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Systematic Review of Cardiovascular Disease Risk Assessment Tools

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Structured Abstract

Objectives: To summarize the current state of cardiovascular disease (CVD) risk modeling literature with a focus on the U.S. patient population, and to describe evidence on which models best predict cardiovascular risk among patients with diabetes.

Data Sources: We searched MEDLINE for articles published January 1, 1999, to February 24, 2009, and reviewed all reference lists of included articles.

Review Methods: We included studies of asymptomatic adults in any geographic setting with any study design in which a CVD clinical risk prediction model was developed or validated. We excluded studies that 1) were not in English; 2) were without information pertinent to the key questions; 3) had fewer than 200 participants at enrollment; 4) were not original studies; and 5) lacked internal or external validation data. We captured study information such as cohort characteristics, risk model characteristics, model performance statistics, and quality review elements. We collected information about the study populations for stratification of results by variables, including sex and geographic area. We also searched online for available tools and documented their location and the model on which they purported to be based. We used the online tools to calculate risk for five test cases to identify variation in estimated risk.

Results: Of the 3,499 articles initially identified, 84 met inclusion criteria, providing data on 102 risk models. The majority of models (87 out of 102) were not externally validated. The most commonly externally validated risk models were the 1991 Framingham (FRS) model for CVD (26 evaluations), the 1998 FRS model for total coronary heart disease (CHD) (24 evaluations), the FRS Adult Treatment Panel III (ATP-III) model for hard CHD (16 evaluations), the Prospective Cardiovascular Münster (PROCAM) model for hard CHD (11 evaluations), and the Systematic Coronary Risk Evaluation (SCORE) model for CVD mortality (11 evaluations).

Conclusion: The FRS models performed well in U.S. populations, but there were absolute risk prediction problems when they were applied to populations substantially different from the source cohort. Sometimes this was due to particularly low or high baseline risk in the destination cohort, and at other times to systematic differences in risk attributable to specific factors. The 2001 ATP-III version demonstrated better risk prediction than older FRS models because it focuses on hard CHD outcomes, excludes patients with diabetes, and includes newer FRS data. Diabetes-specific process measurement variables are significantly related to cardiovascular outcome risk among patients with diabetes, and risk models that incorporate these factors outperform general risk prediction models when applied to these patients. Models excluding patients with diabetes outperformed general risk prediction models that included these patients in their development when applied to non-diabetic cohorts. Unfortunately, external validation of diabetes-specific risk models is lacking, particularly among U.S. cohorts.

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Executive Summary

Introduction

Background

Cardiovascular disease (CVD) is the leading cause of death in the United States and costs the U.S. health care system an estimated \$531 billion in direct and indirect costs.^{1, 2} Because of the high incidence and cost of this disease, clinical practice guidelines target primary prevention, and recommend that providers evaluate patients for cardiac risk factors that may warrant medical treatment.³⁻⁷ However, previous research has shown that providers do not accurately estimate the risk of CVD events on their own.⁸⁻¹³ A number of multivariate risk prediction equations, derived from large prospective cohort studies or randomized trials, have been developed to estimate CVD risk in time intervals ranging from 4 to 12 years.¹⁴⁻²¹ In order to make them more usable to busy clinicians, many of these risk models only require information from a patient's medical history and easily available laboratory tests, and have been adapted for interpretation through simplified charts or tables in paper or computer-based formats.^{3, 22}

The most commonly used CVD risk prediction models in the United States are those based upon the Framingham cohort, a large prospective cohort of U.S. men and women aged 30 to 74 years. These models have been subsequently validated in multiple diverse populations.^{17, 20, 23-26} However, controversy remains regarding which variables are the most important for risk prediction, which outcomes are the most generalizable across populations, and whether remodeling or recalibration needs to be addressed in populations other than the source cohort.

A number of studies showing that patients with diabetes had significantly elevated risk for cardiovascular outcomes prompted the Adult Treatment Panel III (ATP-III) guidelines, which include a risk calculator that excludes patients with diabetes and direct clinicians to consider those patients as already having CVD for the purposes of medical management.^{3, 27, 28} However, other studies have questioned this assertion, both from risk modeling and disease management standpoints.²⁹ In addition, there is a growing literature that suggests that patients with diabetes themselves are a heterogeneous group of patients who require diabetes-specific risk factors to adequately characterize their cardiovascular risk.^{23, 30}

The aim of this systematic review was to summarize the current state of CVD risk models, with a focus on the U.S. patient population. In addition, performance of each of the available models in populations other than the source cohort was assessed, as well as a summarization of which models use which risk factors and the impact that recalibration and reclassification has had in the last few decades on these models. Finally, we sought evidence related to which models are best suited for predicting cardiovascular risk among patients with diabetes, and whether treating diabetes as an outcome equivalent is appropriate.

Key Questions

The key questions for this report were:

KQ1: Do any of the currently available tools for the prediction of cardiovascular risk in a North American population offer clear advantages in discriminatory power over the others in predicting incident coronary heart disease (CHD), cerebrovascular stroke (stratified by thrombotic or

hemorrhagic type), or a combination of these two?

KQ2a: Do tools that treat diabetes as a CHD outcome equivalent have different performance characteristics than those that use diabetes as an independent risk factor for those outcomes?

KQ2b: Is the appropriateness of using diabetes as a coronary risk equivalent modified by the number of other cardiac risk factors that the individual has?

Methods

Literature Search

For this review, we included studies of asymptomatic adults in any setting and country with any study design in which a clinical risk prediction model was developed or validated for predicting CVD risk. We excluded studies that 1) were not published in English; 2) did not report information pertinent to the key questions; 3) had fewer than 200 participants at enrollment; 4) were not original studies; and 5) did not perform any internal or external validation of the model. For this review, the relevant population was men and women who are currently asymptomatic for CVD. As we developed each of the search components with input from previous systematic reviews, we employed an approach of iterative refinement, using a pool of approximately 50 relevant articles previously identified as a quasi-validation set, to assess recall of our search iterations (i.e., whether our searches retrieved or missed known items of interest).³¹⁻³³ In addition to studies identified through the literature search in MEDLINE, we hand-searched the reference lists of all included articles for additional articles. Once we identified articles through the electronic database searches, review articles, and bibliographies, we examined abstracts of articles to determine whether studies met our criteria. Two reviewers separately evaluated the abstracts for inclusion or exclusion. If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it. Of the entire group of 3,499 articles, 636 required full-text review. For the full article review, two reviewers read each article and decided whether it met our inclusion criteria.

Data Abstraction

The data for this project were abstracted into a database designed to capture study information such as cohort characteristics, risk model characteristics, model performance statistics, and quality review elements. We collected information about the study populations to allow for stratification of results by variables, including sex and geographic area.

The team was trained to abstract by pulling relevant data from several articles into the database and then reconvening as a group to discuss the utility of the table design. We repeated this process through several iterations. The content lead reviewed each abstraction to ensure accuracy and completeness.

In addition to assessing the studies and models presented in the literature, we searched for all available tools online and documented their location and the model on which they purported to be based. We then used the online tools to calculate risk for five test cases, in order to identify any variation in estimated risk.

We assessed the quality of individual studies across multiple dimensions using assessment questions developed to reflect the importance of fully characterizing a population in which a model is developed, and the prevalence of missing data and loss to follow-up. In addition,

evaluation methods and measures were pursued. We did not assign quality scores to the individual studies or the literature as a whole, but instead chose to present patterns of quality.

Results

Key Question 1

The literature search identified 3,499 potentially relevant articles of primary CVD risk modeling development or validation. Most of the studies were excluded in the abstract stage because either the study was not relevant to the topic or the study population was not asymptomatic for CVD. In the full-text review stage, most of the studies were excluded, either because the evaluation did not involve a risk prediction tool, the study population was not asymptomatic for CVD, or there were no model performance measurements reported.

A total of 84 articles^{29, 34-82,14, 19, 23-25, 83-110,111} were included in this review, representing a total of 102 risk prediction models. To develop the models, the authors used a total of 100 variations of 73 identifiable patient cohorts. These cohorts provided data on CHD outcomes (52 cohorts), CVD outcomes (31 cohorts), and cardiovascular accident (CVA) outcomes (12 cohorts). Of the 102 models that were identified, only 17 were externally validated in a population other than the one in which the model was developed, and those models were all developed from the following nine primary patient cohorts:

- Scottish Heart Health Extended Cohort (SHHEC)
- Diabetes Audit and Research in Tayside, Scotland (DARTS)
- FINRISK
- Framingham Study (FRS)
- Framingham Offspring Study (FRS-O)
- Prospective Cardiovascular Münster Study (PROCAM)
- QRESEARCH Database
- Systematic Coronary Risk Evaluation (SCORE)
- United Kingdom Prospective Diabetes Study (UKPDS)

Information on these cohorts is available in Appendix G/Summary Table 4. The most commonly externally validated risk models were:

- 1991 FRS model for CVD (with 26 evaluations)
- 1998 FRS model for total CHD (with 24 evaluations)
- FRS ATP-III model for hard CHD (i.e., sudden CHD death or myocardial infarction, with or without cardiac procedures) (with 16 evaluations)
- PROCAM model for hard CHD (with 11 evaluations)
- SCORE model for CVD mortality (with 11 evaluations)

These models are typically considered general population, first-outcome incidence calculators, meaning that they are intended to calculate individual risk for any patient within a certain age range. However, it is important to acknowledge that the FRS ATP-III model excludes patients with diabetes, the PROCAM model excludes women, the DARTS and UKPDS models exclude patients without diabetes, and the Scottish ASSIGN model (derived from SHHEC) includes a non-traditional social deprivation index as a risk factor. Therefore, it is possible that they are not entirely applicable in all general populations.

The majority of models (87 out of 102) identified through our search were not validated in an external data set.^{14, 24, 25, 34-39, 41, 47, 49-52, 55, 57, 60-62, 71, 75, 76, 80, 81, 83, 84, 87, 91, 93, 100, 101, 103, 107, 109, 111-115 Some of the studies published models yet to be externally validated that were directly intended to be used for individual risk prediction.^{54, 59, 60} Some of these models were developed for specific groups of patients with atrial fibrillation,⁵² chronic kidney disease,⁴⁵ renal transplants,⁸² younger age,⁴⁹ or older age,^{64, 69, 93, 102} or were based only on patient-provided information.^{51, 105} Other studies were conducted primarily in order to evaluate whether a variety of non-traditional risk factors improved prediction performance. These non-traditional risk factors include body mass index,³⁴ hemoglobin A_{1c},^{56, 40, 70, 86, 103} apolipoproteins,^{54, 80} socioeconomic factors,^{59, 66} family history,^{59, 76, 80, 103} carotid ultrasonography,⁷² metabolic syndrome,^{65, 75, 79} exercise testing parameters,⁸⁴ and genetic polymorphisms.¹⁰¹ A recent review of non-traditional risk factors in CHD risk prediction concluded that the evidence was insufficient to assess the balance of benefits and harms of using these risk factors in risk prediction.^{117, 118}}

There was significant heterogeneity among outcome definitions, both across all of the studies and among models used for comparison within individual studies. Frequently, cohort outcome data were collected in order to match a particular risk model, but other models with different outcomes were used as comparisons. Nonetheless, since all of the outcomes were variations of CVD, stable relative risk performance was frequently found even when outcomes were mismatched.

Evaluating absolute risk prediction of a risk model with a mismatched outcome between model and cohort has severe limitations, because the baseline outcome event rates are different from the outset. Some interpretation is possible if the prediction error is in the opposite direction of what one would expect; that is, if a cohort outcome is more restrictive, one would expect the model to overpredict the outcome, but if it underpredicts the outcome, then the result can be safely interpreted as poor absolute risk prediction. However, no such assertion can be made if absolute risk prediction is determined to be adequate for mismatched outcomes.

Some of the tools reported thresholds for low- and high-risk patients in order to recommend tailored management of those patients.^{14, 19, 35, 37-39, 41, 43, 46, 47, 51, 54, 56, 58, 61, 70, 73, 84, 88, 97, 99, 103} In addition, some studies evaluated the effects of risk strata reclassification between different models and for additional variable inclusion to an existing model.^{35, 36, 46, 54, 61, 88, 99, 101-103} Results of reclassification evaluations were variably reported, sometimes in tabular format and sometimes by reclassification indices. There was a clear correlation with absolute risk prediction performance and classification performance, and some reclassification evaluations resulted in significantly improved performance. It is also important for cohort and model outcome matching, since low- and high-risk threshold cut-off points are set using the development data (i.e., matched outcome). Separate risk cut-off points must be established in order to appropriately use such tools to risk-stratify patients for outcomes other than those for which they were developed.

Almost all models had good relative and absolute risk prediction in the cohort in which they were developed. Clearly this is not surprising, but it does bring into question the limitations of relying on models that have only been internally validated. The external validations with the strongest evidence were among North American and European cohorts in which the same outcome measure was used in the validation study as in the development study. Asian cohort model evaluations had limited generalizability to U.S. populations because they have been shown to have significantly different outcome event rates of CHD and cerebrovascular disease.

External validation of U.S. models developed in other U.S. cohorts found that most retained good relative and absolute risk prediction performance among white and black populations, but absolute risk prediction was poor among minority populations, such as Hispanics and Asian Americans.^{23, 97, 100} A few evaluations using higher- or lower-risk cohorts, such as siblings of patients with early coronary artery disease or young adults, predictably had poor absolute risk prediction performance.^{42, 49} In all cases, overall model relative risk performance (risk separation) was better for women than men.^{23, 42, 49, 97, 100} Generally, these risk models are most likely to perform accurately in patients representative of the source population in which they were developed.

External validation of U.S. risk models among European cohorts in which the outcomes were matched was more mixed. A few studies with matched outcomes reported acceptable risk model performance, but the European cohorts were generally at higher risk than the source population, including all-diabetic or elderly cohorts.^{48, 89} A few studies reported that the risk models underpredicted the outcomes, but these were almost entirely high-risk patient cohorts, such as patients with diabetes, organ transplants, advanced age, poorly controlled hypertension, or poor access to health care.^{56, 77, 82, 85, 89} Most of the evaluations among European cohorts found that the U.S. risk models overpredicted risk.^{14, 48, 56, 80, 88, 92, 94, 110} This was frequently due to a difference in underlying outcome event rates between the model cohort and the evaluation cohort. In some studies, significant differences between relative risk factor contributions were also found.³⁰

A number of U.S. cohorts that engaged in recalibration or remodeling reported poor absolute risk performance for the original FRS models. However, most of these evaluations had an outcome mismatch between the cohort and model.^{54, 61, 101} Those studies that performed remodeling of the FRS risk variables in the local cohort reported retained or improved relative risk prediction and adequate absolute risk prediction.^{54, 61, 101} It should be noted that it is not surprising that remodeling with an outcome that matches the original model outcome (by definition) would result in improved performance. For example, one study evaluated matched outcomes between the cohort and the original model and found that minority populations were poorly predicted by the model. This study subsequently showed that remodeling resulted in adequate performance for all the cohorts.²³ Two other studies with matched outcomes and inadequate original model performance noted adequate absolute risk prediction after remodeling.⁴⁵ In contrast, recalibration methods (which adjust the baseline outcome event rate intercept in the model but do not adjust the risk variable coefficients) performed more variably, with both adequate and inadequate absolute risk prediction results.^{42, 45} However, in the one study that performed both recalibration and remodeling, recalibration for both.⁴⁵

Key Question 2

There were six diabetic cohorts that were used to develop risk prediction models and 11 diabetic cohorts that were used in external validation of diabetes-specific risk models for CVD, CHD, or stroke outcomes.^{38, 40, 57, 63, 72, 73, 78, 85, 96, 107, 108, 119} There were 13 non-diabetic cohorts used in either primary model development or external validation of risk models excluding diabetes or general purpose models.

The UKPDS risk model¹¹⁹ was the most frequently validated type 2 diabetes model.^{38, 40, 73, 78, 108} However, three of the five studies were from U.K. cohorts, and there were no U.S. validations of this model. Even among the U.K. external validation studies, absolute risk prediction

performance was variable, interpretation was complicated by outcome mismatches, and there was no matched outcome external validation of the model.^{73, 78, 108} In contrast, there was clear evidence that the UKPDS outperformed general cardiovascular risk models when they were directly compared among diabetic populations.^{73, 78} Another externally validated type 2 diabetes cardiovascular risk model is the DARTS model, which was developed in a different British cohort. A third type 2 diabetes model that was only internally validated was developed in Chinese patients.³⁸ In all three models, diabetes-specific risk factors were included.

Evaluation of the contribution of diabetes to the risk of developing cardiovascular outcomes was evaluated in two studies, one consisting of only U.S. cohorts and the other including both U.S. and European cohorts.^{23, 30} The U.S. cohort comparison study found that cohorts comprised of non-white or Hispanic populations had significantly different relative risks among those factors than the Framingham cohort. However, the risk of CVD among patients with diabetes differed significantly from that in the FRS population only for a Native American cohort. A similar comparison that included European studies as well demonstrated different CVD risk in the European cohort relative to the FRS cohort.

These studies also showed the effect of including or excluding variables in a multivariate analysis, since both evaluated some of the same cohorts, but the U.S./European study did not include as many of the traditional risk factors as the U.S.-only study.^{23, 30} Some additional risk was attributed to diabetes when there were fewer variables in the multivariate analysis. This was most likely due to a correlation between diabetes and the variables that were omitted, and reinforces the concept that any risk estimate for a variable includes residual confounding from unmeasured covariates.

Most of the matched outcome external validations performed on diabetic cohorts by cardiovascular risk models that included diabetes as a risk factor found that the models significantly underpredicted the number of outcomes experienced in the cohort, suggesting that developing predictive models in cohorts that combine patients with and without diabetes may be less than ideal.^{73, 78, 85} A few studies showed acceptable observed-to-expected ratios, but had outcome mismatches that were more restrictive in the cohort than the model.^{40, 72} The effect of increased risk of CVD in diabetic populations precludes simply adding a diabetes risk variable to a general model to capture the variance of risk experienced by diabetic populations. In other words, simply including diabetes as a variable in a general model is insufficient to fully capture the level of risk in patients with diabetes. More descriptive variables that have confounding or effect-modifying effects are likely necessary for analyses in these populations, including diabetes control, duration of diabetes, and whether the patient has already experienced end-organ damage.

There were a few studies that evaluated risk models that included diabetes as a risk factor in nondiabetic cohorts. For example, Czech patients without diabetes were evaluated with the 1998 FRS model with matched outcomes, resulting in an overprediction of outcomes.⁵⁶ The Norwegian Counties Study evaluated the SCORE risk model, which does not include a diabetes risk factor but does include patients with diabetes in its source cohort, in patients without diabetes and also found that the model overestimated the number of outcomes.⁴⁴ The internal validation of the QRISK equation for CVD risk excluded patients with diabetes and was used to externally validate the 1991 FRS general risk model.⁴⁶ Again, the 1991 FRS model significantly overpredicted the outcome, although there was a small outcome mismatch. Models including diabetes as a binary variable, in which patients without diabetes are given a value of zero, should in theory perform well in non-diabetic populations, where all individuals would simply have zero risk associated with that condition. The fact that they do not points to the strong likelihood that a dichotomous diabetes risk predictor does not account for all of the cardiovascular risk associated with having diabetes.

In several studies, a risk model with diabetes as a risk factor was directly compared to a diabetesexcluded model. The Women's Health Study, in which 2.9 percent of patients had diabetes, evaluated the FRS ATP-III and 1998 models, but the outcomes were very mismatched in the ATP-III (CVD vs. hard CHD) and 1998 models (total vs. hard CHD), and absolute risk prediction was poor in both.⁵⁴ The Chicago Heart Association Detection Project in Industry study evaluated young men without diabetes for matched outcomes in the ATP-III model and unmatched outcomes in the 1998 model, but absolute risk performance was poor in both because of the young population.⁴⁹

Remodeling efforts among diabetes and diabetes-excluded risk models followed the larger trend of general cardiovascular risk prediction models. Recalibration methods were successful in some cases but inadequate in others.³⁸ However, remodeling methods were almost always successful in producing a model that performed well in the local cohort.³⁸ Among non-diabetic cohorts and general risk models, remodeling was successful in improving performance, although it should be noted that diabetes as a risk factor was dropped from the models.⁵⁶ Among a large U.S. female non-diabetic cohort, remodeling of the FRS ATP-III risk variables did not result in a well-calibrated model.⁶¹

Remodeling of established risk models for use in other cohorts also serves to illuminate systematic relative risk differences between risk factors. For example, although absolute risk prediction was very poor when the UKPDS model was applied to the Hong Kong Diabetes Registry, a direct comparison of the hazard ratios of the same risk variables between the two cohorts did not show significant differences.³⁸ Thus, both the baseline outcome incidence and the relative risk contributions from individual risk factors are relevant to absolute risk performance.

Discussion

Limitations of the Literature

Summarizing this literature is challenged by the tremendous outcome heterogeneity among model evaluation studies. In many cases, only limited comparison was possible between cohorts and models with different outcomes. Minor mismatches were more common than large categorical differences, but this still could have significant impact on the absolute risk prediction performance of a model, as shown by large differences in outcomes in cohorts reporting multiple similar outcomes.

External validation studies showed fair performance when FRS models were applied to U.S. populations that were similar to the source FRS cohort, but failed when applied to some minority populations. European general risk models have not been widely validated in U.S. populations, and U.S. risk models tended to perform poorly in European and Asian cohorts. This suggests, but does not confirm, that European models would likely perform poorly in U.S. cohorts.

Changes in baseline outcome event rates and relative contributions to risk from different risk factors present in either the source model or the application cohort, but not both, clearly led to poor performance in some models. Remodeling, and to a lesser extent, recalibration, have been shown to be successful methods for improving model performance in a variety of cohorts.

However, methodological issues remain, including lack of empirical evidence for the appropriate frequency at which remodeling should occur and the optimal sample sizes for these analyses.

Summary and Interpretation

Overall, the FRS models performed fairly well in U.S. populations, but there were absolute risk prediction problems when they were applied to populations that were substantially different than the source cohort. In some cases, this was due to particularly low or high baseline risk in the destination cohort, and in some cases it was due to systematic differences in risk attributable to specific risk factors. Although all of the FRS risk models were developed from a cohort that was not entirely representative of the U.S. population, the 2001 ATP-III version demonstrated several benefits over the older FRS models, including a focus on a hard CHD outcome, exclusion of patients with diabetes, and incorporation of more current FRS data than the 1991 version. A 2008 CVD model was recently published but has not yet been externally validated.¹²⁰

Recalibration, and to a greater extent, remodeling, demonstrated effectiveness as a means to improving performance in cohorts with substantially different outcome incidence or risk factor prevalence from the source cohort. Questions remain regarding the population sample size necessary to perform these methods and how frequently it should be applied.

Development of risk models for cohorts with risk profiles that are systematically divergent from the general population can also be a successful strategy. However, in many cases, studies taking this approach were more or less remodeling exercises using traditional risk variables in the most common models. Sample size requirements for developing stable risk models are even less clear for these cohorts, and some of these studies had fewer than 1,000 participants. A growing body of literature suggests that specific cohort risk models are likely to be most successful when there are risk factors unique to that population that inform cardiovascular risk.

Even among U.S. cohorts, there was evidence that some ethnically diverse or minority populations had significantly different risk factor contributions to outcomes, even when the baseline prevalence was similar.^{23, 30} Our review did not exclude studies from any geographic area, but in analyzing the data it became clear that there were systematic differences in risk factor prevalence and outcome event rates between Asian cohorts (which were mostly Chinese or Korean) and North American and European cohorts.¹²¹ This makes use of Asian models in a general U.S. population ill-advised.

Diabetes-specific process measurement variables are significantly related to cardiovascular outcome risk among patients with diabetes, and risk models that incorporated these factors outperformed general risk prediction models when applied to these patients. Analysis also suggests that models excluding patients with diabetes outperformed general risk prediction models that included these patients in their development when applied to non-diabetic cohorts. Unfortunately, external validation of diabetes-specific risk models is lacking, particularly among U.S. cohorts. No U.S. diabetes risk model has been externally validated.

Problems with absolute risk prediction were improved or resolved by recalibration and remodeling methods, supporting the need in this literature for periodic recalibration or remodeling for either general or specific populations. However, empirical evidence for determining what time interval is reasonable or for detecting when a population is "significantly" different from the reference population does not yet exist.

Chapter 1. Introduction

Importance of Predicting Risk of Cardiovascular Events

There have been a number of studies that show that medical treatment of cardiovascular risk factors reduces the occurrence of adverse cardiovascular outcomes.¹²²⁻¹²⁸ Because of the high incidence and cost of this disease, clinical practice guidelines target primary prevention, and recommend that providers evaluate patients for cardiac risk factors that may warrant medical treatment.³⁻⁷ However, previous research has shown that providers do not accurately estimate the risk of cardiovascular disease (CVD) events on their own.⁸⁻¹³ A number of multivariate risk prediction equations, derived from large prospective cohort studies or randomized trials, have been developed to estimate CVD risk in intervals ranging from 5 to 10 years.¹⁴⁻²¹ In order to make them more usable to busy clinicians, many of these risk models only require information from a patient's medical history and easily available laboratory tests, and have been adapted for interpretation through simplified charts or tables in paper or computer-based formats.^{3, 22}

The most commonly used CVD risk prediction models in the United States are those based upon the Framingham cohort. These models were developed in a large prospective cohort of U.S. men and women aged 30 to 74 years, have been subsequently validated in multiple diverse populations, and discriminate well among those patients who will have a CVD event and those who will not.^{17, 20, 23-26} However, these models do not accurately predict the risk for some patients, such as those younger than age 30 years or older than age 65 years, Japanese American men, Hispanic men, or Native American women.^{23, 26, 129} In addition, they demonstrate reduced ability to predict accurately in patients with diabetes mellitus, severe hypertension, or left ventricular hypertrophy.¹²⁹⁻¹³¹

Concern over diabetes as a risk factor for CVD escalated in the late 1990s as several studies were published showing highly elevated risk of CVD among patients with diabetes.^{27, 28} One of these was a landmark study by Haffner and colleagues that evaluated 1,373 patients without diabetes and 1,059 patients with diabetes among a Finnish cohort.²⁸ This study found that the 7-year risk of myocardial infarction (MI) among asymptomatic patients was 3.5 percent in patients without diabetes and 20.2 percent in patients with diabetes. MI recurrence rates among those patients who had already experienced an MI were 18.8 percent in patients without diabetes and 45 percent in patients with diabetes. These studies informed the Adult Treatment Panel III (ATP-III) recommendation for diabetes to be considered as a coronary heart disease (CHD) risk equivalent, because the MI recurrence rates in patients without diabetes.

However, there is a growing literature in this domain showing that model performance is highly dependent on how similar the source model cohort is to the cohort in which it is applied.^{17, 23} In addition, diabetes is a high-risk condition for CVD with a number of well-defined process measurements, such as hemoglobin A_{1c} and urine albumin, that have been shown to be predictive of organ damage and adverse outcomes.^{132, 133} Since these risk factors are not present in general CVD risk prediction models, absolute risk prediction performance among patients with diabetes could be poor. We performed a systematic review of CVD risk prediction tools in order to determine whether tools that include diabetes as a risk factor in a general CVD risk model were able to perform adequately compared to those that were developed for only patients with or without diabetes.

The aim of this systematic review is to summarize the current state of CVD risk models, with a focus on models for use in the U.S. patient population. In addition, performance of each of the available models in populations other than the source cohort is assessed, as well as a summarization of which models use which risk factors and the impact that recalibration and reclassification has had in the last few decades on these models. Finally, we address the specific question of whether it is appropriate to treat diabetes as a CVD equivalent or as an independent risk factor.

Key Questions

The key questions for this report were:

KQ1: Do any of the currently available tools for the prediction of cardiovascular risk in a North American population offer clear advantages in discriminatory power over the others in predicting incident CHD, cerebrovascular stroke (stratified by thrombotic or hemorrhagic type), or a combination of these two?

KQ2a: Do tools that treat diabetes as a CVD or CHD outcome equivalent have different performance characteristics than those that use diabetes as an independent risk factor for those outcomes?

KQ2b: Is the appropriateness of using diabetes as a coronary risk equivalent modified by the number of other cardiac risk factors that the individual has?

Technical Expert Panel

Table 1 lists the individuals who served as technical experts, providing feedback on the search, inclusion/exclusion criteria, and scope of the project. In addition, Dr. Diana Petitti provided expert consultation, particularly on the goals, methods, and scope of the project.

Uses of This Report

The report is intended to describe the breadth and state of the literature on cardiovascular risk prediction, with a particular focus on models and tools relevant to the U.S. population. In requesting this review, the U.S. Preventive Services Task Force (USPSTF) sought to determine whether a specific model or tool had better performance characteristics than others, and therefore might be most useful in primary care. Although the report was specifically designed to provide data to the USPSTF for their use in making recommendations, it is hoped that the report may also be useful to researchers working in the field of cardiovascular risk prediction, particularly in areas in which research is currently inadequate for making recommendations.

Chapter 2. Methods

Here we document the procedures that the Vanderbilt Evidence-based Practice Center used to develop this report on tools for predicting cardiovascular risk. We first describe the strategy for identifying articles relevant to the key questions, the inclusion/exclusion criteria, and the process used to abstract relevant information from the eligible articles and generate summary tables.

Literature Review Methods

Inclusion and Exclusion Criteria

The inclusion/exclusion criteria were developed in consultation with the Technical Expert Panel to capture the literature most closely related to the key questions. Inclusion criteria are summarized in Table 2.

We excluded studies that 1) were not published in English; 2) did not report information pertinent to the key questions; 3) had fewer than 200 participants at enrollment; 4) were not original studies; and 5) did not perform any internal or external validation of the model. For this review, the relevant population was men and women who were currently asymptomatic for CVD.

Literature Search and Retrieval Process

Search literature. We began with a focused search on known and unknown CVD risk assessment tools (Appendix A) to get an idea of the size of the literature, and then searched for review articles to provide overview and context.

As we developed each of the search components with input from previous systematic reviews, we employed an approach of iterative refinement, using a pool of approximately 50 relevant articles previously identified as a quasi-validation set to assess recall of our search iterations (i.e., whether our searches retrieved or missed known items of interest).³¹⁻³³

Article selection process. Once we identified articles through the electronic database searches (published January 1, 1999 to February 24, 2009), review articles, and bibliographies, we examined abstracts of articles to determine whether studies met the criteria. Two reviewers separately evaluated the abstracts for inclusion or exclusion (Appendix B). If either reviewer concluded that the article could be eligible for the review based on the abstract, we retained it.

Of the entire group of 3,499 articles, 636 required full-text review. For the full article review, two reviewers read each article and decided whether it met the inclusion criteria (Appendix B).

Literature Synthesis

Development of Summary Tables and Data Abstraction Process

The data for this project were abstracted into a database (Appendix C) designed to capture study information such as cohort characteristics, risk model characteristics, model performance statistics, and quality review elements. We captured information about the study populations to allow for stratification of results by variables, including sex and geographic area.

Summary tables were developed using database queries and then formatted in Microsoft Word for presentation. The tables are designed to provide overviews of the available literature, the diversity of populations used to develop the risk assessment models, and the degree to which the variables in the models and model performance vary.

The team was trained to abstract by pulling relevant data from several articles into the database and then reconvening as a group to discuss the utility of the table design. We repeated this process through several iterations. The content lead (Dr. Matheny) reviewed each abstraction to ensure accuracy and completeness. The full research team met regularly during the article abstraction period and discussed global issues related to the data abstraction process.

Assessment of Available Tools

In addition to assessing the studies and models presented in the literature, we searched for all available online tools and documented their location and the model on which they purported to be based. We then used the online tools to calculate risk for five test cases, in order to identify any variation in estimated risk. The test cases are presented in Table 4.

We used a two-pronged Internet search strategy to find potential sites where online risk assessment tools are available. First, we searched specifically for each model identified through the literature search using the following approaches:

- 1. (model name) + online tool
- 2. (model name) + online tool + CVD
- 3. (model name) + risk score
- 4. (model name) + risk score + CVD
- 5. (model name) + online calculator + CVD
- 6. (model name) + available CVD online calculator

We then searched for additional tools using the following set of terms, and cross-referenced the results with those already identified to find any additional tools:

- 1. CVD available online calculators
- 2. CVD online assessment tools
- 3. Calculating CVD risk online
- 4. Calculating CVD and stroke risk
- 5. CVD online risk assessment tools

Characteristics of five test patients (Table 3) were developed and applied in each of the online tools (Appendix D/Summary Table 1). In addition, statistical analysis software (SAS) models were developed for each of the models that the online tools purported to use, and the test patient characteristics were applied to those as well.

Assessment of Study Quality

We assessed the quality of individual studies across multiple dimensions using the following questions. We did not assign quality scores to the individual studies or the literature as a whole, but chose instead to present patterns of quality. Quality assessment questions were developed to reflect the importance of fully characterizing a population in which a model is developed, and the prevalence of missing data and loss to follow-up. In addition, evaluation methods and measures were pursued.

Does the article state both the inclusion and exclusion criteria, and any additional exclusions that were made after cohort inception? The inclusion and exclusion criteria provide relevant information about how the cohort was formed and characterized. However, some articles use separate criteria to create an analysis subcohort, in which case, the initially established criteria would not adequately describe the cohort.

Was the study population well described? Participant characteristics that might affect outcomes should be fully characterized in order to interpret conclusions or ascertain the relevance of a given model to a new population.

Was the loss to follow-up over the course of the study less than 20 percent? Lack of complete information on the cohort may distort the assessed implications of various predictor variables.

If loss to follow-up was more than 20 percent, did the authors acknowledge the potential effects on the model? The potential for differential loss to follow-up to result in a model that "works" in a non-representative population is high, particularly in studies with long-term followup. It is helpful if authors of studies in which a large proportion of the population is lost to follow-up support the reader's interpretation.

Did missing data cause more than 20 percent of the population to be excluded from the **model?** Even if individuals were not lost to follow-up in a given study, the failure to collect complete data could result in a model being developed in a substantially smaller subcohort that is not entirely reflective of the intended population. Authors should make every attempt to gather data from the greatest number of study participants possible.

If missing data caused more than 20 percent of the population to be excluded, was a missing data technique applied? Approaches to evaluating the potential impact of missing data include sensitivity analyses. These methods can vary from evaluating the change in study results between only the patients with full data to various imputation methods that fill in the missing patient data. Imputation methods can range from simple sample mean imputation to more sophisticated multiple imputation methods.

For validation studies, did the authors report both discrimination and calibration? The degree to which each study evaluated the model performance, regardless of whether it was an internal or external model evaluation, is characterized in this quality assessment. Measures of discrimination include the area under the receiver operating characteristic curve (AUC) and the C statistic. Measures of calibration include the observed-to-expected (O/E) ratio, calibration plots or curves, and the Hosmer-Lemeshow goodness-of-fit test. Less common performance measurements, such as the Brier score, were also occasionally reported.

For model development, did the authors assess internal validation? This item assesses whether the model performance was reported for the cohort in which the model was developed. Any of the discrimination or calibration measures would count for this assessment.

Presentation of Results In This Report

For Key Question 1, we separated all of the modeling studies into three categories, depending on the outcome: CHD, CVD, and cardiovascular accident (CVA). Special emphasis was placed on those models that had been externally validated at least once, because the critical importance of this question relates to the impact model use has on patients in cohorts other than the

development cohort.

For Key Question 2, we separated the modeling studies into three categories, depending on whether the cohort included no, some, or only patients with diabetes. Special emphasis was placed on those models that had been externally validated at least once. Again, this was because the critical importance of this question relates to the impact model use has on patients in cohorts other than the development cohort.

All of the models developed in diabetic populations were summarized in order to discuss which variables were chosen in these models and any recalibration or remodeling that was performed. This was best explored in those studies that collected multiple cohorts and evaluated a common set of risk factors for a matched outcome using an identical method. These multivariate modeling methods can be used equally for risk factor exploration and risk prediction modeling. In the primary inclusion/exclusion criteria, any study that did not report any risk prediction performance characteristic was excluded, but some exclusive risk factor exploration studies are referenced here for completeness.

Key Definitions

In order to interpret these results, it is important to have common definitions of discrimination and calibration. Discrimination is a measurement of how well a model can separate those patients that will experience the outcome from those who will not, but it does not address individual risk predication accuracy. Discrimination also gives a general sense of how much of the underlying information leading to the outcome has been captured by the risk. The most common measurements of discrimination are AUC and the C statistic.¹³⁴ Graphically, this is represented by plotting sensitivity versus 1 minus specificity over all the possible probability cut-off points in the prediction model. The area under that plot is the AUC measurement, with 1.00 reflecting perfect separation between cases and non-cases, and 0.50 reflecting a modeling performance that is no better than chance in detecting the outcome of interest. In some domains in which outcomes are estimated a few days or weeks into the future, the AUC measurement approaches 0.90, while in other domains with very long outcomes and/or difficult-to-capture risk factors, an AUC measurement of 0.60 to 0.70 is considered acceptable. The C statistic, which is also commonly reported in this literature, is also a measure of concordance and discrimination. For binary outcomes, the C statistic is identical to AUC.

Absolute risk estimation is also called calibration in the risk modeling literature, and it is a measure of risk prediction accuracy in individuals or small groups. This is most commonly measured by the Hosmer-Lemeshow goodness-of-fit test, which sorts and separates the cohort into 10 groups and compares the observed and expected number of outcomes in each subgroup (or bin).¹³⁵ Each bin is evaluated with a chi-square test, and the chi-square value from each bin is added together and a P value is calculated. Although 10 bins are standard, a different number may be used. The chi-square value for P=0.05 for 10 bins (8 degrees of freedom) is 15.51. Chi-square values less than (and P values greater than) this are considered adequately calibrated and can be interpreted as a non-significant overall difference between observed and expected outcome event rates (after comparing each bin). A more coarse measurement of calibration is the O/E ratio is only interpretable with confidence intervals. If 1.00 is within the confidence interval, then the O/E ratio is acceptable. However, it should be noted that underprediction in one portion of the risk spectrum and overprediction in another would show up as poor calibration if

the cohort is split into 10 groups, but the model could appear to perform well judging by the O/E ratio.

Model Performance Evaluation Methods Summary

Risk calculators provide a percent risk of an outcome over a set number of years, and both relative risk (discrimination) and absolute risk prediction (calibration) performance measurements can be calculated. O/E ratios are the crudest measurement of absolute risk performance, but can result in an acceptable performance, even when specific ranges of risk are overpredicted while others are underpredicted. The Hosmer-Lemeshow test is a more granular evaluation method which sorts all patients by predicted risk, divides them into 10 categories, evaluates the O/E ratio separately for each category, and sums up the chi-square error in each category to report an aggregate measurement. Absolute risk prediction performance is dependent on both the baseline outcome incidence and the contributions of risk from each risk factor in the source cohort.

Chapter 3. Results

Yield of Literature Searches

Figure 1 presents the yield and results from the searches. In addition to the articles identified through the primary literature search, a number of articles were identified via hand-searching the reference lists of included articles. Therefore, we began with a yield of 3,499 articles, but retained only 84 articles^{29, 34-82,14, 19, 23-25, 83-110,111} that we determined were relevant to the key questions and met the inclusion/exclusion criteria.

Results are divided into three primary sections: a description of all studies (primary model development and validation studies), results specific to Key Question 1, and results specific to Key Question 2.

Definition of Relevant Outcomes

Before describing the results of the literature search, it should be noted that although the search focused entirely on CVD risk prediction, there was considerable heterogeneity in outcome definitions. The following definitions are derived from the literature and were not a priori definitions.

Hard CHD. Among the more restrictive outcomes, there were two definitions of hard CHD, including sudden CHD death and MI with or without cardiac procedures, such as coronary artery bypass graft or percutaneous coronary intervention.

Total CHD. There were three definitions of total CHD, including hard CHD outcome with unstable angina or angina pectoris.

CVA. There were six definitions of CVA, including various subsets of ischemic CVA, hemorrhagic CVA, and transient ischemic attack (Table 4a).

The aggregate outcome of CVD could include some or all of the candidate components from total CHD and CVA, but was required to have at least one component from each, which resulted in 19 different varieties of the CVD outcome (Table 4b). Full definitions for each variety of these outcomes are shown in Table 4b. From this point forward, any outcome mentioned will have a numerical subscript that will reference the outcome definition in Table 4b.

Description of All Studies

We examined studies in which primary models were developed as well as those in which the models were validated in other populations. Appendixes A-N provide a summary of the populations in which the models were developed, as well as the model components and performance. The summary tables are stratified by geographic location and, where appropriate, by sex. The intent is to describe the transition in the model populations as well as the models themselves in order to best consider their applicability to current patient populations. All tables are organized in order of cohort enrollment date, so that the earliest formed cohorts are first and the newest formed cohorts are last. Changes in issues such as population prevalence of disease over time suggest that it is important to consider the original cohort enrollment and end dates that serve as the basis for any model used by clinicians today.

Cardiovascular Disease Risk Assessment Tools

A total of 84 papers^{29, 34-82,14, 19, 23-25, 83-110,111} were included in this review, representing a total of 102 risk prediction models. To develop the models, the authors used a total of 100 variations of 73 identifiable patient cohorts. These cohorts provided data on CHD outcomes (52 cohorts), CVD outcomes (31 cohorts), and CVA outcomes (12 cohorts). The results describe the cohorts that were used in the modeling literature, followed by the models themselves, in each case focusing on those with external validation first.

Primary Model Development

Overview of cohorts. The original description of each of the data sources used in the development of these primary risk prediction models is available in Appendix E/Summary Table 2 (note that each of the cohorts could have been used to develop or assess multiple models).

In some cases, different subsets of a larger cohort were used in the models that we identified (e.g., multiple subsets of the Atherosclerosis Risk in Communities [ARIC] cohort were used to develop risk models in the United States), and we list each of these subcohorts separately. In total, there were 57 cohorts or subcohorts used to develop primary models.^{14, 19, 23-25, 34-42, 46, 47, 49-52, 54-64, 71, 72, 75, 76, 78, 80, 81, 83, 84, 87, 91, 94, 100, 102, 105, 107, 109, 110 Cohort inception ranged from 1954 to 1000. Of these, 27 were in the Americae (United States and Puerto Rice), 24 were in Europe, and}

1999. Of these, 27 were in the Americas (United States and Puerto Rico), 24 were in Europe, and five were in Asia.

A few large studies provide the majority of the available cohorts and subcohorts. For example, six distinct variants or subcohorts of the ARIC study were used to develop primary models with a cardiovascular outcome. Similarly, two subcohorts from the Women's Health Study (WHS) were used in model development. The subcohorts vary in start and end dates, and other population descriptors, such as cardiovascular risk factors or sex.

In Europe, three variants of the QRESEARCH database, two variants of the Uppsala Longitudinal Study of Adult Men (ULSAM), and two variants of the Prospective Cardiovascular Münster (PROCAM) cohort were used in the development of primary models. Cohort size ranged from 229 to 2,285,815, and follow-up ranged from 3.36 to 28.7 years. In Asia, two cohorts had their genesis in the Hong Kong Diabetes (HKD) Registry. Cohort size ranged from 7,067 to 1,223,740, and follow-up ranged from 5.37 to 13 years.

Substantial variation is evident across the populations or subcohorts used to develop models. Appendix F/Summary Table 3 provides an overview of the characteristics of individuals in each of the populations or subcohorts used for model development. We abstracted data on the population variables that we would expect to be presented, but as is clear from the table, there were significant missing data in the articles. We further stratified these data by geographic area and sex.

Description of cohorts. In the 27 American cohorts, ^{19, 23-25, 34, 37, 39, 42, 49, 51, 52, 54, 61, 62, 75, 81, 87, 91, ^{100, 105} the average age ranged from 29.8 to 69.4 years (Appendix F/Summary Table 3). Twentysix cohorts were comprised of all men^{19, 23-25, 37, 39, 42, 49, 51, 52, 62, 75, 81, 105} and 20 were comprised of all women. ^{19, 23, 24, 37, 39, 42, 51, 52, 62, 75, 105} In those cohorts with both sexes, the proportion of women ranged from 10.2 to 62.6 percent.}

The 26 cohorts^{19, 23-25, 37, 39, 42, 49, 51, 52, 62, 75, 81, 105} of American men were developed from seven distinct studies. The populations ranged in average age from 25 to 69.7 years. Prevalence of smokers ranged from 12 to 59.7 percent. Men with diabetes were represented in six studies; the proportion with diabetes ranged from 3.56 to 42 percent. The proportion of male participants

with hypertension ranged from 13 to 61 percent when hypertension was measured by increased blood pressure and from 6.8 to 35.2 percent when it was measured by medication use.

There were 11 studies used to develop the 24 cohorts of American women.^{19, 23, 24, 37, 39, 42, 51, 52, 62, 75, 105} The populations studied ranged in average age from 46.1 to 69.3 years. The prevalence of smokers ranged from 15 to 48.5 percent. Women with diabetes were represented in six of the studies; the proportion with diabetes ranged from 4 to 51 percent. The proportion of female participants with hypertension in these studies ranged from 11 to 62.5 percent when hypertension was measured by increased blood pressure and from 10.7 to 51.7 percent when it was measured by medication use.

In 23 European cohorts, $^{35, 36, 41, 46, 50, 56, 58-60, 63, 64, 71, 72, 76, 78, 80, 84, 94, 102, 104, 107, 109, 110}$ the average age ranged from 46.7 to 71 years. Nine cohorts were comprised of all men^{35, 36, 46, 58, 59, 78, 107} and 10 were comprised of all women.^{35, 36, 46, 58, 59, 78, 107} In those cohorts with both sexes, the proportion of women ranged from 29.4 to 75.4 percent.

The 10 cohorts^{35, 36, 46, 58, 59, 78, 107} of European men used in primary model development were derived from seven studies. The populations studied ranged in average age from 47 to 58.3 years. The prevalence of smokers ranged from 18.5 to 43.8 percent. Men with diabetes were represented in four cohorts;^{59, 78, 107} the proportion with diabetes ranged from 1.5 to 18.8 percent in those studies not exclusively of patients with diabetes.^{58, 59} Two cohorts^{78, 107} consisted only of men with diabetes. The proportion of male participants with hypertension was reported in one study⁵⁸ (41.6 percent) when hypertension was measured by increased blood pressure, and ranged from 0.1 to 29.7 percent when it was measured by medication use.^{35, 58}

The 10 cohorts of European women^{35, 36, 46, 58, 59, 78, 107} used for primary model development were derived from eight studies. The populations studied ranged in average age from 48.8 to 57.6 years. The proportion of smokers among participants was reported for three cohorts^{35, 58, 107} and ranged from 10.6 to 23.1 percent. Women with diabetes were represented in five cohorts, two of which consisted entirely of patients with diabetes;^{78, 107} the proportion with diabetes among the other studies ranged from 1.3 to 14.6 percent. The proportion of participants with hypertension was reported in one study⁵⁸ (47.2 percent) when hypertension was measured by increased blood pressure, and ranged from 6.9 to 33.7 percent when it was measured by medication use.^{35, 46}

In the eight Asian cohorts, ^{38, 47, 55, 57, 83} the average age ranged from 46.6 to 68 years. Three cohorts were comprised of all men^{47, 55, 83} and three were comprised of all women.^{47, 55, 83} In those cohorts with both sexes, the proportion of women ranged from 36.5 to 54.6 percent.

Three cohorts of Asian men were represented in the literature.^{47, 55, 83} The populations studied ranged in average age from 45 to 47 years. The prevalence of smokers ranged from 59 to 68.4 percent. Men with diabetes were represented in two studies; the proportion with diabetes ranged from 4.8 to 6.9 percent. The proportion of participants with hypertension reported in two Asian male cohorts was 29 percent⁸³ and 35.7 percent⁴⁷ when hypertension was measured by increased blood pressure, and was not reported as a measure based on medication use.

There also were three cohorts of Asian women.^{47, 55, 83} The populations studied ranged in average age from 46 to 49 years. The prevalence of smokers ranged from 4 to 6.5 percent. Women with diabetes were represented in two studies; the proportion with diabetes ranged from 4.1 to 5 percent. The reported proportion of participants with hypertension in the cohorts was 22 percent⁸³ and 29.2 percent⁴⁷ when hypertension was measured by increased blood pressure, and

was not reported as a measure based on medication use.

Models with external validations. Of the 102 models identified through the literature search, only 17^{14, 18, 19, 23, 25, 46, 59, 63, 96, 112, 136} were externally validated in a population other than the one in which the model was developed (Table 5). These models were all developed from the following nine primary patient cohorts:

- Scottish Heart Health Extended Cohort (SHHEC)
- Diabetes Audit and Research in Tayside, Scotland (DARTS)
- FINRISK
- Framingham Study (FRS)
- Framingham Offspring Study (FRS-O)
- Prospective Cardiovascular Münster Study (PROCAM)
- QRESEARCH Database
- Systematic Coronary Risk Evaluation (SCORE)
- United Kingdom Prospective Diabetes Study (UKPDS)

A description of these nine cohorts is available in Appendix G/Summary Table 4. Models with external validation data were more likely to be used for individual prediction.

The five most common externally validated risk models (among the 11 total) were:

- 1991 FRS model for CVD₂ (with 21 evaluations)
- 1998 FRS model for total CHD₁ (with 23 evaluations)
- FRS ATP-III model for hard CHD₁ (with 16 evaluations)
- PROCAM model for hard CHD₁ (with 11 evaluations)
- SCORE model for CVD mortality (with 11 evaluations)

The externally validated models are typically considered general population, first-outcome incidence calculators, meaning that they were developed using mixed cohorts of patients meant to be representative of a given geographic area. However, it is important to note that the FRS ATP-III model excludes patients with diabetes, the PROCAM model excludes women, the DARTS and UKPDS models exclude patients without diabetes, and the ASSIGN model (derived from SHHEC) includes a non-traditional social deprivation index as a risk factor. Therefore, they are not entirely applicable in all general populations.

All of the FRS models were developed from the original and/or offspring cohorts of the Framingham Study in the United States. The DARTS, ASSIGN, QRESEACH, and UKPDS models were developed from U.K. patients. The PROCAM model was developed from German patients. The SCORE model was developed from patients in 12 European countries, and the FINRISK model was developed from Finnish patients (and is included as one of the 12 countries in the SCORE model).

Models without external validation. The majority of models (87 out of 102) identified through our search have never been validated in an external data set.^{14, 18, 19, 25, 34-39, 41, 47, 49, 51, 52, 54-57, 60-62, 71, 75, 76, 78, 80, 81, 83, 84, 87, 91, 93, 100, 101, 103, 107, 109, 111, 112, 114, 115, 136 In many cases, these represent a}

subset of studies in which variables were simply added or deleted to assess any change. These are unlikely to ever be used in risk prediction, but because they met inclusion criteria, they are included here. Among the 87 models without any external cohort validation, eight used variants

in risk factors or outcomes or were temporal updates from well-known cohorts with externally validated risk models (Table 6).^{23, 35, 41, 81, 112}

Two models were developed as point score simplifications or evaluations of risk modeling methods other than the Cox proportional hazards model (Table 7).^{14,41}

Ten were developed to compare or improve model performance between a new local model and external validations of more established models, ^{51, 54, 56, 76, 78, 80, 103, 114, 115} and 57 were developed in order to evaluate candidate variables for risk model inclusion (Table 8).^{34, 36, 37, 50, 54, 60, 61, 71, 75, 80, 81, 84, 87, 91, 100, 101, 103, 109}

Five models were developed to evaluate the heterogeneity of risk factors between cohorts (Table 9).^{18, 25, 55, 136}

Twelve models were developed to address specific patient populations, such as elderly patients,⁹³ young patients,⁴⁹ patients with diabetes,^{38, 57, 78, 107} Asian populations,^{38, 47, 57, 83, 111} patients with atrial fibrillation,⁵² and Native American populations⁶² (Table 10).

Model Validation Studies

Cohort descriptions. Appendix I/Summary Table 6 provides an overview of the data sources used to validate the various models described in this report.^{29, 35, 43-45, 48, 53, 54, 63, 65-70, 73, 74, 77, 79, 82, 85, 86, 88-90, 92, 93, 95-99, 101, 104, 106, 108 Cohort inception ranged from 1972 to 2000. Of the validation cohorts identified, nine were in the Americas (United States and Canada), ^{45, 53, 54, 70, 79, 96, 97, 99, 101} 26 were in Europe (including Australia and New Zealand), ^{29, 35, 44, 48, 63, 65-69, 73, 77, 82, 85, 86, 88-90, 92, 104, 106, 108} and four were in Asia.^{74, 95, 98} Cohort size ranged from 230 to 1,072,800, and follow-up} ranged from 3.3 to 21.3 years.

Details on the populations used for validation studies are presented in Appendix J/Summary Table 7. These details are intended to provide an overview of the characteristics of individuals in cohorts that form the basis for the validation studies. Similarly to the data on primary model development, we abstracted data on the population variables that we would expect to be presented, but as is clear from the validation data tables, there were significant missing data in the articles. We further stratified these data by geographic area and sex.

In the American cohorts,^{45, 53, 54, 70, 79, 96, 97, 99, 101} the average age ranged from 52 to 64.7 years. Three cohorts were comprised of all men^{45, 99, 103} and two were comprised of all women.^{45, 99} In the cohorts with both sexes, the proportion of women ranged from 33 to 61.8 percent. The proportion of individuals with diabetes ranged from 2.9 to 14 percent in the cohorts that were not exclusively patients with diabetes; one cohort consisted of patients with diabetes only.⁹⁶

Three cohorts of American men were identified in validation studies.^{45, 99, 103} These cohorts ranged in average age from 50.8 to 65.8 years. The prevalence of smokers ranged from 3.2 to 35.4 percent. Patients with diabetes were represented in two cohorts, with 4.7 percent in one and 14.6 percent in the other. The proportion of participants with hypertension was only reported in one male cohort (35.5 percent)⁴⁵ when hypertension was measured by increased blood pressure, and was not reported as a measure based on medication use.

There were three cohorts of American women used to validate risk models.^{45, 99} The populations studied ranged in average age from 52.6 to 64 years. The prevalence of smokers ranged from 18.2 to 27.2 percent. Patients with diabetes were represented in two of the cohorts, with 4.2 percent in one and 13.7 percent in the other. The proportion of participants with hypertension

was only reported in one female cohort (28.4 percent)⁴⁵ when hypertension was measured by increased blood pressure, and was not reported as a measure based on medication use.

In the European cohorts, the average age ranged from 34.4 to 71.1 years. Twenty-two cohorts were comprised of all men^{35, 43, 44, 66-68, 74, 77, 85, 86, 92, 104, 106} and 15 were comprised of all women.^{35, 43, 44, 48, 66-68, 74, 77, 85, 92, 104, 106} Overall, among those cohorts with both sexes, the proportion of women ranged from 27 to 58 percent.

In the 22 cohorts of European men used in the validation studies, the average age ranged from 32.8 to 68.5 years. The prevalence of smokers ranged from 24 to 83.7 percent. Patients with diabetes were represented in 16 cohorts; the proportion with diabetes ranged from 1.4 to 12 percent. The proportion of male participants with hypertension was reported by two studies (8 percent¹⁰⁶ and 75 percent⁶⁷) when measured by increased blood pressure and was also reported by two studies (6.6 and 8 percent) when it was measured by medication use.⁴³

Validation studies were conducted in 15 cohorts of European women. The populations studied ranged in average age from 36.1 to 71.1 years. The proportion of smokers among participants ranged from 16.7 to 71 percent. Patients with diabetes were represented in eight cohorts; the proportion with diabetes ranged from 1 to 16 percent. The proportion of female participants with hypertension ranged from 6 to 55 percent when hypertension was measured by increased blood pressure and from 10.5 to 12.1 percent when it was measured by medication use.

The average age in the Asian cohorts was 44.7 years. Three cohorts were comprised of all men⁷⁴ and three were comprised of all women.⁷⁴ The three distinct cohorts of Asian men were all derived from the Newcastle Heart Project (NHP), with foci on different subgroups (Pakistan, India, and South Asia). Age and proportion of smokers were not reported. The proportion of men with diabetes ranged from 16 to 26 percent. No hypertension data was reported for the three male cohorts. All three cohorts of Asian women were also similarly derived from the NHP study.⁷⁴ Age and percentage of smokers were not reported. The proportion of women with diabetes ranged from 16 to 28 percent.

Model performance characteristics. Appendix K/Summary Table 8 presents performance data (discrimination and calibration) on all of the models assessed (both primary and validation). There were a total of 260 instances of CHD and CVD model testing in a cohort, including both model development cohorts and external validation cohorts. The studies resulted in an AUC ranging from 0.52 to 0.88. There were 71 studies that reported Hosmer-Lemeshow goodness-of-fit statistics, and among these, 55 percent were adequately calibrated. We describe these data here by region and by whether the data reflect internal or external validation.

Americas – **internal validation.** Model performance characteristics were variably reported for each of the models (Table 11). In most cases, the older, well-validated models did not report AUC-type statistics for internal validation. Among those models developed in the Americas, the internally validated AUC measurement or C statistic ranged from 0.63 to 0.84. It should be noted that many of these were studies in which the main focus was to explore the potential impact of a set of variables. Among those models intended to be "finished" products for external consumption, internally validated AUC-type statistics ranged from 0.65 to 0.83. The total cholesterol and low-density lipoprotein variants of the Wilson FRS model for total CHD₁ both reported a C statistic of 0.74 for men and 0.77 for women.¹⁹ An outcome update for 5-year hard CHD₁ for the total cholesterol version of the Wilson FRS model reported an AUC of 0.79 for men and 0.83 for women.²³ An updated FRS model adapted to point scores by D'Agostino and

colleagues for 12-year CVD₂ reported a C statistic of 0.76 for men and 0.79 for women.¹²⁰ The Reynolds Risk Score for women developed from the WHS cohort for 10-year CVD₃ was measured to have a C statistic of 0.81.⁵⁴ The Reynolds Risk Score for men developed from the Physicians' Health Study II cohort for 10-year CVD₁₅ was measured to have a C statistic of 0.71.¹⁰³ The Personal Heart Early Assessment Risk Tool (HEART) score for hard CHD₂ developed from the ARIC cohort was measured to have an AUC of 0.65 for men and 0.79 for women.⁵¹ The Strong Heart Study (SHS) model developed from the SHS cohort for hard CHD₁ was measured to have a C statistic of 0.70 for men and 0.73 for women.⁶²

Calibration measurements were also not reported for internal validation of the older, wellvalidated models, and were variably reported in the newer studies as an O/E ratio, Hosmer-Lemeshow goodness-of-fit statistic, or a calibration plot, and occasionally as less common measurements, such as the Bayesian or Akaike information criterion. Internal validation of the SHS, D'Agostino CVD, 5-year hard CHD₁ FRS, and Reynolds Risk Score for men and women all reported adequate calibration. The Personal HEART model did not report internal validation calibration measurements.

Americas – external validation. For external validation, outcomes may not exactly match between the cohort and the model. If they are matched, they are designated as such, and if they are not matched, the cohort outcomes will always be listed first (Table 12).

FRS (*Anderson*) *model validations*. This model was evaluated in the South Bay Heart Watch cohort for matched 3-year hard CHD_1 (MI and sudden death models added together), and had an AUC of 0.69, with calibration not reported.¹⁰⁰ The authors also evaluated the effect of outcome mismatching by evaluating 3-year hard CHD_2 /hard CHD_1 and found a non-significant change in AUC to 0.67. The model was evaluated in the Lipid Research Clinics Prevalence Study cohort for CHD mortality/total CHD_1 , and the AUC was 0.83 in men and 0.82 in women, but the authors did not report on calibration. The outcome mismatch occurred because that cohort did not have non-fatal CHD outcomes.

FRS (*Wilson*) *model validations*. D'Agostino and colleagues evaluated five U.S. cohorts for 5year hard CHD₁, using the outcome-matched variant FRS Wilson model.²³ This FRS model was developed in this study using the same cohort and risk variables as the Wilson models; thus, we considered it part of the Wilson family of models. Calibration was evaluated by the Hosmer-Lemeshow goodness-of-fit test, and chi-square values less than 5.5 indicate adequate calibration.

Applying the model to the ARIC cohort produced an AUC of 0.75 in white men, 0.67 in black men, 0.83 in white women, and 0.79 in black women. Calibration was adequate for each of the subcohorts as measured by the Hosmer-Lemeshow test. The ARIC cohort was also evaluated for unmatched 10-year hard CHD_2 /hard CHD_1 , and the AUC was 0.69 for men and 0.81 for women.⁵¹

Applying the model to the SHS cohort resulted in an AUC of 0.69 in Native American men and 0.75 in Native American women. Calibration was adequate for men, but inadequate ($\chi^2 = 22.7$) for women. On the other hand, calibration was adequate for both sexes when the model was applied to the Cardiovascular Health Study (CHS), with an AUC of 0.63 in white men and 0.66 in white women.

Use of the model in the Puerto Rico Heart Health Program (PRHHP) cohort resulted in an AUC of 0.69 in Hispanic men, and calibration was inadequate ($\chi^2 = 142.0$), similar to results using the

Honolulu Heart Program (HHP), in which the AUC was 0.72 in Japanese American men, with inadequate calibration again ($\chi^2 = 66.0$).

Another study combined patients with chronic kidney disease from the ARIC and CHS cohorts and evaluated matched 5- and 10-year hard CHD_1 .⁴⁵ For 5-year outcomes, the C statistic was 0.62 in men and 0.77 in women, and for 10-year outcomes, the C statistic was 0.60 in men and 0.73 in women. Calibration was inadequate for both sexes and outcomes, with chi-square values ranging from 33.4 to 75.1.

The Johns Hopkins Sibling Study was evaluated with the model for matched total CHD₁ among healthy siblings of patients with known premature coronary artery disease (CAD).⁴² The study did not report discrimination, and calibration was adequate for women but inadequate for men ($\chi^2 = 75$). The number of observed outcomes significantly exceeded those predicted in men (O/E ratio, 1.67 [95% confidence interval (CI), 1.34–2.06]), and non-significantly exceeded those predicted in women (O/E ratio, 1.13 [95% CI, 0.74–1.64]).

The Chicago Heart Association Detection Project in Industry study evaluated young men aged 18 to 39 years without diabetes for unmatched 10-year hard CHD_1 /total CHD_1 .⁴⁹ Discrimination was not measured, and the number of observed outcomes was significantly lower than expected (O/E ratio, 0.05 [95% CI, 0.03–0.07]). The Women's Health Initiative evaluated women for unmatched hard CHD_1 /total CHD_1 , and the AUC was 0.69.⁵³ The WHS cohort evaluated women for unmatched CVD₃/total CHD_1 using both the total cholesterol and low-density lipoprotein versions of the model.⁵⁴ The AUC was 0.75 in both cases, and they were both inadequately calibrated. The San Antonio Heart Study cohort evaluated men and women, 68 percent of whom were Hispanic, for unmatched CVD_{15} /total CHD_1 , and the AUC was 0.82.⁷⁹ Finally, the Normative Aging Study evaluated male U.S. military veterans for matched total CHD_1 . The AUC was 0.63, and observed outcomes were non-significantly lower than expected (O/E ratio, 0.93 [95% CI, 0.81–1.06]).

FRS (ATP-III) model validations. The St. Francis Heart Study cohort evaluated men and women for unmatched hard CHD₂/hard CHD₁, and the AUC was 0.68.⁷⁰ The ARIC cohort was evaluated in two studies for unmatched 6-year and mean 11-year hard CHD₂/hard CHD₁.^{75, 105} The 6-year study reported an AUC of 0.65 for men and 0.67 for women, and the mean 11-year study reported an AUC of 0.63 for men and 0.73 for women. The South Bay Heart Watch cohort evaluated men and women without diabetes for matched hard CHD₁, and the AUC was 0.63.⁸⁷ The WHS evaluated women for unmatched CVD₃/hard CHD₁, and the AUC was 0.79, with inadequate calibration.⁵⁴ The Chicago Heart Association study evaluated young men aged 18 to 39 years without diabetes for 10-year matched hard CHD₁.⁴⁹ Discrimination was not reported, and calibration was inadequate (p = 0.07, based on the Hosmer-Lemeshow goodness-of-fit test).

Europe – **internal validation.** Reporting of model performance characteristics in internal cohorts during model development was highly variable (Table 13). Discrimination measurements, either AUC or C statistic, ranged from 0.52 to 0.83 for those models developed in European patients. The QRESEARCH cohort in the United Kingdom was used to develop a series of models under the QRISK name, namely version 1, version 1.1, and version 2.^{35, 43, 46} Version 1 was developed for CVD₄, version 1.1 was developed for CVD₁₀, and version 2 was developed for CVD₁. The AUC for these models ranged from 0.77 to 0.79 among men and from 0.79 to 0.82 among women. Calibration measurements in version 1 were reported using the Brier

score and O/E ratio, and were not significantly different from 1.0. Calibration measurements were reported to be adequate and were represented in graphical form for version 2.

The Swedish National Diabetes Register was used to develop a diabetes-specific risk model that added hemoglobin A_{1c}, age at onset of diabetes, and duration of diabetes to the traditional risk factors for the outcome of CVD₅. The C statistic for the model was 0.70, and it was adequately calibrated by the Hosmer-Lemeshow goodness-of-fit test.¹⁰⁷ The Supplementation en Vitamines et Mineraux Antioxydants (SU.VI.MAX) model was developed in a French cohort of men for the outcome of total CHD₁, and the AUC was 0.75. No calibration measurements were reported. Models were developed from the Second Northwick Park Heart Study (NPHS-II), West of Scotland Coronary Prevention Study, European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk), and the Norwegian Government Study to evaluate diabetes variables, echocardiography characteristics, family history of CAD, fibrinogen, lipoprotein A, apolipoproteins A1 and B, and exercise testing.^{36, 60, 71, 84} The CUORE cohort, consisting of men from Italy, was used to develop a model for the outcome of hard CHD₂.⁷⁶ Internal validation was reported as an AUC of 0.74, with questionable calibration ($\chi^2 = 15.5$). The DARTS cohort consisted of patients with type 2 diabetes in Scotland who were utilized to develop a model for hard CHD₁.⁶³ The AUC in the internal validation was 0.71, and calibration measurements were not reported. The PROCAM cohort of German men was used to develop a risk prediction model for hard CHD₁. The AUC of the model was 0.83, and the calibration was adequate. A cohort from New Zealand was used to develop a risk prediction model for 5-year CVD₂, and the AUC was 0.73 for men and 0.78 for women.⁸⁹ The Intervention as a Goal in Hypertension Treatment (INSIGHT) cohort utilized a multinational cohort including patients with hypertension to develop a model for CVD_{14} and stroke.⁹⁴ The CVD version reported an AUC of 0.66. Calibration was reported by an O/E ratio of 1.0 for the stroke version and 1.25 for the CVD version. A cohort of elderly (aged 60–79 years) Australians in Dubbo, New South Wales was used to generate a risk prediction model for 5- and 10-year CVD₄.⁹³ No discrimination measures were reported, and the calibration was reported as inadequate for both 5- and 10-year outcomes.

Europe – **external validation.** The FRS (Anderson) family of models has been extensively externally validated among European cohorts. The Poole Diabetes Study evaluated men and women with diabetes for unmatched total $CHD_3/total CHD_1$ and CVD_{13}/CVD_2 outcomes with two version of the model.⁷³ The entire cohort as well as a variety of subcohorts (men, women, and patients with treated and untreated hypertension) were evaluated. The same trends were present for all analyses. The CVD outcome analysis found an AUC of 0.67 and 0.68 for men and women, respectively. The CHD outcome analysis found an AUC of 0.73 and 0.70 for men and women, respectively. In the overall cohort, there was inadequate calibration for both outcomes, and the O/E ratio was 1.46 for the CHD outcome and 1.48 for the CVD outcome.

The SHHEC, which consisted of Scottish men and women, was evaluated for the unmatched outcome of 10-year CVD_{11}/CVD_2 . The AUC was 0.72 for men and 0.74 for women. The O/E ratio was 0.71 (95% CI, 0.66–0.76) for men and 0.65 (95% CI, 0.59–0.71) for women, indicating that the model predicted an excess of outcomes. The British Regional Heart Study (BRHS), consisting of men aged 40 to 59 years without diabetes, was evaluated for a series of unmatched outcomes using the total CHD₁ version of the model and 10- and 20-year hard CHD₁, stroke₁, and diabetes mellitus outcomes.⁶⁵ The AUC measurement ranged from 0.63 to 0.69, and the outcomes were purposely mismatched to evaluate the performance of the tool for these outcomes. Calibration was not calculable, except for 20-year hard CHD₁/total CHD₁, which

reported an O/E ratio of 2.5 (95% CI, 2.33–2.68), revealing that the observed outcomes were largely in excess of predicted outcomes.

The Leiden-85 cohort, a group of elderly (age 85 years) men and women from the Netherlands, was evaluated for unmatched CVD mortality/CVD₂.¹⁰² The AUC was 0.53. The Cardiff Diabetes Database cohort, a group of men and women with diabetes, was evaluated for the matched outcome of CVD_2 .⁸⁵ The AUC was 0.64 for men and 0.66 for women. The O/E ratio for men was 0.81 (95% CI, 0.67–0.98) and for women it was 0.86 (95% CI, 0.67–1.08).

A cohort from New Zealand was evaluated for 5-year CVD₂; the AUC was 0.74 for men and 0.77 for women, and the O/E ratio was 1.17 (95% CI, 1.05–1.31) and 1.09 (95% CI, 0.88–1.34) for men and women, respectively.⁸⁹ The QRESEARCH cohort was evaluated for unmatched 10-year CVD₄/CVD₂, and the AUC was 0.76 for men and 0.77 for women.⁴³ The O/E ratio was 0.68 for men and 0.83 for women. The same cohort was evaluated for unmatched 10-year CVD₁₀/CVD₂, and the AUC was 0.76 for men and 0.78 for women.⁴⁶

The British Women's Heart and Health cohort was evaluated for unmatched total CHD₃/total CHD₁ and CVD₁₁/CVD₂.⁶⁴ The AUC was 0.63 for the CHD outcome and 0.64 for the CVD outcome. The O/E ratio for the CHD outcome was 0.97 (95% CI, 0.84-1.11) and for the CVD outcome it was 0.65 (95% CI, 0.57–0.74). The Health Improvement Network cohort was evaluated for 10-year CVD_{10}/CVD_2 , and the AUC for men was 0.74 and for women it was 0.76.⁴³ The O/E ratio for men was 0.76 (95% CI, 0.75–0.76) and for women it was 0.91 (95% CI, 0.90–0.92). The Monitoring Project on Cardiovascular Disease Risk Factors (MP-CVDRF) cohort was evaluated for 10-year CVD mortality/CVD₂.¹⁰⁶ The AUC was 0.86 for all patients, and was 0.69 among smokers, 0.81 in patients with elevated total cholesterol, 0.79 in patients with hypertension, and 0.80 in high-risk patients. The PROCAM cohort was evaluated for the hard CHD₁ outcome.⁹² The O/E ratio for men was 0.56 (95% CI, 0.50–0.63) and for women it was 0.35 (95% CI, 0.24–0.59), and the AUC for men was 0.73 and for women it was 0.88. The Renfrew-Paisley cohort compared manual and non-manual labor employment as a socioeconomic status indicator for the unmatched CVD mortality/CVD₂ outcome.⁶⁶ The O/E ratio for the entire cohort was 1.71 (95% CI, 1.59–1.85) and the AUC was 0.73. The AUC for manual laborers was 0.72 and for non-manual laborers it was 0.74. The Prospective Evaluation of Diabetic Ischaemic Disease by Computed Tomography (PREDICT) cohort of patients with diabetes was evaluated for the unmatched CVD₁₉/CVD₂ outcome, and the AUC was 0.63.¹⁰⁸ An Australian Aboriginal cohort was evaluated for the matched total CHD₁ outcome, and the O/E ratio for men was 2.00 (95% CI, 1.37–2.82) and for women it was 3.92 (95% CI, 2.81–5.32).⁷⁷ The BRHS cohort of men was evaluated for the matched outcomes of CHD mortality and total CHD₁.⁸⁸ The models revealed poor calibration using both model outcome versions, with the CHD mortality version resulting in a chi-square value of 30.2 (p<0.01) and an O/E ratio of 0.68 (95% CI, 0.59–0.79). The total CHD₁ version resulted in a chi-square value of 155 (p<0.01) and an O/E ratio of 0.64 (95% CI, 0.59–0.69). The INSIGHT cohort of middle-aged patients with hypertension was evaluated for the unmatched outcome of CVD₁₄/CVD₂, the matched outcome of total CHD₁, and the matched outcome of stroke₄.⁹⁴ The O/E ratio for the unmatched CVD outcome was 0.39 (95% CI, 0.38–0.44), for the total CHD₁ outcome it was 0.44 (95% CI, 0.36– 0.52), and for the stroke₄ outcome it was 1.00 (95% CI, 0.81–0.22). The MONICA Augsburg cohort was evaluated for unmatched hard CHD₁/CVD₂ and the AUC for men was 0.78 and for women it was 0.88. The O/E ratio for men was 0.50 (95% CI, 0.42–0.59), and for women it was 0.39 (95% CI, 0.27–0.54).⁹² The Wisconsin Epidemiologic Study of Diabetic Retinopathy

(WESDR) cohort of patients with diabetes was evaluated for unmatched stroke mortality/CVD₂, and the O/E ratio was 1.79 (95% CI, 1.37–2.29).⁹⁶ The NHP-Europe cohort was evaluated for unmatched stroke mortality/stroke₄, and the O/E ratio was 3.91 (95% CI, 1.91–7.18).

The FRS (Wilson) family of models has also been extensively externally validated among European cohorts. The EPIC-Norfolk cohort was evaluated for matched total CHD₁, and the AUC for both men and women was 0.71.³⁶ The Study of Atherosclerotic Risk Factors cohort of Czech men without diabetes was evaluated for the matched outcome of total CHD₁, and the AUC was 0.64, with an O/E ratio of 1.28 (95% CI, 1.05–1.54). The Validez de la Ecuación de Riesgo Individual de Framingham de Incidentes Coronarios Adaptada (VERIFICA) cohort of Spanish patients was evaluated for matched total CHD₁.⁵⁸ The AUC for men was 0.68 and for women it was 0.73. Calibration, as evaluated by the Hosmer-Lemeshow goodness-of-fit test, was inadequate for both men ($\chi^2 = 110$) and women ($\chi^2 = 64$). The O/E ratio for men and women, respectively, was 0.45 (95% CI, 0.37–0.54) and 0.44 (95% CI, 0.34–0.55). A cohort of patients with diabetes in Lyon, France was evaluated for unmatched CVD₆/total CHD₁.⁷² The AUC was 0.72, and the O/E ratio was 1.36 (95% CI, 0.96–1.88). The ULSAM cohort of Swedish men was evaluated for unmatched CVD mortality/total CHD₁, and the AUC was 0.58.⁸⁰ The CUORE cohort of Italian men was evaluated for unmatched hard CHD₂/total CHD₁.⁷⁶ The AUC was 0.72, and the O/E ratio was 0.33 (95% CI, 0.29–0.37). The Rotterdam Coronary Calcification Study was evaluated for unmatched CVD_3 /total CHD_1 .⁶⁹ The AUC was 0.73 and 0.68 for men and women, respectively. The MONICA Augsberg cohort of white male patients in Germany was evaluated for unmatched hard CHD₁/total CHD₁, and the AUC was 0.74.⁸⁶ The SU.VI.MAX cohort of French male patients was evaluated for matched total CHD₁.¹¹⁰ The AUC was 0.74 and the O/E ratio was 0.50. A cohort of patients with diabetes in a German university clinic was evaluated for unmatched MI/hard CHD₁, and the AUC was 0.63.¹⁰⁴ A cohort of renal transplant patients in France were evaluated for matched total CHD₁, and the O/E ratio was 1.69 (95% CI, 1.13-2.42).⁸²

The FRS ATP-III model has been externally validated a number of times in European cohorts. A cohort of German clinic patients was evaluated for matched hard CHD₁, and the AUC was 0.63.¹⁰⁴ A cohort of patients aged 55 years and older living in a suburb of Rotterdam, Netherlands was evaluated for matched hard CHD₁. The AUC was 0.63 and 0.73 for men and women, respectively. The O/E ratio was 0.72 (95% CI, 0.65-0.80) for men and 1.02 (95% CI, 0.93–1.12) for women.⁴⁸ The NPHS-II cohort of British men was evaluated for unmatched hard CHD₂/hard CHD₁.⁷¹ The AUC was 0.62, and the O/E ratio was 0.47 (95% CI, 0.41–0.54). The Prospective Epidemiological Study of Myocardial Infarction (PRIME) cohort of Northern Irish men evaluated unmatched 5-year total CHD₁/hard CHD₁.⁹⁰ The AUC was 0.66, and the O/E ratio was 0.75 (95% CI, 0.62–0.89). The PRIME cohort of French men was evaluated for unmatched 5-year total CHD₁/hard CHD₁.⁹⁰ The AUC was 0.68, and the O/E ratio was 0.67 (95% CI, 0.58– 0.77). The ULSAM cohort of Swedish men aged 70 years and older was evaluated for unmatched MI/hard CHD₁, and the AUC was 0.61.⁵⁰ The same cohort was evaluated for matched 10-year hard CHD₁, and the O/E ratio was 0.21 (95% CI, 0.15–0.30). The PROCAM cohort was evaluated for matched hard CHD_1 .¹⁴ The AUC was 0.78, and the calibration, as measured by the Hosmer-Lemeshow goodness-of-fit test ($\chi^2 = 44$; p < 0.01), was inadequate. The Dubbo study of Australian patients aged 60 to 79 years without diabetes was evaluated for matched 10-year CVD₄.⁹³ The O/E ratio for men and women, respectively, was 0.91 (95% CI, 0.75–1.10) and 0.93 (95% CI, 0.74-1.13).

The UKPDS hard CHD₁ risk model for patients with diabetes has been externally validated in other European cohorts. British patients with diabetes were evaluated for unmatched total CHD₃/hard CHD₁. The overall population was found to have an AUC of 0.67, calibration by the Hosmer-Lemeshow test ($\chi^2 = 17.1$; p = 0.03) was inadequate, and the O/E ratio was 1.15 (95% CI, 0.89–1.48). Among men, the AUC was 0.67 and the O/E ratio was 1.11 (95% CI, 0.81–1.49). Among women, the AUC was 0.62 and the O/E ratio was 1.19 (95% CI, 0.74–1.82).⁷³ The National Health Service (NHS) Trust cohort of patients with diabetes at an UK university diabetes clinic was evaluated on the unmatched outcomes of CVD₁₈/hard CHD₁ and total CHD₂/hard CHD₁.⁷⁸ The CVD outcome had an AUC of 0.74 and an O/E ratio of 1.20 (95% CI, 1.08–1.33). The CHD outcome had an AUC of 0.76 and an O/E ratio of 1.60 (95% CI, 1.42–1.80). The PREDICT cohort of British patients with diabetes was evaluated for unmatched CVD₁₉/hard CHD₁ and total CHD₂/hard CHD₂. The CVD outcome had an AUC of 0.67, and the total CHD outcome had an AUC of 0.63.¹⁰⁸ A cohort of patients with diabetes in Munich was evaluated for unmatched MI/hard CHD₁, and the AUC was 0.66.¹⁰⁴

The SCORE model for CVD mortality was externally validated in a number of European cohorts. A cohort of German patients from Ludwig University was evaluated for unmatched hard CHD_1/CVD mortality, and the AUC was 0.66.¹⁰⁴ The Vorarlberg Health Monitoring and Promotion Program of Austrian patients was evaluated for both matched CVD mortality and unmatched CHD mortality/CVD mortality.⁶⁸ The CVD outcome had an AUC of 0.80 for the entire population, 0.76 for men, and 0.78 for women. The O/E ratio for this outcome was 0.73 (95% CI, 0.67–0.80) for everyone, 0.84 (95% CI, 0.75–0.92) for men, and 0.52 (95% CI, 0.42– 0.62) for women. The unmatched CHD outcome had an AUC of 0.75 for men and 0.84 for women, and the O/E ratio was 0.79 (95% CI, 0.70-0.89) for men and 0.46 (95% CI, 0.35-0.60) for women. A cohort of Norwegian patients aged 60 to 69 years without diabetes was evaluated for matched CVD mortality.⁴⁴ The high-risk equation reported an AUC for men and women of 0.65 and 0.68, respectively, and an O/E ratio of 0.45 (95% CI, 0.40–0.50) and 0.37 (95% CI, 0.31–0.44). The low-risk equation reported an O/E ratio for men and women of 0.79 (95% CI, 0.70–0.88) and 0.56 (95% CI, 0.47–0.66), respectively. The Norwegian Counties Study of patients aged 40 to 59 years without diabetes was evaluated for matched CVD mortality.⁴⁴ The high-risk equation reported an AUC for men aged 40 to 49 years of 0.67 and for men aged 50 to 59 years it was 0.68. The AUC for women aged 40 to 49 years was 0.66 and for women aged 50 to 59 years it was 0.72. The O/E ratio for men was 0.53 (95% CI, 0.48-0.58) and for women it was 0.42 (95% CI, 0.34-0.51). The MP-CVDRF cohort of patients aged 20 to 59 years from the Netherlands was evaluated for matched 10-year CVD mortality.¹⁰⁶ The NHP-Europe cohort of patients was evaluated for unmatched CHD mortality/CVD mortality, and the O/E ratio was 3.24 (95% CI. 2.08–4.82).⁷⁴

The PROCAM Cox proportional hazards model for hard CHD_1 was evaluated in a number of European cohorts. The NHS Trust cohort of British patients with diabetes was evaluated for unmatched CVD_{18} /hard CHD_1 and total CHD_2 /hard CHD_1 .⁷⁸ The CVD outcome had an AUC of 0.67 and an O/E ratio of 2.79 (95% CI, 2.51–3.09). The total CHD outcome had an AUC of 0.65 and an O/E ratio of 2.05 (95% CI, 1.82–2.31). The Ludwig University cohort was evaluated for matched hard CHD_1 , and the AUC was 0.65.¹⁰⁴ The Northern Irish PRIME cohort of men was evaluated for 5-year hard CHD_1 ; the AUC was 0.61 and the O/E ratio was 0.56 (95% CI, 0.43–0.72).⁹⁰ The French PRIME cohort of men was evaluated for matched for matched 10-year hard CHD_1 and unmatched MI/hard CHD_1 .⁸⁰ The MI

outcome had an AUC of 0.63, and the hard CHD outcome had an O/E ratio of 0.27 (95% CI, 0.19–0.38). The NPHS-II cohort of white men was evaluated for unmatched hard CHD₂/hard CHD₁.⁷¹ The AUC was 0.63, and the O/E ratio was 0.46 (95% CI, 0.40–0.52). A cohort of German working men in the region of Münster (a subset of the PROCAM cohort) was evaluated for matched hard CHD₁, and the O/E ratio was 0.78 (95% CI, 0.70–0.87).²⁹

The ASSIGN model for CVD_{11} was evaluated in the SHHEC and QRESEARCH cohorts. In the SHHEC cohort, the matched 10-year CVD_{11} outcome was evaluated.⁵⁹ For men, the AUC was 0.73 and the O/E ratio was 0.79 (95% CI, 0.73–0.85). For women, the AUC was 0.77 and the O/E ratio was 0.67 (95% CI, 0.61–0.74). In the QRESEARCH cohort, the unmatched 10-year CVD_4/CVD_1 outcome was evaluated.⁴⁶ For men, the AUC was 0.76 and the O/E ratio was 0.73 (95% CI, 0.72–0.74). For women, the AUC was 0.78 and the O/E ratio was 0.73 (95% CI, 0.72–0.74).

Both the CardioRisk Manager (CRM) and Joint British Societies Risk Prediction Chart (JBSRC) models were evaluated in a single cohort, the NHS Trust. The outcomes in the cohort were total CHD_2 and CVD_{18} ; in both cases, the total CHD_2 outcome was matched to the models and the CVD outcomes were unmatched. The total CHD outcome was evaluated with the JBSRC model and had an AUC of 0.77. The same outcome was evaluated with the CRM model and the AUC was 0.73. The CVD outcome was evaluated in the JBSRC model and the AUC was 0.80, and for the CRM model, it was 0.37.

The DARTS model was evaluated for matched hard CHD_1 in the Salford, England cohort of patients with diabetes.⁶³ The AUC for this model was 0.69.

The QRISK model was quasi-externally evaluated in the QRESEARCH cohort for the unmatched outcome of CVD_1/CVD_4 . The AUC for men was 0.79, and for women it was 0.81.³⁵

The UKPDS-60 model for stroke was evaluated in the WESDR cohort for unmatched stroke mortality/stroke₁. The O/E ratio was 1.13 (95% CI, 0.87–1.45) (Table 14).

Asia – internal validation. Reporting of model performance characteristics in internal cohorts during model development was variable. The discrimination measurements, either AUC or C statistic, ranged from 0.74 to 0.82 for those models developed in European patients. The Cox proportional hazards model developed from the Chinese Multi-Provincial Study (MUCA) cohort evaluated the outcome of hard CHD₁.⁸³ The AUC for men and women was 0.74 and 0.76, respectively. Models for both sexes were also calibrated, with a chi-square value of 12.6 (p=0.13) in men and 14.2 (p=0.08) in women. The MUCA-II cohort was utilized to develop a model for predicting CVD₁₇, and the AUC for the simple version was 0.79 for both sexes. For the point score adaptation, the AUC for men was 0.79 and for women it was 0.78. The National Health Insurance Corporation cohort was used to produce the Korean Stroke Risk Prediction model for 10-year stroke₆. The AUC for men was 0.82 and for women it was 0.81. Models for both sexes were adequately calibrated, with the male model reporting a chi-square value of 7.7 (p=0.56) and the female model reporting a chi-square value of 14.3 (p=0.16). The HKD Registry was used to develop both a total CHD₁ and a stroke₁ risk model. The stroke risk model reported an AUC of 0.79, and the total CHD₁ model reported an AUC of 0.74. The study also evaluated how much mismatched stroke outcomes (stroke₅ and stroke₃) would affect discrimination, and the AUC reported for stroke₅ and stroke₃ was 0.77 and 0.79, respectively (Table 15).

Asia – external validation. The FRS (Wilson) family of models was evaluated in two cohorts in Asia. First, the MUCA cohort was used to evaluate the matched outcome of hard CHD₁. The AUC for men was 0.71, and for women it was 0.74. Neither sex-specific model was calibrated; for men the chi-square value was 646 (p<0.01) and for women it was 148 (p<0.01). The JapanWork cohort of men was used to evaluate matched 5-year and 10-year total CHD₁. The AUC for the 5-year total CHD₁ outcome was 0.71, and for the 10-year total CHD₁ outcome it was 0.62. The O/E ratio was 0.38 for the 5-year outcome and 0.58 for the 10-year outcome.

The UKPDS-56 model for patients with diabetes was evaluated in one Asian cohort, the HKD Registry, for matched hard CHD_1 . The AUC was 0.61. The UKPDS-60, the stroke risk model, was applied to the same cohort for matched stroke₁, and the AUC was 0.61.

A custom FRS model⁵⁵ was applied to the Asia Pacific Cohort Studies Collaboration (APCSC) total Asian cohort for the matched outcome of CVD_8 . The AUC for men was 0.75, and for women it was 0.79. Neither sex-specific model was calibrated, with the male model reporting a chi-square value of 558 (p<0.01) and the female model reporting a chi-square value of 608 (p<0.01). The O/E ratio of the male model was 0.27, and for the female model it was 0.50.

The SCORE risk model was evaluated in the NHP South Asia cohort for unmatched CHD mortality/CVD mortality. The O/E ratio was 4.42.

Finally, the FRS (Anderson) stroke model was applied to the NHP South Asia cohort, and the O/E ratio was 1.88 (Table 16).

Remodeling and Recalibration

Americas. Model recalibration is a method in which the source model's intercepts are adjusted by the outcome incidence in the local population, but the risk variable coefficients remain intact. Remodeling is a method in which the risk variables from a prior equation are used to develop a new model in a local population. For this reason, any models that were generated in new cohorts that used the same variables as a previously published risk prediction model were considered remodeling efforts, not new model development. In addition, remodeling adjusts the new model by definition to matching outcomes between the cohort and model, while recalibration does not, since the risk variable coefficients are unchanged from the source model.

The FRS (Wilson) model was recalibrated or remodeled in a number of other cohorts. WHS data were used to remodel both the total cholesterol and low-density lipoprotein versions of the FRS (Wilson) model for total CHD₁ to the outcome of CVD_3 .⁵⁴ In both cases, the source models had shown inadequate calibration, while both of the remodeled models showed adequate calibration, with an AUC of 0.79 for both. D'Agostino and colleagues evaluated five U.S. cohorts for 5-year hard CHD₁ using the outcome-matched variant FRS Wilson model.²³ Of the five cohorts, the source model failed calibration tests in Native American women in the SHS cohort, Hispanic men in the PRHHP cohort, and Japanese American men in the HHP cohort. The source model was recalibrated in each of those cohorts, and in each case, the recalibrated model had adequate calibration. The Johns Hopkins Sibling Study was evaluated with the model for matched total CHD₁ among healthy siblings of patients with known premature CAD.⁴² The source model was found to be inadequately calibrated for men. The model was recalibrated using the local cohort, and calibration was found to be adequate in the adjusted model. One study combined patients with chronic kidney disease from the ARIC and CHS cohorts and evaluated matched 5- and 10-year hard CHD₁.⁴⁵ Calibration was determined to be inadequate for both outcomes for both

sexes. After recalibration was performed by replacing the baseline incidence using the local cohort, calibration was adequate for both sexes for the 5-year outcome and for women at 10 years, but calibration remained inadequate in men for the 10-year outcome. This study also remodeled the source model in both sexes for the 10-year outcome. This resulted in adequate calibration for both sexes, and significantly improved discrimination in men from 0.60 to 0.68, and in women it improved from 0.73 to 0.81.

The FRS ATP-III model was recalibrated or remodeled in a number of other cohorts. WHS data were used to perform remodeling of the FRS ATP-III model for hard CHD_1 to the outcome of CVD_3 .⁵⁴ The source model had shown inadequate calibration, and the remodeled model was reported to be adequately calibrated, with an AUC of 0.81.

A custom four-variable model from the fourth examination of the FRS was developed to be applied to both the National Health and Nutrition Examination Survey (NHANES) I and II cohorts in order to evaluate model performance in external U.S. cohorts and whether remodeling would result in significant risk variable coefficient changes.²⁵ This study evaluated four of the six variables (excluding diabetes and low-density lipoprotein cholesterol) from the FRS (Wilson) family. All four variables (age, systolic blood pressure, total cholesterol, and smoking) showed significant coefficient variation among models developed from each of the three cohorts in men, but only smoking varied significantly for women. In addition, AUC estimates when each of the cohorts was internally validated or when the custom FRS model was externally validated were nearly identical. Finally, while the O/E ratio was not significantly different than 1.0 for women, the custom FRS model overestimated the mortality rate for men in both NHANES cohorts (Table 17).

Europe. The FRS (Anderson) family of models was recalibrated or remodeled in three separate cohorts. The QRESEARCH cohort was used to recalibrate the model using the Nationwide Instruction for Cardiovascular Education method for the matched outcome of CVD₁.⁴⁶ The AUC for men was 0.78, and for women it was 0.80. The Cardiff cohort was used to perform remodeling for CVD₂, and the AUC for men and women was 0.65 and 0.68, respectively.⁸⁵ Finally, the BRHS cohort of men was used to remodel both CHD mortality and total CHD₁ outcomes.⁸⁸ The new CHD mortality model was adequately calibrated ($\chi^2 = 3.4$; p=0.91), but the total CHD model was inadequately calibrated ($\chi^2 = 24.6$; p<0.01).

The FRS (Wilson) family of models was recalibrated or remodeled in three separate cohorts. The EPIC-Norfolk cohort was used to perform remodeling, and the AUC for men was 0.72, and for women it was 0.80.³⁶ The VERIFICA cohort was used to perform remodeling for the outcome of total CHD₁. The AUC for men was 0.69, and for women it was 0.81. Both sex-specific models reported adequate calibration. The CUORE cohort of men was used to perform remodeling for the hard CHD₂ outcome using both the D'Agostino and Chambless methods.⁷⁶ The D'Agostino method resulted in an AUC of 0.72, but the calibration was inadequate ($\chi^2 = 27.1$; p<0.01). The Chambless method resulted in an AUC of 0.72, and the calibration was also inadequate ($\chi^2 = 19.9$; p=0.01).

The CUORE cohort was also used to remodel the PROCAM model for the outcome of hard CHD_2 , using both the D'Agostino and Chambless methods. In both cases, the AUC was 0.74, and there was inadequate calibration.⁷⁶ For the D'Agostino method, the chi-square value was 220 (p<0.01), and for the Chambless method, it was 53 (p<0.01) (Table 18).
Asia. The FRS (Anderson) family of models was the source for recalibration among both the MUCA and MUCA-II cohorts. The outcome in MUCA was matched hard CHD₁, and in MUCA-II it was matched CVD₁₇. The MUCA cohort reported an AUC in men of 0.74 and in women it was 0.76. The MUCA-II cohort reported an AUC of 0.80 among men and 0.79 among women. The custom FRS model⁵⁵ was remodeled using the APCSC China cohort, and the AUC for men was 0.76, and for women it was 0.80. The model was not adequately calibrated for men ($\chi^2 = 16.7$; p=0.03) but was calibrated for women ($\chi^2 = 12.2$; p=0.15) (Table 19).

Synthesis of Data Specific to Key Question 1

KQ1: Do any of the currently available tools for the prediction of cardiovascular risk in a North American population offer clear advantages over the others in predicting incident CHD, cerebrovascular stroke (stratified by thrombotic or hemorrhagic type), or a combination of these two?

The external validations with the strongest evidence are those with matched outcomes among North American and European cohorts. Asian cohorts are less applicable, as it has been wellestablished that those populations have significantly different outcome event rates of CHD and cerebrovascular disease than the general U.S. population, and are therefore not discussed in this section.

A 5-year version of the 1998 FRS model was evaluated in five different U.S. cohorts for matched outcomes. This study found that prediction performance was superior in women across all cohorts. In addition, while relative risk performance was maintained across all cohorts, absolute risk prediction was poor in Asian American or Hispanic cohorts.²³ The 1991 FRS model was evaluated in high-risk patients (patients with <10 percent FRS risk were excluded at baseline) for matched outcomes and had an acceptable O/E ratio.¹⁰⁰ The 1998 FRS model was evaluated in siblings of patients with early onset CVD for matched outcomes, and the tool significantly underpredicted outcomes.⁴² The 1998 FRS model was evaluated in male veterans for matched outcomes and had an acceptable O/E ratio.⁹⁷ The FRS ATP-III model was evaluated in young adults aged 18 to 39 years for matched outcomes and it significantly overpredicted outcomes.⁴⁹

British patients with diabetes and predominantly white workers from New Zealand were both evaluated using the 1991 FRS equation with matched outcomes.^{85, 89} Female patients with diabetes had an acceptable O/E ratio, but outcomes for men were underpredicted. The male worker outcomes were underpredicted, and the female worker outcomes were acceptably predicted. The 1991 FRS equation was also used to evaluate the PROCAM cohort with matched outcomes, and outcomes were significantly overpredicted.⁹² Australian Aborigines were evaluated with the 1991 FRS model for matched outcomes, and the model significantly underpredicted the outcome rate.⁷⁷ Two outcome versions of the 1991 FRS model were evaluated for matched outcomes in a cohort of British men, and both outcomes were overpredicted.⁸⁸ A multinational cohort of patients from Western Europe and Israel was evaluated with the 1991 FRS model for matched outcomes, and the tool significantly overpredicted outcomes.⁹⁴ The 1998 FRS model was used to evaluate Czech men without diabetes for matched outcomes, and it significantly underpredicted outcomes.⁵⁶ A cohort of Spanish patients was evaluated with the 1998 FRS model for matched outcomes, and it significantly overpredicted outcomes.⁵⁶ A cohort of French men was evaluated with the 1998 FRS model for matched outcomes, and it significantly overpredicted outcomes.¹¹⁰ A cohort of

French renal transplant patients was evaluated with the 1998 FRS model, and it significantly underpredicted outcomes.⁸² A cohort of German patients (including those with diabetes) was evaluated with the ATP-III FRS model for matched outcomes, and the O/E ratio was acceptable.¹⁰⁴ A cohort of elderly patients from the Netherlands was evaluated with the ATP-III FRS model for matched outcomes, and the outcomes were significantly overpredicted for men and acceptably predicted for women.⁴⁸ The German PROCAM cohort of men (including those with diabetes) was evaluated with the ATP-III FRS model for matched outcomes, and the tool significantly overpredicted risk.¹⁴ A cohort of Swedish men was evaluated with the ATP-III FRS model for matched outcomes, and it drastically overpredicted risk.⁸⁰

An Austrian cohort of patients was evaluated with the SCORE model for matched outcomes, and the outcomes were significantly overpredicted.⁶⁸ An elderly cohort of Norwegian patients without diabetes was evaluated with the SCORE model for matched outcomes, and the tool overpredicted risk.⁴⁴ A middle-aged cohort of Norwegian patients without diabetes was evaluated with the SCORE model for matched outcomes, and the high-risk version overpredicted outcomes and the low-risk version underpredicted outcomes.⁴⁴ Another Norwegian cohort of patients aged 20 to59 years was evaluated with the SCORE model for matched outcomes, and the tool overpredicted outcomes.¹⁰⁶ French and Irish cohorts in the PRIME study were evaluated with the PROCAM model, and the tool overpredicted risk.⁹⁰ A Swedish cohort of men was evaluated with the PROCAM model for matched outcomes, and it also overpredicted risk.⁵⁰ A cohort of German men was evaluated with the PROCAM model for matched outcomes, and it overpredicted risk.²⁹ The Salford cohort of patients with diabetes was evaluated using the DARTS model for matched outcomes, and the risk estimation was acceptable.⁶³

Synthesis of Data Specific to Key Question 2

KQ2a: Do tools that treat diabetes as a CVD or CHD outcome equivalent have different performance characteristics than those that use diabetes as an independent risk factor for those outcomes?

KQ2b: Is the appropriateness of using diabetes as a coronary risk equivalent modified by the number of other cardiac risk factors that the individual has?

Six diabetic cohorts were used to develop risk prediction models, and 11 diabetic cohorts were used in external validation of diabetes-specific risk models for CVD, CHD, or stroke outcomes.^{38, 57, 63, 72, 73, 78, 85, 96, 104, 107, 108, 119} Thirteen non-diabetic cohorts were used in either primary model development or external validation of risk models excluding diabetes or general purpose models.

Diabetes Cardiovascular Risk Models

The most widely cited and externally validated risk model for patients with type 2 diabetes is the UKPDS risk model, which was developed in 4,540 white and Afro-Caribbean British patients for hard CHD_1 .¹¹⁹ The tool was developed among patients aged 25 to 65 years to predict greater than 4-year event rates. Events up to 4 years were excluded because the standardized mortality ratio observed in the general population (0.94 for men, 0.96 for women) was less than that, probably because patients with life threatening illnesses and those older than age 65 years at baseline were excluded from the study cohort. Risk variables used in the model are summarized in Table 24.

Another externally validated type 2 diabetes cardiovascular risk model is the DARTS model, which was developed in 4,569 patients in Tayside, Scotland for hard CHD_1 .⁶³ Only 1 percent of the cohort was non-white. Type 1 diabetes was excluded, but there was no severity of illness or age exclusions in this cohort. Risk variables used in the model are summarized in Table 24.

An internally validated type 2 diabetes risk model was developed in 7,067 Chinese patients from the HKD Registry for total CHD_1 .³⁸ It should be noted that 6.2 percent of the cohort had peripheral artery disease and 3.9 percent of the cohort had a prior stroke (Table 20).

Diabetes as a modeling risk factor. There is significant evidence to support the conclusion that the relative risk of the known risk factors for CVD outcomes can vary among different cohorts within the United States, as well as between the United States and Europe or Asia.

In a study by D'Agostino and colleagues for the National Heart Lung and Blood Institute CHD Prediction Workshop, a total of seven U.S. cohorts were evaluated for 5-year hard CHD_1 .²³ For men and women in each cohort, an original and remodeled FRS (Wilson 1998) equation was applied to each sex in each cohort. Among men, there were significant differences between the FRS cohort and the Physicians' Health Study cohort, Japanese Americans in the HHP cohort, Hispanics in the PRHHP cohort, Native Americans in the SHS cohort and the CHS cohort. Among women, there were significant differences between the FRS cohort and African Americans in the ARIC cohort and Native Americans in the SHS cohort. Absolute risk performance for the Framingham risk score in the other cohorts was acceptable for all except for men in the HHP and PRHHP cohorts and women in the SHS cohort. A summary of relative risk for hard CHD₁ among patients with diabetes is shown in Table 21.

A study by the Diverse Populations Collaborative Group Investigators that compared 16 cohorts from the Americas and Europe found that the proportion of patients with diabetes ranged from 0.2 (rural patients in the Yugoslavia Cardiovascular Disease Study) to 9.1 percent (Japanese Americans in the HHP).³⁰ The overall CHD mortality rate per 1,000 person-years ranged from 1.0 (rural patients in the PRHHP) to 6.5 percent (Tecumseh Community Health Study). When comparing multivariate models of age, systolic blood pressure, total cholesterol, current smoking, and diabetes across these cohorts, diabetes relative risk among men varied widely from 1.24 (range, 0.61–2.51) in the control arm of the Multiple Risk Factor Intervention Trial to 8.05 (range, 3.80–17.03) in the random sample of the Lipid Research Clinics Follow-Up Study. Among women, the relative risk varied from 1.32 (range, 0.62–2.82) in the Tecumseh Community Health Study to 8.67 (range, 3.81–19.77) in the Norwegian Counties Study (Table 22).

Remodeling efforts of established risk models for other cohorts also serves to illuminate systematic relative risk differences between risk factors. The UKPDS risk model was remodeled using the HKD Registry, and a comparison of hazard ratios in the UKPDS and remodeled HKD models is shown in Table 23. Comparing the variable estimates between the original and remodeled equation for the Chinese cohort revealed that sex and hemoglobin A_{1c} were significantly different predictors of CHD between the two cohorts.

Diabetes risk model external validations. The model development study by Donnan and colleagues used 4,569 patients from Salford, England to externally validate the model developed in the DARTS cohort.

Diabetic cohorts evaluated by non-specific risk models. A small cohort of French patients with diabetes was evaluated by the 1998 FRS model, and the O/E ratio was acceptable, but the outcomes were fairly mismatched.⁷² The Poole Diabetes Study was evaluated using the 1991 FRS model for both total CHD and CVD, although the definitions varied between cohort and model in each case in very small ways.⁷³ Both outcomes were significantly underpredicted in the cohort by the risk model. The NHS Trust cohort was evaluated by the PROCAM model for a mismatched outcome between total and hard CHD, and the model significantly underpredicted the number of outcomes.⁷⁸ The Cardiff Diabetes Database was evaluated with the 1991 FRS model for a completely matched CVD outcome, and the model underpredicted the number of outcomes sees, but was marginally better for women.⁸⁵ A study on 716 patients in Munich, Germany was evaluated by the 1998 FRS equation for total CHD, and the predicted and observed outcomes were not significantly different.¹⁰⁴ However, there was an outcome mismatch due to measurement of hard CHD in the cohort, which would underestimate the number of outcomes compared to what the model would expect. The PREDICT cohort in London was evaluated with the 1991 FRS equation, but the study did not report calibration or the predicted number of outcomes.¹⁰⁸

Assessment of Tools Available Online

We identified 44 online tools for calculating CVD risk using the approach described in the Methods section. The models on which these tools are based, along with their online location, are listed in Appendix D/Summary Table 1.

We used a set of test patients to predict risk using SAS versions of the original models and the online tools that purported to use those models. We compared our SAS-generated risk to those generated with the online tools (Table 24). All of the online versions had some variation from the referenced source model, but in most cases these differences were modest. FRS (Anderson) Online did show a large difference for Patient 2 (0.19 vs. 0.09). FRS (Wilson) Online also showed a large difference for Patient 2 (0.03 vs. 0.13). In addition, there were large variations among the risk tools for each patient. Some of the variation can be explained by the different outcomes the models were attempting to model. In particular, the FRS (Anderson) model predicts a CVD outcome with a large number of components, which is known to be 2 to 3 times as high as the hard CVD outcome. For patients without diabetes, risk measurements were very consistent across models. For patients with diabetes, risk estimates varied greatly.

Figures 2 and 3 show the variation in predicted outcomes obtained for two of the test patients when only age was varied (from 35 to 65 years). As age increases, the model predictions demonstrate increasing variation.

Quality of the Literature

We assessed the quality of each study included in our review. Individual results for quality scoring are presented in Appendix M/Summary Table 10, and a summary of quality scores is presented in Figure 4, with the proportion of studies achieving each level of each quality measure represented by a horizontal bar.

No quality measure was fully achieved by 100 percent of the included studies. Fewer than half of the studies in any geographic region provided an adequate description of the study population or

the inclusion/exclusion criteria on which the initial cohort was built. Very few studies had adequate follow-up (<20 percent), and among those with substantial loss to follow-up, none accounted for the potential effects of the loss. Internal validation should be a basic requirement for the reporting of model development studies, but fewer than 30 percent overall reported measures of internal validation. Among U.S. studies in which existing models were validated, both discrimination and calibration were almost always (88 percent) reported, although this was not the case among studies in the other geographic areas, which reported these measures less than 40 percent of the time.

Chapter 4. Discussion

The body of literature for this analysis consisted largely of studies that could not be easily pooled or combined quantitatively. Therefore, it is essential when identifying trends in the outcomes to highlight studies that reflect key issues and concepts, and we have done that in this section.

Almost all models retained good relative and absolute risk prediction in the development cohort itself, but since most were not externally validated, the utility of these models must remain in question. Among the small number of externally validated models, the strongest performance was seen in those with matched outcomes among North American and European cohorts. External validation of U.S.-developed models in other U.S. cohorts found that most retained good relative and absolute risk prediction performance among white and black populations, but absolute risk prediction was poor among minority populations, such as Hispanics and Asian Americans.^{23, 97, 100} A few studies that evaluated higher- or lower-risk cohorts, such as siblings of patients with early CAD or young adults, had poor absolute risk prediction performance, which is expected.^{42, 49} In all cases, overall model relative risk performance (risk separation) was superior for women.^{23, 42, 49, 97, 100} Thus, the evidence in this review would suggest that risk models are generally accurate only in patients who are representative of the source population, and for the Framingham cohort, such patients were middle-aged and white or black.

There was a paucity of CVA risk models in the literature. This was primarily due to the exclusion criterion that required the baseline population to be free of CVD at the time of cohort inception. A few of the CVA risk models were externally validated in a population with baseline CVD. While those cohorts and risk models that were developed in the absence of baseline CVD are included here, they are not representative of the overall literature.

Comparison of traditional cardiovascular risk factors among seven U.S. cohorts by D'Agostino and colleagues found that although effects seen across some cohorts were similar, those that comprised Japanese American, Native American, or Hispanic populations had significantly different relative risk associated with risk factors identified in the Framingham cohort.²³ In addition, those cohorts also demonstrated poor performance in absolute risk prediction of the FRS model. While there is clearly some tolerance for changes in cohort characteristics, the degree of tolerance is not entirely known, and overall the evidence suggests that the number and magnitude of differences in relative risk between populations is correlated with poor absolute risk performance. Other studies have identified a direct relationship between the tendency to under- or overpredict based upon the baseline outcome incidence in the model derivation cohort.³⁰

In studies that examined risk factors for CVD using some of the same cohorts, but using slight variations of risk variables sets (four in one; six in another), confounding was clearly present as variables were included or excluded from the models, suggesting that even in the best risk estimates there is likely unmeasured confounding.^{23, 30}

External validation of U.S. risk models among European cohorts in which the outcomes were matched were more mixed. A few studies with matched outcomes reported acceptable risk model performance, but the European cohorts were generally at higher risk than the source population, including populations of patients with diabetes or elderly patients.^{48, 89} Another cohort reported acceptable performance but its results are questionable because the authors evaluated a cohort that included patients with diabetes using a model that was developed excluding diabetes.⁴⁰

Several studies reported that the risk models underpredicted outcomes, but again, these were almost entirely conducted in high-risk patient cohorts.^{56, 77, 82, 85, 89} Most of the evaluations among European cohorts found that the U.S. risk models overpredicted risk, given that underlying outcome event rates between the model cohort and the evaluation cohort differed substantially,^{14, 48, 56, 80, 88, 92, 94, 110} with significant differences observed in the degrees to which individual variables contributed to risk assessment.³⁰

The UKPDS risk model was the most frequently externally validated diabetes model,^{38, 40, 73, 78,} ¹⁰⁸ although evaluation results were mixed. For example, application of the UKPDS model to a Chinese cohort of patients with diabetes drastically overestimated the risk of CHD among those patients,³⁸ largely due to a significantly higher rate of cerebrovascular disease and a significantly lower rate of CVD among Chinese patients compared with U.S. or European cohorts.¹²¹ Among newly diagnosed patients in the British Poole Diabetes Study, absolute risk prediction, as determined by the Hosmer-Lemeshow goodness-of-fit test, was mildly inadequate, but the O/E ratio was acceptable.⁷³ However, the cohort included both soft and hard CHD outcomes, while the model was developed to predict hard CHD only, suggesting that the model would overpredict outcomes in this cohort if the outcomes were appropriately matched. Results of analyses in the NHS Trust cohort of London patients demonstrated that the model significantly underpredicted the number of outcomes.⁷⁸ However, the cohort included both soft and hard outcomes, which left the question of whether the model would have had an acceptable ratio for matched outcomes. Thus, although the UKPDS model had clearly improved performance over non-diabetes-specific risk models when directly compared, confirmed external validation in a matched outcome cohort of patients with diabetes has not yet taken place.^{73, 78}

Most of the external validations performed on diabetic cohorts by non-specific cardiovascular risk models found that the models were significantly underpredicting the number of outcomes.^{73, 78, 85} A few studies showed an acceptable O/E ratio, but had outcome mismatches that were more restrictive in the cohort than the model.^{40, 72} This supports the conclusion that the risk of CVD among patients with diabetes is elevated compared to the general population. In addition, this also suggests that a diabetes risk variable in a general model is insufficient for capturing the variance of risk experienced by diabetic populations; that is, risk is not simply attributed by whether the patient has diabetes or not, but also by other factors such as diabetes control, duration of diabetes, and whether the patient has already experienced end-organ damage.

There were no studies in which a general risk prediction model was compared to a diabetesexcluded model for matched outcomes. WHS, in which 2.9 percent of patients had diabetes, evaluated the FRS ATP-III and 1998 models, but the outcomes were substantially mismatched in the ATP-III (CVD vs. hard CHD) and 1998 models (total vs. hard CHD), and absolute risk prediction was poor in both.⁵⁴ The Chicago Heart Association study evaluated young men aged 18 to 39 without diabetes for matched outcomes in the ATP-III model and unmatched outcomes in the 1998 model, but absolute risk performance was poor in both because of the young population.⁴⁹ Czech patients without diabetes were evaluated with the 1998 FRS model for matched outcomes, and the model overpredicted the number of outcomes.⁵⁶ The Norwegian Counties Study of patients without diabetes evaluated the SCORE risk model, which did not include a diabetes risk factor but did include patients with diabetes in its source cohort, and the model overestimated the number of outcomes, and the overestimation was worse with increasing age.⁴⁴ The internal validation evaluation of the QRISK equation for CVD, which excluded patients with diabetes, also externally validated the 1991 FRS general risk model.⁴⁶ The 1991 FRS model significantly overpredicted the outcome, although there was a small outcome mismatch.

A number of U.S. cohorts that engaged in recalibration or remodeling reported poor absolute risk performance for the original FRS models. However, most of these evaluations had outcome mismatches between the cohort and the model.^{54, 61, 101} Those studies that performed remodeling of FRS risk variables in a local cohort reported retained or improved relative risk prediction and adequate absolute risk prediction.^{54, 61, 101} It should be noted that remodeling results in a model with an outcome that matches the model outcome (by definition), and it is not surprising that this would result in improved performance. One study evaluated matched outcomes between the cohort and the original model and found that minority populations were poorly predicted by the model. This study subsequently showed that remodeling resulted in adequate performance in all the cohorts, based upon the Hosmer-Lemeshow goodness-of-fit test.²³ Two other studies with matched outcomes and inadequate original model performance noted adequate absolute risk prediction after remodeling.⁴⁵ In contrast, recalibration methods (which adjust the baseline outcome event rate intercept in the model but do not adjust the risk variable coefficients) performed more variably, with both adequate and inadequate absolute risk prediction results.^{42, 45} However, one of these studies performed both recalibration and remodeling, and showed that although recalibration was sufficient for women and not men, remodeling resulted in adequate absolute risk prediction for both sexes.⁴⁵

Remodeling efforts among diabetes and diabetes-excluded risk models followed the general trend of cardiovascular risk prediction models. Recalibration methods were successful in some cases, but were inadequate in others. However, remodeling methods were almost always successful in producing a model that performed well in the local cohort.³⁸ Among non-diabetic cohorts and general risk models, remodeling was successful in improving performance, although it should be noted that diabetes as a risk factor was dropped from the models.⁵⁶ Among a large U.S. female non-diabetic cohort, remodeling of the FRS ATP-III risk variables did not result in a well-calibrated model.⁶¹

Remodeling established risk models in other cohorts also serves to illuminate systematic relative risk differences between risk factors. For example, although absolute risk prediction was very poor when the UKPDS model was applied to the HKD Registry, there were no significant differences when comparing the hazard ratios of specific risk variables from the two cohorts,³⁸ suggesting that both the baseline outcome incidence and the relative risk contribution from individual risk factors play into absolute risk performance.

There were some substantial and consistent challenges to analyzing this body of literature. For example, we observed significant heterogeneity among outcome definitions, and this resulted in frequent mismatches between cohort and modeling outcomes. Frequently, cohort outcome data were collected in order to match a particular risk model, or to develop one, and other models with different outcomes were tested in order to directly compare them. Relative risk performance relies on the weight of the risk factors in the model, and is not dependent on the baseline outcome incidence. The C statistic, AUC, and sensitivity and specificity at a specified cut-off point all measure this type of performance. Relative risk performance (discrimination) can be insensitive to outcome mismatches if the relative contribution from each risk factor remains intact. Since all of the outcomes were wariations of CVD, stable relative risk performance was frequently found even when outcomes were mismatched. However, in order to use these tools clinically, low- and high-risk threshold cut-off points are set using the development data (i.e.,

matched outcome). Separate risk cut-off points must be established in order to appropriately use such tools to risk-stratify patients for outcomes other than those for which they were developed.

In addition, many risk calculators provide a percent risk of an outcome rather than a set number of years, which is absolute risk prediction and measured by model calibration statistics. The O/E ratio is the crudest measurement of this type of performance, but it can result in an acceptable ratio when some ranges of risk are overpredicted and some are underpredicted. The Hosmer-Lemeshow goodness-of-fit test is a more granular evaluation method that sorts all patients by predicted risk, divides them into 10 categories, evaluates the O/E ratio for each category separately, and sums the chi-square value in each category to report an aggregate measurement. Absolute risk prediction performance is dependent on both the baseline outcome incidence and the contribution of risk from each risk factor in the source cohort. Evaluating absolute risk prediction with a mismatched outcome between model and cohort has severe limitations, because the baseline outcome event rates are different from the outset. Some interpretation is possible if the prediction error is in the opposite direction of what one would expect; that is, if a cohort outcome is more restrictive, one would expect the model to overpredict the outcome, but if it underpredicts the outcome, then the result can be safely interpreted as poor absolute risk prediction. However, no such assertion can be made if absolute risk prediction is determined to be adequate for mismatched outcomes.

Summary

Overall, the FRS models performed fairly well in U.S. populations, but performance suffered when they were applied to populations that were substantially different from the source cohort. Although the FRS model was developed from a predominantly white cohort and is not representative of the U.S. population as a whole, performance was reasonable in both white and black patients from the ARIC cohort. In some cases, this was due to particularly low or high baseline risk in the destination cohort, and in some cases it was due to systematic differences in risk attributable to specific risk factors. In addition, the 2001 ATP-III version demonstrated several benefits compared to the older FRS models, including a focus on hard CHD outcomes, exclusion of patients with diabetes, and incorporation of more current FRS data than the 1991 version. A 2008 CVD model was recently published but has not yet been externally validated.³⁹

Recalibration, and to a greater extent, remodeling, demonstrated effectiveness as a means to improving performance in cohorts with substantially different outcome incidence or risk factor prevalence compared to the source cohort. However, questions remain regarding the population sample size necessary to perform these methods and how frequently they should be applied.

Development of risk models for cohorts with risk profiles that are systematically divergent from the general population can also be a successful strategy. However, in many cases, studies taking this approach were more or less remodeling exercises using traditional risk variables in the most common models. Sample size requirements for developing stable risk models are even less clear for these cohorts, and some of these studies had fewer than 1,000 participants. A growing body of literature suggests that specific cohort risk models are likely to be most successful when there are risk factors unique to that population that inform cardiovascular risk.

Even among U.S. cohorts, there was evidence that some ethnically diverse or minority populations had significantly different risk factor contributions to outcomes, even when the baseline prevalence was similar.^{23, 30} Our review did not exclude studies on the basis of

geographic area, but in analyzing the data it became clear that there were systematic differences in risk factor prevalence and outcome event rates between Asian cohorts (which were mostly Chinese or Korean) and North American and European cohorts.¹²¹ This makes use of Asian models in a general U.S. population ill-advised.

Diabetes-specific process measurement variables are significantly related to cardiovascular outcome risk among patients with diabetes, and risk models that incorporate these factors outperformed general risk prediction models when applied to these patients. Analysis also suggests that models excluding patients with diabetes outperformed general risk prediction models that included these patients in their development when applied to non-diabetic cohorts. Unfortunately, external validation of diabetes-specific risk models is lacking, particularly among U.S. cohorts. No U.S. diabetes risk model has been externally validated.

Problems with absolute risk prediction were improved or resolved by recalibration and remodeling methods, supporting the need in this literature for periodic recalibration or remodeling for either general or specific populations. However, empirical evidence for determining what time interval is reasonable or for detecting when a population is "significantly" different from the reference population does not yet exist. Future research in this area should focus on carefully matching outcomes between cohorts and risk models. Additional work in recalibration and remodeling methods is needed, as well as external validation of diabetes-only risk models.

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Acronyms/Abbreviations

Abbrev.AbbreviationAFTAccelerated failure timeAHRQAgency for Healthcare Research and QualityAICAkaike information criterionAPCSCAsia Pacific Cohort Studies CollaborationApo AApolipoprotein A1Apo BApolipoprotein BARICAtherosclerosis Risk in CommunitiesASSIGNAssessing Cardiovascular Risk Using SIGN GuidelinesATP-IIIAdult Treatment Panel IIIAUCArea under the curveAvg.AverageBICBayesian information criterionBMIBody mass indexBPBlood pressureBRHSBritish Regional Heart StudyBWHHBritish Regional Heart StudyBWHHBritish Regional Heart StudyCACSCoronary artery bypass graftCACSCoronary artery diseaseCadiciumCadcium scoreCADCoronary artery diseaseCardiff DMCardiff Diabetes DatabaseCeVDCerebrovascular diseaseCHAChicago Heart AssociationChSCardiovascular Health StudyCIConfidence intervalCMCSChinese Multi-Provincial Cohort StudyCP-NorwayCardiovascular Program–NorwayCRF-XClassical risk factorsCRMCardiovascular RoseCRPC-reactive protein
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CRMCardioRisk ManagerCRPC-reactive proteinCVACardiovascular accident
CRPC-reactive proteinCVACardiovascular accident
CVA Cardiovascular accident
CVD Cardiovascular disease
CYA Chicago Young Adults
D' Ag D'Agostino
DARTS Diabetes Audit and Research in Tayside, Scotland
DBP Diastolic blood pressure
DM Diabetes mellitus
DPCGI Diverse Populations Collaborative Group Investigation
Director includeDPCGIDiverse Populations Collaborative Group InvestigationDxDiagnosis

eGFR	Epidermal growth factor receptor
EKG	Electrocardiography
EPC	Evidence-based Practice Center
EPIC	European Prospective Investigation of Cancer
ESC	European Society of Cardiology
F/U	Followun
FamHx	Family history
FrRenal	French Renal cohort
FRS	Framingham Study
FRS-0	Framingham Offspring Study
HDFP	Hypertension Detection and Follow-Un Program
HDI	High-density lipoprotein
$H_{\sigma}h\Delta$	Hemoglobin A.
ндол _{іс}	Honolulu Heart Program
НКЛ	Hong Kong Diabetes Registry cohort
HI GOF	Hosmer-Lemeshow Goodness-of-Fit
heCPD	High sensitivity C reactive protein
HTN	Hypertension
INSIGHT	Intervention as a Goal in Hypertension Treatment
	Intervention as a Obai in Trypertension Treatment
IQK	Loint Pritish Societies Disk Prediction Chart
JDSKC	Johns Honking Sibling Study
JU22 1 62	Joinis Hopkins Storing Study
	Leuden-65 conort
	Low-defisity inpoprotein
LPA	Lipoprotein(a) Lipid Desearch Clipics Provelence Study
LKCPS	Ludwig Maximiliana University
	Ludwig-Maximinans University
	Muccondial information
	MONICA Augeburg schort
MONICA MD CUDDE	Monitoring Project on Condiguescular Disease Disk Festor
MP-CVDKF	Multiple Disk Factor Internentian Trial
MKFII	Chinese Multi Drovingial Study I
MUCA-I	Chinese Multi Drovincial Study I
MUCA-II	Chinese Multi-Provincial Study II
IN, 11 N/A	Not overlable
IN/A NAS	Not available
NAS	Normative Aging Study
NDD	Notwegian Counties Study
NDK NILANES I	National Diabetes Registry
NHANES I EES	National Health and Nutrition Examination Survey I
NHANES I-EFS	National Health and Nutrition Examination Survey I Epidemiological Follow-
NHANES II	up Study National Health and Nutrition Examination Survey U
NUIC	National Health Insurance Comparation
	National Heart Lung and Dlood Institute
	National real Lung and Blood Institute
NHP	Newcastle Heart Project

NHS	National Health Service
NICE	Nationwide Instruction for Cardiovascular Education
NIH	National Institutes of Health
NorGov	Norwegian Government Study
NPHS-I	First Northwick Park Heart Study
NPHS-II	Second Northwick Park Heart Study
NSW	New South Wales
NTRF	Non-traditional risk factors
NZwork	New Zealand workers cohort
O/E	Observed-to-expected ratio
P, p	p value
PCI	Percutaneous coronary intervention
PDS	Poole Diabetes Study
PHS	Physicians Health Study
Post-AF	Post-atrial fibrillation
PREDICT	Prospective Evaluation of Diabetic Ischaemic Disease by Computed Tomography
PRHHP	Puerto Rico Heart Health Program
PRHS	Puerto Rico Heart Study
PRIME	Prospective Epidemiological Study of Myocardial Infarction
PROCAM	Prospective Cardiovascular Münster cohort
Pub.	Publication
PVD	Peripheral vascular disease
RCC	Rotterdam Coronary Calcification Study
REGICOR	Registre Gironi del Cor
RRS	Reynolds Risk Score
SAHS	San Antonio Heart Study
SBHW	South Bay Heart Watch
SBP	Systolic blood pressure
SCORE	Systematic Coronary Risk Evaluation
SFHS	St. Francis Heart Study
SHHEC	Scottish Heart Health Extended Cohort
SHS	Strong Heart Study
SMR	Standard mortality ratio
SNDR	Swedish National Diabetes Registry
Spec.	Specific
STULONG	Study of Atherosclerotic Risk Factors
SU.VI.MAX	Supplementation en Vitamines et Mineraux Antioxydants
TC	Total cholesterol
TC-HDL	Total cholesterol and high-density lipoprotein
TEP	Technical Expert Panel
THIN	The Health Improvement Network
TIA	Transient ischemic attack
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
ULSAM	Uppsala Longitudinal Study of Adult Men
US	United States

USA-PRC	United States of America–People's Republic of China Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology Research Group
USPSTF	U.S. Preventive Services Task Force
val	Value
vars.	Variables
VERIFICA	Validez de la Ecuación de Riesgo Individual de Framingham de Incidentes
	Coronarios Adaptada (Validity of the Adapted Framingham Individual Risk
	Equation for Coronary Incidents Cohort)
VHM&PP	Vorarlberg Health Monitoring and Promotion Program
w/o	without
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy
WGHS	Women's Genome Health Study
WHI	Women's Health Initiative
WHS	Women's Health Study
wk(s)	weeks
WOSCOPS	West of Scotland Coronary Prevention Study
Х	times
yr(s)	Years

Table 1. Technical Expert Panel

	Physician	Other clinician	Researcher	Consumer/ Patient	End User
USPSTF					
Michael L. LeFevre, MD, MSPH	Х		Х		Х
Timothy Wilt, MD, MPH	Х		Х		Х
Russell P. Harris, MD, MPH	Х		Х		Х
Non-USPSTF					
Lucila Ohno-Machado, MD, PhD	Х		Х		Х
Michael Kattan, PhD			X		Х

Table 2. Inclusion Criteria

Category	Criteria
Study population	Asymptomatic adults
Study settings and geography	Any clinical/research settings in any country
Publication languages	English only
Admissible evidence (study design and other criteria)	 <u>Admissible designs</u> Randomized controlled trials, controlled clinical trials, cohorts Study size ≥200 <u>Other criteria</u> Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results Studies must attempt either internal or external validation Studies must report on one or both of the following outcomes: Coronary artery disease (nonfatal and fatal MI and sudden coronary heart disease death) Cerebrovascular stroke (thrombotic/hemorrhagic) Relevant outcomes must be able to be abstracted from data presented in the paper.

Table 3. Test Patient Characteristics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	43	54	58	63	77
Female	No	Yes	Yes	No	Yes
Race	White	Black	White	Black	White
Cholesterol Data*					
Total cholesterol (mg/dL)	220	245	237	197	260
High-density lipoprotein cholesterol (mg/dL)	43	46	35	22	33
Low-density lipoprotein cholesterol (mg/dL)	134	167	133	89	173
Triglycerides (mg/dL)	83	144	236	244	145
Taking lipid medication	No	No	Yes	Yes	No
Hypertension Data					
Systolic blood pressure (mmHg)	118	143	139	151	148
Diastolic blood pressure (mmHg)	76	85	85	93	91
Taking hypertension medication	No	No	Yes	Yes	No
Diabetes Data					
Patient self-report	No	No	Yes	Yes	No
Physician reported diagnosis	No	No	Yes	Yes	No
Fasting baseline glucose	89	104	145	169	135
Diabetes medication use	No	No	Yes	Yes	No
HgbA _{1c} (%)	5.7	5.8	7.4	8.5	6.5
Smoking					
Current	No	No	No	Yes	No
Former	No	No	Yes	No	Yes
Never	Yes	Yes	No	No	No
Other Variables					
Left ventricular hypertrophy by EKG	No	No	Yes	Yes	Yes
Body mass index	24.3	31.4	32.6	28.6	27.6
Family history of premature coronary heart					
disease	No	Yes	No	Yes	Yes
Family history of myocardial infarction	No	Yes	No	Yes	No
Chronic kidney disease	No	No	No	Yes	No
Atrial fibrillation	No	No	No	No	Yes
Rheumatoid arthritis	No	No	No	No	No
Microalbuminuria	No	No	Yes	No	No
Macroalbuminuria	No	No	No	Yes	No

*To convert to mmol/L, divide entry by 38.67 (except for triglycerides).

Table 4a. Outcome Definitions for Total Coronary Heart Disease, HardCoronary Heart Disease, and Cardiovascular Accident

	То	tal C	HD	Har	d CHD			C	:VA		
Name	1	2	3	1	2	1	2	3	4	5	6
Ischemic stroke						Х	Х	Х	Х		Х
Hemorrhagic stroke, all						Х			Х	Х	
Hemorrhagic stroke, embolic & intracerebral											Х
Transient ischemic attack							Х		Х		
Angina pectoris	Х		Х								
Unstable angina	Х	Х	Х								
Myocardial infarction	Х	Х	Х	Х	Х						
Intermittent claudication											
Sudden CHD death	Х	Х	Х	Х	Х						
Cardiac procedure		Х	Х		Х						
Congestive heart failure											

Table 4b. Outcome Definitions for Cardiovascular Disease

		CVD																	
Name	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Ischemic stroke	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х
Hemorrhagic stroke, all		х		Х			х	Х		х	Х		х	х	Х			Х	Х
Hemorrhagic stroke, embolic & intracerebral					х														
Transient ischemic attack	Х	х		Х					Х	х	Х	х	х	х					
Angina pectoris	Х	Х			Х	Х			Х	Х	Х	Х	Х	Х				Х	
Unstable angina	Х	Х			Х	Х			Х	Х	Х	Х	Х	Х				Х	Х
Myocardial infarction	Х	х	х	Х	Х	х	х	Х	Х	х	Х	Х	х	х	Х	Х	Х	Х	х
Intermittent claudication		х							Х			Х	х			Х		Х	
Sudden CHD death	Х	х	х	Х	Х	Х	х	Х	Х	х	Х	х	х	Х	Х	Х	Х	Х	Х
Cardiac procedure			Х		Х		Х		Х		Х		Х		Х	Х		Х	Х
Congestive heart failure		х					х					х	х	х					

Table 5. Externally Validated Models

		Year	Study	Cohort	Enroll	Enroll		
Model Name	Model Outcome	Published	Count	Abbreviation	Start Date	End Date	Enrollment	Followup*
ASSIGN ⁵⁹	CVD ₁₁	2007	2	SHHEC	01/01/1984	12/31/1995	13,297	
FINRISK ⁷⁴	CVD	2005	4	FINRISK			14,694	
FRS (Anderson) ^{18,136}	CVD ₂	1991	21	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
FRS (Anderson) ^{18,136}	Total CHD ₁	1991	8	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
FRS (Anderson) ^{18,136}	Myocardial infarction	1991	1*	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
FRS (Anderson) ^{18,136}	Sudden CHD death	1991	1*	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
QRISK ⁴⁶	CVD ₄	2007	4	QRESEARCH	01/01/1995	04/01/2007	614,553	6.5
SCORE ¹¹²								
High Risk TC								
Low Risk TC	CVD mortality	2003	11	SCORE			205,178	
FRS (Wilson) ¹⁹								
LDL								
ТС	Total CHD ₁	1998	23	FRS, FRS-O	01/01/1948	12/31/1974	5,345	12
FRS (TC) ¹⁹	Hard CHD ₁	2001	8	FRS, FRS-O	01/01/1948	12/31/1974	5,345	12
FRS (ATP-III) ²³	Hard CHD ₁	2001	16	FRS, FRS-O				
PROCAM ¹⁴	Hard CHD ₁	2002	11	PROCAM	01/01/1979	12/31/1985	5,159	10
UKPDS 56 ⁹⁶	Hard CHD ₁	2001	5	UKPDS			4,540	
DARTS ⁶³	Hard CHD ₁	2006	2	DARTS	01/01/1995	06/30/2004	4,569	4.1
FRS (4 variants) ²⁵	CHD mortality	1999	3	FRS	01/01/1954	12/31/1958	4,169	24
FRS ^{18,136}	Stroke ₄	1991	3	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
UKPDS 60 ⁹⁶	Stroke ₁	2002	2	UKPDS	01/01/1977	12/31/1991	4,549	10.5

Table 6. Risk Models Without External Validation That Are Risk Factor Variants, Outcome Variants, or Temporal Updates From Well-Known Cohorts With Externally Validated Risk Models

	Model	Year	Cohort	Enroll	Enroll		
Model Name	Outcome	Published	Abbreviation	Start Date	End Date	Enrollment	Followup*
FRS (D'Agostino) ²³	CVD ₂	2008	FRS, FRS-O	01/01/1968	12/31/1987	8,491	
QRISK2 ³⁵	CVD ₁	2008	QRESEARCH	01/01/1993	03/31/2008	2,285,815	15
SCORE ¹¹²							
High Risk TC-HDL Ratio							
Low Risk TC-HDL Ratio	CVD Mortality	2003	SCORE			205,178	
PROCAM ⁴¹	Stroke ₂	2007	PROCAM	01/01/1978	12/31/1995	7,295	12
ARIC ⁸¹							
Basic							
Basic + Age + Race							
Basic + NTRF + Age + Race	Stroke ₃	2004	ARIC	01/01/1987	12/31/1989	13,161	12.3

Table 7. Risk Models Without External Validation That Are Point Score Simplifications orEvaluations of Modeling Methods Other Than Cox Proportional Hazards

		Year	Cohort	Enroll	Enroll		
Model Name	Model Outcome	Published	Abbreviation	Start Date	End Date	Enrollment	Followup*
PROCAM (Point score) ¹⁴	Hard CHD ₁	2002	PROCAM	01/01/1979	12/31/1985	5,159	10
PROCAM (Weibull model) ⁴¹	Hard CHD ₁	2007	PROCAM	01/01/1978	12/31/1995	7,295	12

Table 8. Risk Models Without External Validation That Compare or Improve Model Performance Between a New Local Model and External Validation of More Established Models

	Model	Year	Cohort	Enroll	Enroll		
Model Name	Outcome	Published	Abbreviation	Start Date	End Date	Enrollment	Followup*
CRM ⁷⁸	CVD	1999	NHS Trust	01/01/1990	12/31/1991	798	
New Zealand Risk Charts ¹¹⁵	CVD ₂	1996					
Reynolds Risk Score (Men) ¹⁰³							
Model A							
RRS + CRP + FamHx	CVD ₁₅	2008	PHS-II	12/01/1995		10,724	10.8
Reynolds Risk Score (Women) ^{54,56}							
Model A							
Model B, Clinically Simplified	CVD ₃	2007	WHS (Val)	09/01/1992		8,158	10.2
JBSRC ⁷⁸	CVD	1998	NHS Trust	01/01/1990	12/31/1991	798	
European Society of Cardiology ¹¹⁴	Total CHD ₁	1994	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
CUORE ⁷⁶	Hard CHD ₂	2005	CUORE	01/01/1983	12/31/1996	6,865	9.1
Personal HEART ⁵¹	Hard CHD ₂	2007	ARIC	01/01/1987	12/31/1989	14,343	
ULSAM ⁸⁰	MI	2004	ULSAM	01/01/1970	12/31/1973	1,108	28.7

Table 9. Risk Models Without External Validation That Evaluate theHeterogeneity of Risk Factors Between Cohorts

	Model	Year	Cohort	Enroll	Enroll		
Model Name	Outcome	Published	Abbreviation	Start Date	End Date	Enrollment	Followup*
NHANES I (4	CHD						
variable) ²⁵	mortality	1999	NHANES I	01/01/1971	12/31/1975	6,611	20
NHANES I & II,	CHD		NHANES I &				
pooled ²⁵	mortality	1999	II			18,542	
NHANES II (4	CHD						
variable) ²⁵	mortality	1999	NHANES II	01/01/1976	12/31/1980	5,705	15
FRS CHD Mortality	CHD						
(4 variable) ^{18, 136}	mortality	1991	FRS, FRS-O	01/01/1948	12/31/1975	5,573	12
FRS (Barzi) ⁵⁵	CVD ₈	2007	FRS, FRS-O	01/01/1948	12/31/1974	5,345	12

Table 10. Risk Models Without External Validation That AddressSpecific Patient Populations Known to Perform Poorly in the MostWidely Used Models

	Model	Year	Cohort	Enroll	Enroll		
Model Name	Outcome	Published	Abbreviation	Start Date	End Date	Enrollment	Followup*
Dubbo ⁹³	CVD ₄	2003	Dubbo-All	01/01/1988		2,102	
USA-PRC ¹¹¹							
Point Scoring							
Simplified	CVD ₁₇	2006	USA-PRC	09/01/1983	10/31/1984	9,903	15.1
CRM ⁷⁸	CVD	1999	NHS Trust	01/01/1990	12/31/1991	798	
107			Swedish				
Swedish NDR ¹⁰⁷	CVD ₅	2008	NDR	01/01/1998	12/31/2003	11,646	5.64
Hong Kong	Total						
Diabetes Score ³⁸	CHD ₁	2008	HKD Registry	01/01/1995		7,067	5.4
Miyasaka Post-	Total						
AF ⁵²	CHD₁	2007	Mayo	01/01/1980	12/31/2000	2,768	6
	Hard						
CMCS ⁸³	CHD ₁	2004	MUCA	01/01/1992	12/31/1999	30,121	
	Hard						
SHS Model ⁶²	CHD ₁	2006	SHS	01/01/1989	12/01/2001	4,372	
Chicago Young	CHD						
Adults ⁴⁹	mortality	2007	CHA	01/01/1967	01/31/1973	10,375	32
Hong Kong							
Diabetes Score ⁵⁷	Stroke ₁	2007	HKD Registry	01/01/1995	07/30/2005	3,541	5.37
Korean Stroke							
Risk Prediction ⁴⁷	Stroke ₆	2008	NHIC	01/01/1992	12/31/1995	1,205,268	13

Table 11. Model Development Performance Characteristics (Americas): Internal Validation

					Hosmer-Lemeshow		emeshow	
Cohort	Outcome				AUC	Goodne	ss-of-Fit	O/E
Abbreviation	(Cohort/Model)	Model Name	Group Name	AUC	Variance	χ ²	Р	Ratio
FRS-O	CVD ₁₂	Wilson AFT CVD ³⁴	All					
		Model A		0.78				
		Model A No BMI		0.78				
		Model B		0.80				
		Model B No BMI		0.80				
FRS-O	Total CHD ₁	Wilson AFT CHD ³⁴	All					
		Model A		0.79				
		Model A No BMI		0.78				
		Model B		0.81				
		Model C		0.80				
		Model D		0.81				
		Model E		0.81				
		Model E No BMI		0.81				
FRS-O	Stroke ₂	Wilson AFT CeVD ³⁺	All					
		Model A		0.79				
		Model A No BMI		0.77				
		Model B		0.80				
		Model C		0.80				
		Model D		0.80				
		Model D No BMI		0.80				
FRS, FRS-O	CVD ₂	D'Agostino CVD ³³	Men	0.76	0.75-0.78	13.5		
			Women	0.79	0.77-0.81	7.8		
	Total CHD ₁ /CVD ₂		Men	0.73	0.71-0.75	18.2		
			Women	0.79	0.76-0.81	14.8		
	Stroke ₄ /CVD ₂		Men	0.83	0.79-0.86	26.1		
			Women	0.77	0.72-0.82	5.3		
	CHF/CVD ₂		Men	0.84	0.80-0.88	27.2		
			Women	0.85	0.80-0.89	9.3		
	PVD/CVD ₂		Men	0.81	0.78-0.85	19.1		
		FDO (TTO) (11/1)19	Women	0.83	0.79-0.87	11.3		
	Hard CHD ₁ (5 yr)	FRS [IC] (Wilson)	Men	0.79				
			Women	0.83				
	Hard CHD ₁ (5 yr)	FRS Best Cox Models	Men	0.79		3.3		
			Women	0.83		3.7		
WHS	CVD ₃	Reynolds Risk Score (Women)		0.01				
		Model A ST	All	0.81				
		Model B, Clinically Simplified	All	0.81				
			All	0.82				
			All	0.81	0.010	E 00		
WGHS	CVD ₃	ATP-III Vars + Genotype ¹⁰¹	All	0.81	0.019	5.96		
	1	RRS Vars + Genotype ¹⁰¹	All	0.81	0.019	7.43		

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Table 11. Model Development Performance Characteristics (Americas): Internal Validation

Cohort	Outcome				AUC Goodness-c		emeshow	O/E
Abbreviation	(Cohort/Model)	Model Name	Group Name	AUC	Variance	χ ²	P	Ratio
PHS-II	CVD ₁₅	Reynolds Risk Score (Men) ¹⁰³	-					
		Model A	All	0.70		11.3		
		RRS + CRP + FamHx	All	0.71		12.9		
	Hard CHD ₂ /CVD ₁₅	Reynolds Risk Score (Men) ¹⁰³						
		Model A	All	0.69				
		RRS + CRP + FamHx	All	0.70				
NHANES-I	CVD7	NHANES-EFS (Gaziano) ³⁷						
EFS		Lab-Based Model	Men	0.78	0.77-0.80	6.7	0.57	
		Non Lab-Based Model	Men	0.78	0.77-0.80	3.5	0.90	
		Lab-Based Model	Women	0.83	0.81-0.85	6.6	0.58	
		Non Lab-Based Model	Women	0.83	0.82-0.85	3.5	0.90	
SHS	Hard CHD ₁	SHS (Lee) ⁶²	Men	0.71		7.18	0.51	
			Women	0.73		7.25	0.45	
SBHW	Hard CHD ₁	Detrano-Data Derived ¹⁰⁰	All	0.68	0.05			
		Detrano-Data Derived + Ca ¹⁰⁰	All	0.71	0.04			
	Hard CHD ₂	Detrano-Data Derived ¹⁰⁰	All	0.69	0.04			
		Detrano-Data Derived + Ca ¹⁰⁰	All	0.72	0.04			
	Hard CHD ₁	FRS (ATP-III) Variables + CACS ⁸⁷	All	0.68				
NHANES I	CHD mortality	NHANES I (4 Variables) ²⁵	Men	0.71				
			Women	0.81				
NHANES II	CHD mortality	NHANES II (4 Variables) ²⁵	Men	0.75				
			Women	0.77				
NHANES I/II	CHD death	NHANES I and II, Pooled ²⁴	White Men	0.77				
			Black Men	0.76				
			White Women	0.84				
			Black Women	0.82				
ARIC	Hard CHD ₂	Metabolic Syndrome Model ⁷⁵	Men	0.63				
		-	Women	0.73				
		Personal HEART ⁵¹	Men	0.65	0.63-0.67			
			Women	0.79	0.77-0.80			
		ARIC, Basic + Liberal DM-Specific ⁹¹	DM Men	0.67				
			DM Women	0.72				
			Non-DM Men	0.79				
			Non-DM Women	0.69				
		ARIC, Basic + Restrictive DM-Specific ⁹¹	DM Men	0.75				
			DM Women	0.70				
			Non-DM Men	0.79				
			Non-DM Women	0.69				
		ARIC, Basic Combined ⁹¹	DM Men	0.65				
			DM Women	0.71				
Table 11. Model Development Performance Characteristics (Americas): Internal Validation

						Hosmer-L	emeshow	
Cohort	Outcome				AUC	Goodne	ss-of-Fit	O/E
Abbreviation	(Cohort/Model)	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
ARIC	Hard CHD ₂	ARIC, Multiple Factors + Liberal DM-	DM Men	0.74				
		Specific ⁹¹	DM Women	0.77				
			Non-DM Men	0.71				
			Non-DM Women	0.80				
		ARIC, DM-Specific Basic ⁹¹	DM Men	0.68				
			DM Women	0.71				
			Non-DM Men	0.68				
			Non-DM Women	0.78				
		ARIC, DM-Specific Basic + Multiple Factors ⁹¹	DM Men	0.70				
			DM Women	0.72				
			Non-DM Men	0.70				
			Non-DM Women	0.78				
		ARIC, DM-Specific Basic + Restrictive DM ⁹¹	DM Men	0.72				
			DM Women	0.70				
	Stroke ₃	Chambless Models ⁸¹						
		Basic	Men	0.76				
		Basic	Women	0.79				
		Basic + Age + Race	Men	0.79				
		Basic + Age + Race	Women	0.81				
		NTRF + Age + Race	Men	0.80				
		NTRF + Age + Race	Women	0.84				
CHA	CHD mortality	CHA ⁴⁹	Men	1				0.95
Mayo	Total CHD ₁	Miyasaka CHD Post-AF ⁵²	Men					0.78
			Women					0.86

Note: If the cohort and model outcomes match, only one outcome is listed; otherwise both are listed. For internal model development, any cohort/model outcome mismatches are intentional to evaluate the effect of outcome mismatching on the performance of the model. O/E ratios are not relevant for internally developed models (they are all close to 1.0).

						Hosmer-Lo	emeshow	
Cohort					AUC	Goodnes	ss-of-Fit	O/E
Abbreviation	Outcome (Cohort/Model)	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
LRCPS	CHD mortality/Total CHD ₁	FRS (Anderson) ⁹⁹	All	0.83	0.81-0.85			
	-		Men	0.83				
			Women	0.82				
SBHW	Hard CHD ₁ *	FRS (Anderson) ¹⁰⁰	All	0.69	0.05			
	Hard CHD ₂ /Hard CHD ₁ *		All	0.67	0.04			1.17
ARIC	Hard CHD₁ (5 yr)	FRS [TC] (Wilson) ²³	White Men	0.75		13.8		
			Black Men	0.67		5.3		
			White Women	0.83		6.2		
			Black Women	0.79		5.0		
HHP	Hard CHD ₁ (5 yr)	FRS [TC] (Wilson) ²³	Men	0.72		66		
PRHHP	Hard CHD ₁ (5 yr)	FRS [TC] (Wilson) ²³	Men	0.69		142		
SHS	Hard CHD₁ (5 yr)	FRS [TC] (Wilson) ²³	Men	0.69		10.6		
			Women	0.75		22.7		
CHS	Hard CHD1 (5 yr)	FRS [TC] (Wilson) ²³	Men	0.63		13.2		
			Women	0.66		10.4		
ARIC/CHS	Hard CHD ₁ (10yr)	FRS [TC] (Wilson) ⁴⁵	Men	0.60		72.3	<0.01	1.49
			Women	0.73		75.1	<0.01	2.02
	Hard CHD ₁ (5yr)		Men	0.62		33.4	<0.01	1.64
			Women	0.77		61.2	<0.01	2.73
JHSS	Total CHD₁	FRS [TC] (1998) ⁴²	Men			75.0	<0.01	1.67
			Women			8.0	0.43	1.13
CHA	Hard CHD ₁ /Total CHD ₁ (10 yr)	FRS [TC] (1998) ⁴⁹	Men					0.05
WHI	Hard CHD ₁ / Total CHD ₁	FRS [?] (Wilson) ⁵³	Women	0.69				
	CVD ₁₅ /Total CHD ₁		Women	0.68				
SAHS	CVD ₁₅ /Total CHD ₁	FRS [?] (Wilson) ⁷⁹	All	0.82				
NAS	Total CHD ₁	FRS [TC] (1998) ⁹⁷	All	0.63				0.93
ARIC	Hard CHD ₂ /Hard CHD ₁	FRS [TC] (Wilson) ²³	Men	0.69	0.67-0.71			
			Women	0.81	0.79-0.82			
WHS	CVD ₃ /Total CHD ₁	FRS [TC] (1998) ⁶¹	Women	0.75			<0.01	
		FRS [LDL] (1998) ⁶¹	Women	0.75			<0.01	
SFHS	Hard CHD ₂ / Hard CHD ₁	FRS (ATP-III) ⁷⁰	All	0.68	0.62-0.74			
ARIC	Hard CHD ₂ /Hard CHD ₁	FRS (ATP-III) ⁷⁵	Men	0.63				
			Women	0.73				
SBHW	Hard CHD ₁	FRS (ATP-III) ⁸⁷	All	0.63				
WHS	CVD ₃ /Hard CHD ₁	FRS (ATP-III) ¹⁰¹	Women	0.79			<0.01	
ARIC	Hard CHD ₂ /Hard CHD ₁ (6 yr)	FRS (ATP-III) ⁷⁵	All	0.72				
			Men	0.65				
			Women	0.67				
CHA	Hard CHD ₁ (10 yr)	FRS (ATP-III) ⁴⁹	Men					0.07

Cohort					AUC	Hosmer-Le Goodnes	emeshow ss-of-Fit	O/E
Abbreviation	Outcome (Cohort/Model)	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
NAS	Total CHD ₁	European Society of	All	0.58				
		Cardiology (ESC) ⁹⁷						

*The model outcome was calculated using the sum of MI and sudden CHD death models from FRS (Anderson).

Note: If the cohort and model outcomes match, only one outcome is listed; otherwise both are listed. AUC refers to AUC or C statistic. The LRCPS study did not clearly state which FRS (Anderson) outcome it used in the study.

Cohort					AUC	Hosmer-Le Goodnes	emeshow s-of-Fit	O/E
Abbreviation	Cohort Outcome	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
QRESEARCH	CVD ₄ (10 yr)	QRISK ⁴³	Men	0.77				1.00
			Women	0.79				0.98
	CVD ₁₀ (10 yr)	QRISK 1.1 ⁴³	Men	0.77	0.77-0.77			
			Women	0.79	0.78-0.79			
	CVD ₁	QRISK 243	Men	0.79	0.79-0.79			
			Women	0.82	0.81-0.82			
Swedish NDR	CVD ₅	Swedish NDR ¹⁰⁷	Risk Grouped	0.70		4.3	0.83	
			Subgroup B	0.69				
SU.VI.MAX	Total CHD ₁	SU.VI.MAX ¹¹⁰	All	0.75				
EPIC-Norfolk	Total CHD ₁	FRS (1998) + EPIC + HbA1c36	Men	0.73	0.70-0.75			
		FRS (1998) + EPIC + HbA1c	Women	0.80	0.78-0.83			
		FRS (1998) + EPIC + w/o DM + HbA1c	Men	0.73	0.70-0.74			
		FRS (1998) + EPIC + w/o DM + HbA1c	Women	0.80	0.77-0.82			
WOSCOPS	Hard CHD ₁	QT Dispersion ⁶⁰	All	0.52				
CUORE	Hard CHD ₂	CUORE ⁷⁶	Men	0.74	0.68-0.80	15.5	0.05	
DARTS	Hard CHD ₁	DARTS ⁶³	All	0.71	0.63-0.79			
PROCAM	Hard CHD ₁	PROCAM CHD (Cox Model) ¹⁴	All	0.83		6.5	0.3	
		PROCAM CHD (Point Score) ¹⁴	All	0.82				
NPHS-II	Hard CHD ₂	Score 1 (Basic) ⁷¹	Men	0.64	0.58-0.70			
_	_	Score 2 (Basic + DM + FamHx)	Men	0.66	0.60-0.71			
		Score 3 (Basic + DM)	Men	0.63	0.58-0.69			
		Score 4 (Basic + FamHx)	Men	0.64	0.59-0.69			
		Score 5 (Basic + Fibrinogen)	Men	0.66	0.60-0.71			
		Score 6 (Basic + LpA)	Men	0.67	0.61-0.72			
		Score 7 (Basic + ApoA1 + ApoB)	Men	0.66	0.60-0.72			
PROCAM	Hard CHD ₁	PROCAM (BMI-modified) ¹⁰⁹	All	0.82				0.88
		PROCAM CHD (Cox Model) ¹³⁷	All	0.82				
NZWork	CVD ₂ (5 yrs)	New Zealand Risk Charts ⁸⁹	Men	0.73	0.72-0.74			
	_ () /		Women	0.78	0.75-0.81			
INSIGHT	CVD ₁₄	INSIGHT CVD ⁹⁴	All	0.661				1.25
PROCAM	Hard CHD ₁ (10 yr)	PROCAM CHD (Cox Model) ⁴¹	All	0.824				
		PROCAM CHD (Weibull Model) ⁴¹	All	0.824				
NorGov	CHD Mortality	Erikssen CRF-X Model ⁸⁴	All					1.00
	,	Erikssen CRF Model	All					
		Erikssen X Model	All					
INSIGHT	Stroke ₄	INSIGHT Stroke ⁹⁴	All					1.00
Dubbo	CVD ₄ (5 yr)	Dubbo Model ⁹³	All		1	107	<0.01	
	CVD ₄ (10 yr)		All			167	< 0.01	
ULSAM (70)	CVD Mortality	FRS (1998) + ECG ⁵⁰	All		0.67			

						Hosmer-Le	emeshow	
Cohort					AUC	Goodnes	s-of-Fit	O/E
Abbreviation	Cohort Outcome	Model Name	Group Name	AUC	Variance	χ ²	Р	Ratio
SHHEC	CVD ₁₁ /CVD ₂ (10 yr)	FRS (1991) ⁵⁹	Men	0.72				0.71
			Women	0.74				0.65
PDS	Total CHD ₃ /Total CHD ₁	FRS (1991) ⁷³	All	0.66	0.58-0.73			1.46
			All (Exclude LVH)	0.67	0.59-0.74			1.50
			Men	0.73	0.64-0.81			1.71
			Women	0.70	0.64-0.76			1.36
			Treated BP	0.67	0.54-0.80	19.8	0.01	1.71
			Untreated BP	0.66	0.57-0.76	22.6	<0.01	1.44
PDS	CVD ₁₃ /CVD ₂	FRS (1991) ⁷³	All	0.67	0.61-0.73			1.48
			All (Exclude LVH)	0.68	0.62-0.74			1.51
			Men	0.67	0.59-0.75			1.54
			Women	0.68	0.58-0.78			1.40
			Treated BP	0.63	0.53-0.74	32.8	<0.01	1.67
			Untreated BP	0.69	0.61-0.77	39.5	<0.01	1.38
BRHS	Hard CHD ₁ + Stroke ₁ + DM ₂ /Total							2.5
	CHD ₁ (20 yrs)	FRS (1991) ⁶⁵	Men	0.67	0.65-0.69			
	Hard CHD ₁ /Total CHD ₁ (10 yrs)	FRS (1991) ⁶⁵	Men	0.73	0.71-0.75			
	Hard CHD ₁ /Total CHD ₁ (20 yrs)	FRS (1991) ⁶⁵	Men	0.68	0.66-0.70			
	Stroke ₁ /Total CHD ₁ (10 yrs)	FRS (1991) ⁶⁵	Men	0.71	0.65-0.77			
	Stroke ₁ /Total CHD ₁ (20 yrs)	FRS (1991) ⁶⁵	Men	0.66	0.62-0.70			
	DM ₂ /Total CHD ₁ (10 yrs)	FRS (1991) ⁶⁵	Men	0.61	0.55-0.67			
	DM ₂ //Total CHD ₁ (20 yrs)	FRS (1991) ⁶⁵	Men	0.6	0.56-0.64			
L85	CVD Mortality/CVD ₂	FRS (1991) ¹⁰²	All	0.53	0.42-0.63			
Cardiff DM	CVD ₂	FRS (1991) ⁸⁵	Men	0.64				0.82
		- ()	Women	0.66				0.86
NZWork	CVD ₂ (5 vrs)	FRS (1991) ⁸⁹	Men	0.74	0.73-0.75			1.17
			Women	0.77	0.74-0.80			1.09
ORESEARCH	CVD_4/CVD_2 (10 yr)	FRS (1991) ⁴³	Men	0.76				0.68
	0 · 2 # 0 · 2 2 (· 0 J ·)		Women	0.77				0.83
BWHH	Total CHD ₂ /Total CHD ₄	FRS (1991) ⁶⁴		0.63	0 59-0 67			0.00
Buttin	CVD_{14}/CVD_{2}	$FRS(1991)^{64}$		0.60	0.61-0.68			0.65
ORESEARCH	CVD_{10}/CVD_{2}	FRS (1991) ⁴³	Men	0.04	0.01 0.00			0.00
GILDLANOIT		11(3(1991)	Women	0.70	0.70-0.77			
	CVD_{1}/CVD_{2} (10 yr)	EBS (1001) ⁴³	Mon	0.70	0.77-0.70			0.76
	CVD_{10}/CVD_2 (10 yl)	FK3 (1991)	Momon	0.74	0.75-0.74			0.70
	O(D) Montolity $O(D)$ (4.0 ym)	FDC (4004) ¹⁰⁶	vvomen	0.70	0.76-0.76			0.91
	$C V D$ inionality/ $C V D_2$ (10 yr)	FK3 (1991)	All Llink viels Deticate	0.86	0.84-0.88			
			Hign-risk Patients	0.80	0.77-0.82			
			56P >140 mmHg	0.79	0.75-0.83			
			IC >6.5 mmol/L	0.81	0.77-0.85			
			Smokers	0.69	0.65-0.74			

						Hosmer-Le	emeshow	
Cohort	Cohort Outcome	Medel Neme	Crown Nama		AUC	Goodnes	s-of-Fit	O/E Datio
Abbreviation			Group Name		variance	χ	Р	Ratio
PROCAM	Hard CHD1"	FRS (1991)*	Ivien Wersen	0.73	0.70-0.75			0.56
Denfrau	C) (D. Martality (C) (D		vvomen	0.88	0.80-0.96			0.35
Renfrew-	CVD Mortality/CVD ₂	FRS (1991)**	All	0.73	0.72-0.75			
Paisley			Manual Labor	0.72	0.70-0.74			4 74
DDEDIOT			Non-manual Labor	0.74	0.71-0.78			1.71
PREDICT	CVD ₁₉ /CVD ₂	FRS (1991)	All	0.63	0.55-0.71			
Aboriginal	Total CHD₁	FRS (1991)''	Men					2.00
DDU 0			vvomen				0.04	3.92
BRHS	CHD Mortality	FRS (1991) CHD Mortality	Men			30.2	<0.01	0.68
BRHS	Total CHD ₁	FRS (1991) ⁶⁶	Men			155	<0.01	0.64
INSIGHT	CVD ₁₄ /CVD ₂	FRS (1991) ³⁴	All					0.39
INSIGHT	Total CHD ₁	FRS (1991) ⁹⁴	All					0.44
LudwigU	Hard CHD ₁ /CVD Mortality	SCORE (?) ⁴⁰	All	0.66	0.62-0.68			
SHHEC	CVD ₁₁ (10 yr)	ASSIGN ⁵⁹	Men	0.73				0.79
			Women	0.77				0.67
PDS	Total CHD ₃ /Hard CHD ₁	UKPDS 56 ⁷³	All	0.67	0.60-0.74			1.15
			Men	0.67	0.59-0.76			1.11
			Women	0.62	0.49-0.75			1.19
			Treated BP	0.70	0.58-0.82			1.26
			Untreated BP	0.65	0.56-0.74	17.1	0.03	1.09
VHM&PP	CVD Mortality	SCORE (Low Risk TC) ⁶⁸	All	0.80	0.79-0.82			0.73
			Men	0.76	0.74-0.79			0.84
			Women	0.78	0.74-0.82			0.52
VHM&PP	CHD Mortality/CVD Mortality	SCORE (Low Risk TC) ⁶⁸	Men	0.75	0.72-0.78			0.79
			Women	0.84	0.80-0.88			0.46
QRESEARCH	CVD ₄ /CVD ₁₁ (10 yr)	ASSIGN ⁴⁶	Men	0.76				0.73
			Women	0.78				0.73
CP-Norway	CVD Mortality	SCORE (High Risk TC)44	Men	0.65				0.45
		(č ,	Women	0.68				0.37
NCS	CVD Mortality	SCORE (High Risk TC)44	Men (40-49 yrs)	0.67				0.53
	,	(3)	Men (50-59 yrs)	0.68				0.53
			Women (40-49 vrs)	0.66				0.60
			Women (50-59 vrs)	0.72				0.45
MP-CVDRF	CVD Mortality (10 vr)	SCORE (?) ¹⁰⁶	All	0.85	0.83-0.87			
			High-risk Patients	0.75	0.72-0.78			
			SBP >140 mmHa	0.76	0.72-0.81			
			TC > 6.5 mmol/L	0.78	0.73-0.82			
			Smokers	0.62	0.55-0.68			
QRESEARCH		QRISK ⁴³	Men	0.79	0.79-0.79			1
	р. — т		Women	0.81	0.81-0.81			

Cardiovascular Disease Risk Assessment Tools

						Hosmer-Lemeshow		
Cohort					AUC	Goodnes	s-of-Fit	O/E
Abbreviation	Cohort Outcome	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
NHS Trust	CVD ₁₈ /Hard CHD ₁	PROCAM (Cox) ⁷⁸	All	0.67	0.62-0.73			2.79
	CVD ₁₈ /Hard CHD ₁	UKPDS 56 ⁷⁸	All	0.74	0.70-0.78		l I	1.20
	Total CHD ₂ /Hard CHD ₁	PROCAM (Cox) ⁷⁸	All	0.65	0.59-0.71			2.05
	Total CHD ₂ /Hard CHD ₁	UKPDS 56 ⁷⁸	All	0.76	0.72-0.80			1.60
EPIC-Norfolk	Total CHD₁	FRS [TC] (1998) ³⁶	Men	0.71	0.69-0.73			
			Women	0.71	0.68-0.74			
LudwigU	Hard CHD ₁	PROCAM (Cox) ⁴⁰	All	0.65	0.62-0.68		l I	
		FRS (ATP-III) ⁴⁰	All	0.63	0.59-0.65			
Rotterdam	Hard CHD₁	FRS (ATP-III) ⁴⁸	Men	0.63	0.52-0.74		l I	0.72
			Women	0.73	0.65-0.83			1.02
STULONG	Total CHD₁	FRS [TC] (1998) ⁵⁶	All	0.638	58.4-69.1			1.282
VERIFICA	Total CHD₁	FRS [TC] (1998) ⁵⁸	Men			110	<0.01	
			Women	0.68		64	<0.01	0.45
			Patients w/Diabetes	0.73		54	<0.01	0.44
NHS Trust	CVD ₁₈ /CVD	JBSR ₂ C ⁷⁸	All	0.80	0.75-0.85		l I	
	CVD ₁₈ /CVD	CRM ⁷⁸	All	0.76	0.72-0.79		l I	2.30
	Total CHD ₂	JBSRC ⁷⁸	All	0.77	0.74-0.80			
	Total CHD ₂	CRM ⁷⁸	All	0.73	0.70-0.77			1.74
NPHS-II	Hard CHD ₂ /Hard CHD ₁	FRS (ATP-III) ⁷¹	All	0.62	0.58-0.66			0.47
PRIME-Belfast	Total CHD ₁ /Hard CHD ₁ (5 yr)	FRS (ATP-III) ⁹⁰	All	0.66				0.75
	Hard CHD ₁ (5 yr)	PROCAM (Cox) ⁹⁰	All	0.61				0.56
PRIME-France	Total CHD ₁ /Hard CHD ₁ (5 yr)	FRS (ATP-III) ⁹⁰	All	0.68				0.67
	Hard CHD ₁ (5 yr)	PROCAM (Cox) ⁹⁰	All	0.64				0.23
PREDICT	CVD ₁₉ /Hard CHD ₁	UKPDS 56 ¹⁰⁸	All	0.67	0.60-0.75			
	Total CHD ₂ /Hard CHD ₁	UKPDS 56 ¹⁰⁸	All	0.63	0.56-0.71			
Lyon	CVD ₆ /Total CHD ₁	FRS [Unknown Version] (1998) ⁷²	All	0.72				1.36
ULSAM (70)	CVD Mortality/Total CHD ₁	FRS [Unknown Version] (1998) ⁵⁰	All	0.58				
ULSAM	MI/Hard CHD ₁	PROCAM (Cox) ⁸⁰	Men	0.63			l I	
		FRS (ATP-III) ⁸⁰	Men	0.61				
CUORE	Hard CHD ₂ /Total CHD ₁	FRS [TC] (1998) ⁷⁶	Men	0.723	0.67-0.78			0.33
RCC	CVD ₃ /Total CHD ₁	FRS [?] (1998) ⁶⁹	All	0.73				
			Age >70 yrs	0.68				
MONICA-	Hard CHD ₁ /Total CHD ₁	FRS [?] (1998) ⁸⁶	All	0.74			l I	
Augsburg								
PROCAM	Hard CHD ₁	FRS (ATP-III) ¹⁴	All	0.78		44	<0.01	
NPHS-II	Hard CHD ₂ /Hard CHD ₁	PROCAM (Cox) ⁷¹	All	0.63	0.59-0.67			0.46
SU.VI.MAX	Total CHD ₁	FRS [?] (1998) ¹¹⁰	All	0.74				0.50
MunichDM	MI/Hard CHD ₁	UKPDS 56 ¹⁰⁴	All	0.66	0.62-0.68			
		FRS [?] (1998) ¹⁰⁴	All	0.63	0.59-0.66			
Salford	Hard CHD ₁	DARTS ⁶³	All	0.69	0.58-0.78			

						Hosmer-Le	meshow	
Cohort					AUC	Goodnes	s-of-Fit	O/E
Abbreviation	Cohort Outcome	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
THIN	CVD ₁₀ /CVD ₄ (10 yr)	QRISK ⁴³	Men	0.76	0.76-0.77			1.15
			Women	0.79	0.79-0.79			1.11
MONICA-	Hard CHD ₁ /CVD ₂	FRS (1991) ⁹²	Men	0.78	0.73-0.84			
Augsburg			Women (55-64 yrs)	0.88	0.80-0.96			0.50
NHP-Europe	Stroke Mortality/Stroke ₄	FRS (1991) Stroke ⁷⁴	All					3.91
INSIGHT	Stroke ₄	FRS (1991) Stroke ⁹⁴	All					1.00
WESDR	Stroke Mortality/CVD ₂	FRS (1991) ⁹⁶	All					1.79
Dubbo	CVD ₄ (10 yr)	FRS (ATP-III) ⁹³	Non-DM Men					0.91
			Non-DM Women					0.93
WESDR	Stroke Mortality/Stroke1	UKPSD 60 ⁹⁶	All					1.14
ULSAM	Hard CHD ₁ (10 yr)	FRS (ATP-III) ⁸⁰	All					0.21
		PROCAM (Cox) ⁸⁰	All					0.27
NHP-Europe	CHD Mortality	SCORE (Unknown Version) ⁷⁴	All					3.24
FrRenal	Total CHD ₁	FRS [?] (1998) ⁸²	All					1.69
MünsterWork	Hard CHD ₁	Procam (Cox) ²⁹	Men					0.78
QRESEARCH	CVD ₁	FRS (1991) NICE Recal ³⁵	Men	0.78	0.78-0.78			
			Women	0.80	0.80-0.80			
EPIC-Norfolk	Total CHD₁	FRS (1998) EPIC ³⁶	Men	0.72	0.70-0.75			
			Women	0.80	0.78-0.83			
VERIFICA	Total CHD ₁	FRS (1998) REGICOR	Men	0.69		5.1	0.08	1.26
		VERIFICA ⁵⁸	Women	0.81		2.7	0.26	1.03
CUORE	Hard CHD ₂	FRS (1998 TC) D'Ag CUORE ⁷⁶	Men	0.72	0.67-0.78	27.1	<0.01	0.78
		PROCAM (Cox) D'Ag CUORE ⁷⁶	Men	0.74	0.68-0.79	220	< 0.01	0.34
		FRS (1998 TC) Chb CUORE ⁷⁶	Men	0.72	0.67-0.78	19.9	0.01	1.01
		PROCAM (Cox) Chb CUORE ⁷⁶	Men	0.74	0.68-0.79	53.0	<0.01	1.01
Cardiff DM	CVD ₂	FRS (1991) Cardiff DM ⁸⁵	Men	0.65				
	_	· · · ·	Women	0.68				
BRHS	CHD Mortality	FRS (1991) BRHS ⁸⁸	Men			3.4	0.91	
	Total CHD₁					24.6	<0.01	
VERIFICA	Total CHD₁	FRS (1998) REGICOR	Patients w/Diabetes					
		VERIFICA ⁵⁸				1.4	0.99	

*The model outcome was calculated using the sum of MI and sudden CHD death models from FRS (Anderson).

						Hosmer-I	_emeshow	
Cohort					AUC	Goodne	ess-of-Fit	O/E
Abbreviation	Cohort Outcome	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
MUCA-II	CVD ₁₇	USA-PRC (Simple) ¹¹¹	Men	0.79	0.76-0.83			
		USA-PRC (Simple)	Women	0.79	0.75-0.82			
		USA-PRC (Points)	Men	0.79	0.76-0.83			
		USA-PRC (Points)	Women	0.78	0.77-0.82			
MUCA	Hard CHD ₁	CMCS Cox Model ⁸³	Men	0.74	0.70-0.78	12.6	0.13	
			Women	0.76	0.70-0.82	14.2	0.08	
NHIC	Stroke ₆ (10 yr)	Korean Stroke Risk Prediction ⁴⁷	Men	0.82	0.80-0.83	7.7	0.56	
			Women	0.81	0.79-0.83	14.3	0.16	
HKD Registry	Stroke ₁	HKD Stroke Risk Score ⁵⁷	All	0.79	0.72-0.78			
	Stroke ₅ /Stroke ₁	HKD Stroke Risk Score ⁵⁷	All	0.77				
	Stroke ₃ /Stroke ₁	HKD Stroke Risk Score ⁵⁷	All	0.79				
	Total CHD ₁	HKD CHD Risk Score ⁵⁷	All	0.74				

						Hosmer-Lemeshow Goodness-of-Fit		
Cohort			Group		AUC	Goodness-of-Fit		O/E
Abbreviation	Cohort Outcome	Model Name	Name	AUC	Variance	χ^2	Р	Ratio
MUCA	Hard CHD ₁	FRS Hard CHD [TC] (1998) ⁸³	Men	0.71	0.67-0.75	646	<0.01	
			Women	0.74	0.69-0.80	148	<0.01	
JapanWork	Total CHD ₁ (5 yr)	FRS [?] (Wilson) ⁹⁵	Men	0.71				0.38
	Total CHD ₁ (10 yr)		Men	0.62				0.58
HKD Registry	Stroke ₁	UKPDS 60 ⁵⁷	All	0.59	0.55-0.63			0.51
	Hard CHD₁	UKPDS 56 ³⁸	All	0.61	0.58-0.64			
APCSC China	CVD ₈	FRS (2007 Barzi) ⁵⁵	Men	0.75	0.72-0.78	558	<0.01	0.27
			Women	0.79	0.74-0.83	608	<0.01	0.50
NHP-South Asia	CHD Mortality/CVD Mortality	SCORE (?) ⁷⁴	All					4.42
	Stroke Mortality/Stroke ₄	FRS (1991) Stroke ⁷⁴	All					1.88

Table 17. Model Recalibration/Remodeling Performance Characteristics (Americas)

Cohort	Outcome				AUC	Hosmer-Le Goodness	meshow s-of-Fit	O/E
Abbreviation	(Cohort/Model)	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
WHS (Val)	CVD ₃	FRS (Wilson TC) WHS ^{54#}	Women	0.79			0.18	
		FRS (Wilson LDL) WHS ^{54#}	Women	0.79			0.16	
WGHS	CVD ₃	FRS (ATP-III) WGHS ^{101#}	Women	0.80	0.78-0.82	6.2	0.62	
		Reynolds Risk Score WGHS ^{101#}	Women	0.81	0.79-0.83	7.8	0.46	
NHANES I	CHD Mortality	FRS (Custom 4 Variable) ²⁵	Men	0.71				
	-		Women	0.80				0.90
NHANES II	CHD Mortality	FRS (Custom 4 Variable) ²⁵	Men	0.74				
	-		Women	0.76				0.65
WHS	CVD ₃	FRS (ATP-III) WHS ^{101#}	Women	0.81			0.25	
SHS	Hard CHD ₁ (5 yr)	SHS Best Cox ²³	Men	0.77		2.7		
			Women	0.86		3.5		
ARIC	Hard CHD1 (5 yr)	ARIC Best Cox ²³	White Men	0.76		5.4		
			Black Men	0.70		7.2		
			White Women	0.84		5.2		
			Black Women	0.85		3.4		
HHP	Hard CHD ₁ (5 yr)	HHP Best Cox ²³	Men	0.74		2.6		
PRHHP	Hard CHD ₁ (5 yr)	PR Best Cox ²³	Men	0.72		7.2		
CHS	Hard CHD ₁ (5 yr)	CHS Best Cox ²³	Men	0.69		6.8		
			Women	0.68		6.8		
JHSS	Total CHD ₁	FRS (Wilson) D'Agostino JHSS ⁴²⁵	Men				9.0	
			Women				8.0	
ARIS/CHS	Hard CHD ₁ (5 yr)	FRS CKD ARIS/CHS ^{45\$}	Men			13.7		
			Women			8.7		
	Hard CHD ₁ (10 yr)	FRS CKD ARIS/CHS ^{45\$}	Men			32.3		
			Women			8.9		
		FRS (1998) CKD Best Cox Remodel ⁴⁵	Men	0.68		4.0		
			Women	0.81		2.5		

Note: If the cohort and model outcomes match, only one outcome is listed; otherwise both are listed. Please note that remodeling changes the outcome to match the cohort, regardless of the source data for the variables. Also note that a model is considered a remodeling effort if it uses the same variables as a previous model. # indicates remodeling based upon the preceding cohort; \$ Indicates recalibrated based upon the preceding cohort.

Table 18. Model Recalibration/Remodeling Performance Characteristics (Europe)

Cohort	Cohort					Hosmer-Lemeshow Goodness-of-Fit		O/E
Abbreviation	Outcome	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
QRESEARCH	CVD ₁	FRS (1991) NICE Recal ^{35\$}	Men Women	0.78 0.80	0.78-0.78 0.80-0.80			
Cardiff DM	CVD ₂	FRS (1991) Cardiff DM ^{85#}	Men Women	0.65 0.68				
BRHS	CHD Mortality	FRS (1991) BRHS ^{88\$}	Men			3.4	0.91	
BRHS	Total CHD1	FRS (1991) BRHS ^{88\$}	Men			24.6	<0.01	
EPIC-Norfolk	Total CHD ₁	FRS (1998) EPIC ^{36#}	Men	0.72	0.70-0.75			
			Women	0.80	0.78-0.83			
VERIFICA	Total CHD ₁	FRS (1998) REGICOR VERIFICA58#	Men	0.69		5.1	0.08	1.26
			Women	0.81		2.7	0.26	1.03
VERIFICA	Total CHD ₁	FRS (1998) REGICOR VERIFICA ^{58#}	Patients w/Diabetes			1.4	0.99	
CUORE	Hard CHD ₂	FRS (1998 TC) D'Ag CUORE ^{76#}	Men	0.72	0.67-0.78	27.1	<0.01	0.78
CUORE	Hard CHD ₂	FRS (1998 TC) Chb CUORE ^{76#}	Men	0.72	0.67-0.78	19.9	0.01	1.01
CUORE	Hard CHD ₂	PROCAM (Cox) D'Ag CUORE ^{76#}	Men	0.74	0.68-0.79	220.0	<0.01	0.34
CUORE	Hard CHD ₂	PROCAM (Cox) Chb CUORE ^{76#}	Men	0.74	0.68-0.79	53.0	<0.01	1.01

Note: If the cohort and model outcomes match, only one outcome is listed; otherwise both are listed. # indicates remodeling based upon the preceding cohort; \$ Indicates recalibrated based upon the preceding cohort.

Table 19. Model Recalibration/Remodeling Performance Characteristics (Asia)

Cohort	Cohort				AUC	Hosmer-Lemeshow Goodness-of-Fit		O/E
Abbreviation	Outcome	Model Name	Group Name	AUC	Variance	χ^2	Р	Ratio
MUCA-II	CVD ₁₇	FRS (1998) MUCA-II ^{111#}	Men	0.80	0.76-0.83			
			Women	0.79	0.76-0.83			
MUCA	Hard CHD ₁	FRS (1998) MUCA ^{83#}	Men	0.74	0.70-0.78	31.5	<0.01	
			Women	0.76	0.70-0.82	16.9	0.03	
APCSC China	CVD ₈	FRS (Barzi 2007) APCSC ^{55#}	Men	0.76	0.73-0.79	16.7	0.03	
			Women	0.80	0.75-0.84	12.2	0.15	

Note: If the cohort and model outcomes match, only one outcome is listed; otherwise both are listed. # indicates remodeling based upon the preceding cohort.

Table 20. Variables Used By Cardiovascular Risk Models for Patients With Diabetes

Variable			HKD ³⁸
Age	At diagnosis	At diagnosis	*
Sex	*	*	*
Race	Afro-Caribbean		
Smoking status	Current	Current & Former	Current
DM diagnosis duration		*	*
eGFR			*
Spot urine A/C ratio			*
Lipid profile	Total/HDL Ratio	Total	Non-HDL
Hemoglobin A ₁ c	*	*	
Systolic BP	*	*	
Treated hypertension		*	
Height		*	

*Indicates that the variable was used by that model, and any text describes the particular subset of the variable in question that was used in the model.

Table 21. Comparison of Relative Risk for Hard CHD₁ Among Patients With Diabetes Across Seven U.S. Cohorts²³

	Diabetes Relative Risk						
Cohort	(95% CI)*						
Men							
Framingham Heart Study	1.69 (1.11-2.57)						
ARIC (White)	2.42 (1.69-2.57)						
ARIC (Black)	1.40 (0.75-2.62)						
Physician's Heart Study	1.54 (1.05-2.26)						
Honolulu Heart Program	2.55 (1.82-3.57)						
Puerto Rico Heart Program	2.07 (1.50-2.85)						
Strong Heart Study	4.29 (2.27-8.10) [#]						
Cardiovascular Health Study	1.47 (0.89-2.44)						
Wome	en						
Framingham Heart Study	2.38 (1.40-4.06)						
ARIC (White)	3.62 (2.21-5.94)						
ARIC (Black)	2.01 (1.16-3.48)						
Strong Heart Study	8.63 (2.55-29.16) [#]						
Cardiovascular Health Study	2.29 (1.23-4.23)						

* These relative risks were adjusted for age, systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, and current smoking status. # indicates significant difference between the cohort and the FRS.

Table 22. Comparison of Diabetes Relative Risk Across 16 NorthAmerican, European, and Asian Cohorts

Cohort	Diabetes Relative Risk* (95% Cl)
Men	
Framingham Heart Study ^{23\$}	1.99 (1.23-3.21)
NHANES I ^{25\$}	2.17 (1.60-2.94)
NHANES II ^{25\$}	1.73 (1.15-2.60)
Honolulu Heart Program ^{23\$}	2.85 (2.17-3.75)
Puerto Rico Heart Health Program ^{23\$}	
Urban	2.88 (2.07-4.03)
Rural	2.86 (1.23-6.60)
HDFP (Regular Care) ^{38\$}	1.79 (1.06-3.05)
MRFIT (Usual Care) ^{138\$}	1.24 (0.61-2.51)
Tecumseh Community Health Study ¹³⁹	1.85 (0.94-3.66)
Renfrew and Paisley Study66	2.73 (1.93-3.87)
Glostrup Cohort ¹⁴⁰	2.52 (1.26-5.02)
Iceland Reykjavik Study ¹⁴¹	1.78 (1.17-2.71)
Israeli Ischemic Heart Disease Study ¹⁴²	2.31 (1.86-2.87)
Norwegian Counties Study44	3.98 (2.62-6.03) [#]
Yugoslavia Cardiovascular Disease Study ¹⁷	4.63 (2.15-9.96) [#]
Lipid Research Clinics Follow-Up Study99	
Random Sample	8.05 (3.80-17.03) [#]
Hyperlipidemia	3.79 (1.60-3.05) [#]
Women	
Framingham Heart Study ²³	4.67 (2.70-8.07)
NHANES I ²⁵	2.50 (1.89-3.30)
NHANES II ²⁵	2.76 (1.92-3.97)
HDFP (Regular Care) ³⁸	2.57 (1.37-4.81)
Tecumseh Community Health Study ¹³⁹	1.32 (0.62-2.82)
Renfrew and Paisley Study	3.65 (2.36-5.65)
Norwegian Counties Study44	8.67 (3.81-19.77)
Iceland Reykjavik Study ¹⁴¹	3.81 (2.25-6.44)

*These relative risks were adjusted for age, systolic blood pressure, total cholesterol, and current smoking status. # indicates significant difference between the cohort and the FRS. \$ indicates a U.S. cohort.

Table 23. Comparison of Variable Coefficients Between UKPDS and HKD Registry for Coronary Heart Disease Outcome in Patients With Diabetes

	UKPDS ¹¹⁹	HKD Registry ³⁸
Variable	(95% CI)	(95% CI)
Age (1 year of age at Dx DM)	1.059 (1.05-1.07)	1.04 (1.03-1.06)
Female	0.525 (0.42-0.63)	0.81 (0.59-1.10)
Afro-Caribbean ethnicity	0.390 (0.19-0.59)	
Current smoker	1.350 (1.11-1.59)	1.40 (0.99-1.98)
HgbA _{1c} (per 1% increase)	1.183 (1.11-1.25)	1.03 (0.95-1.16)
SBP (per 10 mmHg increase)	1.088 (1.04-1.14)	1.09 (1.01-10.17)
Total/HDL lipid ratio	3.845 (2.59-5.10)	2.74 (1.67-4.50)

			Test Patient				
Model	Model Type	Outcome	1	2	3	4	5
FRS (Anderson)							
DBP	Model Generated	CVD ₂	0.05	0.09	0.43	0.66	N/A
SBP	Model Generated	CVD ₂	0.05	0.09	0.49	0.70	N/A
Points	Model Generated	CVD ₂	0.05	0.10	0.42	N/A	N/A
	Online	CVD ₂	0.05	0.19	0.44	N/A	N/A
FRS (Wilson)							
TC	Model Generated	Total CHD ₁	0.06	0.12	0.20	0.51	0.16
LDL	Model Generated	Total CHD ₁	0.05	0.13	0.18	0.33	0.19
	Online	Total CHD ₁	0.03	0.03	0.06	0.39	0.16
FRS (ATP-III)							
Points	Model Generated	Hard CHD ₁	0.02	0.03	Outcome	Outcome	0.22
	Online	Hard CHD ₁	0.03	0.03	Outcome	Outcome	N/A
UKPDS							
	Model Generated	Hard CHD ₁	N/A	N/A	0.16	0.29	N/A
	Online	Hard CHD ₁	N/A	N/A	0.15	0.33	N/A
Other							
PROCAM (Point Score)	Model Generated	Hard CHD ₁	0.01	0.11	0.18	>0.30	N/A
SCORE (High Risk)	Model Generated	CHD Mortality	N/A	0.01	0.02	0.16	N/A

Table 24. Model and Online Tool Comparison

Figure 1. Yield of Literature



*The number of articles excluded exceeds the total number of articles in each category because most of the articles fit into multiple exclusion categories.



Figure 3. Variation in Predicted Outcomes, Patient 3



Figure 4. Summary of Quality Scores

		All (n=83)	Americas (n=28)	Asia (n=8)	Europe (n=47)
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and any additional exclusions that were made after					
conort inception?				Г : : :	F i i i
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	++				
	+				
Vas the study population well described?	-				
	NA				
	++				
Vas the loss to follow-up over the course of the	+				
study less than 20%?					
	NA				
	++				
more than 20% were lost, did the authors	+				
acknowledge the potential effects on the model?	—				
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	NA				
	++				
id missing data cause more than 20% of the	Ŧ				
population to be excluded from the model?					
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missing data, was a missing data technique	-				
applied?					
	NA				
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	NA				
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or model development did the authors assess	+		:		
internal validation?	-				
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Appendix A. Literature Search Terms and Results

SEARCH STRATEGY				
Cardiova	scular Diseases			
1	cardiovascular disease*[tiab]	53,927		
2	cardiovascular diseases[majr:noexp]	40,508		
3	myocardial infarction[majr]	87,024		
4	coronary disease[majr]	111,322		
5	stroke[majr]	34,282		
6	brain ischemia[majr:noexp]	19,070		
7	cerebrovascular accident[tiab]	2,344		
8	death, sudden, cardiac[majr]	3,973		
9	heart diseases[majr:noexp]	31,459		
10	cardiovascular mortality[tiab]	4,367		
11	coronary[tiab]	224,553		
12	artery[tiab]	283,473		
13	disease[tiab]	1,398,642		
14	#11 AND (#12 OR #13)	151,293		
15	stroke[tiab]	88,070		
16	brain[tiab]	480,737		
17	cerebrovascular[tiab]	27,374		
18	cerebral[tiab]	210,834		
19	brainstem[tiab]	25,684		
20	#15 AND (#16 OR #17 OR #18 OR #19)	26,438		
21	intracranial hemorrhages[majr]	29,154		
22	intracranial hemorrhage, traumatic[majr]	5,957		
23	#21 NOT #22	23,197		
24	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	449,543		
	OR #14 OR #20 OR #23			
Risk Ass	essment	00.550		
25	Risk Assessmentimni	93,552		
27	Risk Function*[tiab]	314		
28	Risk Equation*[tiab]	164		
29	Risk Calc*[tiab]	506		
30	Risk Scor*[tiab]	2,957		
31	Risk Predict*[tiab]	1.641		
32	Risk Factor Calc*[tiab]	8		
34	Risk Engine*[tiab]	40		
35	Risk Appraisal*[tiab]	363		
36	Prediction Model*[tiab]	2 107		
37	Risk algorithm[tiab]	43		
38	Scoring* Method*[tiab]	13.615		
39	Scoring Scheme*[tiab]	335		
40	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR	122,344		
-	#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39	, -		
Modeling	Measurements			
41	roc curve[mh]	13,045		
42	Roc curve[tiab]	4,402		
43	Area Under Curve[mh]	14,816		
44	receiver WITH operating WITH curve[tiab]	7,349		
45	c-statistic*[tiab]	510		
46	C index*[tiab]	230		
47	C indices*[tiab]	23		
48	hosmer WITH lemeshow[tiab]	383		
49	validation studies[pt]	35,385		
50	hazard ratio[tiab]	12,036		
51	forecasting[mh]	56,935		
52	models, statistical[mh]	141,871		
53	observ* WITH predict*[tiab]	90.609		
54	Predictive Value of Tests[mh]	84,827		
55	concordance[tiab]	15,712		

Appendix A. Literature Search Terms and Results

56	#41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55	425,065
Corona	rv Artery Disease Risk Models	
57	assign score*[tiab]	22
58	brhs[tiab]	13
59	British regional heart[tiab]	91
60	British national heart[tiab]	12
61	busselton[tiab]	160
62	decode study[tiab]	18
63	Dundee risk score*[tiab]	4
64	erica risk[tiab]	14
65	findris*[tiab]	5
66	framingham equation*[tiab]	117
67	framingham estim*[tiab]	5
68	framingham heart study algorithm[tiab]	2
69	Framingham algorithm[tiab]	24
70	Framingham guideline*[tiab]	232
71	Framingham risk[tiab]	572
72	Framingham score*[tiab]	102
73	Framingham function*[tiab]	28
74	Framingham model*[tiab]	44
75	Glostrup[tiab]	260
76	New Zealand chart*[tiab]	198
77	precard[tiab]	4
78	PROCAM[tiab]	131
79	Reynolds risk score*[tiab]	11
80	score project[tiab]	21
81	Sheffield table*[tiab]	34
82	shaper score*[tiab]	13
83	Systematic Coronary Risk Evaluation[tiab]	40
84	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65	1,863
	OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR	
	#74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82	
-	OR #83	
Summa	tion	
85	#40 OR #84	123,397
86	#24 AND #56 AND #85 AND English[la] AND humans[mh] AND	3,317
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88		131
89		17
90		157
91		3,160

Appendix B. Inclusion/Exclusion Forms

Systematic Review of CVD Risk Assessment Tools

Abstract Review Form

First Author, Year: _____ Ref ID #_____ Abstractor Initials: _____

	Primary Inclusion/Exclusion Criteria						
1.	Relevant to SER topic	Yes	No	Cannot Determine			
2.	Attempts internal or external validation	Yes	Yes No Cann Detei				
3.	Published in English	Yes No Cannot Determin		Cannot Determine			
4.	Original research (exclude reviews, editorials, commentaries, letters to editor, etc.)	Yes	No	Cannot Determine			
5.	Eligible Study types a. Randomized controlled trials b. Controlled clinical trials c. Cohorts d. Case-series	Yes	No	Cannot Determine			
6.	 Reports relevant outcomes: a. Coronary Artery Disease (non fatal and fatal MI and sudden coronary heart disease death) b. Cerebrovascular stroke (thrombotic/hemorrhagic) c. Combination of a and b 	Yes	No	Cannot Determine			
7.	Study size ≥ 200 If No, state study size	Yes	No	Cannot Determine			
8.	Study population is adults asymptomatic for CVD If No, state % symptomatic%	Yes	No	Cannot Determine			

Retain for:

__BACKGROUND/DISCUSSION

REVIEW OF REFERENCES

___Other_____

Systematic Review of CVD Risk Assessment Tools

Full Text Review Form

First Author, Year: _____ Ref ID #_____ Abstractor Initials: _____

1. Relevant to SER topic If NO: a. Post-PCI b. Post-CABG ____ Yes No c. Diagnostic _____ d. Prognostic _____ e. Etiologic ___ f. Not a risk tool ____ g. Other _ 2. Attempts internal or external validation (evaluation of risk model) If YES: a. ROC analysis _____ Yes No b. O/E ratios _____ c. Calibration Plots _____ d. Hosmer-Lemeshow _____ e. Other _ 3. Published in English Yes No 4. Original research (exclude reviews, editorials, commentaries, letters to Yes No editor, etc.) 5. Eligible Study types a. Randomized controlled trials _____ Yes No Controlled clinical trials _____ b. Cohorts ____ c. d. Case-series ___ 6. Reports relevant outcomes: a. Coronary Artery Disease (non fatal and fatal MI and sudden coronary heart Yes No disease death) b. Cerebrovascular stroke (thrombotic/hemorrhagic) Combination of a. and b. c. 7. Study size ≥ 200 Yes No If NO: State study size _____ 8. Study population is asymptomatic for CVD Exclude: Include: PAD MI CAD LEAD CABG Hypertension Renal Disease Stroke Yes No Metabolic Syndrome Unstable Angina Stable Angina If NO: State % symptomatic _____ %

Appendix B. Inclusion/Exclusion Forms

 Study population is adults aged ≥ 18 years old 	Yes	No
 10. Study conducted in the United States If NO: State country 	Yes	No
11. Length of Follow-Up		

Retain for:

_____BACKGROUND/DISCUSSION

_____REVIEW OF REFERENCES

____Other_____

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Enrollment Start Date:	1/1/1968 Study Design: Prospect	ive Cohort 🛛 Quality:	×				
Enrollment Stop Date:	12/31/1987	Refs Reviewed					
Followup Duration (in years): Internal Model Development? If Internally Developed, was the	Followup Measure Type:	<u>▼</u> +/_:					
Description of Internal Validation	n: overfitting estimated by boostrap resampling of the o	riginal dataset as recommended by Harrell					
Primary Reviewer Notes: INCLUDE - both internal development and external validation, enrollment will be based on the above cohorts ****!!! GREAT REVIEW IN DISCUSSION OF OTHER MODELS !! !***							
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HDL-C (mg/dL)	Mean 🔽	Women 🔽	57.6	15.3	SD 💌						
SBP (mm Hg)	Mean 🔽	Women 💌	125.8	20	SD 💌						
Antihypertensive med	Count 🛛 🗸	Women 💌	532		*						
Smoker (Current)	Count 🛛 🗸	Women 💌	1548		~						
Diabetes Mellitus 🗸 🗸	Count 🛛 🗸	Women 💌	170		~						
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Enrollment (Baseline)	Count 🛛 🗸	Men 💌	3969		~						
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HDL-C (mg/dL)	Mean 🗸	Men 💌	44.9	12.2	SD 🗸						
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Observed Outcomes	Women 💌	CVD 💌	D'Agostino CVD FEMALE	✓ 456		count 💌						
C Statistic	Men 💌	CVD 💌	D'Agostino CVD MALE	• 0.763	0.746-0.780	~						
C Statistic	Women 💌	CVD 💌	D'Agostino CVD FEMALE	• 0.793	0.772-0.814	~						
HL GOF (c-hat)	Men 💌	CVD 💌	D'Agostino CVD MALE	✓ 13.48		chi squa 💌						
HL GOF (c-hat)	Men 💌	CVD 💌	D'Agostino CVD MALE	• 0.14		p value 💌						
HL GOF (c-hat)	Women 💌	CVD 💌	D'Agostino CVD FEMALE	7.79		chi squa 🗙						
HL GOF (c-hat)	Women 🗸	CVD 💌	D'Agostino CVD FEMALE	• 0.56		p value 💌						
C Statistic	Men 🗸 🗸	CVD 💌	Framingham Risk Score [Unl	• 0.756	0.739-0.773	~						
C Statistic	Women 🗸	CVD 🔽	Framingham Risk Score [Unl	• 0.778	0.756-0.799	~						
HL GOF (c-hat)	Men 🗸	CVD 🔽	Framingham Risk Score [Unl	32.37		chi squa 🗸						
HL GOF (c-hat)	Women 🗸	CVD 💌	Framingham Risk Score [Unl	• 12.42		chi squa 🐱	~					
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Endnote Study ID:283 Year Published:2008 Primary Reviewer: MEM 2nd Reviewer:MLM		
First Author (Last name, First and Middle Initial D'Agostino, RB NEW MODEL REFRESH ALL		
Basic Study Data Include-Exclude Descriptor Descriptor Data Models Outcomes Statistics Quality1 Quality2		_
Does the arrticle state both the inclusion/exclusion and any additional exclusions that were made after cohort inception?		
U Was the study population well described?		
Is the population asymptomatic for CVD or Stroke?		
· · · · · · · · · · · · · · · · · · ·		
Was there a clear definition of predictor variables?		
For Validation studies, do the definitions of the risk variables match those in the original model?		
Was there a valid and reliable approach to measuring predictor variables?		
V		
Was there a clear description of the outcome variables?		
was there a valiu and reliable approach to measuring outcome variables?		
For validation studies, did the study and original model outcome definitions match?		
Record: II 7 FIF of 119		
patient's preferred phone for contact		

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First Author (Last name, First and Middle Initial D'Agostino, RB NEW MODEL REFRESH ALL	
Basic Study Data Include-Exclude Descriptor Descriptor Data Models Outcomes Statistics Quality1 Quality2	
Was the loss to follow-up over the course of the study less than 20%?	
if more than 20% were lost, did the authors address the potential effects on the model?	-
8	
If more than 20% of data was excluded due to missing data, was a missing data technique applied (imputation, sens. analysis)?	_
Did missing data cause more than 20% of the population to be excluded from the model?	•
8	
Did the authors report both discrimination and calibration for any models developed/evalulated?	
For model development, did the authors assess internal validity?	<u> </u>
For validation studies, was there <= 2 years difference bewteen (mean/median) followup time between development and validation of	ohorts?
	2
Record: 14 7 PPP* of 119	
patient's preferred phone for contact	

Appendix D. Summary Table 1: Online Tools

Madal	Model Deceriction		Date of URL
Framingham	Model Description	URL Accessed	Access
Framingham	Based upon Framingham Hoart Study and ATP III	http://hp2010.1111binin.net/atpii//calculator.asp?usentype=ptoi	0/30/2009
Framingham	based upon Framingham fleart Study and ATF m	https://www.americameari.org/gginisk/locale/eii_00/index.html/gtype	6/30/2000
Framingham	Based upon Framingham Heart Study	http://www.cardiacriskcalculator.org/	6/30/2009
Framingham	Based upon Framingham Heart Study (1998)	http://www.cardiachskcaiculator.org/	6/30/2009
Framingham	Based upon Framingham Heart Study (1998) and ATP III	https://www.stateoder.com/cardiae.ntm	0/30/2003
riannighan	based upon Framingham Freak Olduy (1990) and Alth In	urlstring=	6/30/2009
Framingham	Based upon Framingham Heart Study	http://calculators.epnet.com/?docid=healthcalculators/chd/precalcdoc&	
J		token=8ce583c0-2d91-46f6-af0a-	
		aa4c845a0528&DeliveryContext=coe&CollectionIID=347&frame=pare	
		<u>nt</u>	7/1/2009
Framingham	Based upon Framingham Heart Study and ATP III	http://www.americanheart.org/presenter.jhtml?identifier=3003499	7/1/2009
Framingham	Based upon Framingham Heart Study (2001) and ATP III	http://www.chd-	
		taskforce.com/framingham.php?iSprache=1&iversion=1&SiVersion=0	7/1/2009
Framingham	Based upon Framingham Heart Study	https://www.heartagecalculator.com/HeartHealth/HeartAgeCalculator.a	
		spx?hostID=1503	7/1/2009
Framingham	Based upon Framingham Heart Study, JBS Calculator	http://www.patient.co.uk/showdoc/40000133/	7/1/2009
Framingham	Based upon Framingham Heart Study	http://cvrisk.mvm.ed.ac.uk/calculator/calc.asp	7/1/2009
Framingham	Based upon Framingham Heart Study (ETHRISK)	http://www.epi.bris.ac.uk/CVDethrisk/CHD_CVD_form.html	7/1/2009
Framingham	Based upon Framingham Heart Study	http://www.cardiosmart.org/CardioSmart/Default.aspx?id=298,	
		https://www.itsmyhealthrecord.com/ACCriskform2008.lasso	7/2/2009
Framingham	Based upon Framingham Heart Study	http://my.clevelandclinic.org/ccforms/Heart Center Risk Tool.aspx	7/2/2009
Framingham	Calculators based upon Framingham Heart Study	http://www.framinghamheartstudy.org/risk/index.html	6/30/2009
ATP III	Based upon Framingham Heart Study and ATP III	https://www.americanheart.org/gglRisk/locale/en_US/index.html?gtype	
		<u>=health</u>	6/30/2009
ATP III	Based upon ATP III and Framingham Heart Study	http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof	
			6/30/2009
ATP III	Based upon ATP III	http://www.mayoclinic.com/health/heart-disease-risk/HB00047	
			6/30/2009
ATP III	Based upon Framingham Heart Study (1998) and ATP III	https://www.heartdecision.org/chdrisk/v_hd/main?p=_home_home&_	
		<u>urlstring</u> =	6/30/2009
ATP III	Based upon Framingham Heart Study and ATP III	http://www.americanheart.org/presenter.jhtml?identifier=3003499	
			7/1/2009
ATP III	Based upon Framingham Heart Study (2001) and ATP III	http://www.chd-	
		taskforce.com/framingham.php?iSprache=1&iversion=1&SiVersion=0	7/1/2009
Other	Pocock SJ (2001) multivariate Cox model	http://www.riskscore.org.uk/	6/30/2009
Other	N/A	http://doctorwidget.com/cvd/cvd mathv2.htm	6/30/2009
Other	National Vascular Disease Prevention Alliance (NVDPA)	http://www.cvdcheck.org.au/playerProductInstall2.html	
	for Australia (did not give a mathematical model)		7/2/2009

Appendix D. Summary Table 1: Online Tools

			Date of URL
Model	Model Description	URL Accessed	Access
Other	FDS model for 5-year risk of major CVD (Australia)	http://www.medicine.uwa.edu.au/download.cfm?DownloadFile=75841	
		E31-96BA-5DAE-B9B5B5B8E85E85C3	7/2/2009
Other	N/A	http://ww2.heartandstroke.ca/hs_Risk.asp?media=hsf_hmpg	7/2/2009
Other	N/A	http://www.goredforwomen.org/index.aspx	7/2/2009
Other	N/A	https://www.beverlyhospital.org/services/online-tools/health-risk-	
		assessments/heart-health	7/2/2009
Other	HeartScore (no other model listed)	https://escol.escardio.org/heartscore3/calc.aspx?model=europehigh	7/2/2009
Other	HeartScore	https://escol.escardio.org/heartscore3/calc.aspx?model=europelow	7/2/2009
Other	JBS/BNF	http://cvrisk.mvm.ed.ac.uk/calculator/calc.asp	7/1/2009
Other	BVN RISK does not purport to forecast a vascular event;	http://www.csun.edu/studenthealthcenter/online/BVN_calculator/BVN_	
	instead, it offers a tangible prediction that a vascular study	calculator.php	
	may uncover significant evidence of vascular disease		7/2/2009
Other	Based upon 2002 NHANES and ATP III	http://www.csun.edu/studenthealthcenter/online/BVN_calculator/BVN	
		calculator.php	7/2/2009
Other	QRISK2 Men	http://www.grisk.org	6/30/2009
Other	QRISK2 Women	http://www.grisk.org	6/30/2009
Other	ASSIGN Men	http://assign-score.com/estimate-the-risk/	6/30/2009
Other	ASSIGN Women	http://assign-score.com/estimate-the-risk/	6/30/2009
Other	SHS Men	http://strongheart.ouhsc.edu/CHDcalculator/calculator.html	6/30/2009
Other	SHS Women	http://strongheart.ouhsc.edu/CHDcalculator/calculator.html	6/30/2009
Other	REGICOR model	http://www.regicor.org/conttemp?idioma=angles	6/30/2009
Other	CUORE	http://www.cuore.iss.it/sopra/calc-rischio_en.asp	7/1/2009
Other	UKPDS	http://www.dtu.ox.ac.uk/index.php?maindoc=/riskengine/	7/1/2009
Other	PROCAM	http://www.scopri.ch/riskalgorithms.htm	7/1/2009
Other	ASSIGN	http://cvrisk.mvm.ed.ac.uk/calculator/calc.asp	7/1/2009

Appendix E. Summary Table 2

Enroll	Enroll	First	Year			Cohort	Enrollment	Enrollment	Follow- Up
Start Date	End Date	Author	Published	Country	Cohort	Abbreviation	Base	Final	(yrs)
		Liao Y ¹	1999	U.S.	NHANES I and II (pooled)	NHANES I and		18542	
						II (pooled)			
01/01/1948	12/31/1974	Wilson PWF ²	1998	U.S.	Framingham Cohort (11th exam) or Framingham Offspring	FRS, FRS-O	5345		12
					(1st exam)				
01/01/1954	12/31/1958	Liao Y ³	1999	U.S.	Framingham Heart Study (4th exam)	FRS	4169		24
01/01/1965	12/31/1968	D'Agostino RB ⁴	2001	Puerto Rico	Puerto Rico Heart Health Program	PRHHP		8713	
01/01/1967	01/31/1973	Berry JD ⁵	2007	U.S.	Chicago Young Adults	CHA	10375		32*
01/01/1968	12/31/1987	D'Agostino RB ⁶	2008	U.S.	Framingham Cohort (11th exam) (68-71) & Offspring (1st	FRS, FRS-O	8491		
					exam) (71-75) & Offspring (3rd exam) (84-87)				
01/01/1971		Wilson PWF	2008	U.S.	Framingham Offspring Study	FRS-O	5124	4780	~24
01/01/1971	12/31/1974	D'Agostino RB ⁴	2001	U.S.	Framingham Study (11th exam) or Framingham Offspring	FRS, FRS-O		5251	12**
					Study (1st exam)				
01/01/1971	12/31/1975	Liao Y ¹	1999	U.S.	First National Health and Nutrition Examination Survey	NHANES I	6611		20
01/01/1971	12/31/1992	Gaizano TA [®]	2008	U.S.	First National Health and Nutrition Examination Survey	NHANES-I EFS	14407	6186	21
					Epidemiologic Follow-Up Study				
01/01/1976	12/31/1980	Liao Y ¹	1999	U.S.	Second National Health and Nutrition Examination Survey	NHANES II	5705		15
01/01/1980	12/31/1982	D'Agostino RB ⁴	2001	U.S.	Honolulu Heart Program	HHP		2755	
01/01/1980	12/31/2000	Miyasaka Y ⁹	2007	U.S.	Adult Residents of Olmsted County, MN	Mayo	2768		6* [5.2]
01/01/1983	12/31/1996	Vaidya D ¹⁰	2007	U.S.	John Hopkins Sibling Study	JHSS		784	
01/01/1986	12/31/1989	Mainous AG ¹¹	2008	U.S.	Atherosclerosis Risk in Communities Study	ARIC	9307		
01/01/1987	12/31/1989	Chambless LE ¹²	2004	U.S.	Atherosclerosis Risk in Communities Study	ARIC	13161		12.3†
01/01/1987	12/31/1989	D'Agostino RB ⁴	2001	U.S.	Atherosclerosis Risk in Communities Study	ARIC	14178		
01/01/1987	12/31/1989	Folsom A ¹³	2003	U.S.	Atherosclerosis Risk in Communities Study	ARIC		14054	10.2†
01/01/1987	12/31/1989	Mainous AG ¹⁴	2007	U.S.	Atherosclerosis Risk In Communities Study	ARIC	14343		
01/01/1987	12/31/1989	McNeill AM ¹⁵	2005	U.S.	Atherosclerosis Risk in Communities Study	ARIC		12089	11*
01/01/1989	12/31/1990	D'Agostino RB ⁴	2001	U.S.	Cardiovascular Health Study	CHS		2557	
01/01/1989	12/31/1991	D'Agostino RB ⁴	2001	U.S.	Strong Heart Study (OK and Aberdeen area of ND and SD)	SHS		3782	
01/01/1989	12/01/2001	Lee ET ¹⁶	2006	U.S.	Strong Heart Study	SHS	4372		
01/01/1990	12/31/1992	Greenland P ¹⁷	2004	U.S.	South Bay Heart Watch	SBHW		1029	7†
12/01/1990	12/31/1992	Detrano RC ¹⁸	1999	U.S.	South Bay Heart Watch	SBHW	1196	1194	3.42
09/01/1992		Cook NR ¹⁹	2006	U.S.	Women's Health Study	WHS		15048	10*
09/01/1992		Ridker PM ²⁰	2007	U.S.	Women's Health Study (Validation Cohort)	WHS (Val)		8158	10.2†

Table 2a. Data Sources Summary (Primary Models) - Americas

*Mean. **Other. † Median.

Table 2b. Data Sources Summary (Primary Models) – Europe

Enroll	Enroll		Year			Cohort	Enrollment	Enrollment	Follow-
Start Date	End Date	First Author	Published	Country	Cohort	Abbreviation	Base	Final	Up (yrs)
		Bernard S ²¹	2005	France	Lyon, France	Lyon	229		5**
01/01/1970	12/31/1973	Dunder K ²²	2004	Sweden	Uppsala Longitudinal Study of Adult Men	ULSAM	1108		28.7
01/01/1970	12/31/1973	Strom Moller C ²³	2007	Sweden	Uppsala Longitudinal Study of Adult Men (baseline age 70	ULSAM (70)		1221	23
					cohort)				
08/28/1972	03/30/1975	Erikssen G ²⁴	2004	Norway	Healthy Norwegian men aged 40-60 years recruited from 5	NorGov		2014	26**
					government agencies				
01/01/1975	12/31/1979	Reissigova J ²⁵	2007	Czech Republic	Study of Atherosclerotic Risk Factors	STULONG	646		
01/01/1978	12/31/1995	Assmann G ²⁶	2007	Germany	PROCAM cohort; employees of 52 companies and local	PROCAM		7295	12* [6]

Appendix E. Summary Table 2

Enroll	Enroll		Year			Cohort	Enrollment	Enrollment	Follow-
Start Date	End Date	First Author	Published	Country	Cohort	Abbreviation	Base	Final	Up (yrs)
					government authorities in Germany, aged 20-78 years				
01/01/1979	12/31/1985	Assmann G ²⁷	2002	Germany	PROCAM cohort; employees with followup every 2 years	PROCAM	5389	5159	10**
01/01/1979	12/31/1999	Assmann G ²⁸	2008	Germany	Cohort of men and women employed in Germany	PROCAM		7134	10**
01/01/1983	12/31/1996	Ferrario M ²⁹	2005	Italy	CUORE	CUORE	6865		9.1†
01/01/1984	12/31/1995	Woodward M ³⁰	2007	Scotland	Scottish Hearth Health Extended Cohort	SHHEC	13297		
01/01/1989		Cooper JA ³¹	2005	UK	Second Northwick Park Heart Study	NPHS-II		2732	10.8†
01/01/1989	12/31/1991	Macfarlane PW ³²	2007	Scotland	West of Scotland Coronary Prevention Study	WOSCOPS	6595		4.9*
01/01/1990	12/31/1991	Stephens JW ³³	2004	UK	Diabetes clinic at University College London Hospitals NHS	NHS Trust	798		
					Trust				
01/01/1993	03/31/2008	Hippisley-Cox J ³⁴	2008	UK	Members of the QRESEARCH database	QRESEARCH	2285815		15
03/01/1993	02/28/1998	Simmons RK ³⁵	2008	UK	European Prospective Investigation of Cancer–Norfolk	EPIC-Norfolk	10295		8.5*
01/01/1994	12/31/1995	Vergnaud AC ³⁶	2008	France	Participants in Supplementation en Vitamines et Mineraux	SU.VI.MAX		3440	10**
					Antioxydants randomized primary prevention trial followed				
					annually since 1994/5				
01/01/1994	12/31/1996	Bastuji-Garin S ³⁷	2002	Western Europe	INSIGHT trial cohort of middle-aged patients with hypertension	INSIGHT	4407	4147	3.7†
		00		and Israel					
01/01/1995	12/31/1998	Marrugat J ³⁰	2007	Spain	Validity of the Adapted Framingham Individual Risk Equation	VERIFICA	5732		
		20			for Coronary Incidents cohort				
01/01/1995	06/30/2004	Donnan PT ³⁹	2006	UK	Subjects with type 2 diabetes registered with a Tayside general	DARTS		4569	4.1† [9.5]
	/ /				practitioner				
01/01/1995	04/01/2007	Hippisley-Cox JC ⁺	2007	UK	QRESEARCH database, constructed from 160 general	QRESEARCH	614553		6.5†
					practices in UK; validation cohort	(Val)			
01/01/1997	12/31/1999	Becker A	2008	Germany	Consecutive patients referred by primary care provider for	LudwigU	1726		3.36*
		42			preventive cardiological exam	1.0.7			[0.61]
09/01/1997	09/30/1999	de Ruijter W**	2009	Netherlands	Leiden 85-plus study	L85	302		5
01/01/1998	12/31/2003	Cederholm. J ⁴³	2008	Sweden	Swedish National Diabetes Register	SNDR	11646		5.64*
01/01/1999	12/31/2001	May MD⁴⁴	2006	UK	British Women's Heart and Health Cohort	BWHH	3582		4.7*

*Mean. **Other. †Median.

Table 2c. Data Sources Summary (Primary Models) – Asia

Enroll	Enroll	First	Year			Cohort	Enrollment	Enrollment	Follow-Up
Start Date	End Date	Author	Published	Country	Cohort	Abbreviation	Base	Final	(yrs)
01/01/1974	12/31/1993	Barzi F ⁴⁵	2007	China	Asia Pacific Cohort Studies Collaboration; total Chinese	APCSC China	25682		8.3*
					cohort				
01/01/1992	12/31/1995	Jee SH ⁴⁶	2008	Korea	Koreans insured by National Health Insurance	NHIC	1223740	1205268	13**
					Corporation (NHIC)				
01/01/1992	12/31/1999	Liu J ⁴⁷	2004	China	Chinese Multi-Provincial Cohort study; aged 35-64 years	MUCA	30121		
					from 16 centers in 11 provinces (1992-1993) and Beijing				
					(1996-1999)				
01/01/1993	12/31/1994	Wu Y ⁴⁸	2006	China	MUCA II	MUCA II	9903		11
01/01/1995		Yang X ⁴⁹	2008	China	Hong Kong Diabetes Registry	HKD Registry	7067		5.4* [4.94]
01/01/1995	07/30/2005	Yang X ⁵⁰	2007	China	Hong Kong Diabetes Registry	HKD Registry	7209	3541	5.37* [4.9]

*Median. **Other.
First	Year	Cohort		Mean	Race	Female	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Liao Y ¹	1999	NHANES I and	All			57.5			l `´					
		II (pooled)												
Wilson PWF ²	1998	FRS, FRS-O	All			53.4	39	LDL: 141.8	4.5			32.8	8.9	
								HDL: 51.7						
Liao Y ³	1999	FRS	All	49.8		55.7	47.7	Tot: 238		132.9**	83.3**			
D'Agostino RB ⁴	2001	PRHHP	All	54.1	H: 100	0	44		7			34		
Berry JD ⁵	2007	CHA	All	29.8		0	47	Tot: 189.8	0	134.4**	78.1**			
D'Agostino RB6	2008	FRS, FRS-O	All	48.8		53.3	34.7	HDL: 51.7	5	127.6			11	
-								Tot: 213.9						
Wilson PWF'	2008	FRS-O	All	36.7	W: 100	51.6	45.2	HDL: 50.7	2.8	122.2 (16.67				
				(9.75 [SD])				Tot: 196.8		[SD])				
D'Agostino RB ⁴	2001	FRS, FRS-O	All	49	W: 100	53.6	22.2		4.5			32.2		
Liao Y ¹	1999	NHANES I	All	52	W: 100	58.4	35.2			134.6	84.4			
Gaizano TA ⁸	2008	NHANES-I EFS	All	47.8		54.1	42.9	Tot: 220.8	3.8	132.3			9.7	
Liao Y ¹	1999	NHANES II	All	54.5	W: 100	53.5				132.4	82.9			
D'Agostino RB ⁴	2001	HHP	All	61.9		0	32		14			33		
Miyasaka Y ⁹	2007	Mayo	All			52.4	52		12.8				43.9	73.7
Vaidya D ¹⁰	2007	JHSS	All	45.6	W: 83.3	48.5	33	LDL: 152.4	6.3	133.1	84.7			45.2
-					B: 16.7			HDL: 50.3						
								Tot: 232.6						
Mainous AG ¹¹	2008	ARIC	All	59.7		58	17.7	HDL: 53.9	0	122.8				
								Tot: 207.6						
Chambless LE ¹²	2004	ARIC	All			55.3								
D'Agostino RB ⁴	2001	ARIC	All	54	W: 73.5	56.7	26		8.6			16.8		
-					B: 26.5									
Folsom A ¹³	2003	ARIC	Diabetes		W: 55									
					B: 45									
Folsom A ¹³	2003	ARIC	All			56.8			10.7					
Mainous AG ¹⁴	2007	ARIC	All	54.1	W: 73.7	56.5	26		6.9			14.8	28.2	
					B: 26.3									
McNeill AM ¹⁵	2005	ARIC	All	54	W: 74.6	100	26.6	LDL: 136.7	0			39.1		
					B: 25.6									
D'Agostino RB ⁴	2001	CHS	All	69.4	W: 100	62.6	13.9		11.9			33.7		
D'Agostino RB ⁴	2001	SHS	All	56.1	O: 100	59.6	34.1		47.3			25.2		
Lee ET ¹⁶	2006	SHS	All	56.2		60.6	33.7	LDL: 118.2	44	127.6	76.7			
								Tot: 191.1						
Greenland P ¹⁷	2004	SBHW	All	65.7	W: 84.9	10.2	17.7		0			41.4		
				(7.8 [SD])	B: 5.3									
					H: 4.5									
40					O: 5.2									
Detrano RC ¹⁸	1999	SBHW	All	66 (8 [SD])		11		HDL: 45.3	18	142 (20 [SD])	80 (11 [SD])	32		
Cook NR ¹⁹	2006	WHS	All	54 (8 [SD])		100			0				12	

Table 3a. Data Sources Details (Primary Models) – Americas All

First	Year	Cohort		Mean	Race	Female	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Ridker PM ²⁰	2007	WHS (Val)	All	52*	W: 94.5	100	11.5		2.9	125*	80*	25.3		
				(49-59	B: 1.9					(115-135	(70-80			
				[IQR])	H: 1					[IQR])	[IQR])			
					O: 1.8									

* Median. **Derived.

Table 3b. Data Sources Details (Primary Models) – Americas Men

First	Year	Cohort	-	Mean	Race	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Liao Y ¹	1999	NHANES I and	Men										
		II (pooled)											
Liao Y ¹	1999	NHANES I and	Black	54.5		46.7		5.9	141.7	89.2	61.6		
		II (pooled)	men	(13.4 [SD])					(25.0 [SD])	(14.3 [SD])			
Liao Y ¹	1999	NHANES I and	White	53.5		38.6		3.8	134.9	85	49.1		
		II (pooled)	men	(13.2 [SD])					(20.1 [SD])	(11.5 [SD])			
Wilson PWF ²	1998	FRS, FRS-O	Men			40.4	LDL: 142.9 HDL: 44.8	5.2			36	6.8	
Liao Y ³	1999	FRS	Men	49.6		59.7			132	84			
				(8.5 [SD])					(20 [SD])	(11.7 [SD])			
D'Agostino RB ⁴	2001	PRHHP	Men										
Berry JD ⁵	2007	CHA	Men				Tot: 189.8			78.1			
Berry JD ⁵	2007	CHA	Older	34.5		44.7	Tot: 199.4	0	134.8	79.8			
			(30-39)	(2.9 [SD])					(15.7 [SD])	(10.5 [SD])			
Berry JD ⁵	2007	CHA	Younger	25		49.4	Tot: 180	0	133.9	76.3			
			(18-29)	(3 [SD])					(14.8 [SD])	(10 [SD])			
D'Agostino RB°	2008	FRS, FRS-O	Men	48.5		35.2	HDL: 44.9		129.7			10.1	
				(10.8 [SD])			Tot: 212.5		(17.6 [SD])				
D'Agostino RB ⁴	2001	FRS, FRS-O	Men	48.3		40		5			40		
Liao Y ¹	1999	NHANES I	Men	53.2		41.6			135.6	86.2			
				(10.5 [SD])					(19.7 [SD])	(11.5 [SD])			
Gaizano TA ⁸	2008	NHANES-I EFS	Men	48.3		36.2	Tot: 218.9	3.56	133.8			7.65	
				(14 [SD])					(19.8)				
Liao Y ¹	1999	NHANES II	Men	54.3		37.7			133.4	84.6			
				(10.5 [SD])					(19.3 [SD])	(11.4 [SD])			
Miyasaka Y ⁹	2007	Mayo	Men									35.2	65.5
Vaidya D ¹⁰	2007	JHSS	Men	45.2	W: 88.7		LDL: 149.9		131.7	82.6			39.9
				(7.3 [SD])	B: 11.3		HDL: 44.6		(16.8 [SD])	(9.9 [SD])			
							Tot: 232.8						
Mainous AG ¹¹	2008	ARIC	Men	60		18.7	HDL: 45.5	0	124				
							Tot: 200						
Chambless LE ¹²	2004	ARIC	Men										
D'Agostino RB ⁴	2001	ARIC	Men								17.9		
D'Agostino RB ⁴	2001	ARIC	White	54.6		24		6			13		
-			men										

First	Year	Cohort		Mean	Race	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
D'Agostino RB ⁴	2001	ARIC	Black	53.7		38		14			34		
			men										
Mainous AG ¹⁴	2007	ARIC	Men	54.4	W: 77	27.5					14.7	23.5	
				(5.7 [SD])	B: 23								
McNeill AM ¹⁵	2005	ARIC	Men	54		29.6	LDL: 139				39.9		
				(5.7 [SD])									
D'Agostino RB ⁴	2001	CHS	Men	69.7		12		15			35		
D'Agostino RB ⁴	2001	SHS	Men	55.4		40		42			27		
Lee ET ¹⁶	2006	SHS	Men	55.5			LDL: 118.9	39.7	128	79.4			
							Tot: 189.3						

Table 3c. Data Sources Details (Primary Models) - Americas Women

First	Year	Cohort		Mean	Race	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Liao Y ¹	1999	NHANES I and	White women	52.2		29.3		4.3	132.5	81.7	42.7		
		II (pooled)		(13.8 [SD])					(23.7 [SD])	(11.9 [SD])			
Liao Y ¹	1999	NHANES I and	Black women	50.9		32.8		7.1	141.2	87.2	62.5		
		II (pooled)		(13.8 [SD])					(27.9 [SD])	(14.1 [SD])			
Wilson PWF ²	1998	FRS, FRS-O	Women			37.7	LDL: 140.8	4			30	10.7	
							HDL: 57.7						
Liao Y ¹	1999	FRS	Women	49.9		38.1			133.6	82.7			
				(8.5 [SD])					(24.7 [SD])	(12.3 [SD])			
D'Agostino RB ⁶	2008	FRS, FRS-O	Women	49.1		34.2	HDL: 57.6		125.8			11.8	
				(11.1 [SD])			Tot: 215.1		(20 [SD])				
D'Agostino RB ⁴	2001	FRS, FRS-O	Women	49.6		38		4			29		
Liao Y ¹	1999	NHANES I	Women	51.2		30.7			133.9	83.2			
				(11.0 [SD])					(23.4 [SD])	(11.9 [SD])			
Gaizano TA [®]	2008	NHANES-I EFS	Women	47.4		48.5	Tot: 222.5	4.09	131 (23.3)			11.41	
				(14.1[SD])									
Liao Y'	1999	NHANES II	Women	54.7		29.7			131.5	81.4			
				(10.5 [SD])					(22 [SD])	(11.7 [SD])			
Miyasaka Y [®]	2007	Mayo	Women									51.7	81.1
Vaidya D ¹⁰	2007	JHSS	Women	46.1	W: 77.6		LDL: 155.1		134.5	86.9			50.8
				(7.4 [SD])	B: 22.4		HDL: 56.3		(13.8 [SD])	(9.4 [SD])			
		4.510					1 ot: 232.3		100				
Mainous AG''	2008	ARIC	Women	59.5		17	HDL: 60.3	0	122				
	0001	4.510	14/1 1	50.0		05	Tot: 213						
D'Agostino RB	2001	ARIC	White women	53.9		25		6			11		
D'Agostino RB ⁺	2001	ARIC	Black women	53.3		25		17			28		
D'Agostino RB*	2001	ARIC	Women								15.9		
Mainous AG	2007	ARIC	Women	53.8	W: 71.1	24.8					14.9	32	
		4.510		(5.7 [SD])	B: 28.9		1.51. (0.5						
McNeill AM ¹⁰	2005	ARIC	Women	54		24.7	LDL: 135				38.5		
		0.110		(5.7 [SD])									
D'Agostino RB ⁺	2001	CHS	Women	69.3		15		10			33		
D'Agostino RB*	2001	SHS	Women	56.5		30		51			24		

First	Year	Cohort		Mean	Race	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Lee ET ¹⁶	2006	SHS	Women	56.6			LDL: 117.7	46.7	127.3	75			
							Tot: 192.3						

Table 3d. Data Sources Details (Primary Models) – Europe All

First	Year	Cohort		Mean	Race	Female	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Assmann G ²⁶	2007	PROCAM	All			29.4			6.2					
Assmann G ²⁷	2002	PROCAM	All	46.7		0	31.1	LDL: 148.5	6.7	131.4				
				(7.5 [SD])				HDL: 45.7		(18.4 [SD])				
Bastuji-Garin S ³⁷	2002	INSIGHT	All	64.1		55.3	32		19	166		100		
				(1.6 [SD])						(15 [SD])				
Becker A ⁴¹	2008	LudwigU	All	57.7 (13.3 [SD])		41	34.1		17			52		
Bernard S ²¹	2005	Lyon	All	55.5 [%]		35.4	23.1	LDL: 136.5 Tot: 74.1	100			47.6	25.8	
Cederholm J ⁴³	2008	SNDR	All			43.1	17.8		100	144.5 (18.1 [SD])				
Cooper JA ³¹	2005	NPHS-II	All		W: 100	0			2.1	· · · · ·				
de Ruijter W ⁴²	2009	L85	All			70.7			14.2	154* (144, 167 [IQR])				
Donnan PT ³⁹	2006	DARTS	All	59.5 (12.1 [SD])	W: 99 O: 1	47.4	23.5	Tot: 210.6	100	144 (21 [SD])	82 (11 [SD])		61.9	
Dunder K ²²	2004	ULSAM	All			0	54.5	LDL: 208.65 Tot: 277.29	1.5	132 (18 [SD])	83 (11 [SD])			
Erikssen G ²⁴	2004	NorGov	All	49.8 (5.5 [SD])		0	43.8	Tot: 261.3	0	130.1 (17.9 [SD])			0	
Ferrario M ²⁹	2005	CUORE	All	50.8 (9.2 [SD])		0	39	HDL: 50.2	5	138.5 (20.5 [SD])			10	
Hippisley-Cox J ³⁴	2008	QRESEARCH	All		W: 95.8 B: 0.8 O: 3.4	75.4	25.3		2.9				6.3	
Hippisley-Cox JC ⁴⁰	2007	QRESEARCH (Val)	All			50.3	25.5	Tot: 226.2	0	133.9			10.6	
Macfarlane PW ³²	2007	WOSCOPS	All	55.2		0	44	LDL: 192 HDL: 44	1.2	135.5	84	15.7		
Marrugat J ³⁸	2007	VERIFICA	All	56.3		57.3	24.7	HDL: 53.7	16.4	135.1	81.3	44.8	30.9	
May MD ⁴⁴	2006	BWHH	All	68.6 (5.5 [SD])		100		Tot: 257.4	4.4	148 (25 [SD])				
Reissigova J ²⁵	2007	STULONG	All	51.2 (3.7 [SD])		0			0			54.8		
Simmons RK ³⁵	2008	EPIC-Norfolk	All	57.9		56.2	11.9	HDL: 56.7 Tot: 235.9	2.8	134.5				
Stephens JW ³³	2004	NHS Trust	All		W: 69 B: 5 O: 26	36	19.5		100					

First	Year	Cohort		Mean	Race	Female	Smoker	Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med	HTN or HTN
Author	Published	Abbreviation	Group	Age (yrs)	(%)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)	Med Use (%)
Strom Moller C ²³	2007	ULSAM (70)	All	71		0	20.8	LDL: 152.1		146.8				
				(0.6 [SD])				Tot: 226.2		(18.5 [SD])				
Vergnaud AC ³⁶	2008	SU.VI.MAX	All	52		0		LDL: 152.1	2.4	129.4	83.5			
-				(4.7 [SD])				Tot: 241.8		(13.8 [SD])	(8.5 [SD])			
Woodward M ³⁰	2007	SHHEC	All	48.8		50.8	41	Tot: 245.7	1.4	131.9				

* Median.

Table 3e. Data Sources Details (Primary Models) - Europe Men

First Author	Year Published	Cohort Abbreviation	Mean Age (yrs)	Smoker (%)	Mean Cholesterol Level (mg/dL)	Diabetes (%)	Mean SBP (mmHg)	Mean DBP (mmHg)	HTN (%)	HTN Med Use (%)
Cederholm J ⁴³	2008	SNDR		18.5		100	143.9 (17.4 [SD])			
Hippisley-Cox J ³⁴	2008	QRESEARCH (Derivation)	48* (40-58 [IQR])							5.6
Hippisley-Cox J ³⁴	2008	QRESEARCH		27.6						
Hippisley-Cox J ³⁴	2008	QRESEARCH (Validation)	47* (40-57 [IQR])							5.4
Hippisley-Cox JC ⁴⁰	2007	QRESEARCH Validation)	47* (40-57 [IQR])		Tot: 222.3	0	135.4 (19.7 [SD])			8.5
Marrugat J ³⁸	2007	VERIFICA	55.7 (10.6 [SD])	43.8	HDL: 48.5 Tot: 228.8	18.8	135 (17.8 [SD])	81.9 (10.3 [SD])	41.6	27.1
Simmons RK ³⁵	2008	EPIC-Norfolk	58.3 (9.7 [SD])		HDL: 50 Tot: 232		136.8 (17 [SD])			
Stephens JW ³³	2004	NHS Trust				100				
Woodward M ³⁰	2007	SHHEC	48.9		Tot: 242.97	1.5	133.8 (0.2 [SD])			

* Median.

Table 3f. Data Sources Details (Primary Models) – Europe Women

First	Year	Cohort	Mean Age	Smoker	Mean Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med
Author	Published	Abbreviation	(yrs)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)
Woodward M ³⁰	2007	SHHEC	48.8		Tot: 249.99	1.4	130.1			
							(0.3 [SD])			
Woodward M ³⁰	2007	SHHEC	48.8		Tot: 249.99	1.3	130.1			
							(0.3 [SD])			
Stephens JW ³³	2004	NHS Trust				100				
Hippisley-Cox J ³⁴	2008	QRESEARCH		23.1						
Hippisley-Cox J ³⁴	2008	QRESEARCH	49*							6.9
		(Validation)	(41-59 [IQR])							
Hippisley-Cox J ³⁴	2008	QRESEARCH	49*							7.1
		(Derivation)	(41-60 [IQR])							
Simmons RK ³⁵	2008	EPIC-Norfolk	57.6		HDL: 62		132.7			
			(9.6 [SD])		Tot: 239		(18.7 [SD])			

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First	Year	Cohort	Mean Age	Smoker	Mean Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med
Author	Published	Abbreviation	(yrs)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)
Marrugat J ³⁸	2007	VERIFICA	56.8	10.6	HDL: 57.6	14.6	135.2	80.9	47.2	33.7
			(10.4 [SD])		Tot: 234.1		(18.8 [SD])	(10.8 [SD])		
Hippisley-Cox JC ⁴⁰	2007	QRESEARCH	49*		Tot: 230.1	0	132.4			12.6
		Validation)	(41-59 [IQR])				(21.6 [SD])			
Cederholm J ⁴³	2008	SNDR		16.8		100	145.2			
							(19.0 [SD])			

* Median.

Table 3g. Data Sources Details (Primary Models) – Asia All

First	Year	Cohort	Group	Mean Age	Race	Female	Smoker	Mean Cholesterol	Diabetes	Mean SBP	Mean DBP	HTN	HTN Med
Author	Published	Abbreviation		(yrs)	(%)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(mmHg)	(%)	Use (%)
Barzi F ⁴⁵	2007	APCSC China	All	46.6	O: 100	41.4	42.8	Tot: 175.5		120.6			
Jee SH ⁴⁶	2008	NHIC	All	46.6	O: 100	36.5	39	Tot: 192.5	4.5	123.4		33.3	
Liu J ⁴⁷	2004	MUCA	All		O: 100	46.7	33.3		5.5			25.7	
	2006	MUCA II	All	46	50.6	45				119	77		
Wu Y ⁴⁸				(6 [SD])						(19 [SD])	(11 [SD])		
	2008	HKD Registry	All	57*	O: 100	54.6	20.6		100	134*	76*		33.7
Yang X ⁴⁹				(21 [IQR])						(27 [IQR])	(14 [IQR])		
	2007	HKD Registry	Stroke	68*						144*	77*		34.2
Yang X ⁵⁰				(12 [IQR])						(30 [IQR])	(14 [IQR])		
	2007	HKD Registry	Non-stroke	56*						133*	76*		46
Yang X ⁵⁰				(20 [IQR])						(27 [IQR])	(14 [IQR])		
Yang X ⁵⁰	2007	HKD Registry	All		O: 100	54.5	20.3		100				45.4

*Median.

Table 3h. Data Sources Details (Primary Models) – Asia Men

First	Year	Cohort		Mean Age	Race	Smoker	Mean Cholesterol	Diabetes	Mean SBP	HTN
Author	Published	Abbreviation	Group	(yrs)	(%)	(%)	Level (mg/dL)	(%)	(mmHg)	(%)
Barzi F45	2007	APCSC China	Men	47	O:100	68.4	Tot: 175.5		121	
				(8 [SD])					(18 [SD])	
Jee SH ⁴⁶	2008	NHIC	Men	45	O:100	59.1	Tot: 191.3	4.8	124.5	35.7
				(11.0 [SD])					(16.0 [SD])	
Liu J ⁴⁷	2004	MUCA	Men		O:100	59		6.9		29

Table 3i. Data Sources Details (Primary Models) - Asia Women

First	Year	Cohort	Group	Mean Age	Race (%)	Smoker	Mean Cholesterol	Diabetes	Mean SBP	HTN
Author	Published	Abbreviation		(yrs)		(%)	Level (mg/dL)	(%)	(mmHg)	(%)
Barzi F45	2007	APCSC China	Women	46	O:100	6.5	Tot: 171.6		120	
				(8 [SD])					(20 [SD])	
Jee SH ⁴⁶	2008	NHIC	Women	49.4	O:100	4.1	Tot: 194.5	4.1	121.5	29.2
				(12.1 [SD])					(19.1 [SD])	
Liu J ⁴⁷	2004	MUCA	Women		O:100	4		5		22

		Model	Study					Followup
Model Name	Model Outcome	Pub Year	Count	Cohort Abbrev	Enroll Start	Enroll End	Enrollment	Duration
ASSIGN ³⁰	CVD 11	2007	2	SHHEC	01/01/1984	12/31/1995	13297	
DARTS ³⁹	Hard CHD 1	2006	2	DARTS	01/01/1995	06/30/2004	4569	4.1
FINRISK	CVD	2005	4	FINRISK			14694	
FRS (1991) ^{51, 52}	CVD 2	1991	26	FRS, FRS-O	01/01/1948	12/31/1975	5573	12
FRS (1991) ^{51, 52}	Total CHD 1	1991	5	FRS, FRS-O	01/01/1948	12/31/1975	5573	12
FRS (1991) Stroke ^{51, 52}	Stroke 4	1991	3	FRS, FRS-O	01/01/1948	12/31/1975	5573	12
FRS (ATP) ⁴	Hard CHD 1	2001	16	FRS, FRS-O				
FRS (Custom 4 Variable) ³	CHD Mortality	1999	3	FRS	01/01/1954	12/31/1958	4169	24
FRS [LDL] (1998) ²	Total CHD 1	1998	2	FRS, FRS-O	01/01/1948	12/31/1974	5345	12
FRS [TC] (1998) ²	Total CHD 1	1998	10	FRS, FRS-O	01/01/1948	12/31/1974	5345	12
FRS [Unknown Version] (1998) ²	Total CHD 1	1998	12	FRS, FRS-O	01/01/1948	12/31/1974	5345	12
FRS Hard CHD [TC] (1998) ²	Hard CHD 1	1998	3	FRS, FRS-O	01/01/1948	12/31/1974	5345	12
PROCAM CHD (Cox model) ²⁷	Hard CHD 1	2002	11	PROCAM	01/01/1979	12/31/1985	5159	10
QRISK ⁴⁰	CVD 4	2007	4	QRESEARCH	01/01/1995	04/01/2007	614553	6.5
SCORE (High Risk TC) ⁵³	CVD Mortality	2003	2	SCORE			205178	
SCORE (Low Risk TC) ⁵³	CVD Mortality	2003	3	SCORE			205178	
SCORE (Unknown Version) ⁵³	CVD Mortality	2003	6	SCORE			205178	
UKPDS 56 ⁵⁴	Hard CHD 1	2001	5	UKPDS			4540	
UKPDS 60 ⁵⁴	Stroke 1	2002	2	UKPDS	01/01/1977	12/31/1991	4549	10.5

Primary Models With at Least One External Validation*

*Models in italics are not counted as separate models as they were underspecified in the source manuscript; thus, the exact version of the model that was used could not be determined.

Primary Models With No External Validation*

	Model	Model					Follow-up
Model Name	Outcome	Pub Year	Cohort Abbrev	Enroll Start	Enroll End	Enrollment	Duration
ARIC ¹³							
Version 1: Basic risk factors							
Version 2: Basic & DM-Specific risk factors							
SubVersion A: liberal definition of DM							
SubVersion B: restrictive definition of DM							
Version 3: DM-Specific risk factors							
SubVersion A: liberal definition of DM							
SubVersion B: restrictive definition of DM	Hard CHD 2	2003	ARIC	01/01/1987	12/31/1989	14054	10.2
ATP-III (Remodel) + genotype ⁵⁵	CVD 3	2009	WGHS	01/01/1992	03/31/2004	22129	10.2
Chicago Young Adults⁵	CHD Mortality	2007	CHA	01/01/1967	01/31/1973	10375	32
ARIC Stroke (Chambless) ¹²							
Version 1: Basic							
Version 2: Basic + Age + Race							
Version 3: Basic + NTRF + Age + Race	Stroke 3	2004	ARIC	01/01/1987	12/31/1989	13161	12.3
CMCS Cox Model ⁴⁷	Hard CHD 1	2004	MUCA	01/01/1992	12/31/1999	30121	
CRM ³³	CVD	1999	NHS Trust	01/01/1990	12/31/1991	798	
CUORE ²⁹	Hard CHD 2	2005	CUORE	01/01/1983	12/31/1996	6865	9.1
D'Agostino CVD FEMALE ⁶	CVD 2	2008	FRS, FRS-O	01/01/1968	12/31/1987	8491	
SBHW (Detrano) ¹⁸	Hard CHD 1	1999	SBHW	12/01/1990	12/31/1992	1194	3.42

	Model	Model					Follow-up
Model Name	Outcome	Pub Year	Cohort Abbrev	Enroll Start	Enroll End	Enrollment	Duration
Version 1: Data Derived							
Version 2: Data Derived + Ca							
Dubbo model ⁵⁶	CVD 4	2003	DUBBO-All	01/01/1988		2102	
WOSCOPS ³²							
Version 1: ECG + Age, smoking only							
Version 2: ECG + Clinical Vars							
Version 3: ECG + Age	MI	2007	WOSCOPS	01/01/1989	12/31/1991	6595	4.9
Erikssen NorGov ²⁴							
Version 1: CRF Model							
Version 2: CRF-X Model							
Version 3: X Model	CHD Mortality	2004	NorGov	08/28/1972	03/30/1975	2014	26
European Society of Cardiology (ESC)	Total CHD 1	1994	FRS, FRS-O	01/01/1948	12/31/1975	5573	12
FRS (1991) CHD Mortality	CHD Mortality	1991	FRS, FRS-0	01/01/1948	12/31/1975	5573	12
EPIC-Norfolk HgbA1c ^{oo}							
Version 1: FRS '98 Vars + HgbA1c	Total CUD 1	2008		02/01/1002	02/28/1008	10205	0.5
Version 2: FRS 96 vars w/o Divi + HgbATC FRS (2004 ATR) + $CACS^{1/2}$		2006		03/01/1993	02/28/1998	10295	0.0 7
FRS(2001ATP) + CACS		2004		01/01/1990	12/31/1992	1029	1
FRS(2007 Barzi)	CVD 8	2007		01/01/1948	12/31/1974	5345	12
NUANES EES L (Cariana) ⁸		2007	ULSAWI (70)	01/01/19/0	12/31/19/3	1221	23
Version 1: Lab Based Medel							
Version 2: Non Lab Based Model		2008		01/01/1071	12/21/1002	6196	21
Hong Kong Disbotos Pisk Score ⁵⁰	Stroko 1	2008	HKD Pogistry	01/01/19/1	07/20/2005	2541	5 27
Hong Kong Total CHD Score ⁴⁹		2007		01/01/1995	01/30/2003	7067	5.37
		1008	NHS Truet	01/01/1993	12/31/1001	7007	5.4
Korean Stroke Risk Prediction (KSRR) ⁴⁶	Stroke 6	2008	NHIC	01/01/1990	12/31/1991	1205268	13
Metabolic Syndrome Model ¹⁵	Hard CHD 2	2005	ARIC	01/01/1992	12/31/1995	1203200	13
Miyasaka CHD Post-AF ⁹	Total CHD 1	2003	Mayo	01/01/1980	12/31/2000	2768	6
New Zealand risk charts ⁵⁸		1006	Wayo	01/01/1300	12/31/2000	2700	0
NHANES I (4 Variables) ³	CHD Mortality	1990	NHANESI	01/01/1971	12/31/1075	6611	20
NHANES Land IL pooled ³	CHD Mortality	1000	NHANES Land II (pooled)	01/01/13/1	12/31/19/3	185/2	20
NHANES II (4 Variable) ³	CHD Mortality	1999		01/01/1976	12/31/1980	5705	15
NPHS-II ³¹	OT ID Wortdarty	1000		01/01/10/0	12/01/1000	0100	10
Score 1 (basic)							
Score 2 (basic + DM + Fam Hx)							
Score 3 (basic + DM)							
Score 4 (basic + Fam Hx)							
Score 5 (basic + Fibrinogen)							
Score 6 (basic + Lipoprotein A)							
Score 7 (basic + ApoAI + ApoB)	Hard CHD 2	2005	NPHS-II	01/01/1989		2732	10.8
Personal HEART ¹⁴	Hard CHD 2	2007	ARIC	01/01/1987	12/31/1989	14343	
PROCAM (BMI-modified) ²⁸	Hard CHD 1	2008	PROCAM	01/01/1979	12/31/1999	7134	10
PROCAM CHD (Point Score) ²⁷	Hard CHD 1	2002	PROCAM	01/01/1979	12/31/1985	5159	10
PROCAM CHD (Weibull model) ²⁶	Hard CHD 1	2007	PROCAM	01/01/1978	12/31/1995	7295	12
PROCAM Stroke (Cox model) ²⁶	Stroke 2	2007	PROCAM	01/01/1978	12/31/1995	7295	12
QRISK2 ³⁴	CVD 1	2008	QRESEARCH	01/01/1993	03/31/2008	2285815	15
QT Dispersion ³²	Hard CHD 1	2007	WOSCOPS	01/01/1989	12/31/1991	6595	4.9

	Model	Model					Follow-up
Model Name	Outcome	Pub Year	Cohort Abbrev	Enroll Start	Enroll End	Enrollment	Duration
Reynolds Risk Score (Remodel) + genotype ⁵⁵	CVD 3	2009	WGHS	01/01/1992	03/31/2004	22129	10.2
Ridker Model A ²⁰	CVD 3	2007	WHS (Val)	09/01/1992		8158	10.2
Ridker Model A, PHS-II ⁵⁹	CVD 15	2008	PHS-II	12/01/1995		10724	10.8
Ridker Model B ²⁵	CVD 3	2007	STULONG	01/01/1975	12/31/1979	646	
SCORE (High Risk TC-HDL Ratio) ⁵³	CVD Mortality	2003	SCORE			205178	
SHS Model ¹⁶	Hard CHD 1	2006	SHS	01/01/1989	12/01/2001	4372	
Swedish NDR ⁴³	CVD 5	2008	SNDR	01/01/1998	12/31/2003	11646	5.64
ULSAM ²²	MI	2004	ULSAM	01/01/1970	12/31/1973	1108	28.7
USA-PRC (Point Scoring) ⁴⁸	CVD 17	2006	USA-PRC	09/01/1983	10/31/1984	9903	15.1
USA-PRC (Simplified) ⁴⁸	CVD 17	2006	USA-PRC	09/01/1983	10/31/1984	9903	15.1
WHS Model ¹⁹							
Version 1: Basic							
Version 2: Basic + hsCRP	CVD 3	2006	WHS	09/01/1992		15048	10
Wilson AFT CeVD ⁷							
Model A							
Model A No BMI							
Model B							
Model C							
Model D							
Model D No BMI	Stroke 2	2008	FRS-O	01/01/1971		4780	24
Wilson AFT CHD'							
Model A							
Model A No BMI							
Model B							
Model C							
Model D							
Model E							
Model E No BMI	Total CHD 1	2008	FRS-O	01/01/1971		4780	24
Wilson AFT CVD'							
Model A							
Model A No BMI							
Model B	01/10 40		550.0	04/04/4074		1700	
Model R No BMI	CVD 12	2008	FRS-0	01/01/19/1		4780	24

*Some studies have grouped models in which various variables were added and removed from candidate models in that evaluation.

Model*	AFT (A, No BMI)	AFT (A)	AFT (B)	AFT (C)	AFT (D)	AFT (E)	AFT (E, No BMI)
Outcome	First CHD						
	1.57 (1.49 - 1.64)	1.55 (1.47 - 1.62)	1.53 (1.46 - 1.61)	1.50 (1.43 - 1.58)	1.49 (1.42 - 1.57)	1.48 (1.40 - 1.56)	1.48 (1.40 - 1.56)
Age	(yrs)						
Female	0.35 (0.29 - 0.43)	0.38 (0.31 - 0.47)	0.48 (0.39 - 0.59)	0.40 (0.33 - 0.49)	0.49 (0.40 - 0.60)	0.49 (0.40 - 0.61)	0.49 (0.40 - 0.60)
			1.38 (1.30 - 1.47)		1.38 (1.30 - 1.46)	1.37 (1.29 0 1.46)	1.39 (1.31 - 1.47)
			(TotChol/HDL		(TotChol/HDL	(TotChol/HDL	(TotChol/HDL
Total Cholesterol			mg/dL)		mg/dL)	mg/dL)	mg/dL)
Body Mass Index		1.28 (1.17 - 1.39)	1.17 (1.07 - 1.28)	1.21 (1.11 - 1.33)	1.11 (1.01 - 1.23)	1.10 (1.00 - 1.21)	
				1.18 (1.08 - 1.27)	1.18 (1.09 - 1.28)	1.17 (1.08 - 1.28)	1.20 (1.11 - 1.30)
Systolic BP				(mmHg)	(mmHg)	(mmHg)	(mmHg)
						1.60 (1.16 - 2.21)	1.66 (1.20 - 2.28)
						(fasting glucose	(fasting glucose
Diabetes Mellitus						≥126 or Med use)	≥126 or Med use)
	2.01 (1.68 - 2.41)	2.09 (1.74 - 2.50)	1.91 (1.60 - 2.29)	2.13 (1.78 - 2.55)	1.97 (1.64 - 2.36)	1.97 (1.64 - 2.36)	1.95 (1.63 - 2.33)
Smoker	(Current)						

Table 5a. Model Parameters – Accelerated Failure Time (First CHD)⁷

Table 5b. Model Parameters – Accelerated Failure Time (First CeVD)⁷

Model	AFT (A, No BMI)	AFT (A)	AFT (B)	AFT (C)	AFT (D)	AFT (D, No BMI)
Outcome	First CeVD					
Age	1.70 (1.53 - 1.89) (yrs)	1.66 (1.49 - 1.85) (yrs)	1.64 (1.48 - 1.83) (yrs)	1.59 (1.42 - 1.78) (yrs)	1.58 (1.41 - 1.77) (yrs)	1.58 (1.42 - 1.77) (yrs)
			1.20 (1.03 - 1.40)		1.19 (1.03 - 1.39)	1.23 (1.07 - 1.42)
Total Cholesterol			(TotChol/HDL mg/dL)		(TotChol/HDL mg/dL)	(TotChol/HDL mg/dL)
Body Mass Index		1.35 (1.15 - 1.59)	1.29 (1.09 - 1.54)	1.26 (1.06 - 1.49)	1.21 (1.01 - 1.44)	
				1.25 (1.06 - 1.47)	1.24 (1.05 - 1.47)	1.30 (1.11 - 1.52)
Systolic BP				(mmHg)	(mmHg)	(mmHg)
	1.56 (1.07 - 2.26)	1.62 (1.12 - 2.36)	1.54 (1.06 - 2.24)	1.67 (1.15 - 2.44)	1.60 (1.10 - 2.32)	1.56 (1.07 - 2.27)
Smoker	(Current)	(Current)	(Current)	(Current)	(Current)	(Current)

Table 5c. Model Parameters – Accelerated Failure Time (Total CVD)⁷

Model	AFT (A, No BMI)	AFT (A)	AFT (B)	AFT (B, No BMI)
Outcome	Total CVD	Total CVD	Total CVD	Total CVD
Age	1.59 (1.52 - 1.65) (yrs)	1.56 (1.50 - 1.63) (yrs)	1.49 (1.42 - 1.55) (yrs)	1.49 (1.43 - 1.55) (yrs)
Female	0.42 (0.36 - 0.49)	0.46 (0.39 - 0.54)	0.58 (0.49 - 0.69)	0.57 (0.49 - 0.68)
			1.32 (1.25 - 1.40)	1.34 (1.27 - 1.41)
Total Cholesterol			(TotChol/HDL mg/dL)	(TotChol/HDL mg/dL)
Body Mass Index		1.27 (1.18 - 1.37)	1.09 (1.01 - 1.18)	
			1.23 (1.15 - 1.32)	1.25 (1.17 - 1.33)
Systolic BP			(mmHg)	(mmHg)
			1.66 (1.26 - 2.20)	1.73 (1.31 - 2.28)
			(fasting glucose ≥126	(fasting glucose ≥126
Diabetes Mellitus			or Med use)	or Med use)
	2.01 (1.73 - 2.34)	2.08 (1.79 - 2.42)	2.01 (1.72 - 2.34)	1.99 (1.70 - 2.31)
Smoker	(Current)	(Current)	(Current)	(Current)

Model	ARIC 87-00 (Men)	ARIC 87-00 (Women)
Outcome	Ischemic Stroke	Ischemic Stroke
Age	2.24 (1.76 - 2.86) (Age/10)	1.99 (1.52 - 2.62) (Age/10)
Race (Black)	1.42 (1.07 - 1.89)	1.52 (1.10 - 2.08)
Systolic BP	1.45 (1.28 - 1.63) (mmHg)	1.42 (1.25 - 1.61) (mmHg)
Hypertension	1.58 (1.21 - 2.06) (Med use)	1.50 (1.10 - 2.06) (Med use)
Diabetes Mellitus	2.43 (1.83 - 3.23) (fasting glucose ≥126, nonfasting ≥200)	3.12 (2.26 - 4.29) (fasting glucose ≥126, nonfasting ≥200)
Smoker	2.00 (1.54 - 2.60) (Current)	2.23 (1.64 - 3.03) (Current)
Left Ventricular Hypertropy	1.47 (0.84 - 2.57)	2.24 (1.35 - 3.74)
Previous Coronary Heart Disease	2.08 (1.47 - 2.95)	1.88 (0.98 - 3.58)

Table 5d. Model Parameters – Atherosclerosis Risk in Communities^{4,11-13,15}

Table 5e. Model Parameters – Adult Treatment Panel/Agatston Calcium Score⁶⁰

Model	ATP/Agatston Calcium Score
Hyperlipidemia (Undefined)	2.89 (1.49 - 2.28)
Hypertension	1.97 (1.53 - 2.10) (Arterial, undefined)
Diabetes Mellitus	3.21 (2.11 - 3.89) (Undefined)
Smoker	2.31 (1.59 - 2.71) (Current)
Agatston > 75th percentile	5.2 (4.03 - 6.37)

Table 5f. Model Parameters – CUORE²⁹

Model	CUORE (Men)
Age	1.065 (1.050 - 1.081) (yrs)
Total Cholesterol	1.093 (1.091 - 1.096) (mg/dL)
HDL	0.884 (0.876 - 0891) (mg/dL)
Systolic BP	1.092 (1.086 - 1.098) (mmHg)
Hypertension	1.833 (1.354 - 2.483) (Med use)
Diabetes Mellitus	1.521 (1.034 - 2.238) (self report, FBG ≥126 or Med use)
Smoker	1.876 (1.495 - 2.353) (Current)
Family History	1.377 (1.059 - 1.791) (CVD)

Table 5g. Model Parameters – Framingham Risk Score^{4,6}

Model	FRS D'Agostino (Men)	FRS D'Agostino (Women)
Age	21.35 (14.03 - 32.48) (Natural Log Age yrs)	10.27 (5.65 - 18.64) (Natural Log Age yrs)
Total Cholesterol	3.08 (2.05 - 4.62) (Natural Log Total mg/dL)	3.35 (2.00 - 5.62) (Natural Log Total mg/dL)
HDL	0.39 (0.30 - 0.52) (Natural Log HDL mg/dL)	0.49 (0.35 - 0.69) (Natural Log HDL mg/dL)
	6.91 (3.91 - 12.20) (Natural Log SBP mmHg NoMedTx)	15.82 (7.86 - 31.87) (Natural Log SBP mmHg NoMedTx)
Systolic BP	7.38 (4.22 - 12.92) (Natural Log SBP mmHg MedTx)	16.82 (8.46 - 33.46) (Natural Log SBP mmHg MedTx)
Diabetes Mellitus	1.78 (1.43 - 2.20) (≥140 mg/dL orig, ≥126 offspring, or Med use)	2.00 (1.49 - 2.67) (≥140 mg/dL orig, ≥126 offspring, or Med use)
Smoker	1.92 (1.65 - 2.24) (Current)	1.70 (1.40 - 2.06) (Current)

Table 5h. Model Parameters – HEART (ARIC)¹⁴

Model	HEART [ARIC] (Men)	HEART [ARIC] (Women)
	REF (45-49)	REF (45-49)
	1.15 (0.87 - 1.52) (50-54)	1.57 (1.07 - 2.30) (50-54)
	1.63 (1.26 - 2.12) (55-59)	2.04 (1.40 - 2.96) (55-59)
Age	1.94 (1.50 - 2.51) (60-64)	2.27 (1.55 - 3.32) (60-64)
Hx of Hypercholesterolemia (Pt Report)	1.54 (1.26 - 1.88)	1.58 (1.22 - 2.06)
		REF (<30)
Body Mass Index		1.47 (1.14 - 1.90) (≥30)
Hypertension	1.44 (1.20 - 1.72) (Hx, Pt Report)	2.43 (1.86 - 3.16) (Hx, Pt Report)
Diabetes Mellitus	1.86 (1.42 - 2.44) (Self report)	3.68 (2.74 - 4.96) (Self report)
	REF (Never)	REF (Never)
	1.60 (1.26 - 2.02) (Current)	3.22 (2.47 - 4.22) (Current)
Smoker	1.15 (0.92 - 1.44) (Former)	0.99 (0.69 - 1.42) (Former)
Family History	1.52 (1.09 - 2.10) (CVD)	
	REF (Often/Very Often)	
	1.16 (0.88 - 1.55) (Sometimes)	
Physical Activity	1.39 (1.08 - 1.79) (Seldom/Never)	

Table 5i. Model Parameters – Hong Kong^{49,50}

Model	Hong Kong	Hong Kong
Outcome	CHD	CHD
Age	1.03 (1.01 - 1.04) (yrs)	1.07 (1.05 - 1.08) (yrs)
Female	0.70 (0.51 - 0.97)	
non-HDL Cholesterol (mmol/L)	1.30 (1.15 - 1.48)	
Diabetes Mellitus	1.04 (1.02 - 1.06) (yrs Dx)	1.09 (1.02 - 1.18) (HgbA1c %)
log10	0.62 (0.40 - 0.95) (EGFR) 1.13 (1.03 - 1.25) (1+albumin/creatinine ratio)	1.70 (1.45 - 2.00) (albumin/creatinine ratio)
Smoker	1.55 (1.08 - 2.22) (Current)	
Previous Coronary Heart Disease		1.76 (1.15 - 2.69)

Table 5j. Model Parameters – Intervention as a Goal in Hypertension Treatment³⁷

Model	INSIGHT (Italy)	INSIGHT (Spain)	INSIGHT (France)	INSIGHT (Scandinavia)	INSIGHT (Netherlands)	INSIGHT (UK)
Ago	1.034 (0.961 - 1.113)	1.067 (0.981 - 1.160)	1.066 (0.997 - 1.141)	0.991 (0.893 - 1.100)	1.096 (1.016 - 1.181)	1.011 (0.975 - 1.049)
Age	(yrs)	(yrs)	(yrs)	(yrs)	(yrs)	(yrs)
Female	0.720 (0.302 - 1.717)	0.411 (0.159 - 1.059)	0.478 (0.223 - 1.025)	0.421 (0.135 - 1.311)	0.376 (0.161 - 0.877)	0.807 (0.539 - 1.208)
Total	1.303 (1.045 - 1.625)	1.364 (1.002 - 1.858)	1.083 (0.866 - 1.354)	0.919 (0.630 - 1.340)	1.295 (1.063 - 1.578)	1.221 (1.099 - 1.356)
Cholesterol	(TotChol/HDL mg/dL)					
	1.000 (0.972 - 1.028)	1.014 (0.987 - 1.042)	0.988 (0.960 - 1.018)	1.000 (0.970 - 1.031)	0.999 (0.977 - 1.022)	1.011 (0.999 -1.024)
Systolic BP	(mmHg)	(mmHg)	(mmHg)	(mmHg)	(mmHg)	(mmHg)
	1.270 (0.496 - 3.254)	1.174 (0.449 - 3.071)	2.850 (1.351 - 6.013)	1.187 (0.319 - 4.423)	0.925 (03.09 - 2.773)	1.640 (0.983 - 2.733)
Diabetes	(Med use or FBG ≥140	(Med use or FBG	(Med use or FBG	(Med use or FBG ≥140	(Med use or FBG ≥140	(Med use or FBG ≥140
Mellitus	mg/dL)	≥140 mg/dL)	≥140 mg/dL)	mg/dL)	mg/dL)	mg/dL)
	2.214 (0.912 - 4.946)	1.256 (0.404 - 3.910)	1.482 (0.670 - 3.275)	1.783 (0.579 - 5.490)	1.444 (0.643 - 3.242)	1.248 (0.811 - 1.920)
Smoker	(Current)	(Current)	(Current)	(Current)	(Current)	(Current)

Model	KSRP (Men)	KSRP (Women)
Age	1.085 (1.083 - 1.086) (yrs)	1.082 (1.079 - 1.084) (yrs)
	REF (<200 mg/dL)	REF (<200 mg/dL)
	1.062 (1.023 - 1.104) (200-239 mg/dL)	1.023 (0.973 - 1.076) (200-239 mg/dL)
Total Cholesterol	1.193 (1.133 - 1.256) (≥240 mg/dĽ)	1.131 (1.065 - 1.202) (≥240 mg/dL)
Body Mass Index	1.032 (1.025 - 1.038)	1.022 (1.015 - 1.029)
Systolic BP	1.022 (1.021 - 1.023) (mmHg)	1.016 (1.015 - 1.017) (mmHg)
Diabetes Mellitus	1.800 (1.710 - 1.895) (fasting glucose ≥126 mg/dL)	1.943 (1.813 - 2.083) (fasting glucose ≥126 mg/dL)
	REF (Never)	REF (Never)
	1.319 (1.261 - 1.380) (Current)	1.368 (1.268 - 1.476) (Current)
Smoker	0.976 (0.926 - 1.029) (Former)	1.112 (1.005 - 1.231) (Former)
	1.070 (1.002 - 1.144) (0g/day)	
	0.972 (0.915 - 1.033) (1-24g/day)	
	REF (25-49g/day)	
	1.116 (1.017 - 1.224) (50-99g/day)	REF (0g/day)
Alcohol Intake	1.179 (1.030 - 1.349) (100+g/day)	1.016 (0.954 - 1.083)25-49g/day)
Physical Activity	1.072 (1.034 - 1.111) ("Do you exercise regularly?" Yes/No)	1.074 (1.014 - 1.139) ("Do you exercise regularly?" Yes/No)

Table 5k. Model Parameters – Korean Stroke Risk Prediction⁴⁶

Table 5I. Model Pparameters – Miyasaka Post-Arterial Fibrillation⁹

Model	Miyasaka Post-AF (Men)	Miyasaka Post-AF (Women)
Outcome	CHD	CHD
Age	1.32 (1.18 - 1.46) (Age/10)	1.29 (1.13 - 1.47) (Age/10)
Systolic BP	1.04 (0.96 - 1.13) (BP/10 mmHg)	1.07 (0.99 - 1.14) (BP/10 mmHg)
Hypertension	1.47 (1.02 - 2.12) (Dx, Med use, or ≥HTN Grade 1)	2.23 (1.33 - 3.73) (Dx, Med use, or ≥HTN Grade 1)
Diabetes Mellitus	1.50 (1.04 - 2.17) (Dx, Med use)	2.04 (1.47 - 2.82) (Dx, Med use)
Chronic Renal Disease (Diagnosed)	1.34 (0.91 - 1.96)	1.79 (1.17 - 2.72)
Peripheral Artery Disease (Diagnosed)	1.39 (0.85 - 2.28)	1.67 (1.12 - 2.50)
Valvular Heart Disease (>than mild stenosis/regurg		
by Echo OR prior valve repair/replacement)	1.39 (0.98 - 1.97)	1.44 (1.06 - 1.95)
Obstructive Sleep Apnea (Diagnosed)	1.97 (0.99 - 3.89)	2.43 (0.59 - 9.97)

Model	NHANES I F/U Lab	NHANES I F/U Lab	NHANES I F/U Non-Lab	NHANES I F/U Non-Lab
Outcome	Men	Women	Men	Women
Age	31.311 (22.003 - 44.558)	40.528 (26.024 - 63.115)	35.163 (24.613 - 50.235)	49.6 (32.353 - 76.041)
	(Natural Log Age yrs)	(Natural Log Age yrs)	(Natural Log Age yrs)	(Natural Log Age yrs)
Total Cholesterol	2.153 (1.504 - 3.082) (Natural Log Total mg/dL)	1.78 (1.191 - 2.661) (Natural Log Total mg/dL)		
Body Mass Index			2.068 (1.287 - 3.324)	2.332 (1.582 - 3.438)
Systolic BP	5.506 (3.393 - 8.936)	6.309 (3.79 - 10.502)	5.088 (3.111 - 8.322)	4.687 (2.777 - 7.911)
	(Natural Log BP mmHg)	(Natural Log BP mmHg)	(Natural Log BP mmHg)	(Natural Log BP mmHg)
Hypertension	1.278 (1.041 - 1.571)	1.465 (1.221 - 1.758)	1.246 (1.014 - 1.53) (Med	1.443 (1.205 - 1.728)
	(Med use)	(Med use)	use)	(Med use)
Diabetes Mellitus	1.989 (1.497 - 2.643)	2.036 (1.574 - 2.632)	1.898 (1.428 - 2.522)	1.913 (1.483 - 2.468)
	(Self report)	(Self report)	(Self report)	(Self report)
Smoker	1.728 (1.5 - 1.989)	1.734 (1.474 - 2.041)	1.764 (1.529 - 2.036)	1.77 (1.504 - 2.082)
	(Current)	(Current)	(Current)	(Current)

Table 5m. Model Parameters – National Health and Nutrition Examination Survey Followup⁸

Table 5n. Model Parameters – National Health and Nutrition Examination Survey Men/Women^{1,3}

Model	NHANES I (Men)	NHANES I (Women)	NHANES II (Men)	NHANES II (Women)
Age	1.081 (1.067 - 1.095) (yrs)	1.117 (1.097 - 1.137) (yrs)	1.124 (1.098 - 1.152) (yrs)	1.094 (1.06 - 1.13) (yrs)
Total Cholesterol	1.003 (1.002 - 1.003) (mg/dL)	1.002 (1 - 1.005) (mg/dL)	1.001 (0.998 - 1.005) (mg/dL)	1.002 (0.998 - 1.006) (mg/dL)
Systolic BP	1.014 (1.008 - 1.019) (mmHg)	1.017 (1.012 - 1.022) (mmHg)	1.016 (1.009 - 1.023) (mmHg)	1.023 (1.015 - 1.03) (mmHg)
Smoker	1.64 (1.311 - 2.051) (Current)	2.241 (1.713 - 2.932) (Current)	2.437 (1.791 - 3.316) (Current)	2.505 (1.648 - 3.807) (Current)

Table 5o. Model Parameters – Second Northwick Park Heart Study³¹

Model	NPHS-II
Age	1.19 (0.90 - 1.56) (yrs)
Total Cholesterol	1.26 (1.04 - 1.52) (mmol/L)
Triglycerides (mmol/L)	1.23 (1.02 - 1.48)
Systolic BP	1.23 (1.02 - 1.48) (mmHg)
Diabetes Mellitus	3.10 (1.41 - 6.80) (Undefined)
Smoker (Never)	1.61 (1.10 - 2.35) (Current)
Family History	1.67 (1.15 - 2.44) (CVD)
Fibrinogen (g/L)	1.29 (1.07 - 1.55)
Lipoprotein a (mg/dL)	1.60 (1.05 - 2.42)

Table 5p. Model Parameters – Prospective Cardiovascular Münster ^{26-28,6}
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Model	PROCAM
Outcome	Stroke
Age	1.12 (1.08 - 1.15) (yrs)
Female	0.54 (0.31 - 0.93)
Systolic BP	1.02 (1.01 - 1.03) (mmHg)
Diabetes Mellitus	2.07 (1.03 - 3.33) (Undefined)
Smoker	2.34 (1.52 - 3.60) (Current)

Table 5q. Model Parameters – QRISK^{34,40,62}

Model	QRISK (Men)	QRISK (Women)
Age	50.634 (47.792 - 53.646) [Log (Age/10)]	87.75 (81.34 - 94.66) [Log (Age/10)]
Total Cholesterol	1.001 (0.999 - 1.003) (TotChol/HDL mg/dL)	1.001 (0.999 - 1.002) (TotChol/HDL mg/dL)
Body Mass Index	1.022 (1.019 - 1.025)	1.015 (1.013 - 1.018)
Systolic BP	1.004 (1.004 - 1.005) (mmHg)	1.005 (1.004 - 1.005) (mmHg)
Hypertension	1.847 (1.788 - 1.908) (Med use) 0.993 (0.992 - 0.995) [Interaction {SBP*HTN Med Use)]	1.734 (1.674 - 1.796) (Med use) 0.996 (0.995 - 0.997) [Interaction (SBP*HTN Med Use)]
Smoker	1.417 (1.385 - 1.449) (Current)	1.530 (1.487 - 1.574) (Current)
Family History	1.300 (1.257 - 1.344) (CVD)	1.229 (1.187 - 1.273) (CVD)
Townsend Score	1.017 (1.014 - 1.020)	1.035 (1.031 - 1.038)

Table 5r. Model Parameters – Registre Gironí del Cor³⁸

Model	REGICOR (Men)	REGICOR (Women)
		1.338 (0.866 - 2.067) (yrs)
Age	1.044 (1.020 - 1.069) (yrs)	0.998 (0.994 - 1.002) (>2 yrs)
Total Cholesterol	1.000 (0.996 - 1.008) (mg/dL)	0.999 (0.991 - 1.007) (mg/dL)
HDL	0.980 (0.963 - 0.998) (mg/dL)	0.953 (0.931 - 0.976) (mg/dL)
Optimal BP (SBP < 120 & DBP < 80)	0.555 (0.199 - 1.544)	0.986 (0.248 - 3.919)
Normal BP (SBP 120-129, DBP 80-84)	(REF)	(REF)
High Normal BP (SBP 130-139, DBP 85-89)	0.863 (0.428 - 1.741)	0.958 (0.363 - 2.527)
Hypertension Grade 1 (SBP 140-159, DBP 90-99)	1.404 (0.748 - 2.633)	0.955 (0.400 - 2.280)
Hypertension Grades 2-4 (SBP >=160, DBP >=100)	1.134 (0.510 - 2.524)	1.176 (0.442 - 3.127)
Diabetes Mellitus	1.017 (0.612 - 1.690) (Dx)	2.221 (1.234 - 3.999) (Dx)
Smoker	1.758 (1.153 - 2.679) (Current)	3.983 (1.681 - 9.435) (Current)

Table 5s. Model Parameters – Strong Heart Study^{4,16}

Model	SHS (Men)	SHS (Women)
	REF (45-54)	REF (45-54)
	1.70 (1.33 - 2.17) (55-64)	1.40 (1.09 - 1.80) (55-64)
Age	2.58 (1.92 - 3.46) (65-74)	2.03 (1.53 - 2.70) (65-74)
	REF (<100 mg/dL)	REF (<100 mg/dL)
	1.03 (0.76 - 1.39) (100-129 mg/dL)	1.53 (1.15 - 2.04) (100-129 mg/dL)
	1.67 (1.23 - 2.26) (130-159 mg/dL)	1.61 (1.17 - 2.22) (130-159 md/dL)
LDL	2.44 (1.72 - 3.47) (≥160 mg/dL)	2.17 (1.51 - 3.12) (≥160 mg/dL)
	1.31 (1.04 - 1.64) (<40 mg/dL)	1.10 (0.86 - 1.40) (<40 mg/dL)
	REF (40-59 mg/dL)	REF (40-59 mg/dL)
HDL	0.84 (0.53 - 1.33) (≥60 mg/dL)	0.96 (0.69 - 1.33) (≥60 mg/dL)
Optimal BP (SBP < 120 & DBP < 80)	REF (no Med use)	REF (no Med use)
Pre-Hypertension (SBP 120 - 139, DBP 80-89) And No HTN Med Use	1.78 (1.26 - 2.51)	1.15 (0.83 - 1.59)
Hypertension Grades 1-4 (SBP >=140, DBP>=90) Or HTN Med Use	2.01 (1.43 - 2.83)	1.69 (1.25 - 2.28)
Diabetes Mellitus	1.66 (1.30 - 2.12) (fasting glucose ≥126 or Med use)	2.26 (1.73 - 2.96) (fasting glucose ≥126 or Med use)
Normal albuminuria (<30 albumin/creatinine urine ratio)	(REF)	(REF)
Microalbuminuria (ratio of urine albumin/creatinine was >30 and <300)	1.39 (1.04 - 1.85)	1.33 (1.00 - 1.77)
Macroalbuminuria (ratio of urine albumin/creatinine was >300)	2.11 (1.51 - 2.95)	2.69 (2.02 - 3.59)
Smoker	1.38 (1.10 - 1.72) (Current)	1.44 (1.14 - 1.83) (Current)

Table 5t. Model Parameters – Uppsala Longitudinal Study of Adult Men^{22, 23}

Model	ULSAM
Systolic BP	1.27 (1.08-1.47) (mmHg)
Smoker (Never)	1.23 (1.03 - 1.48) (Current)
Family History	1.34 (1.09-1.62) (MI)
Apo B/Apo A1 Ratio	1.46 (1.24 - 1.71)
Intact proinsulin (pmol/L)	1.46 (1.20 - 1.76)

Table 5u. Model Parameters – USA-People's Republic of China⁴⁸

Model	USA-PRC (men)	USA-PRC (women)
Age	1.07 (1.04 - 1.10) (yrs)	1.09 (1.05 - 1.13) (yrs)
	1 (<140 mg/dL)	1 (<140 mg/dL)
	0.99 (0.59 - 1.69) (140-200 mg/dL)	0.92 (0.44 - 1.93) (140-200 mg/dL)
Total Cholesterol	1.36 (0.79 - 2.34) (200+ mg/dL)	1.30 (0.62 - 2.73) (200+ mg/dL)
	1 (<24)	1 (<24)
Body Mass Index	1.33 (1.00 - 1.78) (≥24)	1.97 (1.34 - 2.88) (≥24)
	0.58 (0.36 - 0.92) (<120 mmHg)	0.44 (0.24 - 0.82) (<120 mmHg)
	REF (120-129 mmHg)	REF (120-129 mmHg)
	1.49 (0.93 - 2.41) (130-139 mmHg)	1.26 (0.68 - 2.32) (130-139 mmHg)
	2.24 (1.43 - 3.51) (140-159 mmHg)	2.22 (1.28 - 3.84) (140-159 mmHg)
	5.50 (3.43 - 8.80) (160-179 mmHg)	3.93 (2.23 - 6.91) (160-179 mmHg)
Systolic BP	12.59 (7.45 - 21.28) (≥180 mmHg)	6.35 (3.42 - 11.80) (≥180 mmHg)
Diabetes Mellitus	1.07 (0.58 - 1.98) (fasting glucose ≥126 or Med use)	2.61 (1.57 - 4.33) (fasting glucose ≥126 or Med use)
Smoker (Never)	2.03 (1.42 - 2.90) (Current)	1.60 (1.11 - 2.32) (Current)

Table 5v. Model Parameters – Wo	men's Health Study ^{19,20}
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Model	WHS
Age	1.076 (1.064 - 1.089) (yrs)
Total Cholesterol	4.801 (2.834 - 8.135) (Natural Log Total mg/dL)
HDL	0.288 (0.192 - 0.43) (Natural Log HDL mg/dL)
Systolic BP	1.032 (1.02 - 1.044) (SBP-125) 0.999 (0.999 - 1) [(SBP-125)^2]
Hypertension	1.302 (1.023 - 1.657) (Med use)
Smoker (Never)	2.624 (2.086 - 3.301) (Current)
Natural Log of hsCRP (mg/L)	1.216 (1.102 - 1.341)

Study			Study 1st	í í		Cohort	Enrollment	Enrollment	Follow Up
Yr Pub	Enroll Start	Enroll End	Author	Country	Cohort	Abbrev	Base	Final	(yrs)
2007	1/1/1993	12/31/1998	Denes P ⁶³	United States	Women's Health Initiative study	WHI	14749		5.6 (mean)
2007			Weiner DE ⁶⁴	United States	Atherosclerosis Risk In Communities and Cardiovascular Health Study trials with CKD	ARIC, CHS	934		
2005	7/1/1996	3/31/1999	Arad Y ⁶⁵	United States	St Francis Heart Study	SFHS	4903	4613	4.3 (other)
2004	1/1/1979	12/31/1988	Stern MP66	United States	San Antonio Heart Study	SAHS	5158	2570	7.5 (other)
2002	1/1/1961		Orford JL ⁶⁷	United States	Normative Aging Study - male veterans	NAS	1393		10 (other)
2000	1/1/1972	12/31/1976	Grover SA ⁶⁸	Canada	Lipid Research Clinics Prevalence Study cohort	LRCPS	2218		12.2 (mean)
2002	7/1/1979	6/30/1980	Kothari V ⁵⁴	United Status	Wisconsin Epidemiologic Study of Diabetic Retinopathy	WESDR	4549		8.3 (mean)
2009	1/1/1992	3/31/2004	Paynter N ⁵⁵	United States	Women's Genome Health Study	WGHS	22129		10.2 (median)
2007	12/1/1995		Ridker P ²⁰	United States	Physicians Health Study II	PHS-II	10724		10.8 (median)

Table 6a. Data Sources Summary (External Validation) – Americas

Table 6b. Data Sources Summary (External Validation) – Europe

Study	Enroll					Cohort Enrollment		Enrollment	
Yr Pub	Start	Enroll End	Study 1st Author	Country	Cohort	Abbrev	Base	Final	Follow Up (yrs)
2004			Lindman AS ⁷¹	France	Consecutive renal transplant patients		344		6 [1.17] (mean)
2005	1/1/1972	12/31/1976	Scheltens T ⁷⁷	Scotland	Renfrew and Paisley Study			12304	10 (other)
2007	1/1/1974	12/31/1988	Silventoinen K ⁷⁸	Norway	Norwegian Counties Study (ages 40-59)	NCS		49144	
2005	1/1/1978	7/31/1980	Simons LA ⁵⁶	UK	British Regional Heart Study, men ages 40-59	BRHS	5128	5077	21.3 (mean)
					British Regional Heart Study; men aged 40-59				
					years at study entry, randomly selected from				
2003	1/1/1978	12/31/1980	Simons LA ⁵⁶	UK	registers of one general practice in each town	BRHS		6643	12 (other)
			70		in men at work in public authorities and large				
2007	1/1/1979		Vliegenthart R ⁷⁹	Germany	companies in the region of Munster, Germany		4818		
			20		PROCAM cohort, drawn from 52 companies and				
2003	1/1/1979	12/31/1985	Empana JP [∞]	Germany	local government authorities	PROCAM	8682		
					MONICA Augsburg cohort, 1984/1985 and	MONICA-			
2003	1/1/1984	12/31/1990	Empana JP [∞]	Germany	1989/1990 surveys	Augsburg	5786		7.8 (median)
					Men randomly selected from the general				
2004	1/1/1984	12/31/1995	Milne R°'	Germany	population in 1984-5, 1989-90, and 1994-5		3435		6.6 (mean)
					Vorarlberg Health Monitoring and Promotion				
					Program (VHM&PP) cohort of individuals				
0005	4/4/4005	40/04/4004	Mana 782	Austria	Undergoing general health examinations in			11010	(a + b - r)
2005	1/1/1985	12/31/1991	Vvang Z	Austria	Vorariberg province		0005	44649	10 (other)
2007	1/1/1985	12/31/1994	Donnan PT ^{®®}	Norway	Cardiovascular Program in Norway (Ages 60-69)	CP-Norway	8085		10
					Participants randomly selected from 3 cities in the				
					Netherlands, aged 20-59 and free from CVD,				
			02		Monitoring Project on Cardiovascular Disease				
2008	1/1/1987	12/31/1992	Bhopal R°°	Netherlands	Risk Factors	MP-CVDRF		39719	10 (other)
					Individuals aged 25-65 years identified from				
					Finnish population register and participating in 3				
			94		cross-sectional risk factor surveys in Finland in				
2005	1/1/1987	12/31/1997	Koller MT ^{⁰⁴}	Finland	1987, 1992, and 1997		17725		9.9 (median)
			04		Dubbo Study cohort of elderly Australians (Ages				
2003	1/1/1988		Hippisley-Cox JC ³⁴	Australia	60-79)	DUBBO		2102	

Study	Enroll					Cohort	Enrollment	Enrollment	
Yr Pub	Start	Enroll End	Study 1st Author	Country	Cohort	Abbrev	Base	Final	Follow Up (yrs)
					Dubbo Study cohort of elderly Australians (Ages	DUBBO (No			
2003	1/1/1988		Hippisley-Cox JC ⁶²	Australia	60-79) without Diabetes	DM)		1800	
2005	1/1/1990	12/31/1993	McEwan P ⁸⁵	Netherlands	Rotterdam Coronary Calcification Study	RCC		1795	3.3 [0.8] (mean)
2003	1/1/1991	12/31/1993	Guzder RN ⁸⁶	France	PRIME cohort study	PRIME	7359		5 (other)
				Northern					
2003	1/1/1991	12/31/1993	Becker A ⁸⁷	Ireland	PRIME cohort study (Belfast Cohort)	PRIME	2399		5 (other)
					Individuals recruited from the workforce ofa				
					nationwide multi-industry corporation (Fletcher				
			00	New	Challenge Ltd 72%) and the general electoral rolls				
2003	1/1/1992	12/31/1993	Elkeles RS ⁸⁸	Zealand	of the Auckland metropolitan region (28%)			6354	5 (other)
2005	1/1/1992	12/31/1995	Lindman AS ⁷¹	Australia	Aboriginal community		687		
2006	1/1/1993	12/31/1998	Scheltens T ⁷⁷	UK	Individuals with diabetes receiving care in Salford	DARTS	6544	3472	
2005	4/1/1993	10/31/1994	Silventoinen K ⁷⁸	UK	Newcastle Heart Project: Europeans	NHP Europe	725		9.6 (median)
2007	12/31/1993	1/1/2006	Simons LA ⁵⁶	Netherlands	Rotterdam Study		6795		12.9 (median)
2008	1/1/1995		Simons LA ⁵⁶	UK	QRESEARCH	QRESEARCH		607733	12 (other)
					THIN Cohort; data from 288 practices in the UK				
					using the INPS Vision system (~20% of UK				
					practices); including 24 practices (54709 patients)				
			70		from Scotland and 14 practices (36904) from				
2008	1/1/1995	3/31/2006	Vliegenthart R ^{/9}	UK	Northern Ireland	THIN		1072800	11 (other)
2004	1/1/1996	12/31/1996	Empana JP ⁸⁰	UK	Cardiff Diabetes Database (type 1 and type 2)			938	4 (other)
2005	5/1/1996	6/30/1998	Empana JP ⁸⁰	UK	Poole Diabetes Study	PDS	428		4.2 [0.62] (median)
2008	1/1/1998	4/3/1999	Milne R ⁸¹	Germany	Munich	MunichDM	716		8.1 [1.1] (mean)
					Individuals with type 2 diabetes aged 50-75 years,				
			80		recruited from outpatient clinics in Central and				
2008	11/1/2000	11/30/2003	Wang Z°²	UK	West London	PREDICT	589		4 (median)

Table 6c. Data Sources Summary (External Validation) – Asia

Study			Study 1st				Enrollment	Enrollment	Follow Up
Yr Pub	Enroll Start	Enroll End	Author	Country	Cohort	Cohort Abbrev	Base	Final	(yrs)
					Males aged 30-59 completing annual				
2001	1/1/1991	12/31/1993	Suka M ⁸⁹	Japan	health examinations between 1991-1993	JapanWork	5611		
					Employee health management center in a				
2002	1/1/1991	12/31/1993	Suka M ⁹⁰	Japan	Japanese Company	JapanWork	5611		
2005	5/1/1995	3/31/1997	Bhopal R ⁸³	Pakistan	Newcastle Heart Project - Pakistani	NHP - Pakistan	264		7.1 (median)
2005	5/1/1995	3/31/1997	Bhopal R ⁸³	India	Newcastle Heart Project - Indian	NHP - India	230		7.1 (median)
				South					
2005	5/1/1995	3/31/1997	Bhopal R ⁸³	Asia	Newcastle Heart Project - South Asians	NHP - South Asia	576		7.1 (median)

Study 1	Study	Cohort	Group	Age		Female	Smoker	Mean Cholesterol	Diabetes	SBP	DBP	HTN	HTN Med	HTN Med Use
Author	Yr Pub	Abbrev	Name	(vrs)	Race	%	(Current) %	Levels (mg/dL)	%	(mmHa)	(mmHa)	Measured %	Use %	Or Measured %
7.00.00		ARIC	Hamo	(3.0)	W: 84 4	70	(ouriond) //	Lovoio (ing/aL)	70	((inouourou /o		er modedrou //
Weiner DE ⁶⁴	2007	CHS	All	64.7	B: 15.6	61.8	17		14			31.2		
								LDL: 166.6						
								HDL: 47.4		127.6	77.3			
Orford JL67	2002	NAS	All	58.2	W: 98	0		Tot: 245.6	2.9	[Mean]	[Mean]			
								LDL: 144.3		128.4	81.5			
Grover SA ⁶⁸	2000	LRCPS	All	53.1		33	32.7	Tot: 218.4	4.6	[Mean]	[Mean]			
					W: 32									
Stern MP ⁶⁶	2004	SAHS	All		H: 68	58			12.6					
					W: 82.5									
Kothari V54	2002	WESDR	All	52	O: 17.5	41.3	30.3		100					
										125				
Paynter N ⁵⁵	2009	WGHS	All	52.4	W: 100	100	11.5		2.6	[Median]			12.2	
					W: 84.3									
					B: 6.4					127.3	75.8			
Denes P ⁶³	2007	WHI	All	62.9	H: 5.4	100	10.5		3.9	[Mean]	[Mean]			57.5
								LDL: 143						
								HDL: 52						
Arad Y ⁹¹	2005	SFHS	All	59	W: 88	35	10	Tot: 224	6			34		

Table 7a. Data Sources Details (External Validations) – Americas All

Table 7b. Data Sources Details (External Validations) – Americas Men

Study 1	Study	Cohort	Group	Age		Smoker	Mean Cholesterol	Diabetes			HTN
Author	Yr Pub	Abbrev	Name	(yrs)	Race	(Current) %	Levels (mg/dL)	%	SBP (mmHg)	DBP (mmHg)	Measured %
		ARIC,			W: 86.6						
Weiner DE ⁶⁴	2007	CHS	Men	65.8	B: 13.4	15.1		14.6			35.5
							LDL: 144.3		127 [Mean]	82.2 [Mean]	
Grover SA ⁶⁸	2000	LRCPS	Men	50.8		35.4	Tot: 214.5	4.7	(17.8 SD)	(10.6 SD)	
Kothari V54	2002	WESDR	Men	51.5							
									128 [Median]		
Ridker P ²⁰	2008	PHS-II	Men	63		3.2			(120-135)		

Table 7c. Data Sources Details (External Validations) – Americas Women

Study 1 st	Study	Cohort	Group	Age		Smoker	Mean Cholesterol	Diabetes	SBP	DBP	HTN
Author	Yr Pub	Abbrev	Name	(yrs)	Race	(Current) %	Levels (mg/dL)	%	(mmHg)	(mmHg)	Measured %
		ARIC,			W: 83						
Weiner DE ⁶⁴	2007	CHS	Women	64	B:17	18.2		13.7			28.4
							LDL: 148.2		131.3 [Mean]	80 [Mean]	
Grover SA ⁶⁸	2000	LRCPS	Women	57.8		27.2	Tot: 226.2	4.2	(20.4 SD)	(10.3 SD)	
Kothari V54	2002	WESDR	Women	52.6							

Study 1st	Study	Cohort	Group	Age	<u> </u>	Female	Smoker	Mean Cholesterol	Diabetes			HTN	HTN Med
Author	Yr Pub	Abbrev	Name	(vrs)	Race	%	(Current) %	Levels (mg/dL)	%	SBP (mmHq)	DBP (mmHq)	Measured %	Use %
				(j = /				· · · · · · · · · · · · · · · · · · ·		136 [Mean]	81 [Mean] (10		
Ducloux D ⁶⁹	2004	FrRenal	All	51		36.9	23.3		10.8	(19 [SD])	(SDI)		
-		Renfrew-											
Brindle PM ⁷⁰	2005	Paisley	All			54.3	50.7		1.2				
Lindman AS ⁷¹	2007	NCS	All	47		50.9	40.7	Tot: 248.04	0	132.4 [Mean]	81 [Mean]		
Wannamethee								HDL: 44.4		145.7 [Mean]	83 [Mean]		
SG ⁷²	2005	BRHS	All	50.3		0	42.1	Tot: 241.3	0	(20.7 [SD])	(13.2 [SD])	78.5	
										143 [Median]	81 [Median]		
										(115-182	(62-104 [95%		
Brindle P ⁷³	2003	BRHS	All			0	41.9		1.1	[95% CI])	CI])		
								LDL: 152.1					
Buyken AE ⁷⁴	2007	MunsterWork	All			0	30.6	Tot: 227.37		124.7 [Mean]	86.2 [Mean]		
Hense HW ⁶¹	2003	PROCAM	All	46.5		36.3	30.6		2.8	131.5 [Mean]			
		MONICA-											
Hense HW ⁶¹	2003	Augsburg	All	49.5		50.6	26.4		3.6	131.8 [Mean]			
		MONICA-						HDL: 51.6		138.7 [Mean]	83.3 [Mean]		
Koenig W ⁷⁵	2004	Augsburg	All	56.4	W: 100	0	27.4	Tot: 245.7	5.8	(derived)	(derived)		
Ulmer HB ⁷⁶	2005	VHM&PP	All	57.3		54.8							
Lindman AS ⁷¹	2007	CP-Norway	All	65.7		53.7	28.5	Tot: 258.57		149.8 [Mean]	83.9 [Mean]		
										120.1 [Mean]	76 [Mean]		
Scheltens T ⁷⁷	2008	MP-CVDRF	All	40.8		53	39.5	Tot: 214.5		(15.4 [SD])	(10.3 [SD])	6.9	
Silventoinen K ⁷⁸	2005	FinCross	All	44.5		53.4		Tot: 222.3	1.5	135.8 [Mean]	82.3 [Mean]	64.3	
										166 [Mean]			
Simons LA ⁵⁶	2003	DUBBO	All	64.1		58	32		19	(15 [SD])			
Vliegenthart R ⁷⁹	2005	RCC	All	71.1		57.5	16.4	Tot: 230.1	12.3			59.8	
					W: 85								
Milne R ⁸¹	2003	NZWork	All		O: 15	27							
Wang Z ⁸²	2005	Aboriginal	All	34.4	O: 100	48.2	77.6	Tot: 183.3	12.5	121.1 [Mean]	74.7 [Mean]		
					W: 99					144 [Mean]	82 [Mean] (11		
Donnan PT ³⁹	2006	DARTS	All	59.5	O: 1	47.4	23.5		100	(21 [SD])	[SD])		
Bhopal R ⁸³	2005	NHP - Europe	All		O: 100	50	30.1	Tot: 222.3	4	127.5 [Mean]			
Koller MT ⁸⁴	2007	Rotterdam	All	70.2		63.9	21.5					30.8	21.5
Hippisley-Cox JC ³⁴	2008	QRESEARCH	All			50.4	25.5	Tot: 226.2	0	133.7 [Mean]			10.1
Hippisley-Cox JC ⁶²	2008	THIN	All			50.6	24.7	Tot: 222.3	0	133.8 [Mean]			8.6
										144 [Mean]			
McEwan P ⁸⁵	2004	Cardiff DM	All	59.6		42.2	22	Tot: 226.2	100	(21 [SD])			
								LDL: 140.4		142 [Mean]	81 [Mean]		
Guzder RN ⁸⁶	2005	PDS	All	58.6		43.7		Tot: 230.1	100	(21.4 [SD])	(12.1 [SD])		31.8
Becker A ⁸⁷	2008	MunichDM	All	55.2		39.9			100				
										131 [Median]	78 [Median]		
										(121-142 [IQ	(72-84 [IQ		
Elkeles RS ⁸⁸	2008	PREDICT	All	63.1	W: 71.1	36.7	15.1		100	Range])	Range])		

Table 7d. Data Sources Details (External Validations) - Europe All

Study 1st	Study	Cohort	Í	Age	Smoker	Mean Cholesterol	Diabetes			HTN	HTN Med
Author	Yr Pub	Abbrev	Group Name	(yrs)	(Current) %	Levels (mg/dL)	%	SBP (mmHg)	DBP (mmHg)	Measured %	Use %
		Renfrew-						145 [Median] (116-			
Brindle PM ⁷⁰	2005	Paisley	Men		55.3		1.4	190 [95th percentile])			
Bhopal R ⁸³	2005	NHP-Europe	Men			Tot: 219.96	5	131 [Mean]			
		MONICA-									
Hense HW ⁶¹	2003	Augsburg	Men		33.7		4.2				
Scheltens T ⁷⁷	2008	MP-CVDRF	Men							8	
								125.5 [Mean]	77.7 [Mean]		
Wang Z ⁸²	2005	Aboriginal	Men	32.8	83.7	Tot: 191.1	9.3	(17.1 [SD])	(13.6 [SD])		
Silventoinen K ⁷⁸	2005	FinCross	Men	45		Tot: 224.64	2	139 [Mean]	85 [Mean]	75	
								131.6 [Mean]			
Hense HW ⁶¹	2003	PROCAM	Men	46.5	33.8		2.9	(0.25 [SD])			
Hippisley-Cox								135.3 [Mean]			
JC ³⁴	2008	QRESEARCH	Men	47	28.2	Tot: 222.3	0	(19.6 [SD])			8
Lindman AS ⁷¹	2007	NCS	Men	47	44.2	Tot: 248.43	0	135.3 [Mean]	83 [Mean]		
Hippisley-Cox								135.6 [Mean]			
JC ⁶²	2008	THIN	Men	48	26.6	Tot: 222.3	0	(19.4 [SD])			6.6
		MONICA-						134.9 [Mean]			
Hense HW ⁶¹	2003	Augsburg	1984-85 Survey Men	49.4	35.4		3.5	(0.44 [SD])			
		MONICA-						135.1 [Mean]			
Hense HW ⁶¹	2003	Augsburg	1989-90 Survey Men	49.6	31.9		5.1	(0.48 [SD])			
Becker A ⁸⁷	2008	MunichDM	Men	55.5			100				
		MONICA-	Men without coronary			HDL: 51.8					
Koenig W ⁷⁵	2004	Augsburg	event	56.2	26.4	Tot: 244.4	5.4	138.5 [Mean]	83.3 [Mean]		
		MONICA-	Men without coronary			HDL: 51.8					
Koenig W ⁷⁵	2004	Augsburg	event	56.2	26.4	Tot: 246.48	5.4	138.5 [Mean]	83.3 [Mean]		
Ulmer HB ⁷⁶	2005	VHM&PP	Men	56.5							
		MONICA-	Men with coronary			HDL: 48.4					
Koenig W ⁷⁵	2004	Augsburg	event	59.2	44.2	Tot: 257.4	12	142.6 [Mean]	83.8 [Mean]		
								142 [Mean]			
McEwan P ⁸⁵	2004	Cardiff DM	Men	59.2	24	Tot: 218.4		(19 [SD])			
		MONICA-	Men with coronary			HDL: 48.4					
Koenig W ⁷⁵	2004	Augsburg	event	59.2	44.2	Tot: 257.4	12	142.6 [Mean]	83.8 [Mean]		
		MONICA-	Men with coronary			HDL: 48.4					
Koenig W ⁷⁵	2004	Augsburg	event	59.2	44.2	Tot: 259.35	12	142.6 [Mean]	83.8 [Mean]		
								150 [Mean]	85 [Mean]		
Lindman AS ⁷¹	2007	CP-Norway	Men	65.6	37.4	Tot: 242.58	0	(20.2 [SD])	(12.2 [SD])		
Koller MT ⁸⁴	2007	Rotterdam	Men	68.5	30.1					25.3	

Table 7e. Data Sources Details (External Validations) – Europe Men

Study 1st	Study	`	Group	Age	Smoker	Mean Cholesterol			DBP	HTN	HTN Med
Author	Yr Pub	Cohort Abbrev	Name	(yrs)	(Current) %	Levels (mg/dL)	Diabetes %	SBP (mmHg)	(mmHg)	Measured %	Use %
								147 [Median]			
Brindle PM ⁷⁰	2005	Renfrew-Paisley	Women		46.9		1.1	(114-196 95th percentile)			
Lindman AS ⁷¹	2007	NCS	Women	46.9	37.3	Tot: 247.26	0	129.6 [Mean]	79 [Mean]		
Hense HW ⁶¹	2003	PROCAM	Women	46.6	24.9		2.6	131.2 [Mean] (0.36 [SD])			
		MONICA-									
Hense HW ⁶¹	2003	Augsburg	Women		19.3		3	128. 6 [Mean]			
Ulmer HB ⁷⁶	2005	VHM&PP	Women	58							
								149.6 [Mean]	83 [Mean]		
Lindman AS ⁷¹	2007	CP-Norway	Women	65.7	20.9	Tot: 272.22		(21.8 [SD])	(12.7 [SD])		
Scheltens T''	2008	MP-CVDRF	Women							6	
Silventoinen K ⁷⁸	2005	FinCross	Women	44		Tot: 218.4	1	133 [Mean]	80 [Mean]	55	
								116.4 [Mean]	71.5 [Mean]		
Wang Z ⁸²	2005	Aboriginal	Women	36.1	71	Tot: 175.5	16	(18.7 [SD])	(12.9 [SD])		
Bhopal R ⁸³	2005	NHP - Europe	Women			Tot: 224.25	3	124 [Mean]			
Koller MT ⁸⁴	2007	Rotterdam	Women	71.1	16.7					33.8	
Hippisley-Cox											
JC ³⁴	2008	QRESEARCH	Women	49	22.9	Tot: 226.2		132.2 [Mean] (21.6 [SD])			12.1
Hippisley-Cox											
JC ⁶²	2008	THIN	Women	49	22.9	Tot: 226.2	0	132.1 [Mean] (21.0 [SD])			10.5
McEwan P ⁸⁵	2004	Cardiff DM	Women	60.2	19	Tot: 234		146 [Mean] (23 [SD])			
Becker A ⁸⁷	2008	MunichDM	Women	54.8			100				

Table 7f. Data Sources Details (External Validations) – Europe Women

Table 7g. Data Sources Details (External Validations) - Asia All

Study 1 st	Study		Group	Age	ĺ.		Smoker	Mean Cholesterol			
Author	Yr Pub	Cohort Abbrev	Name	(yrs)	Race	Female %	(Current) %	Levels (mg/dL)	Diabetes %	SBP (mmHg)	DBP (mmHg)
Suka M ⁸⁹	2001	JapanWork	All	44.7	O:100	0	59.8	Tot: 198.9	8.5	129 [Mean] (17.1 [SD])	80.3 [Mean] (10.6 [SD])
Bhopal R ⁸³	2005	NHP–Pakistan	All		O:100	51.1	17	Tot: 218.4	27	122 [Mean]	
Bhopal R ⁸³	2005	NHP-India	All		O:100	63	6.1	Tot: 216.84	16	125.9 [Mean]	
Bhopal R ⁸³	2005	NHP–South Asia	All		O:100	54.5	15.6	Tot: 216.84	20.5	122.5 [Mean]	

Table 7h. Data Sources Details (External Validations) – Asia Men

Study 1 st	Study		Group		Mean Cholesterol		
Author	Yr Pub	Cohort Abbrev	Name	Race	Levels (mg/dL)	Diabetes %	SBP (mmHg)
Bhopal R ⁸³	2005	NHP-Pakistan	Men	O:100	Tot: 219.18	26	123 [Mean]
Bhopal R ⁸³	2005	NHP-India	Men	O:100	Tot: 219.57	16	124 [Mean]
Bhopal R ⁸³	2005	NHP–South Asia	Men	O:100	Tot: 217.23	21	122 [Mean]

Table 7i: Data Sources Details (External Validations) - Asia Women

Study 1 st	Study		Group		Mean Cholesterol		
Author	Yr Pub	Cohort Abbrev	Name	Race	Levels (mg/dL)	Diabetes %	SBP (mmHg)
Bhopal R ⁸³	2005	NHP-Pakistan	Women	O:100	Tot: 218.01	28	121 [Mean]
Bhopal R ⁸³	2005	NHP-India	Women	O:100	Tot: 215.28	16	127 [Mean]
Bhopal R ⁸³	2005	NHP-South Asia	Women	O:100	Tot: 216.45	20	123 [Mean]

Table 8a. CVD Model Details – Americas

		Group			Model			HLC	GOF
Cohort	Cohort Abbrev	Name	Cohort Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р
Framingham Offspring Study ⁷	FRS-O	All	CVD 12	Wilson AFT Model A No BMI CVD	CVD 12	0.775			
Framingham Offspring Study ⁷	FRS-O	All	CVD 12	Wilson AFT Model A CVD	CVD 12	0.784			
Framingham Offspring Study	FRS-O	All	CVD 12	Wilson AFT Model B CVD	CVD 12	0.801			
Framingham Offspring Study	FRS-O	All	CVD 12	Wilson AFT Model B No BMI CVD	CVD 12	0.8			
National Health and Nutrition Examination									
Survey I Epidemiologic Follow-Up Study ⁸	NHANES-I EFS	Men	CVD 7	Gaziano Lab-Based Model	CVD 7	0.784	0.766-0.801	6.7	0.57
National Health and Nutrition Examination									
Survey I Epidemiologic Follow-Up Study ⁸	NHANES-I EFS	Women	CVD 7	Gaziano Lab-Based Model	CVD 7	0.829	0.813-0.845	6.62	0.579
National Health and Nutrition Examination									
Survey I Epidemiologic Follow-Up Study ⁸	NHANES-I EFS	Men	CVD 7	Gaziano Non-Lab-Based Model	CVD 7	0.783	0.765-0.800	6.61	0.579
National Health and Nutrition Examination									
Survey I Epidemiologic Follow-Up Study ⁸	NHANES-I EFS	Women	CVD 7	Gaziano Non-Lab-Based Model	CVD 7	0.831	0.816-0.847	3.45	0.903
Framingham Cohort (11th) (68-71) &									
Offspring 1st (71-75) & Offspring (3rd 84-87)°	FRS, FRS-O	Men	CVD 2	D'Agostino CVD MALE	CVD 2	0.763	0.746-0.780	13.48	0
Framingham Cohort (11th) (68-71) &									
Offspring 1st (71-75) & Offspring (3rd 84-87)°	FRS, FRS-O	Women	CVD 2	D'Agostino CVD FEMALE	CVD 2	0.793	0.772-0.814	7.79	0.56
Framingham Cohort (11th) (68-71) &									-
Offspring 1st (71-75) & Offspring (3rd 84-87)°	FRS, FRS-O	Men	Total CHD 1	D'Agostino CVD MALE	CVD 2	0.733	0.712-0.754	18.2	0
Framingham Cohort (11th) (68-71) &						0 707		4470	
Offspring 1st (/1-/5) & Offspring (3rd 84-87)°	FRS, FRS-O	Women	Total CHD 1	D'Agostino CVD FEMALE	CVD 2	0.787	0.762-0.812	14.79	0
Framingham Cohort (11th) (68-71) &									
Offspring 1st (71-75) & Offspring (3rd 84-87)*	FRS, FRS-0	Men	Stroke 4	D'Agostino CVD MALE	CVD 2	0.826	0.789-0.863	26.11	0
Framingham Cohort (11th) (68-71) & Offension (2nd 0.4 07) ⁶		14/000000	Otralia 4	DIA mentione CV/D FEMALE		0.700	0 745 0 000	F 00	0.014
Unspring 1st (71-75) & Unspring (3rd 84-87)	FR5, FR5-0	women	Stroke 4	D'Agostino CVD FEMALE	CVD Z	0.769	0.715-0.822	5.26	0.811
Offensing 1et (71 75) & Offensing (2rd 84 87) ⁶		Man	CUE	D'Agastina CV/D MALE		0.044	0 700 0 992	27.22	0
Eramingham Cabort (11th) (69,71) 8	FK3, FK3-0	Wen	СПГ	DAGOSUNO CVD MALE	CVDZ	0.041	0.799-0.003	21.23	0
Offenring 1et (71,75) & Offenring (2rd 84,87) 6		Womon	CHE	D'Agostino CVD EEMALE		0.947	0 802 0 801	0.22	0
Eramingham Cabort (11th) (69,71) 8	FK3, FK3-0	women		D'AGOSUNO CVD FEIMALE	CVDZ	0.047	0.003-0.091	9.32	0
Offenring 1st $(71-75)$ & Offenring $(3rd 84-87)^6$	ERS ERS	Mon	ם//ח	D'Agostino CVD MALE		0.813	0 780-0 847	10.05	0
Framingham Cohort (11th) (68-71) &	110,110-0	INCII		DAGOSTINO CVD WALL	0002	0.015	0.700-0.047	13.05	0
Offspring 1st (71-75) & Offspring (3rd 84-87) ⁶	FRS FRS-0	Women	PVD	D'Agostino CVD FEMALE	CVD 2	0.829	0 786-0 872	11 33	0
Lipid Research Clinics Prevalence Study	110,1100	Women	1.40	D'Igodino OVD I EMIXEE	0102	0.020	0.100 0.012	11.00	•
cohort ⁶⁸	LRCPS	All	CHD Mortality	FRS (1991)	CVD 2	0.83	0.02		
Lipid Research Clinics Prevalence Study		/			0.02	0.00	0.02		
cohort ⁶⁸	LRCPS	Men	CHD Mortality	FRS (1991)	CVD 2	0.83			
Lipid Research Clinics Prevalence Study								1	
cohort ⁶⁸	LRCPS	Women	CHD Mortality	FRS (1991)	CVD 2	0.82			
		White						1	
Atherosclerosis Risk in Communities Study ⁴	ARIC	Men	Hard CHD 1 (5 yr)	FRS (1991)	CVD 2	0.75		13.8	
		White						1	
Atherosclerosis Risk in Communities Study ⁴	ARIC	Women	Hard CHD 1 (5 vr)	FRS (1991)	CVD 2	0.83		6.2	
		Black			Hard			1	
Atherosclerosis Risk in Communities Study ⁴	ARIC	Men	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.67		5.3	

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		Group			Model			HLC	GOF
Cohort	Cohort Abbrev	Name	Cohort Outcome	Model Name	Outcome	AUC	AUC Var	χ ²	Р
		Black			Hard				
Atherosclerosis Risk in Communities Study ⁴	ARIC	Women	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.79		5	
					Hard				
Honolulu Heart Program ⁴	HHP	Men	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.72		66	
					Hard				
Puerto Rico Heart Health Program ⁴	PRHHP	Men	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.69		142	
Strong Heart Study (area of Oklahoma and					Hard				
Aberdeen area of North and South Dakota) ⁴	SHS	Men	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.69		10.6	
Strong Heart Study (area of Oklahoma and					Hard				
Aberdeen area of North and South Dakota)*	SHS	Women	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.75		22.7	
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	Ridker Model A	CVD 3	0.809			0.38
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	Ridker Model B	CVD 3	0.808			0.62
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	FRS (Wilson TC) Remodel	CVD 3	0.791			0.18
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	FRS (Wilson LDL) Remodel	CVD 3	0.791			0.16
Women's Health Study ¹⁹	WHS	All	CVD 3	WHS Model with hsCRP	CVD 3	0.815			0.23
Women's Health Study ¹⁹	WHS	All	CVD 3	WHS Model without hsCRP	CVD 3	0.813			0.039
					Hard				
Cardiovascular Health Study ⁴	CHS	Men	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.63		13.2	
					Hard				
Cardiovascular Health Study ⁴	CHS	Women	Hard CHD 1 (5 yr)	FRS Hard CHD [TC] (1998)	CHD 1	0.66		10.4	
Women's Genome Health Study ⁵⁵	WGHS	All	CVD 3	FRS (ATP) WGHS Remodel	CVD 3	0.803	0.019	6.24	0.62
Women's Health Study ⁵⁵	WHS	All	CVD 3	FRS (ATP) WHS Cook Remodel	CVD 3	0.814			0.25
Women's Genome Health Study	WGHS	All	CVD 3	Reynolds Risk Score Remodel	CVD 3	0.807	0.019	7.75	0.46
Women's Genome Health Study ⁵⁵	WGHS	All	CVD 3	ATP-III (Remodel) + genotype	CVD 3	0.805	0.019	5.96	0.65
				Reynolds Risk Score (Remodel) +					
Women's Genome Health Study ⁵⁵	WGHS	All	CVD 3	genotype	CVD 3	0.809	0.019	7.43	0.49
Physicians Health Study II ⁵⁹	PHS-II	All	CVD 15	Ridker Model A, PHS-II	CVD 15	0.699		11.3	
50				Reynolds Risk Score + CRP +					
Physicians Health Study II	PHS-II	All	CVD 15	parental history	CVD 15	0.708		12.9	
Physicians Health Study II ⁵⁹	PHS-II	All	Hard CHD 2	Ridker Model A, PHS-II	CVD 15	0.689			
50				Reynolds Risk Score + CRP +					
Physicians Health Study II ⁵⁹	PHS-II	All	Hard CHD 2	parental history	CVD 15	0.7			

Table 8b. CHD Model Details – Americas

	Cohort	Group	Cohort		Model			HL	GOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
Framingham Offspring Study ⁷	FRS-O	All	Total CHD 1	Wilson AFT Model E CHD	Total CHD 1	0.813		ⁿ		
Framingham Offspring Study ⁷	FRS-O	All	Total CHD 1	Wilson AFT Model D CHD	Total CHD 1	0.812				1
Framingham Offspring Study	FRS-O	All	Total CHD 1	Wilson AFT Model B CHD	Total CHD 1	0.808				1
Framingham Offspring Study	FRS-O	All	Total CHD 1	Wilson AFT Model A CHD	Total CHD 1	0.791				
Framingham Offspring Study	FRS-O	All	Total CHD 1	Wilson AFT Model A No BMI CHD	Total CHD 1	0.784				
Framingham Offspring Study	FRS-O	All	Total CHD 1	Wilson AFT Model C CHD	Total CHD 1	0.796				
Framingham Offspring Study ⁷	FRS-O	All	Total CHD 1	Wilson AFT Model E No BMI CHD	Total CHD 1	0.814				
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Men	(10yr)	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.6		72.3	0	1.492
Atherosclerosis Risk In Communities and			Hard CHD 1							1
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Women	(10yr)	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.73		75.1	0	2.022
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Women	(10yr)	FRS CKD Best Cox, females	Hard CHD 1	0.81		2.5		
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Men	(10yr)	FRS CKD Best Cox, males	Hard CHD 1	0.68		4		
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Men	(5yr)	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.62		33.4	0	1.636
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Women	(5yr)	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.77		61.2	0	2.727
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Women	(5yr)	FRS CKD Best Cox, females	Hard CHD 1	0.82		0.8		
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Men	(5yr)	FRS CKD Best Cox, males	Hard CHD 1	0.72		4.2		
Atherosclerosis Risk in Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁶⁴	ARIC, CHS	Women	(5 yr)	FRS CKD recal	Hard CHD 1			8.7		
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ^{o4}	ARIC	Women	(10 yr)	FRS CKD recal	Hard CHD 1			8.9	L	
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular Health Study trials with CKD ⁰⁴	ARIC, CHS	Men	(5 yr)	FRS CKD recal	Hard CHD 1			13.7		
Atherosclerosis Risk In Communities and			Hard CHD 1							
Cardiovascular health Study trials with CKD ^{o4}	ARIC, CHS	Men	(10 yr)	FRS CKD recal	Hard CHD 1			32.3	 	
Women's Health Initiative study	WHI	All	Hard CHD 1	FRS [Unknown Version] (1998)	Total CHD 1	0.69			 	
Women's Health Initiative study	WHI	Women	Hard CHD 1	FRS [Unknown Version] (1998)	Total CHD 1	0.69			L	
Women's Health Initiative study	WHI	All	CVD 15	FRS [Unknown Version] (1998)	Total CHD 1	0.68			L	
Women's Health Initiative study	WHI	Women	CVD 15	FRS [Unknown Version] (1998)	Total CHD 1	0.68				_
San Antonio Heart Study ¹⁰	SAHS	All	CVD 15	FRS [Unknown Version] (1998)	Total CHD 1	0.816				
St Francis Heart Study	SFHS	All	Hard CHD 2	FRS (ATP)	Hard CHD 1	0.68	0.62-0.74			
Atherosclerosis Risk in Communities Study	ARIC	Men	Hard CHD 2	Metabolic Syndrome Model	Hard CHD 2	0.631				_
Atherosclerosis Risk in Communities Study	ARIC	Women	Hard CHD 2	Metabolic Syndrome Model	Hard CHD 2	0.729				_
Atherosclerosis Risk in Communities Study ¹⁵	ARIC	Men	Hard CHD 2	FRS (ATP)	Hard CHD 1	0.634			Ļ	
Atherosclerosis Risk in Communities Study ¹⁵	ARIC	Women	Hard CHD 2	FRS (ATP)	Hard CHD 1	0.731			Ļ	
Strong Heart Study	SHS	Men	Hard CHD 1	SHS Model	Hard CHD 1	0.71		7.18	0.51	
Strong Heart Study ¹⁶	SHS	Women	Hard CHD 1	SHS Model	Hard CHD 1	0.73		7.25	0.45	
South Bay Heart Watch cohort ¹⁷	SBHW	All	Hard CHD 1	FRS (ATP)	Hard CHD 1	0.63				

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	Cohort	Group	Cohort		Model			HL	.GOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
South Bay Heart Watch cohort ¹⁷	SBHW	All	Hard CHD 1	FRS (2001 ATP) + CACS	Hard CHD 1	0.68				
Normative Aging Study - male veterans ⁶⁷	NAS	All	Total CHD 1	European Society of Cardiology (ESC)	Total CHD 1	0.58				
Normative Aging Study - male veterans ⁶⁷	NAS	All	Total CHD 1	FRS [TC] (1998)	Total CHD 1	0.63				0.928
Atherosclerosis Risk In Communities Study ¹⁴	ARIC	Men	Hard CHD 2	FRS [TC] (Wilson)	Hard CHD 1	0.691	0.670- 9.712			
Atherosclerosis Risk In Communities Study ¹⁴	ARIC	Women	Hard CHD 2	FRS [TC] (Wilson)	Hard CHD 1	0.808	0.792- 0.823			
Atheroscierosis Risk in Communities Study	ARIC	wen	Hard CHD 2	Personal HEAR I	Hard CHD 2	0.649	0.007		 	
Atherosclerosis Risk In Communities Study ¹⁴	ARIC	Men	Hard CHD 2	Personal HEART	Hard CHD 2	0.649	0.627- 0.671		L	
Atherosclerosis Risk In Communities Study ¹⁴	ARIC	Women	Hard CHD 2	Personal HEART	Hard CHD 2	0.788	0.772- 0.804			
Atherosclerosis Risk In Communities Study ¹⁴	ARIC	Women	Hard CHD 2		Hard CHD 2	0.788			 	<u> </u>
South Bay Heart Watch ¹⁰	SBHW	All	Hard CHD 1	FRS (1991)	Hard CHD 1	0.69	0.05		 	1.165
South Bay Heart Watch ¹⁰	SBHW	All	Hard CHD 1	Detrano - Data Derived	Hard CHD 1	0.68	0.05		 	
South Bay Heart Watch ¹⁰	SBHW	All	Hard CHD 1	Detrano - Data Derived + Ca	Hard CHD 1	0.71	0.04		 	
First National Health and Nutrition Examination Survey ³	NHANES I	Men	CHD Mortality	FRS (Custom 4 Variable)	CHD Mortality	0.71				0.90
First National Health and Nutrition Examination Survey ³	NHANES I	Women	CHD Mortality	FRS (Custom 4 Variable)	CHD Mortality	0.8				
First National Health and Nutrition Examination Survey ³	NHANES I	Men	CHD Mortality	NHANES I (4 Variables)	CHD Mortality	0.71				
First National Health and Nutrition Examination Survey ³	NHANES I	Women	CHD Mortality	NHANES I (4 Variables)	CHD Mortality	0.81				
Second National Health and Nutrition			CHD		CHD					
Examination Survey ³	NHANES II	Men	Mortality	FRS (Custom 4 Variable)	Mortality	0.74				0.649
Second National Health and Nutrition			CHD		CHD					
Examination Survey ³	NHANES II	Women	Mortality	FRS (Custom 4 Variable)	Mortality	0.76				
Second National Health and Nutrition			CHD		CHD					
Examination Survey ³	NHANES II	Men	Mortality	NHANES II (4 Variable)	Mortality	0.75				
Second National Health and Nutrition			CHD		CHD					
Examination Survey	NHANES II	Women	Mortality	NHANES II (4 Variable)	Mortality	0.77				
Framingham Study (11th Exam) or			Hard CHD 1							
Framingham Offspring Study (1st Exam)	FRS, FRS-0	Men	(5 yr)	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.79			 	
Framingham Study (11th Exam) or			Hard CHD 1			0.00				
Framingham Onspring Study (1st Exam)	FR5, FR5-0	women	(5 yr)	FRS Hard CHD [1C] (1998)	Hard CHD 1	0.83			───	┥───┦
Framingham Study (11th Exam) of		Mon	Hard CHD 1	ERS White Male Rest Cox Model		0.70		2.2		
Framingham Onspring Study (1st Exam)	FK3, FK3-U	wen				0.79		3.3	<u> </u>	
Framingham Offspring Study (1st Exam) ⁴	ERS ERS	Women		ERS White Female Best Cox Model	Hard CHD 1	0.83		37		
	110,110	Black				0.00	+	5.7	├ ───	╉───┦
Atherosclerosis Risk in Communities Study ⁴	ARIC	Men	(5 vr)	ARIC Black Male Best Cox Model	Hard CHD 1	07		72	1	
		White	Hard CHD 1			0.1	1	1.2	<u> </u>	+ +
Atherosclerosis Risk in Communities Study ⁴	ARIC	Men	(5 vr)	ARIC White Male Best Cox Model	Hard CHD 1	0.76		5.4	1	
Atherosclerosis Risk in Communities Study ⁴	ARIC	Black	Hard CHD 1	ARIC Black Female Best Cox Model	Hard CHD 1	0.85		3.4		

Cardiovascular Disease Risk Assessment Tools

	Cohort	Group	Cohort		Model			HL	GOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	γ^2	Р	Ratio
		Women	(5 yr)							
		White	Hard CHD 1							
Atherosclerosis Risk in Communities Study ⁴	ARIC	Women	(5 yr)	ARIC White Female Best Cox Model	Hard CHD 1	0.84		5.2		
			Hard CHD 1							
Honolulu Heart Program ⁴	HHP	Men	(5 yr)	HHP Male Best Cox Model	Hard CHD 1	0.74		2.6		
			Hard CHD 1							
Puerto Rico Heart Health Program ⁴	PRHHP	Men	(5 yr)	PR Male Best Cox Model	Hard CHD 1	0.72		7.2		
Strong Heart Study (area of Oklahoma and			Hard CHD 1	SHS Native American Male Best Cox						
Aberdeen area of North and South Dakota) ⁴	SHS	Men	(5 yr)	Model	Hard CHD 1	0.77		2.7		
Strong Heart Study (area of Oklahoma and			Hard CHD 1	SHS Native American Female Best						
Aberdeen area of North and South Dakota) ⁴	SHS	Women	(5 yr)	Cox Model	Hard CHD 1	0.86		3.5		
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	FRS [TC] (1998)	Total CHD 1	0.752			<0.001	
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	FRS (ATP)	Hard CHD 1	0.787			<0.001	
Women's Health Study (Validation Cohort) ²⁰	WHS (Val)	All	CVD 3	FRS [LDL] (1998)	Total CHD 1	0.751			<0.001	
Framingham Cohort (11th Exam) Or										
Framingham Offspring (1st Exam) ²	FRS, FRS-O	Men	Total CHD 1	FRS [LDL] (1998)	Total CHD 1	0.74				
Framingham Cohort (11th Exam) Or										
Framingham Offspring (1st Exam) ²	FRS, FRS-O	Women	Total CHD 1	FRS [LDL] (1998)	Total CHD 1	0.77				
South Bay Heart Watch ¹⁸	SBHW	All	Hard CHD 2	FRS (1991)	Total CHD 1	0.67	0.04			
South Bay Heart Watch ¹⁸	SBHW	All	Hard CHD 2	Detrano - Data Derived	Hard CHD 1	0.69	0.04			
South Bay Heart Watch ¹⁸	SBHW	All	Hard CHD 2	Detrano - Data Derived + Ca	Hard CHD 1	0.72	0.04			
			Hard CHD 1							
Cardiovascular Health Study ⁴	CHS	Men	(5 yr)	CHS White Male Best Cox Model	Hard CHD 1	0.69		6.8		
			Hard CHD 1							
Cardiovascular Health Study ⁴	CHS	Women	(5 yr)	CHS White Female Best Cox Model	Hard CHD 1	0.68		6.8		
			Hard CHD 2							
Atherosclerosis Risk in Communities Study ¹⁵	ARIC	Men	(6 yr)	FRS (ATP)	Hard CHD 1	0.646				
			Hard CHD 2							
Atherosclerosis Risk in Communities Study ¹⁵	ARIC	Women	(6 yr)	FRS (ATP)	Hard CHD 1	0.667				
			Hard CHD 2							
Atherosclerosis Risk in Communities Study ¹⁵	ARIC	All	(6 yr)	FRS (ATP)	Hard CHD 1	0.72				
		Diabetic		ARIC, diabetes-specific basic risk						
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	factors, liberal definition of diabetes	Hard CHD 2	0.672				
		Diabetic		ARIC, diabetes-specific basic risk						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	factors, liberal definition of diabetes	Hard CHD 2	0.721				
		Non-								
		diabetic		ARIC, diabetes-specific basic risk						
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	factors, liberal definition of diabetes	Hard CHD 2	0.786				
		Non-								
40		diabetic		ARIC, diabetes-specific basic risk						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	factors, liberal definition of diabetes	Hard CHD 2	0.688				
				ARIC, diabetes-specific basic risk						
		Diabetic		factors, restrictive definition of diabetes						
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	(only drug-treated diabetes)	Hard CHD 2	0.75				
		Diabetic		ARIC, diabetes-specific basic risk						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	factors, restrictive definition of diabetes	Hard CHD 2	0.7				

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	Cohort	Group	Cohort	t Model			HLGOF		O/E	
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
				(only drug-treated diabetes)						
		Diabetic		ARIC, combined model, basic risk						
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	factors	Hard CHD 2	0.65				
		Diabetic		ARIC, combined model, basic risk						
Atherosclerosis Risk in Communities	ARIC	women	Hard CHD 2	factors	Hard CHD 2	0.71				
		Diabotic		ARIC, diabetes-specific basic +						
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	diabetes	Hard CHD 2	0 74				
	7.0.00	mon		ARIC, diabetes-specific basic +		0.7 1				
		Diabetic		multiple risk factors, liberal definition of						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	diabetes	Hard CHD 2	0.771				
		Non-		ARIC, diabetes-specific basic +						
		diabetic		multiple risk factors, liberal definition of						
Atherosclerosis Risk in Communities ¹⁰	ARIC	men	Hard CHD 2	diabetes	Hard CHD 2	0.711				
		Non-		ARIC, diabetes-specific basic +						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	diabetes	Hard CHD 2	0 796				
	ANO	Diabetic				0.730				
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	ARIC. diabetes-specific basic markers	Hard CHD 2	0.68				
	-	Diabetic								
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	ARIC, diabetes-specific basic markers	Hard CHD 2	0.711				
		Non-								
A.J. J. D. J. D. J. J. 13		diabetic								
Atherosclerosis Risk in Communities	ARIC	men	Hard CHD 2	ARIC, diabetes-specific basic markers	Hard CHD 2	0.679				
		Non-								
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	ARIC diabetes-specific basic markers	Hard CHD 2	0 777				
	7.1.10	Diabetic		ARIC, diabetes-specific basic+multiple		0.111				
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	markers	Hard CHD 2	0.702				
		Diabetic		ARIC, diabetes-specific basic+multiple						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	markers	Hard CHD 2	0.723				
		Non-								
Athennesis Distric Oscience itis 13		diabetic		ARIC, diabetes-specific basic+multiple		0 700				
Atheroscierosis Risk in Communities	ARIC	Men	Hard CHD 2	markers	Hard CHD 2	0.702				
		diabetic		ARIC diabetes-specific basic+multiple						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	markers	Hard CHD 2	0.781				
				ARIC, diabetes-specific basic risk						
				factors, restrictive definition of diabetes						
40		Diabetic		(only physician-diagnosed or -treated						
Atherosclerosis Risk in Communities ¹³	ARIC	men	Hard CHD 2	diabetes)	Hard CHD 2	0.72				
				ARIC, diabetes-specific basic risk						
		Dichotic		ractors, restrictive definition of diabetes						
Atherosclerosis Risk in Communities ¹³	ARIC	women	Hard CHD 2	diabetes)	Hard CHD 2	0.7				
NHANES I and II (pooled) ¹	NHANESI	White	CHD death	NHANES I and II, pooled	CHD	0.77				

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	Cohort	Group	Cohort		Model			HL	.GOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
	and II	men			Mortality					
	(pooled)									
	NHANES I									
	and II	Black			CHD					
NHANES I and II (pooled) ¹	(pooled)	men	CHD death	NHANES I and II, pooled	Mortality	0.76				
	NHANES I									
	and II	White			CHD					
NHANES I and II (pooled) ¹	(pooled)	women	CHD death	NHANES I and II, pooled	Mortality	0.84				
	NHANES I									
	and II	Black			CHD					
NHANES I and II (pooled) ¹	(pooled)	women	CHD death	NHANES I and II, pooled	Mortality	0.82				
Johns Hopkins Sibling Study ¹⁰	JHSS	Women	Total CHD 1	FRS [TC] (1998)	Total CHD 1			8		1.128
Johns Hopkins Sibling Study ¹⁰	JHSS	Men	Total CHD 1	FRS Wilson-D'Agostino Recal	Total CHD 1			9		
Johns Hopkins Sibling Study ¹⁰	JHSS	Men	Total CHD 1	FRS [TC] (1998)	Total CHD 1			7.5		1.671
Johns Hopkins Sibling Study ¹⁰	JHSS	Women	Total CHD 1	FRS Wilson-D'Agostino Recal	Total CHD 1			8		
			Hard CHD 1							
Chicago young adults ⁵	CHA	Men	(10 yr)	FRS [TC] (1998)	Total CHD 1					0.046
			Hard CHD 1							
Chicago young adults⁵	CHA	Men	(10 yr)	FRS (ATP)	Hard CHD 1					0.072
			Hard CHD 1		CHD					
Chicago young adults ⁵	CHA	Men	(30 yr)	CHA	Mortality					0.95
Adult residents of Olmsted County, Minnesota ⁹	Mayo	Men	Total CHD 1	Miyasaka CHD Post-AF	Total CHD 1					0.783
Adult residents of Olmsted County, Minnesota ⁹	Mayo	Women	Total CHD 1	Miyasaka CHD Post-AF	Total CHD 1					0.857

Table 8c. Stroke Model Details – Americas

	Cohort	Group	Cohort		Model		O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	Ratio
Framingham Offspring Study ⁷	FRS-O	All	Stroke 2	Wilson AFT Model A No BMI CeVD	Stroke 2	0.772	
Framingham Offspring Study ⁷	FRS-O	All	Stroke 2	Wilson AFT Model A CeVD	Stroke 2	0.792	
Framingham Offspring Study ⁷	FRS-O	All	Stroke 2	Wilson AFT Model B CeVD	Stroke 2	0.798	
Framingham Offspring Study ⁷	FRS-O	All	Stroke 2	Wilson AFT Model C CeVD	Stroke 2	0.8	
Framingham Offspring Study ⁷	FRS-O	All	Stroke 2	Wilson AFT Model D CeVD	Stroke 2	0.804	
Framingham Offspring Study	FRS-O	All	Stroke 2	Wilson AFT Model D No BMI CeVD	Stroke 2	0.798	
Atherosclerosis Risk in Communities Study ¹²	ARIC	Men	Stroke 3	Chambless Basic Men	Stroke 3	0.756	
Atherosclerosis Risk in Communities Study ¹²	ARIC	Women	Stroke 3	Chambless Basic Women	Stroke 3	0.792	
Atherosclerosis Risk in Communities Study ¹²	ARIC	Men	Stroke 3	Chambless BM + Age + Race	Stroke 3	0.789	
Atherosclerosis Risk in Communities Study ¹²	ARIC	Men	Stroke 3	Chambless BM + NTRF + Age + Race	Stroke 3	0.803	
Atherosclerosis Risk in Communities Study ¹²	ARIC	Women	Stroke 3	Chambless BW + Age + Race	Stroke 3	0.813	
Atherosclerosis Risk in Communities Study ¹²	ARIC	Women	Stroke 3	Chambless BW + NTRF + Age + Race	Stroke 3	0.837	
Wisconsin Epidemiologic Study of Diabetic Retinopathy ⁵⁴	WESDR	All	Stroke Mortality	UKPDS 60	Stroke 1		1.135
Wisconsin Epidemiologic Study of Diabetic Retinopathy ⁵⁴	WESDR	All	Stroke Mortality	FRS (1991)	CVD 2		1.788

Table 8d. CVD Model Details – Europe

	Cohort		Cohort		Model			HLC	GOF	O/E
Cohort	Abbrev	Group Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
Consecutive patients referred by primary care								~		
provider for preventive cardiological exam ⁴¹	LudwigU	All	Hard CHD 1	SCORE (Unknown Version)	CVD Mortality	0.66	0.62-0.68			
Members of the QRESEARCH database ³⁴	QRESEARCH	Validation-Men	CVD 1	QRISK	CVD 4	0.788	0.786-0.791			
		Validation-								
Members of the QRESEARCH database ³⁴	QRESEARCH	Women	CVD 1	QRISK	CVD 4	0.814	0.811-0.817			
Members of the QRESEARCH database ³⁴	QRESEARCH	Validation-Men	CVD 1	QRISK2	CVD 1	0.792	0.789-0.794			
		Validation-								
Members of the QRESEARCH database ³⁴	QRESEARCH	Women	CVD 1	QRISK2	CVD 1	0.817	0.814-0.820			
Members of the QRESEARCH database ³⁴	QRESEARCH	Validation-Men	CVD 1	FRS (1991), NICE-Modified	CVD	0.779	0.776-0.782			
		Validation-								
Members of the QRESEARCH database ³⁴	QRESEARCH	Women	CVD 1	FRS (1991), NICE-Modified	CVD	0.8	0.797-0.803			
Scottish Hearth Health Extended Cohort ³⁰	SHHEC	Men	CVD 11 (10 yr)	ASSIGN	CVD 11	0.727				0.789
Scottish Hearth Health Extended Cohort ³⁰	SHHEC	Women	CVD 11 (10 yr)	ASSIGN	CVD 11	0.765				0.672
Scottish Hearth Health Extended Cohort ³⁰	SHHEC	Men	CVD 11 (10 yr)	FRS (1991)	CVD 2	0.716				0.71
Scottish Hearth Health Extended Cohort ³⁰	SHHEC	Women	CVD 11 (10 yr)	FRS (1991)	CVD 2	0.741				0.651
Diabetes clinic at University College London										
Hospitals NHS Trust ³³	NHS Trust	All	CVD 18	JBSRC	CVD	0.8	0.75-0.85			
Diabetes clinic at University College London										
Hospitals NHS Trust ³³	NHS Trust	All	CVD 18	CRM	CVD	0.76	0.72-0.79			2.301
Diabetes clinic at University College London										
Hospitals NHS Trust ³³	NHS Trust	All	Total CHD 2	JBSRC	CVD	0.77	0.74-0.80			
Diabetes clinic at University College London										
Hospitals NHS Trust ³³	NHS Trust	All	Total CHD 2	CRM	CVD	0.73	0.70-0.77		<u> </u>	1.74
Uppsala Longitudinal Study of Adult Men										
(Baseline Age 70 Cohort) ²³	ULSAM (70)	All	CVD Mortality	FRS (Wilson 1998) + ECG	CVD Mortality	0.67			<u> </u>	
Poole Diabetes Study ⁵⁰	PDS	All	Total CHD 3	FRS (1991)	Total CHD 1	0.657	0.581-0.732	19.8	0	1.471
D 1 D 1 1 0 1 86		All-excluding							-	
Poole Diabetes Study ⁵⁰	PDS	LVH	Total CHD 3	FRS (1991)	Total CHD 1	0.665	0.591-0.740	22.6	0	
Poole Diabetes Study ⁵⁵	PDS	Men	Total CHD 3	FRS (1991)	Total CHD 1	0.726	0.643-0.810	──	 	
Poole Diabetes Study	PDS	Women	Total CHD 3	FRS (1991)	Total CHD 1	0.697	0.635-0.760	──	 	
D I D I I I D I I B B		Pretreated								
Poole Diabetes Study	PDS	blood pressure	Total CHD 3	FRS (1991)	Total CHD 1	0.666	0.538-0.795	<u> </u>	<u> </u>	
		Untreated blood				0.000				
Poole Diabetes Study	PDS	pressure	Total CHD 3	FRS (1991)	Total CHD 1	0.663	0.568-0.758	00.0	<u> </u>	4 5 4 7
Poole Diabetes Study	PDS	All	CVD 13	FRS (1991)	CVD 2	0.673	0.612-0.734	32.8	0	1.517
Deale Dishetes Stude ⁸⁶		All-excluding				0.070	0 040 0 700	20 5		
Poole Diabetes Study	PDS	LVH	CVD 13	FRS (1991)	CVD 2	0.678	0.618-0.739	39.5	0	
Poole Diabetes Study	PDS	Men	CVD 13	FRS (1991)	CVD 2	0.669	0.590-0.747	──	──	
Poole Diabetes Study	PDS	women	CVD 13	FRS (1991)	CVD 2	0.678	0.580-0.776	<u> </u>	<u> </u>	
Decle Dichetes Study ⁸⁶	DDC	Pretreated		FRS (1001)		0.624	0 500 0 700		1	
Fuole Diabetes Study	FD3	Lintracted black	01013	(1991)		0.034	0.550-0.739	—	├──	+
Paolo Diobatan Studu ⁸⁶	DDe			EBS (1001)		0.60	0 612 0 767		1	
Cordiff Dichotop Dotohooo (turo 1 and turo	Cordiff DM	Man		FRS (1991)		0.09	0.013-0.767	──	<u> </u>	0.015
Cardin Diabetes Database (type 1 and type		ivien		FK3 (1991)		0.64	1	1	1	0.015

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	Cohort		Cohort	Model				HLGOF		
Cohort	Abbrev	Group Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
2) ⁸⁵										
Cardiff Diabetes Database (type 1 and type									1	
2) ⁸⁵	Cardiff DM	Women	CVD 2	FRS (1991)	CVD 2	0.66			ł	0.86
Cardiff Diabetes Database (type 1 and type				FRS (1991) Cardiff					Ĩ	
2) ⁸⁵	Cardiff DM	Men	CVD 2	Diabetes Remodel	CVD 2	0.65			1	
Cardiff Diabetes Database (type 1 and type				FRS (1991) Cardiff					i	
2) ⁸⁵	Cardiff DM	Women	CVD 2	Diabetes Remodel	CVD 2	0.68			ł	
Vorarlberg Health Monitoring and Promotion									Ĩ	
Program (VHM&PP) cohort undergoing									ł	
general health exams in Vorarlberg province ⁷⁶	VHM&PP	All	CVD Mortality	SCORE (Low Risk TC)	CVD Mortality	0.8	0.79-0.82		ł	0.731
Vorarlberg Health Monitoring and Promotion									i	
Program (VHM&PP) cohort undergoing									ł	
general health exams in Vorarlberg province ⁷⁶	VHM&PP	Men	CVD Mortality	SCORE (Low Risk TC)	CVD Mortality	0.76	0.74-0.79		ł	0.836
Vorarlberg Health Monitoring and Promotion									i	
Program (VHM&PP) cohort undergoing									ł	
general health exams in Vorarlberg province ⁷⁶	VHM&PP	Women	CVD Mortality	SCORE (Low Risk TC)	CVD Mortality	0.78	0.74-0.82		ł	0.523
Vorarlberg Health Monitoring and Promotion									i	
Program (VHM&PP) cohort undergoing									ł	
general health exams in Vorarlberg province ⁷⁶	VHM&PP	Men	CHD Mortality	SCORE (Low Risk TC)	CVD Mortality	0.75	0.72-0.78		ł	0.79
Vorarlberg Health Monitoring and Promotion										
Program (VHM&PP) cohort undergoing									l	
general health exams in Vorarlberg province ⁷⁶	VHM&PP	Women	CHD Mortality	SCORE (Low Risk TC)	CVD Mortality	0.84	0.80-0.88		1	0.463
Individuals recruited from workforce of a									i	
nationwide multi-industry corporation (Fletcher									ł	
Challenge, Ltd. [72%]) and general electoral									ł	
rolls of Auckland metro region (28%) ⁸¹	NZWork	Men	CVD 2 (5 yrs)	New Zealand risk charts	CVD	0.73	0.72-0.74		I	
Individuals recruited from workforce of a									l	
nationwide multi-industry corporation (Fletcher									ł	
Challenge, Ltd. [72%]) and general electoral									ł	
rolls of Auckland metro region (28%) ⁸¹	NZWork	Women	CVD 2 (5 yrs)	New Zealand risk charts	CVD	0.78	0.75-0.81		I	
Individuals recruited from workforce of a									ł	
nationwide multi-industry corporation (Fletcher									ł	
Challenge, Ltd. [72%]) and general electoral									ł	
rolls of Auckland metro region (28%)	NZWork	Men	CVD 2 (5 yrs)	FRS (1991)	CVD 2	0.74	0.73-0.75		 	1.173
Individuals recruited from workforce of a									ł	
nationwide multi-industry corporation (Fletcher									ł	
Challenge, Ltd. [72%]) and general electoral									ł	
rolls of Auckland metro region (28%) ³¹	NZWork	Women	CVD 2 (5 yrs)	FRS (1991)	CVD 2	0.77	0.74-0.80		 	1.089
			Hard CHD 1 +						ł	
British Regional Heart Study, men aged 40-59			Stroke 1 +						ł	
years'	RKHS	Men	DM2 (20 yrs)	FRS (1991)	Total CHD 1	0.67	0.65-0.69	\parallel		
British Regional Heart Study, men aged 40-59			Hard CHD 1		-				ł	
years	BKHS	Men	(10 yrs)	FRS (1991)	Total CHD 1	0.73	0.71-0.75	\parallel		
British Regional Heart Study, men aged 40-59			Hard CHD 1						ł	
years'	BRHS	Men	(20 yrs)	FRS (1991)	Total CHD 1	0.68	0.66-0.70		i	2.5

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	Cohort		Cohort		Model			HLG	GOF	O/E
Cohort	Abbrev	Group Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
British Regional Heart Study, men aged 40-59			Stroke 1 (10							
years ⁷²	BRHS	Men	yrs)	FRS (1991)	Total CHD 1	0.71	0.65-0.77			
British Regional Heart Study, men aged 40-59			Stroke 1 (20							
years ⁷²	BRHS	Men	yrs)	FRS (1991)	Total CHD 1	0.66	0.62-0.70			
British Regional Heart Study, men aged 40-59			Diabetes, Type							
years ⁷²	BRHS	Men	2 (10 yrs)	FRS (1991)	Total CHD 1	0.61	0.55-0.67			
British Regional Heart Study, men aged 40-59			Diabetes, Type							
years ⁷²	BRHS	Men	2 (20 yrs)	FRS (1991)	Total CHD 1	0.6	0.56-0.64			
QRESEARCH database, constructed from	QRESEARCH									
160 UK general practices; validation cohort ⁴⁰	(Val)	Men	CVD 4 (10 yr)	ASSIGN	CVD 11	0.764				0.734
QRESEARCH database, constructed from	QRESEARCH									
160 UK general practices; validation cohort ⁴⁰	(Val)	Women	CVD 4 (10 yr)	ASSIGN	CVD 11	0.784				0.727
QRESEARCH database, constructed from	QRESEARCH									
160 UK general practices; validation cohort ⁴⁰	(Val)	Men	CVD 4 (10 yr)	FRS (1991)	CVD 2	0.76				0.681
QRESEARCH database, constructed from	QRESEARCH									
160 UK general practices; validation cohort ⁴⁰	(Val)	Women	CVD 4 (10 yr)	FRS (1991)	CVD 2	0.774				0.83
QRESEARCH database, constructed from	QRESEARCH									
160 UK general practices; validation cohort ⁴⁰	(Val)	Men	CVD 4 (10 yr)	QRISK	CVD 4	0.767				1.002
QRESEARCH database, constructed from	QRESEARCH									
160 UK general practices; validation cohort ⁴⁰	(Val)	Women	CVD 4 (10 yr)	QRISK	CVD 4	0.788				0.98
British Women's Heart and Health Cohort ⁴⁴	BWHH	All	Total CHD 1	FRS (1991)	CVD 2	0.63	0.59-0.67			0.97
British Women's Heart and Health Cohort ⁴⁴	BWHH	All	CVD 11	FRS (1991)	CVD 2	0.64	0.61-0.68			0.65
INSIGHT trial cohort of middle-aged patients										
with hypertension ³⁷	INSIGHT	All	CVD 14	INSIGHT CVD	CVD 14	0.661				1.25
INSIGHT trial cohort of middle-aged patients										
with hypertension ³⁷	INSIGHT	All	CVD 14	FRS (1991)	CVD 2					0.385
Cardiovascular Program in Norway (Ages 60-										
(69) ⁷¹	CP-Norway	Men	CVD Mortality	SCORE (High Risk TC)	CVD Mortality	0.65				0.448
Cardiovascular Program in Norway (Ages 60-										
(69) ⁷¹	CP-Norway	Women	CVD Mortality	SCORE (High Risk TC)	CVD Mortality	0.68				0.372
74		Men (40-49								
Norwegian Counties Study (ages 40-59) ⁷¹	NCS	years)	CVD Mortality	SCORE (High Risk TC)	CVD Mortality	0.67				0.53
74		Men (50-59								
Norwegian Counties Study (ages 40-59)'	NCS	years)	CVD Mortality	SCORE (High Risk TC)	CVD Mortality	0.68				0.53
		Women (40-49								
Norwegian Counties Study (ages 40-59) ⁷¹	NCS	years)	CVD Mortality	SCORE (High Risk TC)	CVD Mortality	0.66				0.60
		Women (50-59								
Norwegian Counties Study (ages 40-59) ⁷¹	NCS	years)	CVD Mortality	SCORE (High Risk TC)	CVD Mortality	0.72				0.45
	Renfrew-									
Renfrew and Paisley Study ⁷⁰	Paisley	All	CVD Mortality	FRS (1991)	CVD 2	0.733	0.715-0.750			1.714
		Manual class								
	Renfrew-	(social classes								
Renfrew and Paislev Study ⁷⁰	Paislev	IIIM. IV. V)	CVD Mortality	FRS (1991)	CVD 2	0.72	0.699-0.741			

	Cohort		Cohort		Model			HLGOF		O/E
Cohort	Abbrev	Group Name	Outcome	Model Name	Outcome	AUC	AUC Var	γ^2	Р	Ratio
		Non-manual						~	-	
		class (social								
	Renfrew-	classes I, II,								
Renfrew and Paisley Study ⁷⁰	Paisley	IIIN)	CVD Mortality	FRS (1991)	CVD 2	0.744	0.710-0.777			
QRESEARCH ⁶²	QRESEARCH	Men	CVD 10 (10 yr)	FRS (1991)	CVD 2	0.762	0.759-0.765			
QRESEARCH ⁶²	QRESEARCH	Women	CVD 10 (10 yr)	FRS (1991)	CVD 2	0.776	0.772-0.780			
QRESEARCH ⁶²	QRESEARCH	Men	CVD 10 (10 yr)	QRISK	CVD 4	0.77	0.767-0.773			
QRESEARCH ⁶²	QRESEARCH	Women	CVD 10 (10 yr)	QRISK	CVD 4	0.788	0.784-0.792			
THIN Cohort; data from 288 UK practices										
using INPS Vision system (~20%); including										
24 practices (54709 patients) from Scotland &										
14 practices (36904) from Northern Ireland ⁶²	THIN	Men	CVD 10 (10 yr)	FRS (1991)	CVD 2	0.737	0.734-0.739			0.758
THIN Cohort; data from 288 UK practices										
using INPS Vision system (~20%); including										
24 practices (54709 patients) from Scotland &										
14 practices (36904) from Northern Ireland ⁶²	THIN	Women	CVD 10 (10 yr)	FRS (1991)	CVD 2	0.76	0.756-0.763			0.909
THIN Cohort; data from 288 UK practices										
using INPS Vision system (~20%); including										
24 practices (54709 patients) from Scotland &										
14 practices (36904) from Northern Ireland ⁶²	THIN	Men	CVD 10 (10 yr)	QRISK	CVD 4	0.762	0.759-0.765			1.149
THIN Cohort; data from 288 UK practices										
using INPS Vision system (~20%); including										
24 practices (54709 patients) from Scotland &										
14 practices (36904) from Northern Ireland ⁶²	THIN	Women	CVD 10 (10 yr)	QRISK	CVD 4	0.789	0.786-0.792			1.111
PROCAM cohort; drawn from 52 companies										
and local government authorities ⁶¹	PROCAM	Men	Hard CHD 1	FRS (1991)	CVD 2	0.73	0.70-0.75			0.564
PROCAM cohort; drawn from 52 companies										
and local government authorities ⁶¹	PROCAM	Women	Hard CHD 1	FRS (1991)	CVD 2	0.88	0.80-0.96			0.347
MONICA Augsburg cohort; 1984/1985 and	MONICA-									
1989/1990 surveys ⁶¹	Augsburg	Men	Hard CHD 1	FRS (1991)	CVD 2	0.78	0.73-0.84			0.501
MONICA Augsburg cohort; 1984/1985 and	MONICA-	Women aged								
1989/1990 surveys ⁶¹	Augsburg	55-64 years	Hard CHD 1	FRS (1991)	CVD 2	0.88	0.80-0.96			
		Participants								
42		grouped by								
Swedish National Diabetes Register ⁴³	SNDR	predicted risk	CVD 5	Swedish NDR	CVD 5	0.7		4.29	0.83	
Swedish National Diabetes Register ⁴³	SNDR	Subgroup B	CVD 5	Swedish NDR	CVD 5	0.69				
Monitoring Project on Cardiovascular Disease										
Risk Factors; cohort randomly selected from 3			CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD)"	MP-CVDRF	All	(10 yr)	FRS (1991)	CVD 2	0.86	0.84-0.88			
Monitoring Project on Cardiovascular Disease										
Risk Factors; cohort randomly selected from 3		All high risk	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ^{//}	MP-CVDRF	participants	(10 yr)	FRS (1991)	CVD 2	0.8	0.77-0.82		L	
Monitoring Project on Cardiovascular Disease		Participants with							1	
Risk Factors; cohort randomly selected from 3		SBP >140	CVD Mortality						1	
cities in Netherlands (aged 20-59 & no CVD)	MP-CVDRF	mmHg	(10 yr)	FRS (1991)	CVD 2	0.79	0.75-0.83	1	1	1

Cardiovascular Disease Risk Assessment Tools

	Cohort		Cohort		Model			HLC	GOF	O/E
Cohort	Abbrev	Group Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
Monitoring Project on Cardiovascular Disease										
Risk Factors; cohort randomly selected from 3		Participants with	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	TC >6.5 mmol/L	(10 yr)	FRS (1991)	CVD 2	0.81	0.77-0.85			
Monitoring Project on Cardiovascular Disease		Smokers (men								
Risk Factors; cohort randomly selected from 3		>50 yrs, women	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	>55 yrs)	(10 yr)	FRS (1991)	CVD 2	0.69	0.65-0.74			
Monitoring Project on Cardiovascular Disease										
Risk Factors; cohort randomly selected from 3			CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	All	(10 yr)	SCORE (Unknown Version)	CVD Mortality	0.85	0.83-0.87			
Monitoring Project on Cardiovascular Disease										
Risk Factors; cohort randomly selected from 3		All high risk	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	participants	(10 yr)	SCORE (Unknown Version)	CVD Mortality	0.75	0.72-0.78			
Monitoring Project on Cardiovascular Disease		Participants with								
Risk Factors; cohort randomly selected from 3		SBP > 140 mm	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	Hg	(10 yr)	SCORE (Unknown Version)	CVD Mortality	0.76	0.72-0.81			
Monitoring Project on Cardiovascular Disease										
Risk Factors; cohort randomly selected from 3		Participants with	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	TC >6.5 mmol/L	(10 yr)	SCORE (Unknown Version)	CVD Mortality	0.78	0.73-0.82			
Monitoring Project on Cardiovascular Disease		Smokers (men								
Risk Factors; cohort randomly selected from 3		>50 yrs, women	CVD Mortality							
cities in Netherlands (aged 20-59 & no CVD) ⁷⁷	MP-CVDRF	>55 yrs)	(10 yr)	SCORE (Unknown Version)	CVD Mortality	0.62	0.55-0.68			
Leiden 85-plus Study42	L85	All	CVD Mortality	FRS (1991)	CVD 2	0.53	0.42-0.63			
Dubbo Study; cohort of elderly Australians										
(ages 60-79) without DM ⁵⁶	DUBBO-NoDM	Men	CVD 4 (10 yrs)	FRS (ATP)	Hard CHD 1					0.914
Dubbo Study; cohort of elderly Australians										
(ages 60-79) without DM ⁵⁶	DUBBO-NoDM	Women	CVD 4 (10 yrs)	FRS (ATP)	Hard CHD 1					0.925
Dubbo Study; cohort of elderly Australians										
(ages 60-79) with DM ⁵⁶	DUBBO-All	All	CVD 4 (5 yrs)	Dubbo model	CVD 4				107	
Dubbo Study; cohort of elderly Australians										
(ages 60-79) with DM ⁵⁶	DUBBO-All	All	CVD 4 (10 yrs)	Dubbo model	CVD 4				167	

Table 8e. CHD Model Details – Europe

	Cohort	Group	Cohort		Model			HLC	GOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
European Prospective Investigation of Cancer [EPIC]-								~		1
Norfolk ³⁵	EPIC-Norfolk	Men	Total CHD 1	FRS [TC] (1998)	Total CHD 1	0.71	0.69-0.73			
European Prospective Investigation of Cancer [EPIC]-										
Norfolk ³⁵	EPIC-Norfolk	Women	Total CHD 1	FRS [TC] (1998)	Total CHD 1	0.71	0.68-0.74			
European Prospective Investigation of Cancer [EPIC]-										
Norfolk ³³	EPIC-Norfolk	Men	Total CHD 1	FRS (1998) EPIC Remodel	Total CHD 1	0.72	0.70-0.75			
European Prospective Investigation of Cancer [EPIC]-										
Norfolk ³⁰	EPIC-Norfolk	Women	Total CHD 1	FRS (1998) EPIC Remodel	Total CHD 1	0.8	0.78-0.83			
European Prospective Investigation of Cancer [EPIC]-		14.00				0.70	0 70 0 75			
INORIOIK	EPIC-NOTIOIK	wen	Total CHD 1	FRS (1998) + EPIC + HDA1C	Total CHD 1	0.73	0.70-0.75			
European Prospective Investigation of Cancer [EPIC]-		Womon				0.0	0 70 0 02			
European Brospective Investigation of Concer [EBIC]	EFIC-NUTIOK	women		FRS(1996) + EFIC + HDATC		0.0	0.76-0.65			
Norfolk ³⁵	EPIC-Norfolk	Men	Total CHD 1	\pm HbA1c	Total CHD 1	0.73	0 70-0 74			
European Prospective Investigation of Cancer [EPIC]-		WiCh		FRS(1998) + FPIC w/o DM		0.75	0.70 0.74			+
Norfolk ³⁵	EPIC-Norfolk	Women	Total CHD 1	+ HbA1c	Total CHD 1	0.8	0 77-0 82			
Consecutive patients referred by primary care provider		Women			Total Of D	0.0	0.77 0.02			
for preventive cardiological exam ⁴¹	LudwiaU	All	Hard CHD 1	PROCAM CHD (Cox model)	Hard CHD 1	0.65	0.62-0.68			
Consecutive patients referred by primary care provider	<u> </u>									
for preventive cardiological exam ⁴¹	LudwigU	All	Hard CHD 1	FRS (ATP)	Hard CHD 1	0.63	0.59-0.65			
Rotterdam Study ⁸⁴	Rotterdam	Men	Hard CHD 1	FRS (ATP)	Hard CHD 1	0.63	0.52-0.74			0.723
Rotterdam Study ⁸⁴	Rotterdam	Women	Hard CHD 1	FRS (ATP)	Hard CHD 1	0.73	0.65-0.83			1.021
Study of Atherosclerotic Risk Factors ²⁵	STULONG	All	Total CHD 1	FRS [TC] (1998)	Total CHD 1	0.638	58.4-69.1			1.282
Validity of the Adapted Framingham Individual Risk										
Equation for Coronary Incidents Cohort ³⁸	VERIFICA	Men	Total CHD 1	FRS [TC] (1998)	Total CHD 1	0.68		110.1	0	0.451
Validity of the Adapted Framingham Individual Risk										
Equation for Coronary Incidents Cohort ³⁰	VERIFICA	Women	Total CHD 1	FRS [TC] (1998)	Total CHD 1	0.73		64.3	0	0.44
Validity of the Adapted Framingham Individual Risk				FRS (1998 Wilson)		0.00				4 050
Equation for Coronary Incidents Conort	VERIFICA	Men	Total CHD 1	REGICOR Remodel	Total CHD 1	0.69		5.1	0	1.256
Validity of the Adapted Framingham Individual RISK		14/2002		FRS (1998 Wilson)		0.04		0.7	~	1 00
Equation for Coronary Incidents Conort	VERIFICA	women	Total CHD 1	ERS (1008 Wilcon)	Total CHD 1	0.81		2.7	0	1.03
Faultion for Coronany Incidente Cohort ³⁸		Diabotics		PEGICOP Romodol				1 /	0	
Validity of the Adapted Framingham Individual Risk	VERIFICA	Diabetics		REGICOR Remodel	Total CLID T			1.4	0	+
Equation for Coronary Incidents Cohort ³⁸	VERIFICA	Diabetics	Total CHD 1	FRS (1998 Wilson)	Total CHD 1			54.2	0	
West of Scotland Coronary Prevention Study ³²	WOSCOPS	All	Hard CHD 1	OT Dispersion	Hard CHD 1	0.52		04.2	•	+
		7.01		ERS [Unknown Version]		0.02				+
Lvon, France ²¹	Lvon	All	CVD 6	(1998)	Total CHD 1	0.72				1.36
Diabetes clinic at University College London Hospitals		7	0.20	(1000)		0				
NHS Trust ³³	NHS Trust	All	CVD 18	PROCAM CHD (Cox model)	Hard CHD 1	0.67	0.62-0.73			2.79
Diabetes clinic at University College London Hospitals		1								1
NHS Trust ³³	NHS Trust	All	CVD 18	UKPDS 56	Hard CHD 1	0.74	0.70-0.78			1.201
Diabetes clinic at University College London Hospitals										
NHS Trust ³³	NHS Trust	All	Total CHD 2	PROCAM CHD (Cox model)	Hard CHD 1	0.65	0.59-0.71			2.05

Cardiovascular Disease Risk Assessment Tools
	Cohort	Group	Cohort		Model			HLO	GOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	γ^2	Р	Ratio
Diabetes clinic at University College London Hospitals								ň		
NHS Trust ³³	NHS Trust	All	Total CHD 2	UKPDS 56	Hard CHD 1	0.76	0.72-0.80			1.6
Uppsala Longitudinal Study of Adult Men (Baseline Age			CVD	FRS [Unknown Version]						
70 Cohort) ²³	ULSAM (70)	All	Mortality	(1998)	Total CHD 1	0.58				
		Men								
20		(Prediction								
Uppsala Longitudinal Study of Adult Men ²²	ULSAM	Data)	MI	PROCAM CHD (Cox model)	Hard CHD 1	0.63				
		Men								
22		(Prediction								
Uppsala Longitudinal Study of Adult Men ²²	ULSAM	Data)	MI	FRS (ATP)	Hard CHD 1	0.61				<u> </u>
22			Hard CHD 1							
Uppsala Longitudinal Study of Adult Men-	ULSAM	All	(10 yrs)	FRS (ATP)	Hard CHD 1					0.213
Linnada Lanaitudinal Chudu of Adult Man ²²		A 11	Hard CHD 1							0.074
Deele Diebetee Studi 86	ULSAM	All	(10 yrs)		Hard CHD 1	0.07	0 500 0 740	474		0.271
Poole Diabetes Study	PDS	All	Total CHD 3		Hard CHD 1	0.67	0.598-0.742	17.1	0	+
Poole Diabetes Study	PDS	Wen	Total CHD 3		Hard CHD 1	0.673	0.585-0.761			+
Poole Diabetes Study	PD5	Vvomen	Total CHD 3	UKPDS 56	Hard CHD 1	0.618	0.491-0.746			+
		Pretreated								
Doolo Diobotoo Studu ⁸⁶	DDC	DIOOU				0 606	0 575 0 917			
Foole Diabeles Sludy	FD3	Untroated		UKFD3 50		0.090	0.575-0.617			<u> </u>
		blood								
Poole Diabetes Study ⁸⁶	PDS	pressure	Total CHD 3	LIKPDS 56	Hard CHD 1	0 648	0 559-0 736			
CLIORE ²⁹	CUORE	Men	Hard CHD 2	CLIORE	Hard CHD 2	0.040	0.684-0.796	15 5		+
	OUDINE	WICH		FRS (Wilson 1998 TC)		0.742	0.004 0.730	10.0		+
CUORF ²⁹	CUORE	Men	Hard CHD 2	CUORE D'Ag Remodel	Hard CHD 2	0.723	0.670-0.779	27.1		0.765
				PROCAM (Cox) CUORE		00				000
CUORE ²⁹	CUORE	Men	Hard CHD 2	D'Ag Remodel	Hard CHD 2	0.735	0.678-9.790	220.3		0.87
CUORE ²⁹	CUORE	Men	Hard CHD 2	FRS (TC) (1998)	Total CHD 1	0.723	0.670-0.779			0.328
		-		FRS (Wilson 1998 TC)						
CUORE ²⁹	CUORE	Men	Hard CHD 2	CUORE Chamb Remodel	Hard CHD 2	0.723	0.670-0.779			1.01
				PROCAM (Cox) CUORE						1
CUORE ²⁹	CUORE	Men	Hard CHD 2	Chamb Remodel	Hard CHD 2	0.735	0.678-9.790			1.01
Subjects with type 2 diabetes registered with a Tayside										
GP ³⁹	DARTS	All	Hard CHD 1	DARTS	Hard CHD 1	0.71	0.63-0.79			
				FRS [Unknown Version]						
Rotterdam Coronary Calcification Study ⁷⁹	RCC	All	CVD 3	(1998)	Total CHD 1	0.73				
		age > 70		FRS [Unknown Version]						
Rotterdam Coronary Calcification Study ⁷⁹	RCC	years	CVD 3	(1998)	Total CHD 1	0.682				
Men randomly selected from general population in	MONICA-			FRS [Unknown Version]						
1984-5, 1989-90, and 1994-5 ^{/>}	Augsburg	All	Hard CHD 1	(1998)	Total CHD 1	0.735				
PROCAM; cohort of employees of 52 companies and			1							
local government authorities with f/u every 2 years ²⁷	PROCAM	All	Hard CHD 1	PROCAM CHD (Cox model)	Hard CHD 1	0.829		6.5	0.3	
PROCAM; cohort of employees of 52 companies and		1								
local government authorities with f/u every 2 years ²⁷	PROCAM	All	Hard CHD 1	FRS (ATP)	Hard CHD 1	0.778		43.8	0.001	

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	Cohort	Group	Cohort		Model			HLG	OF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	γ^2	Р	Ratio
PROCAM: cohort of employees of 52 companies and								~		
local government authorities with f/u every 2 years ²⁷	PROCAM	All	Hard CHD 1	PROCAM CHD (Point Score)	Hard CHD 1	0.824				
Individuals with diabetes receiving care in Salford ³⁹	Salford	All	Hard CHD 1	DARTS	Hard CHD 1	0.69	0.58-0.78			
Second Northwick Park Heart Stud ³¹	NPHS-II	All	Hard CHD 2	PROCAM CHD (Cox model)	Hard CHD 1	0.63	0.59-0.67			0.46
Second Northwick Park Heart Study ³¹	NPHS-II	All	Hard CHD 2	NPHS-II score 1 (basic)	Hard CHD 2	0.64	0.58-0.70			
				NPHS-II score 2 (basic + DM						
Second Northwick Park Heart Study ³¹	NPHS-II	All	Hard CHD 2	+ fam hx)	Hard CHD 2	0.66	0.60-0.71			
				NPHS-II score 3 (basic +						
Second Northwick Park Heart Study ³¹	NPHS-II	All	Hard CHD 2	DM)	Hard CHD 2	0.63	0.58-0.69			
				NPHS-II score 4 (basic +						
Second Northwick Park Heart Study ³¹	NPHS-II	All	Hard CHD 2	fam hx)	Hard CHD 2	0.64	0.59-0.69			
				NPHS-II score 5 (basic +		0.0.				+
Second Northwick Park Heart Study ³¹	NPHS-II	All	Hard CHD 2	fibringgen)	Hard CHD 2	0.66	0.60-0.71			
				NPHS-II score 6 (basic +		0.00				+
Second Northwick Park Heart Study ³¹	NPHS-II	All	Hard CHD 2		Hard CHD 2	0.67	0 61-0 72			
		,		NPHS-II score 7 (basic +		0.07	0.01 0.12			+
Second Northwick Park Heart Study ³¹	NPHS-II	АII	Hard CHD 2	A n o A I + A n o B	Hard CHD 2	0.66	0 60-0 72			
Second Northwick Park Heart Study ³¹	NPHS-II		Hard CHD 2	FRS (ATP)	Hard CHD 1	0.60	0.58-0.66			0.47
			Total CHD 1			0.02	0.00 0.00			0.47
PRIME cohort study (Belfast Cohort) ⁸⁰	PRIME-Belfast	ΔII	(5 yr)	FRS (ATP)	Hard CHD 1	0.66				0 746
				TRO (ATT)		0.00				0.740
PPIME cohort study (Bolfast Cohort) ⁸⁰	DRIME Bolfact	A II	(5 vr)			0.61				0.562
						0.01				0.302
DRIME cohort study ⁸⁰	DRIME Franco	A II				0.69				0.672
	FININE-FIANCE	All		FKS (AFF)		0.00	-			0.073
DRIME cohort study ⁸⁰	DRIME Franco	A II				0.64				0 220
Cohort of mon and woman amployed in NW/ Cormany ²⁸				PROCAM (BML modified)	Hard CHD 1	0.04				0.223
Cohort of men and women employed in NW Cermany ²⁸			Hard CHD 1	PROCAM CHD (Cox model)	Hard CHD 1	0.02				0.001
Individuals with type 2 dispetes dispessed by standard	FROCAIVI	All		FROCAM CITE (Cox model)		0.021	-			
aritaria and an standard diabetic therapy (dist. tableta										
inculin) and agod 50.75 years, recruited from outpatient										
clinics in Central and West London ⁸⁸		All		ERS (1001)		0.63	0 55-0 71			
Individuals with type 2 diabetes diagnosed by standard			CVD 13	1 ((391)	0002	0.05	0.00-0.71			+
criteria and on standard diabetic therapy (diet tablets										
insulin) and aged 50-75 years, recruited from outpatient										
clinics in Central and West London ⁸⁸	PREDICT	ΔII	CVD 19		Hard CHD 1	0.67	0 60-0 75			
Individuals with type 2 diabetes diagnosed by standard	TREDICT		00010			0.07	0.00 0.75			
criteria and on standard diabetic therapy (diet tablets										
insulin) and aged 50-75 years recruited from outpatient										
clinics in Central and West London ⁸⁸	PREDICT	ΔII	Total CHD 2		Hard CHD 1	0.63	0 56-0 71			
Participants in Supplementation en Vitamines et	TREDIOT					0.00	0.00 0.7 1			
Minerally Antioxydants randomized primary prevention				ERS [Inknown Version]						
trial followed annually since 1994/1995 ³⁶	SUVIMAX	ΔII	Total CHD 1	(1008)	Total CHD 1	0 74				0 497
Participants in Supplementation on Vitamines of		7 MI				0.74		\vdash		5.731
Minerally Antioxydants randomized primary prevention			1							
trial followed annually since 1001/1005 ³⁶	SILVIMAY	ΔII	Total CHD 1	SUVIMAX	Total CHD 1	0.75				
that, followed annually since 1004/1000		7.01		00.01.00/07		0.10	1			1

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	Cohort	Group	Cohort		Model			HLG	SOF	O/E
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
Munich ⁸⁷	MunichDM	All	MI	UKPDS 56	Hard CHD 1	0.66	0.62-0.68			
				FRS [Unknown Version]						
Munich ⁸⁷	MunichDM	All	MI	(1998)	Total CHD 1	0.63	0.59-0.66			
PROCAM cohort; employees of 52 companies and local			Hard CHD 1							
government authorities in Germany, aged 20-78 years ²⁶	PROCAM	All	(10 Year)	PROCAM CHD (Cox model)	Hard CHD 1	0.824				
PROCAM cohort; employees of 52 companies and local			Hard CHD 1	PROCAM CHD (Weibull						
government authorities in Germany, aged 20-78 years ²⁶	PROCAM	All	(10 Year)	model)	Hard CHD 1	0.824				
Men at work in public authorities and large companies										
in the region of Munster, Germany ⁷⁴	MunsterWork	Men	Hard CHD 1	PROCAM CHD (Cox model)	Hard CHD 1					0.781
Aboriginal community ⁸²	Aboriginal	Men	Total CHD 1	FRS (1991)	Total CHD 1					2
Aboriginal community ⁸²	Aboriginal	Women	Total CHD 1	FRS (1991)	Total CHD 1					3.918
INSIGHT trial cohort of middle-aged patients with										
hypertension ³⁷	INSIGHT	All	Total CHD 1	FRS (1991)	Total CHD 1					0.435
British Regional Heart Study; men aged 40-59 years										
randomly selected from registers of one general			CHD		CHD					
practice in each town ⁷³	BRHS	Men	Mortality	FRS (1991) BRHS Recal	Mortality			3.4		
British Regional Heart Study; men aged 40-59 years										
randomly selected from registers of one general										
practice in each town ⁷³	BRHS	Men	Total CHD 1	FRS (1991) BRHS Recal	Total CHD 1			24.6		
British Regional Heart Study; men aged 40-59 years										
randomly selected from registers of one general			CHD		CHD					
practice in each town ⁷³	BRHS	Men	Mortality	FRS (1991) CHD Mortality	Morality			30.2		0.683
British Regional Heart Study; men aged 40-59 years										
randomly selected from registers of one general										
practice in each town ⁷³	BRHS	Men	Total CHD 1	FRS (1991)	Total CHD 1			155.3		0.637
				FRS [Unknown Version]						
Consecutive renal transplant patients ⁶⁹	FrRenal	All	Total CHD 1	(1998)	Total CHD 1					1.688

Table 8f. Stroke Model Details – Europe

		Group	Cohort			O/E
Cohort	Cohort Abbrev	Name	Outcome	Model Name	Model Outcome	Ratio
INSIGHT trial cohort of middle-aged patients with hypertension ³⁷	INSIGHT	All	Stroke 4	INSIGHT Stroke	Stroke 4	1
INSIGHT trial cohort of middle-aged patients with hypertension ³⁷	INSIGHT	All	Stroke 4	FRS (1991) Stroke	Stroke 4	1
Apparently healthy Norwegian men aged 40-60 years recruited						
from 5 governmental agencies ²⁴	NorGov	All	CHD Mortality	Erikssen - CRF-X Model	CHD Mortality	0.999
Apparently healthy Norwegian men aged 40-60 years recruited						
from 5 governmental agencies ²⁴	NorGov	All	CHD Mortality	Erikssen – CRF Model	CHD Mortality	1
Apparently healthy Norwegian men aged 40-60 years recruited						
from 5 governmental agencies ²⁴	NorGov	All	CHD Mortality	Erikssen – X Model	CHD Mortality	1
Newcastle Heart Project: Europeans ⁸³	NHP-Europe	All	Stroke Mortality	FRS (1991) Stroke	Stroke 4	3.913
Newcastle Heart Project: Europeans ⁸³	NHP-Europe	All	CHD Mortality	SCORE [Unknown Version]	CHD Mortality	3.235

Table 8g. CVD Model Details – Asia

	Cohort	Group	Cohort		Model			HL	GOF	
Cohort	Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	O/E Ratio
Asia Pacific Cohort Studies Collaboration -										
Total Chinese Cohort ⁴⁵	APCSC China	Men	CVD 8	Asian Pacific	CVD 8	0.76	0.73-0.79	16.7	0.033	
Asia Pacific Cohort Studies Collaboration -										
Total Chinese Cohort ⁴⁵	APCSC China	Women	CVD 8	Asian Pacific	CVD 8	0.8	0.75-0.84	12.2	0.15	
Asia Pacific Cohort Studies Collaboration -										
Total Chinese Cohort ⁴⁵	APCSC China	Men	CVD 8	FRS (2007 Barzi)	CVD 8	0.75	0.72-0.78	557.5	0.0001	0.266
Asia Pacific Cohort Studies Collaboration -										
Total Chinese Cohort ⁴⁵	APCSC China	Women	CVD 8	FRS (2007 Barzi)	CVD 8	0.79	0.74-0.83	608	0.0001	0.495
				FRS (1998 Hard CHD1)						
MUCA II ⁴⁸	MUCA-II	Men	CVD 17	MUCA-II Remodel	CVD 17	0.796	0.762-0.829			
				FRS (1998 Hard CHD1)						
MUCA II ⁴⁸	MUCA-II	Women	CVD 17	MUCA-II Remodel	CVD 17	0.791	0.755-0.828			
MUCA II ⁴⁸	MUCA-II	Men	CVD 17	USA-PRC (Simplified)	CVD 17	0.792	0.758-0.825			
MUCA II ⁴⁸	MUCA-II	Women	CVD 17	USA-PRC (Simplified)	CVD 17	0.783	0.746-0.821			
MUCA II ⁴⁸	MUCA-II	Men	CVD 17	USA-PRC (Point Scoring)	CVD 17	0.791	0.757-0.825			
MUCA II ⁴⁸	MUCA-II	Women	CVD 17	USA-PRC (Point Scoring)	CVD 17	0.779	0.741-0.817			

Table 8h. CHD Model Details – Asia

		Group	Cohort		Model			HL	GOF	O/E
Cohort	Cohort Abbrev	Name	Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
Hong Kong Diabetes Registry ⁴⁹	HKD Registry	All	Hard CHD 1	UKPDS 56	Hard CHD 1	0.61	0.581-0.639			
Hong Kong Diabetes Registry ⁴⁹	HKD Registry	All	Total CHD 1	Hong Kong Total CHD Score	Total CHD 1	0.737				
Hong Kong Diabetes Registry ⁴⁹	HKD Registry	All	Total CHD 1	Hong Kong Total CHD Score	Total CHD 1	0.704	0.675-0.733			
Employee health management center in a										
Japanese company ⁹⁰	Japan Work	Men	Total CHD 1	FRS [Unknown Version] (1998)	Total CHD 1	0.62				0.579
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in										
11 provinces (1992-3) and Beijing (1996-9) ⁴⁷	MUCA	Women	Hard CHD 1	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.742	0.686-0.798	147.6		
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in										
11 provinces (1992-3) and Beijing (1996-9) ⁴⁷	MUCA	Men	Hard CHD 1	FRS Hard CHD [TC] (1998)	Hard CHD 1	0.705	0.665-0.746	645.9	0.0001	
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in										
11 provinces (1992-3) and Beijing (1996-9) ⁴⁷	MUCA	Women	Hard CHD 1	CMCS Cox Model	Hard CHD 1	0.759	0.699-0.818	14.2	0.08	
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in										
11 provinces (1992-3) and Beijing (1996-9) ⁴⁷	MUCA	Women	Hard CHD 1	CMCS Cox Model	Hard CHD 1	0.759	0.699-0.818	14.2	0.0001	
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in										
11 provinces (1992-3) and Beijing (1996-9) ⁴⁷	MUCA	Men	Hard CHD 1	CMCS Cox Model	Hard CHD 1	0.736	0.696-0.776	12.6	0.13	
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in				FRS (1998 TC Hard CHD)						
11 provinces (1992-3) and Beijing $(1996-9)^{47}$	MUCA	Women	Hard CHD 1	MUCA Remodel	Hard CHD 1	0.759	0.699-0.818	16.9	0.03	
Chinese Multi-Provincial Cohort Study;										
persons aged 35-64 years from 16 centers in				FRS (1998 TC Hard CHD)						
11 provinces (1992-3) and Beijing $(1996-9)^{47}$	MUCA	Men	Hard CHD 1	MUCA Remodel	Hard CHD 1	0.736	0.696-0.776	31.5	0.0001	
Males aged 30-59 completing annual health										
exams between 1991-389	JapanWork	All	Total CHD 1	FRS [Unknown Version] (1998)	Total CHD 1	0.71				0.382
Newcastle Heart Project–South Asians ⁸³	NHP-South Asia	All	CHD Mortality	SCORE (Unknown Version)	CVD Mortality					4.419

Table 8i. Stroke Model Details – Asia

		Group			Model			HLG	OF	O/E
Cohort	Cohort Abbrev	Name	Cohort Outcome	Model Name	Outcome	AUC	AUC Var	χ^2	Р	Ratio
Hong Kong Diabetes Registry ⁵⁰	HKD Registry	All	Stroke 1	Hong Kong Diabetes Risk Score	Stroke 1	0.79	0.716-0.782			
Hong Kong Diabetes Registry ⁵⁰	HKD Registry	All	Stroke 1	UKPDS 60	Stroke 1	0.588	0.549-0.626			0.514
Hong Kong Diabetes Registry ⁵⁰	HKD Registry	All	Stroke 5	Hong Kong Diabetes Risk Score	Stroke 1	0.77				
Koreans insured by National Health										
Insurance Corporation (NHIC) ⁴⁶	NHIC	Men	Stroke 6 (10 yr)	Korean Stroke Risk Prediction (KSRP)	Stroke 6	0.817	0.799-0.834	7.71	0.56	
Koreans insured by National Health										
Insurance Corporation (NHIC) ⁴⁶	NHIC	Women	Stroke 6 (10 yr)	Korean Stroke Risk Prediction (KSRP)	Stroke 6	0.81	0.788-0.832	14.26	0.16	
Hong Kong Diabetes Registry ⁵⁰	HKD Registry	All	Stroke 3	Hong Kong Diabetes Risk Score	Stroke 1	0.785				
Newcastle Heart Project–South Asians ⁸³	NHP-South Asia	All	Stroke Mortality	FRS (1991) Stroke	Stroke 4					1.875

Table 9a. Outcome Incidence Rates – All

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
Wilson PWF'	2008	US	Framingham Offspring Study	FRS-O	All	51.6	2.8	Stroke 2	4780	111	2.3
Wilson PWF ⁷	2008	US	Framingham Offspring Study	FRS-O	All	51.6	2.8	Total CHD 1	4780	492	10.3
Wilson PWF ⁷	2008	US	Framingham Offspring Study	FRS-O	All	51.6	2.8	CVD 12	4780	684	14.3
Hippisley-Cox J ³⁴	2008	UK	Members of QRESEARCH database	QRESEARCH	All	75.4	2.9	CVD 1	2285815	96709	4.2
Cimmon o DI/ ³⁵	2000		European Prospective Investigation of		A 11	50.0			40005	<u></u>	<u> </u>
Simmons RK	2008	UK	Cancer [EPIC]-Norrolk		All	56.Z	2.8	Total CHD 1	10295	680	6.6
Gaizano TA ⁸	2008	US	Survey I Epidemiologic Follow-Up Study	EFS	All	54.1	3.8	CVD 7	6186	578	9.3
Yang X ⁴⁹	2008	China	Hong Kong Diabetes Registry	HKD Registry	All	54.6	100	Hard CHD 1	7067	157	2.2
Yang X ⁴⁹	2008	China	Hong Kong Diabetes Registry	HKD Registry	All	54.6	100	Total CHD 1	7067	351	5
			Framingham Cohort (11th) (68-71) & Offspring 1st (71-75) & Offspring (3rd 84-								
D'Agostino RB ⁹²	2008	US	87)	FRS, FRS-O	All	53.3	5	CVD 2	8491	1174	13.8
			Consecutive patients referred by primary								
		_	care provider for preventive cardiological								
Becker A*	2008	Germany	exam		All	41	17	Hard CHD 2	1726	380	22
			Consecutive patients referred by primary								
Dealer A ⁴¹	2000	0.000	care provider for preventive cardiological		A 11	14	47		4700	100	10.1
Becker A	2008	Germany	DDOCAM asharti amplayaaa of 52		All	41	17	Hard CHD 1	1726	180	10.4
			PROCAM conort; employees of 52								
Assmann G ²⁶	2007	Germany	authorities in Germany, aged 20-78 yrs	PROCAM	ΔII	20 /	6.2	(10 Year)	7205	345	17
Vaidva D ¹⁰	2007	US	John Honkins Sibling Study	JHSS	All	48.5	6.3	Total CHD 1	784	108	13.8
Valaya D	2001	00	THIN cohort: data from 288 LIK practices	01100	/	40.0	0.0		104	100	10.0
			using INPS Vision system (~20%)								
			including 24 practices (54709 patients)								
			from Scotland and 14 practices (36904)					CVD 10 (10			
Hippisley-Cox JC ⁶²	2008	UK	from Northern Ireland	THIN	All	50.6	0	yr)	1072800	87858	8.2
								CVD 10 (10			
Hippisley-Cox JC ⁶²	2008	UK	QRESEARCH	QRESEARCH	All	50.4	0	yr)	607733	47557	7.8
Hippisley-Cox JC ⁶²	2008	UK	QRESEARCH	QRESEARCH	All	50.4	0	CVD 10	607733	30087	5
			THIN cohort; data from 288 UK practices								
			using INPS Vision system (~20%);								
			including 24 practices (54709 patients)								
co.			from Scotland and 14 practices (36904)								
Hippisley-Cox JC ^{o2}	2008	UK	from Northern Ireland	THIN	All	50.6	0	CVD 10	1072800	44152	4.1
			Cardiovascular Program in Norway (ages	0. T. I.							
Lindman AS'	2007	Norway	60-69)	CP-Norway	All	53.7	0	CVD Mortality	8085	427	5.3
Lindman AS''	2007	Norway	Norwegian Counties Study (ages 40-59)	NCS	All	50.9	0	CVD Mortality	49144	517	1.1
			Atherosclerosis Risk In Communities and								
Mainer DE ⁶⁴	2007		Cardiovascular Health Study trials with		A II	61.0	1.1	Hard CHD 1	024	120	12.0
	2007	05	Athoropoloropio Diels In Communities and	ARIC, CHS	All	01.0	14		934	130	13.9
			Ameroscierosis Risk in Communities and								
Weiner DE ⁶⁴	2007	us		ARIC CHS	All	61.8	14	(5vr)	934	65	7
						01.0	1	\~ <i>J</i> '/			

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
		-	QRESEARCH database, constructed								
			from 160 UK general practices; validation	QRESEARCH							
Hippisley-Cox JC ⁴⁰	2007	UK	cohort	(Validation)	All	50.3	0	CVD 4 (10 yr)	614553	48738	7.9
			Koreans insured by National Health					Stroke 6 (10			
Jee SH ⁴⁶	2008	Korea	Insurance Corporation (NHIC)		All	36.5	4.5	yr)	1205268	42995	3.6
Koller MT ⁸⁴	2007	Netherlands	Rotterdam Study		All	63.9		Hard CHD 1	6795	799	11.8
_								Hard CHD 1			
Berry JD ⁵	2007	US	Chicago young adults	CHA	All	0	0	(10 yr)	10375	24	0.2
_								Hard CHD 1			
Berry JD⁵	2007	US	Chicago young adults	CHA	All	0	0	(30 yr)	10375	271	2.6
			Uppsala Longitudinal Study of Adult Men								
Strom Moller C ²³	2007	Sweden	(baseline age 70 cohort)	ULSAM	All	0		CVD Mortality	1221	139	11.4
			Atherosclerosis Risk In Communities								
Mainous AG ¹⁴	2007	US	Study	ARIC	All	56.5	6.9	Hard CHD 2	14343	1108	7.7
			Men at work in public authorities and								
74		_	large companies in the region of Munster,			_					
Buyken AE'	2007	Germany	Germany		All	0		Hard CHD 1	4818	325	6.7
Miyasaka Y°	2007	US	Adult residents of Olmsted County, MN		All	52.4	12.8	Total CHD 1	2768	463	16.7
Denes P ⁶⁵	2007	US	Women's Health Initiative study	WHI	All	100	3.9	Hard CHD 1	14749	246	1.7
Denes P ^{oo}	2007	US	Women's Health Initiative study	WHI	All	100	3.9	CVD 15	14749	595	4
Ridker PM ²⁰	2007	US	Women's Health Study (validation cohort)	WHS	All	100	2.9	CVD 3	8158	262	3.2
45			Asia Pacific Cohort Studies Collaboration								
Barzi F ^₅	2007	China	- Total Chinese Cohort	APCSC China	All	41.4		CVD 8	25682	542	2.1
- · · · · · · · · · · · · · · · · · · ·		Czech					-				
Reissigova J ²⁰	2007	Republic	Study of Atherosclerotic Risk Factors	STULONG	All	0	0	Total CHD 1	646	106	16.4
Yang X ⁵⁰	2007	China	Hong Kong Diabetes Registry	HKD Registry	All	54.5	100	Stroke 3	3541	150	4.2
Yang X ⁵⁰	2007	China	Hong Kong Diabetes Registry	HKD Registry	All	54.5	100	Stroke 5	3541	32	0.9
Yang X ³⁰	2007	China	Hong Kong Diabetes Registry	HKD Registry	All	54.5	100	Stroke 1	3541	182	5.1
			Validity of the Adapted Framingham								
		a .	Individual Risk Equation for Coronary								
Marrugat J ^{oo}	2007	Spain	Incidencts Cohort	VERIFICA	All	57.3	16.4	Total CHD 1	5732	180	3.1
M/	0007	O south south	O Web Lie			50.0		CVD 11 (10	40007	1105	0.0
woodward we	2007	Scotland	Scottish Hearth Health Extended Conort	SHHEC	All	50.8	1.4	yr)	13297	1165	8.8
Masfarlar DM^{32}	2007	Castland	West of Scotland Coronary Prevention	MOCODO		<u>^</u>	1.0		0505		
Cook ND ¹⁹	2007	Scotland	Study Women's Legith Study	WUSCOPS	All	100	1.2		6595	409	2.2
	2006	05	Strong Lloort Study		All	100	0		10040	490	3.3
Lee ET	2006	05	Strong Heart Study	585	All	60.6	44	Hard CHD 1	4372	724	16.6
Dennen DT ³⁹	2006		Patients with diabetes receiving care in	DADTO	A II	47 4	100		2472		
Donnan PT	2006	UK	Sallolo, UK	DARIS	All	47.4	100		3472		
Dennen DT ³⁹	2006		Subjects with type 2 diabetes registered	DADTO	A 11	47 4	100		4560	040	5.0
Donnan Fi May MD ⁴⁴	2000		Will a Tayside GP	DARIS	All	47.4	100		4309	243	0.0
May MD ⁴⁴	2006		British Women's Heart and Health Cohort	ВМПП	All	100	4.4		3002	240	0.7
Wannamathaa	2000	UN	Pritich Pogional Hoart Study man and		All	100	4.4		300Z	190	5.5
sc ⁷²	2005		A 50 yrs	RDUC	A II	0	0		5077	763	15
Wannamathac	2005		Pritich Pagional Hoart Study: man aged	ыкпо	All	0	U	(20 yis) Diabataa	5077	103	10
	2005		A Solver	PDUC	A II	0	0	Type 2 (20	5077	200	5.0
30	2005	UN	40-09 yis	DKHO	All	U	U	iype∠(∠u	0077	299	5.9

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
-								yrs)			
Wannamethee			British Regional Heart Study; men aged					Stroke 1 (20			
SG ⁷²	2005	UK	40-59 yrs	BRHS	All	0	0	yrs)	5077	291	5.7
Brindle PM ⁷⁰	2005	Scotland	Renfrew and Paisley Study		All	54.3	1.2	CVD Mortality	12304	696	5.7
			Individuals aged 25-65 yrs identified from								
			Finnish population register and particip-								
			ating in 3 cross-sectional risk factor								
Silventoinen K ⁷⁸	2005	Finland	surveys in Finland in 1987, 1992, & 1997		All	53.4	1.5	Stroke 1	17725	324	1.8
			Individuals aged 25-65 yrs identified from								
			Finnish population register and particip-								
			ating in 3 cross-sectional risk factor					All-Cause			
Silventoinen K ⁷⁸	2005	Finland	surveys in Finland in 1987, 1992, & 1997		All	53.4	1.5	Mortality	17725	765	4.3
			Individuals aged 25-65 yrs identified from								
			Finnish population register and particip-								
70			ating in 3 cross-sectional risk factor								
Silventoinen K ⁷⁸	2005	Finland	surveys in Finland in 1987, 1992, & 1997		All	53.4	1.5	Total CHD 1	17725	699	3.9
			Vorarlberg Health Monitoring and								
			Promotion Program (VHM&PP); cohort of								
70			individuals undergoing general health								
Ulmer HB ^{/6}	2005	Austria	examinations in Vorarlberg province	VHM&PP	All	54.8		CHD Mortality	44649	300	0.7
			Vorarlberg Health Monitoring and								
			Promotion Program (VHM&PP); cohort of								
70			individuals undergoing general health								
Ulmer HB [/]	2005	Austria	examinations in Vorarlberg province	VHM&PP	All	54.8		CVD Mortality	44649	487	1.1
Vliegenthart R ⁷⁹	2005	Netherlands	Rotterdam Coronary Calcification Study	RCC	All	57.5	12.3	CVD 3	1795	88	4.9
Arad Y ⁹¹	2005	US	St Francis Heart Study	SFHS	All	35	6	CVD 16	4613	119	2.6
Cooper JA ³¹	2005	UK	Second Northwick Park Heart Study	NPHS-II	All	0	2.1	Hard CHD 2	2732	219	8
Bernard S ²¹	2005	France	Lyon, France		All	35.4	100	CVD 6	229	34	14.8
Guzder RN ⁸⁶	2005	UK	Poole Diabetes Study	PDS	All	43.7	100	Total CHD 3	428	60	14
Guzder RN ⁸⁶	2005	UK	Poole Diabetes Study	PDS	All	43.7	100	CVD 13	428	98	22.9
Guzder RN ⁸⁶	2005	UK	Poole Diabetes Study	PDS	All	43.7	100	Total CHD 3	428	60	14
Guzder RN ⁸⁶	2005	UK	Poole Diabetes Study	PDS	All	43.7	100	CVD 13	428	98	22.9
Bhopal R ⁸³	2005	India	Newcastle Heart Project - Indian	NHP - India	All	63	16		230		
								Stroke			
Bhopal R ⁸³	2005	UK	Newcastle Heart Project - Europeans	NHP Europe	All	50	4	Mortality	725	9	1.2
				NHP-South				Stroke			
Bhopal R ⁸³	2005	South Asia	Newcastle Heart Project - South Asians	Asia	All	54.5	20.5	Mortality	576	3	0.5
				NHP-South							
Bhopal R ⁸³	2005	South Asia	Newcastle Heart Project - South Asians	Asia	All	54.5	20.5	CHD mortality	576	19	3.3
Bhopal R ⁸³	2005	Pakistan	Newcastle Heart Project - Pakistani	NHP-Pakistan	All	51.1	27		264		
Bhopal R ⁸³	2005	UK	Newcastle Heart Project - Europeans	NHP Europe	All	50	4	CHD Mortality	725	22	3
			Atherosclerosis Risk in Communities								
McNeill AM ¹⁵	2005	US	Study	ARIC	All	100	0	Hard CHD 2	12089	879	7.3
	1		Atherosclerosis Risk in Communities	1		1	1	1	1	1	
McNeill AM ¹⁵	2005	US	Study	ARIC	All	100	0	Stroke 3	12089	216	1.8
Ferrario M ²⁹	2005	Italy	CUORE	CUORE	All	0	5	Hard CHD 2	6865	312	4.5
Wang Z ⁸²	2005	Australia	Aboriginal community	1	All	48.2	12.5	Total CHD 1	687	68	9.9

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
			Diabetes clinic at University College								
Stephens JW ³³	2004	UK	London Hospitals NHS Trust		All	36	100	Total CHD 2	798	269	33.7
			Diabetes clinic at University College								
Stephens JW ³³	2004	UK	London Hospitals NHS Trust		All	36	100	CVD 18	798	358	44.9
Stern Michael P ⁶⁶	2004	US	San Antonio Heart Study	SAHS	All	58	12.6	CVD 15	2570	156	6.1
Dunder K ²²	2004	Sweden	Uppsala Longitudinal Study of Adult Men	ULSAM	All	0	1.5	MI	1108	251	22.7
								Hard CHD 1			
Dunder K ²²	2004	Sweden	Uppsala Longitudinal Study of Adult Men	ULSAM	All	0	1.5	(10 yrs)	1108	33	3
10			Atherosclerosis Risk in Communities								
Chambless LE ¹²	2004	US	Study	ARIC	All	55.3		Stroke 3	13161	376	2.9
Ducloux D ⁶⁹	2004	France	Consecutive renal transplant patients		All	36.9	10.8	Total CHD 1	344	27	7.8
			Chinese Multi-Provincial Cohort Study;								
			individuals aged 35-64 yrs from 16								
47			centers in 11 provinces (1992-1993) and								
Liu J"	2004	China	Beijing (1996-1999)	MUCA	All	46.7	5.5	Hard CHD 1	30121	191	0.6
- " - 2 ⁴			Apparently healthy Norwegian men aged								
Erikssen G	2004	Norway	40-60 yrs recruited from 5 govt agencies		All	0	0	CHD Mortality	2014	300	14.9
Na 5	0004		Cardiff Diabetes Database (type 1 and		A 11	40.0	100		000	170	10.0
McEwan P**	2004	UK	type 2)		All	42.2	100	CVD 2	938	172	18.3
Kaania W ⁷⁵	2004	Cormony	Men randomly selected from general		A 11	0	5.0		2425	101	FC
Creanland D ^{1/}	2004	Germany	population in 1984-5, 1989-90 and 1994-5		All	0	5.8	Hard CHD 1	3435	191	5.0
Greenland P	2004	05	South Bay Heart Watch conort	SBHW	All	10.2	0	Hard CHD 1	1029	84	8.Z
			British Regional Heart Study; men aged								
Brindlo P ⁷³	2002		40-59 yrs randonny selected from registers	BDUC	A II	0	1 1		6642	677	10.2
	2003	UK	Drotte general plactice in each town	БКПЭ	All	0	1.1		0043	0//	10.2
			40-59 vrs randomly selected from registers								
Brindle P ⁷³	2003	ПК	of one general practice in each town	BRHS	ΔII	0	1 1	CHD mortality	6643	186	2.8
Brindle I	2000		People from workforce of nationwide multi-	Brand	7.11	U			0040	100	2.0
			industry corporation (Eletcher Challenge,								
			Ltd. [72%]) and general electoral rolls of								
Milne R ⁸¹	2003	New Zealand	Auckland metro region (28%)		All	27		CVD 2 (5 yrs)	6354	411	6.5
		Northern	U U U U U U U U U U U U U U U U U U U					Hard CHD 1			
Empana JP ⁸⁰	2003	Ireland	PRIME cohort study (Belfast cohort)	PRIME	All	0		(5 yr)	2399	61	2.5
· ·		Northern						Total CHD 1			
Empana JP ⁸⁰	2003	Ireland	PRIME cohort study (Belfast cohort)	PRIME	All	0		(5 yr)	2399	120	5
· · ·								Hard CHD 1			
Empana JP ⁸⁰	2003	France	PRIME cohort study	PRIME-France	All	0		(5 yr)	7359	106	1.4
-								Total CHD 1			
Empana JP ⁸⁰	2003	France	PRIME cohort study	PRIME-France	All	0		(5 yr)	7359	197	2.7
Folsom A ¹³	2161	US	Atherosclerosis Risk in Communities	ARIC	All	56.8		Hard CHD 2	14054	1064	7.6
			PROCAM cohort; drawn from 52								
Hense HW ⁶¹	2003	Germany	companies and local govt authorities	PROCAM	All	36.3	2.8	Hard CHD 1	8682	338	3.9
			MONICA Augsburg cohort; 1984/1985	MONICA-							
Hense HW ⁶¹	2003	Germany	and 1989/1990 surveys	Augsburg	All	50.6	3.6	Hard CHD 1	5786	178	3.1
50			Dubbo Study cohort of elderly Australians					CVD 4 (10			
Simons LA ⁵⁶	2003	Australia	(ages 60-79) (with DM)	DUBBO-All	All	58	19	yrs)	2102	459	21.8

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
			Dubbo Study cohort of elderly Australians								
Simons LA ⁵⁶	2003	Australia	(ages 60-79) (with DM)	DUBBO-All	All	58	19	CVD 4 (5 yrs)	2102	211	10
			Dubbo Study cohort of elderly Australians					CVD 4 (10			
Simons LA ⁵⁶	2003	Australia	(ages 60-79) without DM	DUBBO-NoDM	All	58	0	yrs)	1800	192	10.7
07		W. Europe	INSIGHT trial cohort of middle-aged								
Bastuji-Garin S ^{or}	2002	and Israel	patients with hypertension	INSIGHT	All	55.3	19	Stroke 4	4147	96	2.3
		W. Europe	INSIGHT trial cohort of middle-aged								
Bastuji-Garin S"	2002	and Israel	patients with hypertension	INSIGHT	All	55.3	19	CVD 14	4147	231	5.6
D O		W. Europe	INSIGHT trial cohort of middle-aged								
Bastuji-Garin S	2002	and Israel	patients with hypertension	INSIGHT	All	55.3	19	Total CHD 1	4147	124	3
Out - M ⁹⁰	0000	1	Employee health management center in a		A.II	0			5044	004	0.0
Suka M	2002	Japan	Japanese company		All	0		Total CHD 1	5611	384	6.8
Kathari V ⁵⁴	2002	United	Visconsin Epidemiologic Study of		A 11	44.0	100	Stroke	4540	50	1.0
Contant V	2002	Status	Nermetive Aging Study male veterane	WESDR	All	41.3	100		4049	29	1.3
	2002	05	Romative Aging Study - male veterans	INA5	All	0	2.9		1393	200	14.0
			PROCAW control, employees of 52								
Assmann G ²⁷	2002	Germany	f/u every 2 years	PROCAM	ΔII	0	67	Hard CHD 1	5150	325	63
Assinanii O	2002	Germany	Males aged 30-59 completing annual			0	0.7		5155	525	0.5
Suka M ⁸⁹	2001	Janan	health examinations between 1991-1993		ΔII	0	85	Total CHD 1	5611	80	14
Odika IVI	2001	oupun	Framingham Study (11th Exam) or		/ \11	Ŭ	0.0	Hard CHD 1	0011	00	1.4
D'Agostino RB ⁴	2001	us	Framingham Offspring Study (1st Exam)	FRS FRS-0	All	53.6	4.5	(5 vr)	5251	130	2.5
D / Igootino 11D	2001	00	Atherosclerosis Risk in Communities	1110,1110 0	7.01	00.0	1.0	Hard CHD 1	0201	100	2.0
D'Agostino RB ⁴	2001	us	Study	ARIC	All	56.7	8.6	(5 vr)	14178	279	2
								Hard CHD 1			_
D'Agostino RB ⁴	2001	US	Honolulu Heart Program	ННР	All	0	14	(5 yr)	2755	77	2.8
U								Hard CHD 1			
D'Agostino RB ⁴	2001	Puerto Rico	Puerto Rico Heart Health Program	PRHHP	All	0	7	(5 yr)	8713	107	1.2
			Strong Heart Study (area of OK and					Hard CHD 1			
D'Agostino RB ⁴	2001	US	Aberdeen area of ND and SD)	SHS	All	59.6	47.3	(5 yr)	3782	69	1.8
								Hard CHD 1			
D'Agostino RB ⁴	2001	US	Cardiovascular Health Study	CHS	All	62.6	11.9	(5 yr)	2557	115	4.5
00			Lipid Research Clinics Prevalence Study								
Grover SA ⁶⁸	2000	Canada	cohort	LRCPS	All	33	4.6	CHD Mortality	2218	62	2.8
Detrano RC ¹⁰	1999	US	South Bay Heart Watch	SBHW	All	11	18	Hard CHD 2	1194	64	5.4
Detrano RC ¹⁰	1999	US	South Bay Heart Watch	SBHW	All	11	18	Hard CHD 1	1194	46	3.9
			First National Heatlh and Nutrition								
Liao Y ^a	1999	US	Examination Survey	NHANES I	All	58.4		CHD Mortality	6611	588	8.9
Liao Y°	1999	US	Framingham Heart Study (4th Exam)	FRS	All	55.7		CHD Mortality	4169	406	9.7
3			Second National Heatlh and Nutrition								
Liao Y°	1999	US	Examination Survey	NHANES II	All	53.5		CHD Mortality	5705	275	4.8
Paynter Nº	2009	US	Women's Genome Health Study	WGHS	All	100	2.6	CVD 3	22129	/15	3.2
de Ruijter W*	2009	Netherlands	Leiden 85-plus Study	L85	All	/0./	14.2	CVD Mortality	302	35	11.6
Ridker P	2008		Physicians Health Study II	PHS-II	All	0	0	Hard CHD 2	10/24	1072	10
Ridker P	2008	08	Physicians Health Study II	PHS-II	All	0	0	CVD 15	10724	1294	12.1
Becker A ⁸⁷	2008	Germany	Munich	M-DM	All	39.9	100	Hard CHD 1	/16	/6	10.6
Becker A°'	2008	Germany	Munich	M-DM	All	39.9	100	MI	716	40	5.6

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
Becker A ⁸⁷	2008	Germany	Munich	M-DM	All	39.9	100	Hard CHD 2	716	163	22.8
			Atherosclerosis Risk in Communities					Hard CHD 2			
Mainous A ¹¹	2008	US	Study	ARIC	All	58	0	(6 yr)	9307	430	4.6
			Monitoring Project on Cardiovascular								
			Disease Risk Factors; persons randomly								
			selected from 3 cities in Netherlands,					CVD Mortality			
Scheltens T ^{//}	2008	Netherlands	aged 20-59 and no CVD	MP-CVDRF	All	53		(10 yr)	39719	256	0.6
Cederholm J ⁴³	2008	Sweden	Swedish National Diabetes Register		All	43.1	100	CVD 5	11646	1482	12.7
			Patients with type 2 diabetes diagnosed								
			by standard criteria and on standard								
			diabetic therapy (diet, tablets, insulin) and								
			aged 50-75 yrs, recruited from outpatient								
Elkeles RS ⁸⁸	2008	UK	clinics in Central and West London	PREDICT	All	36.7	100		589		
			Cohort of men and women employed in	PROCAM							
Assmann G ²⁸	2008	Germany	northwest Germany	cohort	All	0		Hard CHD 1	7134	404	5.7
			Participants in Supplementation en								
			Vitamines et Mineraux Antioxydants								
			randomized primary prevention trial,								
Vergnaud AC ³⁶	2008	France	followed annually since 1994/1995	SU.VI.MAX	All	0	2.4	Total CHD 1	3440	128	3.7
			Framingham Coorth (11th Exam) Or								
Wilson PWF ²	1998	US	Framingham Offspring (1st Exam)	FRS, FRS-O	All	53.4	4.5	Total CHD 1	5345	610	11.4
				NHANES I and							
Liao Y ¹	1999	US	NHANES I and II (pooled)	II (pooled)	All	57.5		CHD death	18542	1451	7.8

Table 9b. Outcome Incidence Rates – Men

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
Wilson PWF ²	2008	US	Framingham Offspring Study	FRS-O	Men				2313		
			Participants in Supplementation en								
			Vitamines et Mineraux Antioxydants								
			randomized primary prevention trial,								
Vergnaud AC ³⁶	2008	France	followed annually since 1994/1995	SU.VI.MAX	Men			Total CHD 1	3440	128	3.7
Vaidya D ¹⁰	2007	US	John Hopkins Sibling Study	JHSS	Men			Total CHD 1	404	81	20
Becker A ⁴¹	2008	Germany	Munich	M-DM	Men		100		430		
			National Health and Nutrition Examination	NHANES-I							
Gaizano TA ⁸	2008	US	Survey I Epidemiologic Follow-Up Study	EFS	Men		3.56		2837		
Hippisley-Cox J ³⁴	2008	UK	Members of the QRESEARCH database	QRESEARCH	Men			CVD 1	1136761	55667	4.9
			European Prospective Investigation of								
Simmons RK ³⁵	2008	UK	Cancer [EPIC]–Norfolk	EPIC-Norfolk	Men			Total CHD 1	4513	430	9.5
			Atherosclerosis Risk in Communities					Hard CHD 2			
Mainous A ¹¹	2008	US	Study	ARIC	Men		0	(6 yr)	3901	299	7.7
			Framingham Cohort (11th) (68-71) &								
			Offspring 1st (71-75) & Offspring (3rd 84-								
D'Agostino RB ⁶	2008	US	87)	FRS, FRS-O	Men			CVD 2	3969	718	18.1
			Consecutive patients referred by primary								
			care provider for preventive cardiological								
Becker A ⁸⁷	2008	Germany	examination		Men			Hard CHD 1	1018	110	10.8

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
			Consecutive patients referred by primary								
07			care provider for preventive cardiological								
Becker A ⁸⁷	2008	Germany	examination		Men			Hard CHD 2	1018	237	23.3
			THIN cohort; data from 288 UK practices								
			using e INPS Vision system (~20%);								
			including 24 practices (54709 patients)								
			from Scotland and 14 practices (36904)					CVD 10 (10			
Hippisley-Cox JC ^{o2}	2008	UK	from Northern Ireland	THIN	Men		0	yr)	529813	52292	9.9
Lindman AS'	2007	Norway	Norwegian Counties Study (ages 40-59)	NCS	Men		0	CVD Mortality	24359	423	1.7
			Atherosclerosis Risk In Communities and								
64			Cardiovascular Health Study trials with					Hard CHD 1			
Weiner DE ⁰⁴	2007	US	CKD	ARIC, CHS	Men		14.6	(10yr)	357	74	20.7
			Atherosclerosis Risk In Communities and								
64			Cardiovascular Health Study trials with					Hard CHD 1			
Weiner DE ⁶⁴	2007	US	CKD	ARIC, CHS	Men		14.6	(5yr)	357	35	9.8
			QRESEARCH database, constructed								
10			from 160 UK general practices; validation	QRESEARCH							
Hippisley-Cox JC ⁴⁰	2007	UK	cohort	(Validation)	Men		0	CVD 4 (10 yr)	305140	28317	9.3
			Koreans insured by National Health					Stroke 6 (10			
Jee SH ⁺ °	2008	Korea	Insurance Corporation (NHIC)		Men		4.8	yr)	767885	27007	3.5
Koller MT ⁶⁴	2007	Netherlands	Rotterdam Study		Men			Hard CHD 1	2452	351	14.3
-								Hard CHD 1			
Berry JD°	2007	US	Chicago young adults	CHA	Men			(10 yr)	10375	24	0.2
5								Hard CHD 1			
Berry JD [°]	2007	US	Chicago young adults	CHA	Men			(30 yr)	10375	271	2.6
22			Uppsala Longitudinal Study of Adult Men								
Strom Moller C ²³	2007	Sweden	(baseline age 70 cohort)	ULSAM	Men			CVD Mortality	1221	139	11.4
14			Atherosclerosis Risk In Communities								
Mainous AG [™]	2007	US	Study	ARIC	Men				6239		
			Men at work in public authorities and								
74			large companies in the region of Munster,								
Buyken AE	2007	Germany	Germany		Men			Hard CHD 1	4818	325	6.7
Miyasaka Y°	2007	US	Adult residents of Olmsted County, MN		Men			Total CHD 1	1318	227	17.2
45			Asia Pacific Cohort Studies Collaboration								
Barzi F [™]	2007	China	- Total Chinese Cohort	APCSC China	Men			CVD 8	15046	418	2.8
- · · · · · · · · · · · · · · · · · · ·		Czech									
Reissigova J ²⁰	2007	Republic	Study of Atherosclerotic Risk Factors	STULONG	Men			Total CHD 1	646	106	16.4
			Validity of the Adapted Framingham								
			Individual Risk Equation for Coronary						- · · -		
Marrugat J ^{oo}	2007	Spain	Incidencts Cohort	VERIFICA	Men		18.8	Total CHD 1	2447	112	4.6
								CVD 11 (10			
Woodward M ^{ee}	2007	Scotland	Scottish Hearth Health Extended Cohort	SHHEC	Men		1.5	yr)	6540	743	11.4
	000-		vvest of Scotland Coronary Prevention						0505		
Mactarlane PW ³²	2007	Scotland	Study	WOSCOPS	Men				6595		
Lee ET'	2006	US	Strong Heart Study	SHS	Men		39.7	Hard CHD 1	1/22	349	20.3
			Patients with type 2 diabetes registered		l						
Donnan PT ³⁹	2006	UK	with a Tayside GP	DARTS	Men				2403		

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
Wannamethee			British Regional Heart Study; men aged					Hard CHD 1			
SG ⁷²	2005	UK	40-59 yrs	BRHS	Men			(20 yrs)	5077	763	15
Wannamethee			British Regional Heart Study; men aged					Stroke 1 (20			
SG ⁷²	2005	UK	40-59 yrs	BRHS	Men			yrs)	5077	291	5.7
Wannamethee			British Regional Heart Study; men aged					Diabetes type			
SG ⁷²	2005	UK	40-59 yrs	BRHS	Men			2 (20 yrs)	5077	299	5.9
Brindle PM ⁷⁰	2005	Scotland	Renfrew and Paisley Study		Men		1.4		5626		
			Persons aged 25-65 yrs identified from								
			Finnish population register & participating								
70			in 3 cross-sectional risk factor surveys in								
Silventoinen K ^{/*}	2005	Finland	Finland in 1987, 1992, and 1997		Men		2	Stroke 1	8268	177	2.1
			Persons aged 25-65 yrs identified from								
			Finnish population register &								
			participating in 3 cross-sectional risk								
0 ¹¹ 1 1 1 1 78			factor surveys in Finland in 1987, 1992,								
Silventoinen K ^{ro}	2005	Finland	and 1997		Men		2	Total CHD 1	8268	480	5.8
			Persons aged 25-65 yrs identified from								
			Finnish population register &								
			participating in 3 cross-sectional risk								
Silventoinen K ⁷⁸	2005	Finland	factor surveys in Finland in 1987, 1992,		Man		2	All-Cause	0000	100	c
Silventoinen K	2005	Finland	and 1997		Men		2		8268	499	0
Cooper JA	2005	UK	Second Northwick Park Heart Study	NPH5-II	Men		<i>c</i>	Hard CHD 2	2732	219	8
Bhopal R	2005	UK	Newcastle Heart Project: Europeans	NHP Europe	wen		5		362		
Mania: 11 ANA ¹⁵	0005	110	Atheroscierosis Risk in Communities		Man				5000		
	2005	US	Study		Men				5208	24.0	4.5
	2005	Italy		COORE	Men		0.0	Hard CHD 2	0000	312	4.5
wang Z	2005	Australia	Aboriginal community		wen		9.3	Total CHD 1	356	30	8.4
Stanhana IVA/33	2004		Lenden Legenitele NUS Trust		Man		100		504		
Stephens Jw	2004	UK	Athereealereeia Biek in Communities		wen		100		504		-
Champless I E ¹²	2004	110	Atheroscierosis Risk in Communities		Mon			Stroke 2	5007	155	26
	2004	05	Chippen Multi Provincial Cohort Study:	ARIC	wen			Stroke 3	1000	100	2.0
			individuals aged 35.64 yrs from 16								
			contors in 11 provinces (1992-1993) and								
1 iu 1 ⁴⁷	2004	China	Rejijing (1996-1999)	MUCA	Men		69	Hard CHD 1	16065	137	0 9
	2004	Onina	Apparently healthy Norwegian men aged	11100/1	WICH		0.0		10000	107	0.0
Frikssen G ²⁴	2004	Norway	40-60 vrs recruited from 5 govt agencies		Men			CHD Mortality	2014	300	14.9
2			Cardiff Diabetes Database (type 1 and						2011		
McEwan P ⁸⁵	2004	UK	type 2)		Men			CVD 2	542	105	19.4
		0.11	Men randomly selected from general pop-					0.22	0.2		
Koenia W ⁷⁵	2004	Germany	ulation in 1984-5, 1989-90, and 1994-5		Men			Hard CHD 1	3435	191	5.6
			British Regional Heart Study: men aged								
			40-59 vrs randomly selected from registers								
Brindle P ⁷³	2003	UK	of one general practice in each town	BRHS	Men			Total CHD 1	6643	677	10.2
		1	British Regional Heart Study; men aged		1	1	1				
			40-59 yrs randomly selected from registers	5	1						
Brindle P ⁷³	2003	UK	of one general practice in each town	BRHS	Men			CHD mortality	6643	186	2.8

Study 1 st Author Yr. Pub Columity Colume Author Name % Name Enrollment Outcomes % Milne R ⁴¹ 2003 Zealand recruited from workforce of nation Men CVD 2 (5 yr) 4638 325 7 Empana JP ^{ID} 2003 Iteliand PRIME cohor study (Beflast cohort) PRIME Men CVD 2 (5 yr) 4638 325 7 Empana JP ^{ID} 2003 Iteliand PRIME cohor study (Beflast cohort) PRIME Men Hard CHD 1 61 2.5 Simons LA ⁵⁶ 2003 Australia Gapes 60-791 (with DM) DUBBO-All Men CVD 4 (10 78 106 12.1 Simons LA ⁵⁶ 2003 Australia Gapes 60-791 (with DM) DUBBO-All Men CVD 4 (5 yrs) 878 106 12.1 Sike M ⁴⁸ 2002 Jass Normaines and prophyses of 32 Men Total CHD 1 511 384 6.8 Order JL ¹⁴ 2002 US Normaines and local gont authorties with P		Study			Cohort	Group	Female	Diabetes	Outcome			Event
People recruited from workforce of nation- wide multi-indust; opcoration (Fletcher Challenge, Ltd. (72%)) & general electoral Men CVD 2 (5 yrs) 4638 225 7 Milne R ⁴¹ 2002 Zealand Northern Northern Total CHD 1 5 Empana JP ⁴⁰ 2001 Ireland PRIME cohort study (Befast cohort) PRIME Men 120 5 Empana JP ⁴⁰ 2003 Australia Debto Study othor of elder/ Australians DUBBO-All Men 120 5 Simons LA ⁵⁰ 2003 Australia Gapes 60-79) (with DM) DUBBO-All Men CVD 4 (10	Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
wide multi-industry corporation (Pietcher Challenge, Ltd. [72%] & general electoral Men CVD 2 (6 yrs) 4638 325 7 Empana JP ³⁰ 2003 Zealand PRIME cohort study (Belfast cohort) PRIME Men CVD 2 (6 yrs) 4638 325 7 Empana JP ³⁰ 2003 Inteland PRIME cohort study (Belfast cohort) PRIME Men Ictal CHD 1 (5 yr) 2399 61 2.5 Simons LA ⁵⁰ 2003 Australa Dubbo Study cohort of eldetry Australians DUBBO-All Men CVD 4 (10 2299 61 2.5 Simons LA ⁵⁰ 2003 Australa Dubbo Study cohort of eldetry Australians DUBBO-All Men CVD 4 (5 yrs) 878 106 12.1 Simons LA ⁵⁰ 2002 US Normative Aging Study- male veterans NAS Men Total CHD 1 1631 344 6.8 Orford JL ⁵⁰ 2002 US Normative Aging Study- male veterans NAS Men Total CHD 1 1519 25.6 6.3 Suck M ⁶⁰ 2001<				People recruited from workforce of nation-								
Mine R ⁴¹ New Challenge. Ltd. [72%] & general electoral Men CVD 2 (5 yrs) 4638 325 7 Empana JP ⁴⁰ 2003 Ireland PRIME Men (5y) 2399 120 5 Empana JP ⁴⁰ 2003 Ireland PRIME PRIME Men (5y) 2399 12 5 Empana JP ⁴⁰ 2003 Ireland PRIME cohort study (Bellast cohort) PRIME Men (5y) 2399 61 2.5 Simons LA ⁴⁶ 2003 Australia (ages 60-79) (wth DM) DUBBO-All Men (CVD 4 (10) 7 2399 61 2.5 Simons LA ⁴⁶ 2003 Australia (ages 60-79) (wth DM) DUBBO-All Men CVD 4 (5 yrs) 878 222 2.5.3 Simons LA ⁴⁶ 2003 Australia (ages 60-79) (wth DM) DUBBO-All Men Total CHD 1 1691 349.4 6.8 Suba M ⁶⁰ 2002 Japan Apartal exploration control elderly Australians Men Total CHD 1				wide multi-industry corporation (Fletcher								
Milne R ^a 2003 Zealand rolls of Auckand metro region (28%) Men CVD 2 (5 yrs) 4638 325 7 Empana JP ³⁰ 2003 Ireland PRIME cohort study (Belfast cohort) PRIME Men Total CHD 1 (5 yr) 2399 120 5 Empana JP ³⁰ 2003 Iveland PRIME cohort study (Belfast cohort) PRIME Men Hard CHD 1 (5 yr) 2399 61 2.5 Simons LA ⁶⁸ 2003 Australia (ages 60-79) (with DM) DUBBO-All Men CVD 4 (10 yrs) 878 106 12.1 Simons LA ⁶⁸ 2002 Japan Japanese company Men Total CHD 1 5611 384 6.8 Orlord JL ^W 2002 US Normative Aging Study - male veterans NAS Men Total CHD 1 5159 325 6.3 Ska M ⁶⁰ 2002 Germany Hard CHD 1 5159 325 6.3 14.8 Ska M ⁶⁰ 2001 Japan econormany Melas seed 30-59 completing annual conormales a	04		New	Challenge, Ltd. [72%]) & general electoral								
Empana JP ³⁰ Northern PRIME cohort study (Belfast cohort) PRIME Men Total CHD 1 (5 yr) 2399 120 5 Empana JP ³⁰ 2003 Ireland PRIME cohort study (Belfast cohort) PRIME Men (5 yr) 2399 120 5 Simons LA ³⁰ 2003 Australia Dubbo Study cohort of elderly Australians CVD 4 (10 yrs) 878 222 25.3 Simons LA ⁴⁰ 2003 Australia Bege 60-79) (with DM) DUBBO-All Men Yrs) 878 106 12.1 Suka M ⁶⁰ 2002 Japan Japanese company Mas Total CHD 1 5611 384 6.8 Orford JL ^{4rr} 2002 US Normative Aging Study : male veterans NAS Men Total CHD 1 1511 384 6.8 Assmann G ^{4rr} 2002 German J(u every 2 yrs) PROCAM Men Total CHD 1 1511 80 1.4 Assmann G ^{4rr} 2001 Japan Healt examinations between 1931-1939 Men Total CHD 1	Milne R ⁸¹	2003	Zealand	rolls of Auckland metro region (28%)		Men			CVD 2 (5 yrs)	4638	325	7
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Ulmer HB762005AustriaFirst National Heatth and NutritionVHM&PPMenCVD Mortality201683711.8Liao Y11999USExamination SurveyNHANES IMenCHD Mortality275333112Liao Y11999USExamination SurveyNHANES IMenCHD Mortality275328610.4Liao Y11999USExamination SurveyNHANES IMenCHD Mortality275328610.4Liao Y11999USExamination SurveyNHANES IMenCHD Mortality275328610.4Liao Y31999USExamination SurveyNHANES IIMenCHD Mortality26551766.6Lindman AS712007Norway60-69CP-NorwayMen0CVD Mortality37402957.9Hippisley-Cox JC342008UKQRESEARCHQRESEARCHMen0yr)301622276299.2Hense HW ⁶¹ 2003Germanycompanies and local govnt authoritiesPROCAMMen2.9Hard CHD 155273075.6	Olmer HB	2005	Austria	Variations in Vorariberg province	VHIVI&PP	wen			CHD Mortality	20168	244	1.Z
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Liao Y11999USExamination SurveyNHANES IMenCHD Mortality275333112Liao Y11999USFirst National Heatth and Nutrition Examination SurveyNHANES IMenCHD Mortality (15 yr)275328610.4Liao Y31999USSecond National Heatth and Nutrition Examination SurveyNHANES IMenCHD Mortality (15 yr)275328610.4Liao Y31999USExamination SurveyNHANES IIMenCHD Mortality (15 yr)26551766.6Lindman AS712007NorwayCardiovascular Program in Norway (ages 60-69)CP-NorwayMen0CVD Mortality yloc 10 (10 yr)301622276299.2Hippisley-Cox JC342008UKQRESEARCHQRESEARCHMen02.9Hard CHD 155273075.6		2005	Austria	First National Heath and Nutrition		INCL				20100	571	1.0
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Liao Y³1999USExamination SurveyNHANES IIMenCHD Mortality26551766.6Lindman AS ⁷¹ 2007Norway60-69)CP-NorwayMen0CVD Mortality37402957.9Hippisley-Cox JC³42008UKQRESEARCHQRESEARCHMen0CVD 10 (10 yr)301622276299.2Hense HW ⁶¹ 2003GermanyPROCAM cohort; drawn from 52 companies and local govnt authoritiesPROCAMMen2.9Hard CHD 155273075.6		1000	00	Second National Heatly and Nutrition		WICH			(10 yi)	2100	200	10.4
Lindman AS2007NorwayCardiovascular Program in Norway (ages Cardiovascular Program in Norway (ages CP-NorwayCP-NorwayMen0CVD Mortality S7402957.9Hippisley-Cox JC342008UKQRESEARCHQRESEARCHMen0CVD 10 (10 yr)301622276299.2Hense HW612003GermanyPROCAM cohort; drawn from 52 companies and local govnt authoritiesPROCAMMen2.9Hard CHD 155273075.6	Liao Y ³	1999	us	Examination Survey	NHANES II	Men			CHD Mortality	2655	176	6.6
Lindman AS712007Norway60-69)CP-NorwayMen0CVD Mortality37402957.9Hippisley-Cox JC342008UKQRESEARCHQRESEARCHMen0VI301622276299.2Hense HW ⁶¹ 2003GermanyPROCAM cohort; drawn from 52 companies and local govnt authoritiesPROCAMMen2.9Hard CHD 155273075.6		1000	00	Cardiovascular Program in Norway (ages		WICH			on b wortanty	2000	170	0.0
Hippisley-Cox JC ³⁴ 2008 UK QRESEARCH QRESEARCH Men 0 CVD 10 (10 yr) 301622 27629 9.2 Hense HW ⁶¹ 2003 Germany PROCAM cohort; drawn from 52 companies and local govnt authorities PROCAM Men 2.9 Hard CHD 1 5527 307 5.6	Lindman AS ⁷¹	2007	Norway	60-69)	CP-Norway	Men		0	CVD Mortality	3740	295	79
Hippisley-Cox JC342008UKQRESEARCHQRESEARCHMen0yr)301622276299.2Hense HW612003GermanyPROCAM cohort; drawn from 52 companies and local govnt authoritiesPROCAMMen2.9Hard CHD 155273075.6	Lindinariy to	2001	literitay			111011		Ŭ	CVD 10 (10	01.10	200	1.0
Hense HW ⁶¹ 2003 Germany PROCAM cohort; drawn from 52 companies and local govnt authorities PROCAM Men 2.9 Hard CHD 1 5527 307 5.6	Hippisley-Cox JC ³⁴	2008	UK	ORESEARCH	ORESEARCH	Men		0	vr)	301622	27629	9.2
Hense HW ⁶¹ 2003 Germany companies and local govnt authorities PROCAM Men 2.9 Hard CHD 1 5527 307 5.6			1	PROCAM cohort: drawn from 52					, ,			
	Hense HW ⁶¹	2003	Germany	companies and local dovnt authorities	PROCAM	Men		2.9	Hard CHD 1	5527	307	5.6
MONICA Augsburg cohort, 1984/1985 MONICA-				MONICA Augsburg cohort, 1984/1985	MONICA-			-				
Hense HW ⁶¹ 2003 Germany and 1989/1990 surveys Augsburg Men 4.2 Hard CHD 1 2861 146 5.1	Hense HW ⁶¹	2003	Germany	and 1989/1990 surveys	Augsburg	Men		4.2	Hard CHD 1	2861	146	5.1

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1 st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
				NHP-South							
Bhopal R ⁸³	2005	South Asia	Newcastle Heart Project - South Asians	Asia	Men		21		262		
Bhopal R ⁸³	2005	India	Newcastle Heart Project - Indian	NHP-India	Men		16		85		
Bhopal R ⁸³	2005	Pakistan	Newcastle Heart Project - Pakistani	NHP-Pakistan	Men		26		129		
			Atherosclerosis Risk in Communities					Hard CHD 1			
D'Agostino RB ⁴	2001	US	Study	ARIC	Men			(5 yr)	6133	195	3.2
								Hard CHD 1			
D'Agostino RB ^₄	2001	US	Honolulu Heart Program	HHP	Men			(5 yr)	2755	77	2.8
								Hard CHD 1			
D'Agostino RB ^⁴	2001	Puerto Rico	Puerto Rico Heart Health Program	PRHHP	Men			(5 yr)	8713	107	1.2
			Strong Heart Study (OK and Aberdeen					Hard CHD 1			
D'Agostino RB ^₄	2001	US	area of ND and SD)	SHS	Men		42	(5 yr)	1527	46	3
								Hard CHD 1			
D'Agostino RB ^₄	2001	US	Cardiovascular Health Study	CHS	Men		15	(5 yr)	956	71	7.4
- 80								Hard CHD 1			
Empana JP ^{oo}	2003	France	PRIME cohort study	PRIME-France	Men			(5 yr)	7359	106	1.4
80								Total CHD 1			
Empana JP ⁶⁶	2003	France	PRIME cohort study	PRIME-France	Men			(5 yr)	7359	197	2.7
54		United	Wisconsin Epidemiologic Study of								
Kothari V°	2002	Status	Diabetic Retinopathy	WESDR	Men						
	1000		Framingham Coorth (11th Exam) Or	FDO FDO O					o 400		
Wilson PWF	1998	US	Framingham Offspring (1st Exam)	FRS, FRS-O	Men		5.2	Total CHD 1	2489	383	15.4
Cederholm J ¹⁰	2008	Sweden	Swedish National Diabetes Register		Men		100		6628		
			Monitoring Project on Cardiovascular								
			Disease Risk Factors; persons randomly								
Cabaltana T77	2000	N a the and a series	selected from 3 cities in Netherlands,						40047	100	
Scheitens I	2008	Netherlands	aged 20-59 and no CVD		Men			(10 yr)	18217	189	1
0.28	0000	0	Conort of men and women employed in	PROCAM					7404	10.1	
Assmann G	2008	Germany	northwest Germany	conort	Men		<u> </u>	Hard CHD 1	7134	404	5.7
	2008	US	Physicians Health Study II	PHS-II	Men		0	CVD 15	VD 15 10724 1294		12.1
	2008	US	Physicians Health Study II	PHS-II	ivien		0	Hard CHD 2	10724	1072	10
Folsom A ¹⁰	2003	US	Atheroscierosis Risk in Communities	ARIC	Men			Hard CHD 2	6071	719	11.8
11	1000			INHANES I and					7077	770	
LIAO Y	1999	05	INHAINES I and II (pooled)	II (pooled)	Men			CHD death	1811	118	9.9
0	0000	A	Dubbo Study cohort of elderly Australians					CVD 4 (10	755	105	10.0
SIMONS LASS	2003	Australia	(ages 60-79) without DM	DORRO-NODW	ivien			yrs)	155	105	13.9

Table 9c. Outcome Incidence Rates – Women

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
Wilson PWF'	2008	US	Framingham Offspring Study	FRS-O	Women				2467		
Vaidya D ¹⁰	2007	US	John Hopkins Sibling Study	JHSS	Women			Total CHD 1	380	27	7.1
Becker A ⁴¹	2008	Germany	Munich	M-DM	Women		100		286		
			National Health and Nutrition Examination	NHANES-I							
Gaizano TA ⁸	2008	US	Survey I Epidemiologic Follow-Up Study	EFS	Women		4.09		3349		
Paynter N ⁵⁵	2009	US	Women's Genome Health Study	WGHS	Women			CVD 3	22129	715	3.2

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
Hippisley-Cox J ³⁴	2008	UK	Members of the QRESEARCH database	QRESEARCH	Women			CVD 1	1149054	41042	3.6
			European Prospective Investigation of								
Simmons RK ³⁵	2008	UK	Cancer [EPIC]–Norfolk	EPIC-Norfolk	Women			Total CHD 1	5782	250	4.3
			Atherosclerosis Risk in Communities					Hard CHD 2			
Mainous A ¹¹	2008	US	Study	ARIC	Women		0	(6 yr)	5406	131	2.4
			Framingham Cohort (11th) (68-71) &								
			Offspring 1st (71-75) & Offspring (3rd 84-								
D'Agostino RB ⁶	2008	US	87)	FRS, FRS-O	Women			CVD 2	4522	456	10.1
			Consecutive patients referred by primary								
			care provider for preventive cardiological								
Becker A ⁸⁷	2008	Germany	examination		Women			Hard CHD 2	708	144	20.3
			Consecutive patients referred by primary								
			care provider for preventive cardiological								
Becker A ⁸⁷	2008	Germany	examination		Women			Hard CHD 1	708	70	9.9
			THIN cohort; data from 288 UK practices								
			using INPS Vision system (~20%); includ-								
	using INPS Vision system (~20%); inc ing 24 practices (54709 patients) from Scotland and 14 practices (36904) fro		ing 24 practices (54709 patients) from								
60	2008 Germany examination 2008 Germany care provider for preventive cardiological examination 2008 Germany examination 2008 Germany examination 2008 Germany examination 2008 Germany examination THIN cohort; data from 288 UK practices using INPS Vision system (~20%); including 24 practices (54709 patients) from Scotland and 14 practices (36904) from Northern Ireland THIN 2007 Norway Norwegian Counties Study (ages 40-59) NCS Atherosclerosis Risk In Communities and Cardiovascular Health Study trials with 2007 US CKD ARIC, 0 2007 <td></td> <td></td> <td></td> <td></td> <td>CVD 10 (10</td> <td></td> <td></td> <td></td>						CVD 10 (10				
Hippisley-Cox JC ^{o2}	2008	UK	Northern Ireland	THIN	Women		0	yr)	542987	35566	6.6
Lindman AS'	2007	Norway	Norwegian Counties Study (ages 40-59)	NCS	Women		0	CVD Mortality	24785	94	0.4
			Atherosclerosis Risk In Communities and								
64			Cardiovascular Health Study trials with					Hard CHD 1			
Weiner DE ⁶⁴	2007	US	CKD	ARIC, CHS	Women		13.7	(10yr)	577	56	9.7
			Atherosclerosis Risk In Communities and								
			Cardiovascular Health Study trials with					Hard CHD 1			
Weiner DE ⁶⁴	2007	US	CKD	ARIC, CHS	Women		13.7	(5yr)	577	30	5.2
			QRESEARCH database, constructed								
40			from 160 UK general practices; validation	QRESEARCH							
Hippisley-Cox JC ⁴⁰	2007	UK	cohort	(Validation)	Women		0	CVD 4 (10 yr)	309413	20421	6.6
40			Koreans insured by National Health					Stroke 6 (10			
Jee SH ⁴⁰	2008	Korea	Insurance Corporation (NHIC)		Women		4.1	yr)	437383	15988	3.7
Koller MT ⁸⁴	2007	Netherlands	Rotterdam Study		Women			Hard CHD 1	4343	448	10.3
			Atherosclerosis Risk In Communities								
Mainous AG ¹⁴	2007	US	Study	ARIC	Women				8104		
Miyasaka Y ⁹	2007	US	Adult residents of Olmsted County, MN		Women			Total CHD 1	1450	236	16.3
Denes P ⁶³	2007	US	Women's Health Initiative study	WHI	Women			CVD 15	14749	595	4
Denes P ⁶³	2007	US	Women's Health Initiative study	WHI	Women			Hard CHD 1	14749	246	1.7
			Women's Health Study (Validation								
Ridker PM ⁹³	2007	US	Cohort)	WHS Women CVD 3 8158		8158	262	3.2			
			Asia Pacific Cohort Studies Collaboration								
Barzi F ⁴⁵	2007	China	- Total Chinese Cohort	APCSC China	Women			CVD 8	10636	124	1.2
			Validity of the Adapted Framingham								
			Individual Risk Equation for Coronary								
Marrugat J ³⁸	2007	Spain	Incidencts Cohort	VERIFICA	Women		14.6	Total CHD 1	3285	68	2.1
								CVD 11 (10			
Woodward M ³⁰	2007	Scotland	Scottish Hearth Health Extended Cohort	SHHEC	Women		1.4	yr)	6757	422	6.2

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
								CVD 11 (10			
Woodward M ³⁰	2007	Scotland	Scottish Hearth Health Extended Cohort	SHHEC	Women	1	1.3	yr)	6757	422	6.2
Cook NR ¹⁹	2006	US	Women's Health Study	WHS	Women			CVD 3	15048	498	3.3
Lee ET ¹⁶	2006	US	Strong Heart Study	SHS	Women		46.7	Hard CHD 1	2650	375	14.2
			Patients with type 2 diabetes registered								
Donnan PT ³⁹	2006	UK	with a Tayside GP	DARTS	Women				2166		
May MD ⁴⁴	2006	UK	British Women's Heart and Health Cohort	BWHH	Women	1		CVD 11	3582	240	6.7
May MD ⁴⁴	2006	UK	British Women's Heart and Health Cohort	BWHH	Women			Total CHD 3	3582	198	5.5
Brindle PM ⁷⁰	2005	Scotland	Renfrew and Paisley Study		Women		1.1		6678		
			Individuals aged 25-65 yrs identified from								
			Finnish population register & participating								
			in 3 cross-sectional risk factor surveys in								
Silventoinen K ⁷⁸	2005	Finland	Finland in 1987, 1992, and 1997		Women		1	Total CHD 1	9457	219	2.3
			Individuals aged 25-65 yrs identified from								
			Finnish population register & participating								
70			in 3 cross-sectional risk factor surveys in								
Silventoinen K ^{/*}	2005	Finland	Finland in 1987, 1992, and 1997		Women	1	1	Stroke 1	9457	147	1.6
			Individuals aged 25-65 yrs identified from								
			Finnish population register & participating								
70			in 3 cross-sectional risk factor surveys in					All-Cause			
Silventoinen K ^{/*}	2005	Finland	Finland in 1987, 1992, and 1997		Women	1	1	Mortality	9457	266	2.8
Bhopal R ⁸³	2005	UK	Newcastle Heart Project: Europeans	NHP Europe	Women	1	3		363		
45			Atherosclerosis Risk in Communities								
McNeill AM ¹⁵	2005	US	Study	ARIC	Women	1			6881		
Wang Z ⁸²	2005	Australia	Aboriginal community		Women	1	16	Total CHD 1	331	38	11.5
22			Diabetes clinic at University College								
Stephens JW ³³	2004	UK	London Hospitals NHS Trust		Women	1	100		294		
10			Atherosclerosis Risk in Communities								
Chambless LE ¹²	2004	US	Study	ARIC	Women	1		Stroke 3	7274	221	3
			Chinese Multi-Provincial Cohort Study;								
47			individuals aged 35-64 from 16 centers in								
Liu J ⁴⁷	2004	China	11 provinces (1992-3) and Beijing (1996-9) MUCA	Women		5	Hard CHD 1	14056	54	0.4
McEwan P [∞]	2004	UK	Cardiff Diabetes Database (type 1 and 2)		Women			CVD 2	396	67	16.9
			People recruited from workforce of nation-								
			wide multi-industry corporation (Fletcher								
		New	Challenge, Ltd. [72%]) and general elector	-							
Milne R°	2003	Zealand	al rolls of Auckland metro region (28%)		Women	1		CVD 2 (5 yrs)	1716	86	5
			Dubbo Study cohort of elderly Australians								
Simons LA ³⁰	2003	Australia	(ages 60-79) (with DM)	DUBBO-All	Women	1		CVD 4 (5 yrs)	1224	105	8.6
			Dubbo Study cohort of elderly Australians					CVD 4 (10			
Simons LA ³⁰	2003	Australia	(ages 60-79) (with DM)	DUBBO-All	Women	1		yrs)	1224	237	19.4
			Framingham Study (11th Exam) or				1.	Hard CHD 1		1	
D'Agostino RB*	2001	US	Framingham Offspring Study (1st Exam)	FRS, FRS-O	Women		4	(5 yr)	2812	39	1.4
68			Lipid Research Clinics Prevalence Study]	
Grover SA ^{oo}	2000	Canada	cohort	LRCPS	Women	1	4.2		734		
Liao Y'	1999	US	Framingham Heart Study (4th Exam)	FRS	Women			CHD Mortality	2323	153	6.6

	Study			Cohort	Group	Female	Diabetes	Outcome			Event
Study 1st Author	Yr Pub	Country	Cohort	Abbrev	Name	%	%	Name	Enrollment	Outcomes	%
			Vorarlberg Health Monitoring and								
			Promotion Program (VHM&PP); cohort of								
			individuals undergoing general health								
Ulmer HB'°	2005	Austria	examinations in Vorarlberg province	VHM&PP	Women	1		CVD Mortality	24481	116	0.5
			Vorariberg Health Monitoring and								
			Promotion Program (VHIVI&PP); conort of								
Lilmor LIP ⁷⁶	2005	Austria	Individuals undergoing general health		Womon				24401	56	0.2
	2005	Austria	Eirct National Hoath and Nutrition		women				24401	50	0.2
Line V^3	1000	119	First National Fleatin and Nutilition		Womon				2959	257	67
	1999	03	Second National Heatth and Nutrition	INFIANLS I	vvomen			CITID MOITAILTY	3030	237	0.7
Liao Y ³	1999	us	Examination Survey	NHANES II	Women			CHD Mortality	3050	99	32
	1000	00	Cardiovascular Program in Norway (ages		women			on b wortanty	0000	00	0.2
Lindman AS ⁷¹	2007	Norway	60-69)	CP-Norway	Women		0	CVD Mortality	4345	132	3
Lindinari/to	2001	Hornay		or normay			Ŭ	CVD 10 (10	1010	102	0
Hippislev-Cox JC ³⁴	2008	UK QRESEARCH PROCAM cohort; drawn from 52 companies and local govt authorities		QRESEARCH	Women		0	vr)	306111	19928	6.5
			PROCAM cohort: drawn from 52				-	,			
Hense HW ⁶¹	2003	Germany	companies and local govt authorities	PROCAM	Women	1	2.6	Hard CHD 1	3155	31	1
		, , , , , , , , , , , , , , , , , , ,	MONICA Augsburg cohort; 1984/1985	MONICA-							
Hense HW ⁶¹	2003	Germany	and 1989/1990 surveys	Augsburg	Women	1	3	Hard CHD 1	2925	32	1.1
				NHP-South							
Bhopal R ⁸³	2005	South Asia	Newcastle Heart Project - South Asians	Asia	Women	1	20		314		
Bhopal R ⁸³	2005	India	Newcastle Heart Project - Indian	NHP - India	Women		16		145		
Bhopal R ⁸³	2005	Pakistan	Newcastle Heart Project - Pakistani	NHP-Pakistan	Women		28		135		
			Atherosclerosis Risk in Communities					Hard CHD 1			
D'Agostino RB ⁴	2001	US	Study	ARIC	Women			(5 yr)	8045	84	1
			Strong Heart Study (OK and Aberdeen					Hard CHD 1			
D'Agostino RB ^₄	2001	US	area of ND and SD)	SHS	Women	1	51	(5 yr)	2255	23	1
								Hard CHD 1			
D'Agostino RB ⁺	2001	US	Cardiovascular Health Study	CHS	Women	1	10	(5 yr)	1601	44	2.7
54		United	Wisconsin Epidemiologic Study of								
Kothari V ³⁴	2002	Status	Diabetic Retinopathy	WESDR	Women						
	1000		Framingham Coorth (11th Exam) Or					TINGUE	0050	007	7.0
	1998	05	Framingham Offspring (1st Exam)	FRS, FRS-0	women		4	Total CHD 1	2856	227	7.9
Cederholm J	2008	Sweden	Swedish National Diabetes Register		women		100		5018		
			Monitoring Project on Cardiovascular								
			Disease Risk Factors; persons randomly								
Scholtons T ⁷⁷	2008	Nothorlanda	selected from 3 cities in Nethenands,		Womon			(10 vr)	21502	67	0.2
Edison A ¹³	2000		Athorosolorosis Pick in Communities		Womon		1		21302	245	4.2
	2101	00		NHANESLand	**omen				1303	545	4.5
Liao Y ¹	1999	us	NHANES Land II (pooled)		Women			CHD death	10665	673	6.3
	1000		Dubbo Study cohort of elderly Australians		vvomen			CVD 4 (10)	10000	0.0	0.0
Simons I A ⁵⁶	2003	Australia	(ages 60-79) without DM		Women			vrs)	1045	87	8.3
				122222 1020	1		1	1		· • ·	0.0

Table 10a. Quality Grading – Study Breakdown

Year	Author	Does the article state both the inclusion/exclusion criteria and any additional exclusions that were made after cohort inception?	Was the study population well described?	Was the loss to followup over the course of the study less than 20%?	If more than 20% were lost, did the authors acknowledge the potential effects on the model?	Did missing data cause more than 20% of the population to be excluded from the model?	If more than 20% of the data was excluded due to missing data, was a missing data technique applied?	For validation studies, did the authors report both discrimination and calibration?	For model development, did the authors assess internal validation?
				An	nericas				
1999	Detrano RC ¹⁸	+	++	-	NA	-	NA	++	+
1999a	Liao Y ³	+	++	-	NA	-	NA	++	
1999b	Liao Y ¹	++	++	+	NA		NA	NA	
2000	Grover SA ⁶⁸	+	++	-	NA	-	NA	+	NA
2001	D'Agostino RB ⁴	+	++	-	NA	-	NA	++	
2002	Kothari V54	++	+	++	NA		NA	NA	-
2002	Orford JL ⁶⁷	+	+		NA	NA	NA	+	NA
2003	Folsom A ¹³	++	+	-	-	+	NA	++	
2004	Chambless LE ¹²	++	++		NA		NA	+	+
2004	Greenland P ¹⁷	+	+	+	NA		NA	+	
2004	Stern MP66	++	-	-	NA		NA	+	NA
2005	Arad Y ⁹¹	++	+	+	NA	-	-	+	
2005	McNeill AM ¹⁵	++	++	+	NA		NA	+	NA
2006	Cook NR ¹⁹	+	++	-	-	-	-	++	+
2006	Lee ET ¹⁶	+	++	+	NA	-	-	NA	+
2007	Berry JD ⁵	++	+	+	NA		NA	-	NA
2007	Denes P ⁶³	+	++	-	NA		NA	+	
2007	Mainous AG ¹⁴	-	++	-	-	-	-	+	+
2007	Miyasaka Y ⁹	++	++	-	-	+	NA		
2007	Ridker PM ²⁰	++	++	-	-	-	NA	++	+
2007	Vaidya D ¹⁰	+	++	-	NA	-	NA	-	NA
2007	Weiner DE ⁶⁴	++	++	+	NA		NA	++	NA
2008	D'Agostino RB ⁶	+	++	-	NA	-	NA	++	+
2008	Gaizano TA ⁸	++	++	-	+		NA	++	+
2008	Mainous AG ¹¹	-	+	-	-	-	-	+	
2008	Wilson P ⁷	++	++	+	NA		NA	+	
2009	Paynter N ⁵⁵	++	++	-	-		NA	++	
		-			Asia				-
2001	Suka M ⁸⁹	++	++	+	NA	+	NA	++	NA
2002	Suka M ⁹⁰	+	-	-		-		+	NA
2004	Liu J ⁴⁷	+	+	+	NA	+	-	++	
2007	Barzi F ⁴⁵	+	+	-	NA	-	NA	++	
2007	Yang X ⁵⁰	++	++	-	NA	-	NA	++	+
2008	Jee SH ⁴⁶	++	++	+	NA		NA	++	+
2008	Yang X49	+	++	-	NA	-	NA	++	+
		•	·	E	urope		•		
2002	Assmann G ²⁷	+	+	+	NA	-	-	++	

Year	Author	Does the article state both the inclusion/exclusion criteria and any additional exclusions that were made after cohort inception?	Was the study population well described?	Was the loss to followup over the course of the study less than 20%?	If more than 20% were lost, did the authors acknowledge the potential effects on the model?	Did missing data cause more than 20% of the population to be excluded from the model?	If more than 20% of the data was excluded due to missing data, was a missing data technique applied?	For validation studies, did the authors report both discrimination and calibration?	For model development, did the authors assess internal validation?
2002	Bastuji-Garin S37	+	+	-	-	-	-	+	NA
2003	Brindle PM ⁷³	+	+	+	NA		NA	++	NA
2003	Empana JP ⁸⁰	-	+	-	-	-	-	++	NA
2003	Hense HW ⁶¹	+	+	-	-	-	-	+	NA
2003	Milne R ⁸¹	+	-	-	-		NA	+	NA
2003	Simons LA ⁵⁶	-	+			-	-		NA
2004	Ducloux D ⁶⁹	+	++	+	NA		NA		
2004	Dunder K ²²	++	++	+	NA	+		++	+
2004	Erikssen G ²⁴	+	+	+	NA	-	-	NA	+
2004	Koenig W ⁷³	++	++	+	NA		NA	+	
2004	McEwan P ^{oo}	+	+			-	+	+	NA
2004	Stephens JW ³³	++	++		+		NA	++	NA
2005	Bernard S ²¹	+	++	-	-	-	-	+	
2005	Bhopal R ⁶⁵	-	+	-	-	NA	NA		
2005	Brindle PM ⁷⁰	+	++	-	-		NA	+	NA
2005	Cooper JA ³¹	+	++	-	-	-	-	++	NA
2005	Ferrario M ²⁹	+	-	-	-	-	-	++	+
2005	Guzder RN ^{oo}	++	++	+	NA		NA	++	NA
2005	Silventoinen K ^{/*}	-	++	-	-	-	-	+	NA
2005	Ulmer HB ⁷⁶	+	+	-	-	-	-	+	NA
2005	Vliegenthart R ⁷⁹	++	++	+	NA		NA	+	
2005	Wang Z ⁸²	++	++	+	NA	+		-	NA
2005	Wannamethee SG ⁷²	++	++	+	NA		NA	+	
2006	Donnan PT ³⁹	+	++	-	-	+		NA	+
2006	May MD ⁴⁴	+	+	-	-	-	+	++	
2007	Assmann G ²⁶	+	++	-	NA	-	NA	+	+
2007	Buyken AE ⁷⁴	+	-	-	NA	-	NA		NA
2007	Hippisley-Cox JC ⁴⁰	+	++			-	-	++	+
2007	Koller MT ⁸⁴	+	+	+	NA		NA	++	NA
2007	Lindman AS ⁷¹	++	+	-	-		NA	+	NA
2007	Macfarlane PW ³²	+	++	-	-	-	-	NA	
2007	Marrugat J ³⁸	++	+	+	NA		NA	++	NA
2007	Reissigova J ²⁵	++	+	+	NA	-	NA	++	NA
2007	Strom Moller C ²³	++	++			-	-	+	
2007	Woodward M ³⁰	-	++		NA		+	+	
2008	Assmann G ²⁸	+	++	-	-		NA	+	NA
2008	Becker A ⁴¹	++	++	+	NA		NA	+	
2008	Becker A ⁸⁷	+	++	+	NA	-	-	+	NA
2008	Cederholm J ⁴³	-	+	-	-		NA	NA	

Year	Author	Does the article state both the inclusion/exclusion criteria and any additional exclusions that were made after cohort inception?	Was the study population well described?	Was the loss to followup over the course of the study less than 20%?	If more than 20% were lost, did the authors acknowledge the potential effects on the model?	Did missing data cause more than 20% of the population to be excluded from the model?	If more than 20% of the data was excluded due to missing data, was a missing data technique applied?	For validation studies, did the authors report both discrimination and calibration?	For model development, did the authors assess internal validation?
2008	de Ruijter W ⁴²	++	++	-	NA		NA	+	+
2008	Elkeles R ⁸⁸	+	++		NA	-	-	+	NA
2008	Hippisley-Cox JC ⁶²	++	++	+	NA	-	+	++	
2008	Hippisley-Cox JC ³⁴	++	++	-	-	-	+	++	NA
2008	Scheltens T ⁷⁷	+	++	-	-		NA	++	NA
2008	Simmons RK ³⁵	++	++	-	NA		NA	+	
2008	Vergnaud A ³⁶	++	++	+	NA	-	-	++	NA

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Reasons for Exclusion:

- X-1. Not relevant to topic
- X-1a. Post-PCI
- X-1b. Post-CABG
- X-1c. Diagnostic
- X-1d. Prognostic
- X-1e. Etiologic
- X-1f. Not a risk tool
- X-1g. Other
- X-2. Does not attempt internal or external validation (evaluation of risk model)
- X-3. Not published in English
- X-4. Not original research
- X-5. Not an eligible study type
- X-6. Does not report relevant outcomes
- X-7. Study size of <200
- X-8. Study population symptomatic for CVD
- X-9. Study population aged <18 years
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