New approaches to the implementation of cardiovascular disease prevention
Jørstad, H.T.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
CHAPTER 2

THE SYSTEMATIC CORONARY RISK EVALUATION (SCORE) IN A LARGE UK POPULATION

10-YEAR FOLLOW-UP IN THE EPIC-NORFOLK PROSPECTIVE POPULATION STUDY

Jørstad HT, Colkesen EB, Minneboo M, Peters RJ, Boekholdt SM, Tijssen JG, Wareham NJ, Khaw KT

European Journal of Preventive Cardiology, 2013
ABSTRACT

BACKGROUND: The European Society of Cardiology endorses cardiovascular disease (CVD) risk stratification using the Systematic COronary Risk Evaluation (SCORE) algorithm, with separate algorithms for high-risk and low-risk countries. In the 2012 European Guidelines on CVD Prevention in Clinical Practice, the UK has been reclassified as a low-risk country. However, the performance of the SCORE algorithm has not been validated in the UK.

DESIGN: We compared CVD mortality as predicted by SCORE with the observed CVD mortality in the European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) prospective population study, a cohort representative of the general population.

METHODS: Individuals without known CVD or diabetes mellitus, aged 39–65 years at baseline, were included in our analysis. CVD mortality was defined as death due to ischaemic heart disease, cardiac failure, cerebrovascular disease, peripheral artery disease and aortic aneurysm. Predicted CVD mortality was calculated at baseline using the SCORE high-risk and low-risk algorithms.

RESULTS: A total of 15,171 individuals (57.1% female) with a mean age of 53.9 (SD 6.2) years were included. Predicted CVD mortality was 2.85% (95% confidence interval (CI) 2.80–2.90) with the SCORE high-risk algorithm and 1.55% (95% CI 1.52–1.58) with the low-risk algorithm. The observed 10-year CVD mortality was 1.25% (95% CI 1.08–1.44). Similar results were observed across sex and age subgroups.

CONCLUSION: In the large EPIC-Norfolk cohort representative of the UK population, the SCORE low-risk algorithm performed better than the high-risk algorithm in predicting 10-year CVD mortality. Our findings indicate that the UK has been correctly reclassified as a low-risk country.
INTRODUCTION

The European Society of Cardiology (ESC) guidelines on cardiovascular disease (CVD) prevention in clinical practice recommend that treatment decisions be based on the predicted 10-year risk of CVD mortality.1 This risk can be calculated using the Systematic CORonary Risk Evaluation (SCORE) algorithm, which is based on the pooling of several large European population-based cohorts.2 The SCORE algorithm includes age, sex, smoking status, systolic blood pressure, and serum total cholesterol or total/HDL-cholesterol ratio, and can be rapidly calculated using SCORE risk charts. Risk charts have been published for high-risk countries and low-risk countries, in addition to country-specific calibrated versions.2,3 Based on data from the World Health Organization,4 the most recent ESC guidelines have reclassified the United Kingdom (UK) as a low-risk country, with no country-specific calibrated version.1 However, the performance of the SCORE has not been studied in a large, population-based UK cohort.

We compared the predicted 10-year CVD mortality as calculated using the SCORE high-risk and low-risk algorithms with the observed 10-year CVD mortality in the European Prospective Investigation of Cancer- Norfolk (EPIC-Norfolk) prospective population study.5

METHODS

Study population

We used data from the EPIC-Norfolk prospective population study, a cohort of men and women aged 39–79 years residing in the county of Norfolk in the UK. Details of the study have been described elsewhere.5 In brief, between 1993 and 1997, 77,630 adults were invited from general practices to participate in the study. Of these, 25,639 (33%) provided signed informed consent for study participation and attended a baseline health assessment. Participants completed questionnaires about their personal and family history of disease, drug use and lifestyle, including smoking status. Participants were also asked whether a doctor had ever told them that they had any of the following conditions: diabetes mellitus, myocardial infarction, stroke. Anthropometric and blood pressure measurements and non-fasting blood samples were collected at the health assessment. Two measures were taken of diastolic and systolic blood pressure using an Accutorr Sphygomanometer (Datascope, UK) after the participant had sat for 3 min. Measurements were obtained on an arm held horizontally at the level of the mid-sternum. A medium or large cuff size was used according to arm circumference. Calibration was undertaken regularly to check the accuracy of both the equipment and the operators. Total cholesterol, high-density lipoprotein (HDL) cholesterol and triglyceride were measured on an RA 1000 (Bayer Diagnostics, Basingstoke, UK). Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula6 except when triglyceride was >4 mmol/l.

In comparison with the general population of the UK, anthropometric variables, blood pressure and serum lipids in the EPIC-Norfolk cohort are representative of the population studies recorded in the Health Survey of England.5,7 There were, however, fewer current smokers.5 Participants were followed up for the development of cause-specific mortality. Vital status for all EPIC-Norfolk participants was obtained through death certification at the Office for National Statistics. Death
Study design

In keeping with the selection criteria of the SCORE algorithm, we excluded individuals aged over 65 years and those with a history of CVD (myocardial infarction or stroke) or diabetes mellitus at baseline. Additionally, subjects with missing data on SCORE variables were excluded. CVD mortality was defined as death where CVD was coded as the underlying or contributing cause. CVD was defined as ischaemic heart disease (ICD-10 codes I20–I25), cardiac failure (ICD-10 codes I11, I13 and I50), cerebrovascular disease (ICD-10 codes I60–I69), peripheral artery disease (ICD-10 codes I70–I79) and aortic aneurysm (ICD-10 code I71). The SCORE algorithm for high-risk and low-risk countries was applied to the EPIC-Norfolk data.

Statistical methods

Baseline characteristics were summarized separately for men and women, using numbers and percentages for categorical variables, mean and standard deviation (SD) for continuous variables with a normal distribution, and median and interquartile range for continuous variables with a non-normal distribution. Predicted 10-year CVD mortality rates were calculated using the SCORE algorithm for high-risk countries and low-risk countries. As SCORE was designed to predict 10-year CVD mortality, the observed mortality rates in our cohort were limited to the first 10 years of follow-up using Kaplan–Meier (KM) estimates. Ratios of predicted to observed CVD mortality, as well as absolute differences between predicted and observed CVD mortality, were calculated for the total population and stratified by sex and age subgroups in accordance with the SCORE charts. We separately evaluated the coronary heart disease (CHD) mortality risk function and the non-coronary heart disease (NCHD) risk function. Receiver operator characteristic (ROC) curves with corresponding areas under the curve (AUCs) were calculated using the high-risk and low-risk algorithms and compared using C-statistics. In order to assess the calibration of both SCORE algorithms, we used the Hosmer–Lemeshow goodness-of-fit test, which aligns the number of predicted and observed CVD deaths by deciles of predicted risk. To correct for possible confounding due to the non-fasting state of the cholesterol measurements, we performed a sensitivity analysis using adjusted levels of total cholesterol (correction to baseline total cholesterol +0.2 mmol/l if fasting time was 0–2 h, +0.1 mmol/l if fasting time was 2–5 h and no change if fasting time was 5 h), as described by Langsted et al. ROC curves were calculated to compare both algorithms using observed total cholesterol values against corrected total cholesterol values.

RESULTS

The study population consisted of 25,639 participants. A total of 10,468 were excluded because they were older than 65 years (n=8053), had a history of CVD or diabetes mellitus (n=697) or missing data (n=1718) (Figure 1). After exclusion, 15,171 study participants <65 years without a history of CVD or diabetes and with a complete dataset were available for analysis. Table 1 presents the characteristics of the study participants. Mean age was 53.9 years (SD 6.2), 57.1% were female and
13.1% were current smokers. Mean body mass index was 26.0 kg/m² (SD 3.9), mean total cholesterol 6.0 mmol/l (SD 1.1) and mean LDL cholesterol 3.9 mmol/l (SD 1.0), which was slightly above levels recommended by the ESC guidelines.

Table 1. Population characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 15,171)</th>
<th>Male (n = 6509)</th>
<th>Female (n = 8662)</th>
<th>Missing n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.9 ± 6.2</td>
<td>54.1 ± 6.2</td>
<td>53.8 ± 6.2</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>73.3 ± 13.2</td>
<td>80.6 ± 11.3</td>
<td>67.9 ± 11.8</td>
<td>17 (0.1)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.0 ± 3.9</td>
<td>26.2 ± 3.2</td>
<td>25.9 ± 4.3</td>
<td>28 (0.2)</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.84 ± 0.09</td>
<td>0.91 ± 0.06</td>
<td>0.78 ± 0.06</td>
<td>30 (0.2)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>13.1 (1988)</td>
<td>13.4 (871)</td>
<td>12.9 (1117)</td>
<td>106 (0.6)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>131 ± 17</td>
<td>134 ± 16</td>
<td>129 ± 17.1</td>
<td>29 (0.2)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>81 ± 11</td>
<td>84 ± 11</td>
<td>79 ± 10.6</td>
<td>29 (0.2)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.0 ± 1.1</td>
<td>6.0 ± 1.1</td>
<td>6.1 ± 1.1</td>
<td>1125 (6.7)</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.9 ± 1.0</td>
<td>3.9 ± 1.0</td>
<td>3.8 ± 1.0</td>
<td>1605 (9.5)</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.4 ± 0.4</td>
<td>1.2 ± 0.3</td>
<td>1.6 ± 0.4</td>
<td>1605 (9.5)</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.4 (1.0-2.1)</td>
<td>1.7 (1.2-2.4)</td>
<td>1.4 (0.9-1.8)</td>
<td>1126 (6.7)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation, percentage (number) or median (interquartile range). Percentages of missing data are presented as percentage before exclusion of individuals with missing values (n=1718) over the whole population (n=16,889). LDL: low-density lipoprotein; HDL: high-density lipoprotein

Table 2 presents the predicted CVD mortality according to the high-risk and low-risk SCORE algorithms and the observed 10-year CVD mortality. Predicted CVD mortality according to the SCORE high-risk algorithm was 2.85% (95% confidence interval (CI) 2.80–2.90), whereas according to the SCORE low-risk algorithm it was 1.55% (95% CI 1.52–1.58). The observed 10-year CVD mortality (KM estimate) was 1.25% (95% CI 1.08–1.44). Goodness-of-fit for the SCORE high-risk algorithm was $x^2=152.95$ (p<0.001), while for the SCORE low-risk algorithm it was $x^2=21.60$ (p=0.02).

Table 2. Predicted and observed 10-year cardiovascular mortality

<table>
<thead>
<tr>
<th></th>
<th>SCORE High risk</th>
<th>SCORE Low risk</th>
<th>Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (95%-CI)</td>
<td>% (95%-CI)</td>
<td>n %</td>
</tr>
<tr>
<td>Total cardiovascular mortality (n=15,171)</td>
<td>2.85 (2.80-2.90)</td>
<td>1.55 (1.52-1.58)</td>
<td>187 1.25</td>
</tr>
<tr>
<td>Male (n=6509)</td>
<td>4.53 (4.43-4.63)</td>
<td>2.35 (2.29-2.40)</td>
<td>126 1.97</td>
</tr>
<tr>
<td>Female (n=8662)</td>
<td>1.58 (1.55-1.62)</td>
<td>0.95 (0.92-0.97)</td>
<td>61 0.71</td>
</tr>
<tr>
<td>Coronary heart disease mortality</td>
<td>2.03 (1.99-2.07)</td>
<td>1.0 (0.98-1.02)</td>
<td>93 0.62</td>
</tr>
<tr>
<td>Non-coronary heart disease mortality</td>
<td>0.82 (0.80-0.83)</td>
<td>0.55 (0.52-0.77)</td>
<td>94 0.63</td>
</tr>
</tbody>
</table>

SCORE: Systematic COronary Risk Evaluation; CI: confidence interval

The observed 10-year CHD mortality was 0.62% (95% CI 0.51–0.76). Predicted CHD mortality according to the SCORE high-risk algorithm was 2.03% (95% CI 1.99–2.07), with an AUC of 0.84 and goodness-of-fit of $x^2=59.50$ (p < 0.0001). According to the SCORE low-risk algorithm CHD mortality was 1.0% (95% CI 0.98–1.02), with an AUC of 0.84 and a goodness-of-fit of $x^2=30.82$ (p=0.0006). There was no significant difference between the AUCs of both algorithms ($x^2=0.49$) (p=0.5).
Figure 1. Study Population

The observed 10-year NCHD mortality was 0.63% (95% CI 0.52–0.77). Predicted NCHD mortality according to the SCORE high-risk algorithm was 0.82% (95% CI 0.80–0.83), with an AUC of 0.73 and a goodness-of-fit of $x^2=13.28$ ($p=0.21$). According to the SCORE low-risk algorithm NCHD mortality was 0.55% (95% CI 0.54–0.56), with an AUC of 0.73 and a goodness-of-fit of $x^2=10.33$ ($p=0.41$). There was no significant difference between the AUCs of both algorithms ($x^2<0.01$) ($p=0.95$).

Overall, CHD mortality was markedly more over-estimated than NCHD mortality. SCORE high-risk overestimated CHD by 330% compared with 160% by SCORE low-risk. NCHD mortality was overestimated by SCORE high-risk by 30%. Conversely, SCORE low-risk showed an underestimation of 13%.

Among men, the predicted CVD mortality according to the SCORE high-risk algorithm and the SCORE low-risk algorithm was 4.53% (95% CI 4.43–4.63) and 2.35% (95% CI 2.29–2.40), respectively. The observed 10-year CVD mortality (KM estimate) in men was 1.97% (95% CI 1.66–2.34). Among women, the predicted CVD mortality according to SCORE high-risk algorithm was 1.58% (95% CI 1.55–1.62) and 0.95% (95% CI 0.92–0.97) according to the SCORE low-risk algorithm. The observed 10-year CVD mortality in women was 0.71% (95% CI 0.55–0.92).

Across all age–sex groups as defined by SCORE cut-offs, the high-risk algorithm consistently overestimated CVD mortality to a larger extent than the low-risk algorithm (Figure 2 and Appendix 1 in the supplementary material). When using the SCORE high-risk algorithm, this overestimation varied between 107% and 169% in men, and 99% and 218% in women. Using the SCORE low-risk algorithm, over-estimation was considerably lower, varying between 10% and 39% in men and
21% and 82% in women (Figure 3). When applying the ESC treatment threshold of SCORE 10-year predicted CVD mortality ≥5%, the SCORE high-risk algorithm classified an additional 12.4% of the population (1879 individuals) as ≥5% compared with the SCORE low-risk algorithm (2562 (16.9%) individuals by SCORE high-risk algorithm vs. 683 (4.5%) individuals by SCORE low-risk algorithm). Discriminative performance of the high-risk and the low-risk SCORE algorithm in predicting 10-year CVD mortality was virtually identical, with an AUC of 0.78 (95% CI 0.75–0.81) using the high-risk algorithm and 0.78 (95% CI 0.75–0.81) using the low-risk algorithm (Appendix 2). Comparing the ROCs for SCORE high-risk and low-risk yielded an x2=0.16 (p=0.68).

In the sensitivity analysis, the AUC for SCORE in predicting 10-year CVD mortality using corrected versus uncorrected total cholesterol levels did not change the AUC using either the high-risk algorithm (AUC 0.78 vs. 0.78) or the low-risk algorithm (AUC 0.78 vs. 0.78) (Appendix 3).
In individuals excluded from the main analysis due to missing data, mean age was slightly higher (55.7 years (SD 6.2)) and 53% were female. Risk factor control was slightly worse as compared with the study population, with 15.4% current smokers, a mean BMI of 27.4kg/m$^2$ (SD 4.6), a mean systolic blood pressure of 135mmHg (SD 18) and a mean diastolic blood pressure of 84 mmHg (SD 11). LDL-cholesterol was identical (3.9 mmol/l (SD 1.0)) as compared with the study population. The observed 10-year CVD mortality was 1.90% (32 events) (95% CI 1.35–2.67) – slightly higher than in the study population.

**DISCUSSION**

In the EPIC-Norfolk prospective population study, a cohort representative of the general UK population, we observed that the SCORE low-risk algorithm more accurately estimates CVD mortality than the SCORE high-risk algorithm. This concurs with the recent ESC guidelines reclassifying the UK as a low-risk country instead of a high-risk country.

The SCORE cardiovascular risk algorithm was developed using 12 European cohort studies, in which the inclusion dates ranged from 1967 to 1991. In comparison, the EPIC-Norfolk cohort enrolled participants between 1993 and 1997. Mortality rates for CHD have risen during the 20th century, reaching a peak in the 1970s and 1980s in the UK and Western Europe, but showing a decline since then. Factors affecting this reduction in cardiovascular mortality include both improved acute and chronic treatments of cardiovascular diseases, as well as improvements in primary and secondary prevention. For example, statin prescription was negligible before 1995, but has increased significantly since the publication of landmark statin trials. In the EPIC-Norfolk cohort, use of lipid-lowering therapy was negligible at baseline, but has likely increased substantially since then, although no exact data are currently available. These changes could contribute to the discrepancies between predicted risk based on the older SCORE cohorts and findings from our more recent cohort.

Overall, the discriminatory ability was high for both SCORE algorithms. Calibration was suboptimal for both, albeit superior using the low-risk algorithm. Both algorithms performed better in predicting non-coronary heart disease mortality as compared with coronary heart disease mortality. The overestimation of cardiovascular mortality was largely due to an overestimation of CHD mortality using both algorithms, potentially reflecting the changes in CHD mortality due to recent improvements in acute treatment as well as primary and secondary prevention during follow-up. Both algorithms performed better in predicting NCHD mortality, with only a slight overestimation using the high-risk algorithm and a slight underestimation using the low-risk algorithm.

Our findings are similar to those of van Dis et al., who showed that the SCORE high-risk algorithm over-estimates the risk of CVD mortality in a large Dutch population-based cohort. Parallel to the UK, the 2012 ESC guidelines have reclassified the Netherlands as a low-risk country. Conversely, de Bacquer and de Backer showed that the predicted risk of fatal CVD using a calibrated SCORE for Belgium does correspond with observed CVD mortality. However, the UK and the Netherlands were initially classified as high-risk countries, whereas Belgium was classified as a low-risk country. Our findings are consistent with those of Capewell and O’Flaherty, who have shown that several countries classified as high-risk in the 1980s and 1990s, including the UK and the Netherlands, now have similar CVD mortality rates compared with countries previously classified as low risk.

To our knowledge, there have been no publications validating SCORE in a large UK cohort other
than the original SCORE publication.² This may be related to the fact that the UK National Institute for Health and Clinical Excellence (NICE) guidelines recommend the Framingham risk equation in addition to the QRISK and ASSIGN algorithms. QRISK and ASSIGN include classic as well as non-traditional risk factors for cardiovascular disease, such as social deprivation and family history of premature coronary heart disease, and have been validated in a large UK primary care population.⁸⁻¹⁸ If SCORE were to become an accepted risk assessment tool in the UK, the low-risk algorithm is a suitable alternative.

Both SCORE algorithms are based on the same Weibull regression, but use different regression coefficients in high-risk and low-risk countries to calculate the 10-year risk of coronary and non-coronary cardiovascular disease for an individual’s age and age in 10 years’ time – reflected in the different values for \( a \) and \( p \) in the algorithms.² The coefficients for the other relevant risk factors (smoking, total cholesterol, systolic blood pressure) are identical in both algorithms, explaining why the ROC curves for both models are nearly identical when applied to the same individuals. However, our analysis shows that the absolute predicted risk is markedly higher when using the high-risk algorithm as compared with the low-risk algorithm.

The reclassification of the UK as a low-risk country could potentially influence the frequency of initiation of cardiovascular prevention. Using the SCORE low-risk algorithm to estimate cardiovascular mortality risk instead of the high-risk algorithm (as recommended by the 2012 ESC guidelines) resulted in 12.4% fewer study participants reaching this threshold. On a national level, considering that the UK population aged 30–59 years consisted of 24.8 million people in 2010, using the SCORE low-risk instead of the high-risk algorithm may lead to the initiation of cardiovascular prevention in three million fewer individuals. This might decrease short-term health-care spending in primary prevention. However, this could potentially adversely influence long-term risk in individuals with low baseline cardiovascular risk. Periodic re-evaluation is therefore recommended, as per current guidelines.

When interpreting the results of our study, several aspects need to be taken into account. First, while the EPIC-Norfolk cohort recorded detailed baseline information about demographic, anthropometric and lifestyle parameters as well as pharmacological therapy, there is only limited information available about changes in pharmacological therapy over time. The increase in the prescription of lipid-lowering drugs from 1995 onward could potentially be a factor contributing to the lower rate of observed CVD mortality in the EPIC-Norfolk cohort.¹⁹ Furthermore, cardiovascular prevention programmes focusing on risk factors not included in SCORE, particularly on lifestyle, could have had a similar impact. Second, the EPIC-Norfolk cohort is similar to a nationally representative sample for anthropometric variables, blood pressure and serum lipids.⁵,⁷ However, the population in the Norfolk area is healthier than the general UK population, with a standardized mortality ratio of 0.94 (source: Office for National Statistics). Potentially, this contributes to the overestimation of mortality by both algorithms in our study population. Third, we observed a slightly higher CVD mortality in individuals excluded from the main analysis due to missing SCORE variables as compared with our study population. This difference could potentially be explained by the slightly higher age and the slightly inferior risk factor profiles in the excluded individuals. However, we cannot exclude that the missing variables could have influenced this modest difference in CVD mortality. Fourth, while the ICD-10 codes of the outcome events in our study were largely identical to the ICD-9 codes included in the original SCORE project, there are a few differences. Most importantly, conductor disorders (426), cardiac dysrhythmias (427) and ill-defined descriptions and complications of heart disease (429) were not specifically coded in our study population. Potentially, this could have contributed to a low-
er number of outcome events in our study. Fifth, cholesterol levels were measured in a non-uniform fasting state. However, the original cohorts on which SCORE was based likewise included measurements collected during varying fasting states, and the 2012 ESC guidelines on cardiovascular prevention do not specify that cholesterol levels should be obtained in a fasting state. Furthermore, after correcting for non-fasting cholesterol levels in our sensitivity analysis, the differences in calculated risks were negligible.

CONCLUSION

The SCORE high-risk algorithm considerably overestimated the risk of 10-year CVD mortality in the EPIC-Norfolk population. The SCORE low-risk algorithm provided more accurate risk prediction of 10-year CVD mortality. Our findings support the recent reclassification of the UK as a low-risk country.

APPENDICES

Appendix 1: Predicted and observed CVD mortality according to SCORE algorithm by sex and age

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>SCORE High-risk</th>
<th>SCORE Low-risk</th>
<th>Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>39-49</td>
<td>1989</td>
<td>2811</td>
<td>1.68 (1.63-1.72)</td>
<td>0.82 (0.80-0.85)</td>
<td>14</td>
</tr>
<tr>
<td>50-54</td>
<td>1586</td>
<td>2126</td>
<td>3.19 (3.10-3.28)</td>
<td>1.61 (0.56-1.65)</td>
<td>22</td>
</tr>
<tr>
<td>55-59</td>
<td>1471</td>
<td>1216</td>
<td>5.62 (5.44-5.79)</td>
<td>2.91 (2.81-3.00)</td>
<td>30</td>
</tr>
<tr>
<td>60-65</td>
<td>1463</td>
<td>1824</td>
<td>8.77 (8.52-9.02)</td>
<td>4.66 (4.52-4.79)</td>
<td>60</td>
</tr>
<tr>
<td>39-49</td>
<td>1989</td>
<td>2811</td>
<td>0.35 (0.34-0.35)</td>
<td>0.20 (0.19-0.20)</td>
<td>3</td>
</tr>
<tr>
<td>50-54</td>
<td>1586</td>
<td>2126</td>
<td>0.91 (0.88-0.93)</td>
<td>0.53 (0.52-0.55)</td>
<td>8</td>
</tr>
<tr>
<td>55-59</td>
<td>1471</td>
<td>1216</td>
<td>1.94 (1.89-2.00)</td>
<td>1.16 (1.13-1.19)</td>
<td>15</td>
</tr>
<tr>
<td>60-65</td>
<td>1463</td>
<td>1824</td>
<td>3.91 (3.80-4.01)</td>
<td>2.37 (2.30-2.42)</td>
<td>35</td>
</tr>
</tbody>
</table>

Con: Kaplan Meier

Appendix 2: ROC of SCORE high-risk vs low-risk algorithm on predicting 10-year cardiovascular mortality
Appendix 3. ROC of SCORE high-risk with and without correction for non-fasting total cholesterol

Appendix 4. ROC of SCORE low-risk with and without correction for non-fasting total cholesterol
REFERENCES


