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Background—Recent time trends and educational gradients characterizing out-of-hospital coronary deaths (OHCD) are poorly described.

Methods and Results—We identified all deaths from coronary heart disease occurring outside the hospital in Norway during 1995 to 2009. Time trends were explored using Poisson regression analysis with year as the independent, continuous variable. Information on the highest achieved education was obtained from The National Education Database and classified as primary (up to 10 years of compulsory education), secondary (high school or vocational school), or tertiary (college/university). Educational gradients in OHCD were explored using Poisson regression, stratified by sex and age (<70 and ≥70 years), and results were expressed as incidence rate ratios (IRRs) and 95% CIs. Of 100,783 coronary heart disease deaths, 58.8% were OHCDs. From 1995 to 2009, age-adjusted OHCD rates declined across all education categories (primary, secondary, and tertiary) in younger men (IRR = 0.35; 95% CI 0.32-0.38; IRR = 0.38; 95% CI 0.35-0.42; IRR = 0.33; 95% CI 0.28-0.40), younger women (IRR = 0.47; 95% CI 0.40-0.56; IRR = 0.55; 95% CI 0.45-0.67; IRR = 0.28; 95% CI 0.16-0.47), older men (IRR = 0.20; 95% CI 0.19-0.22; IRR = 0.20; 95% CI 0.18-0.22; IRR = 0.20; 95% CI 0.17-0.23), and older women (IRR = 0.26; 95% CI 0.24-0.28; IRR = 0.25; 95% CI 0.23-0.28; IRR = 0.28; 95% CI 0.22-0.34). Tertiary education was associated with lower risk of OHCD compared to primary education (IRR = 0.37; 95% CI 0.35-0.40 in younger men, IRR = 0.26; 95% CI 0.22-0.30 in younger women, IRR = 0.52; 95% CI 0.49-0.55 in older men, and IRR = 0.61; 95% CI 0.57-0.66 in older women). These gradients did not change over time (P interaction = 0.25).

Conclusions—Although OHCD rates declined substantially during 1995 to 2009, they displayed educational gradients that remained constant over time. (J Am Heart Assoc. 2017;6:e005236. DOI: 10.1161/JAHA.116.005236.)

Key Words: coronary artery disease • educational inequalities • epidemiology • mortality • Norway • out-of-hospital coronary • trends
analyzing CHD mortality have not distinguished between deaths occurring in or outside the hospital. Few studies have analyzed CHD mortality trends by death location\textsuperscript{2,4,11,12} or focused on SES gradients among patients dying out of hospital.\textsuperscript{4,9,13,14} Most of these studies used small or regional data sets\textsuperscript{11,13} and were not recent.\textsuperscript{4,11,14} Thus, they do not reflect the major changes characterizing CHD occurrence and treatment during the last decades. Further, information on SES was reported on area rather than individual level. Therefore, up-to-date information on time trends and potential SES gradients characterizing OHCD is limited.

In the current study we describe the burden of, and analyze time trends and educational differences in, the risk of OHCD in the Norwegian population during a 15-year time period (1995-2009).

Methods

Data Sources

The Cardiovascular Disease in Norway 1994-2009 Project (www.cvdnor.no)

Detailed information on data collection, content, and quality has been previously published (The Cardiovascular Disease in Norway [CVDNOR] Project).\textsuperscript{15,16} All hospital stays with a cardiovascular disease (CVD) or diabetes-related discharge diagnosis were retrieved from electronic patient administrative systems from all Norwegian hospitals for the period 1994 to 2009. Information included hospitalization and discharge dates, up to 20 discharge diagnoses, and medical (diagnostic and treatment) procedures related to each hospital stay. Information on the date, place, and underlying cause of death for all Norwegian residents dying during the same time period (irrespective of previous hospitalizations for CVD) was obtained from the Norwegian Cause of Death Registry\textsuperscript{17} and merged with hospitalization data.

The National Education Database

The National Education Database (NEDB) contains information on the highest achieved education for all persons with a permanent address in Norway. It is based on reports from educational institutions to Statistics Norway and is updated yearly. The highest achieved education is coded according to the Norwegian Standard Classification. For the purpose of this study, we classified educational level into 3 categories: primary (up to 10-year compulsory education), secondary (high school or vocational school), and tertiary education (college/university).

Information on the total population of Norway, stratified by year, sex, education, and age, was obtained from the Population Registry.

Coronary Deaths

Among all Norwegian residents aged 35 to 89 years during 1995 to 2009, we identified those who died from CHD (ICD-9 codes 410-414, 798, or ICD-10 codes I20-I25, R96).

Based on place of death we distinguished between deaths occurring during a hospital stay (in-hospital coronary deaths) and those occurring outside the hospital (in nursing homes, other nonhospital health institutions, at home, during transportation, at work, or other public places).

Data Quality

The CVDNOR Project

A quality control analysis compared the information obtained from the patient electronic administrative systems with that obtained from patients’ hospital records and found that 99% of the data were correct with regard to date, time of admission, and main diagnosis.\textsuperscript{18} When data from CVDNOR were further compared with other sources of information (ie, The Western Norway Cardiovascular Registry), the results were very similar.\textsuperscript{16}

The Cause of Death Registry

Information on the underlying cause of death in Norway is provided for more than 98% of all deaths.\textsuperscript{19} In a recent analysis assessing the quality of cause-of-death data using a multidimensional score (The Vital Statistics Performance Index), the Norwegian Cause of Death Registry was ranked in the best group, with a total point score of 87.6 out of 100.\textsuperscript{20}

Statistical Analysis

We present continuous variables as means and SDs and categorical variables as percentages. Changes over time in the proportion of OHCD within all CHD deaths were assessed using logistic regression with OHCD as the outcome and calendar year as a continuous exposure variable, adjusted for age.

Trends in Out-of-Hospital Coronary Death Rates

For each educational category we calculated age-standardized OHCD rates by the direct standardization method, using 5-year age strata and the Norwegian population in year 2009 as the standard population. The obtained rates were then joined using Lowes-smoothed lines in STATA.
Trends over time were explored using Poisson regression analysis with count of OHCD as the outcome, calendar year as the independent, continuous variable, and the population of Norway as the offset variable. The model assumed a log-linear trend in rates over time. The total change in OHCD rates from 1995 to 2009 was calculated from the obtained regression coefficient \( b \) using the formula \( \text{IRR} = e^{14b} \). The results are expressed as IRRs.

**Educational Gradients in the Risk of OHCD**

Education gradients in the risk of OHCD were explored using Poisson regression with educational category as a 3-level exposure variable, adjusted for age, calendar year, and history of previous CHD. Results are expressed as IRRs comparing individuals with secondary or tertiary to those with primary education only (the reference category).

We tested for interactions between (1) educational level and sex, (2) educational level and age, and (3) educational level and year. The first 2 interactions were statistically significant. Consequently, all analyses were stratified by sex and age group (younger individuals [35-69 years] and older individuals [70-89 years]).

To avoid the potential influence of nonrandom use of ICD-10 R codes (classified as “ill-defined” codes for causes of death), we repeated the analyses using a more restrictive definition of coronary deaths (ICD-9 codes 410-414 or ICD-10 codes I20-I25).

All statistical analyses were performed using STATA (College Station, TX) version 13. No informed consent was given by study participants because that requirement is waived in register-based research in Norway. The study protocol was approved by the Regional Committee for Medical and Health Research Ethics, Health Region West (2015/2050).

### Results

A total of 100,783 individuals aged 35 to 89 years died from CHD during the period 1995 to 2009 in Norway. Of these, 58,923 (58.5%) were men. Mean (SD) age was 74.5 (10.7) years for men and 79.9 (8.2) years for women \((P<0.001)\).

Characteristics of individuals dying from CHD are summarized in Table 1. Overall, 58.7% of CHD deaths among men and 59.0% among women occurred out of hospital. Individuals who died out of hospital were younger \((P<0.001)\) and less often had a prior history of CHD \((P<0.001)\) compared to those who died in a hospital.

During the study period, the proportion of OHCD within all CHD deaths increased among younger individuals (from 61.5% in 1995 to 68.9% in 2009, \(P\) for trend <0.001 in men, and from 58.4% to 62.9%, \(P\) for trend <0.001 in women) but declined among those aged \(\geq 70\) years (from 58.2% in 1995 to 55.4% in 2009; \(P\) for trend <0.001 in men and from 60.4% in 1995 to 58.3% in 2009; \(P\) for trend=0.044 in women) (Figure 1).

More detailed information on place of death among individuals dying out of hospital is given in Table 2. Most OHCD in younger individuals (67.0% of men and 76.4% of women) occurred at home. In older individuals most OHCD occurred at home among men (53.6%) and in nursing homes among women (56.2%).

### Time Trends in Out-of-Hospital Coronary Death Rates

During the study period, the age-standardized rates of OHCD declined both among younger \((\text{IRR}=0.36, 95\%\text{CI} 0.34-0.38\text{ in men}; \text{IRR}=0.44, 95\%\text{CI} 0.38-0.50\text{ in women})\) and older \((\text{IRR}=0.39, 95\%\text{CI} 0.37-0.40\text{ in men}; \text{IRR}=0.45, 95\%\text{CI} 0.43-0.48\text{ in women})\).

| Table 1. Characteristics of Men and Women Dying From CHD in Norway 1995 to 2009: A CVDNOR Project |
|---|---|---|---|---|---|---|
| Coronary Deaths | Men (n=58,923) | | | | | |
| Out-of-Hospital Deaths (n=34,401) | In-Hospital Deaths (n=24,322) | | | | | |
| Age (y), mean (SD) | 73.6 (11.3) | 75.7 (9.7) | <0.001 | 80.2 (8.4) | 79.4 (9.7) | <0.001 |
| Age group, n (%) | | | | | | |
| 35 to 69 years | 10,503 (30.4) | 5293 (21.8) | 2513 (10.2) | 1711 (10.0) |
| 70 to 89 years | 24,098 (69.6) | 19,029 (78.2) | 22,167 (89.8) | 15,469 (90.0) |
| Education, n (%) | | | | | | |
| Primary | 17,732 (51.8) | 12,188 (50.7) | 16,142 (66.0) | 11,420 (67.1) |
| Secondary | 13,505 (39.5) | 9620 (40.0) | 7281 (29.8) | 4886 (28.7) |
| Tertiary | 2994 (8.7) | 2236 (9.3) | 1031 (4.2) | 713 (4.2) |
| Previous CHD, n (%) | 12,343 (35.7) | 11,337 (46.6) | <0.001 | 8536 (34.6) | 7132 (41.5) | <0.001 |

CHD indicates coronary heart disease; CVDNOR, Cardiovascular Disease in Norway Project.
0.43-0.47 in women) individuals, contributing to the decline in total CHD death rates (Figure S1).

All education categories contributed to the decline in OHCD rates (Figure 2). Over the study period, the rates declined by 65% (IRR = 0.35, 95%CI 0.32-0.38), 62% (IRR = 0.38, 95%CI 0.35-0.42), and 67% (IRR = 0.33, 95%CI 0.28-0.40) in young men with primary, secondary, and tertiary education, respectively. The corresponding declines in younger women were 53% (IRR = 0.47, 95%CI 0.40-0.56), 45% (IRR = 0.55, 95%CI 0.45-0.67), and 72% (IRR = 0.28, 95%CI 0.16-0.47). In older individuals OHCD rates declined by 80% (IRR = 0.20, 95%CI 0.19-0.22), 80% (IRR = 0.20, 95%CI 0.18-0.22), and 80% (IRR = 0.20, 95%CI 0.17-0.23) in men and 74% (IRR = 0.26, 95%CI 0.24-0.28), 75% (IRR = 0.25, 95%CI 0.23-0.28), and 72% (IRR = 0.28, 95%CI 0.22-0.34) in women with primary, secondary, and tertiary education, respectively (Figure 2).

**Educational Gradients in the Risk of Out-of-Hospital Coronary Deaths**

Higher education was associated with decreased risk of OHCD (Table 3), although the strength of the association differed by sex (P for interaction=0.001) and age group (P for interaction <0.001).

In younger men secondary and tertiary education were associated with 35% (IRR = 0.65, 95%CI 0.62-0.67) and 63% (IRR = 0.37, 95%CI 0.35-0.40) lower risk of OHCD compared to primary education. In younger women secondary and tertiary education was associated with 51% (IRR = 0.49, 95%CI 0.45-0.54) and 69% (IRR = 0.34, 95%CI 0.31-0.37) lower risk of OHCD compared to primary education.

Table 2. Place of Death for Men and Women Dying From CHD Outside Hospitals in Norway 1995 to 2009: A CVDNOR Project

<table>
<thead>
<tr>
<th>Place of Death</th>
<th>Men All (n=34,601)</th>
<th>35 to 69 Years (n=10,503)</th>
<th>70 to 89 Years (n=24,098)</th>
<th>Women All (n=24,680)</th>
<th>35 to 69 Years (n=25,13)</th>
<th>70 to 89 Years (n=22,167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing home</td>
<td>8950 (25.9)</td>
<td>417 (4.0)</td>
<td>8533 (35.4)</td>
<td>12,659 (51.3)</td>
<td>207 (8.3)</td>
<td>12,452 (56.2)</td>
</tr>
<tr>
<td>Other health institutions*</td>
<td>203 (0.6)</td>
<td>62 (0.6)</td>
<td>141 (0.6)</td>
<td>144 (0.5)</td>
<td>18 (0.7)</td>
<td>126 (0.5)</td>
</tr>
<tr>
<td>Home</td>
<td>19,950 (57.6)</td>
<td>7036 (67.0)</td>
<td>12,914 (53.6)</td>
<td>10,602 (43.0)</td>
<td>1920 (76.4)</td>
<td>8682 (39.2)</td>
</tr>
<tr>
<td>During transportation</td>
<td>519 (1.5)</td>
<td>195 (1.9)</td>
<td>324 (1.3)</td>
<td>296 (1.2)</td>
<td>59 (2.3)</td>
<td>237 (1.1)</td>
</tr>
<tr>
<td>Other places†</td>
<td>4980 (14.4)</td>
<td>2794 (26.6)</td>
<td>2186 (9.1)</td>
<td>979 (4.0)</td>
<td>309 (12.3)</td>
<td>670 (3.0)</td>
</tr>
</tbody>
</table>

CHD indicates coronary heart disease; CVDNOR, Cardiovascular Disease in Norway Project.
*General practitioner office or emergency room.
†At work or public places.

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Figure 1. Proportion of out-of-hospital deaths within all coronary deaths by sex and age group in Norway: a CVDNOR project. Numbers in the parentheses represent the 95%CI. CVDNOR indicates Cardiovascular Disease in Norway Project.
education were associated with 42% (IRR = 0.58, 95%CI 0.54-0.64) and 74% (IRR = 0.26, 95%CI 0.22-0.30) lower risk of OHCD compared to primary education (Table 3).

In older men secondary and tertiary education were associated with 24% (IRR = 0.76, 95%CI 0.74-0.79) and 48% (IRR = 0.52, 95%CI 0.49-0.55) lower risk of OHCD compared to primary education. In older women the corresponding risk reductions were 23% (IRR = 0.77, 95%CI 0.75-0.80) and 39% (IRR = 0.61, 95%CI 0.57-0.66) (Table 3). The educational gradients in OHCD did not change significantly over the study period (P for interaction = 0.25).

Restricting the outcome to only deaths coded as 410 to 414 in ICD-9 or I20 to I25 in ICD-10 resulted in 6867 fewer OHCD cases but did not substantially change the results compared to those presented in the main analyses (Table S1).

Discussion

In this nationwide analysis we observed that most (58.8%) CHD deaths during 1995 to 2009 in Norway occurred out of hospital. The proportion of OHCDs within all CHD deaths increased over the study period among younger (35-69 years) but declined among older (70-89 years) individuals. The majority of men died at home, whereas the majority of women died in nursing homes. The OHCD rates declined substantially across all sex and age group categories. The risk of dying outside the hospital due to CHD was inversely associated with the level of education, and the observed educational gradients remained unchanged over the study period.

OHCD accounted for 75.3% of all CHD deaths in Sweden from 1991 to 2006, 70.8% of all CHD deaths in Finland from 1983 to 1997, and 63.3% of all coronary deaths in the United States from 1989 to 1998. Differences in the proportion of OHCD between studies are likely to be influenced by differences in the cutoff criteria used for age and study period and may also reflect potential differences in the populations studied and/or the structure of the health care systems.

Declines in the OHCD rates have been reported previously in other countries. Among individuals aged 28 to 62 years in the Framingham Heart study, OHCD rates declined by 49%
between 1950 to 1969 and 1990 to 1999. In a regional study conducted in Finland from 1983 to 1997, OHCD rates declined by 6.1% per year in men and 7.0% a year in women aged 35 to 64 years. In Scotland OHCD rates fell by one-third in men and one-fourth in women aged ≥55 years from 1986 to 1995. More recently (1991-2006), OHCD rates fell by 2.2% per year in Sweden among individuals aged 35 to 84 years. The observed yearly decline of 5% to 7% per year in our study is in line with previous reports but steeper than those reported from Sweden. However, the definition of OHCD differed between the 2 studies: in the Swedish study, only incident OHCDs were included, whereas we included all CHD deaths occurring out of hospital regardless of prior history of CHD. Further, differences in the upper age limit (85 years in the Swedish study vs 89 years in ours) and different measures of associations used (odds ratios in the Swedish study vs IRR in ours) might have contributed to the differences.

When trends in OHCD rates were stratified by level of education, we observed comparable declines in all 3 educational strata within each age group and sex category, similar to a previous report from Scotland covering an earlier time period (1986-1995). The association between SES and risk of OHCD has been addressed by a few small, regional studies. Soo et al reported higher incidence of out-of-hospital cardiac arrest among residents of the most deprived areas compared to the most affluent areas in Nottinghamshire County, UK from 1991 to 1994. The ARIC study also showed an inverse association between neighborhood SES and OHCD from 1992 to 2002, irrespective of SES indicator used. In the OREO-SUD study conducted in the United States from 2002 to 2004, Reinier et al reported a higher incidence of out-of-hospital cardiac arrest in the lowest SES quartile compared to the highest. The relative difference in the incidence of out-of-hospital cardiac arrest varied from 30% to 80%, depending on the SES measure used. In a pooled analysis including 7 metropolitan areas in the United States and Canada from 2006 to 2007, the same group of authors reported that the incidence of cardiac arrest in the lowest SES quartile was nearly doubled (IRR=1.9) compared to that in the highest quartile. Our study, the first to link SES measured at the individual level and risk of OHCD, demonstrated that educational level (a reliable measure of SES during the adult life) is inversely associated, in a dose-response pattern, with the risk of dying outside the hospital.

Low education has been associated with a higher burden of coronary risk factors, leading to a more severe CHD phenotype. In addition, individuals with lower SES have longer delays in seeking medical assistance compared to individuals with higher SES. A more severe CHD phenotype combined with delays in seeking medical assistance in individuals with low SES compared to those with high SES, may account for the observed differences in the proportion of coronary deaths occurring outside the hospital.

In younger individuals we observed a stronger association between educational level and OHCD risk among women than among men. This may be related to sex differences in the pathophysiological and clinical characteristics of CHD in this age group. In younger women CHD occurs less often and can feature an “atypical” clinical presentation, often leading to an underappreciation of risk. Hence, the recognition of symptoms and decision to seek medical assistance might require better knowledge and awareness of CHD risk among women, rendering the role of education among them relevant. In younger men CHD occurs more frequently, and its clinical expression is more often “straightforward,” rendering the

<table>
<thead>
<tr>
<th>Educational Category</th>
<th>IRR (95%CI)</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
<td>Model 1</td>
</tr>
<tr>
<td>35 to 69 years</td>
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<td></td>
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</tr>
<tr>
<td>Primary</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
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<tr>
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<tr>
<td></td>
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<tr>
<td>70 to 89 years</td>
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</tr>
<tr>
<td>Primary</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Secondary</td>
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<tr>
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<td>0.52 (0.49-0.55)</td>
<td>0.60 (0.56-0.64)</td>
</tr>
</tbody>
</table>

Model 1 is adjusted for age and year. Model 2 is adjusted for age, year, and history of coronary heart disease. CI indicates confidence interval; CVDNOR, Cardiovascular Disease in Norway Project; IRR, incidence rate ratio; OHCD, out-of-hospital coronary deaths.
Symptoms and recognition of risk less dependent on education. A complementary explanation may be the existence of a stronger educational gradient in coronary risk factors (including obesity, hypertension, and elevated total cholesterol and triglyceride levels) among women compared to men as reported in a community-based study conducted in Norway.27

In older individuals the strength of the association between education and OHCD was weaker among women than among men. This might be influenced by the fact that women died on average 5 years later than men and more often in nursing homes. Nursing home residents encompass a vulnerable population in which comorbidities and frailty are common, and as previously shown, 70% to 80% of nursing home residents in Norway suffer from cognitive impairment or dementia.28 As pointed out in a recently published meta-analysis, these comorbidities and other factors, unrelated to SES status, play an important role in determining the place of death in this population subset.29 Hence, the association of education and OHCD risk is less decisive among older women compared to older men who die more often at home. Another possible explanation is that level of education in older women might not capture SES as well as in men or younger people.

Implications of Our Findings

The substantial decline in OHCD rates has a major impact on the favorable changes observed for CHD mortality during the last decades in Norway. However, the existence of important SES gradients in the risk of OHCD deserves further investigation. We observed that SES gradients in the risk of OHCD were more pronounced in younger than older individuals. Although OHCDs in younger individuals comprise only 10% of all OHCDs, they account for a substantial number of years of potential life lost and often affect active members of the workforce and parents caring for children. Recent literature has shown that in-hospital mortality among younger individuals is very low and decreasing.30 Thus, if younger individuals with signs and symptoms compatible with acute coronary syndrome are quickly admitted to hospitals, coronary mortality may be substantially reduced in this group. Efforts are needed to increase public awareness of CHD as a life-threatening condition requiring immediate medical assistance. On the other hand, more effective prevention strategies targeting the most deprived subgroups would help reduce the extra burden of risk factors and potentially reduce SES differences in the severity of CHD clinical expression. Further, stronger efforts to improve adherence to treatment and adaptation of a healthy lifestyle among individuals with existing CHD, especially among those with lower education, would help further reduce OHCD rates and narrow SES differences.

Strength and Limitations

The current study adds to previous knowledge on the association between education level and risk of OHCD. The use of a nationwide cohort without geographic, age or sex restrictions minimizes the risk of selection bias in this study. The national personal identification number allowed us to link data from several sources of information, thus improving the quality and completeness of information and reporting. Further, our study is the first to provide information on SES at the individual level in the context of OHCD epidemiologic research.

Our study has some potential limitations as well. Most deaths occurring outside the hospital are not followed by a medical autopsy.31 To date, no information is available on the frequency of medical autopsies following out-of-hospital deaths at a national level. In our material, only 7.2% (17.7% of younger and 5.9% of older) individuals dying outside the hospital underwent medical autopsy. A previous study based on a highly selected sample reported that autopsy findings might lead to a change in the underlying cause of death.32 However, we do not believe that it is plausible that differential reclassification would occur in the underlying cause of death according to education achieved should the autopsy have taken place.

Due to its observational nature, results from our study point to an association between education and risk of OHCD. The lack of information on coronary risk profile, medication use and presence of comorbidities prior to death can potentially lead to residual confounding. These limitations should be kept in mind when interpreting our results.

Conclusion

Over the study period, OHCD rates declined substantially in Norway across all education categories. However, most coronary deaths still occur outside the hospital and are characterized by educational differences, especially among younger individuals. Prevention strategies and greater focus on information about the importance of seeking medical assistance once coronary symptoms develop will help to reduce the burden of OHCD.

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Disclosures
None.

References
SUPPLEMENTAL MATERIAL

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<thead>
<tr>
<th>Educational category</th>
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<th>Women</th>
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<td>Model 2</td>
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<td>Tertiary</td>
<td>0.50 (0.46–0.53)</td>
<td>0.51 (0.49–0.54)</td>
<td>0.56 (0.51–0.60)</td>
<td>0.58 (0.54–0.63)</td>
</tr>
</tbody>
</table>

IRR indicates incidence rate ratio; CI, confidence interval.
Model 1 is adjusted for age and year.
Model 2 is adjusted for age, year and history of coronary heart disease.
Figure S1. Age-standardized rates of coronary heart disease; overall and by death location, Norway 1995–2009: a CVDNOR project
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