 1). Regarding mode of treatment, fewer Indigenous women underwent a lumpectomy and more underwent a mastectomy (56 % vs. 66 % and 44 % vs. 34 %, respectively, $p = 0.17$) compared to their counterparts. Time from diagnosis to treatment was available for 96 % Indigenous and 99 % non-Indigenous women; there was no significant difference in time from diagnosis to treatment ($p = 0.26$) or completion rates of treatment ($p > 0.05$) between groups, nor in number of cycles of chemotherapy ($p = 0.55$) or dose of radiotherapy ($p = 0.81$).

There was no difference in oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) expression between Indigenous and non-Indigenous women, for the small number of cases with available results. Rates of tamoxifen use, the hormone treatment generally prescribed for women with oestrogen receptive tumours (National Health and Medical Research Centre 2001), were similar for those with data recorded (80 % in each group, $p = 0.17$).

Breast cancer recurrence and survival

There was no difference in the percentage of Indigenous and non-Indigenous women who had a recurrence of their breast cancer recorded (25 % vs. 21 %, $p = 0.61$). Significantly, more Indigenous women were deceased by the end of the follow-up period (32 % vs. 18 %, $p = 0.01$), although they tended to die of causes other than breast cancer than non-Indigenous women (26 % vs. 16 %, not statistically significant) (Table 1). The majority of Indigenous women who died survived for up to 2 years after diagnosis. To explore why more Indigenous women had died overall, the characteristics of deceased Indigenous women were compared to those of deceased non-

Table 1 Demographic and clinical characteristics, cancer treatment, time and cause of death among Australian Indigenous and non-Indigenous women diagnosed with breast cancer between 1998 and 2004 in Queensland

	Indigenous (<i>N</i> = 110) <i>N</i> (%)	Non-Indigenous (<i>N</i> = 105) <i>N</i> (%)	<i>p</i> value
Age			
18–39 years	13 (12)	13 (12)	0.95
40–59 years	59 (54)	54 (51)	
60+ years	38 (35)	38 (36)	
Area of remoteness (ARIA)			
Highly accessible/accessible	48 (44)	47 (44)	0.81
Moderately accessible	35 (32)	36 (34)	
Remote/very remote	27 (25)	22 (21)	
Socioeconomic status (SEIFA)			
Most disadvantaged	47 (43)	21 (20)	<0.01
Disadvantaged	28 (25)	31 (30)	
Intermediate advantage	22 (20)	39 (36)	
Advantaged	11 (10)	13 (12)	
Most advantaged	3 (3)	1 (1)	
Stage at diagnosis (SEER score)*	<i>N</i> = 101	<i>N</i> = 94	
Localized cancer	45 (45)	57 (61)	0.02
Advanced disease**	56 (55)	37 (39)	
Histology of breast cancer	<i>N</i> = 110	<i>N</i> = 105	
Ductal adenocarcinoma	94 (86)	85 (81)	0.46
Other (mixed types, adenofibroma, Pagets)	16 (14)	20 (19)	
Charlson Comorbidity Index			
0	64 (58)	86 (82)	<0.01
1	28 (26)	9 (9)	
2+	18 (16)	10 (9)	
Diabetes			
Yes	29 (26)	11 (11)	<0.01
No	81 (74)	94 (89)	
Circulatory disease			
Yes	25 (23)	9 (8)	<0.01
No	85 (77)	97 (92)	
Any treatment given ^a			
Treatment	106 (96)	103 (98)	0.12
No treatment or not known	4 (4)	0	
Curative treatment given ^b	<i>N</i> = 92	<i>N</i> = 89	
Curative treatment	88 (96)	85 (96)	1.0
No curative treatment	4 (4)	4 (4)	
Mode of treatment ^c	<i>N</i> = 88	<i>N</i> = 85	
Lumpectomy only, or concomitant with chemotherapy and/or radiotherapy	49 (56)	56 (66)	0.17
Mastectomy only, or concomitant with chemotherapy and/or radiotherapy	39 (44)	29 (34)	
Recurrence	<i>N</i> = 110	<i>N</i> = 105	
Recurrence recorded	27 (25)	22 (21)	0.61
No recurrence recorded	76 (69)	73 (69)	
Not enough information	7 (6)	10 (10)	

Table 1 continued

	Indigenous (<i>N</i> = 110) <i>N</i> (%)	Non-Indigenous (<i>N</i> = 105) <i>N</i> (%)	<i>p</i> value
Time from diagnosis to death			
Alive at 31st December 2006	75 (68)	87 (83)	0.09
Deceased in <12 months	7 (6)	3 (3)	
Deceased 12 months–2 years	9 (8)	6 (6)	
Deceased greater than 2 years	19 (17)	9 (8)	
Cause of death	<i>N</i> = 35	<i>N</i> = 19	
Cancer death	26 (74)	16 (84)	0.45
Non-cancer death	9 (26)	3 (16)	

* Cases with unknown stage excluded (*n* = 20)

** Regional and metastatic disease combined

^a Information missing for 2 women

^b Metastatic cases excluded

^c Includes women with non-metastatic disease and those who had treatment

Indigenous women. There was no significant difference in age, cancer stage at diagnosis, or remoteness between the women who had died at the end of the follow-up period; however, from the highest two socioeconomic strata, six Indigenous women were deceased compared to no non-Indigenous women ($p = 0.01$). Furthermore, deceased Indigenous women were more likely to have a comorbidity than non-Indigenous women who were also deceased (60 % vs. 30 %, $p < 0.01$).

The crude HR of all-cause mortality among Indigenous women as compared to non-Indigenous was 2.09 (95 % CI 1.18, 3.70). After adjustment for stage, prevalence of comorbidities and any treatment, the risk of dying was not significantly different (HR 1.56 95 % CI 0.83, 2.90) (Table 2). Similarly, there was no significant difference in death rates between Indigenous and non-Indigenous women with localized cancer or advanced cancer at diagnosis. The crude risk of dying from breast cancer was marginally higher for Indigenous women (HR 1.88, 95 % CI 1.00, 3.56) but when adjusted for stage, comorbidities and any treatment, there was no significant survival difference (HR 1.39, 95 % CI 0.71, 2.76).

Disability-adjusted life years

For DALYs, we noted a larger loss of healthy life years in non-Indigenous women with breast cancer as compared with Indigenous women (Fig. 1: 665 and 469 per 100,000, respectively). In addition to estimates of DALYs and its components, we calculated YLLs as a proportion of total DALYs, to illustrate which component of the DALYs was more important. In both Indigenous and non-Indigenous women, premature mortality contributed to more than half of the total burden, though among Indigenous women the

Table 2 Hazard ratios for all-cause and breast cancer death, for Australian Indigenous women in Queensland, compared to non-Indigenous women between 1998 and 2004

	Hazard ratios	95 % (CI)
Unadjusted all-cause death	2.09	(1.18, 3.70)
All cause death adjusted for		
Stage, CCI ^a , any treatment	1.52	(0.81, 2.84)
Unadjusted breast cancer death	1.88	(1.00, 3.56)
Cancer death adjusted for		
Stage ^b	1.64	(0.86, 3.13)
SEIFA ^c	1.92	(0.99, 3.73)
Stage, CCI	1.54	(0.79, 3.02)
Stage, CCI, treatment ^d	1.39	(0.71, 2.76)

^a CCI (Charlson Comorbidity Index) in three categories: 0, 1, 2+

^b Stage in four categories: 1 localized, 2 regional spread, 3 metastatic disease, 9 not sure

^c SEIFA (socioeconomic index for area) in five categories: 1 most disadvantaged, 2 disadvantaged, 3 intermediate advantage, 4 advantaged, 5 most advantaged

^d Treatment in two categories: any and none

proportion was relatively larger (YLL/DALY: 63 vs. 59 %).

Discussion

This study found that Indigenous women with breast cancer were more likely to be socially disadvantaged, have serious comorbidity and more advanced disease at diagnosis than non-Indigenous women. Indigenous women had no treatment delays compared to others in this study, and the mode of treatment as well as completion rates was similar

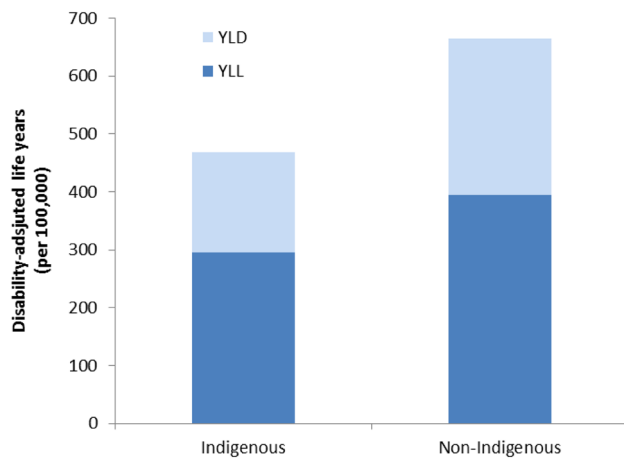


Fig. 1 Age-adjusted disability-adjusted life years per 100,000 population from breast cancer among Indigenous and non-Indigenous women in Queensland, Australia in 2001. *YLD* years of life lived with disability, *YLL* years of life lost

between groups. There was no difference in breast cancer survival outcomes between Indigenous women and other women treated in Queensland public hospitals, after adjusting for stage, comorbidity and treatment.

The finding that Australian Indigenous women had more advanced breast cancer at diagnosis than non-Indigenous women has been reported previously (Condon et al. 2005; Valery et al. 2006). A range of Indigenous cultural beliefs and understanding about cancer have been reported as possible factors inhibiting an early cancer diagnosis (Shahid and Thompson 2009), as has lower rates of participation in breast screening programs compared to non-Indigenous women (54 % compared to 36 %). A greater understanding of these beliefs would inform policy and practice for screening programs. Community education strategies are also required to increase Indigenous women's understanding about breast cancer and encourage health care-seeking behaviour among women.

Compared to non-Indigenous women, Indigenous women scored significantly higher comorbidity scores overall, and those with later stage cancer were over twice as likely to have a comorbidity, in particular diabetes, which has been shown in a meta-analysis to increase the risk of breast cancer and the risk of death from breast cancer (Larsson et al. 2007). A greater burden of comorbidity has been associated with later stage at diagnosis of breast cancer in another study; competing demand for other health care may override screening and earlier diagnosis (Gonzalez et al. 2001). Although women with serious comorbidities reported receiving less breast cancer treatment when compared to those without comorbidity (Louwman et al. 2005), our study found Indigenous women were as likely to receive curative cancer treatment as other women.

Whilst acknowledging the small numbers of cases with available ER, PR and HER2 receptor status, in view of a lack of similar data for Indigenous Australian women, this data is important to report. We found the majority of women in both groups were diagnosed with hormone receptor-positive tumours, in contrast to studies among Indigenous women in New Zealand (McKenzie et al. 2008) and West Africa (Gukas et al. 2008; Huo et al. 2009) which reported a predominance of hormone receptor-negative breast cancers. However, the response of Indigenous women to tamoxifen compared to non-Indigenous women is not known. A higher proportion of non-Indigenous women received breast conserving therapy (lumpectomy with or without chemotherapy/radiotherapy) while a large proportion of Indigenous women received radical surgery (mastectomy with or without chemotherapy/radiotherapy), however, the difference was not significant. Similar rates of breast conserving therapy between Indigenous and non-Indigenous women were reported in a surgical review in far north Queensland (Shaw and Elston 2003), and a Western Australian study (Hall et al. 2004) but higher rates of mastectomy have been reported in New South Wales (Supramaniam et al. 2014) and South Australia (Roder 2007).

There was no significant difference in the percentage of women who had recurrent breast cancer recorded on the medical chart. Numbers in both groups may not be complete as some of those with recurrence may have been lost to follow-up, may not have been biopsied, or may have presented to a private hospital with their recurrence; however, there is no reason to assume that incomplete information on recurrence was differentially biased. Although not significantly different, more Indigenous than non-Indigenous women had died by the end of the follow-up period, and that was more likely to be a non-cancer death. Other studies have reported lower 5-year survival for Indigenous women in comparison to other Australian women, from all causes (Australian Institute of Health and Welfare and Cancer Australia 2012) and also from breast cancer (Chong and Roder 2010). A study of First Nation women in Ontario, Canada with early stage breast cancer, reported that the existence of a pre-existing health condition accounted for the survival disparity (Sheppard et al. 2011), a factor which may also have contributed to poorer overall survival among Indigenous women in our cohort.

Overall survival among Indigenous women was half that of non-Indigenous, although survival disparities diminished after adjustment for stage, comorbidities and treatment. This contrasts with the survival differential reported for Indigenous and non-Indigenous women with breast cancer in the Northern Territory (NT, Relative Risk adjusted for age and stage 2.4, 95 % CI 1.1, 5.2) (Condon et al. 2005). However, the NT study results were not adjusted for

comorbidity and they compared Indigenous women with all women in the territory with breast cancer, whereas our study compared only those treated primarily in public hospitals, where most Indigenous people receive their cancer care. We acknowledge that the small numbers of Indigenous women with breast cancer in our Queensland sample may have resulted in non-significant results and that a larger study is required for their confirmation. However, based on a 2010 report (Moore et al. 2010), we would have expected approximately 152 Indigenous women to be diagnosed with breast cancer and treated in Queensland public hospitals during 1998–2004, for whom 72 % of records were ascertained.

Overall DALYs were less for Indigenous compared to non-Indigenous women with breast cancer. For both groups more than half of the burden was due to premature mortality, yet this was proportionally larger among the Indigenous women (63 vs. 59 %), reflecting higher fatality rates or lower survival.

In Australia, ethnicity is defined by self-assessment (Robertson et al. 1995) and therefore not all Indigenous women with cancer may have been identified by the Registry. There is also the potential for misclassification. However, we believe the Indigenous to non-Indigenous comparison is internally valid, with little, if any, misclassification as medical charts were carefully reviewed to verify Indigenous status. Information about treatment and stage was obtained retrospectively from the medical charts and therefore subject to coding and interpretative uncertainties, but were probably not differentially biased. Our study of survival was also limited by small numbers of breast cancer deaths in the cohort.

Conclusion

In summary, Australian Indigenous women received comparable breast cancer treatment to non-Indigenous women treated in public hospitals in Queensland. Differences in comorbidity and stage at diagnosis between the two groups reinforce the need for early detection and improved management of co-existing disease in Indigenous women with breast cancer.

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Compliance with ethical standards

Authors' contributions SP Moore participated in the conception, design, analyses of the data, interpretation of results, writing and editing the manuscript. I Soerjomataram conducted analysis of DALYs, interpretation of results, and editing of the manuscript. A Green participated in the conception, design, analyses of the data, interpretation of results and editing the manuscript. G Garvey participated in the interpretation of results and editing the manuscript. J Martin participated in the interpretation of results and editing the manuscript. P Valery participated in the conception, design, analyses of the data, interpretation of results and editing the manuscript. We confirm that all authors have seen and approved its final version.

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