New Zealand Diabetes Cohort Study cardiovascular risk score for people with Type 2 diabetes: validation in the PREDICT cohort

Tom Robinson MBChB, MPH, FNZCPHM, FRNZCGP;[1,3] **C Raina Elley** MBChB, FRNZCGP, PhD;[1] **Sue Wells** MBChB, FRNZCGP, FNZCPHM, PhD;[2] **Elizabeth Robinson** MSc;[2] **Tim Kenealy** MBChB, FRNZCGP, PhD;[1] **Romana Pylypchuk** MPH, MSc;[2] **Dale Bramley** MBChB, MPH, FNZCPHM;[3] **Bruce Arroll** MBChB, FRNZCGP, PhD;[1] **Sue Crengle** MBChB, FNZCPHM, FRNZCGP, PhD;[4] **Tania Riddell** MBChB, MPH, FNZCPHM;[2] **Shanthi Ameratunga** MBChB, FRACP, FNZCPHM, PhD;[2] **Patricia Metcalf** PhD;[5] **Paul L Drury** MA, MB BChir, FRCP, FRACP[6]

[1] Department of General Practice and Primary Health Care, The University of Auckland, Auckland, New Zealand

[2] Section of Epidemiology and Biostatistics, The University of Auckland

[3] Waitemata District Health Board, Auckland

[4] Te Kupenga Hauora Maori, The University of Auckland

[5] Department of Statistics, The University of Auckland

[6] Auckland Diabetes Centre, Auckland District Health Board

ABSTRACT

INTRODUCTION: New Zealand (NZ) guidelines recommend treating people for cardiovascular disease (CVD) risk on the basis of five-year absolute risk using a NZ adaptation of the Framingham risk equation. A diabetes-specific Diabetes Cohort Study (DCS) CVD predictive risk model has been developed and validated using NZ Get Checked data.

AIM: To revalidate the DCS model with an independent cohort of people routinely assessed using PREDICT, a web-based CVD risk assessment and management programme.

METHODS: People with Type 2 diabetes without pre-existing CVD were identified amongst people who had a PREDICT risk assessment between 2002 and 2005. From this group we identified those with sufficient data to allow estimation of CVD risk with the DCS models. We compared the DCS models with the NZ Framingham risk equation in terms of discrimination, calibration, and reclassification implications.

RESULTS: Of 3044 people in our study cohort, 1829 people had complete data and therefore had CVD risks calculated. Of this group, 12.8% (235) had a cardiovascular event during the five-year follow-up. The DCS models had better discrimination than the currently used equation, with C-statistics being 0.68 for the two DCS models and 0.65 for the NZ Framingham model.

DISCUSSION: The DCS models were superior to the NZ Framingham equation at discriminating people with diabetes who will have a cardiovascular event. The adoption of a DCS model would lead to a small increase in the number of people with diabetes who are treated with medication, but potentially more CVD events would be avoided.

KEYWORDS: Cardiovascular disease; diabetes; prevention; risk assessment; reliability and validity

Introduction

Globally there is an epidemic of Type 2 diabetes.[1,2] It was estimated that in 2010 there were over 195 000 people in New Zealand (NZ) with diabetes—5.6% of the adult population.[3] People with diabetes are at increased risk of dying of cardiovascular disease (CVD) which accounts for almost 50% of all deaths amongst people with diabetes.[4,5]

There is considerable evidence that energetic management of risk factors such as blood pressure, dyslipidaemia, and glycaemia reduces the risk of CVD in people with diabetes.[6–11] However, it is accepted that rather than treating risk factors separately, clinicians should use absolute CVD risk to guide patient management.[12,13]

NZ guidelines for cardiovascular risk assessment use a predictive risk equation adapted from

J PRIM HEALTH CARE
2012;4(3):181–188.

CORRESPONDENCE TO:
Tom Robinson
Department of General Practice and Primary Health Care, The University of Auckland, PB 92019
Auckland, New Zealand
t.robinson@auckland.ac.nz

the United States Framingham Heart Study.[14,15] This equation has a number of disadvantages for predicting risk of CVD amongst people with diabetes in NZ. In particular, the Framingham cohort was from the United States, did not include ethnic groups that are important in NZ, and only included a small number of people with diabetes.[16] In addition, the equation does not include a number of diabetes-specific variables—such as duration of diabetes, glycaemic control, and albuminuria—that are predictive of cardiovascular outcomes.[17–20] The NZ adaptation of the Framingham model does include adding a single additional five-year risk of 5% for these factors.[14]

In 2010, Elley et al. reported two predictive CVD equations based on the New Zealand Diabetes Cohort Study (DCS). This was a prospective open cohort that used data from a national primary care diabetes programme (Diabetes Get Checked), which commenced in 2000.[21] Full details of the derivation and validation of the equation are described in the original article.[21] Briefly, data from 36 127 people with Type 2 diabetes, but without pre-existing CVD, were matched to national hospitalisation and mortality databases. Predictor variables for the first equation (DCS-A) included age at diagnosis, duration of diabetes, sex, ethnicity, smoking status, systolic blood pressure, HbA1c, total cholesterol: HDL cholesterol ratio (TC/HDL), and the presence of micro- or macroalbuminuria. A second equation (DCS-B) also included current antihypertensive treatment. The performance of both equations was tested on 10 030 individuals from a different geographic area in NZ with discrimination and calibration superior to the original Framingham equation.[21]

Before using a prognostic model in clinical practice it is important to validate it using data from other independent populations of patients.[22] This study aimed to validate the DCS models using data from a cohort of people routinely assessed in NZ general practice with PREDICT, a CVD risk assessment and management programme.

Methods

Design

This validation study uses data from primary care to assess the discrimination, calibration and reclassification implications of the DCS equations in predicting CVD events, compared with actual events over five years.

Study population

PREDICT is a web-based, real-time decision support programme that has been integrated with most practice management software in use in NZ primary care.[23] General practitioners and practice nurses enter required clinical data to create a risk profile. This profile is sent by a secure internet connection to a central server that returns the patient's NZ Framingham five-year cardiovascular risk score with management recommendations. At the same time, an electronic profile is stored and linked to an encrypted National Health Index (NHI) number. These were anonymously linked to national hospitalisation, pharmaceutical dispensing and mortality outcomes and also to regional laboratory data.

Individuals identified as having Type 2 diabetes and no known pre-existing CVD with a PREDICT assessment between 27 August 2002 and 31 December 2005 were included. Individuals were said to have diabetes if they were identified by their primary care physician as having diabetes at first risk assessment, or if they had been identified as having diabetes in the national hospitalisation database, or had been prescribed insulin or an oral hypoglycaemic agent prior to or on their first PREDICT assessment date. If the type of diabetes was unclear, we assigned them as Type 2 if they were never on insulin, if they had been on an oral hypoglycaemic agent, or if their age of onset was over 30 years in Maori and Pacific or over 50 in other ethnic groups. Pre-existing CVD was identified from the primary care physician's risk assessment record.

Risk variables

Risk factor variables required for the DCS equations were extracted for each individual. Data on some of the variables were missing from early PREDICT risk assessments. Duration of diabetes was included if it could be calculated from any subsequent PREDICT risk assessment record. Missing laboratory data were obtained from laboratory records where results from up to five years prior to the baseline assessment or two

weeks after the assessment were available. After the addition of these data, only individuals with a complete minimum dataset were included in the final study cohort. Ethnicity was derived from both the primary care practitioner records and the encrypted NHI database and was prioritised in the order: Maori, Pacific, South Asian, East Asian, 'Other' and European.

Outcome measures

Primary care data were linked to national hospitalisation and mortality databases by NHI number to identify all CVD events over the five years following baseline for each individual. CVD events included hospital admission or death from ischaemic heart disease, cerebrovascular disease or peripheral vascular disease. These were identified from national hospital and mortality databases coded according to ICD-9 and ICD-10 (see the appendix in the web version of this paper).[21] Five-year risk was calculated for each individual according to both the NZ Framingham and the DCS equations.[21]

Analyses

We compared predicted risk with observed outcomes. To assess discrimination, the ability of the models to distinguish between individuals who do or do not have a subsequent CVD event, we calculated the area under the receiver operating characteristic (ROC) curve (C statistic).[13,22,24] Calibration was assessed by comparing the observed and predicted probabilities of CVD events in the pre-specified deciles of DCS model risk, and performing a Hosmer–Lemeshow test for equivalence. The effect of reclassification of risk from the NZ Framingham model to the DCS models was measured using a 15% five-year cardiovascular risk threshold. NZ guidelines recommend drug treatment with five-year risks above 15%. A scatter plot of risks predicted by the two models with these pre-determined risk categories was also produced.[24] All analyses were undertaken using Stata® 11.2.

Ethical approval

This validation study was approved by the Multi-region Ethics Committee (WGT/04/09/077) as part of the Diabetes Cohort Study. The PREDICT cohort study and research process was approved by the Northern Region Ethics Committee Y in 2003 (AKY /03/12/314) with subsequent annual approval by the National Multi-region Ethics Committee since 2007 (MEC/07/19/EXP).

WHAT GAP THIS FILLS

What we already know: People with Type 2 diabetes are at high risk of a cardiovascular event. A locally derived Diabetes Cohort Study CVD risk equation—http://www.nzssd.org.nz/cvd/—has been found to be more valid for those with diabetes in New Zealand than the currently used Framingham equation.

What this study adds: Before incorporating the new equation into national recommendations for management, further validation was required using an independent cohort. The Diabetes Cohort Study CVD risk equation predicted risk more accurately than the currently used adjusted Framingham equation among people with diabetes in the New Zealand PREDICT cohort.

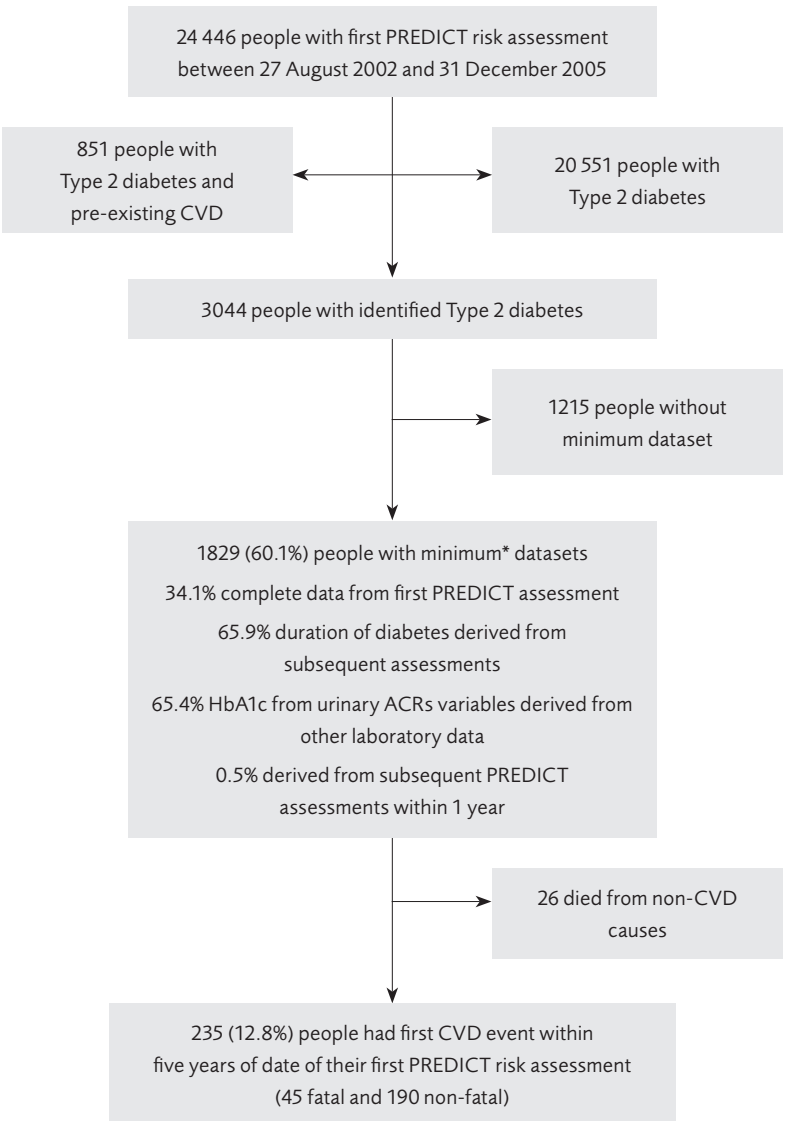
Results

Study population

The derivation of the study cohort and subsequent CVD events is shown in Figure 1. We classified 3044 (13.3%) people on the database as people with Type 2 diabetes without pre-existing CVD. Of these, 1829 (60.1%) had the minimum dataset of risk variables required and formed the final cohort for the study. About two-thirds of these individuals (65.9%) were included after having data added from sources other than the first risk assessment record. These data were diabetes-specific variables (HbA1c, urinary albumin/creatinine ratio, diabetes duration, and age of onset of diabetes). All individuals were followed for five years from their initial CVD risk assessment. During that time, 235 had first CVD events (12.8%), in which 45 (2.5%) were fatal and 190 (10.4%) were non-fatal events.

Baseline characteristics of participants are presented and compared with those of the 1215 people excluded due to missing variables in Table 1. Compared with those included, a higher proportion of the excluded group were European and a lower proportion Pacific. Excluded participants had slightly higher systolic blood pressures and TC/HDL ratios and were less likely to be recorded as being past smokers. Although the two groups had similar risks of CVD events

Figure 1. Flow diagram of participants through study



* Minimum dataset = age at diagnosis, gender, duration of diabetes, smoking status, systolic blood pressure, HbA1c, fasting serum total cholesterol and HDL, urine albumin-creatinine ratio, ethnicity, antihypertensive medication

according to the NZ Framingham equation and observed events during follow-up, the excluded group had higher fatal CVD and other-cause mortality. Differences in duration, HbA1c, and albuminuria between the 'Included' and 'Excluded' groups may not reflect a true underlying difference, as information on these variables was missing for many in the 'Excluded' group.

Discrimination

The ROC curves for the DCS-B equation (with antihypertensive status included) and the modified NZ Framingham equation are shown in Figure 2. The area under the ROC curve (C statistic) was 0.678 (95% CI 0.642–0.714) for the DCS-A equation (without antihypertensive status included) and 0.684 (95% CI 0.648–0.720) for the DCS-B equation. The C statistic for the NZ Framingham equation in this study was 0.648 (95% CI 0.612–0.684) and the unadjusted Framingham equation was 0.649 (95% CI 0.613–0.685). Both DCS equations had significantly higher C statistics than the NZ Framingham equation (p=0.04 DCS-A equation and p=0.01 DCS-B equation). The DCS-B equation C statistic was also significantly higher than the DCS-A equation (p=0.04). The C statistics for the DCS equations in this study were similar to those found in the original DCS validation study (0.69).[21]

Calibration

Figure 3 compares the mean predicted risk with the mean observed five-year event rate for each decile of predicted risk for DCS-B and NZ Framingham equations. The DCS equations predicted higher risks than the NZ Framingham equation for people in the higher deciles of risk. The Hosmer–Lemeshow test showed that estimated risks based on the baseline risk profile tended to be higher than the real event rate for all equations (p<0.001 for DCS-A, p=0.001 for DCS-B, and p=0.02 for NZ Framingham).

Reclassification

The effect of reclassification of risk from the NZ Framingham model to the DCS models was measured using a 15% five-year cardiovascular risk threshold. Figure 4 plots the predicted five-year risk of a CVD event for each individual using the DCS-B and NZ Framingham equations. Horizontal and vertical lines represent the 15% five-year risk cut-offs above which drug therapy is usually recommended in NZ. Area B in the graph represents individuals that are classified as being at low risk under the DCS equation, but high risk under the NZ Framingham equation. Area D on the graph represents people who were classified as

Table 1. Characteristics at baseline for study cohort compared with those excluded due to missing variables

Characteristic	Included	Excluded		P value
	Mean (SD) or Median (IQR)* or n (%)	Data available, n (%)	Mean (SD) or Median (IQR)* or n (%)	
N	1829	1215		
Age (years)	57.3 (10.7)	1215 (100)	57.0 (12.5)	0.6
Age at diagnosis (years)	51.7 (11.1)	360 (30)	53.4 (11.3)	0.01
Diabetes duration (years)*	4 (2-8)	360 (30)	1 (0-4)	<0.001
Gender		1215 (100)		
Men	926 (50.6%)		668 (55.0%)	0.02
Ethnicity		1215 (100)		<0.001
European	550 (30.1%)		575 (47.3%)	
Maori	245 (13.4%)		155 (12.8%)	
Pacific	756 (41.8%)		296 (24.4%)	
South Asian	162 (8.9%)		93 (7.7%)	
East Asian	82 (4.5%)		80 (6.6%)	
Other	25 (1.4%)		16 (1.3%)	
Systolic blood pressure	134.8 (15.6)	1215 (100)	137.8 (19.0)	<0.001
Total cholesterol:HDL ratio	4.1 (1.2)	1214 (100)	4.3 (1.3)	<0.001
HbA1c (%)*	7.4 (6.5-8.6)	803 (66)	6.8 (6.2-7.9)	<0.001
Smoking status		1215 (100)		<0.001
Current smoker	342 (18.7%)		211 (17.4%)	
Previous smoker	386 (21.1%)		95 (7.8%)	
Albuminuria		458 (38)		<0.001
Microalbuminuria	301 (16.5%)		100 (21.8%)	
Macroalbuminuria	88 (4.8%)		36 (7.9%)	
Taking medications		1215 (100)		
Antihypertensives	213 (11.7%)		186 (15.3%)	0.003
Lipid-lowering meds	185 (10.1%)		143 (11.8%)	0.1
5-year CVD risk †*	14.8 (10.6-19.3)	1213 (100)	15.0 (10.1-20.7)	0.6
Outcomes		1215 (100)		
Any CVD event	235 (12.8%)		154 (12.7%)	0.9
Fatal CVD event	45 (2.5%)		70 (5.8%)	<0.001
Non-CVD deaths	26 (1.4%)		45 (3.7%)	<0.001

* Median and inter-quartile range (IQR) given as distribution is skewed.
† NZ-adjusted Framingham equation

high risk under the DCS equation, but low risk under the NZ Framingham equation. Areas A and C represent people who are given the same classification by both models. There are more people who subsequently have CVD events in area D than in area B, indicating that, although there were both successes and failures in reclassification, sensitivity for the DCS equation was superior. However, there are also more people who did not have events who were reclassified to high risk.

Moving from the NZ Framingham equation to the DCS-B equation improves sensitivity from 63.8% to 77.0% (Table 2), but decreases specificity from 54.0% to 51.4%. DCS-A behaves similarly. The positive predictive values (PPVs) and the negative predictive values (NPVs) are higher for the two DCS equations than the NZ Framingham equation. These results are based upon our study cohort five-year prevalence of CVD events of 12.8% (95% CI, 11.3–14.4%). Sensitivity analysis around the 95% confidence intervals of CVD

Figure 2. Receiver operating curves for the DCS-B equation and the NZ Framingham CVD equation (five-year risk)

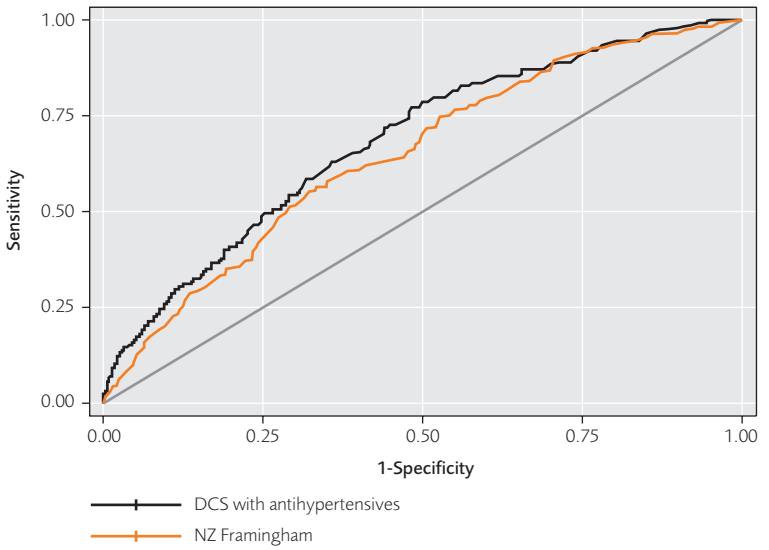
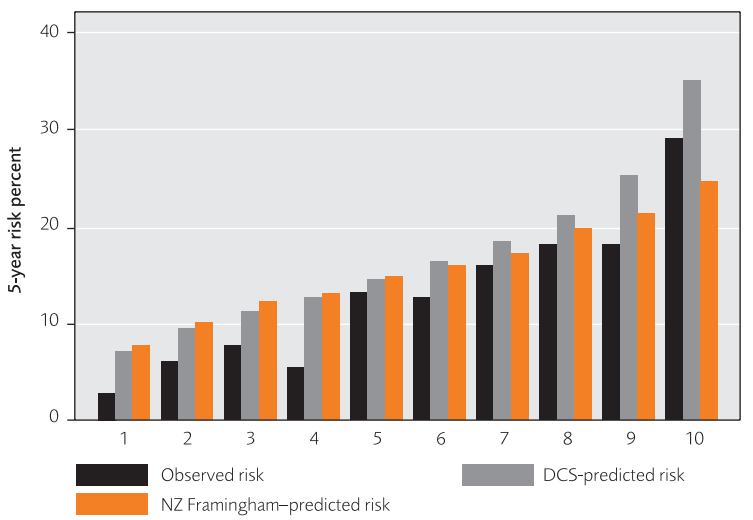


Figure 3. Five-year risks observed in the study cohort compared with those predicted by the DCS-B equation and the NZ Framingham equation for different deciles of risk



event prevalence does not change the relative performance of the models (results not shown).

Discussion

Main finding

For this cohort of people with Type 2 diabetes, the DCS equations were better at discriminating risk of a first CVD event than the NZ Framingham equation currently being used in primary care in NZ. The latter model in this cohort had an area under the ROC curve of 0.65 while the DCS equation gave an area of 0.68.

Strengths and limitations

The use of diabetes duration, HbA1c levels, and degrees of albuminuria are likely to contribute to better discrimination, particularly for higher risk groups. In addition, the DCS equation was developed in a cohort of much greater relevance to the NZ diabetes population than the Framingham equation, even though adjustments were made by the NZ guidelines.[14]

There are a number of important methodological limitations in this validation study. One is that these equations were developed and validated on a cohort of people who may have being treated for their CVD risk. Indeed, the PREDICT programme, from which this cohort is gathered, is specifically intended to lower risk of CVD events by encouraging appropriate treatment. Historically, these equations have been used to predict the outcomes for patients if they were not treated. It is therefore likely that the risk of CVD events in this scenario would be higher than the observed risk in this cohort.

All three equations overestimated risk when compared to actual events in the cohort. This was in contrast to the initial validation study, where the DCS equations underestimated risk of first CVD event.[21] The first possibility is the effectiveness of the PREDICT programme in reducing risk, as discussed above. A second possibility is that the PREDICT cohort is at lower risk than the original DCS cohort, possibly because people with higher risk and comorbidities were enrolled earlier into the Get Checked programme. It is also possible that the difference is due to random error due to the relatively small number of observed events in this study. The overall five-year CVD incidence estimation is somewhat imprecise (12.8%, 95% CI 11.3–14.4%).

A further limitation is that an equation should ideally be validated on a population that is representative of the population on which it will eventually be used. It is a strength of this study that the PREDICT cohort is much more repre-

sentative of NZ people with diabetes than the original Framingham equation cohort. Nevertheless, the baseline characteristics table suggested that this cohort was not completely representative of NZ people with diabetes. For example, Pacific people were over-represented compared to the overall diabetes population. It is also possible that our inability to obtain data on all patients in the original cohort has introduced a selection bias to our final validation cohort. As discussed, included subjects may have been at a slightly lower risk than those excluded. However, it is important that equations discriminate across diverse as well as representative populations.

In validating any equation, it is important to have accurate data on the cohort being studied. The PREDICT data are collected by primary care physicians in routine care rather than by researchers and therefore may contain some inaccuracies. As previously mentioned, some data were not available from the baseline risk assessment and had to be obtained from either laboratory data or subsequent risk assessment records. It is possible that other data, such as smoking status or diabetes duration, may be inaccurately recorded. Such deficiencies would lead to poorer discrimination of the equations. The degree to which they might also lead to systematic under- or overestimation of the predicted risks is more difficult to judge. However, these limitations also reflect the 'real-life' clinical situation in which these tools are used.

Implications for clinical practice

Whilst the current NZ guidelines for managing cardiovascular risk provide guidance for management across a broad range of risks, an important decision point is when to begin treatment of risk with medications.[14] At a population level, changing from the current NZ Framingham equation to one of the DCS equations would have a substantial impact on the way diabetes is managed in NZ. If this cohort were representative of people with diabetes in NZ, then changing to the DCS-B equation would result in recommending treating 53% of people with diabetes with lipid-lowering and antihypertensive medication instead of 49%. Using the Ministry of Health estimates of the number of people with Type 2 diabetes in NZ, and excluding the estimated 22% of people with diabetes who have pre-existing CVD, then 6503 extra people should be offered treatment. However, the benefit would be that an additional 2587 people, who would have had a first CVD event over the next five years, would be correctly identified and offered preventive therapy. As researchers interested in the population manage-

Figure 4. Scatter plot of five-year risk of CVD events predicted by the DCS-B equation against the NZ Framingham equation with 15% five-year risk cut-offs shown

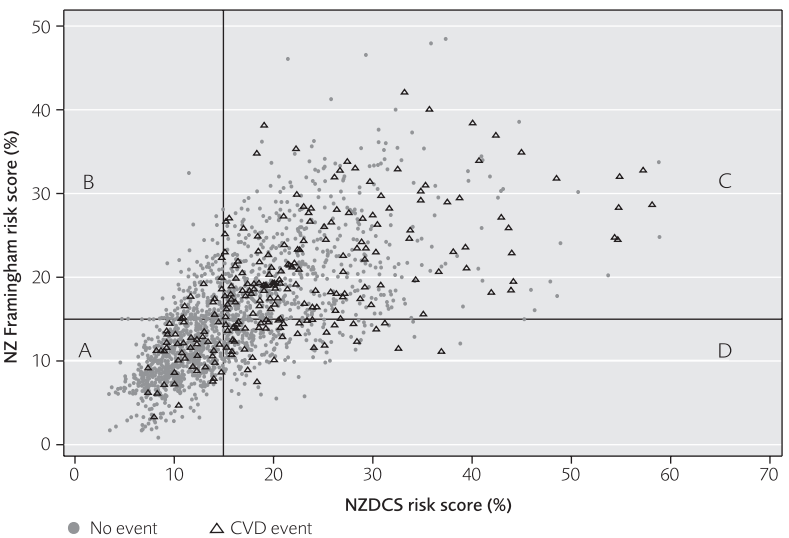


Chart area	A	B	C	D	
NZ Framingham classification	Low	High	High	Low	Total
DCS classification with antihypertensives	Low	Low	High	High	
Outcome					
No event	634	185	549	226	1594
Proportion	40%	12%	34%	14%	100%
CVD event	43	11	139	42	235
Proportion	18%	5%	59%	18%	100%
All patients	677	196	688	268	1829
Proportion	37%	11%	38%	15%	100%

Table 2. Sensitivity, specificity, positive predictive value, and negative predictive value for predicted vs actual CVD events using the DCS and Framingham equations with a 15% risk cut-off (12.9% event prevalence)

	DCS-A	DCS-B	NZ Framingham
Sensitivity	79.6%	77.0%	63.8%
Specificity	45.3%	51.4%	54.0%
Positive predictive value	17.7%	18.9%	17.0%
Negative predictive value	93.8%	93.8%	91.0%

ment of diabetes, we believe this would be a very worthwhile trade-off.

At an individual level, the person with diabetes or their clinician needs to know, firstly, that on average over a five-year period, 13 people out of 100 will have a CVD event. Secondly, of these 13 people, the DCS equation will correctly identify 10 of these people so they can be offered treatment, whereas the current NZ Framingham equation will successfully predict eight. However, to achieve this, 53 of the 100 people will need to take medication (or five more than currently would be the case). Since it is impractical to offer individual patients the choice of model, we believe it is important to consult both clinicians and patient representatives as to which model is preferable. Should the DCS equation be approved, then it can be seamlessly added to the PREDICT decision support engine and available at the point of care.

In conclusion, we have validated the previously developed DCS equations using a different cohort of people with diabetes from the PREDICT dataset and compared its performance with the currently used NZ Framingham equation. We have shown that it has advantages over the current equation at a technical and population health level. From a patient perspective, it will lead to an increased chance of treatment, but also the opportunity to prevent more first CVD events.

ACKNOWLEDGEMENTS
We would like to acknowledge the patients, practices and primary care organisations who contributed data both to the Diabetes Cohort Study and the PREDICT study, and Diagnostic MedLab Ltd who provided anonymous matched laboratory data.

FUNDING
We would like to acknowledge the NZ Health Research Council and Auckland Medical Research Foundation for supporting the collection of data for the original cohort studies and for supporting this validation study. One author (T Riddell) is the recipient of a National Heart Foundation fellowship.

COMPETING INTERESTS
None declared.

References

1. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet. 2011;378(9785):31–40.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(5):1047–53.
3. Wright C. Estimated prevalence of Type 2 Diabetes in New Zealand. In: Robinson T, editor. Wellington: Ministry of Health; 2011.
4. Seshasai SR, Kaptoge S, Thompson A, Di Angelantonio E, Gao P, Sarwar N, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med. 2011;364(9):829–41.
5. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with Type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339(4):229–34.
6. SIGN. Management of diabetes: a national clinical guideline: Scottish Intercollegiate Guidelines Network. Edinburgh: Scottish Intercollegiate Guidelines Network; 2010.
7. Marso SP, Kennedy KF, House JA, McGuire DK. The effect of intensive glucose control on all-cause and cardiovascular mortality, myocardial infarction and stroke in persons with Type 2 diabetes mellitus: a systematic review and meta-analysis. Diab Vasc Dis Res. 2010;7(2):119–30.
8. Selvin E, Bolen S, Yeh HC, Wiley C, Wilson LM, Marinopoulos SS, et al. Cardiovascular outcomes in trials of oral diabetes medications: a systematic review. Arch Intern Med. 2008;168(19):2070–80.
9. Brugts JJ, Yetgin T, Hoeks SE, Gotto AM, Shepherd J, Westendorp RG, et al. The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials. BMJ. 2009;338:b2376.
10. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in Type 2 diabetes. New Eng J Med. 2008;359(15):1577–89.
11. Holman RR, Paul SK, Bethel MA, Neil HA, Matthews DR. Long-term follow-up after tight control of blood pressure in type 2 diabetes. New Eng J Med. 2008;359(15):1565–76.
12. Jackson R, Lawes CM, Bennett DA, Milne RJ, Rodgers A. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. Lancet. 2005;365(9457):434–41.
13. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743–53.
14. New Zealand Guidelines Group. Evidence-based best-practice guideline. The assessment and managment of cardiovascular risk. Wellington: New Zealand Guidelines Group; 2003.
15. New Zealand Guidelines Group. New Zealand cardiovascular guidelines handbook: a summary resource for primary care practitioners. 2009 edition. Wellington: New Zealand Guidelines Group; 2009.
16. Anderson K, Odell P, Wilson P, Kannel W. Cardiovascular disease risk profiles. Am Heart J. 1991;121:293–8.
17. Elley CR, Kenealy T, Robinson E, Drury PL. Glycated haemoglobin and cardiovascular outcomes in people with Type 2 diabetes: a large prospective cohort study. Diabet Med. 2008;25(11):1295–301.
18. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004;141(6):421–31.
19. Fox CS, Sullivan L, D'Agostino RB Sr, Wilson PW. The significant effect of diabetes duration on coronary heart disease mortality: the Framingham Heart Study. Diabetes Care. 2004;27(3):704–8.
20. Newman DJ, Mattock MB, Dawnay AB, Kerry S, McGuire A, Yaqoob M, et al. Systematic review on urine albumin testing for early detection of diabetic complications. Health Technol Assess. 2005;9(30):iii–vi, xiii–163.
21. Elley C, Robinson E, Kenealy T, Bramley D, Drury P. Derivation and validation of a new cardiovascular risk score for people with Type 2 diabetes: The New Zealand Diabetes Cohort Study. Diabetes Care. 2010;33(6):1347–52.
22. Altman DG, Vergouwe Y, Royston P, Moons KG. Prognosis and prognostic research: validating a prognostic model. BMJ. 2009;338:b605.
23. Bannink L, Wells S, Broad J, Riddell T, Jackson R. Web-based assessment of cardiovascular disease risk in routine primary care practice in New Zealand: the first 18 000 patients (PREDICT CVD-1). N Z Med J. 2006;119(1245):U2313.
24. McGeechan K, Macaskill P, Irwig L, Liew G, Wong TY. Assessing new biomarkers and predictive models for use in clinical practice: a clinician's guide. Arch Intern Med. 2008;168(21):2304–10.

APPENDIX A

Diabetes Cohort Study and PREDICT CVD Outcome Codings
as of 05/07/2009

A_Diagnoses and Conditions	ICD-9-CM-A	ICD-10-AM 1st Edition	ICD-10-AM 2nd Edition	ICD-10-AM 3rd Edition
Acute Coronary Heart Disease (CHD) (with examples below)				
Coronary artery disease (Other forms chronic ischaemic heart disease and atherosclerosis of coronary arteries —use for mortality only)	(410x, 411, 431x, except 4110) 4149 (mortality only)	(120x to 124x except 1241)	(120x to 124x except 1241)	(120x to 124x except 1241) 125.8, 12511
Diabetic circulatory complication (only for mortality)	25070, 25071		E1150, E1159, E1450, E1459	E1150, E1159, E1450, E1459
Cardiac arrest				
Cardiac arrest (resuscitated or unspecified) Sudden cardiac death	4275	146x 1461, R96, R98	146x 1461, R96, R98	146x 1461, R96, R98
Old coronary heart disease (not used for outcomes, only for history)				
Old MI Old CABG and old coronary stent	412	1252	1252	1252 Z95.1 Z95.5
Ischaemic stroke				
Ischaemic stroke Transient Ischaemic Attack (TIA)	434x, 436x, 4371 435x	163x, 164x, 166x, 1678 G45x (except G453)	163x, 164x, 166x, 1678 G45x (except G453), G46x	163x, 164x, 166x, G45x (except G453 G45.4), G46x
Old cerebrovascular disease (not used for outcomes, only for history)				
Late effects/sequelae of cerebrovascular disease	438x	1693, 1694, 1698	1693, 1694, 1698	1693, 1694, 1698
Acute Haemorrhagic Stroke (excludes traumatic intracranial haemorrhage)				
Acute Haemorrhagic Stroke	430, 431	160x–162x	160x–162x	160x–162x
Old haemorrhagic stroke (not used as outcome, only for history)				
Sequelae of haemorrhagic stroke (i.e. old event)		1690, 1691, 1692	1690, 1691, 1692	1690, 1691, 1692
Atherosclerotic peripheral vascular disease (PVD)				
Occlusion and stenosis of precerebral arteries	433x, 4410, 4411,	165x	165x	165x
Aotic aneurysm and dissection (other arterial dissection)	4413, 4415, 4416, 4432	1710, 1711, 1713, 1715, 1718	1710, 1711, 1713, 1715, 1718	1710, 1711, 1713, 1715, 1718
Arterial embolism and thrombosis	444x	174x	174x	174x
Intermittent claudication, gangrene, or diabetic peripheral angiopathy with or without gangrene	44021, 44022, 44023, 44024, 25073		17021, E1052, E1452	17021, 17022, 17023, 17024, E1052, E1452

Note: Atherosclerosis 440x (ICD-9) excluded (are signs, not outcomes)

Diabetes Cohort Study and PREDICT CVD Outcome Codings
as of 05/07/2009

A_Procedures	ICD-9-CM-A	ICD-10-AM 1st Edition	ICD-10-AM 3rd Edition
Coronary procedures			
Coronary endarterectomy, aneurysmectomy, repair ventricular septal rupture		3850500	3850500
Coronary angioplasty or stent Percutaneous coronary intervention	360x except 3604	3530306, 3530400-3530501, 3530906-3530908, 3531000-3531005	3530306, 3530400-3530501, 3530906-3530908, 3531000-3531005
CABG	361x	3849700-3850304, 9020100-9020103	3849700-3850304, 9020100-9020103
Re-operation and other procedures on coronary arteries		3863700, 3845619, 3865308	3863700, 3845619, 3865308
Heart revascularisation by arterial implant	362x		
Peripheral procedures			
Operative management of acute rupture or dissection of thoracic aorta 3857200 but other codes (repair of ascending [684][685] and descending [686], or replacement of aneurysm with graft [715] will be coded first) other aortic repair procedures [693]			3857200, [684][685] 3855000-3857101 (except 3855303, 3856202 and 3857100), [693] 3870600), [693] 3870600, 3870601, 3871200
Repair aneurysm [714][715]			330x-331x
Peripheral arterial shunts/bypasses: Peripheral arterial bypass, endarterectomy, repair aneurysm, peripheral arterial bypass graft Aorto-subclavian-carotid bypass	392	3270000-3354200, 3335400, 9021100-9021210, 9022900	
Artrial bypass graft [711][712][713]			3270000-3276318
Aorto-renal bypass Angioplasty/stent peripheral	3924		
Aorto-iliac-femoral bypass	3925	3530000-3530305, 3530600-3530905	
Other intra-abdominal vascular shunt or bypass	3926		
Other (peripheral) vascular shunt or bypass	3928		
Bypass (graft):axillary-brachial/axillary-femoral [axillofemoral] (superfical)/brachial/femoral-femoral/femoroperoneal/femoropopliteal (arteries)/ femorotibial (anterior) (posterior)/popliteal/vascular NOS	3929		3276319
Arterial atherectomy		3531200-3531501	3531200-3531501
Embolectomy/thrombectomy incision of vessel-embolectomy/thrombectomy	380x	3380000-3380612, 9023000	3380000-3380612, 9023000
Endarterectomy and patch graft artery	381x		[700][701][707] 3350000-3355400, 9022900
Resection of vessel with replacement	384x except 3847, 3849		