The prevalence of aortic stenosis in Māori undergoing clinically indicated echocardiography compared to New Zealand Europeans

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ABSTRACT

AIM: There are limited data on the prevalence of calcific aortic valve disease (CAVD) in Māori and known inequities in outcomes after aortic valve intervention. Our study aimed to investigate the prevalence of CAVD in Māori.

METHODS: Data from initial clinically indicated echocardiograms performed between 2010 to 2018 in patients aged ≥18 years were linked to nationally collected outcome data. Ethnicity was defined using protocols from the Ministry of Health.

RESULTS: Of the 23,635 patients, 1,312 (5.6%) identified as Māori, and 22,323 (94.4%) as European. Prevalence of aortic stenosis was 5.3% in Māori and 9.9% in Europeans. Age-specific prevalence did not differ between the two groups. Māori with CAVD were more than twice as likely to have advanced cardiac impairment (right ventricular dysfunction) than Europeans (10.1% vs 4.6, p<0.001).

CONCLUSIONS: Age-specific CAVD rates did not differ between Māori and Europeans, though Māori had a higher proportion of advanced cardiac impairment, which is likely unrelated to CAVD. Differences in population structure likely explain the difference in overall prevalence of CAVD. The improving life expectancy in Māori may lead to increasing incidence of CAVD, thus strategies to improve detection and medical management of CAVD should begin as soon as possible.

Calcific aortic valve disease (CAVD) consists of a spectrum of abnormalities, from thickening and calcification of the valve without haemodynamic significance (aortic sclerosis [ASc]) to calcification of the leaflets and reduction in valve opening (aortic stenosis [AS]) resulting in increased left ventricular afterload. AS affects over 9 million people world-wide, with age being a key risk factor for CAVD, alongside other markers of general cardiovascular risk including diabetes, dyslipidaemia and hypertension.[1–4] Variants in certain genes have also been associated with CAVD,[5,6] but while there has been significant progress in understanding the pathobiology of the disease and interventional treatment of severe disease, there have been no advances in medical therapies.[7–9]

The most recent data for the prevalence of CAVD in New Zealand came from the National Health Committee in 2014, which found that Māori had a lower age-standardised prevalence of severe CAVD compared to non-Māori.[10] There are currently no peer-reviewed publications examining the prevalence or incidence of CAVD in Māori. Recent work found markedly worse outcomes for Māori following treatment for severe CAVD, with Māori patients having significantly reduced survival following both transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (SAVR) compared to Europeans, despite being significantly younger.[11,12]

Thus, we sought to investigate the prevalence and significance of CAVD in Māori undergoing clinically indicated echocardiography to provide information to researchers and clinicians.

Methods

Study cohort and approval

The study cohort for this retrospective study consisted of all patients over 18 years old who underwent clinically indicated echocardiography at Dunedin Hospital or Invercargill Hospital over a 9-year period between 1 January 2010 and 31 December 2018. Consultation with Māori was undertaken with the Ngāi Tahu Research Consultation Committee, and ethical approval was granted by the New Zealand Central Health

and Disability Ethics Committee (ref: 21/CEN/15). Locality approval was provided by Health New Zealand – Te Whatu Ora Southern.

Collection and cleaning of echocardiographic data

Data were stored in the syngo Dynamics echocardiographic picture archiving and communication system (PACS) (version VA20F, Siemens Healthineers, Erlangen, Germany), and extracted using the syngo Dynamics Data Miner. Subsequent studies on the same patient and any studies with missing CAVD status (n=1,323) were excluded, leading to an initial cohort size of 24,699. Of these, 23,635 identified as either Māori or European. Details of data extraction, cleaning, comprehensive variable definitions and non-ethnicity stratified outcomes are described in detail elsewhere.[13,14] Categorical variables, including CAVD status, were defined using tailored functions that analysed free-text fields for relevant phrases. CAVD classification was hence based on the reading cardiologist's clinical description in the echocardiography report. Mild-to-moderate and moderate-to-severe stenosis were coded as mild and moderate disease, respectively. Patients who had undergone previous SAVR or TAVI were described separately. When aggregating CAVD severity, those who had undergone aortic valve implantation (AVI) were included in the AS category.

Determination of extravalvular cardiac impairment

In order to further identify differences in CAVD phenotype, patients were categorised into CAVD stages using a previously developed staging system based on extravalvular cardiac impairment.[15] For clarity in this manuscript, "impairment" refers to this staging system, whereas "severity" refers to the common clinical understanding of mild, moderate and severe stenosis. While CAVD is not necessarily the cause of any identified extravalvular impairment, especially at lower levels of CAVD severity, higher stages of disease have been shown to be good predictors of prognosis in patients with CAVD.[16,17] Left ventricular (LV) mass was calculated using the Devereux formula. Body surface area was frequently not available in our dataset, so the upper limits of the normal range of absolute LV mass were used.[18] Similarly, E/e', a surrogate measure of mean left atrial pressure, is not measured in those with significant mitral valvular disease, mitral annular calcification, arrhythmia or other settings where E/e' is known to be inaccurate, and hence was assumed to be abnormal if it was not recorded.[19]

- Stage 0: No extravalvular cardiac impairment
- Stage 1: LV mass >224 (male) or >162 (female), E/e' >14 or not measured, or left ventricular ejection fraction <40%
- Stage 2: Moderately or worse dilated left atrium, atrial fibrillation, or moderate or worse mitral regurgitation
- Stage 3: Right ventricular systolic pressure >60mmHg, or moderate or worse tricuspid regurgitation
- Stage 4: Moderately or worse impaired right ventricular systolic function

Data validation

To investigate the accuracy of Data Miner output, 100 studies were randomly selected, with the dataset categorisation compared to the final echocardiography report. This revealed excellent agreement.[13]

Statistical analysis

All analysis was performed on a de-identified dataset with National Health Index numbers replaced by anonymous identifiers. Continuous data are expressed as mean (standard deviation) if normally distributed, and otherwise as median (interquartile range). Data were analysed using the Mann–Whitney U-test if continuous and non-normally distributed, and with ANOVA if normally distributed. Categorical variables were analysed using the Chi-squared test. All analyses, including data cleaning, were performed using RStudio with R version 3.6.3.[20–22] Age standardisation was performed using the RStudio package epitools.[23]

Results

Of the 23,635 people in the cohort, 1,312 (5.6%) identified as Māori, and 22,323 (94.4%) were European (Table 1). Māori were significantly younger than European patients (55.4 years vs 64.9 years, p<0.001), but the sex distribution was not significantly different between the two ethnicities (p=0.64). The proportion of bicuspid aortic valve disease appeared similar in both ethnicities (1.3% vs 1.6%).

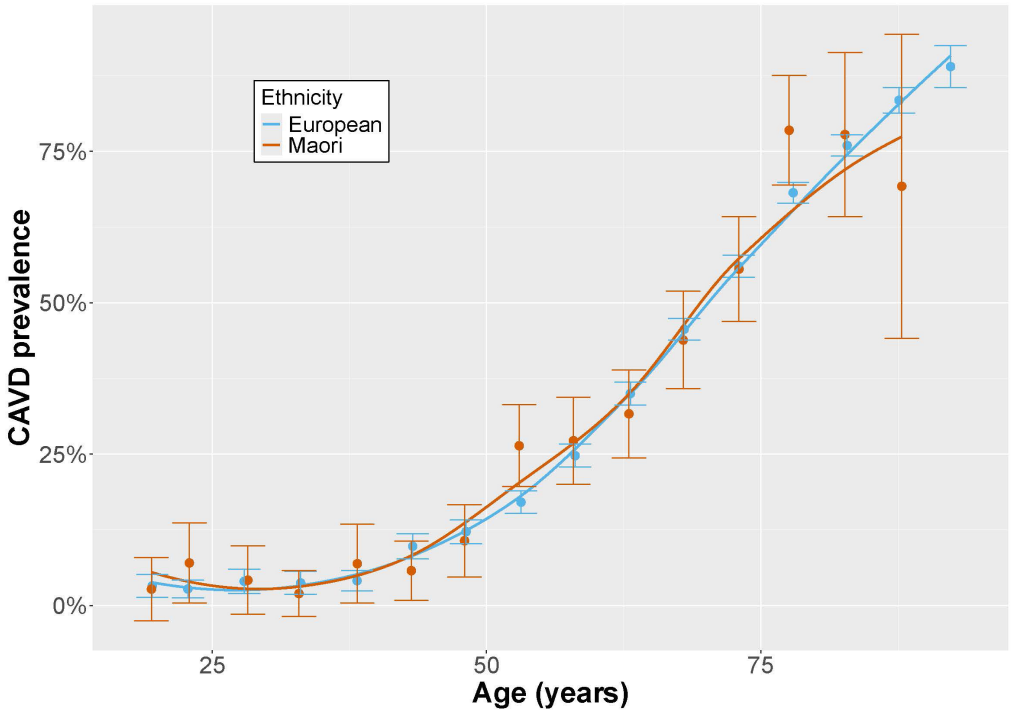
The proportion of any CAVD increased markedly with age. It was present in 50% of 70-year-olds

Table 1: Cohort characteristics.

	Overall (N=23,635)	**Māori (N=1,312)**	**European (N=22,323)**
Age (years)			
Mean (SD)	64.40 (16.70)	55.40 (16.70)	64.90 (16.60)
Sex			
Female	11,027 (46.7)	621 (47.3)	10,406 (46.6)
Male	12,608 (53.3)	691 (52.7)	11,917 (53.4)
Aortic valve maximum velocity (m/s)			
Mean (SD)	1.47 (0.87)	1.32 (0.69)	1.47 (0.88)
Not reported	2,374 (11.2)	134 (11.4)	2,240 (11.2)
CAVD severity			
No CAVD	13,464 (57.0)	915 (69.7)	12,549 (56.2)
Sclerosis	7,839 (33.2)	327 (24.9)	7,512 (33.7)
Mild	895 (3.8)	25 (1.9)	870 (3.9)
Moderate	522 (2.2)	16 (1.2)	506 (2.3)
Severe	370 (1.6)	8 (0.6)	362 (1.6)
AVI	545 (2.3)	21 (1.6)	524 (2.3)
Mitral annular calcification			
Yes	3,302 (14.0)	108 (8.2)	3,194 (14.3)
No	19,988 (84.6)	1,186 (90.4)	18,802 (84.2)
Not reported	345 (1.5)	18 (1.4)	327 (1.5)
Bicuspid aortic valve			
Yes	311 (1.3)	21 (1.6)	290 (1.3)
No	23,324 (98.7)	1,291 (98.4)	22,033 (98.7)

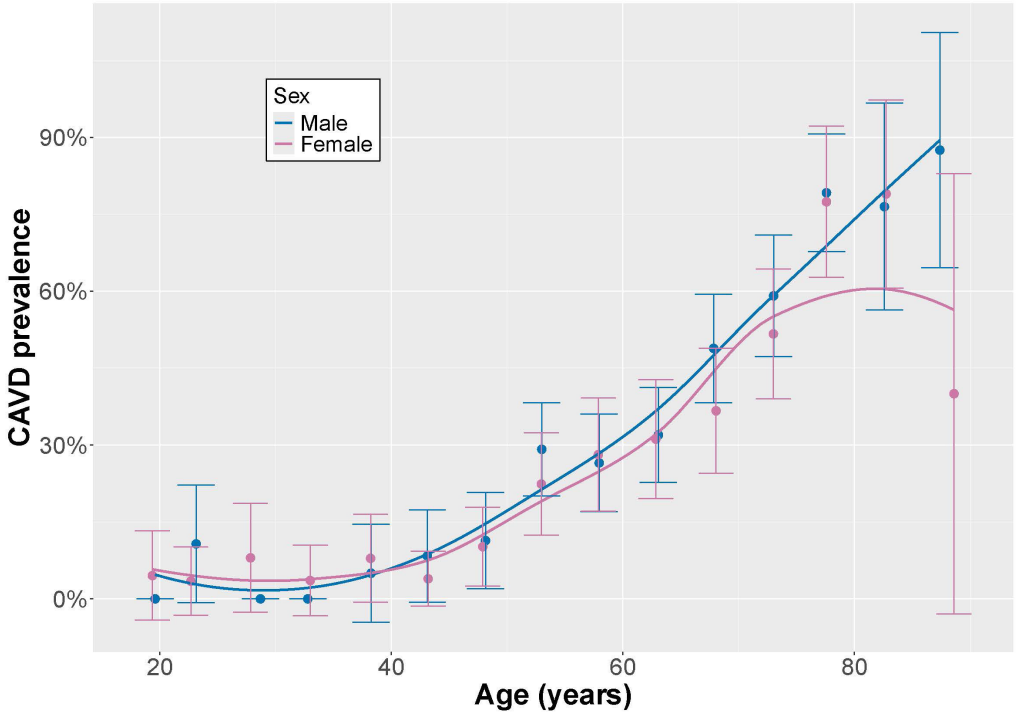
SD = standard deviation; CAVD = calcific aortic valve disease; AVI = aortic valve intervention.

Figure 1: Age-related prevalence of calcific aortic valve disease stratified by ethnicity in patients undergoing clinically indicated echocardiography.



Points are the proportion within each 5-year age band and the average age within each band. Error bars represent 95% confidence intervals. The plotted curve was fitted using locally weighed smoothing (LOESS regression function).

Figure 2: Age-related prevalence of calcific aortic valve disease in Māori, stratified by sex.



Points are the proportion within each 5-year age band and the average age within each band. Error bars represent 95% confidence intervals. The plotted curve was fitted using locally weighed smoothing (LOESS regression function).

Table 2: Proportion of Māori and Europeans with different severity of CAVD.

	Māori (n=1,313)	European (n=22,323)	Corrected p-value
Aortic sclerosis	327 (24.9)	7,512 (33.7)	<0.001
Aortic stenosis	70 (5.3)	2,262 (10.1)	<0.001
Any CAVD	397 (30.2)	9,774 (43.8)	<0.001

Cell values are expressed in n (%) and P determined using a two-sided Z-test (with Bonferroni correction for multiple testing).
CAVD = calcific aortic valve disease.

Table 3: Age-standardised rates per 100,000 of CAVD by ethnicity with 95% confidence intervals in patients undergoing clinically indicated echocardiography.

	Māori	European
Aortic sclerosis	9,100 (7,700–11,300)	7,900 (7,600–8,300)
Aortic stenosis	2,100 (1,500–3,600)	2,600 (2,400–3,000)
Any CAVD	11,200 (9,700–13,400)	10,600 (10,100–11,100)

CAVD = calcific aortic valve disease.

in the cohort (Figure 1). Across all age brackets, CAVD prevalence did not appear to differ between Māori and Europeans. Similarly, the prevalence of CAVD in Māori did not differ by sex (Figure 2). However, the overall prevalence of CAVD, AS and ASc were all significantly lower in Māori than in Europeans (Table 2).

In order to identify the effect of underlying age distributions, the prevalence of ASc, AS and any CAVD was age standardised using the World Health Organization standard population (Table 3). Rates of age-standardised CAVD were not different between the two ethnicities.

Rates of specific comorbid pathologies of the heart and surrounding structures in those with any CAVD are presented in Table 4. Using a previously developed staging system for extra-valvular cardiac impairment, patients were categorised into stages (Table 5). Notably, Māori had twice the proportion of stage 4 impairment compared with Europeans (10.1% vs 4.6%, p<0.001), and a slightly reduced proportion of stage 1 impairment (49.7% vs 55.7% in Europeans, p<0.01). Rates of stage 0, 2 and 3 impairment were similar between the two ethnicities.

Discussion

In this large descriptive study of over 20,000 patients undergoing clinically indicated echocardiography, including 1,313 Māori patients, overall rates of CAVD were lower in Māori than in Europeans (30.2% vs 40.3%). Age-unadjusted prevalence of AS in Europeans was almost double that in Māori (9.9% vs 5.3%). However, when age standardised, prevalence of CAVD was similar between the two groups (11.2 per 1,000 in Māori vs 10.6 per 1,000 in Europeans). There did not appear to be sex-related differences in CAVD in Māori.

Recent epidemiological data on the rate of CAVD in Māori are limited. The National Health Committee's review of AS in New Zealand, published in 2014, found that Māori had a lower age-standardised prevalence of severe AS than non-Māori.[10] This is concordant with our non-adjusted data, noting that low numbers prevented accurate age-standardisation for severe AS on its own. Comparisons with international data can be challenging. This is because routinely acquired data (such as hospital discharges) often only report clinically significant, usually severe, AS, and because the age groups studied and definitions of CAVD used can differ between reports. A 2013 meta-analysis found a pooled AS prevalence of 12.4% in those over 75 years old, which is similar to the overall rate in Europeans in our cohort, but over double that of Māori.[1] International evidence shows that CAVD is less

Table 4: Rate of comorbid pathologies of the heart and surrounding structures in those with any CAVD (sclerosis or aortic stenosis).

	Māori (N=397)	European (N=9,774)	Overall (N=10,171)
Left ventricular systolic dysfunction			
Normal	258 (65.0%)	6,725 (68.8%)	6,983 (68.7%)
Hyperdynamic	3 (0.8%)	150 (1.5%)	153 (1.5%)
Mild	37 (9.3%)	1,026 (10.5%)	1,063 (10.5%)
Moderate	21 (5.3%)	637 (6.5%)	658 (6.5%)
Severe	25 (6.3%)	424 (4.3%)	449 (4.4%)
Not reported	53 (13.4%)	812 (8.3%)	865 (8.5%)
Right ventricular systolic dysfunction			
Normal	268 (67.5%)	7,739 (79.2%)	8,007 (78.7%)
Hyperdynamic	0 (0%)	13 (0.1%)	13 (0.1%)
Mild	56 (14.1%)	767 (7.8%)	823 (8.1%)
Moderate	27 (6.8%)	328 (3.4%)	355 (3.5%)
Severe	15 (3.8%)	112 (1.1%)	127 (1.2%)
Not reported	31 (7.8%)	815 (8.3%)	846 (8.3%)
Right ventricular systolic pressure ≥25mmHg			
Yes	160 (40.3%)	4,032 (41.3%)	4,192 (41.2%)
No	93 (23.4%)	2,085 (21.3%)	2,178 (21.4%)
Not reported	144 (36.3%)	3,657 (37.4%)	3,801 (37.4%)
Mitral stenosis			
None	375 (94.5%)	9,361 (95.8%)	9,736 (95.7%)
Mild	0 (0%)	57 (0.6%)	57 (0.6%)
Moderate	0 (0%)	17 (0.2%)	17 (0.2%)
Severe	1 (0.3%)	5 (0.1%)	6 (0.1%)
MVR/repair	9 (2.3%)	69 (0.7%)	78 (0.8%)
Rheumatic valve	3 (0.8%)	9 (0.1%)	12 (0.1%)
Not reported	9 (2.3%)	256 (2.6%)	265 (2.6%)
Aortic regurgitation			
None	337 (84.9%)	8,445 (86.4%)	8,782 (86.3%)
Mild	51 (12.8%)	1,213 (12.4%)	1,264 (12.4%)

Table 4 (continued): Rate of comorbid pathologies of the heart and surrounding structures in those with any CAVD (sclerosis or aortic stenosis).

	Māori (N=397)	European (N=9,774)	Overall (N=10,171)
Moderate	8 (2.0%)	84 (0.9%)	92 (0.9%)
Severe	1 (0.3%)	32 (0.3%)	33 (0.3%)
Mitral regurgitation			
None	261 (65.7%)	6,394 (65.4%)	6,655 (65.4%)
Mild	78 (19.6%)	2,348 (24.0%)	2,426 (23.9%)
Moderate	16 (4.0%)	352 (3.6%)	368 (3.6%)
Severe	9 (2.3%)	73 (0.7%)	82 (0.8%)
Not reported	33 (8.3%)	607 (6.2%)	640 (6.3%)
Pulmonary regurgitation			
None	243 (61.2%)	5,111 (52.3%)	5,354 (52.6%)
Mild	18 (4.5%)	457 (4.7%)	475 (4.7%)
Moderate	0 (0%)	7 (0.1%)	7 (0.1%)
Severe	1 (0.3%)	2 (0.0%)	3 (0.0%)
Not reported	135 (34.0%)	4,197 (42.9%)	4,332 (42.6%)
Tricuspid regurgitation			
None	253 (63.7%)	6,343 (64.9%)	6,596 (64.9%)
Mild	82 (20.7%)	1,899 (19.4%)	1,981 (19.5%)
Moderate	22 (5.5%)	327 (3.3%)	349 (3.4%)
Severe	5 (1.3%)	40 (0.4%)	45 (0.4%)
Not reported	35 (8.8%)	1,165 (11.9%)	1,200 (11.8%)

CAVD = calcific aortic valve disease; MVR = mitral valve replacement.

Table 5: Stage of cardiac impairment in those with any CAVD, stratified by ethnicity.

	Māori (n=376)	European (n=9,250)
Stage 0	53 (14.1)	1,313 (14.2)
Stage 1	187 (49.7)	5,152 (55.7)
Stage 2	86 (22.9)	2,099 (22.7)
Stage 3	12 (3.2)	263 (2.8)
Stage 4	38 (10.1)	423 (4.6)

Cells are formatted as n (%). Chi-squared test: X-squared=25.578, df=4, p<0.001. CAVD = calcific aortic valve disease.

prevalent in certain ethnic groups, with this work primarily occurring in the United States of America (USA). There are limited data on the prevalence of CAVD in Indigenous populations; however, there is literature relating to non-European minority populations. Comparison with this work is useful, as inequities in health outcomes and access to care exist in those nations, and it is therefore important to note if similar or different findings have been made. Prior research has identified that African American patients have a lower prevalence of severe AS when compared to Caucasian patients (0.29% vs 0.91%).[24] This gap in prevalence existed across age bands, which was not observed in our study. A further study of Medicare beneficiaries in the USA found a similar result, with white patients having a higher overall prevalence of AS compared to Black, Hispanic or Asian/North American Native patients.[25] However, they also found that outcomes of all-cause hospitalisation, heart failure hospitalisation and 1-year mortality were significantly worse for Black patients than white patients. Unfortunately, a similar trend has been observed in New Zealand when examining outcomes following both TAVI and SAVR: Māori have significantly worse survival than Europeans (80.1% vs 93.9%), despite being over a decade younger at the time of TAVI (67.9 vs 80.6 years),[11] and worse survival even at 30 days post-SAVR.[12]

Certain key comorbidities were examined to determine if there were differences in cardiac impairment, outside the degree of stenosis. We applied a previously described staging criteria, based on the degree of cardiac impairment, to those with CAVD.[15] Strikingly, Māori were more than twice as likely to have stage 4 impairment compared with Europeans (10.1% vs 4.6, $p<0.001$). This finding suggests that although Māori have similar rates of CAVD to Europeans of the same age, their overall burden of cardiac impairment is significantly greater. The cardiac impairment is not likely to be directly related to CAVD in the majority of patients—there is no direct causal explanation for how ASc or mild AS, for example, would lead to right ventricular dysfunction. However, more advanced cardiac impairment is likely to impact on future mortality, as well as make subsequent valve intervention a higher-risk procedure. This may, for example, make less invasive approaches such as TAVI more appropriate in the setting of significant extravalvular cardiac impairment. In addition, earlier detection of extravalvular cardiac impairment will allow earlier management of this prior to any requirement for valvular intervention.

To our knowledge, this is the first large study to examine prevalence of CAVD in Māori undergoing clinically indicated echocardiography. A particular strength of our study is not just in its numbers, but in the availability of other echocardiographic information that allows us to further characterise the structural aspects of the heart. Several limitations to our study exist. For instance, we do not have information available on other cardiovascular risk factors, such as hypertension and diabetes, which are known to be associated with CAVD and are more prevalent in Māori.[2,26,27] Secondly, our study population might not be generalisable to all Māori in New Zealand, as the study locale was entirely in the lower South Island. It was also restricted to patients that were referred and received clinically indicated echocardiography and thus cannot explore the true population prevalence of CAVD. There may be a referral or access bias to echocardiography. Māori are more likely to live in remote and rural locations and may have limited access to healthcare overall,[28] so the numbers noted here may well be an under-estimate. Exploratory analyses revealed that there would be insufficient statistical power to draw valid inferences around outcomes following diagnosis of CAVD, and hence further longitudinal analysis was not performed.

In summary, there are similar age-specific rates of CAVD in Māori and Europeans, but with Māori having a higher proportion of more advanced cardiac impairment. The lower non-adjusted prevalence of CAVD in Māori is due to the different population structure, with lower life expectancy in Māori, rather than any apparent difference in prevalence at any specific point over the lifespan. As such, the lower non-adjusted prevalence is likely another representation of the health inequity faced by Māori—in short, we do not see as much CAVD in Māori because Māori do not live long enough to get it.

In the future, the improving life expectancy in Māori may well lead to increasing incidence of CAVD. The higher proportion of cardiac impairment means that attempts to improve detection through access to echocardiography, and, ideally, medical management of both the valve disease and associated cardiac impairment, should begin as soon as possible.

COMPETING INTERESTS
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