The addition of depression to the Framingham Risk Equation model for predicting coronary heart disease risk in women

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The addition of depression to the Framingham Risk Equation model for predicting coronary heart disease risk in women

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ABSTRACT

**Background:** Depression is widely considered to be an independent and robust predictor of Coronary Heart Disease (CHD), however is seldom considered in the context of formal risk assessment. We assessed whether the addition of depression to the Framingham Risk Equation (FRE) improved accuracy for predicting 10-year CHD in a sample of women.

**Design:** A prospective, longitudinal design comprising an age-stratified, population-based sample of Australian women collected between 1993-2011 (n=862).

**Methods:** Clinical depressive disorder was assessed using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID-I/NP), using retrospective age-of-onset data. A composite measure of CHD included non-fatal Myocardial Infarction, unstable angina coronary intervention or cardiac death. Cox proportional-hazards regression models were conducted and overall accuracy assessed using Area Under Receiver Operating Characteristic (ROC) curve analysis.

**Results:** ROC curve analyses revealed that the addition of baseline depression status to the FRE model improved its overall accuracy (AUC:0.77, Specificity:0.70, Sensitivity:0.75) when compared to the original FRE model (AUC:0.75, Specificity:0.73, Sensitivity:0.67). However, when calibrated against the original model, the predicted number of events generated by the augmented version marginally over-estimated the true number observed.

**Conclusions:** The addition of a depression variable to the FRE equation improves the overall accuracy of the model for predicting 10-year CHD events in women, however may over-estimate the number of events that actually occur. This model now requires validation in larger samples as it could form a new CHD risk equation for women.

**KEY WORDS:** Depression, coronary heart disease, women, risk factor assessment, prevention
INTRODUCTION

Burden of Cardiovascular Disease (CVD)

Despite notable improvements in survival rates over the past century(1), cardiovascular disease (CVD) remains the leading cause of death in females in most high income countries. More women now die of CVD than they do from breast cancer(2), with coronary heart disease (CHD) one of the most common forms. As a number of studies have reported particularly high mortality rates following myocardial infarction (MI) in younger women(3), the provision of appropriate and effective assessment tools that can accurately identify future risk of CHD in women may allow prevention, early detection and intervention to improve long-term clinical outcomes.

Risk factors for CHD

In addition to more putative risk factors, including smoking, physical inactivity, poor diet, overweight, hypertension and elevated cholesterol levels, the INTERHEART study(4) indicated that psycho-social factors such as depression were key contributors to the Population Attributable Risk (PAR) for CHD, specifically MI. These observations have since been corroborated by a burgeoning evidence-base providing support for the role of depression in the development of CHD, particularly among women. Women report a higher prevalence of depressive symptoms and increases in severity are directly linked to greater CHD risk(5). Prospective and observational data generated over the past decade have provided consistent and compelling evidence that depression may be a risk factor for CHD, over both the short and long term(6). Recently, the American Heart Association has recommended that depression be elevated to ‘risk factor’ status for poor prognosis in acute coronary syndrome (ACS) patients(7).
However, despite convincing evidence that CHD is the leading killer women globally, that depression precipitates CHD and depression predicts CHD-related mortality (8), this condition remains a neglected risk factor for CHD in the context of risk assessment in clinical and research settings.

**CHD risk assessment**

As the majority of CHD-related deaths are preventable, risk assessment plays a significant role in the control of CVD-related morbidity and mortality(9). Formal CHD risk scoring is clinically useful as it takes into account interactions between risk factors and weights these accordingly. The Framingham Risk Equation (FRE) is currently recommended for use in many medical settings in the United States and Australia. While the FRE possesses predictive ability (c-statistic 0.63 to 0.83 in different populations) that has been considered equal or superior to that of other methods for calculating absolute CHD risk(10), it possesses several well documented limitations. The FRE (i) has been shown to underestimate risk of subclinical coronary artery disease among asymptomatic women(11) and (ii) considers only the risk factors identified from the original and subsequent Framingham CHD studies conducted between the 1940s and 1970s that were contemporary at that time. Importantly, the National Vascular Disease Prevention Alliance (NVDPA), which the leading authority in CVD prevention, further argues that the omission of important, less conventional risk factors, such as depression, is a serious deficiency affecting the accuracy of the FRE(10). While endorsing the use of the FRE for clinicians wanting to calculate patient risk, the NVDPA suggest that incorporating more contemporary risk factors into absolute CVD risk assessment may improve their predictive ability, however such methods have not yet been fully developed (10). We therefore sought to determine whether including depression in the
FRE model improved its predictive accuracy in a nationally representative sample of women over a 10-year period.

METHODS

Study sample: Details of the Geelong Osteoporosis Study (GOS) have been published elsewhere(12). Briefly, the GOS was initiated in 1993, comprising an age-stratified, population-based sample of women (aged 20-94 years) who were randomly selected from electoral rolls for the Barwon Statistical Division (BSD) in South-Eastern Australia. As voting is compulsory in Australia for adults aged 18-years and over, this sampling technique provides a random sample of citizens registered with the Australian Electoral Commission. The area is well suited to epidemiological research as it has a defined population consisting of a range of social, cultural and geographical settings, with a centralised health provider that is comparable with national levels for Australia(12). The total population and female population according to the 2006 census was 259,013 and 132,124 (98,740 aged 20 years and over), respectively. Women randomly selected from the electoral roll were mailed an invitation letter, with a request to contact the research center. Those residing in the area for <6 months or unable to provide informed consent were excluded. During the years 1993–97, 2390 women were invited to participate, of whom 432 lapsed and 444 declined to participate. Personal reasons (53.2%), old age (18%) and illness (12.6%) were the most common reasons for declining the invitation. At least 100 women were recruited in each 5-year age group from 20 to 69 years and 200 for both the age groups of 70–79 years and 80 years and over. Those eligible were subsequently invited to attend the research center located at the largest public hospital in the region (previously Barwon Health; now University Hospital Geelong). Participants provided written, informed consent at each
assessment. The sample size at baseline was 1494 participants (overall participation=77%)(12, 13). This sub-study included the women for whom we had (i) psychiatric diagnostic data at baseline, (ii) FRE variables at baseline (lipids, BP, age, smoking status, and exposure to drug therapy for hypertension) and (iii) coronary heart disease data over 10 year follow up (excluding those with established CHD at baseline (See Table 1). The Barwon Health Human Research Ethics Committee approved the study and all participants provided written informed consent.

Procedure: While the GOS study comprises ongoing, regular health assessments, this study utilized psychiatric, anthropometric, demographic, medications, other health (non-CHD) data and blood samples (from which to diagnose diabetes) drawn from the major GOS assessment at baseline. Trained Research Assistants collected clinical, anthropometric and questionnaire data conducted the mental health assessments following specific training in using the selected tool. In 2011, CHD events data were extracted retrospectively from hospital medical records for the 10-years following the GOS baseline assessment.

Study measurement:

Predictors: FRE scores were calculated from data collected at the GOS baseline assessment and imputed into a FRE calculator(14). Age, smoking status, and exposure to drug therapy for hypertension and hyperlipidemia were obtained through self-report. Systolic BP was taken twice by qualified research assistants using a digital meter (A&D Company, model UA-751) where the cuff was placed on the right upper arm while the arm was resting on a table and the participant was seated. BP was taken on 2 occasions and the average reading was used.
Blood samples were taken from participants following an overnight fast, at the time of baseline assessment at a local pathology laboratory and stored at University Hospital Geelong. Blood samples were stored in serum/plasma aliquots at -80 Celsius and fasting serum lipid profile and blood glucose analyzed using standard laboratory procedures. Lipid profile data were generated through batch analysis at the Molecular Medicine Research Facility at Deakin University. To maintain internal validity, biochemical analyses of blood samples were performed using de-identified samples, blinded to outcome and other exposure data. Those variables contributing to the FRE calculation are displayed in Table 2.

*Depression* – The Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Non-patient edition (SCID-I/NP)(15) was used to identify those ever meeting criteria for a depressive disorder, regardless whether it was a primary or secondary diagnosis. This assessment tool allowed for the identification of lifetime/current depressive disorders including; Major Depressive Disorder (MDD), bipolar disorder, dysthymia, minor depression, substance-induced mood disorder, and mood disorder due to a general medical condition. Depression at baseline was derived from retrospective age-of-onset data generated from the SCID-I/NP interviews at the GOS 10-year follow up. Research has shown that the SCID-I/NP question sequence addressing age-of-onset yields responses with a more plausible age-of-onset distribution than other techniques(16). At baseline assessment, all participants were asked whether they were using anti-depressant medication.

*Outcomes*: The primary outcome was the occurrence of a CHD event that resulted in hospital presentation over the 10-year period, with a formal diagnosis of: cardiac death, non-fatal MI
based on clinical criteria including troponin levels and electrocardiographic changes (subcategorized as ST segment elevation MI (STEMI) or non-STEMI), unstable angina and coronary revascularization subcategorized as percutaneous coronary intervention (PCI) (with or without bare metal, drug-eluting or bio-absorbable vascular stent), or coronary artery bypass grafting (CABG). Data were extracted from the catchment area hospital medical records held at Barwon Health by medically trained Research Fellows. Where there was uncertainty around classification of an event (n=2), the Research Fellows consulted with an adjudication panel comprising a senior endocrinologist and cardiologist. Panel members reviewed the patient files independently and in both cases, agreed on the classification of the event. This procedure is likely to capture the majority of CHD events in the region for three key reasons: (i) Barwon Health was the sole emergency facility in a regional catchment area national health service at the time, (ii) admission remains accessible to the general public with no out-of-pocket expense and (iii) only a small percentage of participants moved away from the region during follow up (82/1494; 5%). Participants gave consent for hospital admission records to be accessed, regardless of retention status over the follow up period.

Statistical approach: We proposed a three-step approach for assessing the potential improvement of the risk prediction model with the addition of baseline depression. Cox proportional-hazards regression models were used to test the effect of the established FRE predictors alone and then paired with baseline depression. Depression was weighted by its contribution to the prediction model, relative to the established predictors. This weighting scheme indicated a 9-point increase for the presence of depression. Thus, a simple algorithm was employed whereby those without depression maintained their standard FRE score and those with
depression were awarded 9 additional points. As per techniques used in previous studies (17),
calibration involved ranking participants according to their percentage risk, generating scores
comparing mean predicted risk with observed outcome where those who have had the event yield
higher predicted risk than those who have not. In order to determine whether FRE models over-
or under-estimated risk, the ratio of predicted risk to observed incidence was calculated. Receiver
operating characteristic (ROC) curve analysis was applied to plot differences in sensitivity and
specificity against the original FRE model to determine discrimination.

RESULTS

Baseline characteristics

Key characteristics of the sample included in this study are shown in Table 1. Of the 148 with
depression, 74.5% recorded MDD while the remaining one-quarter had another depressive
disorder including minor depression, bipolar, mood disorders and/or dysthymia. Groups
(depressed versus not) were comparable in most demographic, clinical and behavioral variables,
including CHD risk as predicted by the established FRE (depressed = 5.04%, non-depressed =
5.23%). A higher proportion of those with depression completed secondary school. At baseline,
seven participants reported a past history of coronary disease and were subsequently excluded
from the analyses.

Coronary heart disease outcome events

Thirty-five women recorded at least 1 CHD event that met criteria over the 10-year period; 12 of
these had clinical depression. This included 4 cardiac deaths, 11 myocardial infarcts (all
STEMI), 5 unstable angina and 15 coronary revascularization events (1 PCI, 11 CABG).
Predictive ability of FRE model that includes depression on 10-years CHD events

Table 2 presents the results of the Cox regression model for the FRE predictors. Using only the original variables comprising the FRE model, age, smoking, and blood pressure (BP) medication (presence versus absence) were the only significant predictors of CHD endpoints at 10 years. Table 2 also presents the results of the model with baseline depression added to the conventional predictors. While age was no longer a significant predictor of CHD in this model, use of blood pressure medication and baseline depression were positive predictors of CHD over the 10-year period. As the FRE includes BP medication to correct for the predictive utility of Systolic BP (SBP), we re-ran all models with and without SBP to avoid duplicating the predictive ability of blood pressure (its inclusion had no bearing on any results).

We also re-ran the model substituting the diagnostically-defined depression variable for the antidepressant use variable collected at baseline. The accuracy of the model was maintained using this self-reported, proxy measure of depression (Table 2).

Figure 1 presents the ROC curves for the prediction of CHD endpoints with the original FRE scores (AUC: 0.75, with a specificity of 0.73 and sensitivity of 0.67) and when it is augmented by baseline depression status (AUC: 0.77, with a specificity of 0.70 and sensitivity of 0.75); the latter model demonstrating superior overall accuracy and sensitivity (p>0.05; data not shown). However, when calibrated against the original model, the predicted number of events generated by the augmented version marginally over-estimated the true number observed (Table 3).
**DISCUSSION**

Our primary finding suggests that the augmented FRE model containing clinically-defined depression has the potential to improved diagnostic parameters for CHD over a 10-year period. While compromising a small degree of specificity, the augmented model produced non-significant, yet superior overall accuracy as well as sensitivity when compared with the original model. However, when calibrated against the original model, the predicted number of events generated by the augmented version marginally over-estimated the true number observed.

This study builds upon the work of others who have incorporated non-conventional risk factors into CVD risk assessment, more broadly. For example, the QRISK model was developed to include social support and has been shown to be superior to conventional risk equations for predicting lifetime CVD in the British population (18). Our study is guided by the evidence from the seminal INTERHEART study comprising over 50,000 individuals demonstrating that poor psychosocial profile, including depression, accounted for 32.5% of the population-attributable risk (PAR) for MI. This level of risk is comparable to that of smoking and greater than high blood pressure and diabetes (4). Indeed, the SIGN Group for Risk Estimation has argued that the application of risk assessment tools that ignore these less acknowledged risk factors and comprise only ‘traditional’ risk factors for heart disease (including the original version of the FRE) can lead to the “under-treatment of the socially deprived compared to the socially advantaged in relation to their future disease burden, thus enhancing disparities” (19). Equally, the under-treatment of individuals with a high prevalence of mental disorder such as depression, who are already disproportionally over-represented with physical health conditions, compared to those without, further perpetuates inequities. From a global health perspective, this study
addresses calls for “all countries…to identify the various at-risk populations more accurately (in order) to initiate and sustain treatment more consistently in those identified at risk”(20).

More broadly, a greater focus on female-specific prevention and management strategies in cardiovascular medicine is warranted. Traditionally, there has been an under-representation of women in clinical trials of MI(21) as well as evidence of differential symptomatology and severity(22). Other disparities in treatment exist, whereby female patients with existing CHD are less likely to be referred for surgical procedures(23), yield fewer benefits from such interventions even when referred (including mental health interventions after a cardiac event)(24, 25) and are under-represented in cardiac rehabilitation programs(26). Additionally, there is evidence that disease may manifest differentially for women due to genetic differences in immuno-inflammatory, hormonal, reproductive and social factors as well as coagulation(27, 28); all of which impact on the course and trajectory of disease. In fact, a review of the evidence base by the American Heart Association and American Stroke Association has led to the release of a position statement recommending female specific risk prediction calculators be developed for stroke.(29)

A key strength of this study was the randomly selected, population-based sample. While clinical depression was identified using psychiatric diagnostic interviewing, we acknowledge that the use of retrospective diagnosis by the SCID at 10-years to define baseline status was not optimal compared to diagnosis of current depression status. Further, the number of participants for whom CHD events occurred over the follow up periods was low; given that events were extracted retrospectively using hospital records data, it is plausible cases may have been missed. This
model therefore requires replication with larger, samples that prospectively collect events data and that may have greater power to observe even larger magnitude of changes in specificity and sensitivity. Further validation is underway in order to determine its utility for predicting risk in males, and for predicting cardiovascular events including stroke.

Depression is a polythetic syndrome whereby individuals present with different symptom manifestations, chronicity, severity and genesis; all of which may have their own impact on heart health. While it is plausible that these factors confer differential CHD risk, due to insufficient power, we were unable to consider this in the model. Our future studies will validate this model with sufficient power to address these potentially important issues using tools that capture depressive symptomatology. While we do not have depression data from self-report inventories (such as those used in primary care settings e.g. Patient Health Questionnaire 9) against which to validate our findings, short, validated self-report tools are indeed available and may yield comparable information that may be utilized for screening patients(30); an approach that is more feasible and timely than undertaking a full clinical assessment of depression in the context of general practice. If the augmented model was applied in clinical practice in its current form, clinicians would need to consider a number of issues. First, from a psychometric perspective, we found that while this model is likely to correctly identify a greater number of women at risk of experiencing a CHD event (ie. true positives) it is at the expense of a small increase in the false positive rate, when compared with the currently used model. Second, from a clinical perspective, is whether the magnitude of benefit gained by adding depression is clinically meaningful to warrant the added time and complexity. A CHD risk equation that includes a mental health component that uses self-report information or a proxy marker of depression (e.g. anti-depressant
medication usage, for example) does warrant further investigation as it could be attractive to patients and clinicians alike, enhancing its utility in clinical practice(31). Indeed, the current recommendations of the American Heart Association(32) advocate screening for depression, in the least. Future studies are required to explore the feasibility of implementing this augmented risk factor assessment in clinical settings.

CONCLUSION
The addition of a depression variable to the FRE equation improves the overall accuracy of the model for predicting 10-year CHD events in women, however may over-estimate the number of events that actually occur. This model now requires validation in larger samples as it could form a new CHD risk equation for women.
Acknowledgments

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Conflict of Interest Statement

MB has received Grant/Research Support from the NIH, Cooperative Research Centre, Simons Autism Foundation, Cancer Council of Victoria, Stanley Medical Research Foundation, MBF, NHMRC, Beyond Blue, Rotary Health, Geelong Medical Research Foundation, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Organon, Novartis, Mayne Pharma, Servier and Woolworths, has been a speaker for Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen Cilag, Lundbeck, Merck, Pfizer, Sanofi Synthelabo, Servier, Solvay and Wyeth, and served as a consultant to Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen Cilag, Lundbeck Merck and Servier. MB, AO, FNJ have received funding from Meat and Livestock, Australia. AO has received an honorarium from Novartis Pharmaceuticals. None of the aforementioned are related to this work.
REFERENCES


Table 1. Key characteristics of sample (depressive disorders versus controls at baseline) (Geelong Osteoporosis Study, Australia, 1993) (n=862)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 714)</th>
<th>Depressive disorders (n = 148)</th>
<th>p value</th>
<th>Missing Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of CHD Events</td>
<td>n = 23</td>
<td>n = 11</td>
<td>.02</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Continuous, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.3 (16.1)</td>
<td>46.4 (13.5)</td>
<td>0.33</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>26.5 (5.4)</td>
<td>27.0 (5.8)</td>
<td>0.40</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>76.3 (11.4)</td>
<td>76.8 (13.09)</td>
<td>0.65</td>
<td>20 (2%)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>121.3 (20.0)</td>
<td>119.4 (18.7)</td>
<td>0.58</td>
<td>19 (2%)</td>
</tr>
<tr>
<td>Pulse (beats per minute)</td>
<td>70.1 (10.6)</td>
<td>70.9 (11.7)</td>
<td>0.43</td>
<td>32 (4%)</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>2.9 (0.9)</td>
<td>3.0 (0.8)</td>
<td>0.14</td>
<td>57 (7%)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.2 (0.4)</td>
<td>1.3 (0.4)</td>
<td>0.61</td>
<td>48 (6%)</td>
</tr>
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<td>Triglycerides (mmol/L)</td>
<td>1.3 (0.8)</td>
<td>1.3 (0.8)</td>
<td>0.33</td>
<td>64 (7%)</td>
</tr>
<tr>
<td>hS-CRP (mg/L)</td>
<td>3.6 (5.5)</td>
<td>3.7 (5.1)</td>
<td>0.92</td>
<td>36 (4%)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>39.9 (6.4)</td>
<td>40.6 (4.3)</td>
<td>0.11</td>
<td>1 (0.1%)</td>
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<tr>
<td># Years Smoker</td>
<td>6.2 (11.1)</td>
<td>7.4 (11.1)</td>
<td>0.22</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>FRE % scores</td>
<td>5.23 (6.03)</td>
<td>5.04 (7.23)</td>
<td>0.78</td>
<td>61 (7%)</td>
</tr>
<tr>
<td>Antidepressant Use, No. (%)</td>
<td>18 (2.5%)</td>
<td>14 (9.5%)</td>
<td>.006</td>
<td>1 (0.1%)</td>
</tr>
</tbody>
</table>

Boldface indicates statistical significance (p<0.05); FRE, Framingham Risk Equation; HDL, high density lipoprotein; hS-CRP, high sensitivity C-Reactive Protein; LDL, low density lipoprotein; SD, Standard Deviation
Table 2: Cox proportional-hazards regression for CHD endpoints over 10-year follow-up
(Geelong Osteoporosis Study, Australia, 1993)

<table>
<thead>
<tr>
<th>FRE variables only</th>
<th>HR</th>
<th>95% CI</th>
<th>p value</th>
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</thead>
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<tr>
<td>Age</td>
<td>1.04</td>
<td>1.01, 1.08</td>
<td><strong>0.005</strong></td>
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<tr>
<td>Smoker</td>
<td>2.70</td>
<td>1.16, 6.29</td>
<td><strong>0.02</strong></td>
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<tr>
<td>HDL (mmol/L)</td>
<td>0.43</td>
<td>0.16, 1.18</td>
<td>0.10</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>1.28</td>
<td>0.95, 1.73</td>
<td>0.10</td>
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<tr>
<td>Systolic Blood Pressure (mm Hg)</td>
<td>1.00</td>
<td>0.98, 1.02</td>
<td>0.89</td>
</tr>
<tr>
<td>Blood Pressure Medication</td>
<td>2.36</td>
<td>1.09, 5.11</td>
<td><strong>0.03</strong></td>
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<th>FRE variables plus depression</th>
<th>HR</th>
<th>95% CI</th>
<th>p value</th>
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<td>Age</td>
<td>1.05</td>
<td>1.02, 1.08</td>
<td><strong>0.003</strong></td>
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<td>Smoker</td>
<td>2.26</td>
<td>0.95, 5.38</td>
<td>0.07</td>
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<td>HDL (mmol/L)</td>
<td>0.44</td>
<td>0.17, 1.15</td>
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<td>Total Cholesterol (mmol/L)</td>
<td>1.23</td>
<td>0.90, 1.68</td>
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<td>Systolic Blood Pressure (mm Hg)</td>
<td>1.00</td>
<td>0.98, 1.02</td>
<td>0.95</td>
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<td>Blood Pressure Medication</td>
<td>2.34</td>
<td>1.07, 5.14</td>
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<tr>
<td>Baseline Depression Status</td>
<td>2.62</td>
<td>1.22, 5.60</td>
<td><strong>0.01</strong></td>
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Boldface indicates statistical significance (*p<0.05); FRE, Framingham Risk Equation; HR, Hazard Ratio; HDL, high density lipoprotein; mm Hg, millimeter of mercury; mmol/L, millimoles per liter
Table 3. Calibration of prediction models (n=800).

<table>
<thead>
<tr>
<th>Fifth of Risk</th>
<th>Participant N</th>
<th>Event N</th>
<th>Predicted %</th>
<th>Observed %</th>
<th>Ratio</th>
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<tr>
<td></td>
<td>Framingham Risk Equation</td>
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Figure 1. ROC curve for original Framingham Risk Equation (solid line) and when augmented for diagnostically-defined depression (dashed) over 10-year follow-up (Geelong Osteoporosis Study, Australia, 1993).
HIGHLIGHTS

- We assess the accuracy of a Framingham Risk Equation (FRE) that include depression
- The model improves overall accuracy yet may over-estimate the number of events.
- This tool has potential to form a new cardiovascular risk equation for women.
- Clinicians should consider if the magnitude of benefit warrants the time/complexity