Marital status and ischaemic heart disease incidence and mortality in women: a prospective study

Sarah Floud¹, Angela Balkwill¹, Dexter Canoy¹, F Lucy Wright¹, Gillian Reeves¹, Jane Green¹, Valerie Beral¹, Benjamin J Cairns¹, for the Million Women Study Collaborators

Sarah Floud: sarah.floud@ceu.ox.ac.uk * corresponding author
Angela Balkwill: angela.balkwill@ceu.ox.ac.uk
Dexter Canoy: dexter.canoy@ceu.ox.ac.uk
F Lucy Wright: lucy.wright@ceu.ox.ac.uk
Gillian Reeves: gill.reeves@ceu.ox.ac.uk
Jane Green: jane.green@ceu.ox.ac.uk
Valerie Beral: pa.valerie.beral@ceu.ox.ac.uk
Benjamin J Cairns: ben.cairns@ceu.ox.ac.uk

¹: Cancer Epidemiology Unit, University of Oxford, Roosevelt Drive, Oxford, OX3 7LF
Abstract

Background

Being married has been associated with a lower risk of mortality from ischaemic heart disease (IHD) in men, but there is less evidence of an association for women, and it is unclear whether the associations with marriage are similar for incident and for fatal IHD. Our aim was to examine the relation between being married and IHD incidence and mortality in a large cohort of UK women.

Methods

A total of 734,626 women (mean age 59.7 (SD 5) years at baseline) without previous heart disease, stroke, or cancer, were followed prospectively for cause-specific hospital admissions and deaths. We used Cox regression models to calculate relative risks (RRs) for IHD in married (including cohabiting) versus unmarried (including divorced, widowed, or never married) women, and to investigate the role of 14 socio-economic, lifestyle and other potential confounding factors.

Results

Overall 81% of women reported being married. Compared to those who were not married, married women were less likely to live in deprived areas, to smoke, or to be physically inactive, but had a higher alcohol intake; there was no difference in body mass index. During 8.8 years of follow-up, 30,747 women had a first IHD event (hospital admission or death) and 2,148 died from IHD. Married women had a similar risk of a first IHD event (hospital admission or death) to unmarried women (adjusted RR=0.99, 95% confidence interval (CI) 0.96-1.02), but a significantly lower risk of IHD mortality (adjusted RR=0.72, 95% CI 0.66-0.80, p<0.0001). The reduced risk of IHD death for married women was evident both in women with and without a prior IHD hospital admission (respectively: adjusted RR=0.72, 95% CI 0.60-0.85, p<0.0001, n=683; and 0.70, 95% CI 0.62-0.78, p<0.0001, n=1,465). The findings were similar in women of different socio-economic groups and with different lifestyle and other factors.

Conclusions

After adjustment for socioeconomic, lifestyle and other factors, being married was not associated with women’s risk of developing IHD in this cohort, but married women had a substantially lower IHD mortality than unmarried women.

Keywords: marital status, ischaemic heart disease, incidence, mortality, women

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Introduction
Studies conducted over several decades and on different populations have shown that being married is associated with a lower risk of all-cause mortality [1-3]. Being married is also associated with a lower risk of ischaemic heart disease (IHD) mortality in men [4-8], but in women the reported lower risks have not been statistically significant [6, 8]. It may be that the presence of a spouse influences prognosis after the onset of IHD through encouragement to seek early medical attention for symptoms or to comply with a treatment regime [9, 10]. It has been also proposed that being married may protect against developing disease by encouraging a healthier lifestyle [11, 12] or by providing social support [13, 14] or financial security [11], but the published data do not clearly show whether being married influences the onset of IHD for either men [7, 15-17] or women [16, 17].

We investigated the association of marital status with IHD incidence and mortality in a large prospective cohort of middle-aged women in the UK. We also examined the risk of IHD death in women after a first hospital admission for IHD, and the extent to which socio-economic, lifestyle and other factors might explain any association of being married on IHD incidence or mortality.

Methods

Study design and participants
Between 1996 and 2001, 1.3 million women were recruited to the Million Women Study via the UK national breast screening programme [18]. After an average of 3 years, these women were resurveyed using a new postal questionnaire, with a
response rate of 65%. In the resurvey, participants were asked for the first time about their marital status, and the date of the resurvey is therefore the baseline for the current analysis. The respondents gave written consent to participate and ethics approval was provided by the Oxford and Anglia Multi-Centre Research Ethics Committee. All participants are linked by their unique NHS identification number to NHS Central Registers, through which they are followed for death, emigration and cancer registration. Information on the date of admission and discharge and diagnoses associated with each hospital admission, coded to the World Health Organisation’s International Classification of Diseases 10th revision (ICD-10) [19], was obtained by electronic record linkage to the Hospital Episode Statistics for England (HES) [20] and Scottish Morbidity Records in Scotland [21].

**Marital status and covariates**

Marital status at baseline was assessed by asking “Are you currently married or living with a partner?”. Those who replied “yes” are referred to as married and those who did not are referred to as unmarried. The unmarried category thus includes women who were never married, as well as women who were divorced, separated, or widowed. It is likely that a large proportion of the unmarried category were divorced or widowed, since the General Household Survey for 2002 reported that 71% of women aged 55-64 years old were married, 3% were cohabiting, 4% were single, 13% were divorced or separated and 9% were widowed [22]. We compared marital status at baseline with marital status reported at the next resurvey and found excellent agreement after an average of 4.5 years (SD 1.2 years): 94% of women married at baseline again reported being married, and 94% of unmarried women again reported being unmarried (kappa statistic for agreement = 0.81). We therefore used marital status at baseline in our analyses. We also compared marital status at
baseline with reports of living arrangements 9 years later. Only 12% of women who were married at baseline were living alone compared to 79% of the unmarried women at baseline.

Socio-economic status was measured at recruitment and assessed using quintiles of the Townsend area deprivation score [23] and two measures of education: highest qualification (O levels, A levels, Nursing/Teaching, College/University, none of the preceding categories) and age left school (left school before or at minimum leaving age, left school after minimum leaving age, no schooling). This latter variable took into account the change in the minimum leaving age from 14 to 15 which occurred on 1st April 1947 in both England [24] and Scotland [25].

The lifestyle risk factors assessed were cigarette smoking (never, past, current <15 per day, current ≥15 per day), alcohol intake (0, <7, 7-14, ≥15 drinks per week), strenuous exercise (rarely or never, <once per week, ≥once per week), body mass index (BMI) (<22.5, 22.5-24.9, 25.0-27.4, 27.5-29.9, ≥30 kg/m²), sleep duration (<7, 7, 8, ≥9 hours) and hormone replacement therapy use (never, ever). These variables were recorded at baseline, except strenuous exercise, which was recorded at recruitment.

Other factors assessed were two measures of well-being: reported happiness at baseline (rarely/never, sometimes, usually, most of the time) and treatment for depression reported at recruitment or baseline (yes, no). In addition, three measures which reflected social contact were assessed: parity recorded at recruitment (nulliparous, parous), current employment at baseline (not in paid work, part-time, full-time) and participation in group activities, such as religious group, voluntary work,
art/craft class, sports club, dancing group, music group, bingo, yoga and other group activity, at baseline (none, 1, 2, ≥3 groups).

**Ischaemic heart disease (IHD)**

A first IHD event was defined as a first hospital admission for IHD or death with IHD as the underlying cause. The definition of a hospital admission for IHD was any mention of an IHD diagnosis (ICD-10: I20-I25) in a primary or other diagnosis field in the hospital record. In a study of vascular disease outcomes in this cohort, IHD information based on hospital records and general practice records were consistent in 92% of 796 randomly selected women with a hospital record of IHD [26]. IHD mortality was defined as death with IHD as the underlying cause (ICD-10: I20-I25) at any point during follow up, with or without a prior hospital admission. First IHD events were also subdivided into: (i) death from IHD with no prior hospital admission and (ii) first hospital admission for IHD. The small number of women (n = 76) who died on the day of first hospital admission for IHD were classed as IHD deaths.

**Analysis**

A total of 866,334 women completed the baseline survey and had follow-up for these analyses. We excluded 74,693 (8.6%) women who reported heart disease or stroke or had been admitted to hospital for these conditions, and 42,827 (4.9%) women who had a cancer registration (except non-melanoma skin cancer), prior to baseline. A further 14,188 (1.6%) women were excluded for whom information on marital status was missing. The remaining 734,626 women formed the population at risk for these analyses.

We used Cox regression to estimate relative risks (RR) and 95% confidence intervals (CI) of first IHD events and IHD mortality. Relative risks were also estimated
separately for: IHD death without prior hospital admission; first IHD hospital admission; and IHD death after hospital admission. Person-years were calculated from baseline until the date of hospital admission for IHD, death, emigration or end of follow-up, whichever came first. Women were followed until 31 March 2011 in England and 31 December 2008 in Scotland (7% of women in analysis lived in Scotland), because complete hospital admission data were not available after these dates.

The regression models used attained age as the underlying time variable and were stratified by region of residence at recruitment (Scotland, and nine regions in England) and adjusted separately and simultaneously for three groups of covariates: (i) indicators of socio-economic status, (ii) lifestyle risk factors, and (iii) other factors. Missing data for the adjustment variables (<2.1% for each variable) were assigned to a separate category. Heterogeneity in the associations between marital status and first IHD events or IHD mortality by sub-groups of age, region and socio-economic, lifestyle and other factors, was assessed using a chi-squared contrast test [27].

For risk of IHD death after hospital admission for IHD, person-years at risk were calculated from first hospital admission for IHD to death, emigration or end of follow-up. Any difference in risks of IHD death associated with marital status during the hospital stay and after discharge was investigated by splitting the follow-up period at 28 days after first hospital admission.

To assess the possibility of reverse causation, where early symptoms of disease might affect the likelihood of marriage breakdown [28], we conducted two sensitivity analyses. In one sensitivity analysis we excluded the first five years of follow-up and, in the other, we restricted the analysis to women who rated their health as “good” or
“excellent” at baseline. All analyses used Stata 12.1 (StataCorp., College Station, TX, USA).

Results

At baseline, the mean age of the women was 59.7 years (SD 4.8 years); 81% reported being married or living with a partner (Table 1). The main differences between married and unmarried women were that married women were less likely to live in deprived areas, to smoke, or to be physically inactive, but there was little difference in mean BMI, and married women had a slightly higher intake of alcohol (Table 1). Married women were also less likely to report low levels of happiness or that they had been treated for depression. They were more likely to be employed than unmarried women but less likely to report participation in group activities.

During an average follow-up of 8.8 years per woman, there were 30,747 first IHD events (including 29,282 hospital admissions for IHD, and 1,465 deaths without prior hospital admission), and overall, 2,148 women died of IHD (Table 1). With minimal adjustment for age and region of recruitment only, married women had a lower risk of a first IHD event and lower IHD mortality than unmarried women, but adjustment for lifestyle risk factors, particularly smoking and area deprivation attenuated the risk estimates (Table A1). After adjustment for all socioeconomic, lifestyle and other risk factors, married women had a similar risk of a first IHD event to unmarried women (adjusted RR=0.99, 95% CI 0.96-1.02) but had a lower IHD mortality (adjusted RR=0.72, 95% CI 0.66-0.80) (Figure 1).
When first IHD events were subdivided into whether the event was a hospital admission or a death, married women had a similar risk of first hospital admission for IHD to unmarried women (adjusted RR=1.01, 95% CI 0.98-1.04) but a lower risk of death from IHD with no prior hospital admission (adjusted RR=0.70, 95% CI 0.62-0.78) (Table 2).

The findings did not differ materially by sub-groups of age, region, or level of area deprivation, by life-style factors such as smoking, alcohol intake, and body mass index, or by measures of well-being, happiness and treatment for depression (Figure 2). There was no evidence of heterogeneity across sub-groups of the remaining factors (age left school, strenuous activity, sleep duration, HRT use, parity, employment, participation in group activities), except for weak evidence of a difference for first IHD events by whether the women were in paid work or not; this difference could have arisen by chance, due to the large number of significance tests performed (Figure A1). The risk estimates were not materially changed when we excluded the first 5 years of follow-up (Table A2) nor when we restricted the analysis to women who rated their health as “good” or “excellent” (Table A3).

Among the 29,282 women who had a hospital admission for IHD, the relationships between marital status and socioeconomic, lifestyle and other characteristics were similar to those found in the main sample (Table A4). When their survival was examined over a mean follow-up period of 3.7 years per woman, married women were less likely than unmarried women to die from IHD after their first hospital admission for IHD (adjusted RR=0.72, 95% CI 0.60-0.85; n = 683) (Table 2). The lower risks for married women were evident both in the first 28 days following a hospital admission, and in later follow-up (respective adjusted RRs: 0.74, 95% CI 0.57-0.98, n = 350; and 0.69, 95% CI 0.54-0.89, n = 333).
Discussion

In this large prospective cohort of middle-aged UK women, married women had similar risks of a first IHD event to unmarried women, after adjustment for socio-economic, lifestyle and other risk factors. In contrast, married women were at a lower risk of IHD mortality and this lower risk remained after adjustment for the same factors. The lower risk of IHD death for married women was found in women both with and without a prior hospital admission for IHD and was similar irrespective of socio-economic, lifestyle and other characteristics. Unlike previous studies, the large sample size of the Million Women Study cohort allowed us to investigate whether the associations between marital status and IHD differed across a range of subgroups of socio-economic, lifestyle and other factors. After accounting for the multiplicity of statistical tests, we found that there was little evidence that the associations varied between subgroups of these factors.

To our knowledge, this is the first study of women to investigate the effect of marital status on both IHD incidence and mortality within the same cohort, although our finding of a lower risk for IHD mortality, but not incidence, has also been reported in men [7, 15]. The previous evidence on incident IHD events in women in relation to marital status is sparse. Two previous cohort studies of women have examined the association between marital status and incident IHD. A population-based cohort study in Sweden with 507 incident IHD events reported no difference in risk by marital status [16], but a recent register-based study in Finland, with 7,193 incident myocardial infarctions, reported a lower risk for married women, without adjustment for socio-economic or lifestyle risk factors [17].
In our study, the small association between marital status and incident IHD was attenuated after adjustment for area deprivation and lifestyle risk factors, which suggests that any influence of marital status on the development of IHD may be confounded with or mediated through these factors. Methodologically, it is difficult to distinguish between factors which may be confounders of the association, and those which may be mediators, but marital status has been proposed to influence risk factors for IHD in several ways. For example, spousal influences on behaviour may encourage healthier lifestyles [11, 12], or there may be negative changes in lifestyle after divorce or separation [29, 30]. However, people may choose partners who share their behaviours, and therefore marriage or cohabitation may reinforce both beneficial and harmful lifestyle choices. Area deprivation might act as another mediator, given that getting married can enhance one’s financial resources, whereas divorce or widowhood can have the reverse effect [11]. Social support has also been proposed to mediate the association between marital status and health [13, 14, 31], but in this study adjustment for variables which could indicate social interaction, including parity, participation in group activities and employment, and measures of well-being such as reported happiness and treatment for depression, had little effect on the risk estimates.

There is little previous evidence on IHD mortality in relation to marital status in women in the general population. Being married has been associated with lower risks of overall cardiovascular mortality in women [3, 8, 32] but these associations could be driven by common vascular diseases other than IHD, such as stroke and venous thromboembolism. The two cohort studies that have investigated mortality from IHD included relatively few women, and reported no significant difference in risk between married and unmarried women [6, 8]. We found lower risks of IHD death in
married women with no prior hospital admission, consistent with evidence that being married is associated with lower risks of out-of-hospital sudden cardiac arrest [33], pre-hospital deaths from myocardial infarction [17] and lower case fatality rates for first day of a coronary event [16]. We also found lower risks of IHD mortality in married women after a hospital admission for IHD. This fits with evidence from smaller patient populations (of up to 1,500 patients) in which there were higher risks of deaths following hospitalisation for IHD for unmarried patients or those living alone [34-38], although two larger studies (up to 16,000 patients) did not find a higher risk of IHD death associated with living alone [39, 40].

The lower risk of IHD mortality for married women in our study was only partly attenuated after all adjustments, suggesting that marital status may influence IHD mortality in part by modifying a woman’s response to the disease. In this cohort, unmarried women tended to live alone and married women with others, so a possible explanation for the lower risk of death among married women may be that they have someone at home who can respond to symptoms and help them seek appropriate treatment [9, 41]. Spouses have been shown to encourage their partners to comply with effective medication regimes [42], facilitate attendance at cardiac rehabilitation programmes [10], and support modification of lifestyle risk factors [29, 43]. Spouses can also provide emotional support to cope with the distress of having had a cardiac event [14]. One alternative explanation for the improved survival after hospital admission among married women is that they may tend to have less severe disease on admission to hospital, but we were unable to assess this due to lack of data on disease severity.

Marital status itself was relatively stable during follow-up in this study, but we do not know if the women who were unmarried at baseline were never married, divorced or
widowed, although the 2002 General Household Survey indicated that most would be divorced or widowed [22]. It could be that being divorced or widowed rather than never married places women at higher risk of IHD, but findings from previous cohort studies show little consistency in the associations between IHD mortality and the various unmarried states for women [8, 16, 44]. It is possible that healthy women may be less likely to divorce [28]. However we were able to limit bias associated with this by excluding women with pre-existing disease, and also through two sensitivity analyses that showed no material change in the adjusted risk estimates.

**Conclusions**

In this large UK cohort of middle-aged women, being married does not appear to affect the risk of developing IHD after adjustment for socioeconomic, lifestyle, and other factors. However, there remains a substantial, unexplained lower risk of death from IHD for married compared to unmarried women.

**Additional material**

Additional file 1

Figure A1 Relative risk of first ischaemic heart disease (IHD) event and IHD mortality comparing married to unmarried women, within further subgroups

Table A1 Relative risk of first ischaemic heart disease (IHD) event and IHD mortality comparing married to unmarried, with separate adjustments for various characteristics
Table A2 Relative risk of first ischaemic heart disease (IHD) event and IHD mortality comparing married to unmarried women, excluding first five years of follow up

Table A3 Relative risk of first ischaemic heart disease (IHD) event and IHD mortality comparing married to unmarried women, restricted to women who rated their health as “good” or “excellent” at baseline

Table A4 Characteristics and details of follow-up for ischaemic heart disease (IHD) mortality in the subsample of women whose first event was a hospital admission for IHD, by marital status

**Abbreviations**
BMI: body mass index; ICD-10: International Statistical Classification of Disease and Related Health Problems: Tenth Revision; IHD, ischaemic heart disease; NHS: National Health Service.

**Competing interests**
The authors declare that they have no competing interests.

**Authors’ contributions**
VB, GR and JG were involved in the conception, design and data acquisition for the Million Women Study. SF, BJC, AB and VB analysed and interpreted the data. SF drafted the first version of the manuscript. All authors contributed to drafting revised versions of the manuscript and gave their final approval of the version to be published.
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The co-ordinating staff for the Million Women Study are: Hayley Abbiss, Simon Abbott, Miranda Armstrong, Angela Balkwill, Vicky Benson, Valerie Beral, Judith Black, Kathryn Bradbury, Anna Brown, Benjamin Cairns, Dexter Canoy, Andrew Chadwick, Barbara Crossley, Francesca Crowe, Dave Ewart, Sarah Ewart, Lee Fletcher, Sarah Floud, Toral Gathani, Laura Gerrard, Adrian Goodill, Jane Green, Lynden Guiver, Michal Hozak, Sau Wan Kan, Tim Key, Oksana Kirichek, Mary Kroll, Nicky Langston, Isobel Lingard, Maria Jose Luque, Kath Moser, Lynn Pank, Kirstin Pirie, Gillian Reeves, Keith Shaw, Emma Sherman, Evie Sherry-Starmer, Julie Schmidt, Helena Strange, Sian Sweetland, Alison Timadjer, Sarah Tipper, Ruth Travis, Lyndsey Trickett, Lucy Wright, Owen Yang, Heather Young.

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References

Figure 1 Relative risk of first ischaemic heart disease (IHD) event and IHD mortality in relation to marital status

Relative risks presented with 95% confidence intervals (95% CI). Fully adjusted for: age, region, area deprivation, age left school, highest educational qualification, smoking, alcohol intake, strenuous exercise, body mass index, HRT use, sleep duration, happiness, treatment for depression, parity, employment, participation in group activities

Figure 2 Relative risk of first ischaemic heart disease (IHD) event and IHD mortality in relation to marital status, by various characteristics

Relative risks presented with 95% confidence intervals (95% CI). The dotted line represents the RR of IHD mortality for all women, comparing married to unmarried. RRs are adjusted as appropriate for age, region, area deprivation, age left school, highest educational qualification, smoking, alcohol intake, strenuous exercise, body mass index, HRT use, sleep duration, happiness, treatment for depression, parity, employment, participation in group activities
Table 1 Characteristics and details of follow-up for ischaemic heart disease (IHD), by marital status

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Married</th>
<th>Unmarried</th>
<th>All Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 594,675</td>
<td>n = 139,951</td>
<td>n = 734,626</td>
</tr>
<tr>
<td></td>
<td>(81%)</td>
<td>(19%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>59.5 (4.7)</td>
<td>60.8 (5.2)</td>
<td>59.7 (4.8)</td>
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<tr>
<td><strong>Socio-economic factors:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most deprived quintile, %</td>
<td>14.0</td>
<td>24.4</td>
<td>16.0</td>
</tr>
<tr>
<td>Left school ≤ minimum leaving age, %</td>
<td>48.4</td>
<td>47.0</td>
<td>48.1</td>
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<tr>
<td>No educational qualifications, %</td>
<td>49.0</td>
<td>46.3</td>
<td>48.5</td>
</tr>
<tr>
<td><strong>Lifestyle factors:</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Current smoker, %</td>
<td>11.1</td>
<td>17.1</td>
<td>12.2</td>
</tr>
<tr>
<td>Mean alcohol, drinks/week (SD)</td>
<td>4.7 (5.8)</td>
<td>3.7 (5.6)</td>
<td>4.5 (5.8)</td>
</tr>
<tr>
<td>Strenuous exercise rarely/never, %</td>
<td>43.0</td>
<td>45.5</td>
<td>43.5</td>
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<tr>
<td>Mean BMI, kg/m² (SD)</td>
<td>26.0 (4.4)</td>
<td>26.1 (4.9)</td>
<td>26.0 (4.5)</td>
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<tr>
<td>Never users of HRT, %</td>
<td>45.1</td>
<td>50.9</td>
<td>46.2</td>
</tr>
<tr>
<td>Mean number of hours asleep (SD)</td>
<td>7.3 (1.1)</td>
<td>7.2 (1.3)</td>
<td>7.3 (1.2)</td>
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<tr>
<td><strong>Other factors:</strong></td>
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<td></td>
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<tr>
<td>Rarely/never/sometimes happy, %</td>
<td>15.2</td>
<td>23.7</td>
<td>16.8</td>
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<td>Treatment for depression, %</td>
<td>9.1</td>
<td>14.9</td>
<td>10.2</td>
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<tr>
<td>Mean number of children (SD)</td>
<td>2.1 (1.1)</td>
<td>1.9 (1.4)</td>
<td>2.1 (1.2)</td>
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<td>Not in work, %</td>
<td>52.9</td>
<td>56.1</td>
<td>53.5</td>
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<tr>
<td>No participation in group activities, %</td>
<td>36.4</td>
<td>32.8</td>
<td>35.7</td>
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<td><strong>Follow-up for IHD incidence and mortality (I20-I25)</strong></td>
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<tr>
<td>Mean years of follow-up (SD)</td>
<td>8.8 (1.9)</td>
<td>8.6 (2.0)</td>
<td>8.8 (1.9)</td>
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<tr>
<td>First IHD event, n</td>
<td>23,816</td>
<td>6,931</td>
<td>30,747</td>
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<td>IHD deaths without prior IHD hospital admission, n</td>
<td>974</td>
<td>491</td>
<td>1,465</td>
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<tr>
<td>First hospital admissions for IHD, n</td>
<td>22,842</td>
<td>6,440</td>
<td>29,282</td>
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<tr>
<td>All IHD deaths, n</td>
<td>1,442</td>
<td>706</td>
<td>2,148</td>
</tr>
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*Percentages were calculated based on women with complete information for that specific variable.*
Table 2 Relative risk of ischaemic heart disease (IHD) first event and IHD mortality comparing married to unmarried women

<table>
<thead>
<tr>
<th>Population at risk (n)</th>
<th>FIRST IHD EVENT</th>
<th>IHD MORTALITY</th>
<th>SUBDIVISIONS OF FIRST IHD EVENT</th>
<th>SURVIVAL</th>
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<tr>
<td></td>
<td>IHD hospital admission or IHD death</td>
<td>All IHD deaths</td>
<td>IHD death with no prior hospital admission</td>
<td>IHD hospital admission</td>
</tr>
<tr>
<td></td>
<td>734,626</td>
<td>734,626</td>
<td>734,626</td>
<td>734,626</td>
</tr>
<tr>
<td>Cases (n)</td>
<td>30,747</td>
<td>2,148</td>
<td>1,465</td>
<td>29,282</td>
</tr>
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<td></td>
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<tr>
<td>Adjusted for age and region only</td>
<td>0.88 (0.85-0.90)</td>
<td>0.55 (0.51-0.61)</td>
<td>0.53 (0.47-0.59)</td>
<td>0.90 (0.88-0.93)</td>
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<tr>
<td>Additionally adjusted only for socio-economic factors$^a$</td>
<td>0.91 (0.89-0.94)</td>
<td>0.59 (0.54-0.65)</td>
<td>0.57 (0.51-0.64)</td>
<td>0.94 (0.91-0.96)</td>
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<tr>
<td>Additionally adjusted only for lifestyle factors$^b$</td>
<td>0.96 (0.94-0.99)</td>
<td>0.68 (0.62-0.74)</td>
<td>0.65 (0.58-0.72)</td>
<td>0.99 (0.96-1.02)</td>
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<tr>
<td>Additionally adjusted only for other factors$^c$</td>
<td>0.88 (0.86-0.91)</td>
<td>0.56 (0.51-0.62)</td>
<td>0.54 (0.49-0.61)</td>
<td>0.91 (0.88-0.93)</td>
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<tr>
<td>Adjusted for all the above$^d$</td>
<td>0.99 (0.96-1.02)</td>
<td>0.72 (0.66-0.80)</td>
<td>0.70 (0.62-0.78)</td>
<td>1.01 (0.98-1.04)</td>
</tr>
</tbody>
</table>

$^a$ adjusted for age, region, area deprivation, age left school, highest educational qualification
$^b$ adjusted for age, region, smoking, alcohol intake, strenuous exercise, body mass index, HRT use, sleep duration
$^c$ adjusted for age, region, happiness, treatment for depression, parity, employment, participation in group activities
$^d$ fully adjusted for age, region, area deprivation, age left school, highest educational qualification, smoking, alcohol intake, strenuous exercise, body mass index, HRT use, sleep duration, happiness, treatment for depression, parity, employment, participation in group activities
First IHD event (n = 30747):
- Adjusted for age and region only: 0.88 (0.85-0.90)
- Fully adjusted: 0.99 (0.96-1.02)

IHD mortality (n = 2148):
- Adjusted for age and region only: 0.55 (0.51-0.61)
- Fully adjusted: 0.72 (0.66-0.80)

Figure 1
### FIRST IHD EVENT

#### Age at baseline
- **< 70 years**
  - Cases: 21541
  - RR (95% CI): 1.00 (0.96-1.03)
- **≥ 70 years**
  - Cases: 9206
  - RR (95% CI): 0.97 (0.92-1.01)
- Test for heterogeneity: *p = 0.3*

#### Region
- **South**
  - Cases: 17133
  - RR (95% CI): 0.99 (0.95-1.02)
- **North**
  - Cases: 13614
  - RR (95% CI): 0.99 (0.95-1.03)
- Test for heterogeneity: *p = 0.8*

#### Deprivation tertile
- **Least deprived areas**
  - Cases: 8397
  - RR (95% CI): 0.95 (0.90-1.01)
- **Middle tertile**
  - Cases: 9501
  - RR (95% CI): 0.98 (0.93-1.03)
- **Most deprived areas**
  - Cases: 12842
  - RR (95% CI): 1.00 (0.96-1.05)
- Test for heterogeneity: *p = 0.3*

#### Smoking status
- **Current**
  - Cases: 6053
  - RR (95% CI): 0.99 (0.93-1.05)
- **Past or never smoker**
  - Cases: 24831
  - RR (95% CI): 0.97 (0.94-1.01)
- Test for heterogeneity: *p = 0.6*

#### Alcohol intake
- **< 7 drinks per week**
  - Cases: 24307
  - RR (95% CI): 0.98 (0.95-1.01)
- **≥ 7 drinks per week**
  - Cases: 6358
  - RR (95% CI): 0.97 (0.91-1.04)
- Test for heterogeneity: *p = 0.9*

#### Body mass index
- **< 25 kg/m²**
  - Cases: 10964
  - RR (95% CI): 0.98 (0.94-1.03)
- **≥ 25 kg/m²**
  - Cases: 19031
  - RR (95% CI): 1.00 (0.96-1.03)
- Test for heterogeneity: *p = 0.7*

#### Happiness
- **Sometimes/rarely/never**
  - Cases: 5878
  - RR (95% CI): 1.02 (0.96-1.08)
- **Usually/most of the time**
  - Cases: 23801
  - RR (95% CI): 0.98 (0.95-1.02)
- Test for heterogeneity: *p = 0.3*

#### Treatment for depression
- **Yes**
  - Cases: 4529
  - RR (95% CI): 0.96 (0.90-1.02)
- **No**
  - Cases: 26216
  - RR (95% CI): 1.00 (0.97-1.03)
- Test for heterogeneity: *p = 0.3*

### IHD MORTALITY

#### Age at baseline
- **< 70 years**
  - Cases: 1317
  - RR (95% CI): 0.70 (0.62-0.79)
- **≥ 70 years**
  - Cases: 831
  - RR (95% CI): 0.75 (0.65-0.88)
- Test for heterogeneity: *p = 0.4*

#### Region
- **South**
  - Cases: 1217
  - RR (95% CI): 0.71 (0.63-0.81)
- **North**
  - Cases: 931
  - RR (95% CI): 0.73 (0.63-0.85)
- Test for heterogeneity: *p = 0.8*

#### Deprivation tertile
- **Least deprived areas**
  - Cases: 484
  - RR (95% CI): 0.68 (0.55-0.84)
- **Middle tertile**
  - Cases: 828
  - RR (95% CI): 0.65 (0.55-0.78)
- **Most deprived areas**
  - Cases: 1027
  - RR (95% CI): 0.77 (0.68-0.88)
- Test for heterogeneity: *p = 0.3*

#### Smoking status
- **Current**
  - Cases: 704
  - RR (95% CI): 0.73 (0.62-0.85)
- **Past or never smoker**
  - Cases: 1433
  - RR (95% CI): 0.71 (0.63-0.80)
- Test for heterogeneity: *p = 0.8*

#### Alcohol intake
- **< 7 drinks per week**
  - Cases: 1741
  - RR (95% CI): 0.72 (0.65-0.80)
- **≥ 7 drinks per week**
  - Cases: 385
  - RR (95% CI): 0.73 (0.57-0.92)
- Test for heterogeneity: *p = 0.9*

#### Body mass index
- **< 25 kg/m²**
  - Cases: 818
  - RR (95% CI): 0.72 (0.62-0.84)
- **≥ 25 kg/m²**
  - Cases: 1259
  - RR (95% CI): 0.72 (0.64-0.82)
- Test for heterogeneity: *p = 0.9*

#### Happiness
- **Sometimes/rarely/never**
  - Cases: 447
  - RR (95% CI): 0.66 (0.54-0.81)
- **Usually/most of the time**
  - Cases: 1559
  - RR (95% CI): 0.75 (0.67-0.84)
- Test for heterogeneity: *p = 0.3*

#### Treatment for depression
- **Yes**
  - Cases: 306
  - RR (95% CI): 0.66 (0.52-0.84)
- **No**
  - Cases: 1842
  - RR (95% CI): 0.74 (0.66-0.82)
- Test for heterogeneity: *p = 0.4*

#### Overall
- **< 70 years**
  - Cases: 2148
  - RR (95% CI): 0.72 (0.66-0.80)
Additional files provided with this submission:

Additional file 1: Final_ADDITIONAL_FILE_1_20131213.docx, 122K
http://www.biomedcentral.com/imedia/1512667626115977/supp1.docx