High-Sensitivity Cardiac Troponin I Improves Cardiovascular Risk Prediction in Older Men: HIMS (The Health in Men Study)

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Background—The Framingham Risk Score estimates the 10-year risk of cardiovascular events. However, it performs poorly in older adults. We evaluated the incremental benefit of adding high-sensitivity cardiac troponin I (hs-cTnI) to the Framingham Risk Score.

Methods and Results—The HIMS (Health in Men Study) is a cohort study of community-dwelling men aged 70 to 89 years in Western Australia. Participants were identified from the electoral roll, with a subset undergoing plasma analysis. Hs-cTnI (Abbott Architect i2000SR) was measured in 1151 men without prior cardiovascular disease. The Western Australia Data Linkage System was used to identify incident cardiovascular events. After 10 years of follow-up, 252 men (22%) had a cardiovascular event (CVE+) and 899 did not (CVE−). The Framingham Risk Score placed 148 (59%) CVE+ and 415 (46%) CVE− in the high-risk category. In CVE−men, adding hs-cTnI affected the risk categories of 244 (27.2%) men, with 64.8% appropriately reclassified to a lower and 35.2% to a higher category, which decreased the number of high-risk men in the CVE− to 39%. In CVE+ men, adding hs-cTnI affected the risk categories of 61 (24.2%), with 50.8% appropriately reclassified to a higher and 49.2% to a lower category and 82.5% remaining above the 15% risk treatment threshold. The net reclassification index was 0.305 (P<0.001). Adding hs-cTnI increased the C-statistic modestly from 0.588 (95% CI, 0.552–0.624) to 0.624 (95% CI, 0.589–0.659) and improved model fit (likelihood ratio test, P<0.001).

Conclusions—Adding hs-cTnI to the Framingham Risk Score provided incremental prognostic benefit in older men, especially aiding reclassification of individuals into a lower risk category. (J Am Heart Assoc. 2019;8:e011818. DOI: 10.1161/JAHA.118.011818.)

Key Words: aging • cardiovascular disease • cardiovascular disease prevention • cardiovascular disease risk factors • risk prediction • risk stratification • troponin

Cardiovascular disease (CVD) is a major cause of morbidity and mortality, which imposes a substantial burden on healthcare expenditure. The Framingham Risk Score (FRS) is a widely used model to estimate 10-year risk of cardiovascular events and aids in deciding on the use of primary prevention therapies. However, this was validated in white middle-aged populations. Studies have demonstrated that the FRS performs poorly in older adults, suggesting that conventional risk factors are not as predictive of cardiovascular events in older people.

High-sensitivity cardiac troponin I (hs-cTnI) assays can measure 10-fold lower concentrations with more precision...
Clinical Perspective

What Is New?

- Addition of high-sensitivity cardiac troponin I to the Framingham Risk Score significantly improved risk prediction in older men.
- There was a greater impact on the predicted risks for the men who did not experience a cardiovascular event during follow-up than in men who did.
- The new model was able to identify a cohort previously misclassified as high cardiovascular risk who had a lower risk of cardiovascular disease over a 10-year period.

What Are the Clinical Implications?

- The ability to identify a group of older adults with a relatively low risk of cardiovascular disease using high-sensitivity cardiac troponin I would allow more judicious use of preventative medications in this age group, thus avoiding side effects and drug-interactions.

The aim of this study was to evaluate the incremental benefit of adding hs-cTnI to the FRS for cardiovascular risk stratification in older men.

Methods

This study was conducted as part of the HIMS (Health in Men Study), which is a cohort study of community-dwelling men aged 70 to 89 years from Perth, Western Australia. The HIMS recruitment process and study population have been previously described in detail. In brief, HIMS was conducted in 2 waves; 12,203 men completed a questionnaire and underwent physical examination between 1996 and 1999, and 4,248 of these men were reassessed and had venesection between 2001 and 2004. The population for this arm of the study was selected from wave 2, as these participants had undergone pathology testing and had stored plasma samples. All participants provided written consent, and the University of Western Australia Human Research Ethics Committee approved the study. Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the Western Australian Centre for Health & Ageing at wacha@uwa.edu.au.

Physical assessments were performed by research nurses and included height, weight, and blood pressure. Participants completed a medical history survey and various questionnaires to assess smoking status, activity, memory, and psychosocial factors as previously described.

Hypertension was defined as blood pressure of ≥140/90 mm Hg, hypertension listed in the medical history, or the use of antihypertensive medications. Diabetes mellitus was defined as fasting blood glucose of ≥7.0 mmol/L, nonfasting blood glucose of ≥11.1 mmol/L, a stated history of diabetes mellitus, or the use of glucose-lowering medication. Dyslipidemia was defined as a fasting high-density lipoprotein of <0.9 mmol/L, low-density lipoprotein of ≥3.4 mmol/L, triglycerides of ≥1.8 mmol/L, total cholesterol of ≥5.5 mmol/L, or the use of lipid-lowering therapy.

Preexisting CVD was defined as a self-reported history of angina, myocardial infarction, stroke, or abdominal aortic aneurysm. The FRS to estimate 10-year cardiovascular event risk was calculated only for men without prior CVD.

Blood samples were collected between 8:00 AM and 10:30 AM. Samples collected into lithium heparin plasma separator (gel) tubes were promptly centrifuged at 2000g for 10 minutes. Cholesterol, triglycerides, high-density lipoprotein cholesterol, and creatinine were analyzed on the day of collection in an accredited laboratory. Low-density lipoprotein cholesterol was calculated using the Friedewald equation. Samples of serum were prepared and frozen at −80°C in 0.8-ml aliquots. Measurement of cardiac troponin I was done on one of these serum aliquots, which was thawed and recentrifuged prior to analysis. Samples were analyzed for cardiac troponin I using an Abbott Architect i2000SR assay over several days using a single reagent lot. This assay has a coefficient of variation of 10% at 6 ng/L in this laboratory.

The Western Australia Data Linkage System was used to determine occurrence of cardiovascular events and death over 10 years of follow-up. This system collates information from hospital morbidity and mortality data, emergency departments, and the death registry at 6-month intervals. The primary outcome measure, cardiovascular events over 10 years, was defined as a composite of coronary heart disease events (including coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular disease events (including ischemic stroke, hemorrhagic stroke, and transient ischemic attack), peripheral artery disease events (including intermittent claudication), and heart failure.
Statistical analysis was performed using SAS 9.4 (SAS Institute, Cary, NC) and STATA (StataCorp, College Station, TX). Categorical variables are described as absolute numbers and percentages. Continuous variables are described as mean and SD, while skewed data are also described as median and interquartile range. The 99th percentile value for hs-cTnI was calculated as the absolute single upper 99th percentile value using hs-cTnI results for men without preexisting CVD at baseline. Nonparametric data were compared using the Wilcoxon rank-sum test. A P<0.05 was used to define statistical significance. Logistic regression was used to assess the association of hs-cTnI with 10-year mortality.

Propportional hazards regression modeling was used to examine the association between covariates of the FRS and cardiovascular events over 10 years. Hs-cTnI was then added as a continuous predictor to the Cox regression model to form a new model. The traditional FRS was compared with the new model using the C-statistic, which measures discriminatory ability by indicating the correct ranking of each individual’s risk, and the likelihood ratio test of improved model fit. Predicted 10-year risks were also compared using the continuous net reclassification improvement, which quantifies improvement offered by a new marker. Density plots, receiver operating curves, and recalibration plots were used to graphically display differences between models. Reclassification tables were constructed for people who did or did not experience a cardiovascular event during follow-up, where comparison is made between quartiles of risk calculated with the FRS and the new model.

### Results

A total of 4248 men contributed data to the second wave of HIMS. The majority were born in Australia (62.0%), Northern Europe (26.7%), and the Mediterranean (5.2%). During a planned analysis of 4248 patient samples for another study, the last 2111 samples were accessible for analysis of hs-cTnI, which then formed the cohort of this study. There were 1137 men aged 70 to 74 years, 843 aged 75 to 79 years, and 131 aged 80 years or older. Baseline characteristics are presented in Table 1.

The hs-cTnI distribution for the entire cohort (n=2111) was nonparametric, as shown in Figure 1. Overall, the mean hs-cTnI was 9.4 ng/L, with a median of 5.9 ng/L and an interquartile range of 4.6 ng/L. The 25th and 75th percentiles were 4.2 and 8.8 ng/L, respectively. There were 42 men with hs-cTnI concentrations ≥40.0 ng/L, with a range of 40.7 to 398.5 ng/L. Increased age, current smoking, presence of baseline comorbidities, and CVD were associated with increased hs-cTnI concentration, as presented in Table 2.

Figure 1 also shows the distribution of hs-cTnI concentrations for men without CVD (n=1151) at baseline. The mean hs-cTnI for this group was 6.9 ng/L, with a median of 5.3 ng/L and an interquartile range of 3.5 ng/L. The 25th and 75th percentiles were 3.9 and 7.4 ng/L, respectively. The 99th percentile for all men without CVD was 30.0 ng/L (95% CI, 24.1–50.3 ng/L). There were 9 men with hs-cTnI concentrations ≥40.0 ng/L, with a range of 41.6 to 216.2 ng/L.

All-cause mortality after 10 years was 23.2% and CVD mortality was 7.8% in the men without prior CVD. The FRS to estimate 10-year cardiovascular event risk was calculated for men without prior CVD (n=1151). After 10 years of follow-up, 252 (22%) had a cardiovascular event (CVE+) and the remaining 899 (78%) did not (CVE—). The score placed 148 (59%) CVE+ men and 415 (46%) CVE— men in the high-risk category (10-year risk >20%).

The addition of log(troponin) increased the C-statistic modestly from 0.588 (95% CI, 0.552–0.624) to 0.624 (95% CI, 0.592–0.656). Table 1. Baseline Characteristics

| Characteristic* | Without CVD (n=1151) | With CVD (n=960) | Overall (n=2111) |
|-----------------|----------------------|-----------------|-----------------|
| Age, y          |                      |                 |                 |
| 70 to 74        | 700 (60.8)           | 437 (45.5)      | 1137 (53.9)     |
| 75 to 79        | 437 (38.0)           | 406 (42.3)      | 843 (39.9)      |
| >80             | 14 (1.2)             | 117 (12.2)      | 131 (6.2)       |
| Smoking status  |                      |                 |                 |
| Never           | 424 (36.8)           | 280 (29.1)      | 704 (33.3)      |
| Former          | 656 (57.0)           | 620 (64.6)      | 1276 (60.4)     |
| Current         | 71 (6.2)             | 60 (6.3)        | 131 (6.2)       |
| BMI, kg/m²      |                      |                 |                 |
| <20             | 21 (1.8)             | 22 (2.3)        | 43 (2.0)        |
| 20 to <25       | 374 (32.5)           | 272 (28.4)      | 646 (30.6)      |
| 25 to <30       | 599 (52.0)           | 493 (51.5)      | 1092 (51.8)     |
| ≥30             | 157 (13.7)           | 170 (17.8)      | 327 (15.5)      |
| Diabetes mellitus | 137 (11.9)         | 187 (19.5)      | 324 (15.3)      |
| Hypertension    | 450 (39.1)           | 579 (60.3)      | 1029 (48.7)     |
| Dyslipidemia    | 433 (38.9)           | 674 (72.2)      | 1107 (54.1)     |
| Malignancy      | 223 (19.4)           | 191 (19.9)      | 414 (19.6)      |
| Troponin, ng/L  | 5.3 (3.5)            | 7.0 (6.8)       | 5.9 (4.6)       |
| Creatinine, μmol/L | 90.5 (20.0)       | 101.7 (36.9)    | 95.6 (29.5)     |
| eGFR, mL/min per 1.73 m² | 79.0 (16.5) | 71.9 (19.2) | 75.8 (18.2) |

BMI indicates body mass index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.

*Troponin is expressed as median (interquartile range). Creatinine and eGFR are expressed as mean (SD). All other variables are expressed as count (%).
0.589–0.659) but significantly improved model fit (likelihood ratio test of improvement in fit, \(P<0.001\)). Receiver operating characteristic curves showing improvement in the model with addition of hs-cTnl (C-statistic 0.624 versus 0.588) is shown in Figure 2. Comparison of the 2 models using regression analysis is presented in Table 3. The addition of hs-cTnl to the

**Figure 1.** The distribution of high-sensitivity cardiac troponin I for the entire cohort (top) and for men without prior cardiovascular disease (CVD) (bottom).
FRS adjusted for only the effect of age, with no effect on the other covariates.

The predicted risk using the FRS and with the addition of hs-cTnI are presented as reclassification tables (Tables 4 and 5). The net reclassification index was 0.305 ($P < 0.001$). There was a greater impact on the predicted risk in the CVE−/C0 men than in CVE+ men. In the 899 CVE−/C0 men, the addition of hs-cTnI affected the risk categories of 244 (27.2%). In these men, 64.8% were appropriately reclassified to a lower category and 35.2% to a higher category. This decreased the number of men in the high-risk category from 46% with the FRS model to 39% with the FRS plus hs-cTnI model. In the 252 CVE+ men, the addition of hs-cTnI affected the risk categories of 61 (24.2%). In these men, 50.8% were appropriately reclassified to a higher risk category and 49.2% to a lower risk category, with 82.5% remaining above the treatment threshold of 15% risk.

Density plots showing improvements in predicted risk for CVE−/C0 and for CVD+ men are presented in Figure 3. Calibration plots showing improvement in the prediction of 10-year risk of cardiovascular events for those CVE− and CVD+ men are shown in Figure 4.

A modified 10-year CVD risk calculator was derived using the original FRS variables (Table S1) and with the addition of hs-cTnI (Table S2). The risk associated with individual scores is shown in Tables S3 and S4. Hs-cTnI was independently associated with risk of cardiovascular events, even at concentrations considerably lower than the 99th percentile, with increasing hs-cTnI concentrations predicting elevated cardiovascular risk. Furthermore, hs-cTnI had a greater impact on the risk score compared with other covariates due to the wider range of points allocated, which allowed for a wider range of 10-year risk estimates (Tables S1 through S4).

**Discussion**

This is the first study to demonstrate that the addition of hs-cTnI to the FRS significantly improves the prediction of cardiovascular events in this cohort, and identifies a cohort of elderly men previously misclassified as high cardiovascular risk.
risk who had a lower risk of cardiovascular events over a 10-year period. There was a greater impact on the predicted risks for the men who did not experience a cardiovascular event than in men who did.

The FRS is unable to identify older adults with relatively low cardiovascular risk, as it attributes points based on age. Furthermore, the association between conventional risk factors such as hypertension and hyperlipidemia with CVD in older adults is not the same as it is for younger populations. The original FRS performs relatively poorly in older men, with a C-statistic of 0.588, found in both the current study and an American study, compared with a C-statistic of 0.76 in the Framingham cohort. The addition of hs-cTnI to the model resulted in a C-statistic of 0.624 and an improvement in model fit (likelihood ratio test, P<0.001).

Recently, an Australian study on hs-cTnI in older women with a mean age of 75 years and a Swedish study on hs-cTnI in men aged 70 years found that hs-cTnI was independently associated with cardiovascular events. Both studies also found that the addition of cTnI to the FRS may improve risk prediction. Using a cohort twice the size and a wider age range, our study supports the concept that hs-cTnI can aid in prognostic discrimination and, in addition, can significantly improve reclassification.

The ability to identify a group of older adults with a relatively low risk of cardiovascular events using hs-cTnI would allow more judicious use of preventative medications in this age group, thus avoiding side effects and drug interactions. There is currently insufficient evidence for statin use in older adults for primary prevention, with some studies showing a possible increase in mortality in this setting.

On the other hand, reclassification into a high-risk category may prompt clinicians to consider preventative therapies. In a randomized controlled trial of patients without CVD and a normal cholesterol, those with higher concentrations of hs-cTnI had a greater reduction in absolute risk of cardiovascular events while on rosuvastatin therapy. This was however, conducted in a relatively younger cohort.

Our study also establishes the 99th percentile of hs-cTnI using the Abbott Architect assay in this community-based cohort of men aged over 70 years. Various studies have published different results for the 99th percentile of hs-cTnI, which can be due to differences in reference population selection. The 99th percentile for older men without a history of self-reported CVD in our study was 30.0 ng/L, which is similar to that reported in other studies of people from a wide range of age groups. In addition, there have been studies in presumably healthy and considerably younger men that have quoted slightly higher concentrations of between 33 and 36 ng/L using the same assay.

### Table 3. Regression Analysis for Comparison of Models

| Variable                  | Framingham Model | Framingham Model Plus log(troponin) |
|---------------------------|------------------|-------------------------------------|
| log(age)                  | 5.134            | 3.042                               |
| log(cholesterol)          | 0.951            | 0.793                               |
| log(HDL)                  | -0.414           | -0.395                              |
| log(SBP), untreated       | -0.727           | -1.105                              |
| log(SBP), treated         | 2.130            | 2.184                               |
| Hypertension treated      |                  |                                     |
| No                        | 0.000            | 0.000                               |
| Yes                       | 0.322            | 0.230                               |
| Current smoker            |                  |                                     |
| No                        | 0.000            | 0.000                               |
| Yes                       | 0.350            | 0.254                               |
| Prior diabetes mellitus   |                  |                                     |
| No                        | 0.000            | 0.000                               |
| Yes                       | 0.182            | 0.081                               |
| log(troponin)             |                  |                                     |
| No                        |                  |                                     |
| Yes                       |                  |                                     |
| AIC                       | 3483.326         | 3453.170                            |
| BIC                       | 3523.713         | 3498.605                            |
| C                         | 0.588            | 0.624                               |

AIC indicates Akaike Information Criterion; BIC, Bayesian Information Criterion; C, C-statistic; HDL, high-density lipoprotein; SBP, systolic blood pressure.

### Table 4. Predicted Risk in Men Who Did Not Experience a Cardiovascular Event

| Framingham Risk Score | Framingham Risk Score Plus Troponin I |
|-----------------------|---------------------------------------|
|                       | 6% to 10%  | 11% to 15%  | 16% to 20%  | >20%  | Total  |
| 6% to 10%             | 0 (0.00)  | 3 (0.26)    | 0 (0.00)   | 0 (0.00) | 3 (0.33) |
| 11% to 15%            | 33 (2.87) | 62 (5.39)   | 19 (1.65)  | 10 (0.87) | 124 (13.8) |
| 16% to 20%            | 18 (1.56) | 145 (12.6)  | 132 (11.5) | 62 (5.39) | 357 (39.7) |
| >20%                  | 1 (0.09)  | 16 (1.39)   | 124 (10.8) | 274 (23.8) | 415 (46.2) |
| Total                 | 52 (5.78) | 226 (25.1)  | 275 (30.6) | 346 (38.5) | 899 (100)  |

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of 3.9, 5.3, and 7.4 ng/L, respectively, in our study is higher than 2.0, 3.2, and 4.6 ng/L or 1.5, 2.7, and 4.6 ng/L, respectively, in other studies in younger adults. Some studies have found that elevations of hs-cTnI are commonly seen in older adults, independent of comorbidities. As such, there is debate over whether older adults should have higher diagnostic thresholds for the diagnosis of acute myocardial infarction. Our findings demonstrate that the 99th percentile of hs-cTnI in healthy older men is comparable to that in healthy younger men. Taken together, these findings suggest that increasing cardiac troponin I concentrations may reflect concurrent morbidity or progressive myocardial impairment rather than a benign process associated with aging.

Additionally, we found that hs-cTnI increased with age, comorbidities, and the presence of CVD. Although hs-cTnI was greater in current smokers compared with never smokers, as one may expect, this finding is in contrast with that from another large cohort study. The complex relationship between smoking, hs-cTnI, and cardiovascular risk therefore requires further elucidation in subsequent studies.

The strengths of our study include the large population and wide age range for an older population. This study also includes a long period of follow-up, in excess of 10 years in older adults, which has not been previously reported. Moreover, the study had very robust data linkage ensuring that mortality and morbidity data are captured. HIMS benefited from an extensive initial recruitment process, as participants were invited from the electoral role, where enrollment to vote is compulsory in Australia. Furthermore, the study involved collection of very extensive baseline data from which to draw associations. However, further validation studies are required for our modified risk prediction model.

Limitations include that this cohort is predominantly white in origin, includes only men, and is located in a major metropolitan area. Our findings would need to be confirmed in other populations. Not all participants in the second wave of the HIMS had hs-cTnI measured, and all results are based on blood samples collected at a single point in time. It has previously been shown that dynamic changes in cardiac troponin are associated with dynamic changes in risk of CVD mortality, and serial measurements may play a future role in

### Table 5. Predicted Risk in Men Who Experienced a Cardiovascular Event

| Framingham Risk Score | Framingham Risk Score Plus Troponin I |
|-----------------------|--------------------------------------|
| 6% to 10%             | 6% to 10%                             |
| 11% to 15%            | 11% to 15%                            |
| 16% to 20%            | 16% to 20%                            |
| >20%                  | >20%                                  |
|                       | Total                                 |

| Framingham Risk Score | 6% to 10% | 11% to 15% | 16% to 20% | >20% | Total |
|-----------------------|-----------|------------|------------|------|-------|
| 6% to 10%             | 0 (0.00)  | 0 (0.00)   | 0 (0.00)   | 0 (0.00) | 0 (0.00) |
| 11% to 15%            | 3 (0.26)  | 12 (1.04)  | 5 (0.43)   | 4 (0.35) | 24 (9.52) |
| 16% to 20%            | 2 (0.17)  | 21 (1.82)  | 33 (2.87)  | 24 (2.09) | 80 (31.7) |
| >20%                  | 0 (0.00)  | 6 (0.52)   | 29 (2.52)  | 113 (9.8) | 148 (58.7) |
| Total                 | 5 (1.98)  | 39 (15.5)  | 67 (26.6)  | 141 (56.0) | 252 (100) |

Figure 3. Density plots showing improvement in predicted risk after addition of high-sensitivity cardiac troponin I for men who did not experience a cardiovascular disease (CVD) event and for men who experienced a cardiovascular disease event during follow-up.

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risk stratification. In addition, variations in hs-cTnI, such as that from analytical imprecision, may limit the utility of single hs-cTnI measurements for risk prediction and the performance of risk prediction tools that use hs-cTnI. In our laboratory, the coefficient of variation (analytical imprecision) for the hs-cTnI assay used is 10% at 6 ng/L.

We did not study the incremental benefit of adding high-sensitivity cardiac troponin T to the FRS in our cohort of patients. However, increased high-sensitivity cardiac troponin T levels, like hs-cTnI, have been associated with incident heart failure and cardiovascular mortality in older adults and could potentially add to current risk prediction scores in this cohort. In addition, the incremental benefit of other biomarkers such as N-terminal pro-brain–type natriuretic peptide and C-reactive protein was not studied. Furthermore, residual confounding due to unmeasured clinical and laboratory prognostic factors or random error are additional limitations of this study.

We conclude from this study of community-dwelling older men in Australia that the 99th percentile of hs-cTnI was comparable to that of younger healthy men seen in previous studies. Hs-cTnI was associated with 10-year cardiovascular events and provided incremental prognostic value when added to the FRS. The combined model especially aided in reclassification of individuals into a lower risk category and identifies a group of older adults at a relatively lower risk of cardiovascular events.

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Disclosures

None.

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Figure 4. Calibration plots showing improvement in predicted risk after addition of high-sensitivity cardiac troponin I for men who did not experience a cardiovascular disease (CVD) event and for men who experienced a cardiovascular disease event during follow-up.
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SUPPLEMENTAL MATERIAL
Table S1. CVD Model Scoring Matrix.

| Points | Age   | Total Cholesterol | HDL  | Current Smoker | Prior Diabetes | SBP Not Treated | SBP Treated |
|--------|-------|-------------------|------|----------------|----------------|-----------------|-------------|
| -5     |       |                   |      |                |                |                 | <120        |
| -4     |       |                   |      |                | 160+           |                 |             |
| -3     |       |                   |      |                | 60+            |                 |             |
| -2     |       |                   |      |                | 140-159        | 120-129         |             |
| -1     | 70-74 | <160              | 45-49| No             | No             | 120-129         | 130-139     |
| 0      | 35-44 |                   |      |                |                | <120            |             |
| 1      |       |                   |      |                |                |                 |             |
| 2      |       |                   |      |                |                |                 |             |
| 3      | 160-199|                  |      |                | Yes            | 140-159         |             |
| 4      |       |                   |      |                |                |                 |             |
| 5      | 74-79 |                   |      |                | Yes            |                 |             |
| 6      | 200-239|                  |      |                |                |                 |             |
| 7      |       |                   |      |                |                |                 |             |
| 8      |       |                   |      |                |                |                 |             |
| 9      | 240-279|                  |      |                |                | 160+            |             |
| 10     | 80+   | 280+              |      |                |                |                 |             |
| 11     |       |                   |      |                |                |                 |             |
Table S2. CVD plus Troponin Scoring Matrix.

| Points | Age | Total Cholesterol | HDL | Current Smoker | Prior Diabetes | SBP Not Treated | SBP Treated | Troponin |
|--------|-----|-------------------|-----|----------------|----------------|----------------|-------------|----------|
| -12    |     |                   |     |                |                |                |             | <120     |
| -11    |     |                   |     |                |                |                |             |          |
| -10    |     |                   |     |                |                |                |             | 160+     |
| -9     |     |                   |     |                |                |                |             |          |
| -8     |     |                   |     |                |                |                |             | 120-129  |
| -7     |     |                   |     |                |                |                |             |          |
| -6     |     |                   |     |                |                |                |             |          |
| -5     |     | 60+               |     |                |                |                |             | 140-159  |
| -4     |     |                   |     |                |                |                |             | 130-139  |
| -3     |     |                   |     |                |                |                |             |          |
| -2     |     |                   |     |                |                |                |             | 130-139  |
| -1     |     |                   |     |                |                |                |             |          |
| 0      |     | 70-74             | <160| 45-49         | No             | No             | 120-129     | <2       |
| 1      |     |                   |     |                | Yes            |                |             |          |
| 2      |     | 35-44             | Yes | <120          | 140-159        |                |             |          |
| 3      |     |                   |     |                |                |                |             |          |
| 4      |     |                   |     |                | Yes            |                |             |          |
| 5      |     | 74-79             | 160-199 |                |                |                |             |          |
| 6      |     |                   |     |                | Yes            |                |             |          |
| 7      |     |                   |     |                |                |                |             |          |
| 8      |     |                   |     |                |                |                |             | 2-2.9    |
| 9      |     |                   |     |                |                |                |             | 2-2.9    |
| 10     |     | 80+               |     |                |                |                |             |          |
| 11     |     |                   |     |                |                |                |             |          |
| 12     |     | 240-279           |     |                |                |                |             | 160+     |
| 13     |     |                   |     |                |                |                |             | 3-3.9    |
| 14     |     | 280+              |     |                |                |                |             |          |
| 15     |     |                   |     |                |                |                |             |          |
| 16     |     |                   |     |                |                |                |             |          |
| 17     |     |                   |     |                |                |                |             | 4-4.9    |
| 18     |     |                   |     |                |                |                |             |          |
| 19     |     |                   |     |                |                |                |             |          |
| 20     |     |                   |     |                |                |                |             | 5-5.9    |
| 21     |     |                   |     |                |                |                |             |          |
| 22     |     |                   |     |                |                |                |             | 6-6.9    |
| 23     |     |                   |     |                |                |                |             | 7-7.9    |
| 24     |     |                   |     |                |                |                |             | 8-8.9    |
| 25     |     |                   |     |                |                |                |             | 9-9.9    |
| 26     |     |                   |     |                |                |                |             |          |
| 27     |     |                   |     |                |                |                |             |          |
| 28     |     |                   |     |                |                |                |             |          |
| 29     |     |                   |     |                |                |                |             |          |
| 30     |     |                   |     |                |                |                |             |          |
| 31     |     |                   |     |                |                |                |             |          |
| 32     |     |                   |     |                |                |                |             |          |
| 33     |     |                   |     |                |                |                |             |          |
| 34     |     |                   |     |                |                |                |             |          |
| 35     |     |                   |     |                |                |                |             |          |
| 36     |     |                   |     |                |                |                |             |          |
| 37     |     |                   |     |                |                |                |             |          |
| 38     |     |                   |     |                |                |                |             |          |
| 39     |     |                   |     |                |                |                |             | 10+      |
Table S3. CVD Model Scores and associated risk estimates.

| CVD Model Score | 10-year Risk |
|-----------------|--------------|
| -7              | 0.09         |
| -5              | 0.10         |
| -4              | 0.11         |
| -3              | 0.12         |
| -2              | 0.12         |
| -1              | 0.13         |
| 0               | 0.14         |
| 1               | 0.15         |
| 2               | 0.16         |
| 3               | 0.17         |
| 4               | 0.18         |
| 5               | 0.19         |
| 6               | 0.21         |
| 7               | 0.22         |
| 8               | 0.23         |
| 9               | 0.25         |
| 10              | 0.26         |
| 11              | 0.28         |
| 12              | 0.29         |
| 13              | 0.31         |
| 14              | 0.33         |
| 15              | 0.35         |
| 16              | 0.37         |
| 17              | 0.39         |
| 18              | 0.41         |
| 19              | 0.43         |
| 20              | 0.45         |
| 21              | 0.48         |
| 22              | 0.50         |
| 24              | 0.55         |
Table S4. CVD plus Troponin Model Scores and associated risk estimates.

| CVD plus Troponin Model Score | 10-Year Risk |
|-------------------------------|--------------|
| -3                            | 0.07         |
| -2                            | 0.07         |
| 0                             | 0.08         |
| 1                             | 0.08         |
| 2                             | 0.08         |
| 3                             | 0.09         |
| 4                             | 0.09         |
| 5                             | 0.10         |
| 6                             | 0.10         |
| 7                             | 0.11         |
| 8                             | 0.11         |
| 9                             | 0.11         |
| 10                            | 0.12         |
| 11                            | 0.12         |
| 12                            | 0.13         |
| 13                            | 0.13         |
| 14                            | 0.14         |
| 15                            | 0.14         |
| 16                            | 0.15         |
| 17                            | 0.15         |
| 18                            | 0.16         |
| 19                            | 0.17         |
| 20                            | 0.17         |
| 21                            | 0.18         |
| 22                            | 0.18         |
| 23                            | 0.19         |
| 24                            | 0.19         |
| 25                            | 0.20         |
| 26                            | 0.21         |
| 27                            | 0.22         |
| 28                            | 0.22         |
| 29                            | 0.23         |
| 30                            | 0.24         |
| 31                            | 0.25         |
| 32                            | 0.25         |
| 33                            | 0.26         |
| 34                            | 0.27         |
| 35                            | 0.28         |
| 36                            | 0.29         |
| 37                            | 0.30         |
| 38                            | 0.31         |
| 39                            | 0.32         |
| 40                            | 0.33         |
| 41                            | 0.34         |
| 42                            | 0.35         |
| 43                            | 0.36         |
| 44                            | 0.37         |
| 45                            | 0.38         |
| 46                            | 0.40         |
|   |     |
|---|-----|
| 46| 0.41|
| 47| 0.42|
| 48| 0.44|
| 49| 0.45|
| 50| 0.46|
| 51| 0.48|
| 52| 0.49|
| 53| 0.50|
| 55| 0.53|
| 56| 0.55|
| 58| 0.58|
| 59| 0.59|
| 60| 0.61|
| 62| 0.64|
| 63| 0.65|
| 65| 0.68|
| 67| 0.71|