Is the Framingham coronary heart disease absolute risk function applicable to Aboriginal people?

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ABSTRACT

Objective: To determine the extent to which the Framingham function predicts the risk of coronary heart disease (CHD) in Aboriginal people.

Design and setting: Cohort study in an Aboriginal community in the Northern Territory.

Participants: 687 Aboriginal people aged 20–74 years were followed up from a baseline examination in 1992–1995 through to 31 December 2003.

Main outcome measure: First CHD events were identified through hospital and death records during the follow-up period.

Methods: An original Framingham function was used to predict CHD risk according to the duration of follow-up and the values of traditional risk factors, which included age, sex, total cholesterol level, high-density lipoprotein (HDL) cholesterol level, blood pressure, the presence of diabetes, and smoking status. The predicted CHD incidence using the Framingham function was 4.4 per 1000 person-years, while the observed incidence was 11.0 (95% CI, 8.7–13.9) per 1000 person-years. The observed number of CHD events (68) was 2.5 times the number predicted (27) using the Framingham function. The observed incidence was about four and three times the predicted incidence for age groups < 35 and 35–44 years, respectively, and about twice the predicted incidence for those over 45 years of age. The Framingham function was a particularly unreliable predictor for women, especially younger women, in whom the observed CHD rate was 30 times the predicted rate.

Conclusions: The Framingham function substantially underestimates the actual risk of CHD observed in Aboriginal people in a remote community, especially for women and younger adults. This implies that traditional risk factors have different degrees of impact and/or that other factors are contributing to risk. A population-specific risk function is needed.

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Aboriginal people have a high mortality rate from coronary heart disease (CHD).[1] An understanding of its pathogenesis is critical to primary prevention at the population level, as well as to the appropriate management of high-risk individuals. Clinical guidelines recommend that the intensity of preventive treatment for CHD be based on the assessment of absolute risk level for individual patients.[2-4] Multiple variable risk prediction equations have been developed to estimate CHD risk, with those derived from the Framingham Heart Study most commonly recommended.[2,4,5] The Framingham equations predict CHD risk well in white American and African American adults, but not as well in Japanese American, Hispanic men and Native American women, in all of whom the risk of 5-year CHD events was systematically overestimated.[6,7] Those equations also overestimate the CHD risk for some European populations,[8-12] but underestimate the risk for South Asians in the United Kingdom.[13]

Australian lipid management guidelines[3] define absolute risk using the New Zealand cardiovascular disease absolute risk charts,[14] which were derived from Framingham data.[15] The performance of Framingham risk scores for predicting CHD death has been assessed in a non-Aboriginal Australian sample in Western Australia. Considerable differences were found in relative risks for some CHD risk factors, such as systolic blood pressure and smoking, although it was concluded that the use of Framingham risk scores would not be misleading in white Australian populations.[16]

It remains unclear whether the Framingham equations can accurately predict CHD risk in Aboriginal Australians. Using cohort data with a 10-year follow-up, we assessed the ability of the Framingham risk equation to predict coronary events in Aboriginal people living in a remote region of the Northern Territory.

METHODS

Participants and measurements

From 1992 to 1995, a community-wide screening program for renal disease was conducted in a remote region of the Northern Territory. It involved 897 adults (more than 80% of the adult population in the Aboriginal community) aged 20–74 years. The traditional risk factors used in the Framingham equation,[15,17] including age, sex, systolic blood pressure, cholesterol level, high-density lipoprotein cholesterol level, diabetes status and cigarette smoking, were measured during the baseline examination. ECG-LVH (left ventricular hypertrophy by electrocardiography) status was not collected.

All participants were followed up to 31 December 2003. During the follow-up period, CHD events, including myocardial infarction, angina pectoris and other ischaemic heart disease, were identified through hospital and death records using codes of the *International classification of diseases* (*ICD 9-CM* codes 410–414, and *ICD 10-AM* codes I20–I25). Only the first-ever CHD incidents (fatal or non-fatal) were included in the analysis. For those participants who reached a CHD event endpoint during follow-up, their follow-up time was the time from the date of their initial screening visit to the date of the first CHD event. Those who did not reach an endpoint were censored at 31 December 2003.

Eight participants were excluded because their hospital records showed pre-existing CHD events. CHD risk could not be estimated using the Framingham function in

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1 Framingham equations for coronary heart disease (CHD) risk

Equation 1 $$\mu = \Sigma \beta_i x_i$$

Equation 2 $$\sigma = e^{\theta_0 + \theta_1}$$

Equation 3 $$u = \frac{\log(t) - \mu}{\sigma}$$

Equation 4 $$p = 1 - e^{-e^{u}}$$

x_i are risk factors (eg, blood pressure or age) and β_i, θ_0 and θ_1 are coefficients estimated from the Framingham study;[17] t is the time of follow-up, and p is the predicted probability of CHD by time, t.

202 participants because data for their baseline risk factors were not complete. The final analysis included 687 participants who were free from CHD at baseline and had a complete set of data for baseline risk factors.

Analysis

Follow-up data were partitioned into four age groups: < 35, 35–44, 45–54 and ⩾ 55 years. For individuals who were in two age groups during the follow-up period, the proportions of follow-up time were assigned to the two age groups using the method described by Clayton and Hills.[18] Predicted CHD risk was estimated using the Framingham equations (Box 1).[15,17] Parameters βi, θ_0, and θ_1 in the equations had been estimated using a Weibull accelerated failure time model.[17] The CHD outcomes in the Framingham equations included myocardial infarction, death from CHD, angina pectoris and coronary insufficiency.[15] The original Framingham equations were presented in two forms: systolic blood pressure (SBP) and diastolic blood pressure equations. Although, in general, the results are similar, the equation incorporating SBP is recommended, because SBP is more accurately determined, has a wider range of values and is a stronger predictor in the Framingham study.[17] As our study did not collect ECG-LVH status, two sets of predictions were calculated, using two different assumptions: that the prevalence of ECG-LVH in the study participants was (i) similar to that of the Framingham population, or (ii) 10 times that of the Framingham population (to obtain conservative predicted values).

According to baseline values of risk factors and the duration of follow-up, risk probability for CHD was estimated for each participant using the Framingham equation. The predicted numbers of CHD events and incidence rates per 1000 person-years according to sex and age group were estimated based on individuals' risk probabilities. The observed CHD rates and their 95% CIs were calculated and compared with the predicted values. All analyses were performed using Stata 8.2 software.[19]

Ethics approval

The project was approved by the Behavioural and Social Science Ethical Review Committee of the University of Queensland, the Human Research Ethics Committee of the Northern Territory Department of Health and Community Services and Menzies School of Health Research and the community health board.

RESULTS

Among 889 participants who were free from CHD at baseline and who were followed up for a total of 7535 person-years, 92 participants developed at least one CHD event during the follow-up period. Sixty-eight first CHD events occurred among the 687 participants with a complete set of data for risk factors recorded; they had 6188 person-years of follow-up, with an incidence rate of 11.0 (95% CI, 8.7–13.9) per 1000 person-years. Their characteristics are shown in Box 2. Among those 202 participants who were not included for further analysis, the CHD incidence rate was higher — 17.8 (95% CI, 11.9–26.6) per 1000 person-years — than for those whose data were used to assess the Framingham equation.

The predicted numbers of CHD events and rates according to the Framingham function are presented in Box 3. Even under the extreme assumption that the prevalence of ECG-LVH of the study population was 10 times that of the Framingham study, the observed number of total CHD events (68) was 2.5 times the predicted value of 27. The observed incidence rate for the whole study sample (11.0 per 1000 person-years) was 2.5 times the predicted rate of 4.4 per 1000 person-years.

The underestimation of CHD risk by the Framingham function occurred in all age groups. The observed CHD rate was about 4.5 times the predicted rate (3.2 v 0.7) for the youngest age group (< 35 years), and about twice the predicted rate for the older age groups. The differences between expected and observed rates were statistically significant in all age groups for women and for both sexes combined (Box 4, A and B). For men, although expected values were lower than observed (Box 4, C), the difference did not reach statistical significance for older men, possibly because of the small sample size in those subgroups. The Framingham function performed more poorly for Aboriginal women (especially younger women) than for men, as shown in Box 3 and Box 4. The predicted CHD rates were low for women under 35 years (0.1 per 1000 person-years), while the observed rate was about 30 times higher (3.3 per 1000 person-years). For women aged 35–44 years, the observed CHD rate was about six times the predicted rate.

DISCUSSION

The Framingham equation produced substantial underestimates of CHD risk in Aboriginal people. The underestimation occurred in all age–sex groups, and was most marked in women and younger groups.

Our findings are consistent with results from a cross-sectional study on the same population, which suggests that, although the prevalence of CHD risk factors is different from that of the general Australian population,[20] the higher risk may not be fully

2 Characteristics of participants in our study*

	Women	Men
Number	331	356
Age (years)	36.1 (12.5)	32.8 (10.7)
Systolic BP (mmHg)	116.4 (18.7)	125.5 (17.1)
Diastolic BP (mmHg)	71.5 (12.9)	77.7 (13.6)
Total cholesterol level (mmol/L)	4.5 (1.1)	4.9 (1.0)
HDL cholesterol level (mmol/L)	1.0 (0.2)	1.1 (0.2)
Body mass index (kg/m^2)	24.1 (5.7)	23.2 (4.6)
Waist circumference (cm)	91.2 (14.0)	86.9 (13.1)
Number (%) with diabetes	53 (16.0%)	33 (9.3%)
Number (%) of smokers	235 (71.0%)	298 (83.7%)

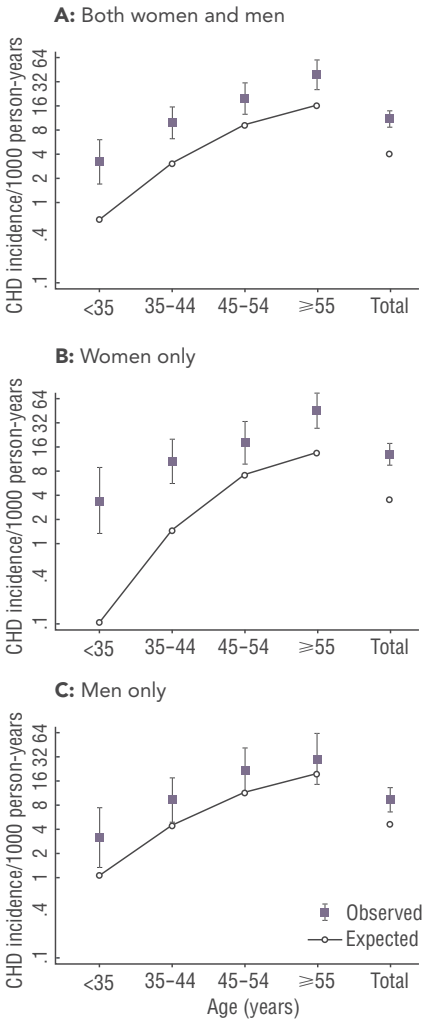
BP = Blood pressure. HDL = High-density lipoprotein. *Figures represent mean (SD) unless otherwise specified.

3 Predicted coronary heart disease (CHD) rates per 1000 person-years, based on the Framingham equation, compared with observed CHD rates in Aboriginal people*

		Expected 1†		Expected 2‡		Observed	
Age (years)	Person-years	Events	Rate	Events	Rate	Events	Rate (95% CI)
Both sexes							
< 35	2822	1.7	0.6	2.0	0.7	9	3.2 (1.7–6.1)
35–44	1827	5.5	3.0	6.2	3.4	18	9.8 (6.2–15.5)
45–54	949	8.6	9.1	9.5	10.0	19	19.7 (12.6–30.9)
⩾ 55	562	8.9	15.8	9.6	17.1	22	39.2 (25.8–59.5)
Total	**6188**	**24.7**	**4.0**	**27.4**	**4.4**	**68**	**11.0 (8.7–13.9)**
Women							
< 35	1197	0.1	0.1	0.1	0.1	4	3.3 (1.3–8.9)
35–44	858	1.3	1.4	1.5	1.6	9	10.5 (5.5–20.2)
45–54	553	4.0	7.1	4.4	8.0	10	18.1 (9.7–33.6)
⩾ 55	329	4.4	13.4	4.8	14.6	15	45.6 (27.5–75.6)
Total	**2936**	**9.7**	**3.4**	**10.7**	**3.7**	**38**	**12.9 (9.4–17.8)**
Men							
< 35	1625	1.6	1.0	1.9	1.2	5	3.1 (1.3–7.4)
35–44	983	4.2	4.3	4.8	4.8	9	9.2 (4.8–17.6)
45–54	411	4.6	11.1	5.1	12.1	9	21.9 (11.4–42.1)
⩾ 55	232	4.5	19.2	4.9	20.5	7	30.1 (14.4–63.2)
Total	**3252**	**15.0**	**4.5**	**16.7**	**5.1**	**30**	**9.2 (6.5–13.2)**

* Expected values were based on the Framingham function, which included age, sex, total cholesterol level, HDL cholesterol level, systolic blood pressure, smoking status, diabetes and ECG-left ventricular hypertrophy. † Assuming the prevalence of the ECG-left ventricular hypertrophy in the study sample was the same as in the Framingham population. ‡ Assuming the prevalence of the ECG-left ventricular hypertrophy was 10 times that of the Framingham population.

4 Expected versus observed coronary heart disease incidence (showing 95% CIs), by age*



* "Expected 1" values in Box 3 were used.

explained by the difference in the prevalence of traditional CHD risk factors. One explanation is that the contributions of traditional CHD risk factors in Aboriginal people might not be the same as those expressed by the Framingham function. People with the same values of risk factors might progress faster toward CHD in the study population. For example, the female "advantage effect" on CHD risk found in other populations does not exist in Aboriginal people.[21] Another explanation is that "non-traditional" factors may be partly responsible for the increased CHD risk in Aboriginal people. Cross-sectional data indicate that levels of C-reactive protein, a marker of inflammation, are high in Aboriginal populations and are associated with CHD risk factors.[22,23] Our study population had a very high prevalence of chronic renal disease.[24] Several studies, including one in the study population, have shown that pathological albuminuria is associated with increased risk for cardiovascular events, independent of traditional risk factors.[25-27] Another potential predictor is waist circumference, which is a measure of central obesity and predicts cardiovascular disease risk in this population.[28] Finally, early-life factors, such as intrauterine growth retardation reflected in low birth weight, might be playing an important role in the predisposition to cardiovascular and related chronic diseases.[29] Obviously, identification of non-traditional risk factors and quantification of their contribution to CHD risk are important for primary prevention. Also, the lack of preventive treatment, low socioeconomic status and poor nutrition in Aboriginal people might be partly responsible for the accelerated CHD progression.

Recalibration of the Framingham function may be one way to correct the underestimation of CHD risk. This method has been performed in several populations.[6,11,12] Alternatively, or in addition, a new function can be developed using local data on traditional and possibly additional risk factors.

Several potential biases may influence the findings of our study. Firstly, the difference in the outcome measurement (CHD diagnosis) must be considered. Unrecognised myocardial infarctions (silent myocardial infarction) were included in the Framingham risk function,[15] but only clinically manifested myocardial infarctions were included in our study. Some CHD cases might have been missed because of some participants being lost to follow-up. Such a difference would tend to result in an underestimate of events in our study population, and thus would not explain the higher observed risk. Secondly, only 77% of initially eligible participants were included in the final analysis because of missing values on at least one of the risk factors. However, those who were not included in the final analysis had a higher incidence of CHD, so it is likely that

the observed CHD incidence is lower than the true incidence in the study population. Thirdly, because risk factors were measured at baseline, data on the progress of CHD risk factors are not available.

In conclusion, our results suggest that the Framingham function substantially underestimates the risk of coronary events in Aboriginal people. The magnitude of underestimation is higher for women and young adults. Underestimation of an individual's true risk has implications for a population screening test. This will undermine a clinician's and patient's ability to make an informed choice about starting preventive treatment. Efforts should be made either to correct the existing function, taking into account the underestimation — especially in women and young adults — or to develop a function from local data. In addition, identification of an expanded menu of risk factors would have important implications for primary prevention.

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COMPETING INTERESTS

None identified.

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