Title:
Increasing Incidence of Endometrial Carcinoma in a High-Risk New Zealand Community

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Abstract

Background:

Endometrial carcinoma (EC) is increasing in incidence, attributed largely to the obesity epidemic. Ethnic differences in NZ have long been recognised, with Pacific women bearing the greater burden of disease. We hypothesise that the pooled national incidence rates underestimate the true burden of EC in our high-risk community.

Aims:

We aimed (1) to determine the incidence, trends and outcome of EC in the high-risk community served by our hospital, relative to national data, and (2) to examine associated demographic, and clinicopathological features with reference to risk factors, to identify potential clinical and population intervention points.

Materials and Methods:

All area-resident women treated for EC at Middlemore Hospital from 2000-2014 were identified from records, and clinicopathological data obtained. Incidence and time trend analysis was performed with reference to tumour type, age and ethnicity.

Results:

The study included 588 women. Pacific, followed by Māori women had the highest incidence of EC (RR=5.11 and 2.47 respectively, relative to “Other” women). The incidence increased for all ethnicities (APC of 7.3 [95% CI 3.6-11.1]), most marked in women aged below 50years (APC of 12.2: 95% CI 5.2-19.7). This occurred predominantly in Pacific women, who had a high prevalence of potentially reversible risk factors. Disease-specific survival was worse in Pacific, and to a lesser extent, Māori women.

Conclusions:

Prompt investigation of symptomatic, high-risk women regardless of age may detect endometrial abnormalities at an early, potentially reversible stage. The prevention and management of identifiable high risk factors would help mitigate the risk of EC and associated diseases.

Introduction

Endometrial cancer (EC) is the fifth most common cancer in New Zealand (NZ) women with a current estimated average annual incidence of 14/100 000 and mortality of 3/100 000[1;2;3]. There are strong environmental risk factors, seen in the wide range in global incidence from 4.1/100 000 women in less developed regions, to 34.1/100 000 women in North America [3]. The incidence, both globally and in New Zealand is increasing, attributed largely to a rise in risk factors associated with the obesity epidemic.

Most risk factors for EC, of which excess body weight is the most important (RR=2-11), appear related to the stimulatory effects of increased oestrogen on endometrium [4;5]. There is evidence to suggest that excess weight is implicated in the development of both types 1 and 2 EC[6;7], and is estimated to account for more than 40% of all EC globally[8]. Other risk factors include diabetes, hypertension, sedentary lifestyle and diet. Progestins, the oral contraceptive, parity, lactation, physical activity, diet (low fat, high plant food), and smoking appear protective. Familial cancer syndromes account for an estimated 2-5% of cases[9].

It has long been recognised that Pacific, and to a lesser extent, Māori women bear the greater burden of EC in NZ, with both increased incidence and mortality[10;11]. This has been attributed largely to the high prevalence of risk factors, particularly obesity, in these populations. An estimated 48.6% (CI 46.8-50.4) of Māori women and 69.1% (95% CI 65.9-72.1) of Pacific women are obese[12], with approximately 37% of EC in Māori women and 48% of EC in Pacific women attributed to increased BMI[13]. Socioeconomic deprivation factors compound this risk, linked both to increased obesity, (1.5x increase in people living in the most deprived compared with the least deprived areas), and to overall cancer incidence, where the most socioeconomically deprived quintile shows a 25% higher rate for all cancers than the least deprived group[14].

Our hospital serves an area (Counties Manukau) with a high proportion of Māori (16%) and Pacific peoples (21%), with substantial socioeconomic deprivation factors; overall 36% live in the most socioeconomically deprived quintile, NZDep2013 quintile 5 areas (increasing to 58% for our Māori population and 76% for our Pacific peoples). Nearly half of all Pacific women have either class 2 (21.7%: 95% CI 17.5-26.7) or class 3 obesity (28.1%: 95% CI 23.8-32.8)[12]. The reported incidence rates for EC based on national population data are

therefore likely to under-estimate the true incidence of EC in this high-risk community, which accounts for approximately 14% of the total National Cancer Registry cases[1]. We hypothesise that increased risk factors for EC in our community are likely to operate as the main drivers of the EC burden in Pacific women.

The aims of this study are as follows: (1) to determine the incidence, trends and outcome of EC in a single, high risk community-based hospital, relative to the available national data[1;3], and (2) to examine the associated demographic, and clinicopathological features with particular reference to risk factors, to identify potential clinical and population intervention points.

Materials and Methods

Ethics consent was obtained from the NZ Health and Disability Committee (14/NTA/4/AM06). Women diagnosed with EC between 2000 and 2014 and resident in Counties Manukau (CM) were identified from the hospital histopathology database. Our hospital serves as the referral hospital for Counties Manukau. Excluded were women treated entirely in the private sector (n=43), non-residents, and women with cervical tumours, sarcomas and metastasis to the uterus. Demographic, clinical and pathological data was extracted from records.

Tumours were classified into type 1 (comprising mainly endometrioid adenocarcinoma) and type 2 (mainly serous, clear cell and Mixed Mullerian tumours). Ethnicity was based on patient self-identification, with three groups, Māori, Pacific, "Other" (mainly European, and various Asian ethnic groups) recognised to reflect national ethnic data. Women were divided into those aged 20 to 49 years, and 50+ years for further analysis. All cancers were re-staged to reflect the 2009 FIGO staging system[15].

Data on risk factors collected from clinical records included BMI, type 2 diabetes, hypertension, hyperlipidaemia and parity. BMI was calculated as current weight (kg) divided by the square of height (meters) (kg/m2). The WHO categories recognized were BMI <30, 30-34 (class 1 obesity), 35-39 (class 2 obesity) and 40+ (class 3 obesity).

Population data for 2001-2014 by age and ethnicity were sourced from Statistics New Zealand (via the Ministry of Health and CM population health team), and were consistent with Statistics New Zealand hedpublis population statistics. EC is an adult cancer, therefore calculations were based on women aged 20+ years. Age standardisation was performed using the World Health Organisation standard population. Data was analysed by tumour type, ethnicity, age group (20-49 years and 50+ years), and BMI. Statistical trend analysis was performed using the Joinpoint regression program[16]. Uncorrected Chi squared with the two-tailed test was used to test comparisons. Multivariate Cox-regression analysis was used to investigate for factors independently associated with disease-specific survival (age group, ethnicity, BMI group, treatment intent, tumour type, grade, stage, and lymphovascular space invasion). For patients who were alive, date of last follow-up was used as the censored observation. A p-value of < 0.05 was determined to be statistically significant.

Results

A total of 588 women were diagnosed with EC, comprising 82 Māori women (13.9%), 242 Pacific women (41.2%) and 264 women of "Other" ethnicities (44.9%). The overall median age of presentation was 59 years (range 23 to 94 years), with the median for Pacific, Māori and "Other" women being 55, 57 and 64 years respectively. Nearly 40% of Pacific women were aged <50years (with 8.5% aged <40years), compared to 14% of "Other" women. Type 1 EC accounted for approximately 80% of EC across all ethnic groups. Predictably, type 2 EC occurred largely in women aged 50+ years. The results are summarised in Table 1 and Figure 1.

EC increased in incidence for all women over the 15-year study period with an annual percentage change (APC) of 7.3 [95% CI 3.6-11.1]), with similar rates of increase for both types 1 and type 2 cancers (Table 2). Pacific women had a higher rate of increase in EC incidence (APC of 9.3 [95% CI 4-14.9]) than Māori (APC of 7.2 [95% CI 0.2-14.6]) and "Other" women (APC of 3.4, [95% CI 0.5-6.4]). Women <50years had an APC of 12.2 (95% CI 5.2-19.7), substantially higher than those aged 50+years (APC of 5.2 [95% CI 2.3-8.2]). The disease specific mortality for all women increased in parallel with the rise in incidence (APC of 7.3 [95% CI 3.7-11.1]).

The majority of women had identifiable risk factors (Table 1; Figure 1). Class 2 or 3 obesity was present in three quarters of Pacific women, two thirds of Māori women, but in only a third of "Other" women. Conversely, EC in non-obese women (BMI<30) occurred overwhelmingly in "Other" women (112 of 133 women; 84.2%), and in women 50+ years (113 of 133 women; 85%). The prevalence of class 2 and 3 obesity increased in Māori women (from 31.3% to 78.3%) over the study period, and remained stable in "Other" women. Class 2 obesity decreased in Pacific women from 20.6% to 18.0%, but class 3 obesity increased by 26% (from 47.1% to 59.4%).

Overall, diabetes or pre-diabetes was present in nearly two thirds of women in this study (37.4% at diagnosis and 24.3% diagnosed subsequently). Hypertension (53.4%), hyperlipidaemia (33.2%) and nulliparity (22.1%) were also common (Table 1).

The majority of women were treated surgically (88.1%), although hysterectomy was subtotal in 27 women and abandoned in three women due to obesity-related difficulties. Median follow up was 65 months (range 0-214 months). Local or distant relapse occurred in 45 women (median time to relapse of 17 months, range 3-106 months). Ten of the 24 women who relapsed locally died of their disease. Overall, 107 women (18.2%), died of EC, half of whom had type 2 EC (Table 1). A significantly worse EC-related survival on multiple regression analysis (Table 3; Figure 2) occurred in women aged 50+ years (compared to those aged <50 years) and in Pacific women (compared to "Other" ethnicity). Māori women also had a worse survival compared to "Other" women, although this was not significant. On all-survival analysis, a worse outcome occurred with BMI50+ than BMI<30 (HR: 1.12: 95% CI 0.66-1.90), although this was not significant, whereas those with a BMI of 30-39 and 40-49 had a survival advantage (HR: 0.64; 95% CI 0.42-0.96 and HR: 0.62: 95% CI: 0.38-1.00 respectively).

Predictably, adverse histological features (type 2/unclassified type EC, lymphovascular space invasion [LVI], higher grade and stage EC), and treatment with palliative intent were associated with an adverse outcome compared to those with type 1, grade 1, stage 1 disease, absence of LVI, and treatment with curative intent.

Discussion

Our study highlights the burden of EC in this high-risk community, where incidence rates and time trends were substantially worse than those reported for all NZ women. The APC in incidence of 7.3 [95% CI 3.6-11.1]) over the 15-year study period exceeds the most recently reported national APC of 2.01 (95% CI 1.40-2.60)[17], and is attributed largely to the high rates in Pacific women. The relative risk of EC with reference to "Other" women (RR=1) was 2.47 in Māori women and 5.11 in Pacific women.

There was a statistically significant increase in incidence for all ethnic groups over the 15year study period, most marked in Pacific women with a very concerning and significant trend from 37.1/100 000 in 2000-2004, to 90.11/100 000 in 2010-14 (APC = 9.3; [95% CI 4.0-14.9]). This substantially exceeds the national trend for Pacific women (APC=3.96 ([95% CI 1.9-6.1]) (17). The incidence trends for Mãori (APC=7.2; [95% CI 0.2-14.6]) and "Other" women (APC=3.4; [95% CI 0.5-6.4]) also exceed national trends (APC=2.4; [95% CI 0.7-4.1], and APC=1.2; [95% CI 0.6-1.8] respectively). The APC for "Other" women was similar to other developed countries[18;19].

A particularly concerning finding was the statistically significant high growth rate over the study period in women aged <50years (APC=12.2 [95% CI 5.2 -19.7]). This occurred predominantly in Pacific women, where the incidence increased from 13.38/100 000 women in 2000-2004, to 46.06/100 000 in 2010-2014. The incidence for the most recent 2010-2014 period was 97% higher than the national incidence for Pacific women aged <50years for a similar period[20]. The high risk factors in our region, such as the effects of socioeconomic deprivation, and obesity levels with associated diseases are likely to account for this difference.

The obesity epidemic is the presumed main driver of the increasing rates of EC, with obesity and associated diseases such as diabetes projected to increase over the coming decades[21]. The association of EC with BMI is non-linear, with class 2 and 3 obesity conferring a greater relative risk, possibly more important in pre-menopausal women[22]. A higher proportion of Māori and Pacific women had a BMI of 35+ (64.6% and 75.6% respectively) compared to "Other" women (33%), and the difference is significant. The prevalence of class 2 and 3

obesity remained largely stable in “Other” women over the study period, but doubled in Māori women, while class 3 obesity in Pacific women increased by 26%. In addition, significantly higher proportions of Māori and Pacific women had type 2 diabetes or impaired glucose tolerance (40.2% and 47.5% respectively vs 28.4%) and were nulliparous (23.2% and 28.9% respectively vs 15.5%), compared to “Other” women. Effective intervention strategies are likely to benefit Māori and Pacific women the most. While the majority of women survived their disease, their risk factors persisted, and substantial numbers developed pre-diabetes or diabetes during the subsequent follow up period.

Women aged <50 years with EC represent a rapidly growing group, particularly in our region. When compared to women aged 50+ years, they had a significantly higher association with type 1 EC (93.0% vs. 77.7%), class 2 and 3 obesity (70.7% vs. 49.2%), FIGO grade 1 (70.7% vs 57.1%) and stage 1 disease (79% vs 69.6%), nulliparity (46.5% vs 13.2%), and lower mortality (9.6% vs. 21.3%). Their risk factors were substantially higher than for NZ women of comparable age (25-54years) included the NZ Health survey, with a 70.7% prevalence of class 2 and 3 obesity in our study (increasing to 83% in Pacific women) vs. 9.5-10.3% for all NZ women[14]. They also had a higher prevalence of hypertension (31.8%), type 2 diabetes (27.4%) and hyperlipidaemia (15.9%) than women of comparable age included in the national data (0.4-14.2%, 0.8-4.1% and 0.6-7.0% respectively). Further, nearly half were nulliparous, compared with 13.2% of the women aged 50+ years, which is likely to represent both a risk factor for EC, and a consequence of obesity. Our data suggests that potentially preventable factors have a greater causative role in EC in younger women, providing an important opportunity for intervention.

Māori and Pacific women did not present with higher grade or stage EC compared to “Other” women, contrary to the reports of others[10]. However, both Māori and Pacific women experienced a worse disease-specific survival compared to “Other” women, which was statistically significant in Pacific women. As expected, women aged <50years had a disease-specific survival advantage over those aged 50+years. Others have reported an increased long term risk of mortality from all causes associated with increasing degrees of obesity, attributed to increased obesity-associated co-morbidities[22]. Women in the BMI 50+ group had a worse, although not significant all-survival rate compared to those with BMI<30, however, those in the BMI 30-39 and 40-49 groups did not. This may reflect the stronger association of type 2

EC, which has a lower disease specific survival (Table 3), with low BMI. By contrast, type I EC was more common in women with BMI 35+, and the difference is significant.

The main strength of our study lies in the detailed analysis of a high-risk group of women whose EC burden is underestimated by pooled national data. Ethnic self-classification was available for all participants, as well as data for major risk factors, in particular BMI. We were able to correlate clinicopathological data and potentially preventable risk factors with demographic features, providing a comprehensive view of EC by ethnicity. A potential weakness is that the population estimates for our region, while based on census data, may underestimate the true population in some ethnic groups. However, the population data are based mainly on the 2011 census, which shows good agreement with cancer registries[23]. Further, we were unable to evaluate the effect of socioeconomic deprivation. We were also unable to determine whether or not younger women, in whom abnormal bleeding could be erroneously attributed to benign causes, experienced delays in diagnosis.

We have highlighted the burden of EC in Pacific women in this high-risk community, and demonstrated that potentially preventable risk factors are present in the vast majority of women, and in particular, young women. Urgent strategies are required to facilitate early detection of endometrial abnormalities prior to the development of EC, where treatment with high dose progestins is likely to be more successful in reversing early oestrogen-driven endometrial abnormalities, and may result in restoration of fertility in young women[24;25]. Tissue diagnosis should be considered in symptomatic, high-risk young women regardless of age, and local protocols have been implemented to reduce the age recommendations for endometrial sampling in presumed dysfunctional uterine bleeding in younger women. Prevention and management of obesity, including both improved nutrition and increased physical activity, would also address independent risk factors for EC, and help to mitigate risk not only of EC, but of associated diseases which collectively confer a substantial health burden beyond EC.

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TABLE 1: Endometrial Carcinoma: Demographic Features, Risk Factors and Outcome

	Total		Maori		Pacific		"Other"	
No of EC	**N=588**	***100%***	**N=82**	***100%***	**N=242**	***100%***	**N=264**	***100%***
Tumour type								
Type 1	**481**	***81.8%***	64	*78.0%*	203	*83.9%*	214	*81.1%*
Type 2	**98**	***16.7%***	15	*18.3%*	36	*14.9%*	47	*17.8%*
Not typed	**9**	***1.5%***	3	*3.7%*	3	*1.2%*	3	*1.1%*
Age group								
	59years (23-94)		57years (31-85)		55years (26-90)		64years (23-94)	
<50 years	**157**	***26.7%***	24	*29.3%*	96	*39.7%*	37	*14.0%*
50+ years	**431**	***73.3%***	58	*70.7%*	146	*60.3%*	227	*86.0%*
BMI women aged <50years								
Total	**157**	***100%***	**24**	***100%***	**96**	***100%***	**37**	***100%***
BMI <30	**20**	***12.7%***	0	*0%*	4	*4.2%*	16	*43.2%*
BMI 30-34 (class 1)	**18**	***11.5%***	4	*16.7%*	7	*7.3%*	7	*18.9%*
BMI 35-39 (class 2)	**29**	***18.5%***	5	*20.8%*	21	*21.9%*	3	*8.1%*
BMI 40+ (class 3)	**82**	***52.2%***	15	*62.5%*	59	*61.4%*	8	*21.6%*
BMI Unknown	**8**	***5.1%***	0	*0%*	5	*5.2%*	3	*8.1%*
BMI women aged 50+ years								
Total	**431**	***100%***	**58**	***100%***	**146**	***100%***	**227**	***100%***
BMI <30	**113**	***26.2%***	11	*19.0%*	6	*4.1%*	96	*42.3%*
BMI 30-34 (class 1)	**88**	***20.4%***	12	*20.7%*	32	*21.9%*	44	*19.4%*
BMI 35-39 (class 2)	**69**	***16.0%***	12	*20.7%*	21	*14.4%*	36	*15.9%*
BMI 40+ (class 3)	**143**	***33.2%***	21	*36.2%*	82	*56.2%*	40	*17.6%*
BMI Unknown	**18**	***4.2%***	2	*3.4%*	5	*3.4%*	11	*4.8%*
All women: Other Risk and associated factors †								
Diabetes/ IGT‡	**220**	***37.4%***	33	*40.2%*	115	*47.5%*	72	*27.3%*
Subsequent Diabetes/ IGT‡	**143**	***24.3%***	23	*28.0%*	62	*25.6%*	58	*22%*
Hypertension	**314**	***53.4%***	48	*58.5%*	125	*51.7%*	141	*53.4%*
Hyperlipidaemia	**195**	***33.2%***	25	30.5%	85	*35.1%*	85	32.2%
Nulliparity	**130**	***22.1%***	19	*23.2%*	70	*28.9%*	41	*15.5%*
Treatment								
Surgery	**518**	***88.1%***	74	*90.2%*	203	*83.9%*	241	*91.3%*
No surgery	**70**	***11.9%***	8	*9.8%*	39	*16.1%*	23	*8.7%*
Grade (FIGO 2009)								
Grade 1	**360**	***61.2%***	43	*52.4%*	153	*63.2%*	165	*62.5%*
Grade 2	**85**	***14.5%***	16	*19.5%*	31	*12.8%*	38	*14.4%*
Grade 3	**132**	***22.4%***	21	*25.6%*	54	*22.3%*	58	*22.0%*
Not graded	**11**	***1.9%***	2	*2.5%*	4	*1.7%*	3	*1.1%*
Stage (FIGO 2009)								
1	**428**	***72.8%***	61	*74.4%*	174	*71.9%*	193	*73.1%*
2	**24**	***4.1%***	2	*2.4%*	6	*2.5%*	16	*6.1%*
3	**36**	***6.1%***	4	*4.9%*	14	*5.8%*	18	*6.8%*
4	**57**	***9.7%***	11	*13.4%*	27	*11.2%*	19	*7.2%*
Stage incomplete or un-staged	**43**	***7.3%***	4	4.9%	21	*8.7%*	18	*6.8%*
Outcome								
Disease specific mortality: All tumour types	**107**	***18.2%***	15	*18.3%*	48	*19.8%*	44	*16.7%*
Type 1	**52**	***8.9%***	7	*8.6%*	27	*11.2%*	18	*6.8%*
Type 2	**49**	***8.3%***	6	*7.3%*	19	*7.8%*	24	*9.1%*
Type unknown	**6**	***1.0%***	2	*2.4%*	2	*0.8%*	2	*0.8%*

† Some women had multiple risk factors

‡ IGT = Impaired Glucose Tolerance

TABLE 2: Average age standardised incidence rates, mortality, and annual percentage change for all women between 2000 and 2014, stratified by tumour type, ethnicity and age group

	Average age standardised incidence (WHO)/100 000	Annual percentage change	95% lower confidence limit	95% upper confidence limit
Incidence: All women				
All women	22.97	**7.3**	**3.6**	**11.1**
Incidence by Tumour type				
Type 1	18.89	**7.7**	**4**	**11.6**
Type 2	3.84	**8.1**	**2.5**	**14.1**
Incidence by Ethnicity				
Mãori	32.33 (RR=2.47)	**7.2**	**0.2**	**14.6**
Pacific	66.88 (RR=5.11)	**9.3**	**4.0**	**14.9**
"Other"	13.09 (RR=1.00)	**3.4**	**0.5**	**6.4**
Incidence by ethnicity and age group				
<50 years				
All women	9.48	**12.2**	**5.2**	**19.7**
Mãori	9.98 (RR=7.1)	*		
Pacific	31.87 (RR=22.8)	*		
"Other"	1.40 (RR=1.0)	*		
50+years				
All women	43.95	**5.2**	**2.3**	**8.2**
Mãori	76.82 (RR=2.4)			
Pacific	136.58 (RR=4.19)			
"Other"	32.61 (RR=1.0)			
Disease-specific mortality rate: All women				
All women	4.14	**7.3**	**3.7**	**11.1**

Note: Bold type indicates statistically significant result
*Numbers of EC insufficient for trend analysis

TABLE 3: Multivariate Analysis of Association between Disease-Specific Survival and Risk Factors

Characteristic	Hazard Ratio	95% CI	*p*
Age: Reference 50+ vs <50years	3.47	1.83-6.59	*<0.001*
BMI group: Ref <30			
30-39	0.83	0.47-1.46	*0.52*
40-49	0.62	0.32-1.21	*0.16*
50-59	1.25	0.62-2.52	*0.54*
Ethnicity: Ref "Other"			
Māori	1.40	0.73-2.69	*0.31*
Pacific	1.78	1.07-2.97	*0.026*
Tumour type: Ref Type 1 vs Type 2 and Type unknown	6.88	4.47-10.59	*<0.001*
Aim of treatment: Ref curative vs palliative	18.27	11.55-28.89	*<0.001*
Lymphovascular space invasion: Ref absent vs present	10.11	5.60-18.25	*<0.001*
Grade: Ref=grade 1 vs 2/3	18.41	7.83-43.31	*<0.001*
Stage: Ref=stage 1/2 vs 3/4	18.74	11.54-30.41	*<0.001*

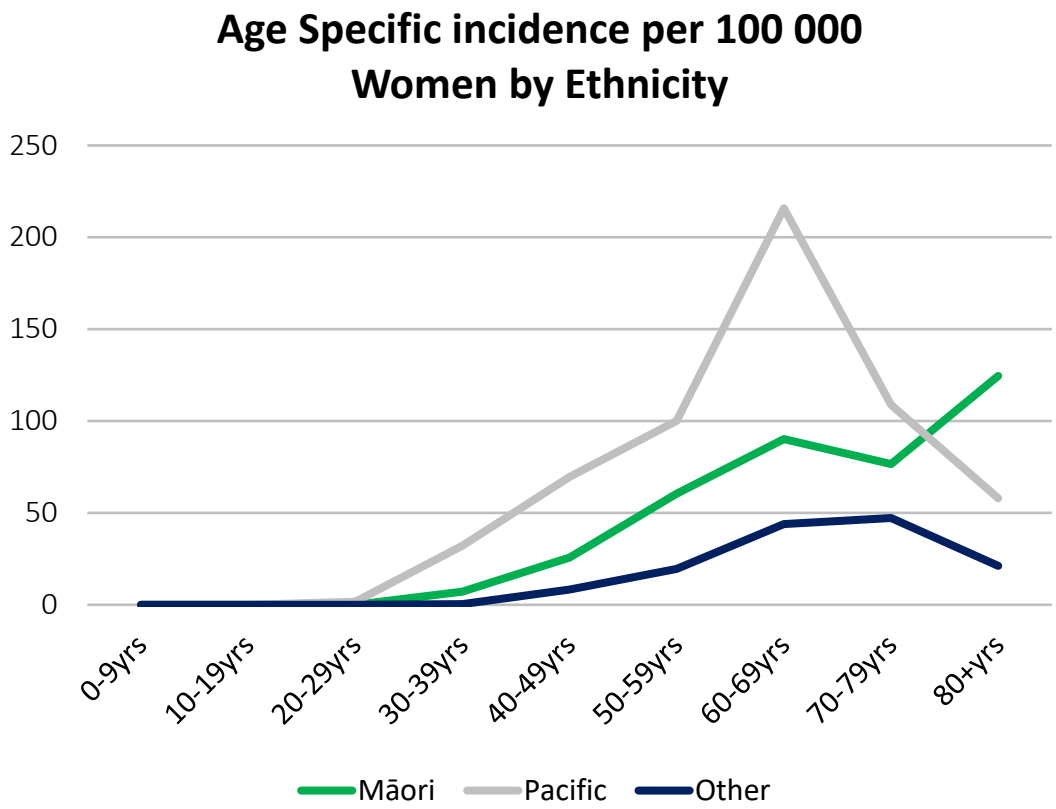
Hazards Ratio: HR>1 indicates that time to death is negatively associated in comparison to the reference group.
Ref = Reference

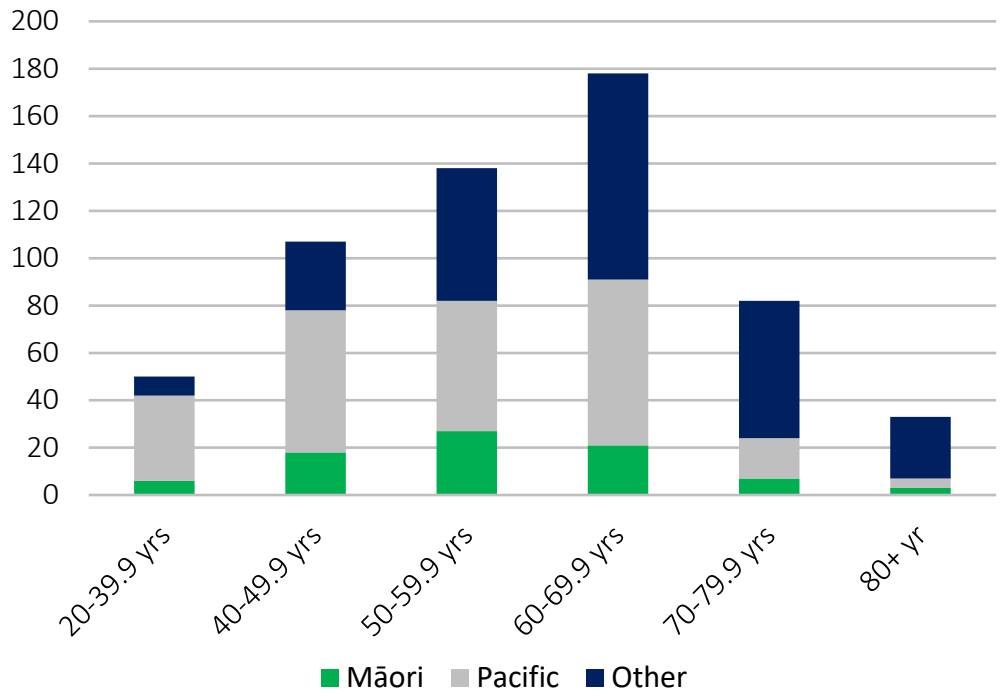
Figure Legends:

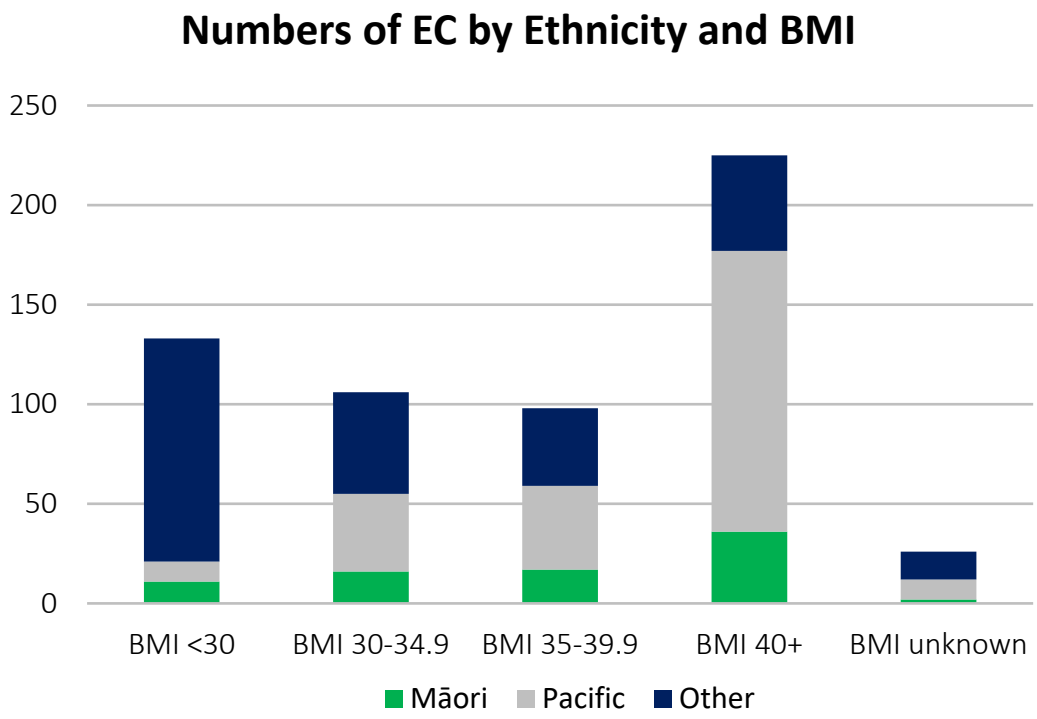
FIGURE 1: (a) Age specific incidence of EC by ethnicity, (b) Numbers of EC by age group and ethnicity, (c) Numbers of EC by ethnicity and BMI, and (d) Time trends in numbers of EC by Ethnicity

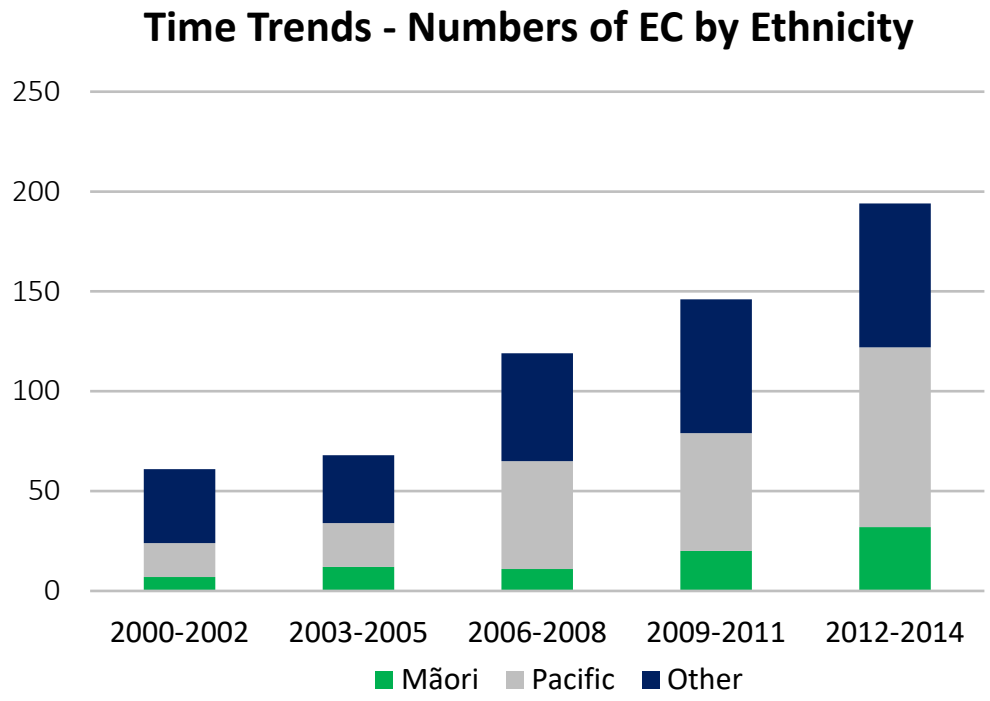
FIGURE 2: Kaplan-Meier disease specific survival by (a) BMI group, b) age group, (c) and ethnic group

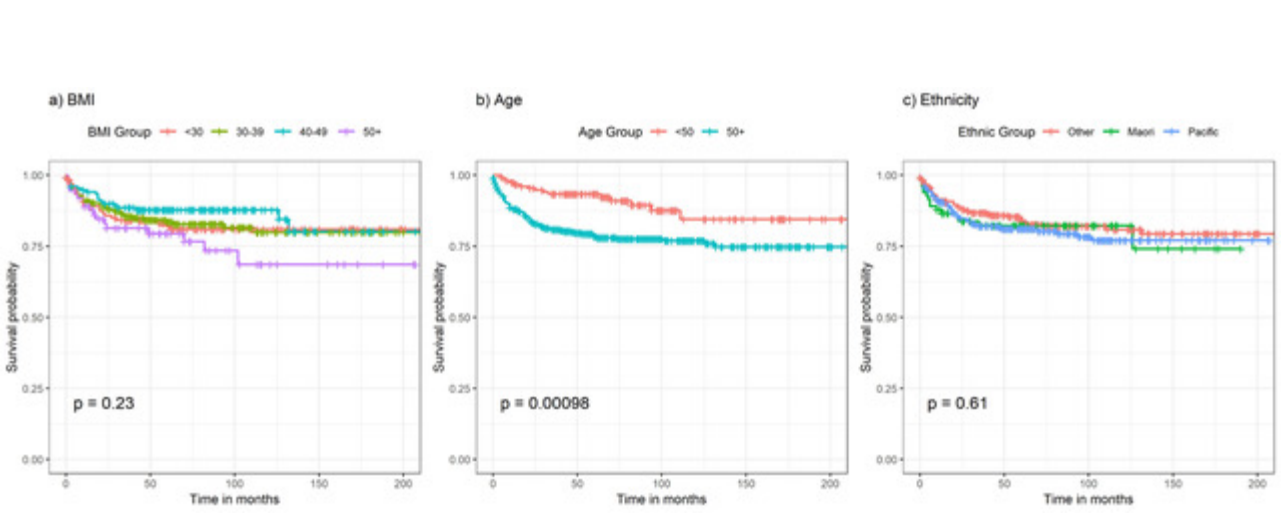
TABLE 1: Endometrial Carcinoma: Demographic Features, Risk Factors and Outcome


Age Specific incidence per 100 000 Women by Ethnicity
250
200
150
100
50
0
0-9yrs
10-19yrs
20-29yrs
30-39yrs
40-49yrs
50-59yrs
60-69yrs
70-79yrs
80+yrs
Māori
Pacific
Other


Numbers of EC by Age Group and Ethnicity
200
180
160
140
120
100
80
60
40
20
0
20-39.9 yrs
40-49.9 yrs
50-59.9 yrs
60-69.9 yrs
70-79.9 yrs
80+ yr
Māori
Pacific
Other


Numbers of EC by Ethnicity and BMI
250
200
150
100
50
0
BMI <30
BMI 30-34.9
BMI 35-39.9
BMI 40+
BMI unknown
Māori
Pacific
Other


Time Trends - Numbers of EC by Ethnicity
250
200
150
100
50
0
2000-2002
2003-2005
2006-2008
2009-2011
2012-2014
Māori
Pacific
Other


a) BMI
BMI Group
<30
30-39
40-49
50+
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.23
0
50
100
150
200
Time in months
b) Age
Age Group
<50
50+
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.00098
0
50
100
150
200
Time in months
c) Ethnicity
Ethnic Group
Other
Maori
Pacific
Survival probability
1.00
0.75
0.50
0.25
0.00
p = 0.61
0
50
100
150
200
Time in months