Missing data on body mass index in a breast cancer register: how is it associated with patient characteristics and clinical outcomes?

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ABSTRACT

AIM: To assess the completeness of data on body mass index (BMI) in a regional breast cancer register, and its association with patient characteristics and clinical outcomes.

METHODS: This analysis used the data from the Waikato Breast Cancer Register and involved all women who were diagnosed with primary breast cancer in the Waikato District Health Board Region between January 2000 and June 2014. Patients with recorded BMI were compared with those with missing data in terms of demographics, disease factors and treatment factors. Cox regression modelling was performed, and hazards of specific outcomes associated with missing data on BMI were assessed.

RESULTS: Of the 3,536 patients included in this analysis, 27.4% had missing data on BMI. Missing data was more frequent in older patients, rural dwellers, patients with comorbidities, screen detected patients, patients with early stage or low grade cancer and hormone receptor positive patients, but was minimal in patients who received chemotherapy. Patients with missing data were less likely to experience loco-regional recurrence (although not significant), metastasis and breast cancer specific mortality, but more likely to experience death from other causes even after demographic, disease and treatment factors were adjusted.

CONCLUSIONS: Height or weight or both were not recorded for more than one quarter of the patients. Missing data was differential by specific patient characteristics and clinical outcomes.

Breast cancer is the most common cancer in New Zealand women, accounting for almost 30% of all new cancer cases and 14% of all cancer deaths in 2012, with a higher rate observed in Māori, Pacific women and those living in deprived area.[1,2] New Zealand has poorer survival from breast cancer compared to some other developed nations,[3] including its neighbour Australia.[4,5]

The outcomes of breast cancer can be influenced by a range of factors, including demographic, biological and treatment factors. One important factor is obesity, assessed by body mass index (BMI, weight/height^2). A meta-analysis of 82 studies reported an increased risk of total mortality with a hazard ratio of 1.41 (95% CI: 1.29-1.53) for women with a BMI over 30 compared to those with normal weight (BMI 18.5-25.1).[6] While a few studies have shown no effect, most studies show worse outcomes in patients with higher BMI, including metastatic disease and first recurrences.

In New Zealand, three in ten adults are obese, and the rate is significantly higher in Māori, Pacific women and those living in deprived areas.[7] Yet the ability of researchers to explore the contribution of BMI to breast cancer outcomes is limited, as the national and regional cancer registries do not routinely collect information on patient height and weight, although some regional registries have started collecting the data recently. An exception is the Waikato Breast Cancer Register, which captures newly diagnosed breast cancer cases in the Waikato District Health Board Region, and has recorded patient height and weight at the time of diagnosis since 1991.

This paper assessed the completeness of data on patient height, weight and BMI in the Waikato Breast Cancer Register and its association with specific patient characteristics and clinical outcomes.

Methods

Data sources

This analysis used the data from the Waikato Breast Cancer Register and involved all women who were diagnosed with primary breast cancer in the Waikato District Health Board Region between January 2000 and June 2014. Compared with the national data sources, the register contains more comprehensive and accurate information on many factors,[8,9] and records patient demographics such as age, ethnicity and health domicile code, height, weight, year of cancer diagnosis, mode of presentation (screen or symptomatic), tumour characteristics such as stage at diagnosis, grade, histological type and hormone receptor status, treatments undertaken such as surgery, radiotherapy, chemotherapy, hormonal therapy and biological treatment and health care facility where primary treatment was undertaken. Information on patient height and weight was obtained from the medical oncology new patient clinical letter or the surgical admission form or both, which record measured weight. If such information was not available, the patient history form was used, which records measured or self-completed (with help from a nurse) height and weight. The health domicile codes represent patients' usual residential address, and were categorised as urban (main urban, satellite urban and rural with high urban influence) and rural areas (others) based on Statistics New Zealand's Urban/Rural Profile.[10] To assess the degree of neighbourhood deprivation, the domicile codes were also mapped on to the 2006 New Zealand Deprivation Index (NZDep),[11] with decile ten the most deprived and decile one the least. Each woman was followed prospectively through public and private clinic follow-ups, and outcomes such as loco-regional recurrence, metastasis and death were recorded.

The data were linked to the National Minimum Dataset (NMDS) to obtain information on comorbidities. The NMDS contains information about all day patients and inpatients discharged from all public hospitals and over 90% of private hospitals in New Zealand.[12] Comorbidity was measured using a C3 index score, which is a cancer-specific index of comorbidity based on the presence of 42 chronic conditions recorded in the NMDS for a period of five years prior to the diagnosis of cancer.[13] Each condition was weighed to its impact on one-year non-cancer mortality in a cancer cohort, and the weights were then summed to get a final comorbidity score.

This analysis was undertaken as part of a wider project aiming to improve outcomes for women with breast cancer in New Zealand. Ethical approval for the project was obtained from the New Zealand Northern 'A' Ethics Committee (Ref. No. 12/NTA/42).

Analyses

All analyses were performed using SAS (release 9.4, SAS Institute Inc., Cary, North Carolina). Missing values except for BMI were computed using multiple imputation with ten complete datasets created by the Markov chain Monte Carlo method,[14] incorporating all baseline characteristics and outcomes. Baseline data were presented as percentages, and compared between patients with recorded height, weight and BMI and those with missing data by using a $\chi 2$ test.

Cumulative incidences for specific outcomes (loco-regional recurrence, metastasis, breast cancer-specific mortality, death from other causes and overall mortality) in the presence of competing risks were computed. For loco-regional recurrence and metastasis, death from any cause as the first event was considered as a competing risk. For breast cancer-specific mortality, death from other causes as the first event was considered as a competing risk. For death from other causes, breast cancer-specific death as the first event was considered as a competing risk. Cox proportional hazards regression modelling was then performed and hazards of the specified outcomes associated with missing data on BMI were assessed. Hazard ratios (HRs) were adjusted for all baseline characteristics except HER-2 status (as about one-third of the records had missing values).

Results

There were 3,536 patients who were diagnosed with primary breast cancer between January 2000 and June 2014. Height was not recorded on 25.4% of patients and weight not recorded on 16.2% so that BMI was unavailable for 27.4% (Table 1). There were significant differences in baseline characteristics of patients with recorded vs. unrecorded height, weight and BMI. Generally, missing data was more frequent in patients who were older and of European ethnicity, resided in semi-urban or rural areas and had a higher comorbidity index. Missing data was also more common in screen-detected patients, patients with early stage (0 and 1) or low-grade cancer and hormone receptor-positive patients. BMI information was available on almost all patients who had adjuvant chemotherapy but was missing on about 40% of other patients. The amount of missing data has declined over time but was still 17.1% in the most recent period, 2012–14.

Table 1: Baseline characteristics of patients by missing height, weight and BMI.

Characteristics	Total	Height			Weight			BMI		
		Missing	%	p-value	Missing	%	p-value	Missing	%	p-value
Total	3,536	897	25.4		573	16.2		968	27.4	
Age										
<40	179	15	8.4	<0.0001	4	2.2	<0.0001	15	8.4	<0.0001
40–59	1,642	322	19.6		226	13.8		355	21.6	
60–79	1,367	385	28.2		242	17.7		416	30.4	
80+	348	175	50.3		101	29.0		182	52.3	
Menopausal status										
Pre-menopause	915	122	13.3	<0.0001	84	9.2	<0.0001	139	15.2	<0.0001
Peri-menopause	139	23	16.5		14	10.1		25	18.0	
Post-menopause	2,461	743	30.2		470	19.1		795	32.3	
Missing/unknown	21	9	42.9		5	23.8		9	42.9	
Ethnicity										
European	2,845	770	27.1	0.0001	503	17.7	<0.0001	832	29.2	<0.0001
Māori	534	98	18.4		56	10.5		106	19.9	
Pacific	60	13	21.7		4	6.7		13	21.7	
Asian	90	15	16.7		9	10.0		16	17.8	
Others	7	1	14.3		1	14.3		1	14.3	
NZDep 2006										
1–2	362	77	21.3	0.1	56	15.5	0.98	85	23.5	0.3
3–4	420	102	24.3		65	15.5		113	26.9	
5–6	781	199	25.5		131	16.8		214	27.4	
7–8	1,063	298	28.0		177	16.7		310	29.2	
9–10	878	212	24.1		139	15.8		234	26.7	
Missing/unknown	32	9	28.1		5	15.6		12	37.5	

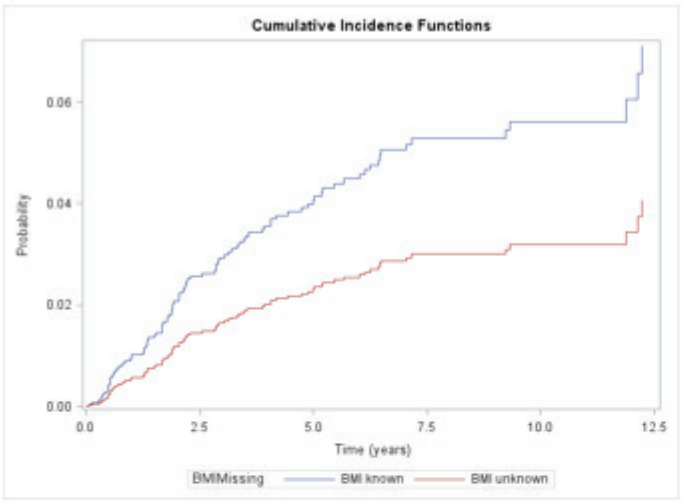
Table 1: Baseline characteristics of patients by missing height, weight and BMI (Continued).

Area of residence										
Urban	1,939	438	22.6	<0.0001	286	14.7	0.03	474	24.4	<0.0001
Semi-urban or rural	1,469	415	28.3		265	18.0		447	30.4	
Missing/unknown	128	44	34.4		22	17.2		47	36.7	
C3 index score										
0	2,737	611	22.3	<0.0001	421	15.4	0.04	669	24.4	<0.0001
1	311	99	31.8		56	18.0		105	33.8	
2	195	60	30.8		33	16.9		64	32.8	
3+	293	127	43.3		63	21.5		130	44.4	
Screen-detected										
Yes	1,441	408	28.3	0.0008	266	18.5	0.003	446	31.0	<0.0001
No	2,095	489	23.3		307	14.7		522	24.9	
Stage at diagnosis										
0	466	182	39.1	<0.0001	116	24.9	<0.0001	194	41.6	<0.0001
I	1,181	402	34.0		263	22.3		435	36.8	
II	1,240	223	18.0		131	10.6		241	19.4	
III	466	48	10.3		31	6.7		52	11.2	
IV	178	37	20.8		27	15.2		41	23.0	
Missing/unknown	5	5	100.0		5	100.0		5	100.0	
Grade										
I	736	253	34.4	<0.0001	174	23.6	<0.0001	278	37.8	<0.0001
II	1,682	387	23.0		237	14.1		423	25.1	
III	808	135	16.7		72	8.9		141	17.5	
Missing/unknown	310	122	39.4		90	29.0		126	40.6	
Histology										
Ductal	2,443	543	22.2	<0.0001	344	14.1	<0.0001	585	23.9	<0.0001
Lobular	336	66	19.6		47	14.0		83	24.7	
Other	750	100	13.3		175	23.3		293	39.1	
Missing/unknown	7	6	85.7		7	100.0		7	100.0	
ER/PR										
ER+/PR+	2,088	540	25.9	<0.0001	366	17.5	<0.0001	594	28.4	<0.0001
ER+/PR-	667	154	23.1		87	13.0		161	24.1	
ER-/PR+	34	5	14.7		3	8.8		6	17.6	
ER-/PR-	512	90	17.6		40	7.8		94	18.4	
Missing/unknown	235	108	46.0		77	32.8		113	48.1	

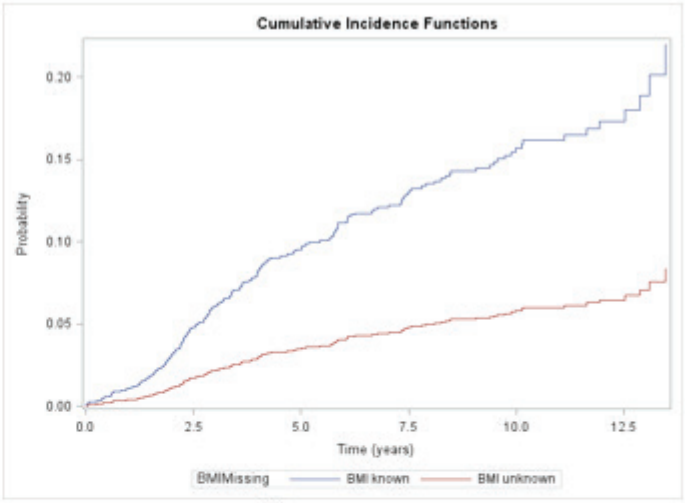
Table 1: Baseline characteristics of patients by missing height, weight and BMI (Continued).

HER-2										
Positive	475	55	11.6	<0.0001	24	5.1	<0.0001	57	12.0	<0.0001
Equivocal	178	71	39.9		41	23.0		76	42.7	
Negative	1,869	372	19.9		250	13.4		417	22.3	
Missing/unknown	1,014	399	39.3		258	25.4		418	41.2	
Loco-regional treatment										
Breast conserving surgery with radiotherapy	1,615	423	26.2	<0.0001	293	18.1	<0.0001	460	28.5	<0.0001
Breast conserving surgery without radiotherapy	395	131	33.2		79	20.0		139	35.2	
Mastectomy with radiotherapy	523	31	5.9		14	2.7		37	7.1	
Mastectomy without radiotherapy	718	200	27.9		100	13.9		213	29.7	
No primary surgery	285	112	39.3		87	30.5		119	41.8	
Adjuvant treatment										
Chemotherapy alone	345	6	1.7	<0.0001	2	0.6	<0.0001	6	1.7	<0.0001
Hormonal/biological therapy alone	1,500	520	34.7		330	22.0		563	37.5	
Chemotherapy and hormonal/biological therapy	727	11	1.5		4	0.6		12	1.7	
None	964	360	37.3		237	24.6		387	40.1	
Facility where primary treatment was undertaken										
Private	992	243	24.5	0.5	203	20.5	<0.0001	263	26.5	0.5
Public	2,544	654	25.7		370	14.5		705	27.7	
Diagnostic year										
2000–2002	579	195	33.7	<0.0001	110	19.0	<0.0001	197	34.0	<0.0001
2003–2005	719	324	45.1		181	25.2		328	45.6	
2006–2008	765	154	20.1		116	15.2		178	23.3	
2009–2011	754	116	15.4		89	11.8		142	18.8	
2012–2014	719	108	15.0		77	10.7		123	17.1	

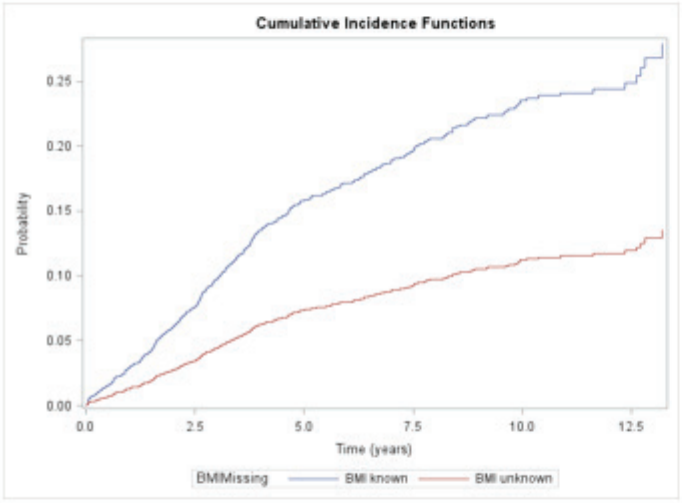
Figure 1: Cumulative incidence of specific outcomes in patients with known BMI vs. unknown BMI.



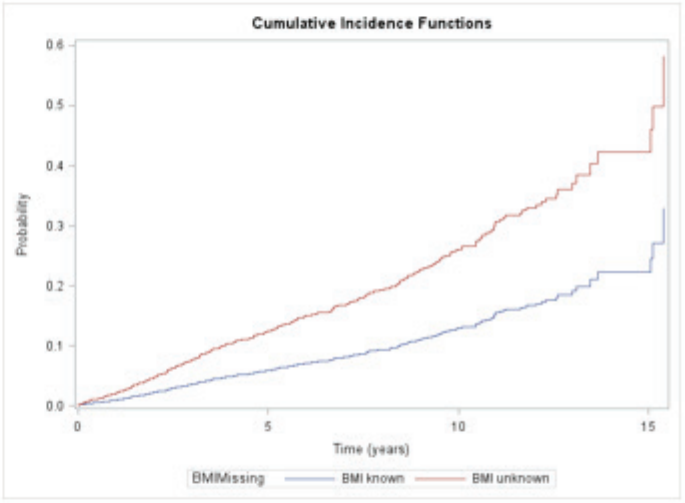
(a) Loco-regional recurrence



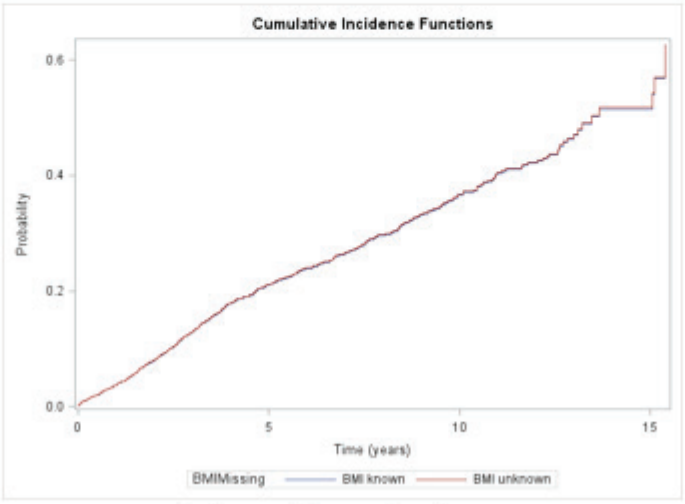
(b) Metastasis



(c) Breast cancer specific death



(d) Death from other causes



(e) Overall mortality*

* Figure 1 (e) has two lines which are overlapping.

Patients with missing data on BMI were less likely to experience loco-regional recurrence (crude HR: 0.56; 95% CI: 0.35, 0.90; adjusted HR: 0.61; 95% CI: 0.37, 1.02), metastasis (crude HR: 0.35; 95% CI: 0.24, 0.50; adjusted HR: 0.38; 95% CI: 0.25, 0.58) and breast cancer-specific mortality (crude HR: 0.44; 95% CI: 0.34, 0.57; adjusted HR: 0.64; 95% CI: 0.46, 0.88), but were more likely to experience death from other causes (crude HR: 2.19; 95% CI: 1.78, 2.70; adjusted HR: 1.28; 95% CI: 1.00, 1.63) (Figure 1 and Table 2). The HRs were adjusted for all baseline characteristics mentioned in Table 1, except HER2-status.

Discussion

In the Waikato Breast Cancer Register, height was not recorded on one in four patients and weight not recorded on one in six patients. Missing data was differential by several demographic, disease and treatment factors as well as specific outcomes.

In general, patients with missing data were older, had early-stage cancer, did not receive chemotherapy and had better cancer-specific outcomes. It is possible that older patients were less likely to have their BMI measured or to complete height and weight fields in the patient history form, and hence had more missing data. It is not surprising that BMI data is almost complete for patients who received chemotherapy, as BMI is important in the prescribing of chemotherapy. These patients also tend to have more aggressive cancer and hence have poorer outcomes. Importantly, our findings indicate that analyses restricted to patients with recorded BMI could be biased, possibly away from the null.

The amount of missing data in the register has been declining over time, reflecting efforts made by the registry staff to ensure that BMI data is collected. However, there is room for improvement as BMI was not available for about 17% of patients who were diagnosed between 2012 and 2014. Patient height and weight should be recorded in all population-based cancer registries for several reasons. First, obesity rates in New Zealand are among the highest in the OECD countries.[15] In particular, two in three Pacific women and one in two Māori women are obese.[7] Second, there is increasing evidence linking obesity to development and prognosis of breast cancer[6,16] and also several other cancers.[17] Possible mechanisms include hormonal imbalance, suboptimal treatment and related comorbidities,[6,18,19] and may be different across population subgroups (eg, across racial/ethnic groups[16]). Yet the impact of obesity on breast cancer has rarely been evaluated in New Zealand. Such evaluation would benefit Māori and Pacific women most, as they bear a disproportionate burden of obesity and related diseases including cancer.

Table 2: Clinical outcomes in patients with recorded vs. unrecorded BMI.

Outcome	BMI	Crude HR (95% CI)	Adjusted HR* (95% CI)
Loco-regional recurrence	BMI recorded	1.00	1.00
	BMI unrecorded	0.56 (0.35, 0.90)	0.61 (0.37, 1.02)
Distant metastasis	BMI recorded	1.00	1.00
	BMI unrecorded	0.35 (0.24, 0.50)	0.38 (0.25, 0.58)
Breast cancer specific death	BMI recorded	1.00	1.00
	BMI unrecorded	0.44 (0.34, 0.57)	0.64 (0.46, 0.88)
Death from other/unknown causes	BMI recorded	1.00	1.00
	BMI unrecorded	2.19 (1.78, 2.70)	1.28 (1.00, 1.63)
Overall mortality	BMI recorded	1.00	1.00
	BMI unrecorded	0.99 (0.87, 1.20)	1.03 (0.85, 1.25)

* Adjusted for all baseline characteristics mentioned in Table 1 except HER2-status.

An initial step in New Zealand would be to routinely record height and weight in the NMDS, as hospital records are the primary source of information for cancer registries and contain data on objectively measured height and weight. An earlier US study found height and weight to be available in the hospital record of most cancer patients (more than 80%) at the time of diagnosis, but acknowledged that manually abstracting height and weight for each patient was resource-intensive.[20] However, the data collection process should be simpler, quicker and cheaper with the growing movement toward electronic health records, advances in data linkage and availability of digital medical scales, which can be connected to a PC or smartphone.

Potential limitations of this analysis should be noted. Misclassification of the cause of death may occur, but such errors are likely to be similar in the two groups being compared, and will only act to reduce observed differences to a small extent. NZDep2006 used in this analysis measures area-level deprivation and may not reflect an individual's actual socioeconomic status, although it has been validated previously.[21] Tumour grade and ER/PR status were missing for some patients (9% and 7% respectively) as patients with stage 0 or in-situ cancer were included in this analysis. HER-2 status was missing for 29% of the patients and was excluded from this analysis, as most patients with missing HER-2 were diagnosed prior to 2006 when HER-2 testing was not routine in New Zealand.

To conclude, height or weight or both were not recorded for more than one quarter of the patients in the Waikato Breast Cancer Register. Importantly, missing data was differential by specific patient characteristics and clinical outcomes. To be able to evaluate the associations between BMI and breast cancer outcomes in New Zealand, patient height and weight should be recorded in hospital and computerised data systems.

Competing interests:
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REFERENCES:

1. Ministry of Health. Cancer: New registrations and deaths 2012. Wellington: Ministry of Health; 2015.
2. Haynes R, Pearce J, Barnett R. Cancer survival in New Zealand: Ethnic, social and geographical inequalities. Soc Sci Med. 2008; 67:928–37.
3. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2014; 385:977–1010.
4. Aye PS, Elwood JM, Stevanovic V. Comparison of cancer survival in New Zealand and Australia, 2006-2010. N Z Med J. 2014; 127:14–26.
5. Elwood JM, Aye PS, Tin Tin S. Increasing disadvantages in cancer survival in New Zealand compared to Australia, between 2000–05 and 2006–10. PLoS One. 2016; 11:e0150734.
6. Chan DS, Vieira AR, Aune D, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014; 25:1901–14.
7. Ministry of Health. Annual Update of Key Results 2013/14: New Zealand Health Survey. Wellington: Ministry of Health; 2014.
8. Seneviratne S, Campbell I, Scott N, et al. Accuracy and completeness of the New Zealand Cancer Registry for staging of invasive breast cancer. Cancer Epidemiol. 2014; 38:638–44.
9. Gurney J, Sarfati D, Dennett E, et al. The completeness of cancer treatment data on the National Health Collections. N Z Med J. 2013; 126:69–74.
10. Statistics New Zealand. New Zealand: An Urban/Rural Profile. Wellington: Statistics New Zealand; 2007.
11. Salmond C, Crampton P, Atkinson J. NZDep2006 Index of Deprivation. Wellington: Department of Public Health, University of Otago; 2007.
12. Ministry of Health. National Minimum Dataset (Hospital Inpatient Events): Data Marts - Data DIctionary V7.5. Wellington: Ministry of Health; 2012.
13. Sarfati D, Gurney J, Stanley J, et al. Cancer-specific administrative data-based comorbidity indices provided valid alternative to Charlson and National Cancer Institute Indices. J Clin Epidemiol. 2014; 67:586–95.
14. Schafer J. Analysis of incomplete multivariate data. London: Chapman & Hall, 1997.
15. Organisation for Economic Co-operation and Development (OECD). Obesity Update. Paris: OECD; 2014.
16. Bandera EV, Maskarinec G, Romieu I, et al. Racial and ethnic disparities in the impact of obesity on breast cancer risk and survival: A global perspective. Adv Nutr. 2015; 6:803–19.
17. Ligibel JA, Alfano CM, Courneya KS, et al. American Society of Clinical Oncology Position Statement on Obesity and Cancer. J Clin Oncol. 2014; 32:3568–74.
18. Ioannides SJ, Barlow PL, Elwood JM, et al. Effect of obesity on aromatase inhibitor efficacy in postmenopausal, hormone receptor-positive breast cancer: a systematic review. Breast Cancer Res Treat. 2014; 147:237–48.
19. Goodwin PJ, Boyd NF. Body size and breast cancer prognosis: a critical review of the evidence. Breast Cancer Res Treat. 1990; 16:205–14.
20. Keegan THM, Le GM, McClure LA, et al. Availability and utility of body mass index for population-based cancer surveillance. Cancer Causes Control. 2008; 19:51.
21. Salmond CE, Crampton P. Development of New Zealand's deprivation index (NZDep) and its uptake as a national policy tool. Can J Public Health. 2012; 103:S7–11.