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# Thyroid cancer in Pacific women in New Zealand

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#### **Abstract:**

**Aim** To describe trends in incidence rates of thyroid cancer in New Zealand between 1981–2004 with a particular focus on Pacific women.

**Method** Linked census-cancer registration data was used to calculate age standardised cancer incidence rates for thyroid cancer. Both trends over time amongst Pacific women, and differences in rates between Pacific and European/Other women in New Zealand, were assessed.

**Results** Rates of thyroid cancer in New Zealand were higher for women than men. The highest rates of thyroid cancer in were observed amongst Pacific women with a pooled age-standardised incidence rate of 18.5/100,000 (95%CI 14.6–22.4/100,000) compared to 5.2/100,000 (95% 4.8–5.5/100,000) for European/Other; SRR 3.58 (95%CI 2.87–4.47). Sparse data mean it is difficult to clearly identify a trend over time for Pacific women but European women experienced a 73% increase from 4.0/100,000 (95%CI 3.3–4.6/100,000) in 1981–1986 to 6.9/100,000 (95%CI 5.9–7.8/100,000) in 2001–2004 (*P*trend=0.05).

Conclusions Pacific women in New Zealand have the highest rates of thyroid cancer among resident ethnic groups. Risk was highest for Pacific women over 45 years of age. More research needs to be done looking at which specific ethnicities are driving rates of thyroid cancer in New Zealand and whether the risk is influenced by birthplace and age at migration to New Zealand.

Thyroid cancer constitutes 1% of all cancers worldwide<sup>1</sup> but is the most common malignancy of the endocrine system.<sup>2,3</sup> Worldwide, the incidence of thyroid cancer between 1973–2002 has increased with an average rise of about 50% among males and about two-thirds among females,<sup>4</sup> but there is large geographic variation with the greatest increases reported in South Australia (178% increase in men and 252% increase in females).<sup>4,5</sup>

Thyroid cancer most frequently presents in the fourth or fifth decade of life and is two to four times more frequent in females than males suggesting that sex hormone elements may be involved in pathogenesis.<sup>3,6</sup> With the exception of exposure to ionising radiation in childhood and female gender, risk factors for thyroid cancer are unclear, making it difficult to understand why there has been an observed increase in incidence rates or why this increase has varied by social group.<sup>7</sup>

Potential risk factors for this disease that have been suggested include iodine deficiency, <sup>8,9</sup> family history of thyroid cancer or personal history of benign thyroid disease, <sup>10</sup> low consumption of fresh fruit and vegetables, <sup>11</sup> and more recently, exposure to radiation associated with increasing computed tomography (CT) scanning. <sup>12</sup>

An alternative explanation for the increasing trend is increased detection of subclinical tumours through the escalating use of ultrasonography and fine needle aspiration, <sup>13,14</sup> but whilst this will account for an increase in small tumours, it does not explain the observed rise in incidence of larger tumours. <sup>7,15,16</sup>

Most thyroid cancers arise from the thyroid follicular cell,<sup>17</sup> are well differentiated and follow an indolent course with 10-year survivals in excess of 90%.<sup>3</sup> The well-differentiated types include papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) and Hürthle cell carcinoma.

PTC is the most common type of thyroid cancer<sup>19</sup> and is associated with exposure to ionising radiation. <sup>18,19</sup> as evidenced by the increase in cases in Chernobyl. <sup>20</sup> It comprises approximately 85% of all thyroid cancers and is the main driver of increasing incidence rates; rates of FTC and medullary thyroid cancer (MTC; a non-follicular type) have remained relatively stable over time. <sup>4</sup>

The non-follicular types are responsible for a small proportion of thyroid cancers. MTC arises from thyroid C-cells and tends to pursue a more aggressive course. Thyroid lymphoma is rare. Anaplastic carcinoma accounts for <5% of thyroid cancers but is responsible for 50% of the mortality of thyroid cancer. Poor prognostic factors are tumour histology (high grade), extrathyroidal extension, metastases, age >40 years and male gender.

Women in New Caledonia, Hawaii and French Polynesia have the highest rates of thyroid cancer in the world with documented rates over five times greater than New Zealand Europeans.<sup>21</sup> Such is the importance of this disease in French Polynesia that thyroid cancer was the second most commonly diagnosed malignancy for women in parts of this region<sup>22</sup> whilst a relative rarity in most other populations.

High incidence rates have also been reported in Fiji, Vanuatu, Marshall Islands, Palau and the Northern Marianas.<sup>21</sup> However, such high rates are not uniform for all Pacific nations.

Thyroid cancer is uncommon in Samoa with an incidence rate amongst Samoan women considerably lower than Polynesian women in Hawaii and Melanesian women in New Caledonia. <sup>23,24</sup> Previous work in New Zealand has reported a higher incidence rate of thyroid cancer among Pacific than Māori or European people in New Zealand. <sup>25</sup>

The aim of this paper is to describe trends in incidence rates of thyroid cancer, by age, in New Zealand between 1981–2004 with a particular focus on Pacific women living in New Zealand. Numbers were too small amongst men to examine trends over time.

#### **Methods**

The dataset was created by linking New Zealand Cancer Registry (NZCR) records to the 5-yearly New Zealand census of population and dwellings (the census) data, and is published in detail elsewhere. <sup>26,27</sup> Briefly, five closed cohorts were created of the New Zealand usual resident population (all ages) on census night 1981, 1986, 1991, 1996, 2001, followed up for incident cancer(s) until the subsequent census or in the case of the 2001 cohort, until 31 December 2004 (the most recent data available at the time of the study's record linkage). The NZCR is a population based cancer register that collects data on the full population of New Zealand, including all thyroid cancers (ICD code C73).

Between 71% to 82% of eligible thyroid cancers were linked to a census record. To avoid underestimation of rates due to linkage bias, weights were calculated for strata based on age, sex, ethnicity and small-area deprivation. For example, if 20 out of 30 cancer registrations for Pacific females aged 45–64 living in moderately deprived areas were linked, each of the 20 linked records was assigned a weight of 30/20=1.5, making the 20 records representative of the 30 eligible records. All analyses used these weights

Approval was granted for this project under the Statistics New Zealand Data Integration Policy, and the Wellington Ethics Committee granted ethics approval for CancerTrends (Ref 04/10/093).

A modified total ethnicity approach was used for this work. Total ethnicity places an individual in all ethnic groups that they identify with. If individuals indicated any/all of Māori, Pacific and/or Asian ethnic affiliation they were placed in any/all of Total Māori, Total Pacific, Total Asian ethnic groups. The residual people who did not indicate any of the above ethnic affiliations were placed in the non-Māori /Pacific/Asian (referred to as European/Other hereafter).

Incidence rates and rate ratios (and 95% confidence intervals) were calculated after direct standardisation of the cohorts to the age structure of the 2001 WHO world standard population.

Analyses were carried out for all adults (aged 15+ years), and by <45 years and ≥45 years for women. These age groups were chosen to parallel other studies that have suggested differential risk according to pre- and post-reproductive age.

Statistical tests of trend were conducted for rates, and of the log transformed rate ratios. All measures were also calculated for all five cohorts pooled. All these analyses were conducted in SAS v9

#### **Results**

There were a total of 2541 thyroid cancers for the entire study period. Of these, 189 cancers were diagnosed amongst Pacific women (with 1.26 million person years), 261 cancers for Māori and 1407 for European/Other women (3.48 and 25.64 million person years respectively).

There were 33 cancers diagnosed amongst Pacific men (with 1,182,637 person years), 78 cancers for Māori and 573 cancers for European/Other men (3,249,289 and 23,977,590 person years respectively). Pooled standardised incidence rates (SR) for Pacific, Māori and European/Other men were 2.7/100,000 (95%CI 1.3–4.1/100,000), 3.2/100,000 (95%CI 2.5–4.3/100,000) and 2.2/100,000 (95%CI 2.0–2.4/100,000) respectively.

Corresponding rates for women were 18.5/100,000 (95%CI 14.6–22.4/100,000), 8.3/100,000 (95%CI 7.0–9.6/100,000) and 5.2/100,000 (95%CI 4.8–5.5/100,000). Table 1 shows the standardised incidence rates (to the 2001 WHO World Population) for males and females (ethnic groups pooled). Rates were clearly higher for females, with a pooled standardised rate ratio (SRR) of 2.71 (95%CI 2.45–3.01) for females compared with males.

Across time, Pacific women have had the highest rates of thyroid cancer (Figure 1a). Table 2 shows SRs and SRRs for females <45 years, 45+ years and total females (15+ years) by ethnicity. The pooled SRR across time for Pacific compared to European/Other females was 3.58 (95%CI 2.87–4.47). Māori rates were intermediary with a pooled SR for all women of 8.3/100,000 (95%CI 7.0–9.6/100,000), and an SRR compared to European/Other of 1.61 (95%CI 1.35–1.92).

Ethnic differences among males were less marked, with Pacific and Māori SRRs of 1.27 (95%CI 0.74–2.18)) and 1.55 (95%CI 1.11–2.18) compared to European/Other (pooled over time and ages).

Over the time period, European/Other women experienced a statistically significant 73% increase from 4.0/100,000 (95%CI 3.3–4.6/100,000) in 1981–1986 to 6.9/100,000 (95%CI 5.9–7.8/100,000) in 2001–2004 (*P*trend=0.05). However, there was no apparent trend among Pacific women—although statistical imprecision at each time point renders the analysis 'weak' in terms of statistical power for detecting any trend for Pacific people.

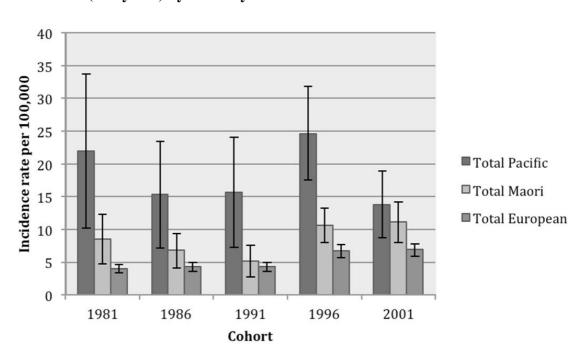


Figure 1. Age-standardised incidence rates (with 95% confidence intervals) for all women (15+ years) by ethnicity

Thyroid cancer incidence rates were higher in those aged  $\geq$ 45 years than <45 years for men and women alike. The pooled SR for total women <45yr was 4.7/100,000 (95%CI 4.3–5.1/100,000) and 8.1/100,000 (95%CI 7.5–8.7/100,000) for  $\geq$ 45 years. For men, these values were 1.2/100,000 (95%CI 1.0–1.4/100,000) and 3.6/100,000 (95%CI 3.2–4.0/100,000) respectively.

By ethnicity, the pooled over time SR for Pacific females <45 years of age was 9.7/100,000 (95%CI 7.6–11.9/100,000) and for  $\geq$ 45 years was 31.9/100,000 (95%CI 22.8–41.1/100,000) giving rate ratios for Pacific compared to European/Other women of 2.40 (95%CI 1.84–3.03) and 4.60 (95%CI 3.40–6.20) for younger and older women respectively.

Noting the non-overlap in the confidence intervals for the Pacific-European/Other SRRs, we can confidently conclude that the elevated Pacific female rates are more pronounced at older ages. For Māori women, pooled SRs were 5.3/100,000 (95%CI 4.2−6.4/100,000) and 13.0/100,000 (95%CI 10.0−15.9/100,000) for <45 years and ≥45 years respectively to give corresponding SRRs of 1.28 (95%CI 1.02−1.62) and 1.87 (95%CI 1.47−2.38).

Table 1. Age-standardised incidence rates (SR) among for 15+ years, 15–44 years and 45+ years (standardised to the 2001 WHO world population), pooled across ethnicity and by sex

Sex	Cohort	SR (95% CI)				
		15+yr	15-44yr	45+yr		
Males	1981-1986	1.9 (1.3–2.5)	1.0 (0.6–1.5)	3.4 (2.0–4.7)		
	1986–1991	1.7 (1.3–2.1)	1.2 (0.1–1.6)	2.4 (1.6–3.2)		
	1991–1996	2.3 (1.8–2.8)	1.0 (0.6–1.5)	4.0 (2.8–5.1)		
	1996-2001	3.0 (2.5–3.5)	1.7 (1.2–2.2)	5.1 (3.9-6.2)		
	2001–2004	2.7 (2.2–3.2)	1.3 (0.8–1.9)	5.1 (3.9-6.3)		
	Ptrend over time	0.07	0.29	0.07		
	Pooled	2.2 (2.0-2.4)	1.2 (1.0-1.4)	3.6 (3.2–4.0)		
Females	1981-1986	5.7 (4.7-6.6)	3.8 (3.0-4.7)	8.4 (6.3-10.5)		
	1986-1991	5.3 (4.5-6.0)	3.3 (2.6-4.1)	8.4 (6.7-10.0)		
	1991-1996	5.0 (4.3-5.8)	3.6 (2.8-4.4)	7.2 (5.7-8.8)		
	1996-2001	8.8 (7.8-9.8)	7.5 (6.3-8.7)	11.6 (9.9-13.3)		
	2001-2004	8.1 (7.2-9.0)	5.9 (4.8-6.9)	11.8 (10.0-13.5)		
	Ptrend over time	0.15	0.18	0.15		
	Pooled	5.9 (5.6-6.2)	4.7 (4.3-5.1)	8.1 (7.5-8.7)		

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Table 2. Age-standardised incidence rates (SR) and rate ratios (SRR) among women by ethnicity for 15+ years, 15–44 years and 45+ years (standardised to the 2001 WHO world population)

Ethnicity	Cohort	SR (95% CI)			SRR (95% CI)		
		15+ yr	15-44yr	45+ yr	15+ yr	15-44yr	45+ yr
European/Other	1981-1986	4.0 (3.3–4.6)	3.3 (2.5–4.1)	5.1 (4.0-6.2)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	1986–1991	4.3 (3.6–5.0)	2.8 (2.0–3.6)	6.9 (5.6–8.3)			
	1991-1996	4.3 (3.6–5.0)	3.3 (2.4–4.3)	5.9 (4.7–7.0)			
	1996-2001	6.7 (5.7–7.7)	6.1 (4.7–7.5)	8.2 (6.8–9.6)			
	2001-2004	6.9 (5.9–7.8)	5.4 (4.1–6.7)	9.2 (7.7–10.7)			
	Ptrend over time	0.05	0.13	0.05			
	Pooled	5.2 (4.8–5.5)	4.1 (3.7–4.6)	7.0 (6.4–7.5)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Pacific	1981–1986	21.9 (10.2–33.7)	6.5 (2.2–10.8)	47.1 (17.5–76.7)	5.52 (3.15–9.68)	1.98 (0.98–4.01)	9.23 (4.74–17.98)
	1986–1991	15.3 (7.1–23.4)	8.3 (3.8–12.9)	23.4 (5.3–41.4)	3.54 (2.03–6.15)	2.97 (1.61–5.49)	3.36 (1.52–7.45)
	1991–1996	15.7 (7.3–24.1)	8.1 (4.1–12.1)	24.7 (5.6–43.7)	3.67 (2.09–6.43)	2.42 (1.37–4.26)	4.22 (1.91–9.34)
	1996-2001	24.6 (17.5–31.8)	17.1 (10.7–23.4)	41.0 (24.1–58.0)	3.66 (2.64–5.07)	2.81 (1.82–4.34)	5.00 (3.19–7.83)
	2001-2004	13.8 (8.7–18.9)	8.3 (4.1–12.5)	20.9 (10.2–31.6)	2.01 (1.35–2.99)	1.55 (0.88–2.70)	2.28 (1.33–3.89)
	Ptrend over time	0.65	0.49	0.49	0.06	0.64	0.12
	Pooled	18.5 (14.6–22.4)	9.7 (7.6–11.9)	31.9 (22.8–41.1)	3.58 (2.87–4.47)	2.36 (1.84–3.03)	4.59 (3.40-6.20)
Maori	1981–1986	8.5 (4.7–12.3)	5.1 (2.6–7.7)	12.2 (4.0–20.4)	2.14 (1.33–3.46)	1.55 (0.89–2.71)	2.40 (1.18–4.87)
	1986–1991	6.8 (4.1–9.4)	4.6 (2.0–7.2)	10.8 (5.0–16.6)	1.56 (1.02–2.39)	1.64 (0.87–3.10)	1.56 (0.88–2.76)
	1991-1996	5.2 (2.8–7.6)	2.3 (1.3–4.3)	8.0 (2.7–13.3)	1.22 (0.74–1.99)	0.84 (0.46–1.52)	1.36 (0.69–2.71)
	1996-2001	10.6 (8.0–13.3)	8.1 (5.5–10.7)	14.7 (9.1–20.3)	1.58 (1.18–2.12)	1.34 (0.90–1.98)	1.79 (1.18–2.73)
	2001-2004	11.1 (8.0–14.2)	6.0 (3.5–8.4)	21.2 (13.2–29.2)	1.62 (1.18–2.22)	1.11 (0.69–1.77)	2.31 (1.53–3.48)
	Ptrend over time	0.29	0.57	0.24	0.49	0.33	0.61
	Pooled	8.3 (7.0-9.6)	5.3 (4.2-6.4)	13.0 (10.0–15.9)	1.61 (1.35-1.92)	1.28 (1.02–1.62)	1.87 (1.47-2.38)

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## **Discussion**

Thyroid cancer is more common in females than males in New Zealand and this is consistent with a female preponderance observed worldwide. The highest rates of thyroid cancer in New Zealand are amongst Pacific women. Whilst this is in keeping with what is known about thyroid cancer in the Pacific basin, it is not clear why this is the case.

Between 1966 and 1974, France conducted 41 atmospheric nuclear tests in French Polynesia but the high rates of thyroid cancer here cannot be completely attributed to nuclear fallout because rates of thyroid cancer have remained stable since the 1950s<sup>32</sup> and it does not explain the high rates of thyroid cancer across multiple Pacific Islands at a considerable distance from the nuclear testing areas.<sup>21</sup>

The predominance of this disease amongst women worldwide has supported a role for hormonal and reproductive factors. In fact, in the same way that breast cancers express oestrogen receptors, it has been observed that thyroid tumours also have a high level of oestrogen receptor expression. <sup>33</sup>

In New Caledonia, where Melanesian women have the highest rates in the world, a population-based study found an association between parity and thyroid cancer risk<sup>31</sup> but the evidence in support of this is mixed.<sup>29,30,34</sup> A pooled analysis of case-control studies found a non-significant 20% increase in risk for multiparous compared to nulliparous women. Notwithstanding this, if parity were related to risk, it would not explain the apparent low rates in Samoan women, or the variation between Pacific Island nations.

Artificial menopause increases the risk of thyroid cancer by 80% compared to women who have a natural menopause and in contrast to known risks for breast cancer related to oestrogen exposure, later age at menarche and age at first birth are only weakly associated with thyroid cancer risk.<sup>35</sup>

The relationship between iodine and thyroid function is complex. Both iodine deficiency and excess can inhibit thyroid hormone synthesis and cause goiter. Goiter and benign thyroid nodules/adenomas are the strongest risk factors for thyroid cancer apart from radiation in childhood with pooled ORs of 5.9 (95%CI 4.2–8.1) and 29.9 (95%CI 14.5–62.0) respectively.

Due to such high rates of thyroid cancer in the Pacific, where seafood consumption is high and consequently iodine intake, it has been proposed that iodine excess is contributory. However, this hypothesis was not supported in an international pooled analysis of case-control studies that looked specifically at fish and shellfish intake. Nonetheless, it is possible that there is a differential effect depending on iodine status.

When examining only those studies from areas with an iodine rich diet (e.g. Hawaii, Japan, Norway), there was a non-significant mild increase in risk for the highest ( $\geq$ 3 times/week) compared to the lowest (<1 times/week) intake of fish or shellfish (OR 1.13, 95%CI 0.85–1.5).

Conversely, for low iodine and goiter endemic areas (e.g. Sweden, Switzerland), a high intake was protective with an OR of 0.65 (95%CI 0.48–0.88) for the highest versus the lowest intake groups. A high intake of butter and cheese has been found to be associated with thyroid cancer<sup>37</sup> and this is likely related to BMI. In a systematic review examining risk of cancer with a 5kg/m<sup>2</sup> increase in BMI, the risk of thyroid cancer was found to increase by14% in women (RR 1.14, 95%CI 1.06–1.23) and 33% in men (RR 1.33, 95%CI 1.04–1.70).<sup>41</sup>

Whilst this may account for some of the disparity in thyroid cancer incidence rates between Pacific and European/Other women in New Zealand, it does not explain the very large disparity nor the variation between women in different Pacific Island nations.

In the United States, Southeast Asian migrants (largely Filipino and Vietnamese) have high rates of thyroid cancer compared to United States Caucasian women and Northern Asian women living in the United States (largely Chinese and Japanese). However, this relationship is complex, with Phillipine-born men and women living in the United States having incidence rates of thyroid cancer exceeding both their US-born counterparts and white men and women. This effect by birthplace was not seen for Chinese men or women.

A study examining thyroid cancer risk amongst Asian women living in the United States found that for Asian women <50 years, a large proportion of the difference in thyroid cancer rates when compared to white women was due to goiter/nodules and dietary differences (i.e. low consumption of isoflavones). For older women ( $\geq$ 50 years), whilst these were also contributory, recent migration was important with a risk over 2.5 times higher for Asian women who had spent <30% of their lifetime in the United States compared to Asian women who had spent  $\geq$ 30% (OR 2.7, 95%CI 1.2–6.0). This suggests an early life exposure amongst these migrant populations which may affect thyroid cancer risk.

Increased diagnostic scrutiny is unlikely to be the reason for the higher rate seen in Pacific women. Evidence from New Zealand is that, if differences are present, Māori and Pacific people are likely to be under-served in relation to diagnostic and other services relative to the New Zealand European population.  $^{44-46}$ 

## **Conclusion**

Although thyroid cancer is a relatively rare disease in developed countries, it continues to be of importance in the Pacific and amongst Pacific women in New Zealand. Given that rates in Samoan women have been reported to be low, more work needs to be done to identify which Pacific groups are driving the incidence rates observed in New Zealand and whether thyroid cancer risk is affected by birthplace and migrant status.

Finally, we hypothesise that thyroid cancer rates among Pacific women will be largely among those born in the Pacific, due to the high iodine diets among children and young people living in the Pacific. The finding of larger relative differences in thyroid cancer between Pacific and European/Other women at older ages in this study is consistent with this hypothesis (older Pacific women living in New Zealand are more

likely to have been born in the Pacific than younger women), and sufficiently large datasets to test this hypothesis may be available following further linkage of census and cancer registration data.

Further work is required to investigate dietary iodine in the Pacific, including seaweed consumption, and monitoring iodine excess by way of urinary iodine and serum TSH and  $T_4$ .

**SNZ disclaimer:** Access to the data used in this study was provided by and sourced from Statistics New Zealand under conditions designed to give effect to the security and confidentiality provisions of the Statistics Act 1975. The results presented in this study are the work of the authors, not Statistics New Zealand.

Competing interests: Nil.

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