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Cardiovascular risk estimation in older persons: SCORE O.P.

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Abstract

Aims: Estimation of cardiovascular disease risk, using SCORE (Systematic COronary Risk Evaluation) is recommended by European guidelines on cardiovascular disease prevention. Risk estimation is inaccurate in older people. We hypothesized that this may be due to the assumption, inherent in current risk estimation systems, that risk factors function similarly in all age groups. We aimed to derive and validate a risk estimation function, SCORE O.P., solely from data from individuals aged 65 years and older.

Methods and results: 20,704 men and 20,121 women, aged 65 and over and without pre-existing coronary disease, from four representative, prospective studies of the general population were included. These were Italian, Belgian and Danish studies (from original SCORE dataset) and the CONOR (Cohort of Norway) study. The variables which remained statistically significant in Cox proportional hazards model and were included in the SCORE O.P. model were: age, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, smoking status and diabetes. SCORE O.P. showed good discrimination; area under receiver operator characteristic curve (AUROC) 0.74 (95% confidence interval: 0.73 to 0.75). Calibration was also reasonable, Hosmer–Lemeshow goodness of fit test: 17.16 (men), 22.70 (women). Compared with the original SCORE function extrapolated to the $\geq$65 years age group discrimination improved, $p = 0.05$ (men), $p < 0.001$ (women). Simple risk charts were constructed. On simulated external validation, performed using 10-fold cross validation, AUROC was 0.74 and predicted/observed ratio was 1.02.

Conclusion: SCORE O.P. provides improved accuracy in risk estimation in older people and may reduce excessive use of medication in this vulnerable population.

Keywords

Risk estimation, elderly, primary prevention, risk factors, cardiovascular disease

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Introduction

Over the last 50 years, the world's population has been aging. This global and progressive phenomenon has substantial societal implications, particularly with regard to the need for medical care. Between 1950 and 2000, the number of persons aged over 60 years tripled to 600 million worldwide and this number is expected to triple again in the next 50 years to two billion.[1] The rate of increase is currently fastest in the developed world, with the proportion of older individuals expected to rise from one-fifth in 2000 to one-third in 2050. Even in the developing world the proportion

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is expected to increase from 8% in 2000 to 20% in 2050.[1]

The rising proportion of older individuals will increase the burden of chronic disease considerably, signalling the need for increased attention to prevention of chronic disease in this population.

Cardiovascular diseases (CVDs) account for the majority of deaths in this age group and are also responsible for considerable morbidity and reduction in quality of life.[2] In addition to the substantial evidence indicating that most conventional risk factors continue to function in the older age group[3–6] there is now randomized controlled trial evidence demonstrating the benefit in terms of reduction in hard cardiovascular (CV) endpoints which results from treatment of risk factors, including blood pressure[7] and lipids[8] and observational evidence indicating the benefits of smoking cessation.[9,10] In the case of hypertension this applies not only to over 65 s,[11] but has recently been extended to the very old.[7] Therefore, CVD should be considered preventable even in this age group.

Guidelines on the prevention of CVD recommend the use of risk estimation systems so that preventive measures can be directed towards those at highest total CV risk, who will derive the greatest benefit.[12–15] To date, however, available risk estimation systems have been shown to be inaccurate in older people.[16–18]

Current risk estimation systems have used data from primarily younger age groups for the derivation dataset,[19–22] and have assumed that risk factor effects are constant regardless of age. However, although risk factors for CVD still function in the older age group, the strengths of the effects of the different risk factors change with age with some risk factors, such as physical activity, assuming greater importance and others, such as body mass index (BMI), less.[6] Therefore, we hypothesize that one of the reasons existing systems predict risk poorly in older people is because the beta coefficients (or relative risks) assigned to the risk factors have been derived from a younger population and it may be inappropriate to apply these to the older age group. Interactions between age and some of the other risk factors have been incorporated into QRISK2[19] and the NCEP ATP III version of Framingham,[15] but whether this improves risk estimation in older people has not been tested.

SCORE (Systematic COronary Risk Evaluation) is the risk estimation system recommended by the European guidelines on CVD prevention.[21] It was developed from 12 pooled cohort studies. Currently, it estimates risk 10 year risk of CVD mortality based on age, gender, total cholesterol (TC) or total cholesterol:high-density lipoprotein (HDL) cholesterol ratio, systolic blood pressure (SBP) and smoking status. However, at present the system is only recommended for use in persons aged between 40 and 65 years.[21]

Our objective in this analysis was to derive and validate a risk estimation function, similar to SCORE, for use in the 65 years and older age group. In line with the above hypothesis this will be derived using only longitudinal data collected in the older age group. Depending on the results it may be appropriate to incorporate this into the interactive version of SCORE, HeartScore, in the future.

Study populations

The original SCORE function was derived from a pooled dataset of 12 European cohort studies. This pooled dataset included over 205,000 individuals, representing 2.1 million person-years of observation.[21] Of these 12 studies, three had data available for individuals aged 65 years and over – Denmark, Italy and Belgium. The dataset used for the derivation of SCORE O.P. included the 6154 individuals aged 65 years and over from these three studies,[23–25] to which was added data from a large cohort of 40,825 individuals aged 65 years and over from the Cohort of Norway (CONOR) prospective study.[26]

Supplementary Material Table 1 online gives details of the population, recruitment and sampling, years of recruitment and number included for each of the individual studies in the dataset used for this analysis.

Methods

Detailed methods of the data collection methods, follow-up methods and case ascertainment for the individual studies have been published elsewhere.[23–26]

The endpoints were defined as in the original SCORE project with coronary heart disease (CHD) mortality defined as ICD9 codes 410–414 inclusive and non-CHD CVD mortality defined as 401–409, 426–443, 798.1 and 798.2 with the exception of the following definitely non-atherosclerotic causes of death: 426.7, 429.0, 430.0, 432.1, 437.3, 437.4 and 437.5. Corresponding ICD10 codes were used where cohort studies recorded using this system. Those with previous history of myocardial infarction were excluded as well as those with missing data on any of the required covariables. Individuals were not excluded on the basis of co-morbidities or medication usage.

The statistical methods for derivation of the function are given in the Supplementary Material online.

The performance of the function was tested in terms of discrimination including area under receiver operating characteristic curve and Harrell's C statistic, which is more reliable in the situation of variable follow-up. The calibration of the function was assessed in terms of

Table 1. Baseline characteristics and numbers included for each of the countries included in the analysis.

	Women					Men				
	Belgium	Denmark	Italy	Norway	All	Belgium	Denmark	Italy	Norway	All
Number	619	683	1680	17,139	20,121	770	653	1749	17,532	20,704
No. events CHD	30	53	26	733	842	40	67	65	982	1154
No. events non-CHD CVD	25	47	20	1019	1111	43	35	30	929	1037
Rate CHD (per 1000 person-years[a])	4.5	11.7	2.9	5.5	5.5	6.1	17.7	5.9	8.1	8.1
Rate non-CHD CVD (per 1000 person-years[a])	4.4	10.4	1.9	7.7	7.2	6.6	9.2	2.7	7.6	7.3
Median follow-up (years)	10.1	8.8	6.0	7.9	7.8	10.1	6.2	6.0	6.8	6.8
IQR follow-up (years)	10.1–10.1	2.4–9.7	5.0–7.0	5.51–10.3	5.3–10.2	7.4–10.1	2.4–9.2	5.0–7.0	5.3–8.9	5.2–9.1
Median age (years)	69.4	70.3	67.0	73.6	72.9	69.6	70.3	67.0	72.3	71.6
Age range (years)	65–75	69–80	65–99	65–99	65–99	65–75	69–80	65–93	65–101	65–101
% diabetes	6%	6%	6%	7%	7%	4%	7%	6%	7%	7%
% smokers	4%	34%	9%	16%	16%	49%	51%	32%	23%	26%
Mean TC (mmol/l)	7.0	6.9	6.2	6.8	6.7	6.2	6.1	5.7	6.1	6.0
Mean HDL (mmol/l)	1.5	1.6	1.4	1.6	1.5	1.3	1.3	1.3	1.4	1.3
Mean SBP (mmHg)	151	150	154	155	155	145	147	150	150	149

CHD: coronary heart disease; CVD: cardiovascular disease; IQR: interquartile range; TC: total cholesterol; HDL: high-density lipoprotein; SBP: systolic blood pressure [a]Percentage 10 year mortality risk.

predicted/observed ratios and Hosmer–Lemeshow goodness of fit testing.[27] Hosmer–Lemeshow testing was only possible for the five year function because complete follow-up to 10 years was not available for some of the cohorts. The sample option in the HL command of Stata was used to account for the fact that the same dataset was used for the derivation and validation of the function.

A simulated external validation of the 10 year function was performed using the 10-fold cross validation approach.[28,29] The dataset was divided into 10 groups using randomly generated numbers. The function was derived on 9 of these groups and validated on the remaining group. This approach was repeated 10 times, eliminating a different group each time the function was derived. We calculated AUROC and predicted/observed ratios as measures for assessing the discrimination and calibration of the function, respectively. We have presented the average of the 10 results as well as the individual 10 results. It was not possible to calculate the Harrell's C statistic, because in Stata this can only be performed as a post estimation command and is therefore it is only possible to calculate the Harrell's C statistic for the derivation dataset. However, AUROC is also an appropriate measure for assessing discrimination. Hosmer Lemeshow test has not been performed because we performed 10-fold cross validation on the 10 year function only.

Sensitivity analysis

To test the hypothesis that using the specific risk factors which were particularly important in the older age group and deriving the beta coefficients for these risk factors specifically from the older age group improves risk estimation, we compared the performance of the original SCORE function and SCORE O.P. The test dataset contained only those aged 65 years and over. Because the CONOR cohort was not included in the derivation cohort of the original SCORE function, the Norwegian data had to be excluded from the test dataset for this particular sensitivity analysis. Inclusion of the CONOR data in the test dataset would have resulted in an inequitable 'home advantage' for the SCORE O.P. function compared with the original SCORE function.

All statistical analyses were performed using Stata 9.

Results

The analysis included 20,121 women and 20,704 men. This was after the exclusion of those who had a previous history of myocardial infarction ($n = 4291$) and those with missing data on any of the included variables ($n = 1863$). Median follow-up was 7.8 years for women and 6.8 years for men. In men and women respectively 842 and 1154 fatal CHD events occurred during the follow-up period. The corresponding figures for the

non-CHD CVD mortality endpoint were 1111 and 1037. The proportion of the CVD mortality rate caused by CHD mortality in this older dataset was considerably less than the proportion in the SCORE dataset of under 65 year olds (same countries); 40% in older women compared with 59% in younger women and 52% in older men compared with 78% in younger men.

Baseline characteristics for the entire group and subdivided by cohort and gender are given in Table 1. The rates of CHD and non-CHD CVD mortality in each country are also shown in Table 1.

Results of the multivariable analysis

The following variables remained significant in the model for CHD mortality: TC, HDL cholesterol, diabetes, smoking status, SBP and age. For the non-CHD CVD mortality model the same variables were significant predictors, except for TC. BMI was not a significant predictor of either endpoint on multivariable analysis. The hazard ratios for each of the risk factors for each endpoint are shown in Table 2. The hazard ratios for each risk factor stratified by age group (65 to 75 years and 75 to 85 years) are shown in the Supplementary Table 2. The hazard ratios for the risk factor in the group, excluding those with diabetes, are shown in Supplementary Table 3.

SCORE O.P. function. Supplementary Table 4 shows the beta coefficients for each of the risk factors. It also shows the adjusted baseline survivals to 10 and five years for men and women for the CHD and non-CHD CVD mortality functions for the high and low risk functions. These figures can be used in conjunction with equation 1 (Supplementary Material) to allow calculation of the SCORE O.P. for an individual.

Examples of SCORE O.P. charts for men and women for use in low and high risk European regions are shown in Figure 1, for illustration purposes only. Because only five variables can be accommodated in the two-dimensional paper charts these charts assume a HDL of 1.2 in men and 1.4 in women and non-diabetic status. However, inclusion of the SCORE O.P. function in the interactive HeartScore system would enable incorporation of all variables.

Internal validation of the SCORE O.P. function. On internal validation the SCORE O.P. function demonstrated good discrimination, with an area under receiver operator characteristic curve (AUROC) of 0.74 (0.73

Table 2. Hazard ratios for each of the risk factors for each endpoint (all listed variables were included as covariables in the multivariable model).

	CHD mortality endpoint		Non-CHD CVD mortality endpoint	
Risk factors	Women	Men	Women	Men
SBP per 10 mmHg	1.07 (1.04 to 1.10)	1.08 (1.05 to 1.11)	1.08 (1.05 to 1.10)	1.07 (1.04 to 1.10)
TC per 1 mmol/l	1.13 (1.07 to 1.19)	1.23 (1.17 to 1.30)		
HDL per 0.5 mmol/l	0.76 (0.69 to 0.82)	0.81 (0.75 to 0.88)	0.93 (0.86 to 1.00)	0.87 (0.80 to 0.94)
Smoking	1.88 (1.56 to 2.26)	1.79 (1.58 to 2.03)	1.53 (1.29 to 1.83)	1.76 (1.54 to 2.01)
Diabetes	2.30 (1.89 to 2.79)	1.84 (1.53 to 2.21)	1.92 (1.61 to 2.31)	1.61 (1.31 to 1.98)
Age per one year	1.16 (1.15 to 1.17)	1.13 (1.11 to 1.14)	1.18 (1.16 to 1.19)	1.15 (1.14 to 1.16)

CHD: coronary heart disease; CVD: cardiovascular disease; SBP: systolic blood pressure; TC: total cholesterol; HDL: high-density lipoprotein cholesterol

Table 3. Internal validation results (discrimination and calibration) for SCORE O.P. non-coronary cardiovascular mortality.

	Women	Men	All
AUROC	0.78 (0.76 to 0.79)	0.70 (0.69 to 0.71)	0.74 (0.73 to 0.75)
Harell's C statistic – CHD	0.761	0.693	0.732
Harell's C statistic – non-CHD CVD	0.770	0.706	0.739
Hosmer–Lemeshow (p value) Five year function	22.70 (0.0038)	17.16 (0.0285)	24.33 (0.0020)
Predicted/observed ratio	1.03	1.05	1.04

AUROC: area under receiver operator characteristic curve; CHD: coronary heart disease; CVD: cardiovascular disease

Table 4. Performance of SCORE O.P. compared with the original SCORE function in those aged 65 years and over.

	AUROC		Hosmer–Lemeshow (*p* value)	
	Men	Women	Men	Women
SCORE O.P. function	0.7036	0.7919	15.26 (0.0543)	9.98 (0.2664)
Original SCORE function	0.6849	0.7436	20.96 (0.0073)	16.64 (0.0340)
p for difference	0.05	<0.001	–	–

AUROC: area under receiver operating characteristic curve

to 0.75) in the overall group. The AUROC and Harell's C statistics for the function SCORE O.P. are shown in Table 3. The summary calibration results – Hosmer Lemeshow tests and predicted/observed ratios are also shown in Table 3. The function resulted in a minor overestimation of risk overall.

Internal validation – sensitivity analysis. Table 4 shows the AUROC and Hosmer–Lemeshow goodness of fit testing (five-year function) for both SCORE O.P. and the original SCORE function in the 65 years and over age group. As mentioned above only the countries (Italy, Belgium, Denmark) included in both the original SCORE derivation dataset and the SCORE O.P.

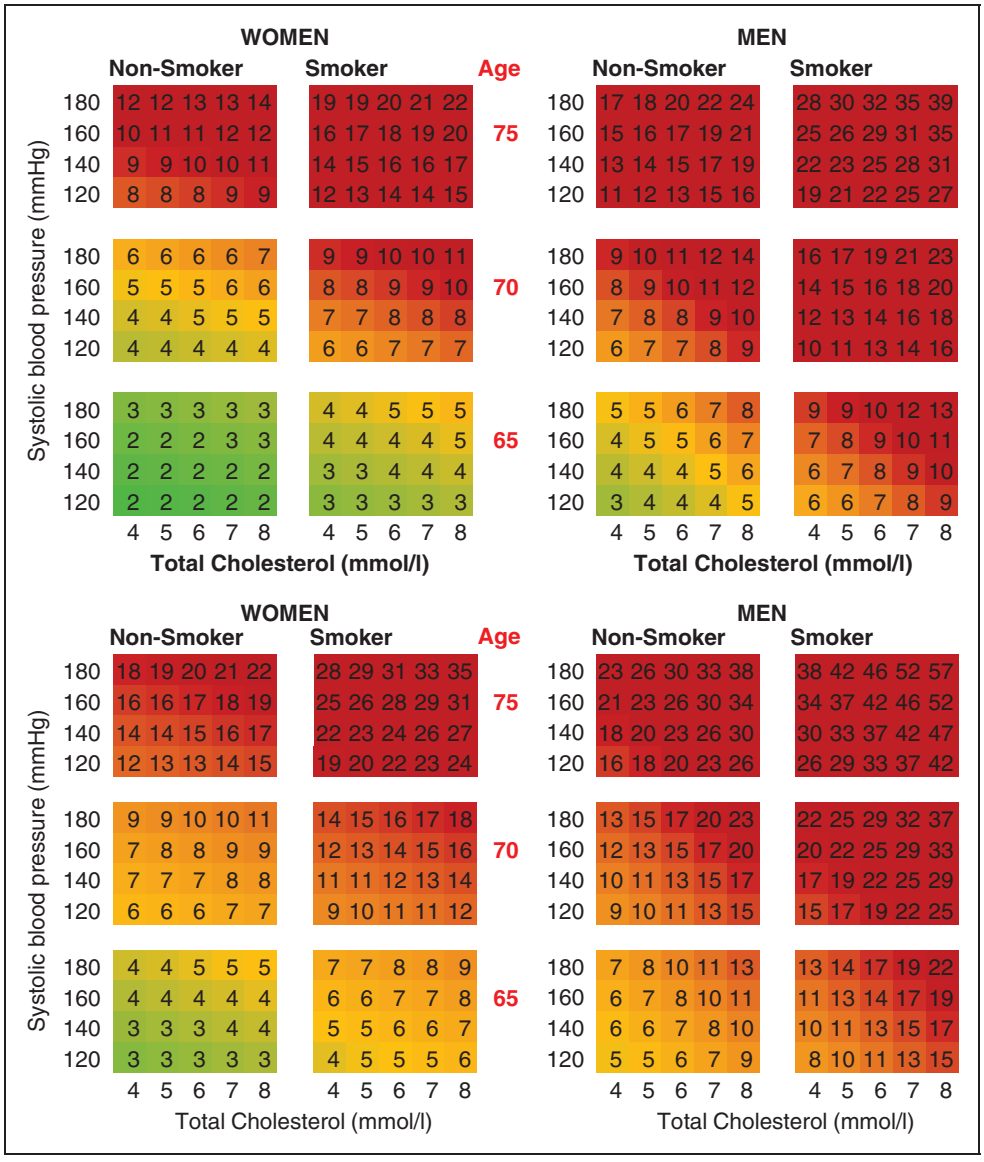

Figure 1. SCORE O.P. charts for use in low (upper) and high (lower) risk regions. Assumes high-density lipoprotein 1.2 mmol/l for men, 1.4 mmol/l for women, and non-diabetic status. Numbers indicate estimated % 10 year cardiovascular mortality risk.

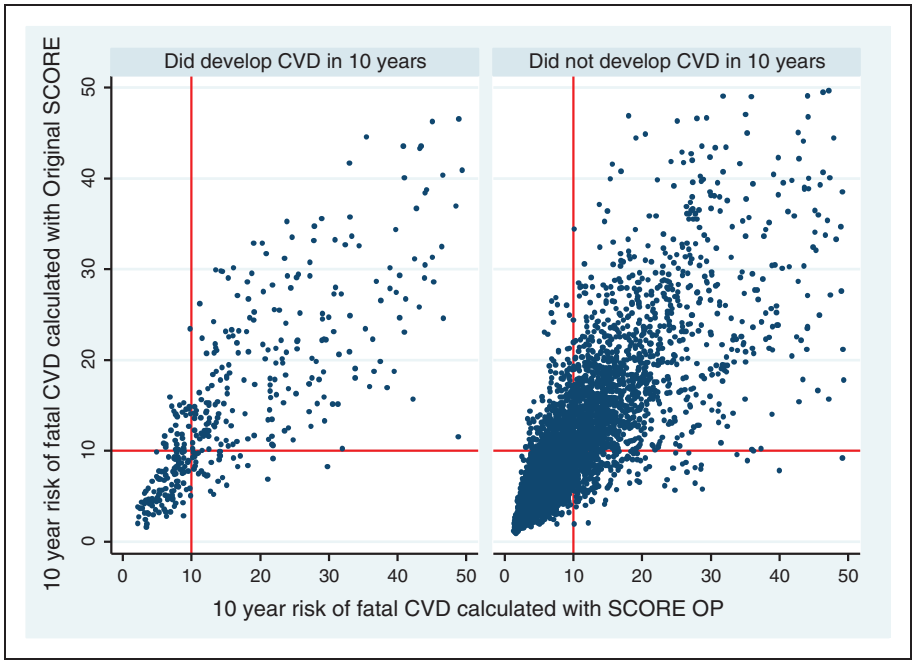

Figure 2. SCORE O.P. and original SCORE in each individual in the test dataset.
CVD: cardiovascular disease

dataset were included in this test dataset. This ensured that both functions were internally validated on a dataset which was included in the derivation cohort for the function. As shown in the AUROC figures, discrimination was significantly better in the SCORE O.P. function. Calibration was also marginally improved.

Figure 2 shows a scatterplot of SCORE O.P. values plotted against original SCORE values, separately in those who did and did not develop CVD over the 10 years. Taking 10% risk as an arbitrary threshold for high risk, 524 of 5673 individuals who did not develop CVD were reclassified downwards, compared with only 288 reclassified upwards. For those who did develop CVD, the same number were reclassified upwards as downwards. This indicates that SCORE O.P. results in fewer false positives without any increase in false negatives.

Simulated external validation – 10-fold cross validation

The results of the discrimination and calibration on 10-fold cross validation were similar to those of the main function. The overall AUROC was 0.74. Table 5 details the AUROC and observed/predicted ratios for the entire group and stratified by gender. Supplementary Tables 5 and 6 detail the AUROC and predicted/observed ratios for each individual group.

Table 5. Ten-fold cross validation results (discrimination and calibration) for SCORE O.P.

	Women	Men	All
AUROC	0.78	0.70	0.74
Average 10 year CVD mortality risk (predicted)	12.755	15.741	14.269
Average 10 year rate of CVD mortality (observed)	12.742	15.349	13.996
Predicted/observed ratio	1.001	1.026	1.020

AUROC: area under receiver operating characteristic curve; CVD: cardiovascular disease

Discussion

We have demonstrated that several conventional risk factors continue to predict CVD in the older age group and that total CVD risk can be accurately estimated in this age group. The main difference between our function and that of other risk estimation functions is that the selection of risk factors to be included and the beta coefficients or relative risk weightings assigned to each of the risk factors have been based on analyses restricted to the older age group. This is the first risk estimation system for use specifically in older men and women that has been derived from the age group to which it is to be applied. Although the ability to predict occurrence of future events in this group has been

studied previously, no study has published a risk estimation system which can be used to calculate risks in this age group in clinical practice.[17,18,30] The system functions well, including on simulated external validation.

Our sensitivity analysis suggests that this change in methods may result in more accurate risk estimation in this age group. However, this requires confirmation by testing in an external dataset. In particular the new system results in fewer false positives – older individuals who are designated as high risk, but who will not develop disease. This is not accompanied by an increase in false negatives. This has substantial implications in terms of reducing the over treatment of older individuals.

Comparison with other studies

Previous assessments of the Framingham and other risk estimation functions in the older age group have been limited, but in general have shown poor discrimination in this age group. For example, the AUROC for Framingham in the Leiden plus cohort was 0.53 (95% confidence interval: 0.43 to 0.64).[17] Another study from the Netherlands in individuals aged over 70 years showed similarly poor discrimination with AUROCs of 0.55 and 0.60 for the PROCAM and Framingham functions respectively for the prediction of CVD mortality.[16] It is important to remember that these are external validations and our discrimination figures are based on an internal validation. However, even risk functions derived from the same data they were tested in did not perform well in this age group.[17,18] Risk scores containing conventional risk factors showed poor discrimination when validated in the data from which they were derived, with AUROCs of 0.53 and 0.69, for studies conducted in the Netherlands[17] and Sweden,[18] respectively. Interestingly, in the Swedish study the addition of biomarkers to the model significantly improved accuracy of risk estimation.[18] The value of incorporating additional biomarkers has been less consistent in other studies.[31]

To date, risk functions which have been derived solely from the older age group are very limited. One exception is an analysis of prediction of CVD in the elderly in the Uppsala Longitudinal Study of Adult Men.[18] Their risk function containing conventional risk factors resulted in an AUROC of 0.688 in men aged over 65 years on internal validation. However, this function is only applicable to older men and the authors have not provided a means of using this function to estimate risk in older people in clinical practice.

Regarding the effect of risk factors in different age groups, the prospective studies collaboration has also examined the effect of systolic blood pressure and cholesterol levels on vascular mortality in different age bands.[32,33] The results cannot be directly compared with our results due to substantial differences in methods, particularly their lack of adjustment for other risk factors. The relationship across age bands was similar with successive decreases in relative risk associated with the risk factors with increasing age.[32,33] Their hazard ratios for a 20 mmHg lower SBP were 0.60 in men and 0.55 in women for the CHD mortality endpoint (70–79 year age band).[32] Using similar methods in our population the hazard ratios were 0.76 for men and 0.74 for women. Their hazard ratios for a 1 mmol/l lower TC were 0.80 in men and 0.86 in women for the CHD endpoint (70–79 year age band).[33] Using similar methods in our population the hazard ratios were 0.85 in men and 0.94 in women. Their higher relative risks may be related to their use of 'usual' risk factor levels in the Prospective Studies Collaboration, which was possible due to the availability of repeated measurements. We examined the hazard ratios associated with risk factors in older and younger participants in our dataset and demonstrated a reduction in the effect of conventional risk factors in the older subgroup (apart from HDL cholesterol as we have noted previously[34]), which would be consistent with the results from the Prospective Studies Collaboration.[32,33]

Comparing SCORE O.P. with the original SCORE function and Framingham. The original SCORE function provided risk estimation up to the age of 65 years. SCORE O.P. has been developed to estimate risk up to the age of 80. At the 65 year age band the two charts overlap and the risk estimates can be compared – see Figure 3. Comparing the two charts, the risk estimates appear to be much lower using SCORE O.P. However, the baseline risk is very similar in both charts. For example, using SCORE O.P. a 65 year old woman with TC 4.0 mmol/l and SBP 120 mmHg and non-smoking has a 2.7% 10-year risk of fatal CVD; the risk estimate using SCORE for the same individual is 2.0%. For men the corresponding figures are 4.8% and 4.4% respectively. When one takes into consideration that the SCORE O.P. charts assume beneficial levels of two other risk factors, which are not included in original SCORE (mean HDL cholesterols and non-diabetic status), it is apparent that the risk estimate at low levels of risk factors is actually higher in SCORE O.P. The reason for this is that the low levels of risk factors are having less of a protective effect in SCORE O.P, mainly because the risk factors in general are associated with a lower relative risk in the older age group.

The reason that the SCORE O.P. charts produce lower risk estimates compared with the SCORE charts in older people is because when risk factors are present the added risk (in addition to the baseline risk)

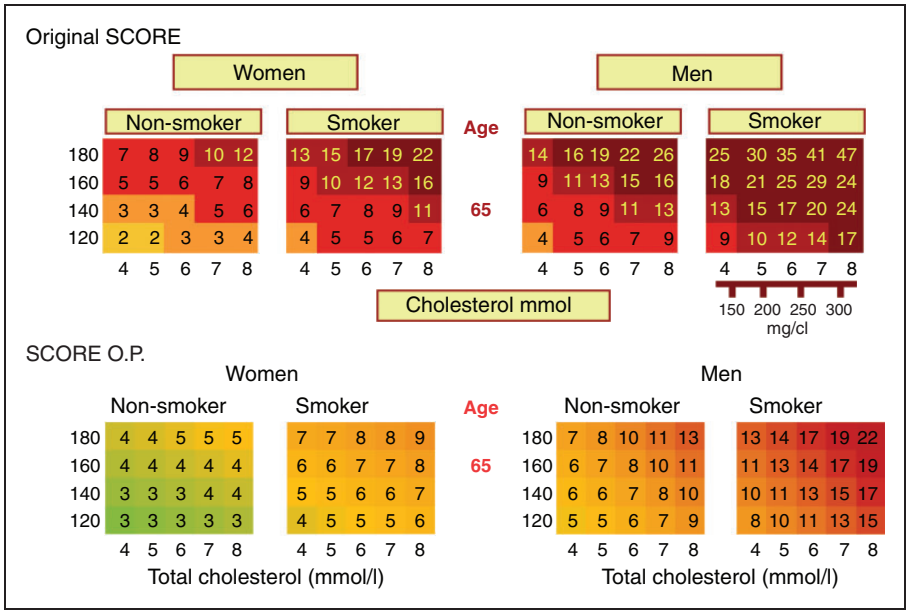

Figure 3. Comparing SCORE O.P. and original SCORE (for high risk regions) at the 65 years age band.

due to these is less in SCORE O.P. compared with SCORE. In general, when comparing two risk charts one intuitively tends to look at the top right hand box. This is probably a particularly ineffective method, given the very small number of individuals who would actually have this combination of risks (male smoker with TC 8 mmol/l and SBP 180 mmHg). When looking at the risk estimate for this combination of risk factors the difference between SCORE O.P. and SCORE is marked (47% *vs.* 22% respectively). This is because the SCORE chart over-estimates the risk associated with risk factors in the older age group because the beta coefficients for the risk factors have not been calculated using data from older persons but the entire group, which contains primarily middle aged individuals. This difference between relative risks associated with risk factors has been demonstrated in our analysis as well as in other studies.[6,33] Comparison with Framingham is discussed in the Supplementary Material.

Other approaches to improving risk estimation in older people

Some studies have shown an improvement in risk estimation in older people when biomarkers and markers of sub-clinical disease are added to risk estimation.[16,18] However, the addition only resulted in a maximum AUROC of 0.74, similar to that of the present study. We believe that the measurement of these biomarkers may both complicate and reduce the cost effectiveness of risk estimation. On this basis, our approach to improving risk estimation in the older age group may be preferable. Additionally, we have no evidence that altering these newer risk factors results in reductions in CVD risk.

Another approach to risk estimation in the elderly is the inclusion of interactions between age and several other risk factors, as in the second version of QRISK[19] and the NCEP ATP III version of the Framingham function.[15] This allows for some of the difference in effect of risk factors at different ages and may result in superior risk estimation in older age groups; however, this issue has not been examined to date.

Implications for the prevention of CVD in older people in clinical practice

The recent demonstrations in randomized controlled trials of the morbidity and mortality benefits of preventive measures in older individuals, even in the very old,[7] have substantial implications for the prevention of CVD in this age group. Guidelines on prevention of CVD in clinical practice recommend the use of risk estimation systems so that preventive measures can be targeted towards those at highest risk.[13–15,35] Therefore, it is clearly important to have a system which estimates risk accurately in this age group.[36] We believe this work adds to currently available evidence in this area. The reduction in overestimation of risk and therefore overtreatment is equally important, especially when pharmacotherapy is associated with increased adverse effects in older people.

This analysis raises some questions about the primary prevention of CVD in the elderly. If the use of

preventive measures is based on total CV risk then using the conventional threshold for high risk (>5% 10 year risk of CVD mortality), the majority would require intensive risk factor modification and this may result in over-medication of older persons.[37] The most appropriate threshold for high risk would depend on the risk/benefit ratio and the resources available. We suggest that this could be investigated by re-analysing the results of randomized controlled trials of preventive measures and calculating the number needed to treat for each preventive measure in each risk category. Our newly derived function presents an opportunity for this risk stratification.

Limitations and further work

We were limited in that we did not have an additional dataset in which to perform an external validation. However, the high agreement of the results when simulated external validation was performed gives reassurance about the reliability of the function. The next important aspect of this project is to test SCORE OP in an external dataset and additionally compare with the Framingham function[38] and also to the original SCORE function,[21] extrapolated to the older age group. This will enable further testing of the hypothesis that derivation of the function specifically from the older age group results in improved risk estimation in older persons.

There may be some inaccuracy in the causes of death in this analysis due to the reliance on death certificate information, which has been shown to be less accurate in the older age group.

A function containing the option of including whether the individual is on anti-hypertensives would be useful. Unfortunately, all of the cohorts used here did not have this information and therefore it has not been possible to include it in SCORE O.P. The incorporation of use of anti-hypertensives as an extra variable in the function was analysed in a sensitivity analysis, using the Norwegian data only. The use of anti-hypertensives was based on self-report at baseline in the Norwegian data. Full details are given in the Supplementary Material. In brief, it showed that inclusion of anti-hypertensive medication as an extra variable results in only minor changes in risk estimations and accuracy of the function. Use of anti-hypertensives and statins to prevent cardiovascular disease have increased considerably over the last 20 years in Norway.[39] It was not possible to adjust for initiation of use of statins or antihypertensives during follow-up in the present study. This may have led to an underestimation of risk associated with hypertension and high cholesterol.

The risk of dying from other causes will influence the absolute risk of dying from CVD. Competing risk is more important as age increases, and is not accounted for in any of the current risk systems. This may have led to overestimation of the CVD risk.

Some consider the use of CVD mortality as opposed to combined CVD non-fatal and fatal events to be a limitation. This was preferred as the endpoint in SCORE because of the difficulties associated with standardization of the definitions of the non-fatal CVD events, especially when dealing with several different cohort studies. The subject is fully discussed in the work of Catherine McGorrian on the SCOREplus project (unpublished work, McGorrian 2010). Additionally, the use of CVD mortality facilitates the process of recalibration of functions to allow for time trends and geographical variations, through the use of the widely available and reliable World Health Organization statistics on cause of death.

Conclusions

This is the first risk estimation system which has been developed specifically for the estimation of risk in older men and women and as such adds to the current evidence in this area. We have shown higher discrimination compared with previous systems with an AUROC of 0.74. This high discriminatory value held on simulated external validation. Importantly, the new function resulted in a decrease in false positives, which could lead to a reduction in over-treatment.

Instead of extrapolating the effect of risk factors from younger to older individuals as in previous systems, SCORE O.P. has been specifically derived from data from older individuals. We believe this methodology may account for our results. The next step will be to extend the validation process by using an external data set.

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Conflict of interest

The authors declare that there is no conflict of interest.

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