Inequitable Long-Term Outcomes for an Indigenous Population After Definitive Treatment of Patients With Graves Disease

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Background: Māori, the indigenous people of Aotearoa/New Zealand, have an increased incidence of Graves disease and often require more than one radioiodine (RAI) dose, raising the question as to whether surgery may be preferable in this population. However, there is a lack of outcome data after definitive therapy in an indigenous population.

Aim: To assess ethnic differences in thyroid status after definitive therapy for Graves disease.

Methods: Single-center retrospective review of patients treated by RAI or thyroidectomy from 1 December 2001 to 31 March 2013. TSH levels at 1, 2, 5, and 10 years after treatment were recorded.

Results: A total of 798 patients were included: 589 received RAI, and 209 underwent surgery. Overall, 48% of patients were euthyroid at 1 year after definitive treatment, and 63.5% were euthyroid by 10 years. Māori were less likely to be euthyroid when compared with Europeans at all time points (*e.g.*, 29.7% vs 57.3% at 1 year and 52.2% vs 70.9% at 10 years, $P < 0.0005$). Māori were more likely to receive more than one dose of RAI compared with Europeans (30.2% vs 14.2%, $P < 0.0005$). Persistent thyrotoxicosis at 1 year after RAI was seen in 25.8% of Māori compared with 8.3% of Europeans ($P < 0.0005$).

Conclusions: Māori have lower rates of optimal thyroid levels than their European counterparts at all time points studied. Early disparity was associated with a higher RAI failure rate. Late differences were due to higher rates of untreated hypothyroidism. Overall, euthyroid rates were low, indicating the need for improvement in care, particularly for indigenous peoples.

Graves disease (GD) is responsible for ~64% of hyperthyroidism in Aotearoa/New Zealand [1]. Māori, the indigenous people of New Zealand, have a higher incidence of GD when compared with non-Māori [2] and, unlike the rest of the New Zealand population, are more likely to

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Abbreviations: GD, Graves disease; RAI, radioiodine; RR, relative risk.

require more than one dose of therapeutic radioiodine (RAI) [3], raising the question as to whether surgery may be a preferable treatment of this population.

Total thyroidectomy results in a near 100% remission rate of thyrotoxicosis [4]. After surgery, thyroid hormone replacement is commenced on the first postoperative day due to the predictable requirement for thyroid replacement. Levothyroxine replacement in an uncomplicated adult patient is considered straightforward, with a starting dose of 1.7 μg/kg ideal body weight, which can be titrated until a normal TSH is achieved [5]. However, in patients who receive RAI, the development of hypothyroidism is less predictable, with a 78.6% local remission rate of thyrotoxicosis after a single dose [4] and a 2.8 odds lower remission rate in Māori [3]. As such, unlike the surgical group, the optimal time to begin thyroid hormone replacement is less clear after RAI, and patients require ongoing biochemical monitoring to identify the development of a hypothyroid state. Studies of patients with primary hypothyroidism have shown low euthyroid rates (45% to 52%) [6–9], but minimal data are available on iatrogenic hypothyroidism [10], in particular for indigenous peoples.

Due to complex social and political factors, indigenous populations frequently experience disparate health outcomes when compared with nonindigenous groups [11], and in New Zealand Māori are no different [12]. As such, we hypothesize that Māori are at risk for poorer outcomes after definitive treatment for GD. The aim of this study was to assess whether there is an ethnic disparity in the proportion of patients who are biochemically euthyroid after definitive therapy for GD.

1. Methods

A. Inclusion and Exclusion Criteria

A retrospective chart review was performed of all patients who received definitive treatment for GD with either RAI or thyroidectomy from 1 December 2001 to 31 March 2013 at Waikato Hospital, Hamilton, Aotearoa/New Zealand. Data were retrieved from electronic and physical hospital records and from community laboratories. There were no exclusion criteria.

B. Radioactive Iodine

The practice in our unit is to administer a fixed dose of RAI of 555 MBq (15 mCi) to patients with thyrotoxicosis. All doses were administered at Waikato Hospital and long-term follow-up performed by the patient's family doctor, unless there was persistent thyrotoxicosis. In that situation, the patient would usually remain under the care of an endocrinologist or general physician and receive an additional doses of RAI (usually at least 6 months apart) until they became euthyroid or hypothyroid. Patients who had received multiple doses of RAI were followed from the time of their first dose. Patients who received both RAI and surgery were categorized by the first modality received.

C. Thyroidectomy

A high-volume specialist endocrine surgeon performed the majority of the thyroid surgeries. Surgical options were subtotal thyroidectomy (leaving >1 g thyroid tissue), near-total thyroidectomy (leaving <1 g thyroid tissue), and total thyroidectomy (removing all macroscopic thyroid tissue). In our unit, the usual operation for GD is total thyroidectomy [13]. Patients were reviewed 6 weeks postoperatively by the surgeon and/or endocrine service, and long-term follow-up was performed by the patient's general practitioner.

D. Variables

The primary variable of interest was thyroid state post-treatment, ascertained by TSH level. A patient was considered euthyroid if the TSH concentration was within the reference interval (0.3 to 5.0 mIU/L). Because most community tests did not include free thyroid hormone levels, for the purposes of this study TSH values <0.3 mIU/L were grouped into overt

hyperthyroidism (<0.1 mIU/L) and subclinical hyperthyroidism (0.1 to 0.29 mIU/L). TSH values above the reference interval were grouped into subclinical hypothyroidism (5.1 to 9.9 mIU/L) and overt hypothyroidism (≥10.0 mIU/L). For the purposes of statistical analysis of TSH as a continuous variable, TSH levels outside the detection limits of the assay (<0.01 and >100 mIU/L) were assigned values of 0.01 and 101 mIU/L, respectively.

TSH values were recorded at four time points: 1 year post-treatment (±6 months), 2 years post-treatment (±6 months), 5 years post-treatment (±1 year), and 10 years post-treatment (±1 year). Patients who were deceased, who had not yet made it to that time point, or who did not have a TSH level measured were censored from the analysis. Missed tests were recorded and compared. For patients who had multiple TSH values available within a particular time period, the value closest to the treatment anniversary was included.

Demographic variables collected included age at definitive treatment, sex, and ethnicity. Ethnicities collected from hospital records were self-reported ethnicity reported by the New Zealand National health care system. A prioritization approach was used to manage multiple ethnicities within individuals into European, Māori, Pacific Peoples, Asian, MELAA (Middle Eastern/Latin American/African), and Other (included unknown) categories [14]. Māori were compared with the European group only for ethnicity comparisons due to the small numbers of patients in the remaining groups.

E. Statistical Analysis

Analyses were performed using STATA version 13.1 (StataCorp, College Station, TX). Given the nonlinear scale of TSH measurement, geometric averages with 95% CIs are presented. These were calculated by logarithmic transformation of the TSH values prior to calculation, with exponentiation for reporting of mean. The two-sample t test was used to assess the relationship between continuous variables, and the two-sample Wilcoxon rank-sum (Mann-Whitney) test was used to assess the relationship between categorical variables when assessing two within-group categories. When there were three or more within-group categories, one-way ANOVA was used for continuous variables, the χ^2 or Fisher test for categorical variables, and multinomial logistic regression testing for regression analysis. A P value <0.05 was considered to refute the null hypothesis.

F. Ethics

The study was conducted in accordance with the National Health Advisory Committee's Ethical Guidelines for Observational Studies and with permission from the institutional review committee (RD014031) and the Waikato Endocrine Department.

2. Results

A. General

Demographic data are shown in Table 1. A total of 798 patients were included in the study. European patients comprised 58.3% of the total group, and Māori comprised 28.7%. Of note, 14.9% of the local population identified as Māori during this time period [14]. RAI was administered to 73.8% (n = 589) of patients, with 209 patients (26.2%) undergoing surgery. Most patients received pretreatment with antithyroid medications (98.5% and 97.3% for the RAI and surgical groups, respectively). The majority of patients treated with RAI (n = 474, 80.5%) received one dose (range, one to four doses). Two patients received two doses of RAI and then underwent surgery (both Māori), and one European patient underwent surgery after three doses of RAI due to treatment failure. Māori were more likely to receive more than one dose for persistent thyrotoxicosis (69.8% received one dose, 25.3% received two doses, 2.7% received three doses, and 2.2% received four doses) compared with Europeans (85.8% received one dose, 10.7% received two doses, 3% received three doses, and 0.6% received four doses; $P \leq 0.0005$).

Two patients early in the study period underwent subtotal thyroidectomy. Of these, one developed recurrent GD and was subsequently treated with RAI (requiring two doses).

Table 1. Demographic Data

		European, n (%)		466 (58.3)	
Prioritized ethnicity		Māori, n (%)		229 (28.7)	
		Pacific Peoples, n (%)		22 (2.8)	
		Other,[a] n (%)		38 (4.8)	
		Unknown, n (%)		43 (5.4)	
		Total	Māori	European	P
	n (%)	798	229 (28.7)	466 (58.3)	
Age	Median age, y [5th, 95th percentile]	47 (25, 71)	43 (26, 61)	50 (26, 74)	<0.0005
Sex	Female, n (%)	634 (79.5)	183 (79.9)	382 (82.0)	0.512
	Male, n (%)	164 (20.6)	46 (20.1)	84 (18.0)	
Treatment	Radioactive iodine, n (%)	589 (73.8)	182 (79.5)	337 (72.3)	0.041
	Thyroidectomy, n (%)	209 (26.2)	47 (20.5)	129 (27.7)	

[a]In the "other" subgroup, 35 of 38 subjects were Asian.

Nine surgical patients (4%), of whom two were Māori, experienced a complication (two wound infections; one recurrent laryngeal nerve injury; and seven cases of permanent hypoparathyroidism, defined as requiring calcium and/or calcitriol >6 months after surgery irrespective of PTH level). Median time from definitive treatment to last laboratory review was 3504 days (1996 days for the surgical group [Europeans 2022 days, Māori 1910 days] and 3814 for the RAI group [Europeans 3709 days, Māori 4125 days], $P < 0.0005$).

B. Overall Euthyroid Rates

The overall percentage of individuals euthyroid or otherwise is shown in Fig. 1. TSH levels were available at 1 year in 733 of 798 (91.9%) patients. At 1 year, 47.7% of the patients were euthyroid, 26.3% were hyperthyroid, and the remainder was hypothyroid, with 15.7% of the cohort having overt hypothyroidism. By 10 years, TSH data were available for 318 patients, with 33 patients known to have died and 395 of 798 not yet having reached 10 years of follow-up. At 10 years, 63.5% of patients were euthyroid, 10.7% were hyperthyroid (5.3% overt and 5.3% subclinical), and 25.8% were hypothyroid (11.3% overt and 14.5% subclinical). Of those thyrotoxic at each time point, notes were reviewed to ascertain whether this was due to levothyroxine over-replacement (as in all surgical cases except for one patient with recurrent GD after subtotal thyroidectomy) or failed RAI. In the RAI group, persistent thyrotoxicosis was the cause in 74 of 168 patients at 1 year (42 Māori), in 23 of 106 patients at 2 years (11 Māori), and in 7 of 57 at 5 years. Only one patient was biochemically thyrotoxic due to failure of RAI by 10 years, with a further eight patients (seven Māori) still receiving ATDs to maintain a euthyroid state.

C. Ethnic Differences in Rates of Euthyroidism

C-1. Differences between Māori and European ethnic groups

Māori were younger than European patients (median age, 43 years compared with 50 years; $P < 0.0005$) and were more likely to receive RAI (79.5%) than surgery (20.5%) ($P = 0.041$). Ethnic differences in TSH levels and euthyroid rates are shown in Fig. 2A and 2B and in Tables 2 and 3. At all time points studied, Māori were less likely to be euthyroid than the European group and were more likely to be over-represented in the overt hyper- and hypothyroid groups; at 1 year 29.7% of Māori were euthyroid compared with 57.3% of Europeans ($P < 0.0005$), and by 10 years 52.2% of Māori were euthyroid compared with 70.9% of Europeans ($P < 0.0005$). Regression analysis controlling for age, sex, private health care use, and definitive therapy form (RAI or surgery) showed an increased risk of hypothyroidism for Māori at all time points and an early risk of hyperthyroidism (Table 3). The median TSH for hypothyroid Māori patients at 1 year was 18.7 mIU/L compared with 9.72 mIU/L in the European cohort, indicating Māori patients who were not euthyroid were more severely affected. Of the 53 patient episodes with severe
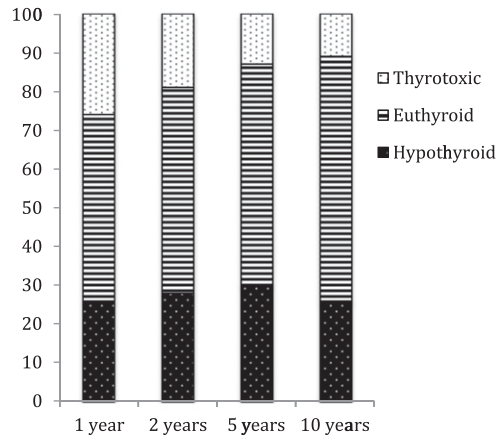
Figure 1. Thyroid status after definitive treatment (RAI and surgery combined and all ethnic groups combined).

hypothyroidism (arbitrarily defined as a TSH >50 mIU/L), 27 Māori accounted for 33 episodes, 11 Europeans for 12 episodes, and other ethnic groups the remainder. For Māori with severe hypothyroidism, 4 of 33 were euthyroid at the next blood test, and 2 of 33 were over-replaced. Of the remaining 27 Māori who were still hypothyroid, 15 had a TSH >50 mIU/L. For European patients with severe hypothyroidism by the next blood test, one was euthyroid, one was over-replaced, and 10 were hypothyroid (eight of whom had a TSH >50 mIU/L).

The rate of laboratory testing according to ethnicity was assessed. Early on, Māori were less likely to have their TSH measured (at 1 year 88.6% [202/228] of Māori vs 93.5% [434/464] of European and at 2 years 76.0% [171/225] of Māori vs 86.6% [399/461] of Europeans; $P =$ 0.025 and $P < 0.0005$, respectively). Later in the follow-up period, there was no difference between TSH testing in Māori or European patients (at 5 years 80.5% [173/215] of Māori vs 85.0% [380/447] of European and at 10 years 76.0% [92/121] of Māori vs 83.9% [182/217] of European; $P =$ 0.140 and 0.078, respectively).

C-2. Which treatment resulted in a higher euthyroid rate for Māori?

For Māori at 1 year, there was a difference in euthyroid state between treatment modalities, although the proportion of euthyroid subjects was low in both groups (28.8% for the RAI group and 33.3% for the surgical group, $P =$ 0.016). There was a significantly higher rate of thyrotoxicosis in the RAI group, as compared with the surgical group (38.7% vs 15.4%, respectively), with the rates of hypothyroidism showing the converse (32.5% in the RAI group compared with 51.3% in the surgical group, $P < 0.016$). At 2 years there were no significant differences in thyroid status between treatment modalities for Māori ($P = 0.273$), and the lack of difference remained at 5 and 10 years ($P = 0.242$ and 0.425, respectively). The excess of thyrotoxicosis in the Māori RAI group as compared with the European group, seen at 1 and 2 years ($P = 0.006$), had resolved by 5 years, when the thyrotoxicosis rates were similar (10.4% vs 12.2%, respectively). However, at 5 years the proportion of Māori who were hypothyroid was significantly higher than that for the European group (54.1% vs 20.0%, $P < 0.0005$). This persisted at 10 years, with 42.5% of the Māori RAI group being hypothyroid compared with 17.1% for the European RAI group ($P < 0.0005$). In addition, at all time points a higher proportion of Māori hypothyroid patients had overt hypothyroidism than Europeans (*e.g.*, at 1 year 78% of hypothyroid Māori had a TSH >10 mIU/L compared with 45% of hypothyroid Europeans) (Fig. 2).

3. Discussion

Given the relatively straightforward treatment of hypothyroidism, we expected that the majority (>80%) of patients would be euthyroid at any time point after definitive treatment,
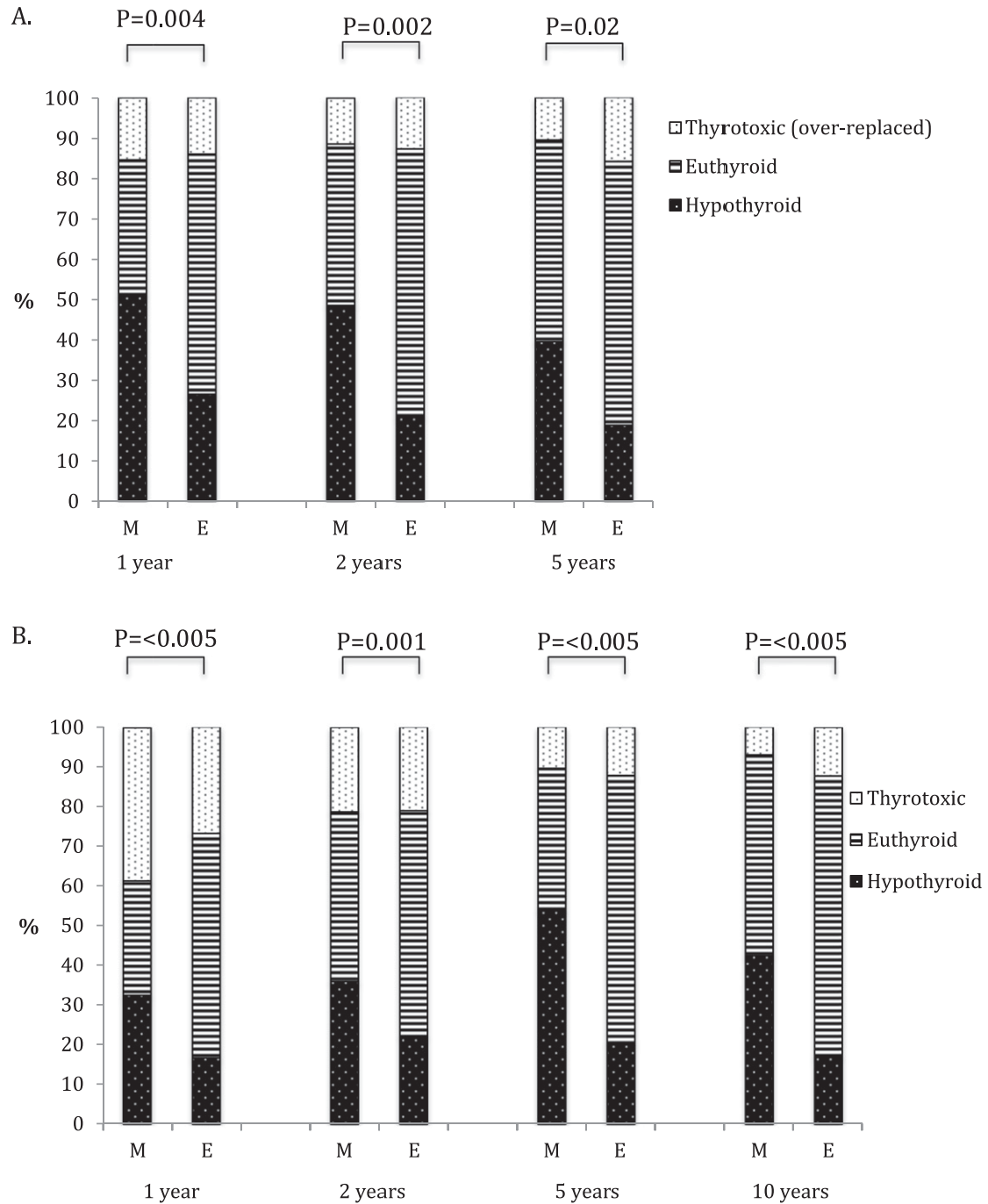
Figure 2. Thyroid status by ethnicity after definitive therapy. (A) Results 1, 2, and 5 y after surgery. (B) Results 1, 2, 5, and 10 y after RAI therapy. E, European; M, Māori.

particularly for surgery due to the predictable need for levothyroxine replacement post-operatively. However, in this study the percentage of patients who were euthyroid after definitive treatment was far lower than expected. Overall, at 1 year after definitive treatment less than half of all patients (47.8%) were euthyroid. This increased with time (52.4%, 57.4%, and 63.5% at 2, 5, and 10 years, respectively). These rates are comparable to those reported for patients with primary hypothyroidism (45% to 52%) [6–9] but significantly lower than a previous study in which patients were followed in a thyroid referral center rather than in a primary care facility [10].

Table 2. Thyroid Status According to Ethnicity

Follow-up (y)	Ethnicity	N	Hyper, n (%)	OHyper, n (%)	SHyper, n (%)	Euthy, n (%)	Hypo, n (%)	SHypo, n (%)	OHypo, n (%)	P^a
1	Māori	202	69 (34.2)	58 (28.7)	11 (5.5)	60 (29.7)	73 (36.1)	16 (7.9)	57 (28.2)	<0.0005
	European	434	101 (23.3)	60 (13.8)	41 (9.5)	249 (57.3)	84 (19.4)	46 (10.6)	38 (8.8)	
2	Māori	171	33 (19.3)	22 (12.9)	11 (6.4)	72 (42.1)	66 (38.6)	22 (12.9)	44 (25.7)	<0.0005
	European	399	75 (18.8)	40 (10.0)	35 (8.8)	237 (59.4)	87 (21.8)	50 (12.5)	37 (9.3)	
5	Māori	173	18 (10.4)	12 (6.9)	6 (3.5)	67 (38.7)	88 (50.9)	27 (15.6)	61 (35.3)	<0.0005
	European	380	50 (13.2)	27 (7.1)	23 (6.1)	254 (66.8)	76 (20.0)	45 (11.8)	31 (8.2)	
10	Māori	92	6 (6.5)	1 (1.1)	5 (5.4)	48 (52.2)	38 (41.3)	21 (22.8)	17 (18.5)	<0.0005
	European	182	21 (11.5)	11 (6.0)	10 (5.5)	129 (70.9)	32 (17.6)	20 (11.0)	12 (6.6)	

Abbreviations: Hyper, hyperthyroid (*i.e.*, TSH <0.3 mIU/L; combines overt [OHyper TSH <0.1 mIU/L] and subclinical [SHyper TSH 0.1–0.29 mIU/L] groups); Euthy, euthyroid (TSH 0.3–5.0 mIU/L); Hypo, hypothyroid (*i.e.*, TSH >5.0 mIU/L; combines both overt [OHypo TSH >10.0 mIU/L] and subclinical [SHypo TSH 5.1–9.9 mIU/L] groups).
^{a}The P value is derived from a χ^2 comparison statistic of thyroid status between Māori and European at each time point.

When analyzing the data by ethnicity, the results were even more concerning, with Māori less likely to be euthyroid than the European group (29.7% vs 57.3%) at 1 year, and this inequity persisted through all follow-up points. Even when available factors were controlled for, Māori had a higher relative risk (RR) than the European group of both hyperthyroidism at the first year (RR, 2.34) and hypothyroidism at all study time points (RR, 3.09, 2.08, 3.80, and 2.52). The persistent thyrotoxicosis after RAI was due to a lower rate of response to RAI rather than over-replacement with thyroxine, particularly at 1 year, and is consistent with our previous findings that Māori are more likely to need more than one RAI dose than European patients [3]. The reasons for this difference are not known because it persists when adjusted for age and disease severity, but it may be due to the larger thyroid size seen in Māori with thyrotoxicosis compared with European patients [2]. The reason for the higher rate of hypothyroidism in Māori as compared with European patients is not known but is not explained by simple demographics. When assessing those with severe hypothyroidism (arbitrarily defined as a TSH >50 mIU/L), Māori comprised 60% of the group and were over-represented among patients who had a severely elevated TSH at more than one of the time points studied, indicating chronicity to this finding.

As the 'Tangata Whenua' (*i.e.*, the indigenous people) of New Zealand, Māori, who are 14.9% of the Aotearoa/New Zealand population [15], have the right to equitable health outcomes [12]. However, for complex social and political reasons, Māori are not accorded equity in many health measures [16]. This study presents another health outcome in which a health disparity occurs for Māori. There are many potential reasons for this disparity, in the form of system factors (cost of medications, transport, general practitioner visits), clinician factors (health explanations, underinvestigation, and undertreatment), and patient factors (medication adherence, socioeconomic status, health literacy). Often, patient noncompliance and disengagement with health services are presented as the primary factors of interest in the ethnic disparities seen between Māori and Europeans. Although there was a difference in blood test completion rate between Māori and European in the early years of this study, the effect size was small (89% compared with 95%, $P = 0.025$), and the difference was not seen in subsequent years (years 5 and 10). Information is not available on the factors influencing this reduced monitoring of TSH in the early years of this study. Overall, thyroid function testing was high, but this did not correspond to the high rates of euthyroidism. Therefore, failure to have blood testing to assess the adequacy of thyroid hormone replacement cannot explain the large disparity in outcomes for Māori. These data suggest that reasons other than patient participation with health care are responsible for this inequality. Most likely, combinations of factors are involved, and research to review all levels of potential disparity (system, clinician, and patient) is needed to understand this better. In addition, although this is a single-center study focusing on the New Zealand indigenous population, it is likely that these findings are not limited to this region and that similar studies in other indigenous or minority groups need to be undertaken.

Table 3. Relative Risk of Thyroid Status According to Ethnicity Using Multinomial Logistic Regression (Māori Compared With European)

Follow-up (y)	Hyperthyroid		Euthyroid[a]	Hypothyroid	
	RR (95% CI)	P		RR (95% CI)	P
1	2.34 (1.52–3.62)	<0.0005	1.00	3.09 (1.98–4.82)	<0.0005
2	1.37 (0.83–2.29)	0.221	1.00	2.08 (1.35–3.21)	0.001
5	1.41 (0.74–2.67)	0.291	1.00	3.80 (2.46–5.88)	<0.0005
10	0.74 (0.27–2.01)	0.555	1.00	2.52 (1.38–4.59)	0.003

Multinomial logistic regression analysis of thyroid state outcome, including age, sex, private health care, and treatment modality (radioactive iodine or surgery).
Hyperthyroid = TSH <0.3 mIU/L (combines overt [TSH <0.1 mIU/L] and subclinical [TSH 0.1–0.29 mIU/L] groups). Euthyroid = TSH 0.3–5.0 mIU/L. Hypothyroid = TSH >5.0 mIU/L (combines overt [OHypo TSH >10 mIU/L] and subclinical [SHypo TSH 5.1–9.9 mIU/L] groups).
[a]Euthyroid state used as baseline for comparison in regression.

Strengths of this paper include the number of patients (n = 798) and that, as an observational study rather than a randomized trial, this study portrays the real-life management of thyroid disease after definitive therapy for GD. In addition, we have reviewed euthyroid rates out to a median of 9.6 years after definitive therapy. However, due to a recent shift in practice in our unit to recommending surgery over RAI to young patients with GD, long-term follow-up rates after surgery were low, with 167 patients having at least 5 years of follow-up and only 29 patients having 10 years of follow-up. Although we have data about whether a suppressed TSH was due to over-replacement or failure of treatment, an important limitation in interpreting our results is the lack of information regarding each patient's levothyroxine replacement regimen. Without this information, an abnormal TSH result is unable to be attributed to a specific cause, such as taking an inappropriate dosage, noncompliance, or whether action was taken to correct the abnormal result. Previous work has reported that, despite the abnormal TSH levels, there is often a failure by clinicians to adjust levothyroxine replacement. In a study performed in the United Kingdom, 56% of hypothyroid patients with high TSH had no dose increase, and 89% with low TSH had no dose reduction (rarely was noncompliance recorded as the reason for no action) [17]. If practice in our region of dosing inaction parallels that seen in this study from the United Kingdom, it is important to note that Māori, as an ethnic minority, are more severely affected by this undertreatment. A small British qualitative interview study of only 16 participants (including general practitioners, pharmacists, practice nurses, and a nurse practitioner) reported inadequate knowledge of levothyroxine medication interactions and pharmacokinetics by prescribers, and lack of time was identified as a barrier to improving thyroid management [18]. Although we would expect that standard practice would be to alter dosage and to recheck levels after ~6 to 8 weeks (*i.e.*, 42 to 56 days), we found that the median time to rechecking levels in the severely hypothyroid group was double this at 112 days, only one-third of these patients had a repeat blood test within 90 days, and 45% of repeat levels were still severely hypothyroid (data not shown).

Regardless of the reason for abnormal TSH levels, we have demonstrated that the outcome of patients after definitive treatment is frequently inadequate and worse for Māori patients. This is important not just for potential effects on quality of life but also for mortality, with patients with thyrotoxicosis demonstrating an increase in mortality for every 6 months of a decreased TSH [19]. These data also raise questions about recommendations for treatment of patients with subclinical hyperthyroidism [20, 21] because the results of this study suggest that long-term thyroid status may well be worse after definitive treatment than prior to such therapy.

4. Conclusions

After definitive therapy for GD, Māori have significantly lower rates of optimal thyroid levels than their European counterparts, and this inequity was present at all time points and

irrespective of treatment modality, indicating the need for improved care particularly for indigenous peoples.

Acknowledgments

References and Notes

1. Brownlie BE, Wells JE. The epidemiology of thyrotoxicosis in New Zealand: incidence and geographical distribution in north Canterbury, 1983-1985. *Clin Endocrinol (Oxf).* 1990;**33**(2):249–259.
2. Tamatea JAU, Reid P, Conaglen JV, Elston MS. Thyrotoxicosis in an Indigenous New Zealand Population - a prospective observational study (unpublished data).
3. Tamatea JA, Conaglen JV, Elston MS. Response to radioiodine therapy for thyrotoxicosis: disparate outcomes for an indigenous population. *Int J Endocrinol.* 2016;**2016**:7863867.
4. Genovese BM, Noureldine SI, Gleeson EM, Tufano RP, Kandil E. What is the best definitive treatment for Graves' disease? A systematic review of the existing literature. *Ann Surg Oncol.* 2013;**20**(2): 660–667.
5. Jonklaas J. Sex and age differences in levothyroxine dosage requirement. *Endocr Pract.* 2010;**16**(1): 71–79.
6. Parle JV, Franklyn JA, Cross KW, Jones SR, Sheppard MC. Thyroxine prescription in the community: serum thyroid stimulating hormone level assays as an indicator of undertreatment or overtreatment. *Br J Gen Pract.* 1993;**43**(368):107–109.
7. Somwaru LL, Arnold AM, Joshi N, Fried LP, Cappola AR. High frequency of and factors associated with thyroid hormone over-replacement and under-replacement in men and women aged 65 and over. *J Clin Endocrinol Metab.* 2009;**94**(4):1342–1345.
8. Mithal A, Dharmalingam M, Tewari N. Are patients with primary hypothyroidism in India receiving appropriate thyroxine replacement? An observational study. *Indian J Endocrinol Metab.* 2014;**18**(1): 83–88.
9. Okosieme OE, Belludi G, Spittle K, Kadiyala R, Richards J. Adequacy of thyroid hormone replacement in a general population. *QJM.* 2011;**104**(5):395–401.
10. Solter D, Solter M. Do we treat hypothyroidism properly? A survey of 2488 patients from University Hospital Center, Zagreb, Croatia. *Ann Endocrinol (Paris).* 2013;**74**(1):27–29.
11. Anderson I, Robson B, Connolly M, Al-Yaman F, Bjertness E, King A, Tynan M, Madden R, Bang A, Coimbra CE, Jr, Pesantes MA, Amigo H, Andronov S, Armien B, Obando DA, Axelsson P, Bhatti ZS, Bhutta ZA, Bjerregaard P, Bjertness MB, Briceno-Leon R, Broderstad AR, Bustos P, Chongsuvivatwong V, Chu J, Deji, Gouda J, Harikumar R, Htay TT, Htet AS, Izugbara C, Kamaka M, King M, Kodavanti MR, Lara M, Laxmaiah A, Lema C, Taborda AM, Liabsuetrakul T, Lobanov A, Melhus M, Meshram I, Miranda JJ, Mu TT, Nagalla B, Nimmathota A, Popov AI, Poveda AM, Ram F, Reich H, Santos RV, Sein AA, Shekhar C, Sherpa LY, Skold P, Tano S, Tanywe A, Ugwu C, Ugwu F, Vapattanawong P, Wan X, Welch JR, Yang G, Yang Z, Yap L. Indigenous and tribal peoples' health (The Lancet-Lowitja Institute Global Collaboration): a population study. *Lancet.* 2016;**388**(10040):131–157.
12. United Nations. The United Nations declaration on the rights of indigenous peoples. Geneva: United Nations; 2013.
13. Tamatea JA, Tu'akoi K, Conaglen JV, Elston MS, Meyer-Rochow GY. Thyroid cancer in Graves' disease: is surgery the best treatment for Graves' disease? *ANZ J Surg.* 2014;**84**(4):231–234.
14. Ministry of Health. Ethnicity data protocols for the health and disability sector. Ministry of Health, Wellington, UK. 2004.
15. Statistics New Zealand. Census quickstats about Maori. 2013; www.stats.govt.nz. Accessed 8 September 2015.
16. Robson B, Harris R. *Hauora: Maori Standards of Health IV: A Study of the Years 2000-2005.* Wellington, New Zealand: University of Otago.
17. De Whalley P. Do abnormal thyroid stimulating hormone level values result in treatment changes? A study of patients on thyroxine in one general practice. *Br J Gen Pract.* 1995;**45**(391):93–95.

18. Dew R, King K, Okosieme OE, Pearce SH, Donovan G, Taylor PN, Hickey J, Dayan CM, Leese G, Razvi S, Wilkes S. Attitudes and perceptions of health professionals towards management of hypothyroidism in general practice: a qualitative interview study. *BMJ Open.* 2018;**8**(2):e019970.
19. Lillevang-Johansen M, Abrahamsen B, Jørgensen HL, Brix TH, Hegedüs L. Excess mortality in treated and untreated hyperthyroidism is related to cumulative periods of low serum TSH. *J Clin Endocrinol Metab.* 2017;**102**(7):2301–2309.
20. Biondi B, Bartalena L, Cooper DS, Hegedüs L, Laurberg P, Kahaly GJ. The 2015 European Thyroid Association guidelines on diagnosis and treatment of endogenous subclinical hyperthyroidism. *Eur Thyroid J.* 2015;**4**(3):149–163.
21. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid.* 2016;**26**(10):1343–1421.