

## Original Article

# Vitamin D status of Māori and non-Māori octogenarians in New Zealand: a Cohort Study (LiLACS NZ)

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**Background and Objectives:** This study assessed vitamin D status and its determinants in a cohort of octogenarians living within New Zealand's Bay of Plenty and Lakes Districts. **Methods and Study Design:** Serum 25-hydroxyvitamin D [25(OH)D] concentration was measured in 209 Māori (aged 80-90 years) and 357 non-Māori (85 years), along with demographic, lifestyle, supplement use and other health data. **Results:** Mean [95% CI] 25(OH)D concentration was 69 [67 to 72] nmol/L, with 15% >100 nmol/L and 6 individuals >150 nmol/L. Concentrations in Māori (59 [55 to 62] 4 nmol/L) were lower than in non-Māori (75 [72 to 78] nmol/L;  $p < 0.001$ ), a difference maintained when adjusted for day-of-year measured. Vitamin D supplementation was reported by 98 participants (18%): including a greater proportion of women (24%) than men (11%;  $p < 0.001$ ) and of non-Māori (24%) than Māori (7%;  $p < 0.001$ ). Of those taking vitamin D, 49% took high oral doses ( $\geq 25$   $\mu\text{g}/\text{day}$  or equivalent) and five individuals took  $> 50$   $\mu\text{g}/\text{day}$ . Vitamin D supplement use strongly and independently predicted seasonally-adjusted 25(OH)D concentration and was associated with 28 nmol/L higher levels than non-use. Other predictors included Māori ethnicity (10 nmol/L lower concentration than for non-Māori), and female gender (11 nmol/L lower). **Conclusions:** Vitamin D status in New Zealand octogenarians appears higher than previously reported, particularly in non-Māori compared to Māori. Prescribed and non-prescribed oral vitamin D supplementation is prevalent in this group and a strong indicator of vitamin D status.

**Key Words:** calciferol, seasonal variation, ethnic groups, aged 80 and over, elderly

## INTRODUCTION

Low vitamin D status has been linked to a wide range of prevalent medical conditions with serious consequences for older people. These conditions include osteoporosis, falls, fractures, cardiovascular disease, cancer (particularly colorectal) and diabetes.<sup>1</sup> Vitamin D status in healthy adult populations is determined largely by exposure of the skin to direct ultraviolet sunlight in the B spectral range.<sup>2</sup> Intake from supplements, fortified foods, and a small number of foods in which vitamin D is naturally occurring may also play a role, and intake has been shown to prevent severe deficiency when serum 25-hydroxyvitamin D [25(OH)D] concentration is low, as in winter.<sup>3</sup>

Older people commonly have low circulating levels of 25(OH)D.<sup>4</sup> This is due to a combination of factors including reduced outdoor time, increased clothing cover,<sup>5</sup> deliberate avoidance of direct sun exposure, and reduced epidermal synthesis of pre-vitamin D.<sup>6</sup> Octogenarians are likely to have very low serum 25(OH)D concentrations and an increased risk from adverse health outcomes. Lower concentrations have been documented in those  $\geq 80$  years compared to those 60-79 years in a 1988-1994 US national survey,<sup>7</sup> and in Auckland women  $\geq 80$  years whose serum 25(OH)D was 7 nmol/L lower than women aged  $\geq 55$

years.<sup>8,9</sup>

Vitamin D status is relatively poor in New Zealand (populated between latitudes 34 and 47°S) despite a temperate climate, 25(OH)D concentration being approximately 20 nmol/L lower in New Zealand and the UK<sup>8,10,11</sup> than in Canada and the US.<sup>7,12</sup> Higher North American levels probably result from mandatory fortification of milk,<sup>10</sup> but may also reflect temporal and regional differences in the prevalence of vitamin D supplement use. Differences between studies of vitamin D status may also result from the use of different assays<sup>13</sup> or because of uneven distribution of measurements throughout the year. Substantial seasonal variation in 25(OH)D concentration has been noted,<sup>14-16</sup> with decreased winter levels arising

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from lower solar zenith angle and reduced outdoor sun exposure to bare skin.<sup>2</sup>

Although many large cohort studies, such as Longitudinal Aging Study Amsterdam (LASA), Osteoporotic Fractures in Men Study (MrOS), Uppsala Longitudinal Study of Adult Men (ULSAM), and the UK National Diet and Nutrition Survey: 65 years and over (NDNS 65+) have investigated vitamin D status in healthy populations of predominantly Caucasian people 65 years and older,<sup>17-20</sup> much less data exist about status in healthy adults >80 years old or other ethnic groups.

Determinants of vitamin D status for cohorts >80 years are unclear. In younger cohorts, men generally display higher 25(OH)D concentration than women.<sup>21</sup> In addition, vitamin D status correlates with various health and lifestyle factors: positively with physical activity<sup>8,22-24</sup> and self-reported health status<sup>25</sup> and inversely with obesity<sup>24,26</sup> and frailty (when 25(OH)D concentration is <75 nmol/L).<sup>27,28</sup> It is unclear whether the same predictors of vitamin D status apply for cohorts >80 years of age.

Darker skin pigmentation screens ultraviolet light from the innermost strata of the epidermis, which contain the highest concentrations of the vitamin D precursor 7-dehydrocholesterol.<sup>29</sup> Correspondingly, African Americans have lower vitamin D status than White Americans, with Hispanic Americans showing intermediate concentrations of 25(OH)D,<sup>7,30</sup> and from a global perspective darker skin pigmentation is recognised as a risk factor for vitamin D insufficiency or deficiency.<sup>31</sup> In New Zealand, whilst vitamin D status has been shown to be lower, and insufficiency more common in Māori compared to non-Māori adults<sup>10</sup> and children,<sup>32</sup> there is no knowledge about the degree of vitamin D insufficiency or its correlates in Māori in advanced age. The aims of this study were to establish vitamin D status, as well as its correlates and determinants in Māori and non-Māori >80 years of age, based on measurements of serum 25(OH)D concentration.

## MATERIALS AND METHODS

### Recruitment

Data for the study came from participants in the Life and Living in Advanced Age: a Cohort Study in New Zealand (Te Puāwaitanga o Nga Tapuwae Kia Ora Tonu) LiLACS NZ. Māori aged 80-90 years and non-Māori aged 85 years living within the defined district health board areas of Bay of Plenty and Rotorua Lakes (excluding Taupo) were recruited throughout the year from January to December, 2010, using an ethically-approved population-based recruitment strategy detailed previously.<sup>33,34</sup> There was a slight lull in recruitment during summer months, particularly for non-Māori. In brief, all potential participants were identified from the electoral role, primary health care databases, word of mouth, or invited by someone known to them, usually the general practitioner or through Māori networks. Ethical approval for the study was granted by the New Zealand Northern X Health and Disability Ethics Committee (NTX/09/09/088 and 10/12/127).

Extensive efforts throughout the planning and implementation of this study were made to develop and maintain communication with study participants and their communities, and to honour the wairua/spirit of blood,

which according to Māori tradition lives on after donation or death.<sup>34,35</sup>

### Interview & vitamin D supplement use

Participants were interviewed by research-trained interviewers using standardised methods and completed either a comprehensive interview about health, social, cultural and environmental factors or a brief interview of core questions. Socio-demographic characteristics were assessed using adapted items from the 2006 New Zealand Census and deprivation index assigned from the participant's address at the time of interview.

For those opting to complete the full questionnaire, trained research nurses conducted a physical assessment including grip strength, height, weight, and body composition, and collected a blood sample. Medications and supplements were viewed to confirm reported use and total vitamin D dose was calculated.

### Body composition, physical activity & health status measurements

Stature was measured in duplicate (or triplicate if variation >1 cm) using a Seca 213 free-standing stadiometer [Seca, Hamburg, Germany]. Body mass and percent fat were assessed via footplate bioelectrical impedance using Tanita Innerscan Body Composition Monitor, BC-545 [Tanita Corporation, Tokyo, Japan]. Grip strength was measured using a Takei digital handgrip dynamometer-Grip D. All participants completed a subset of items from the Nottingham Extended Activities of Daily Living Scale,<sup>36</sup> which were scored positively if respondents indicated that they were able to complete the activity alone, to produce a score out of 10. For those who completed the full questionnaire, level of physical activity was assessed using Physical Activity Scale for the Elderly,<sup>37</sup> and health-related quality of life was determined using the physical and mental component composite scores of the Medical Outcomes Study Short Form Health Survey (SF-12) and reported as standardised scores.<sup>38</sup>

### Blood collection

Following an overnight fast, blood was collected by the research nurse at the participants' residence or using local laboratory services. Samples were stored temporarily at -20° C then at -80° C and were transported on ice or dry ice. Blood samples were analysed using isotope dilution high-performance liquid chromatography (HPLC)-tandem mass spectrometry for serum 25(OH)D and BioRad Variant HPLC for glycated haemoglobin (HbA1c) at Canterbury Health Laboratories, which participates in the Vitamin D External Quality Assessment Scheme. Other assays, including cholesterol, lipids, glucose, creatinine and parathyroid hormone (PTH) were analysed via an automated HPLC Abbott Architect assay.

### Seasonal adjustment of 25-hydroxyvitamin D concentration

In order to determine if sufficient seasonal variation in this cohort indicated seasonal-adjustment of levels, four repeated measures ANOVA models testing for the effect of month of blood collection were performed for Māori and non-Māori men and women separately in those not

taking vitamin D supplements.

Methods for individual seasonal adjustment of 25(OH)D concentrations have been described previously in detail<sup>39</sup> and validated in separate cohorts.<sup>40</sup> In summary, the seasonal trend for each gender/ethnic group separately was determined by fitting sine curves to the relationship between 25(OH)D against day of the year using Prism (Graph Pad Software Inc., La Jolla, CA, USA). Using the amplitude and phase-shift characteristics of these four sinusoidal relationships an annual baseline was predicted for each individual, which represented the mean serum 25(OH)D concentration expected for that person during the year. The following formula was applied:

$$\text{baseline} = \text{amplitude} * \sin(\text{frequency} * x + \text{offset}) - y$$

where x was expressed as the day of the year (January 1 = 1; December 31 = 365) and the offset represented the horizontal translation along the x-axis.

### Data analysis

Data were analysed using SPSS Statistics Version 19 [SPSS Inc., an IBM Company]. Serum 25(OH)D concentrations were categorised dichotomously at four cut-points: 25 nmol/L, 50 nmol/L, 75 nmol/L, and 100 nmol/L to determine prevalence of deficiency, insufficiency (two definitions) and high levels. Chi-square tests were used to determine gender and ethnicity differences in prevalence. Univariate associations between explanatory variables and seasonally-adjusted and unadjusted 25(OH)D were tested using Pearson's or Spearman's correlation analysis. For multiple linear regression models, we used seasonally-adjusted 25(OH)D as a continuous dependent variable. Independent variables were included

in the regression models regardless of their association with the dependent variable. To reduce the effects of multicollinearity, the models were assessed using the variance inflation factor (VIF). Independent variables in the regression with a VIF>3 were removed. The level of significance for statistical testing was set at  $\alpha=0.05$ . Data are reported as mean [95% confidence interval] unless otherwise stated.

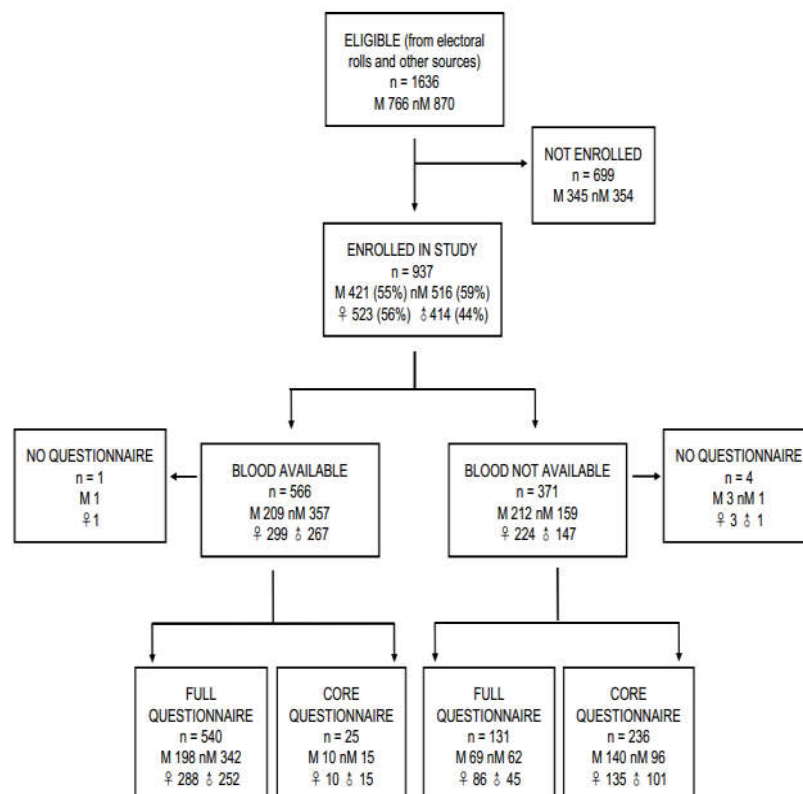
## RESULTS

### Response and participant characteristics (Figure 1)

From a pool of 1,636 eligible participants, 937 were enrolled into the study (421 Māori; 56% women). Of these, 566 agreed to the blood sample and had blood available for 25(OH)D analysis: 209 Māori and 357 non-Māori.

Those with blood available for analysis were less likely to be Māori ( $p<0.001$ ) and female ( $p=0.03$ ); had higher educational qualifications ( $p=0.007$ ); were slightly younger 84.8 [83.3 to 85.3] years (median [interquartile range; IQR]) versus 85.0 [83.0 to 85.6] years ( $p=0.004$ ); and reported a higher ADL score 9 [8 to 10] versus 8 [6 to 10];  $p<0.001$  (median [interquartile range; IQR]). They were also less fat, 33.0 [32 to 34] percent body fat versus 38.2 [37 to 40]% ( $p<0.001$ ); had lower BMI, 27.7 [27 to 28] kg/m<sup>2</sup> versus 29.2 [28 to 31] kg/m<sup>2</sup> ( $p=0.02$ ); had higher grip strength, 24.6 [24 to 25] versus 21.9 [20 to 24]  $\pm$  2 kg ( $p=0.004$ ); reported greater physical activity levels, PASE score 98 [54 to 152] versus 72 [29 to 125] (median [IQR];  $p<0.001$ ); and had a slightly higher mental health-related quality of life (QoL) score, 55 [54 to 56] versus 52 [51 to 54] ( $p=0.02$ ).

For the 566 participants included in main analyses (Ta-



**Figure 1.** Numbers of eligible participants who had blood available for analysis and completed full questionnaire. M: Māori; NM: non-Māori; ♀: female; ♂: male.

ble 1), women, compared to men, were less active, had a weaker hand-grip strength, though had a greater ADL score, had greater percent body fat, total and HDL cholesterol, lower creatinine ( $p<0.001$  for all), and reported a lower physical health-related QoL score ( $p=0.002$ ). Māori compared to non-Māori were younger due to the different inclusion criteria ( $p<0.001$ ), had a higher deprivation index ( $p<0.001$ ), higher ADL score ( $p<0.02$ ) and grip strength ( $p<0.01$ ), greater percent body fat ( $p=0.01$ ) and BMI ( $p<0.001$ ), higher glucose ( $p=0.001$ ), creatinine ( $p=0.01$ ), and HbA1c ( $p<0.001$ ), and lower total ( $p=0.04$ ) and HDL cholesterol ( $p=0.01$ ; Table 1).

#### **Vitamin D status**

Monthly variation in 25(OH)D was restricted to those not known to be taking oral vitamin D. When those taking vitamin D were excluded, monthly variation was present only for Māori men ( $p=0.01$ ) and non-Māori men ( $p<0.001$ ), but not for women of either ethnicity (Figure 2). In contrast, when analysis was completed for only those who reported taking vitamin D, none of the four demographic groups showed monthly variation ( $p=0.2-0.7$ ). As a consequence of these findings, individual 25(OH)D levels were seasonally adjusted to reflect predicted mean annual concentration, only for Māori and non-Māori men not taking vitamin D.

Unadjusted 25(OH)D concentration did not differ between men and women for the entire cohort or for analyses of just Māori or non-Māori, however levels in Māori were 16 [12 to 21] lower than non-Māori (Table 1). Seasonal adjustment did not affect the difference between Māori and non-Māori but resulted in increased 25(OH)D concentration in men, with levels 8 [3 to 13] nmol/L higher than in women ( $p=0.001$ ; Table 1).

Only 12 individuals (2%) recorded seasonally-adjusted 25(OH)D concentration  $<25$  nmol/L, 133 individuals (23%) were  $<50$  nmol/L and 305 (54%) were  $<75$  nmol/L. Whether seasonally-adjusted or not, 86 participants (15%) attained 25(OH)D concentrations  $>100$  nmol/L, and 6 individuals (5 if seasonally-adjusted) were  $>150$  nmol/L.

#### **Vitamin D and calcium supplementation**

Of the 538 individuals for whom this information was available, 98 (18%) reported taking oral vitamin D either from non-prescribed supplements or listed medications. For those taking vitamin D, doses ranged from 2.5-82  $\mu\text{g/day}$  (100-3,288 IU/day), with almost one half (49%) reporting high oral doses  $\geq 25$   $\mu\text{g}$  (1,000 IU) daily or equivalent, and five individuals reporting  $>50$   $\mu\text{g}$  (2,000 IU) equivalent daily dose. Similarly, 89 individuals (17%) reported taking calcium, with doses ranging from 10-2,560 mg/day (500 [285 to 875] median; [IQR]).

A greater proportion of women (24%) than men (11%) reported taking vitamin D supplements ( $p<0.001$ ). Only 7% of Māori participants reported taking vitamin D supplements, and 25% non-Māori ( $p<0.001$ ). In addition to gender and ethnicity differences, vitamin D takers, compared to non-takers, were slightly older ( $p<0.001$ ), had lower BMI ( $p=0.02$ ) and lower physical health-related QoL score ( $p=0.003$ ), recorded lower PTH ( $p<0.001$ ), higher creatinine ( $p<0.001$ ), lower glucose ( $p=0.001$ ) and

HbA1c ( $p=0.03$ ), and higher total and HDL cholesterol concentrations (Table 2).

#### **Vitamin D status in relation to supplementation**

Seasonally-adjusted 25(OH)D was higher in those taking vitamin D supplements (96 [91 to 101] nmol/L) compared to those not (67 [65 to 70] nmol/L), and compared to the 28 individuals in whom supplementation status was unknown (68 [55 to 80] nmol/L;  $p<0.001$  for ANOVA and *post-hoc* comparisons). Prevalence of insufficiency ( $<50$  nmol/L) and deficiency ( $<25$  nmol/L) was very low in those taking vitamin D (Table 3).

Amongst non-vitamin-D-supplement takers, seasonally-adjusted 25(OH)D concentration was lower in women compared to men (59 [56 to 62] and 75 [72 to 78] nmol/L respectively;  $p<0.001$ ). Concentration in Māori were lower (61 [57 to 64] nmol/L than in non-Māori 71 [68 to 75] nmol/L ( $p<0.001$ ). Similarly, women were more likely to be deficient or insufficient compared to men ( $p<0.001$ ) and Māori more likely than non-Māori to be insufficient ( $p=0.02$ ; Table 3). For those taking vitamin D, in contrast, there were no differences in 25(OH)D concentration or prevalence of insufficiency between Māori and non-Māori, or between genders (Table 3).

High levels ( $>100$  nmol/L) were present in those known to be taking vitamin D, as well as in those indicating no vitamin D supplementation, and in those whose vitamin D supplementation status was unknown (Table 3). Concentration above 100 nmol/L was more frequent in women compared to men who took vitamin D supplements ( $p=0.03$ ), but were more frequent in men compared to women who indicated not taking them ( $p=0.003$ ; Table 3). Amongst non-supplement takers, Māori were less likely than non-Māori to have concentrations  $>100$  nmol/L ( $p=0.01$ ; Table 3).

#### **Correlations with demographic, blood, and health and lifestyle measurements**

Correlates of seasonally-adjusted 25(OH)D for the whole cohort included PTH ( $r=-0.24$ ;  $p<0.001$ ), BMI ( $r=-0.16$ ;  $p<0.001$ ), percent fat ( $r=-0.14$ ;  $p<0.001$ ), deprivation index ( $r=-0.11$ ;  $p=0.008$ ), glucose ( $r=-0.09$ ;  $p<0.03$ ) and PASE score ( $r=0.09$ ;  $p=0.03$ ), and creatinine ( $r=0.09$ ;  $p=0.04$ ). For analyses of Māori and non-Māori cohorts separately, deprivation index was not significantly correlated with 25(OH)D in either group, and BMI and percent fat correlations only attained significance for Māori. Statistically significant correlations were largely restricted to those not reporting vitamin D supplementation (data not shown).

#### **Determinants of vitamin D status (Table 4)**

To determine the independent associations of the inter-related explanatory variables with seasonally-adjusted 25(OH)D and to establish models for its prediction, linear regression models were applied. The primary regression model included presence of vitamin D supplementation, age, gender, Māori versus non-Māori ethnicity, high deprivation index (quintile 5), PASE score, BMI, and physical and mental health-related QoL scores. Percent fat, ADL score, maximum grip strength, and HbA1c were removed from models to reduce multicollinearity, as they

**Table 1.** Characteristics of participants

	Women		Men		Gender	<sup>§</sup> <i>p</i> value		Cohort
	Māori	Non-Māori	Māori	Non-Māori		Ethnicity	Interaction	
N	119	180	90	177				566
<sup>†</sup> No. taking vitamin D (%)	12 (10)	58 (32)	2 (2)	26 (15)	<0.001	<0.001	–	98 (17)
Age (years)	82 (81-85)	85 (85-85)	82 (81-84)	85 (85-85)	0.5	<0.001	–	85 (84-85)
Deprivation index	8 (6-10)	6.5 (4-8)	8 (6-10)	6 (4.5-8)	0.7	<0.001	–	7 (5-9)
25(OH)D (nmol/L)	59±26	74±31	58±27	76±29	0.8	<0.001	0.5	69±30
<sup>‡</sup> Adjusted	Not adjusted	Not adjusted	66±23	81±27	0.003	<0.001	1.0	72±29
Blood biomarkers								
PTH (pmol/L)	5.1±2.6	4.8±2.4	4.7±2.4	4.9±3.0	0.6	1.0	0.3	4.9±2.6
Creatinine (µmol/L)	86±24	78±21	111±37	105±34	<0.001	0.01	0.7	93±32
Glucose (mmol/L)	5.8±1.6	5.3±0.9	5.9±1.6	5.5±0.9	0.1	<0.001	0.7	5.6±1.2
HbA1c (mmol/mol)	41±9	37±6	41±12	37±8	0.7	<0.001	0.6	39±9
Total cholesterol (mmol/L)	5.2±1.2	5.6±1.0	4.6±1.0	4.7±1.0	<0.001	0.04	0.1	5.1±1.1
HDL cholesterol (mmol/L)	1.6±0.4	1.7±0.4	1.4±0.4	1.4±0.3	<0.001	0.01	0.2	1.5±0.4
Triglyceride (mmol/L)	1.5±0.6	1.5±0.8	1.4±0.9	1.3±0.7	0.1	0.8	0.6	1.4±0.7
Health & lifestyle factors								
PASE score	94 (52-134)	84 (40-128)	116 (53-205)	112 (63-172)	<0.001	0.2	–	98 (54-152)
ADL score	10 (9-10)	9 (8-10)	9 (8-10)	9 (8-10)	<0.001	0.02	–	9 (8-10)
Grip strength (kg)	20±5	18±4	32±7	30±6	<0.001	0.01	0.8	25±8
Percent fat	37±7	37±7	31±8	28±6	<0.001	0.01	0.02	33±8
Body mass index (kg/m <sup>2</sup> )	29±6	27±4	30±5	27±4	0.1	<0.001	0.04	28±5
SF12-PHRQoL	43±12	39±12	45±11	44±12	0.002	0.1	0.2	42±12
SF12-MHRQoL	54±9	55±8	54±8	55±8	0.9	0.1	0.9	55±8

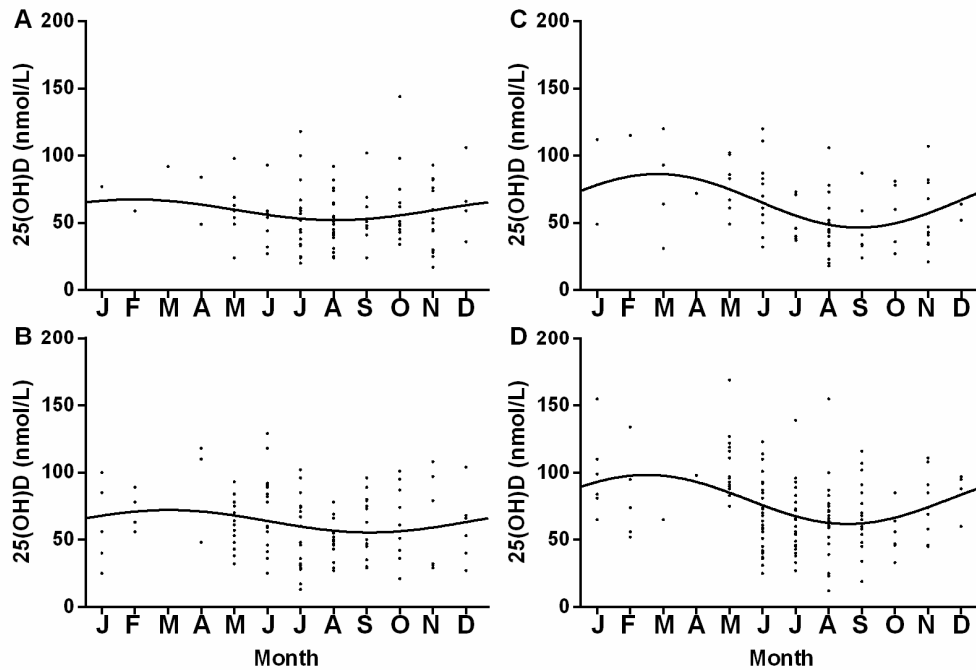
No.: number; 25(OH)D: 25-hydroxyvitamin D; PTH: parathyroid hormone; PASE: Physical Activity Scale for the Elderly<sup>37</sup>; ADL: activities of daily living<sup>36</sup>; HbA1c: glycated haemoglobin; HDL: high density lipoprotein; SF12-PHRQoL: Short Form Physical Health-Related Quality of Life standardised score<sup>38</sup>; SF12-MHRQoL: Short Form Mental Health-Related Quality of Life standardised score<sup>38</sup>.

Data are mean±SD except for numbers of participants which are frequencies and age, deprivation index, PASE and ADL scores which are reported as median (interquartile range) due to severely non-normal distribution.

<sup>†</sup>Number who reported taking oral vitamin D supplements.

<sup>‡</sup>Serum 25(OH)D concentrations (nmol/L) adjusted for the day of the year that blood was collected by gender and ethnicity when seasonal variation was indicated.

<sup>§</sup>Differences via Chi-square test for frequency and 2-way ANOVA (gender x ethnicity) for continuous variables, except for age, deprivation index, PASE and ADL for which Mann-Whitney test was performed.



**Figure 2.** Variation in 25-hydroxyvitamin D levels [25(OH)D] by month of year for those not reporting vitamin D supplement use. Variation across months of measurement shown for A. Māori Women ( $p=0.08$ ); B. non-Māori Women ( $p=0.2$ ); C.; Māori men ( $p=0.01$ ); D. non-Māori men ( $p<0.001$ ).

**Table 2.** Characteristics according to vitamin D supplement use

	Taking (n=98)	†Not taking (n=440)	‡Difference ( $p$ value)
No. females: males	70:28	217:223	<0.001
No. Māori: non-Māori	84:14	182:258	<0.001
Age (years)	85.0 (84.7-85.4)	84.9 (82.8-85.3)	0.001
Deprivation index	7 (5-8)	7 (5-9)	0.2
25(OH)D (nmol/L)	96 (80-110)	63 (44-82)	<0.001
§Adjusted	Not adjusted	67 (48-85)	<0.001
PTH (pmol/L)	42 (3.0-4.9)	5 (3.3-5.6)	<0.001
Creatinine ( $\mu\text{mol/L}$ )	82 (67-91)	96 (74-109)	<0.001
Glucose (mmol/L)	5.3 (4.8-5.5)	5.6 (4.9-5.8)	0.001
HbA1c (mmol/mol)	36.8 (33.0-40.0)	38.9 (34.0-41.0)	0.03
Total cholesterol (mmol/L)	5.5 (4.9-6.1)	5.0 (4.2-5.6)	<0.001
HDL cholesterol (mmol/L)	1.7 (1.6-1.9)	1.5 (1.2-1.8)	0.003
Triglyceride (mmol/L)	1.4 (1.0-1.6)	1.4 (1.0-1.7)	0.7
PASE score	88 (53-141)	101 (54-159)	0.2
ADL score	9 (8-10)	9 (8-10)	0.4
Grip strength (kg)	21.0 (15.1-26.4)	25.4 (18.9-31.6)	<0.001
Percent fat	33 (29-39)	33 (27-39)	0.5
Body mass index ( $\text{kg/m}^2$ )	26.4 (23.9-28.5)	28.0 (24.9-30.3)	0.002
SF12-PHRQoL	39 (31-48)	43 (34-53)	0.003
SF12-MHRQoL	54 (50-59)	55 (50-61)	0.2

No.: number; 25(OH)D: 25-hydroxyvitamin D; PTH: parathyroid hormone; PASE: Physical Activity Scale for the Elderly<sup>37</sup>; ADL: activities of daily living<sup>36</sup>; HbA1c: glycated haemoglobin; HDL: high density lipoprotein; SF12-PHRQoL: Short Form Physical Health-Related Quality of Life standardised score<sup>38</sup>; SF12-MHRQoL: Short Form Mental Health-Related Quality of Life standardised score<sup>38</sup>.

Data are mean (95% confidence interval) except for numbers of participants which are frequencies and Age, Deprivation Index, PASE and ADL score which are reported as median (interquartile range).

†Participants who received a full interview but did not indicate vitamin D use.

‡Differences via Chi-square test for frequency,  $t$ -test for continuous variables except for age, deprivation index, PASE and ADL for which Mann-Whitney test was performed.

§Serum 25(OH)D (nmol/L) concentration adjusted for the day of the year that blood was collected by gender and ethnicity when seasonal variation was indicated.

were less strongly associated with the dependent variables that their correlates: BMI, PASE score, gender and fasting glucose. Following their removal all variables had a VIF<1.75. The model explained 23% of the variance in seasonally-adjusted 25(OH)D. Vitamin D supplementa-

tion was the strongest independent predictor (positively), whilst female gender, Māori ethnicity, and physical health-related QoL score (inversely) were also independently associated with seasonally-adjusted 25(OH)D (Table 4).

**Table 3.** Prevalence of vitamin D deficiency [ $\dagger$ 25(OH)D <25 nmol/L], insufficiency [ $\dagger$ 25(OH)D <50 nmol/L and <75 nmol/L], and high levels [ $\dagger$ 25(OH)D >100 nmol/L] according to vitamin D supplement use in Māori and non-Māori

	Women		Men		$\ddagger$ p value	$\ddagger$ p value
	Maori	Non-Maori	Maori	Non-Maori	Gender	Ethnicity
Taking vitamin D	n=12	n=58	n=2	n=26		
<75 nmol/L	1 (8)	12 (21)	1 (50)	3 (12)	0.6	0.7
<50 nmol/L	0 (0)	2 (3)	0 (0)	0 (0)	0.4	0.6
<25 nmol/L	0 (0)	0 (0)	0 (0)	0 (0)	–	–
>100 nmol/L	4 (33)	28 (48)	0 (0)	6 (23)	0.03	0.4
Not taking vitamin D	n=102	n=115	n=80	n=143		
<75 nmol/L	82 (80)	58 (73)	51 (64)	62 (43)	<0.001	<0.001
<50 nmol/L	44 (43)	38 (48)	18 (23)	19 (13)	<0.001	0.02
<25 nmol/L	6 (6)	5 (6)	1 (1)	0 (0)	0.009	0.06
>100 nmol/L	4 (4)	9 (11)	6 (8)	25 (17)	0.003	0.01
Unknown	n=5	n=7	n=8	n=8		
<75 nmol/L	4 (80)	2 (29)	7 (88)	3 (38)	0.5	0.006
<50 nmol/L	2 (40)	1 (14)	3 (38)	2 (25)	0.7	0.3
<25 nmol/L	0 (0)	1 (14)	0 (0)	1 (13)	0.8	0.2
>100 nmol/L	0 (0)	2 (29)	13 (2)	2 (25)	0.9	0.2

Data show number of individuals (percentage of gender/ethnicity category).

$\dagger$ Serum 25-hydroxyvitamin D [25(OH)D] concentrations for males not taking vitamin D are adjusted for season of measurement.

$\ddagger$ Level of statistical significance of difference in frequencies by gender and ethnicity from Chi-square test.

**Table 4.** Determinants of 25(OH)D adjusted for the day-of-year of measurement (seasonally-adjusted)

	n	Predictors	$\beta$ -coefficient	SE $\beta$	p
Whole cohort	519	VitD supp	27.9	3.0	<0.001
		Female gender	-11.0	2.4	<0.001
		Māori ethnicity	-10.4	3.1	0.001
		Physical QoL	-0.22	0.11	0.04
		PASE	0.033	0.018	0.06
		BMI	-0.47	0.26	0.07
		MODEL $r^2 = 0.23$			
Not taking vitamin D $\dagger$	422	Female gender	-13.9	2.5	<0.001
		Māori ethnicity	-11.2	3.2	<0.001
		PASE	0.036	0.018	0.0498
		Age	-1.29	0.74	0.08
		MODEL $r^2 = 0.14$			
Māori – not taking vitamin D $\ddagger$	172	Female gender	-10.2	3.6	0.006
		Age	-1.37	0.71	0.05
		BMI	-0.62	0.34	0.07
		MODEL $r^2 = 0.10$			
Non Māori – not taking vitamin D $\ddagger$	250	Female gender	-16.5	3.5	<0.001
		PASE	0.051	0.028	0.07
		Physical QoL	-0.29	0.17	0.08
		MODEL $r^2 = 0.12$			

Predictor variables include presence of vitamin D supplementation (VitD supp), gender (female versus male), ethnicity (Māori versus non-Māori), age, high deprivation index (quintile 5), body mass index (BMI), physical activity score (PASE),<sup>37</sup> physical health composite quality of life T-score (Physical QoL),<sup>38</sup> mental health composite quality of life T-score.<sup>38</sup>

$\dagger$ Vitamin D supplementation removed from model.

$\ddagger$ Vitamin D supplementation and ethnicity removed from model.

Percent fat, activities of daily living score, grip strength and HbA1c were removed from all models due to high correlation with BMI, PASE score, gender and glucose respectively; lower predictive power on dependent variables than related variables; as well as improved collinearity statistics following their removal.

Because it may be useful to predict costly 25(OH)D concentration measurements from other routinely-measured blood variables an additional analysis included PTH, total and HDL-cholesterol, triglyceride and glucose measurements in addition to the above variables. Vitamin D supplementation, creatinine, and HDL-cholesterol (positively) and PTH, Māori ethnicity, and female gender

inversely attained independent association with seasonally-adjusted 25(OH)D and cumulatively explained 29% of its variance (data not shown).

Female gender and Māori ethnicity (inversely) and PASE (positively) were significant predictors of seasonally-adjusted 25(OH)D when analysis was restricted to those not taking vitamin D. For Māori and non-Māori

separately, only female gender (inverse predictor) attained statistical significance for prediction of seasonally-adjusted 25(OH)D.

## DISCUSSION

### *Vitamin D status*

From this study, we set out to determine vitamin D status of a cohort of Māori and non-Māori octogenarians, residing in the central North Island of New Zealand. Similar data from octogenarians, are relatively rare compared to slightly younger cohorts, and almost non-existent for Māori.

Overall, levels here are 20 nmol/L higher than those reported previously in older adults in New Zealand<sup>8,10</sup> and the UK.<sup>11</sup> Mean levels of 25(OH)D of 43 nmol/L for women and 55 nmol/L for men in those  $\geq 65$  years were observed in New Zealand in the 1997 National Nutrition Survey;<sup>10</sup> 51 nmol/L in postmenopausal women aged 74 $\pm$ 4 years (mean $\pm$ SD) living in the greater Auckland region;<sup>8</sup> and levels of 52 nmol/L in 50-64 year olds in the UK.<sup>11</sup> In fact, the higher levels (72 nmol/L for seasonally-adjusted levels) in the present study are very similar to levels previously reported from North American surveys: in those  $\geq 60$  years in NHANES III<sup>7</sup> or in 60-79 year olds in Canada.<sup>12</sup> Furthermore, the prevalence of deficiency is low. For those not taking vitamin D supplements, only 11 women and a single man in this group were vitamin D deficient (25(OH)D $<$ 25 nmol/L) and most displayed seasonally-adjusted levels  $>$ 50 nmol/L.

Different assay use or uneven distribution of measurements throughout the year may explain differences in vitamin D status between surveys. Assay inconsistency may explain, in part, the difference in 25(OH)D levels reported between the 1997 survey,<sup>10</sup> derived from Diasorin radioimmunoassay and the current study, which reports HPLC-MS assay data. Whilst past studies indicate that Diasorin RIA results are comparable to LC-MS assays,<sup>13,41</sup> differences of the magnitude reported here cannot be entirely discounted.

Our data show that vitamin D supplementation limited seasonal fluctuation in this cohort. Longitudinal seasonal variation in 25(OH)D levels has previously been demonstrated in older people,<sup>42,43</sup> particularly those with low oral vitamin D intakes.<sup>44</sup> In the present study, we failed to show significant annual variation in women not on vitamin D. This is in contrast to past differences between summer peak and winter nadir of between 25 and 28 nmol/L that have been shown cross-sectionally in older women in Auckland (37°S)<sup>8</sup> and Southeastern Australia (38-39°S),<sup>45</sup> when those taking high-dose vitamin D supplements were excluded. In line with our findings of seasonal variation in men's 25(OH)D levels, an Auckland study showed large peak – nadir differences of 40 nmol/L in men aged  $\geq 40$  years.<sup>23</sup> and a more recent study without this exclusion criterion reported seasonal differences of only 16 nmol/L, in independently-living Australian men aged  $\geq 70$  years.<sup>24</sup>

Of note, we have reported that several participants had high levels of 25(OH)D. Because skin production of vitamin D is self-limiting,<sup>46</sup> it seems likely that these levels resulted from over-supplementation, possibly caused by the use of multiple vitamin-D-containing products or because

the practice of prescribing infrequent high-dose vitamin D may not have been apparent from the study assessment.

### *Generalisability of findings*

Several factors may have resulted in over-estimation of 25(OH)D levels in this study, compared to all those eligible or to the wider population of octogenarians. Firstly, it is possible that those not agreeing to take part in the study or provide blood samples differed in vitamin D status from those agreeing. Blood samples were obtained in 35% of all people eligible for the study according to the electoral roll. Furthermore, those agreeing to provide blood reported less difficulty with performing daily living tasks independently, and were younger, leaner, and more active than those not providing blood, and thus may also have had greater exposure to outdoor sunlight and higher 25(OH)D concentration than the population at large. While it is not possible to estimate the effect size of this response bias on reported vitamin D status, the response rate here is higher than the effective response rate of  $\approx 23\%$  for New Zealanders  $\geq 65$  years in the 1997 survey, from whom mean 25(OH)D concentrations around 20 nmol/L lower were reported.<sup>10</sup> Secondly, these Central North Island regions of New Zealand are sunny areas and people residing here might be expected to have higher than average vitamin D status.

In contrast to the possibility of over-estimation, the over-sampling of Māori versus non-Māori people in this study might underestimate 25(OH)D, since levels in Māori were lower than in non-Māori. A broader age range of Māori compared to non-Māori, was recruited to ensure comparable numbers, given a large ethnic disparity in longevity.<sup>33</sup> Seasonally-adjusted 25(OH)D in Māori was 16 nmol/L lower than in the combined cohort.

### *Vitamin D status in Māori*

Lower levels of 25(OH)D have been previously reported in Māori compared to non-Māori<sup>10,47,48</sup> and a higher incidence of deficiency (levels  $<$ 25 nmol/L) noted in Māori living in a low socio-economic urban area.<sup>49</sup> Scragg et al<sup>47</sup> randomly selected 390 people from a large survey of workers aged 40 to 64 years. Levels of 25(OH)D in those describing their ethnicity as other than Māori or Pacific Island were 7 nmol/L higher than in those identifying as Māori, and 10 nmol/L higher than Pacific Islanders. Vitamin D status data from two National nutritional surveys of adults  $\geq 15$  years old, conducted in 1997 and 2008 also showed levels in Māori to average approximately 8 nmol/L<sup>10</sup> and 3 nmol/L<sup>48</sup> lower than in non-Māori respectively. Unique to the present study are vitamin D data from a sizable sample of Māori who have lived into their 80s. Here, disparity in seasonally-adjusted 25(OH)D levels between Māori and non-Māori participants was much greater than in previous studies, at approximately 16 nmol/L. Ethnicity, but not deprivation index, was independently predictive of levels in regression models.

The reasons for the large ethnic differences noted here are not completely clear. Previous studies have attributed lower levels of 25(OH)D in Māori compared to non-Māori to darker skin tone;<sup>47</sup> higher melanin concentration blocks ultraviolet-dependent conversion of 7-dehydrocholesterol to pre-vitamin D.<sup>29</sup> Skin tone amongst those identifying as Māori in New Zealand varies widely, and more recent



data suggest that neither natural skin colour (of the upper, inner arm),<sup>50</sup> self-reported skin type,<sup>51</sup> nor skin reflectance<sup>52</sup> are associated with vitamin D status in New Zealand populations. In addition to skin reflectance, McKenzie et al<sup>52</sup> assessed the effect of body mass index, gender and ethnicity on 25(OH)D response to a standard full-body dose of artificial ultraviolet radiation in 201 volunteers from Auckland and Dunedin, New Zealand. Of these independent variables, only ethnicity (categorised as European, Māori, Pacific or Asian) significantly predicted changes in 25(OH)D. Somewhat paradoxically, Māori recorded the greatest change in 25(OH)D levels and calculated sensitivity relative to ultraviolet dose, 1.8x higher than for Europeans. Potentially, whatever the underlying cause of lower vitamin D status in Māori applies across a broad age range and accumulates with advanced years.

In some population studies, age has been shown to be inversely related to 25(OH)D levels,<sup>8,10</sup> with declines in levels particularly at ages >80 years, and in women more than men.<sup>23</sup> Age was not a significant predictor of vitamin D status in the present study. In any case, age differences would not explain differences in vitamin D status with ethnicity reported here since Māori, being on average 3 years younger than non-Māori because of the different inclusion criteria, would be expected to have had higher, not lower levels of 25(OH)D. In addition, Māori indicated greater functional independence, with higher ADL score and grip strength, also ordinarily connected with higher, rather than lower, levels of 25(OH)D in elderly.<sup>8,23</sup> One possible reason for the larger difference in vitamin D status with ethnicity reported here might be changing societal attitudes over recent years regarding self-perception of Māori ethnicity. It is possible that these changing attitudes may have resulted in a broader cross-section of people identifying as Māori and thus a reduction in ethnic differences in vitamin D status. This effect might be greater for younger age-groups than for people in their 80s.

Although 25(OH)D levels were lower in Māori than non-Māori, only 2.9% of Māori were vitamin D deficient (<25 nmol/L) and 21% insufficient (<50 nmol/L), compared to 1.7% and 16% of non-Māori. The skeletal and other health consequences of this are unclear, particularly for Māori. There is substantial uncertainty about optimal levels of 25(OH)D. Whilst some in the field argue strongly in favour of minimum reference levels of 75-80 nmol/L,<sup>53-55</sup> others have questioned the reliance for these conclusions on observational data and maintain that sufficient evidence justifies only a minimum reference level of 50 nmol/L.<sup>56-58</sup> Moreover, it is not clear whether the effect of 25(OH)D on skeletal health is consistent across different ethnic groups. Two studies have demonstrated paradoxical inverse associations between 25(OH)D and indices of bone morphology and strength in older men,<sup>59</sup> and fracture risk in older women of African American descent.<sup>60</sup> A recent study has also identified lower levels of vitamin D binding protein in older black Americans, suggesting that lower serum 25(OH)D may have less effect on bioavailability than in white counterparts.<sup>61</sup> In New Zealand, fracture rates are lower for Māori than non-Māori,<sup>62</sup> despite these apparent differences in vitamin D status.

### **Determinants of vitamin D status**

Vitamin D supplement use was the strongest determinant of 25(OH)D levels and prevalence of vitamin D supplement use was an important reason for differences in vitamin D status between Māori and non-Māori. With correction for other predictors, those taking supplements had 25(OH)D levels 27-30 nmol/L higher than those not. Furthermore, there were no differences between Māori and non-Māori in 25(OH)D levels or insufficiency prevalence for those taking vitamin D supplements. Nonetheless, in models containing supplement use, Māori ethnicity still independently explained variance in 25(OH)D levels, with Māori being 10-12 nmol/L lower than non-Māori when other variables were accounted for in the model. Thus, it appears that approximately a third of the difference between Māori and non-Māori is due to differences in vitamin D supplement use. Shea et al<sup>63</sup> also note the importance of vitamin D supplementation in vitamin D status of 70-81 year old Americans, particularly in those of African descent. The prevalence of vitamin D supplement use was higher in that study with 34% and 44% of participants of African and Caucasian descent respectively taking vitamin D, compared to 7% and 25% of Māori and non-Māori participants in the current study.

In agreement with some past studies of older people,<sup>21,23</sup> we found that men have higher 25(OH)D levels than women when adjusted for seasonal variation. Physical activity levels, physical health-related QoL, and BMI also predicted 25(OH)D. Predictive effects of physical activity levels<sup>8,22-24</sup> and adiposity indices<sup>8,23,24,26</sup> are in agreement with previous studies investigating determinants of vitamin D status in older men and women. However, in the present study, none of these variables were strong predictors and the associations mainly disappeared when the dependent variable was seasonally-adjusted, or for Māori 80-90 year olds.

### **Conclusion**

In conclusion, these regional data suggest that vitamin D status in octogenarians in New Zealand is higher than comparable studies of older adults conducted 10-15 years ago, and appears to be associated with the use of high-dose oral vitamin D preparations. In this group measures such as physical activity, body composition and quality of life, were not strongly predictive of vitamin D status adjusted for the time-of-year of measurement. Data arising from analysis of human tissue, including blood, is particularly scarce for Māori. Our data address this lack and show that levels of 25(OH)D in Māori are substantially lower than in non-Māori, with around a third of the difference explained by higher prevalence of vitamin D supplement use amongst non-Māori. Despite this difference, vitamin D status of both Māori and non-Māori octogenarians is relatively high, even for those not on vitamin D. Whilst the health implications of these levels are not clear from cross-sectional data, our data show common use of high-dose vitamin D preparations in people aged in their 80s, much of which may be obtained over-the-counter, and health practitioners should enquire about supplement use before considering vitamin D prescription.

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## AUTHOR DISCLOSURES

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## Original Article

## Vitamin D status of Māori and non-Māori octogenarians in New Zealand: a Cohort Study (LiLACS NZ)

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### 新西兰毛利族和非毛利族八旬老人维生素 D 状况：一项队列研究

**背景与目的：**本研究评估了队列研究中生活在新西兰湾和湖泊区域的八旬老人的维生素 D 状况及其决定因素。**方法与研究设计：**测量 209 名毛利人（80-90 岁）和 357 名非毛利人（85 岁）的血清 25-羟维生素 D（25(OH)D）的浓度，同时收集研究对象的体格测量指标、生活方式、补充剂的应用和其它健康资料。**结果：**平均 25(OH)D 浓度为 69（95% CI：67-72）nmol/L，其中 15% 的研究对象 >100 nmol/L，6 个研究对象 >150 nmol/L。毛利人的 25(OH)D 浓度（59 nmol/L，95% CI: 55-62 nmol/L）低于非毛利人（75 nmol/L，95% CI：72-78 nmol/L， $p < 0.001$ ），校正测量日期后，差异仍然存在。98 名（占 18%）研究对象报告补充了维生素 D，女性中补充者所占的比例（24%）高于男性（11%， $p < 0.001$ ），非毛利人中补充者所占的比例高于毛利人。补充维生素 D 的人中，49% 的人摄入高剂量（每天  $\geq 25 \mu\text{g}$  或相当剂量），5 个研究对象每天摄入维生素 D  $\geq 50 \mu\text{g}$ 。维生素 D 补充剂的应用能够强而独立地预测季节校正的 25(OH)D 浓度，并且使用者比不用者高 28 nmol/L。其它预测指标包括毛利族（比非毛利族低 10 nmol/L）和女性性别（比男性低 11 nmol/L）。**结论：**新西兰八旬老人维生素 D 浓度高于以前的报告，尤其是非毛利人。这个人群中处方和非处方口服维生素 D 补充剂普遍存在，并且是维生素状态的强预测指标。

**关键词：**骨化醇、季节变化、民族、年龄在 80 岁及其以上、老年人