Estimated 10-year cardiovascular mortality seriously underestimates overall cardiovascular risk

Harald T Jørstad, 1 Ersen B Colkesen, 1 S Matthijs Boekholdt, 1 Jan G Tijsse, 1 Nicholas J Wareham, 2 Kay-Tee Khaw, 3 Ron J Peters 1

ABSTRACT

Objective The European Society of Cardiology’s prevention guideline suggests that the ratio of total (fatal plus non-fatal) cardiovascular disease (CVD) may be calculated from the ratio of CVD mortality using a fixed multiplier (3 × ). However, the proposed multiplier has not been validated. We investigated the ratio of total CVD to CVD mortality in a large population-based cohort.

Methods CVD mortality and total CVD (fatal plus non-fatal CVD requiring hospitalisation) were analysed using Kaplan-Meier estimates among 24 014 men and women aged 39–79 years without baseline CVD or diabetes mellitus in the prospective population-based European Prospective Investigation of Cancer and Nutrition-Norfolk cohort. CVD outcomes included death and hospitalisations for ischaemic heart disease, heart failure, cerebrovascular disease, peripheral artery disease or aortic aneurysm. The main study outcome was the ratio of 10-year total CVD to 10-year CVD mortality stratified by age and sex.

Results Ten year CVD mortality was 3.9% (900 CVD deaths, 95% CI 3.6% to 4.1%); the rate of total CVD outcomes was 21.2% (4978 fatal or non-fatal CVD outcomes, 95% CI 20.7% to 21.8%). The overall ratio of total CVD to CVD mortality was 5.4. However, we found major differences in this ratio when stratified by gender and age. In young women (39–50 years), the ratio of total CVD to CVD mortality was 28.5, in young men (39–50 years) 11.7. In the oldest age group, these ratios were considerably lower (3.2 in women and 2.4 in men aged 75–79 years).

Conclusions The relationship between 10-year total CVD and CVD mortality is dependent on age and sex, and cannot be estimated using a fixed multiplier. Using CVD mortality to estimate total CVD risk leads to serious underestimation of risk, particularly in younger age groups, and particularly in women.

INTRODUCTION

The most recent ESC guidelines on cardiovascular disease (CVD) prevention suggest that there is a fixed relationship between CVD mortality and the total burden of CVD events, defined as the composite of fatal and non-fatal CVD. 1 2 It is suggested that in high-risk individuals with a 10-year CVD mortality risk of ≥5%, as estimated using Systematic COronary Risk Evaluation (SCORE), total CVD is threefold higher, and possibly more in young men, and less in women and in older individuals. 1 2 This has led to the suggestion of using a fixed multiplier (3 × ) for calculating total CVD based on CVD mortality only. From a patient’s perspective, total CVD risk is the most relevant parameter for initiating CVD prevention, 4 and using CVD mortality only can result in underestimation of the total CVD burden. 5 Although mortality is a more robust clinical outcome, cardiovascular morbidity is equally relevant to providers of healthcare, policy makers and insurance companies. Currently, the relationship between total CVD and CVD mortality in the general population is unclear, and the proposed multiplier for conversion from CVD mortality to total CVD has not been validated.

We hypothesised that the ratio of total CVD (fatal and non-fatal events) and CVD mortality is dependent on age and sex. We tested this hypothesis in the European Prospective Investigation of Cancer and Nutrition-Norfolk (EPIC-Norfolk), a large prospective population-based cohort, with detailed information on various chronic diseases, including CVD mortality and morbidity.

METHODS

Source population

We used data from the EPIC-Norfolk prospective population study, a cohort of 25 639 men and women aged 39–79 years residing in the county of Norfolk, UK. Details of the study have been described elsewhere. 6 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. Participants were also asked whether a doctor had ever told them that they had any of the following conditions: diabetes mellitus, myocardial infarction or stroke. Anthropometric and blood pressure measurements were performed and non-fasting blood samples were collected at the health assessment. The EPIC-Norfolk cohort was similar to a nationally representative sample for anthropometric indices, blood pressure measurements and serum lipid levels, but with a lower proportion of smokers. 6 The participants’ National Health Service number was used to determine their hospital stay through the East Norfolk Health Authority database, which records all hospital contacts throughout England and Wales for Norfolk residents. Vital status for all EPIC-Norfolk participants was obtained through death certification at the Office for National Statistics. The underlying
Strapping with 1000 iterations with the same sample size as the original sample. SCORE was calculated using the algorithm for low-risk countries in individuals younger than 65 years, using age at baseline, sex, smoking status, total cholesterol and systolic blood pressure. SCORE was only calculated in individuals with a complete data set of the abovementioned variables. Statistical analyses were performed in SPSS V.21 and STATAV.12.

RESULTS
A total of 25 639 individuals attended the baseline visit. Of these participants, 1625 had diabetes mellitus or a history of vascular disease. The study population consisted of 24 014 men and women without prevalent CVD or diabetes mellitus. Table 1 shows baseline characteristics of the study participants. In total, 56.2% of the study participants were women. Mean age was 58.8 (SD 9.3) years, and 11.8% were current smokers. Mean values for body mass index, total cholesterol and low-density lipoprotein (LDL) cholesterol were slightly above levels recommended in primary prevention setting, respectively, at 26.3 kg/m² (SD 3.9) and 6.2 mmol/L (SD 1.2) and 4.0 mmol/L (SD 1.1). There were no clinically relevant differences in CVD risk factors between men and women.

Figure 1 shows the 10-year KM curves for cardiovascular mortality and morbidity. A total of 4978 study participants died of or were hospitalised for CVD, yielding a 10-year cumulative event rate for total CVD of 21.2% (95% CI 20.7% to 21.8%). A total of 900 study participants died of a CVD event or, yielding a 10-year CVD mortality rate of 3.9% (95% CI 3.6% to 4.1%). The overall ratio of total CVD/CVD mortality was 5.4.

Of the 4978 study participants with a CVD or event, 360 individuals had a fatal event as first event (7.2% of total CVD); when 30-day CVD mortality was included this number was 643 (12.9% of total CVD). Of the 4618 non-fatal CVD events/hospitalisations, the majority was ischaemic heart disease (45.6%) followed by peripheral arterial disease (19.7%) and congestive heart failure (16.9%). Only 2.9% of the non-fatal events/hospitalisations were caused by an aortic aneurysm (table 2).

Table 3 presents 10-year CVD mortality and total CVD by age and sex. In men, the KM estimate for total CVD was 24.9%, for CVD mortality this was 5.4%, yielding an overall ratio of 4.6. In women, total CVD was 18.4%, CVD mortality 2.7%, with an overall ratio of 6.8. Among 2219 men aged 39–50 years, the KM estimate for total CVD was 8.2% and for CVD mortality 0.7%, resulting in a ratio of 11.7. Among 3061
women aged 39–50 years, total CVD was 5.7% and CVD mortality 0.2%, resulting in a ratio of 28.5. Event rates increased with age. Among 328 men aged 75–79 years, total CVD was 56.3% and CVD mortality 24.9%, amounting to a ratio of 2.4. Among 366 women aged 75–79 years, total CVD was 47.3% and CVD mortality 14.6%, resulting in a ratio of 3.2. Neither the ratio of nor the difference between total CVD and CVD mortality was constant across categories of age in either sex (table 3, right panels; figure 2). Overall, the total CVD/CVD mortality ratios were inversely related to age, and with greater variation among women as compared with men (figure 2).

SCORE was calculated in 15 171 individuals up to 65 years of age as shown in table 4. Mean predicted CVD mortality according to SCORE was 1.55% (95% CI 1.52% to 1.58%); in men 2.35% (95% CI 2.29% to 2.40%) and in women 0.95% (95% CI 0.92% to 0.97%). In individuals with ≥5% SCORE, 10-year CVD mortality was 7.3%, whereas 10-year total CVD was 41.2%, yielding a ratio of 5.6. In men with a SCORE ≥5%, this ratio was 5.4, in women 9.4. In individuals with a SCORE <5%, these ratios varied considerably: 12.5 in the total population, in men 10.4, in women 15.9.

Total CVD/CVD mortality ratios as assessed using bootstrap resampling were comparable across the total population and the subset wherein SCORE was calculated. Only in the youngest age group, in women more than men, these ratios were higher when calculated using bootstrap resampling (women aged 39–50 years KM-ratio 28.5 vs bootstrap ratio 36.06 [95% CI 35.28 to 36.88], men aged 39–50 years KM-ratio 11.7 vs bootstrap ratio 12.21 [95% CI 12.07 to 12.36]), most likely related to the low number of mortality events in these subgroups.

**DISCUSSION**

Our analysis demonstrates a complex relationship between 10-year total CVD and CVD mortality in the EPIC-Norfolk prospective population study, a large European cohort. Men and women showed a decreasing CVD morbidity/mortality ratio with increasing age, and with a greater ratio for women in all age groups. Thus, our results suggest that the ratios of total CVD/CVD mortality are age-dependent and sex-dependent. Furthermore, only 12.9% of first CVD events were fatal. By focusing on CVD mortality only, the overall burden of CVD is seriously underestimated, leaving large numbers of individuals untreated, despite the fact that their risk of CVD events is substantial.

The ESC prevention guidelines use the 10-year cardiovascular mortality risk predictor SCORE as a decision-making tool in primary prevention. Using SCORE risk charts, clinicians can identify individuals with a high risk (≥5%) of 10-year CVD mortality. Based on data from the FINRISK study, it is suggested that at the level at which risk management is recommended (5% risk of 10-year cardiovascular mortality), total event risk, that is, including morbidity, is about three times higher (15%). The guideline suggests this ratio may be used as a multiplier in calculating total CVD risk based on estimated CVD mortality.1–3 In our study, the total CVD/CVD mortality ratio in individuals with a SCORE ≥5% was markedly higher (5.6) than the suggested multiplier (3), more so in women (9.4) as compared with men (5.4). Noteworthy is that only 77 women up to 65 years of age had a SCORE≥5%. Also when not stratified by SCORE, these ratios were overall higher (total population 5.4, in men 4.6, in women 6.8). The ratio was especially high (28.5 in women, 11.7 in men) in the lower age subgroups (39–50 years), and decreased with age. While risk scores such as SCORE identify individuals at high risk of CVD mortality, our findings show that risk of CVD mortality cannot be readily extrapolated to risk of total CVD using a fixed multiplier. A high risk of CVD mortality suggests a high risk of total CVD, regardless of age and sex, with all inherent implications for primary prevention. However, our study shows that a low risk of CVD mortality does not translate into a proportionally low risk of CVD morbidity, particularly in young individuals, and in women more than men. This discrepancy should be taken into account in the clinical decision-making process regarding preventive measures in young patients.

The majority of first non-fatal events or hospitalisations were caused by ischaemic CVD (in total 77.6%) including ischaemic heart disease, ischaemic cerebrovascular disease and peripheral arterial disease). As healthy lifestyles and preventive medication have been shown to significantly reduce the risk for such events, this underlines the need for preventive measures in these individuals. Although CVD mortality is clearly the most robust clinical outcome, cardiovascular morbidity is likely to be at least as substantial.
Cardiac risk factors and prevention

Figure 2  Ratios of 10-year cumulative total CVD to CVD mortality by sex and age groups. CVD, cardiovascular disease.

Table 3  Cumulative 10-year CVD mortality and total CVD by sex and age

<table>
<thead>
<tr>
<th>Age group</th>
<th>10-year CVD mortality</th>
<th>10-year total CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n KM rate 95% CI</td>
<td>n KM rate 95% CI</td>
</tr>
<tr>
<td></td>
<td>KM difference KM ratio BSP ratio 95% CI of BSP ratio</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>39–50</td>
<td>2219 15 0.7 (0.4 to 1.1)</td>
<td>181 8.2 (7.2 to 9.5)</td>
</tr>
<tr>
<td>50–55</td>
<td>1780 26 1.5 (1.0 to 2.2)</td>
<td>260 14.8 (13.2 to 16.5)</td>
</tr>
<tr>
<td>55–60</td>
<td>1637 34 2.1 (1.5 to 3.0)</td>
<td>320 19.9 (18.6 to 22.0)</td>
</tr>
<tr>
<td>60–65</td>
<td>1632 67 4.2 (3.4 to 5.4)</td>
<td>462 29.0 (26.8 to 31.3)</td>
</tr>
<tr>
<td>65–70</td>
<td>1622 127 8.3 (7.0 to 9.8)</td>
<td>565 36.5 (34.2 to 39.0)</td>
</tr>
<tr>
<td>70–75</td>
<td>1290 209 17.7 (15.6 to 20.0)</td>
<td>586 48.8 (46.0 to 51.7)</td>
</tr>
<tr>
<td>75–79</td>
<td>328 65 23.3 (18.7 to 28.8)</td>
<td>167 56.3 (50.6 to 62.1)</td>
</tr>
<tr>
<td>Total</td>
<td>10 509 543 5.4 (4.9 to 5.8)</td>
<td>2541 24.9 (24.1 to 25.7)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>39–50</td>
<td>3061 5 0.2 (0.07 to 0.4)</td>
<td>173 5.7 (4.9 to 6.6)</td>
</tr>
<tr>
<td>50–55</td>
<td>2333 11 0.5 (0.3 to 0.9)</td>
<td>225 9.8 (8.6 to 11.1)</td>
</tr>
<tr>
<td>55–60</td>
<td>2129 17 0.8 (0.5 to 1.3)</td>
<td>299 14.2 (12.8 to 15.8)</td>
</tr>
<tr>
<td>60–65</td>
<td>2014 43 2.2 (1.6 to 2.9)</td>
<td>395 20.1 (18.4 to 21.9)</td>
</tr>
<tr>
<td>65–70</td>
<td>1995 86 4.5 (3.6 to 5.5)</td>
<td>556 28.8 (26.8 to 30.9)</td>
</tr>
<tr>
<td>70–75</td>
<td>1607 145 9.5 (8.2 to 11.1)</td>
<td>624 40.7 (38.3 to 43.2)</td>
</tr>
<tr>
<td>75–79</td>
<td>366 50 14.6 (11.3 to 18.8)</td>
<td>165 47.3 (42.2 to 52.7)</td>
</tr>
<tr>
<td>Total</td>
<td>13 505 357 27 (2.4 to 3.0)</td>
<td>2437 18.4 (17.8 to 19.1)</td>
</tr>
</tbody>
</table>

CVD mortality is death from a CVD. Total CVD is all fatal and non-fatal CVD or events requiring hospitalisation. Cumulative total CVD and CVD mortality rates were calculated using the KM method. KM difference is difference of total CVD and CVD mortality of the KM estimates. KM ratio is the ratio of total CVD to CVD mortality of the KM estimates. BSP ratio is the ratio of total CVD to CVD mortality of the bootstrap procedure estimates. BSP, bootstrap procedure; CVD, cardiovascular disease; KM, Kaplan-Meier.

relevant to patients, providers of healthcare, policy makers and insurance companies. Currently, 10% of the global disease burden is attributed to CVD, with CVD being responsible for 151.377 million disability-adjusted life years. CVD mortality alone contributed to 17.3 million deaths in 2008, representing 30% of all global deaths, with a projected number of deaths of almost 23.6 million in 2030. The burden of total CVD is likely to show a similar or even greater increase, as CVD mortality has declined relative to CVD morbidity in recent decades. This relative decline in mortality can be attributed to improved acute and chronic CVD treatments, as well as improvements in primary and secondary prevention. Considering the individual, economic and societal implications of CVD morbidity, guidelines could be significantly improved by including morbidity in the estimation of risk.

Different fatal/non-fatal ratios have been published in previous studies, for which several explanations may be found. Similar to our results, van Dis et al showed that the ratio of total CVD to CVD mortality was 4.0 in men and 5.2 in women in a large Dutch population. However, they did not present ratios across different age groups. In a number of primary prevention trials in selected populations, the ratios of total CVD to CVD mortality varied between 3.2 and 4.5 for the overall population. In comparison to our study, these trials were conducted in a predominantly male study population, and did not report numbers of events in sex and age subgroups.

In the landmark trials of aspirin use in primary prevention of coronary heart disease, this ratio was 3.7 (fatal CVD vs non-fatal myocardial infarction and stroke) in the US Physicians Health Study, while the British counterpart study showed a ratio of 1.1 (fatal CVD vs non-fatal myocardial infarction). Both studies used different diagnostic categories which were narrower than those used in our study. It has previously been hypothesised that these differences in ratios reflect diagnostic differences (such as ascertainment and diagnostic thresholds) rather than underlying disease differences. Furthermore, study power may play a role. Greenland et al showed lower ratios of non-fatal myocardial infarction to fatal CVD, especially in the very young (ages 18–39 years men 1.5, women 2.2, ages 40–59 years men 0.8, women 0.9). However, the number of non-fatal outcome events in our study was roughly 10-fold the number in their study. In our study, we chose to address CVD (all arterial
towards telemedicine services, including mental health support.

Some aspects of our study warrant consideration. First, we used data from a prospective cohort, originally designed for the investigation of parameters other than cardiovascular events and hospitalisations, with the limitations inherent in this type of analysis. Second, while we were able to calculate SCORE in a large number of individuals (15,717), there were only 77 women with a SCORE of ≥5%, meaning that nearly all women had a SCORE under the threshold where risk management is recommended. These women had a very low rate of fatal CVD, but a considerable risk of non-fatal CVD, contributing to the very high ratios of total/fatal-CVD. This underlines the fact that CVD mortality cannot readily be used to calculate total CVD, and we do not recommended using these ratios to calculate total CVD from fatal CVD. However, these ratios illustrate the limitations of mortality as a single outcome parameter, particularly at young ages and in women, and emphasise the need to include non-fatal outcomes in estimations of the risk of cardiovascular events.

Finally, the definition of CVD events is essential in any study investigating the relationship between total CVD and CVD mortality. We defined total CVD as any event or disease requiring hospitalisation, including ischaemic heart disease, cardiac failure, cerebrovascular disease, peripheral artery disease and aortic aneurysm. CVD not requiring hospitalisation, including ‘mild’ peripheral artery disease, ‘mild’ heart failure or stable angina pectoris, was not included in our analysis. While these variants of CVD frequently do not require hospitalisation, they are expressions of clinically relevant atherosclerotic disease and form a relevant indicator for the initiation or intensification of preventive measures in individual patients. Using a broader definition of CVD events would result in a higher rate of non-fatal CVD, leading to a further increase in the overall ratios of total CVD/ CVD mortality, and potentially change the threshold for preventive therapy.

Conclusion
In summary, among patients without a history of CVD or diabetes mellitus, the relation between total CVD including hospitalisations and CVD mortality is highly variable. The total CVD to CVD mortality ratio is inversely related to age, and is higher in women as compared with men. Our findings do not support using a fixed multiplier to calculate total CVD risk based on CVD mortality risk, and caution is warranted when extrapolating the risk of CVD mortality to the risk of total CVD. Future guidelines may be revised to reflect these relationships.

Table 4  Cumulative 10-year CVD mortality and total CVD by sex and SCORE

<table>
<thead>
<tr>
<th>Score</th>
<th>N</th>
<th>10-year CVD mortality</th>
<th>10-year total CVD</th>
<th>10-year CVD mortality</th>
<th>10-year total CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>KM rate</td>
<td>95% CI</td>
<td>n</td>
<td>KM</td>
</tr>
<tr>
<td>Total population</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5%</td>
<td>14,491</td>
<td>139</td>
<td>1.0</td>
<td>(0.8 to 1.2)</td>
<td>1783</td>
</tr>
<tr>
<td>≥5%</td>
<td>680</td>
<td>48</td>
<td>7.3</td>
<td>(5.5 to 9.6)</td>
<td>274</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5%</td>
<td>5906</td>
<td>81</td>
<td>1.4</td>
<td>(1.1 to 1.7)</td>
<td>842</td>
</tr>
<tr>
<td>≥5%</td>
<td>603</td>
<td>45</td>
<td>7.7</td>
<td>(5.8 to 10.2)</td>
<td>246</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5%</td>
<td>5855</td>
<td>58</td>
<td>0.7</td>
<td>(0.5 to 0.9)</td>
<td>941</td>
</tr>
<tr>
<td>≥5%</td>
<td>77</td>
<td>3</td>
<td>4.0</td>
<td>(1.3 to 11.2)</td>
<td>28</td>
</tr>
</tbody>
</table>

CVD mortality is death from a CVD. Total CVD is all fatal and non-fatal CVD or events requiring hospitalisation. Cumulative total CVD and CVD mortality rates were calculated using the KM method. Ratios are total CVD to CVD mortality. BSP, bootstrap procedure; CVD, cardiovascular disease; KM, Kaplan-Meier; SCORE, Systematic Coronary Risk Evaluation.

Strengths and limitations
There are several strengths to our study. First, our analysis was performed in a large, population-based cohort with long-term follow-up and detailed information on mortality and hospitalisations, and we were able to estimate cumulative mortality and hospitalisation rates in the overall population and in large age and sex subgroups. Second, the EPIC-Norfolk cohort is similar to a nationally representative sample for anthropometric variables, blood pressure and serum lipids. However, it should be noted that the population in the Norfolk area is healthier than the general UK population with a standardised mortality ratio of 0.94 (source: Office for National Statistics). Third, we have previously shown that the SCORE low-risk algorithm performs better than the high-risk algorithm in prediction 10-year CVD mortality. The recent reclassification of the UK as a low-risk country in the ESC prevention guidelines is in line with our findings.

Some aspects of our study warrant consideration. First, we used data from a prospective cohort, originally designed for the investigation of parameters other than cardiovascular events and hospitalisations, with the limitations inherent in this type of analysis. Second, while we were able to calculate SCORE in a large number of individuals (15,717), there were only 77 women with a SCORE of ≥5%, meaning that nearly all women had a SCORE under the threshold where risk management is recommended. These women had a very low rate of fatal CVD, but a considerable risk of non-fatal CVD, contributing to the very high ratios of total/fatal-CVD. This underlines the fact that CVD mortality cannot readily be used to calculate total CVD, and we do not recommended using these ratios to calculate total CVD from fatal CVD. However, these ratios illustrate the limitations of mortality as a single outcome parameter, particularly at young ages and in women, and emphasise the need to include non-fatal outcomes in estimations of the risk of cardiovascular events.

Finally, the definition of CVD events is essential in any study investigating the relationship between total CVD and CVD mortality. We defined total CVD as any event or disease requiring hospitalisation, including ischaemic heart disease, cardiac failure, cerebrovascular disease, peripheral artery disease and aortic aneurysm. CVD not requiring hospitalisation, including ‘mild’ peripheral artery disease, ‘mild’ heart failure or stable angina pectoris, was not included in our analysis. While these variants of CVD frequently do not require hospitalisation, they are expressions of clinically relevant atherosclerotic disease and form a relevant indicator for the initiation or intensification of preventive measures in individual patients. Using a broader definition of CVD events would result in a higher rate of non-fatal CVD, leading to a further increase in the overall ratios of total CVD/ CVD mortality, and potentially change the threshold for preventive therapy.

Conclusion
In summary, among patients without a history of CVD or diabetes mellitus, the relation between total CVD including hospitalisations and CVD mortality is highly variable. The total CVD to CVD mortality ratio is inversely related to age, and is higher in women as compared with men. Our findings do not support using a fixed multiplier to calculate total CVD risk based on CVD mortality risk, and caution is warranted when extrapolating the risk of CVD mortality to the risk of total CVD. Future guidelines may be revised to reflect these relationships.
Key messages

What is already known on this subject?

- The European Society of Cardiology’s Prevention Guideline suggests that total (fatal and non-fatal) cardiovascular disease (CVD) risk may be calculated from the risk of CVD mortality by using a fixed multiplier (3x).
- The relationship between total CVD and CVD mortality in the general population is unclear, and the suggested fixed multiplier has not been validated.

What might this study add?

- The relationship between 10-year total CVD and CVD mortality is dependent on age and sex, and cannot be estimated using a fixed multiplier.
- Using CVD mortality to estimate total CVD risk leads to serious underestimation of risk, particularly in younger age groups, and particularly in women.

How might this impact on clinical practice?

- These findings have major implications for individual decision making on preventive therapy and for future guidelines on prevention.
- A significantly greater proportion of individuals will benefit from preventive treatments than is estimated by current European Society of Cardiology guidelines, particularly in young age groups.

Acknowledgements

The authors thank the participants, general practitioners and staff in EPIC-Norfolk.

Contributors

All authors contributed to the planning, conduct and reporting of the study.

Funding

EPIC-Norfolk is supported by programme grants from the Medical Research Council UK (MRC G0401527, MRC G0701863, MRC G1000143) and Cancer Research UK (CRUK 8257).

Competing interests

None declared.

Ethics approval

Norfolk Local Research Ethics Committee.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

Requests for additional data can be directed to the corresponding author.

Open Access

This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES

Estimated 10-year cardiovascular mortality seriously underestimates overall cardiovascular risk

Harald T Jørstad, Ersen B Colkesen, S Matthijs Boekholdt, Jan G Tijssen, Nicholas J Wareham, Kay-Tee Khaw and Ron J Peters

*Heart* published online August 10, 2015

Updated information and services can be found at: [http://heart.bmj.com/content/early/2015/08/10/heartjnl-2015-307668](http://heart.bmj.com/content/early/2015/08/10/heartjnl-2015-307668)

**References**

This article cites 21 articles, 8 of which you can access for free at: [http://heart.bmj.com/content/early/2015/08/10/heartjnl-2015-307668#BIBL](http://heart.bmj.com/content/early/2015/08/10/heartjnl-2015-307668#BIBL)

**Open Access**

This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: [http://creativecommons.org/licenses/by-nc/4.0/](http://creativecommons.org/licenses/by-nc/4.0/)

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**

Articles on similar topics can be found in the following collections

- Open access (237)
- Epidemiology (3752)
- Drugs: cardiovascular system (8842)
- Diabetes (842)
- Metabolic disorders (1030)

**Notes**

To request permissions go to: [http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to: [http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to: [http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)