Marital status and risk of cardiovascular diseases: A systematic review and meta-analysis

Running title: Marital status and risk of cardiovascular disease

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Abstract

Background: The influence of marital status on the incidence of cardiovascular disease (CVD) and prognosis after CVD is inconclusive. We systematically reviewed the literature to determine how marital status influences CVD and prognosis after CVD.

Methods: A search of MEDLINE and EMBASE in January 2018 without language restriction was performed to identify studies that evaluated the association between marital status and risk of CVD. Search terms related to both marital status and CVD were used and included studies had to be prospective in design. The outcomes of interest were CVD, coronary heart disease (CHD) or stroke incidence and mortality. We performed random effects meta-analysis stratified by the types of population by calculating odds ratios and 95% confidence intervals.

Results: Our analysis included thirty-four studies with more than two million participants. Compared to married participants, being unmarried (never married, divorced or widowed) was associated with increased risk of CVD (OR 1.43;95%CI 1.00-2.02), CHD (1.16;1.04-1.28), CHD death (1.43;1.28-1.60) and stroke death (1.55;1.16-2.08). Being divorced was associated with increased risk of CHD ($P<0.001$) for both men and women while widowers were more likely to develop a stroke ($P<0.001$). Single men and women with myocardial infarction had increased mortality (1.42;1.14-1.76) compared to married participants.

Conclusions: Marital status appears to influence CVD and prognosis after CVD. These findings may suggest that marital status should be considered in the risk assessment for CVD and outcomes of CVD based on marital status merits further investigation.

Key Questions:

What is already known about this subject?

- While 80% of the risk for future cardiovascular disease (CVD) can be predicted from known cardiovascular risk factors such as hypertension, smoking and diabetes mellitus, the determinants for the remaining 20% risk remain unclear.
- One factor which may be associated with CVD is marital status and studies have reported inconsistent findings.

What does this study add?

- Our analysis showed that compared to married individuals, being unmarried was associated with increased all cause mortality, coronary heart disease (CHD) and both CHD and stroke mortality in the general population.
- Similarly, we observed a greater risk of death from CHD and stroke in divorced compared to married individuals.
- In the widowed population only stroke incidence was elevated with similar risks in both sexes.

How might this impact on clinical practice?

- These findings may suggest that marital status should be considered in the risk assessment for CVD.

Introduction

Cardiovascular disease (CVD) is associated with significant morbidity and mortality.[1] In order to reduce the burden of CVD, there is great interest in identifying risk factors in the general population so that those deemed to be at high risk for future cardiovascular events can be targeted for intervention. While 80% of the risk for future CVD can be predicted from known cardiovascular risk factors such as old age, male sex, hypertension, hyperlipidaemia, smoking and diabetes mellitus, the determinants for the remaining 20% risk remain unclear.[2]

One factor which may be associated with CVD is marital status and studies have reported inconsistent findings. The benefits of marriage on health and mortality have been demonstrated for both sexes, in different ethnic groups and appear to be independent of various sociodemographic characteristics.[3,4] Better prognosis in married individuals has been reported both after myocardial infarction[3,5-10] and stroke,[11,12] whereas, other studies found no influence of marital status on risk of future CVD.[13-15] In addition, sex differences have been observed where the degree of "protection" conferred from being married in men tends to be greater.[16,17] The interpretation of marital status and CVD becomes more complex with the addition of divorced and widowed groups.[15,18-20]

In view of these disparate findings reported in the literature, we conducted a systematic review and meta-analysis to evaluate the risk of CVD based on marital status and the influence of marital status on prognosis after CVD.

Methods

This systematic review and meta-analysis was conducted and reported according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis.[21]

Eligibility criteria

We selected studies which evaluated cardiovascular events or mortality in participants according to marital status. The included studies had at least two groups (married and unmarried, divorced or widowed) and followed participants for incident cardiovascular events or mortality outcome after incident CVD. Studies of patients with suspected coronary heart disease were also included but not pooled with other studies with myocardial infarction. Only prospective studies published since 2000 were retained for analysis to limit issues related to quality of study reporting and generalisability to contemporary clinical practice. There was no exclusion of studies based on the length of follow up, language of publication or definition of cardiovascular events such as ischaemic heart disease, coronary heart disease, myocardial infarction and stroke. However, we excluded studies of heart failure, retrospective analyses, case-control studies and those studies which did not report the numerical association between marital status and outcome. Reviews were examined for additional studies that met the inclusion criteria.

Search strategy

We searched MEDLINE and EMBASE from 2000 onwards using OVID SP with no date or language restriction. This search was last updated in January 2018. The exact free search terms were (marital status or married or unmarried or widowed or divorced) AND (myocardial infarction or acute coronary syndrome or coronary heart disease or ischaemic heart disease or ischemic heart disease or heart attack or stroke or cerebrovascular disease or

cerebrovascular accident). We checked the bibliography of relevant studies and reviews for additional studies that met the inclusion criteria.

Study selection process and data collection process

Two reviewers (CWW and CSK) independently screened all titles and abstracts retrieved from the search for studies that met the inclusion criteria. The full articles of studies that potentially met the inclusion criteria were reviewed and the final decision to include or exclude was made with the other reviewers. Independent double extractions were performed by two reviewers (CWW and CSK) collecting data on study design, year, country, number of participants, mean age, % male, participant inclusion criteria, comparison groups and results while independent double extractions for quality assessment table were completed by CWW and another reviewer (AN).

Risk of bias assessment

Quality assessment of the studies was conducted based on the recommendations of the Cochrane Handbook for Systematic Review and previous published systematic reviews of observational studies.[22]

Data analysis

We used Review Manager V.5.3.5 (Nordic Cochrane Centre) to conduct random effects meta-analysis stratified by the type of population which were either general population, post stroke or post myocardial infarction and marital status. We used random effects because the studies were conducted in a wide range of settings in different populations, hence the need to take heterogeneity into account for the pooled effect estimate. Where possible, we chose to pool reported adjusted risk estimates from primary studies and when these data were not available, raw data were used to calculate unadjusted risk estimates. We

used the I^2 statistic to assess statistical heterogeneity. I^2 values of 30–60% represent moderate levels of heterogeneity and sensitivity analysis was performed to evaluate analyses with high statistical heterogeneity. Publication bias was assessed by asymmetry testing with funnel plots if there is no evidence of significant heterogeneity.[23] Further subgroup analyses were performed to investigate the impact of sex differences combined with marital status on various cardiovascular outcomes. Further analyses were also performed with the exclusion of studies with unclear marital status ascertainment and another with the exclusion of studies with only crude results or unadjusted results available.

Results

Description of studies included in analysis

The process of study selection is shown in Figure 1. After screening, 32 studies were retained for inclusion and 2 additional studies were identified from a review yielding a total of 34 studies for analysis. Table 1 summarises the study designs and participant characteristics. These 34 studies, which took place in various countries including Russia, Denmark, Spain, USA, Sweden, UK, Canada, Israel, Gulf States, Japan, Finland, Greece, Turkey, Norway and China between 1963 and 2015. The follow-up period from these studies ranged from 30 days to 34 years. There were a total of 2,174,437 participants (ranging from 135 to 734,626 participants). Data on age is available for 1,137,571 participants from 25 studies with a mean of 58.4 year (range 42 to 77 years). The definition of unmarried used in each study is presented in Supplementary Table 1.

Quality assessment of included studies

The quality assessment of included studies is summarised in Supplementary Table 2. 24 studies were found to have used reliable methods for ascertaining the marital status which involved utilising databases, [7,11,14-16,20,24,25] questionnaires, [2,9,13,17,18,26-29] and

interviews. [9,12,19,25,30-34] Reliable outcome ascertainment was found in 25 studies either from databases, [6,7,11,13-18,20,24,25,28-30,32,33,35-37] medical records, [6,7,13,16,17,30,31,34] or assessment by healthcare professionals or research teams. [2,18,19,29] 18 studies reported a low rate of loss to follow-up of <10%. [2,6,7,9,13-15,17-20,24,29,30,32-34] 29 studies included adjusted analyses, [3,6,7,8,10,13-20,24-27,29,31,33-38] 3 studies included unadjusted analysis [9,11,12] and 5 studies had only crude results available.[2,32,34,39,40]. For assessment of publication bias, the funnel plots conducted showed no significant asymmetry in the pattern of distribution of studies (Supplementary figures 1-14).

Pooled analysis of marital status and cardiovascular outcomes

Mortality in general population

The results for the general population as well a by gender are summarised in Table 2, Table 3, Table 4, Supplementary Table 2 and Supplementary Figures 1-2 and 4-13. Compared to married participants, unmarried participants were more likely to die from both CHD (OR 1.43 95% CI 1.28-1.60, I^2=57%, P<0.001, n=5) and stroke (OR 1.55 95% CI 1.16-2.08, I^2= 0%, P=0.003, n=2). (Figure 2A).

Being divorced was associated with an increased risk of CHD mortality (OR 1.33 95% CI 1.04-1.70, I^2=0%, n=3) (Supplementary Figure 4) and stroke mortality (OR 2.33 95% CI 1.11-4.89, I^2=0%, P=0.03, n=1) (Supplementary Figure 6). Widowed participants of either sex in these studies did not have increased CHD mortality or stroke mortality (Supplementary Figures 5 and 7).

Cardiovascular risks in general population

Unmarried participants were 1.4 times more likely to develop CVD (OR 1.42 95% CI 1.00-2.01, P=0.05, n=1) (Figure 3C) with a slight increase in the risk of developing CHD (OR 1.16 95% CI 1.04-1.28, I^2=69%, P=0.006, n=8) (Figure 3A) but no difference was observed for incident stroke (P=0.15, n=4) compared to married participants (Figure 3B).

Results for divorced and widowed patients is shown in Table 3. Being divorced in both sexes were 1.3 times more likely to develop CHD (OR 1.35 95% CI 1.20-1.53, I^2=0%, P<0.001, n=3) (Supplementary Figure 10) with slight increase in incident stroke risk (OR 1.15 95% CI 1.01-1.29, I^2=53% P=0.02, n=4) (Supplementary Figure 12). In contrast, widowed participants were more likely to develop a stroke (OR 1.16 95% CI 1.09-1.23, I^2=0%, P<0.001, n=4) (Supplementary Figure 13) but not CHD (P=0.07, n=1) (Supplementary Figure 11).

Mortality in CVD population (MI and stroke)

Results for participants with CVD, for the whole population and stratified by gender are summarised in Figure 4 and Table 4. Mortality was significantly higher for unmarried patients who sustained a myocardial infarction (OR 1.42 95% CI 1.14-1.76, I^2=83%, P<0.002, n=11) (Figure 4A). Being divorced is not associated with increased mortality after MI (P=0.13, n=3) (Figure 4B). For widowed participants, the increased risk of death post-MI was almost 1.7 times (OR 1.68 95% CI 1.30-2.17, I^2=85%, P<0.001, n=4) (Figure 4C).

After a stroke, there was no difference in mortality between unmarried and married participants (P=0.47, n=3) (Supplementary Figure 14).

Mortality in post-cardiac catheterization population

In the post-cardiac catheterization population consisting of a heterogeneous cohort of patients under elective investigation for possible coronary artery disease or acutely following

a myocardial infarction, there was no significant difference in all-cause mortality in the unmarried, divorced and widowed groups when compared to married participants with adjusted Hazard Ratio (aHR) 1.14 95%CI 0.95-1.37; aHR 1.23 95%CI 0.98-1.55; aHR 1.24 95%CI 0.99-1.54, respectively. Both the unmarried and widowed participants were at increased risk of cardiovascular death; corresponding aHR 1.33 95%CI 1.06-1.68 and aHR 1.62 95%CI 1.23-2.13, respectively but the risk was not significant in divorced participants aHR 1.27 95% CI 0.95-1.69.

Discussion

To the best of our knowledge, this is the first evidence synthesis to quantify the evidence base using meta-analysis to evaluate the relationship between marital status and cardiovascular disease. Our analysis showed that compared to married individuals, being unmarried was associated with increased CHD and both CHD and stroke mortality in the general population. Similarly, we observed a greater risk of death from CHD and stroke in divorced compared to married individuals. Finally, in the widowed population only stroke incidence was elevated with similar risks in both sexes. Our analysis also describes important differences in prognosis with regard to mortality according to marital status in patients with incident cardiovascular disease. In participants who suffered a myocardial infarction, being unmarried was associated with greater odds of mortality compared to a married individual, with a non-significant trend in widowed or divorced individuals. In our analysis, no significant gender effect was observed for any risks of developing CVD and death from CVD in any groups of participants., although differences in total mortality were noted.

We have built upon the current understanding of marital status and adverse outcomes in several ways. Firstly, a previous meta-analysis of 53 studies demonstrated higher all-cause mortality in never married, divorced and widowed married versus married individuals[41] but

the study did not explore any specific causes of death or cardiovascular disease. A more recent review published by Manfredini et al describes the improved health status and reduced cardiovascular risk with married status but it did not quantify the relationships with meta-analysis.[42] Our updated review with 34 studies has built upon the findings of these reviews to quantify the relationship between marital status and CVD whilst considering unmarried, divorced and the widowed status of the populations assessed.

Several mechanisms have been suggested to account for the observed protective effect of marital status on CVD especially in men. Social causation theory suggests that individuals benefit from spousal support.[43] For example living with another person allows earlier recognition and response to warning symptoms[16,25] especially if a myocardial infarction becomes instantly disabling.[25] Studies have reported that unmarried patients had longer delays in seeking medical help[7,8,16,44] and longer total ischaemic times[44] which directly influences both the timing and proportion of participants being treated with either thrombolysis or invasive cardiac procedures that reduce mortality.[7,8] In addition, spouses, particularly wives encourage concordant health behaviour such as a healthy lifestyle[13,16,19,45] and adherence to treatment[5,13,16,19,45] that promote cardiovascular health. In contrast, marital dissolution is noted to affect the health behaviour mentioned above negatively.[29] Moreover, Wu et al reported that compared with married individuals, unmarried individuals were twice more likely to be non-adherent to their prescribed medications which was the strongest predictor of better outcome in their study.[45] There are greater financial resources especially in households with a dual income making better health care more accessible.[13,16,30] Furthermore, one of the benefits of being married or with a partner may be increased participation in cardiac rehabilitation which improves outcomes after cardiovascular disease.[46]

Stress-related theory suggests that partner loss or poor-quality relationships may have a negative impact on the economic, behavioural and emotional wellbeing of an individual which may reduce one's ability to prevent, detect and treat illness.[33] Biologically, stress may ultimately worsen cardiovascular risk factors such as hypertension, reduced heart rate variability, impaired vagal tone, hyperlipidemia, diabetes and the progression of atherosclerosis.[9,29,32] The buffering hypothesis suggests that informational or emotional resources from a spouse promote adaptive behaviour and may reduce excessive neuroendocrine response to acute or chronic stressors.[17,35] This translates into decrease in progression of atherosclerosis and other pathological processes thus reducing the risk of CVD.

Furthermore, selection theory has been introduced which assumes that individuals with poor health are less likely to establish or maintain long-term relationship such as marriage.[5,33] Also, Floud et al suggested the possibility that healthy women may be less likely to divorce,[13] although Akimova et al reported that divorced and single women were more highly educated and had a higher qualified occupation which results in greater financial independence and better quality of life.[35]

In widowed populations, there is less variation in CVD and mortality risk between sexes with some studies showing women did more poorly than men. Vujcic et al showed that the proportion of women who lived alone increased with age while the proportion of men who lived alone decreased with age.[9] Possible explanations include women tend to be younger than their husbands and have a longer life expectancy.[9] Thus, it is postulated that widowed women tend to be older and more support is needed to meet their healthcare requirement. This study has several strengths and limitations. This is the largest study to date with a sample size of 2,174,437 compared to the smaller sample sizes of previous reviews.[41,42] We were able to quantify the risk with meta-analysis which was not performed in the previous studies.[42] In terms of generalisability, the current review

included populations from various age groups, ethnicities and geographic locations making the findings generalisable to different populations. We used a comprehensive search strategy of the literature and excluded case-control and retrospective studies to reduce the possibility of bias. Finally, results with the greatest extent of adjustments were used for the analysis in this study.

The major limitation of this study is the inconsistent variable adjustments across studies, which poses a risk of confounding. Adjustment for cardiovascular risk factors was often incomplete in many of the studies analysed, which may have influenced our result. In addition, this review is not an individual patient meta-analysis so information is solely derived from published material. The lack of information on same-sex spouses and quality of marriage limit further insight into the impact of marriage. Moreover, heterogeneity exists across studies in terms of study methodology. For example, the definition of CVD varied across the studies and the follow up period was inconsistent with some long-term studies (>15 years of follow up) where management might have changed over time.[7,19,20,30,36,37]

Future work should focus on whether marital status is a surrogate marker of other adverse health behaviour or cardiovascular risk profiles that underlies our reported findings and whether targeted interventions should focus on such high-risk groups. The association between cohabitation/living with someone and CVD should be explored as it may be a confounding factor in this study. In Quinones et al, the replacement of marital status with cohabitation yielded the same protective effect although slightly less pronounced.[33] Fournier et al suggested that having information of “living alone” versus “living with someone” instead of married versus not married would have been more useful.[43]

In conclusion, being married appears to be associated a lower cardiovascular mortality and incidence of CVD in a general population and mortality after myocardial infarction. Sex differences were also noted where men who were unmarried showed a higher

risk compared to women. While current evidence may demonstrate an association between marital status and mortality and CVD, lack of social support might be a mitigating factor. Future research should focus around whether marital status is a surrogate marker for other adverse health behaviour or cardiovascular risk profiles that underlies our reported findings, or whether marital status should be considered as a risk factor by itself.

Contributorship

MAM and CSK conceived and planned the study. CSK and CWW performed the search for relevant studies. Data was screened, extracted and analyzed by CSK and CWW. CWW wrote the first draft of the paper. All authors contributed to the interpretation of the findings and critically revised it for intellectual content.

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Competing Interests

None.

List of Tables and Figures

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Supplementary Figure 5. Forest plot of CHD death in widowed vs married in general population and funnel plot

Supplementary Figure 6. Forest plot of stroke death in divorced vs married in general population and funnel plot

Supplementary Figure 7. Forest plot of stroke death in widowed vs married in general population and funnel plot

Supplementary Figure 8. Forest plot of CVD death in divorced vs married in general population and funnel plot

Supplementary Figure 9. Forest plot of CVD death in widowed vs married in general population and funnel plot

Supplementary Figure 10. Forest plot of CHD events in divorced vs married in general population and funnel plot

Supplementary Figure 11. Forest plot of CHD events in widowed vs married in general population and funnel plot

Supplementary Figure 12. Forest plot of stroke events in divorced vs married in general population and funnel plot

Supplementary Figure 13. Forest plot of stroke events in widowed vs married in general population and funnel plot

Supplementary Figure 14. Forest plot of post stroke death in unmarried vs married and funnel plot

Table 1: Study design and participant characteristics

Study ID	Study design; Country; Design	Total participants	Mean age	% Male	Inclusion criteria
Akimova 2014[35]	Prospective cohort study; Russia; 1996-2008	1,609	-	49.4	Participants were Tyumen citizens aged 25-64 years.
Andersen 2011[11]	Prospective cohort study; Denmark; 2000-2007	26,818	71.2	51.5	Participants were patients with first-ever ischaemic stroke admission aged 18 and above in the Danish National Indicator Project.
Bell 2013[26]	Post-hoc analysis of trial and cohort study; US; 1993-2010	3,173	Mean age at stroke was 72.6	0	Participants were post-menopausal women aged 50-79, who were stroke-free at baseline with incident stroke prior to 2005 in the Women's Health Initiative trial.
Consuegra-Sanchez 2015[6]	Prospective cohort study; Spain; 1998-2013	7,408	66.1	73.3	Participants were patients with acute MI aged 18 and above who were admitted to Coronary Care Unit of two hospitals in the Murcia region within 24 hours.
Dupre 2015[19]	Prospective cohort study; USA; 1992-2010	15,827	54.3	45.9	Participants were ever married adults aged 45-80 years in the Health and Retirement Study.
Dupre 2016[30]	Prospective cohort study; USA; 1992-2010	2,197	69.5	55.1	Participants had MI during the follow up period in the Health and Retirement Study.
Eaker 2007[31]	Prospective cohort study; USA; 1971-1987	3,682	48.5	48.1	Participants were in the Framingham Offspring Study, consisting of the offspring (and their spouses) of the Framingham Heart Study Original Cohort, enrolled in 1971 to 1974.
Engstrom 2000[14]	Prospective cohort study; Sweden; 1977-1994	9,351	48.5	0	Participants were women aged 28-55 years who attended the health examination programme at the Department of Preventive Medicine in Malmo.
Engstrom 2004[28]	Prospective cohort study; Sweden; 1990-2000	118,134	60	44.8	Participants were individuals aged between 40-89 years in Malmo, Sweden.
Engstrom 2006[20]	Prospective cohort study; Sweden; 1974-1997	6,075	46.8	100	Participants were men without history of MI, stroke or cancer aged 28-61 years in Malmo, Sweden.
Floud 2014[13]	Prospective study; UK; 1996-2011	734,626	59.7	0	Participants were women without history of heart disease or stroke in the Million Women Study.
Gerward 2010[7]	Prospective cohort study; Sweden; 1974-2004	3,542	-	85.7	Participants were individuals aged 27-61 years without history of MI in the Malmo Preventive Project.
Ghosh-Swaby 2016[38]	Prospective cohort study; Canada; Published in 2016	2,100	-	-	Participants had PCI after MI in the Canadian Observational Antiplatelet Study.
Golbourt 2010[36]	Prospective cohort study; Israel; 1963-1997	10,059	49.2	100	Participants were male civil servants and municipal employees in the Israeli Ischaemic Heart Disease study.
Hadi 2012[8]	Prospective cohort study; Gulf States; 2008-2009	5,334	56.8	79.0	Participants were post-ACS patients in the 2nd Gulf Registry of Acute Coronary Events.
Ikeda 2009[17]	Prospective cohort study; Japan; 1990-2004	90,987	51.9	47.7	Participants were Japan residents aged 40-69 years in the first and second cohort of the Japan Public health Centre-based Prospective Study.
Janzon 2004[24]	Prospective cohort study; Sweden; 1977-1998	10,621	49.6	0	Participants were women without history of MI or stroke aged between 28-58 in Malmo, Sweden.
Jayaram 2013[39]	Prospective cohort study; US; 2003-2008	4,853	50 to 80	66.7	Participants were post-acute MI patients aged 50 to 80 years from 31 USA sites.
Kilpi 2015[16]	Prospective cohort study;	299,281	-	49.4	Participants were individuals aged above 15 years in Finland.

	Finland; 1987-2007				
Kriegbaum 2008[15]	Prospective cohort study; Denmark; 1980-2005	8,865	28 to 39	100	Participants were men born in Copenhagen in 1953 and living in Denmark in 1968.
Malyutina 2004[18]	Prospective cohort study; Russia; 1984-1998	11, 404	25 to 64	56.9	Participants were residents in Novosibirsk aged 25-64 years in the WHO MONICA Project.
Maselko 2009[31]	Prospective cohort study; USA; 1992-2006	22,818	63.9	56	Participants were individuals born between 1900-1947 aged 50 years or above without history of stroke in the Health and Retirement Study.
Matthews 2002[29]	Post-hoc analysis of clinical trial; USA; Published in 2002	10,904	46.4	100	Participants were men without definite evidence of clinical CHD but with above-average risk for death due to CHD because of high blood pressure, elevated serum cholesterol levels, and/or cigarette smoking in the Multiple Risk Factor Intervention Trial.
Orth-Gomer 2000[32]	Prospective cohort study; Sweden; 1991-1997	292	55.8	0	Participants were female acute MI or unstable angina patients aged 30-65 years in the Stockholm Female Coronary Risk Study.
Panagiotakos 2008[3]	Prospective cohort study; Greece; 2003-2004	2,090	66.7	75.9	Participants were patients hospitalized with ACS in the GREECS study.
Quinones 2014[33]	Prospective cohort study; Germany; 2000-2010	3,766	28 to 74	75.4	Participants were patients with first episode of MI in Germany who survived longer than 28 days in the MONICA/KORA-myocardial infarction registry.
Samanci 2004[12]	Prospective cohort study; Turkey; 1995-2001	147	62.6	53	Participants were patients with first ischaemic stroke aged 18 and above who were admitted to Akdeniz University hospital.
Schultz 2017[34]	Prospective cohort study; US; 2003-2015	6,051	63	64	Participants were patients who underwent cardiac catheterization for suspected or known coronary artery disease in the Emory Cardiovascular Biobank.
Sorlie 2004[25]	Prospective cohort study; US; 1973-1989	Approximately 700,000	≥25	-	Participants were individuals aged 25 and above in the US National Longitudinal Mortality Study.
Strand 2004[37]	Prospective cohort study; Norway; 1974-2000	44,684	42	50.8	Participants were individuals without history of heart disease aged 35 to 49 years in Norway.
Vujcic 2014[9]	Prospective cohort study; Belgrade; 2002-2011	135	57.8	75.6	Participants were patients admitted to coronary care unit of Institute of Cardiovascular Diseases, Clinical Centre of Serbia due to MI.
Wolinsky 2009[40]	Prospective cohort study; USA; 1993-2005	5,511	77	38	Participants were individuals aged 70 and above in the Survey on Assets and Health Dynamics among the Oldest Old.
Xie 2016[2]	Prospective cohort study; China; 2002-2012	1,739	57.7	35.8	Participants were individuals from 11 villages in Beijing drawn from the original cohort of the People's Republic of China-United States of America Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology.
Yokoyama 2014[10]	Prospective cohort study; Japan; Published in 2014	354	63	100	Participants were men who had acute MI.

Table 2: Follow up and results

Study ID	Population	Follow up	Results
Akimova 2014[35]	General population.	12 years.	CV mortality in men vs married: lonely aOR 4.08 (2.17-7.80) vs widowed aOR 3.19 (1.22-8.34) vs divorced aOR 3.18 (1.90-5.34). CV mortality in women vs married: lonely aOR 0.17 (0.01-1.09) vs widowed aOR 0.37 (0.10-1.04) vs divorced aOR 0.17 (0.03-0.84). CV mortality in men vs not married: married aOR 0.28 (0.18-0.44). CV mortality in women compared to not married: married aOR 3.21 (1.28-8.06).
Andersen 2011[11]	Post-ischaemic stroke.	30 day and 1 year.	All-cause mortality for single vs living with someone: 30 day mortality OR 1.02 (0.78-1.35), 1 year OR 1.14 (0.96-1.34).
Bell 2013[26]	Post-stroke.	12-17 years.	Mortality in not married vs married: aHR 0.95 (0.77-1.16).
Consuegra-Sanchez 2015[6]	Post-MI.	Median 6.1 years.	All-cause mortality in widowed vs married: aHR 1.29 (1.13-1.47). All-cause mortality in single vs married: aHR 1.04 (0.79-1.35). All-cause mortality in divorced vs married: aHR 0.84 (0.43-1.38).
Dupre 2015[19]	General population.	18 years.	Acute MI in men vs continuously married: divorced aHR 1.27 (0.98-1.65), remarried aHR 1.13 (0.96-1.34). Acute MI in women compared to continuously married: divorced aHR 1.36 (1.04-1.78), remarried aHR 1.35 (1.07-1.70).
Dupre 2016[30]	Post-MI.	18 years.	Crude results only see Online Supplements.
Eaker 2007[31]	General population.	10 years.	Incident CHD in men in married vs not married: aRR 0.92 (0.51-1.65). Incident CHD in women in married vs not married: aRR 0.85 (0.43-1.70). Mortality in men in married vs not married: aRR 0.54 (0.35-0.83). Mortality in women in married vs not married: aRR 1.04 (0.62-1.74).
Engstrom 2000[14]	General population.	10.7 years.	Cardiac events in single vs married: aHR 1.05 (0.69-1.6).
Engstrom 2004[28]	General population.	>10 years.	Stroke incidence in men vs married: divorced aRR 1.29 (1.15-1.44), widowed aRR 1.13 (0.99-1.28), never married aRR 0.89 (0.77-1.02). Stroke incidence in women vs married: divorced aRR 1.22 (1.09-1.37), widowed aRR 1.13 (1.02-1.24), never married has no result.
Engstrom 2006[20]	General population	18.7 years.	Coronary events vs married: never married aRR 1.29 (1.00-1.7), divorced aRR 1.51 (1.2-1.9), widowed aRR 1.78 (0.94-3.3). Stroke vs married: never married aRR 1.25 (0.8-1.9), divorced aRR 1.44 (0.98-2.1), widowed aRR 1.18 (0.3-4.8).
Floud 2014[13]	General population.	8.8 years.	IHD in partnered vs not partnered women: aRR 0.99 (0.96-1.02). IHD mortality in partnered vs not partnered women: aRR 0.72 (0.66-0.80).
Gerward 2010[7]	Post-coronary event.	21 years.	Mortality post coronary event in men vs married: never married aOR 2.14 (1.63-2.81), divorced aOR 1.91 (1.50-2.43), widowed aOR 1.49 (0.77-2.89). Mortality post coronary event in women vs married: never married aOR 2.32 (0.93-5.81), divorced aOR 1.87 (1.04-3.36), widowed aOR 2.74 (1.03-7.28).
Ghosh-Swaby 2016[38]	Post-MI.	15 months.	Mortality vs married/common law and living together: never married aOR 1.09 (0.30-3.91), separated/divorced/widowed aOR 0.64 (0.24-1.68). MACE vs married/common law and living together: never married aOR 1.31 (0.79-2.16), separated/divorced/widowed aOR 0.77 (0.50-1.23). MI vs married/common law and living together: never married aOR 1.51 (0.68-3.38), separated/divorced/widowed aOR 1.02 (0.49-2.16). Stroke vs married/common law and living together: never married aOR 4.06 (0.91-18.14), separated/divorced/widowed aOR 0.60 (0.10-3.49).
Golbourt 2010[36]	Male working adults.	34 years.	Fatal stroke in unmarried vs married men: aHR 1.64 (1.18-2.30).
Hadi 2012[8]	Post-ACS.	1 year.	In-hospital mortality vs married: single aOR 1.35 (0.46-3.99), widowed aOR 1.97 (1.23-3.18).
Ikeda 2009[17]	General population.	Median 11 years.	CHD in men for alone vs spouse: aHR 1.23 (0.74-2.02). CHD mortality in men for alone vs spouse: aHR 1.43 (0.73-2.81). All-cause mortality in men for alone vs spouse: aHR 1.47 (1.26-1.72). CHD in women for alone vs spouse: aHR 1.77 (0.92-3.39). CHD mortality in women for alone vs spouse: aHR 2.72 (1.37-5.38). All-cause mortality in women for alone vs spouse: aHR 1.09 (0.92-1.31).
Janzon 2004[24]	General population.	14 years.	Cardiac events in women not married vs married never smoked: never smoked aRR 0.8 (0.4-1.7), ex-smoker aRR 1.5 (0.7-3.3) and current smokers aRR 5.0 (3.3-7.6). Cardiac events in women married vs married never smoked: ex-smoker aRR 1.4 (0.8-2.4), current smoker aRR 4.7 (3.2-6.9).
Jayaram 2013[39]	Post-MI.	2 years.	Crude results only see Online Supplements.
Kilpi 2015[16]	General	12 years.	MI events vs marital partner in men: cohabitation aHR 1.16 (1.04-1.30), living with others aHR 1.10 (0.99-1.21), living alone aHR 1.18 (1.08-

	population.		1.28). MI events vs marital partner in women: cohabitation aHR 1.08 (0.85-1.37), living with others aHR 1.19 (0.97-1.45), living alone aHR 1.16 (0.99-1.36). Mortality in MI vs marital partner in men: cohabitation aHR 1.07 (0.86-1.33), living with others aHR 1.80 (1.46-2.23), living alone aHR 1.50 (1.29-1.75). Mortality in MI vs marital partner in women: cohabitation aHR 2.00 (1.26-3.17), living with others aHR 1.11 (0.75-1.64), living alone aHR 1.06 (0.80-1.40).
Kriegbaum 2008[15]	General population.	12 years.	IHD in men vs cohabitant: never cohabitant aHR 0.89 (0.62-1.30), broken partnership aHR 1.28 (1.03-1.58).
Malyutina 2004[18]	General population.	10.3 years.	All-cause mortality in men vs married: non-married aRR 1.28 (1.00-1.64), single aRR 1.36 (0.87-2.11), divorced aRR 1.43 (1.02-2.00), widowed aRR 0.87 (0.50-1.52). CVD mortality in men vs married: non-married aRR 1.22 (0.84-1.77), single aRR 0.89 (0.38-2.01), divorced aRR 1.78 (1.13-2.82), widowed aRR 0.61 (0.25-1.50). CHD mortality in men vs married: non-married aRR 1.20 (0.74-1.95), single aRR 0.62 (0.19-1.99), divorced aRR 1.84 (1.04-3.26), widowed aRR 0.77 (0.24-2.44). Stroke mortality in men vs married: non-married aRR 1.19 (0.56-2.49), single aRR 0.81 (0.11-5.85), divorced aRR 2.40 (1.03-5.58). All-cause mortality in women vs married: non-married aRR 1.37 (0.92-2.04), single aRR 0.99 (0.31-3.18), divorced aRR 1.86 (1.07-3.24), widowed aRR 1.16 (0.70-1.93). CVD mortality in women vs married: non-married aRR 1.15 (0.67-1.97), single aRR 0.62 (0.08-4.59), divorced aRR 1.41 (0.63-3.18), widowed aRR 1.05 (0.54-2.04). CHD mortality in women vs married: non-married aRR 1.14 (0.55-2.39), single aRR 1.25 (0.16-9.55), divorced aRR 1.44 (0.49-4.26), widowed aRR 1.00 (0.40-2.50). Stroke mortality in women vs married: non-married aRR 1.52 (0.53-4.33), divorced aRR 2.11 (0.45-9.82), widowed aRR 1.44 (0.42-4.90).
Maselko 2009[31]	General population.	9.4 years.	Incident stroke in men vs married: divorced/separated aHR 1.01 (0.79-1.29), never married aHR 1.15 (0.80-1.67), widowed aHR 1.23 (0.99-1.53). Incident stroke in women vs married: divorced/separated aHR 0.95 (0.77-1.16), never married aHR 1.27 (0.95-1.69), widowed aHR 1.11 (0.97-1.28).
Matthews 2002[29]	General population.	9 years.	Mortality vs married: separated aRR 1.24 (0.98-1.57), divorced aRR 1.37 (1.09-1.72). Cardiovascular mortality vs married: separated aRR 1.43 (1.05-1.96), divorced aRR 1.40 (1.01-1.92). CHD mortality vs married: separated aRR 1.02 (0.67-1.57), divorced aRR 1.66 (1.17-2.36). MI mortality compared to married: separated aRR 1.31 (0.76-2.26), divorced aRR 1.15 (0.64-2.06).
Orth-Gomer 2000[32]	Post-ACS.	5 years.	Crude results only see Online Supplements.
Panagiotakos 2008[3]	Post-ACS.	30 days.	Mortality vs married: never married aOR 2.70 (1.82-3.99), widowed/divorced aOR 1.21 (0.42-3.53). CVD compared to married: never married aOR 1.07 (0.41-2.82), widowed/divorced aOR 1.21 (0.42-3.53).
Quinones 2014[33]	Post-MI.	Median 5.3 years.	Mortality in married vs not married: aHR 0.83 (0.68-1.01).
Samanci 2004[12]	Post-stoke.	1 year.	Mortality in single/widowed vs married: OR 2.03 (1.22-8.51).
Schultz 2017[34]	Post-cardiac catheterisation or CHD.	Median 3.7 years.	Mortality vs married: unmarried aHR 1.14 (0.95-1.37), divorced aHR 1.23 (0.98-1.55), widowed aHR 1.24 (0.99-1.54). Cardiovascular death vs married: unmarried aHR 1.33 (1.06-1.68), divorced aHR 1.27 (0.95-1.69), widowed aHR 1.62 (1.23-2.13). Cardiovascular death and MI vs married: unmarried aHR 1.46 (1.22-1.76), divorced aHR 1.41 (1.10-1.81), widowed aHR 1.71 (1.32-2.20).
Sorlie 2004[25]	General population.	Up to 11 years.	Out-of-hospital all-cause death in not married vs married: aOR 1.33 (1.28-1.38). Out-of-hospital CHD death in not married vs married: aOR 1.60 (1.50-1.71).
Strand 2004[37]	General population.	23.6 years.	IHD death in men vs married: not married aRR 1.28 (1.12-1.46), divorced/separated aRR 1.21 (0.84-1.76), widowed aRR 0.28 (0.07-1.14). IHD death in women vs married: not married aRR 1.33 (0.85-2.09), divorced/separated aRR 1.35 (0.69-2.63), widowed aRR 0.87 (0.43-1.76).
Vujcic 2014[9]	Post-MI.	Median 77 months.	Mortality in others vs married: OR 2.38 (1.14-4.98). Mortality in living alone vs not alone: aOR 7.60 (1.99-29.08).
Wolinsky 2009[40]	Elderly population.	12 years.	Crude results only see Online Supplements.
Xie 2016[2]	General population.	10 years.	Crude results only see Online Supplements.

Yokoyama 2014[10]	Post-MI.	1.7 years.	Mortality unmarried vs married: aHR 3.84 (1.22-10.2).

MI=myocardial infarction, ACS=acute coronary syndrome, CHD=coronary heart disease, IHD=ischaemic heart disease, CV=cardiovascular, CVD=cardiovascular disease, PCI=percutaneous coronary intervention

Table 3. Risk of adverse outcomes considering marital status in general population

Outcome	Marital status and subgroups	Studies	No. of participants (Not applicable, [NA] for studies with no crude result available)	Risk Ratio [95% CI]	Overall effect, P value	Heterogeneity, I^2	Subgroup differences between men only and women only (P value, I^2)
CHD death	Unmarried vs married						
	All	5	>766272 (2 NA)	1.43 [1.28, 1.60]	<0.001	57%	
	Men only	3	>16137 (1 NA)	1.28 [1.13, 1.45]	<0.001	0%	0.35, 0%
	Women only	4	>750135 (1 NA)	1.44 [1.16, 1.78]	<0.001	25%	
	Men and women	1	NA	1.60 [1.50, 1.71]	<0.001	-	
	Divorced vs married						
	All	3	>10378 (2 NA)	1.33 [1.04, 1.70]	0.02	0%	
	Men only	3	>6139 (2 NA)	1.32 [1.00, 1.73]	0.05	0%	0.90, 0%
	Women only	2	>4239 (1 NA)	1.37 [0.78, 2.43]	0.27	0%	
	Widowed vs married						
	All	2	>10105 (1 NA)	0.78 [0.48, 1.25]	0.29	0%	
	Men only	2	>5940 (1 NA)	0.50 [0.19, 1.34]	0.17	16%	0.30, 8.7%
	Women only	2	>4165 (1 NA)	0.92 [0.52, 1.60]	0.76	0%	
	Separated vs married						
	Men only	1	10330	1.31 [0.76, 2.26]	0.33	-	
Stroke death	Unmarried vs married						
	All	2	>11404 (1 NA)	1.55 [1.16, 2.08]	0.003	0%	
	Men only	2	>6485 (1 NA)	1.55 [1.15, 2.11]	0.005	0%	0.97, 0%
	Women only	1	4919	1.52 [0.53, 4.34]	0.43	-	
	Divorced vs married						
	All	1	10724	2.33 [1.11, 4.89]	0.03	0%	
	Men only	1	6485	2.40 [1.03, 5.59]	0.04	-	0.89, 0%
	Women only	1	4239	2.11 [0.45, 9.86]	0.34	-	
	Widowed vs married						

	All	1	10105	1.09 [0.39, 3.09]	0.86	0%	
	Men only	1	5940	0.55 [0.08, 3.85]	0.55		0.41, 0%
	Women only	1	4165	1.44 [0.42, 4.92]	0.56	-	
CVD death	Unmarried vs married						
	All	2	>11404 (1 NA)	1.20 [0.55, 2.65]	0.65	89%	
	Men only	2	>6485 (1 NA)	2.07 [0.72, 5.94]	0.17	92%	0.16, 49.4%
	Women only	2	>4919 (1 NA)	0.63 [0.18, 2.26]	0.48	83%	
	Divorced vs married						
	All	3	>20769 (1 NA)	1.56 [0.95, 2.56]	0.08	73%	
	Men only	3	>16530 (1 NA)	1.93 [1.22, 3.06]	0.005	71%	0.25, 24.7%
	Women only	2	>4239 (1 NA)	0.56 [0.07, 4.37]	0.58	80%	
	Widowed vs married						
	All	2	>10105 (1 NA)	0.96 [0.43, 2.16]	0.93	69%	
	Men only	2	>5940 (1 NA)	1.38 [0.27, 6.99]	0.70	84%	0.48, 0%
	Women only	2	>4165 (1 NA)	0.70 [0.26, 1.90]	0.48	57%	
	Separated vs married						
	Men only	1	10330	1.43 [1.05, 1.95]	0.02	-	
All-cause mortality	Unmarried vs married						
	All	4	>33145 (2 NA)	1.31 [1.19, 1.45]	<0.001	42%	
	Men only	3	>16137 (1 NA)	1.45 [1.26, 1.66]	<0.001	11%	0.01, 83.3%
	Women only	3	>17008 (1 NA)	1.12 [0.96, 1.30]	0.16	0%	
	Men and women	1	NA	1.33 [1.28, 1.38]	<0.001	-	
	Divorced vs married						
	All	2	>10378 (1 NA)	1.43 [1.20, 1.71]	<0.001	0%	
	Men only	2	>6139 (1 NA)	1.39 [1.15, 1.68]	<0.001	0%	0.33, 0%
	Women only	1	4239	1.86 [1.07, 3.24]	0.03	-	
	Widowed vs married						
	All	1	10105	1.02 [0.70, 1.48]	0.93	0%	
	Men only	1	5940	0.87 [0.50, 1.52]	0.62	-	0.45, 0%
	Women only	1	4165	1.16 [0.70, 1.93]	0.57	-	
	Separated vs married						

	Men only	1	NA	1.24 [0.98, 1.57]	0.07	-	
CVD events	Unmarried vs married						
	Men and women	1	1739	1.42 [1.00, 2.01]	0.05	-	
CHD events	Unmarried vs married						
	All	8	>1011397 (2 NA)	1.16 [1.04, 1.28]	0.006	69%	
	Men only	5	>134152 (2 NA)	1.21 [1.14, 1.30]	<0.001	0%	0.20, 40.2%
	Women only	5	>867894 (2 NA)	1.10 [0.96, 1.26]	0.19	41%	
	Men and women	1	9351	1.05 [0.69, 1.60]	0.82	-	
	Divorced vs married						
	All	3	>12812 (1 NA)	1.35 [1.20, 1.53]	<0.001	0%	
	Men only	3	>5389 (1 NA)	1.35 [1.18, 1.55]	<0.001	0%	0.97, 0%
	Women only	1	NA	1.36 [1.04, 1.78]	0.02	-	
	Widowed vs married						
	Men only	1	4754	1.78 [0.95, 3.34]	0.07	-	
	Remarried vs married						
	All	1	NA	1.21 [1.02, 1.44]	0.03	33%	
	Men only	1	NA	1.13 [0.96, 1.34]	0.15	-	0.22, 33.1%
	Women only	1	NA	1.35 [1.07, 1.70]	0.01	-	
Stroke events	Unmarried vs married						
	All	4	>19829 (2 NA)	1.23 [0.93, 1.63]	0.15	78%	
	Men only	3	>8640 (2 NA)	1.01 [0.81, 1.26]	0.93	41%	0.21, 35%
	Women only	1	8268	1.27 [0.95, 1.69]	0.10	-	
	Men and women	1	2921	1.93 [1.34, 2.78]	<0.001	-	
	Divorced vs married						
	All	4	>26843 (1 NA)	1.15 [1.02, 1.29]	0.02	53%	
	Men only	3	>14532 (1 NA)	1.22 [1.02, 1.46]	0.03	46%	0.47, 0%
	Women only	2	>9279 (1 NA)	1.09 [0.86, 1.39]	0.47	77%	
	Men and women	1	3032	0.94 [0.62, 1.43]	0.77	-	
	Widowed vs married						
	All	4	>29692 (1 NA)	1.16 [1.09, 1.23]	<0.001	0%	
	Men only	3	>13728 (1 NA)	1.16 [1.03, 1.29]	0.01	0%	0.69, 0%

	Women only	2	>10948 (1 NA)	1.12 [1.04, 1.22]	0.004	0%	
	Men and women	1	5016	1.33 [1.12, 1.57]	<0.001	-	

Table 4. Risk of adverse outcomes considering marital status in specific groups of participants.

Outcome	Marital status and subgroups	Studies	No. of participants (Not applicable, [NA] for studies with no crude result available)	Risk ratio [95% CI]	Overall effect, P value	Heterogeneity, I^2	Subgroup differences between men only and women only (P value, I^2)
Mortality post stroke	Unmarried vs married						
	All	3	29419	1.08 [0.88, 1.32]	0.47	43%	
	Women only	1	3156	0.95 [0.77, 1.17]	0.62	-	
	Men and women	2	26263	1.24 [0.83, 1.84]	0.29	24%	
Mortality post MI	Unmarried vs married						
	All	11	>21456 (3 NA)	1.42 [1.14, 1.76]	0.002	83%	
	Men only	2	>2453 (1 NA)	1.76 [1.24, 2.49]	0.001	80%	0.56, 0%
	Women only	2	> 374 (1 NA)	1.38 [0.67, 2.86]	0.38	61%	
	Men and women	9	>18629 (2 NA)	1.35 [1.00, 1.83]	0.05	84%	
	Divorced vs married						
	All	3	>4158 (1 NA)	1.36 [0.92, 2.01]	0.13	85%	
	Men only	1	2525	1.91 [1.50, 2.43]	<0.001	-	0.95, 0%
	Women only	1	447	1.87 [1.04, 3.36]	0.04	-	
	Men and women	2	>1186 (1 NA)	1.08 [0.95, 1.22]	0.23	0%	
	Widowed vs married						
	All	4	>9171 (1 NA)	1.68 [1.30, 2.17]	<0.001	85%	
	Men only	1	2136	1.49 [0.77, 2.89]	0.24	-	0.31, 2.3%
	Women only	1	368	2.74 [1.03, 7.28]	0.04	-	
	Men and women	3	>6667 (1 NA)	1.65 [1.24, 2.20]	<0.001	92%	
MI post MI	Unmarried vs married						
	All	2	1964	0.72 [0.14, 3.60]	0.69	77%	
	Women only	1	222	0.29 [0.08, 1.08]	0.07	-	

	Men and women	1	1742	1.51 [0.68, 3.37]	0.31	-	
MACE post MI	Unmarried vs married						
	Men and women	1	1742	1.31 [0.79, 2.17]	0.29	-	
Major bleeding post MI	Unmarried vs married						
	Men and women	1	1742	2.11 [0.55, 8.10]	0.28	-	
CVD post MI	Unmarried vs married						
	Men and women	1	1813	1.07 [0.41, 2.81]	0.89	-	

Figure 1: Flow diagram of study selection

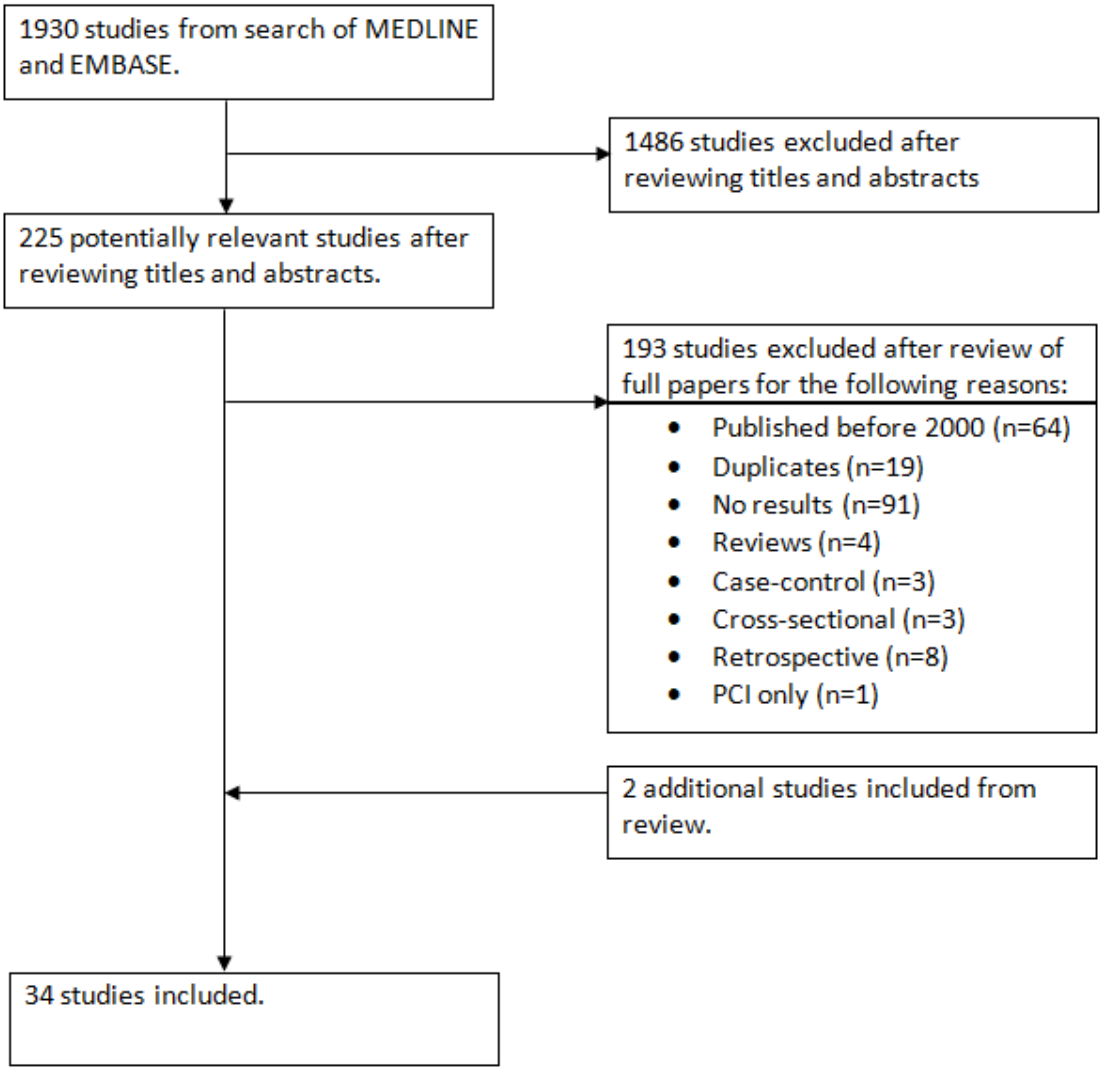
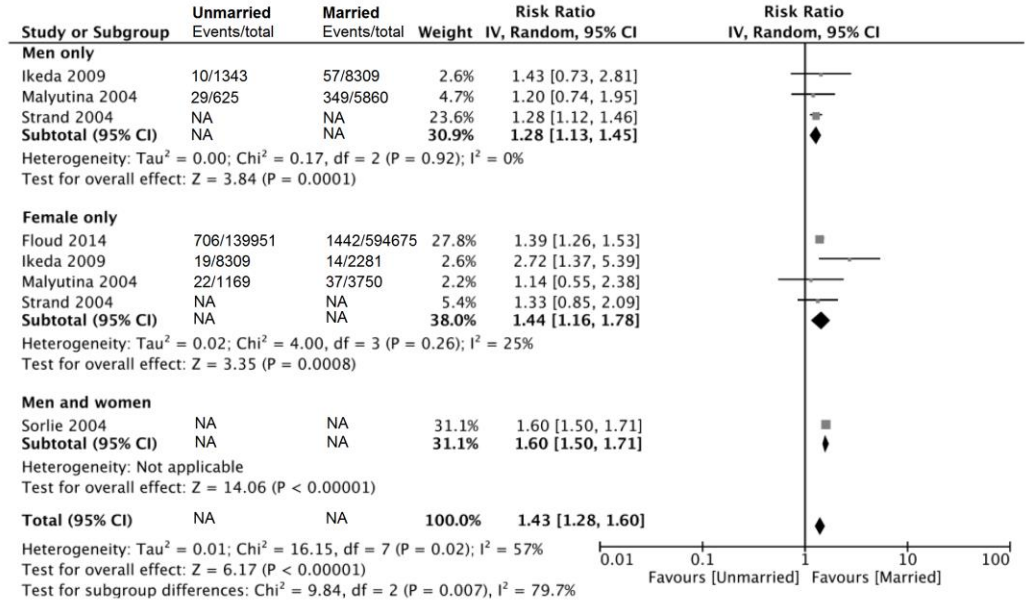
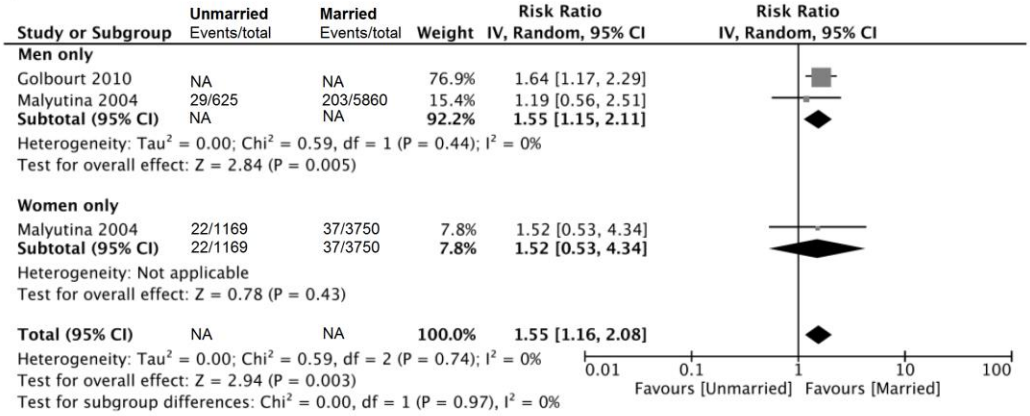


Figure 2. Forest plot of CHD, stroke and CVD deaths in unmarried vs married in general population.

A) CHD death



B) Stroke deaths



C) CVD death

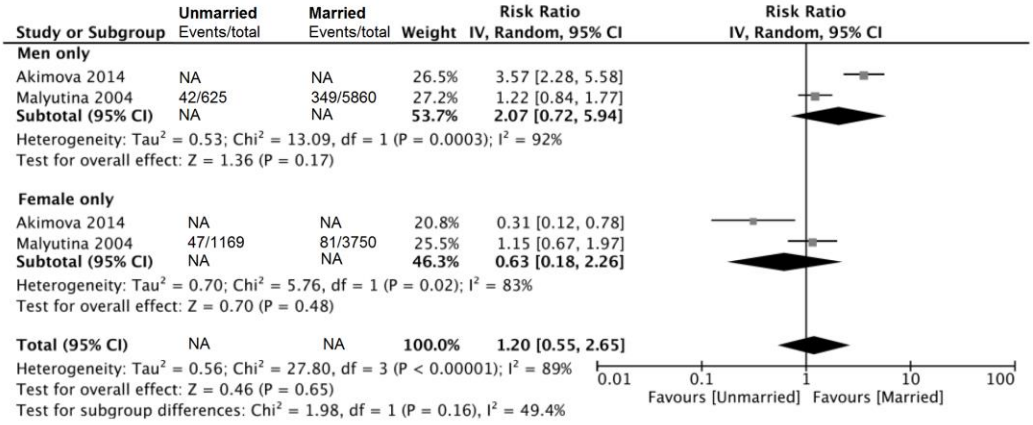
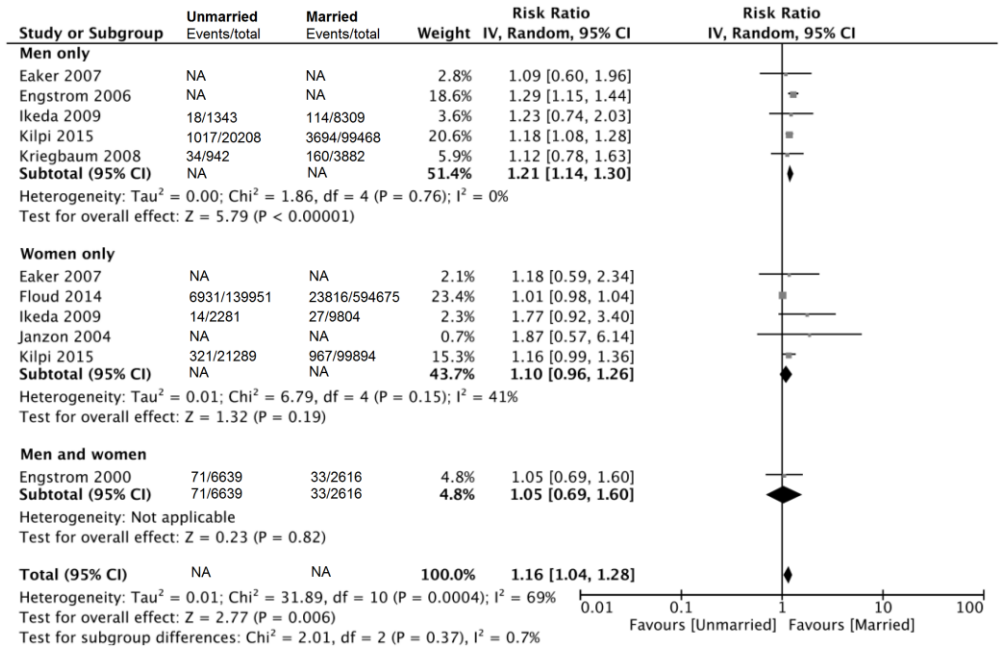
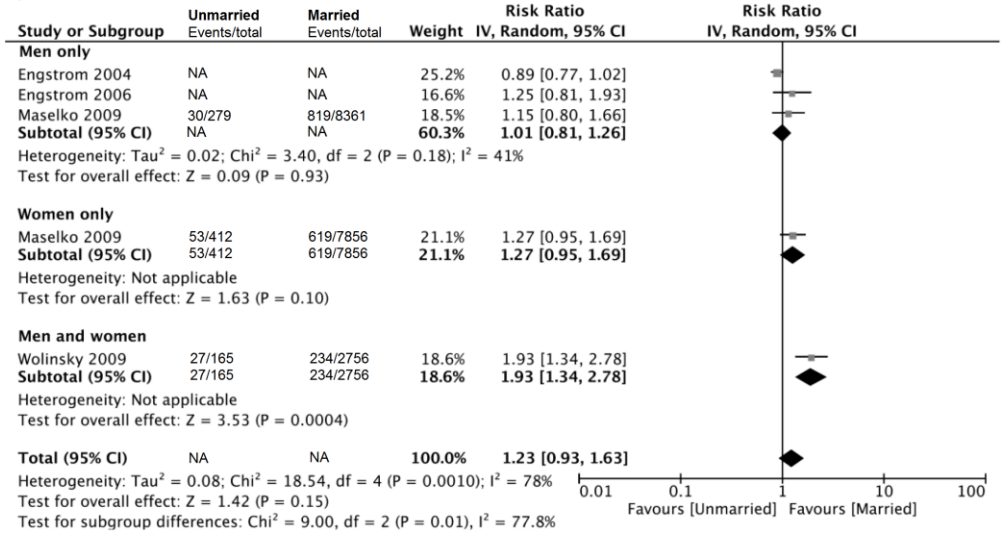


Figure 3. Forest plot of CHD, stroke and CVD events in unmarried vs married in general population.

A) CHD events



B) Stroke events



C) CVD events

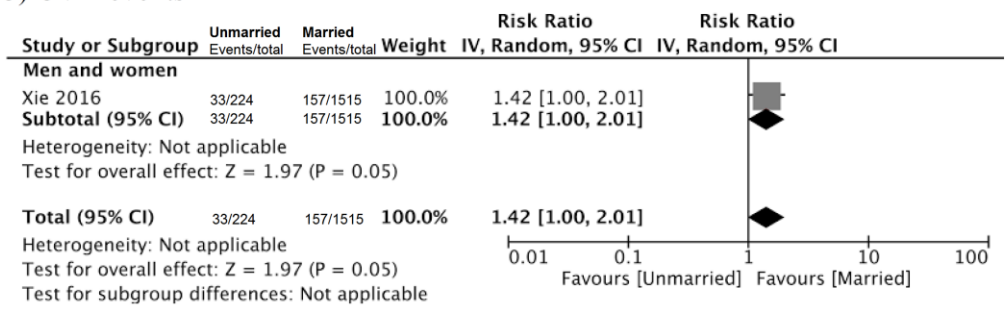
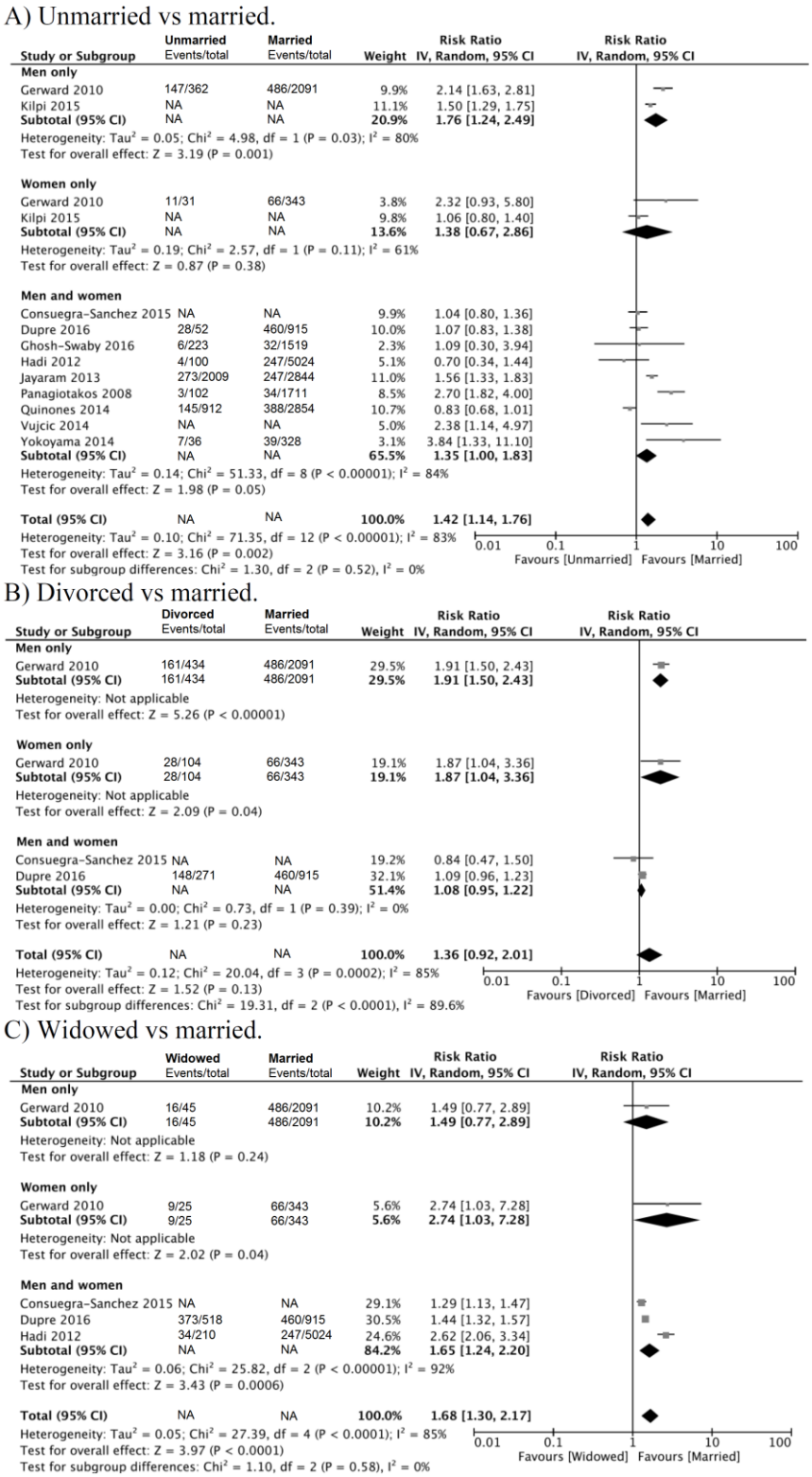


Figure 4. Forest plot of post MI mortality by marital status



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Supplementary Table 1: Definition of unmarried in included studies

Study ID	Definition of unmarried	If unmarried = never married, availability of result in other group(s)
Akimova 2014[35]	Men: Never married (36.4%), divorced (56.5%) and widowed (7.1%). Women: Never married (38.4%), divorced (47.4%) and widowed (14.2%). Total: Never married (37.6%), divorced (51.4%) and widowed (11.0%).	
Andersen 2011[11]	Never married, divorced and widowed. (Dichotimised into currently married vs never/not married.)	
Bell 2013[26]	Never married, divorced and widowed. (Dichotimised into married/cohabiting vs single.)	
Consuegra-Sanchez 2015[6]	Never married.	Divorced and widowed.
Dupre 2015[19]	No result.	
Dupre 2016[30]	Never married.	Divorced and widowed.
Eaker 2007[27]	Never married, divorced and widowed. (Dichotimised into currently married vs not currently married.)	
Engstrom 2000[14]	Never married, divorced and widowed. (Dichotimised into married vs single.)	
Engstrom 2004[28]	Never married.	Divorced and widowed.
Engstrom 2006[20]	Never married.	Divorced and widowed.
Floud 2014[13]	Never married, divorced and widowed. (Dichotimised into partnered vs unpartnered.)	
Gerward 2010[7]	Never married.	Divorced and widowed.
Ghosh-Swaby 2016[38]	Never married.	Divorced and widowed.
Golbourt 2010[36]	Never married (46.9%), divorced and widowed (divorced and widowed were combined, 53.1%).	
Hadi 2012[8]	Never married.	Widowed.
Ikeda 2009[17]	Never married, divorced and widowed. (Results included 'living alone' and 'living with spouse' groups.)	
Janzon 2004[24]	Never married, divorced and widowed. (Dichotimised into married vs single.)	
Jayaram 2013[39]	Never married, divorced and widowed. (Dichotimised into married vs unmarried.)	
Kilpi 2015[16]	Never married, divorced and widowed. (Results included 'living alone' and 'marital partner' groups.)	
Kriegbaum 2008[15]	Never married.	Divorced.
Malyutina 2004[18]	Men: Never married (44.4%), divorced (44.4%) and widowed. (11.1%) Women: Never married (21.7%), divorced (43.5%) and widowed (34.8%). Total: Never married (29.6%), divorced (42.8%) and widowed (27.6%).	
Maselko 2009[31]	Never married.	Divorced and widowed.
Matthews 2002[29]	No result.	
Orth-Gomer 2000[32]	Never married.	Divorced and widowed.
Panagiotakos 2008[3]	Never married.	Divorced and widowed.
Quinones 2014[33]	Never married, divorced and widowed. (Dichotimised into married vs unmarried.)	
Samanci 2004[12]	Never married and widowed.	

	(Dichotimised into married vs single/widowed.)	
Schultz 2017[34]	Never married.	Divorced and widowed.
Sorlie 2004[25]	Never married, divorced and widowed. (Dichotimised into married vs not married.)	
Strand 2004[37]	Never married.	Divorced and widowed.
Vujcic 2014[9]	Never married (10.9%), divorced and widowed (divorced and widowed were combined, 89.1%).	
Wolinsky 2009[40]	Never married	Divorced and widowed.
Xie 2016[2]	Never married, divorced and widowed. (Dichotimised into have spouse vs no spouse.)	
Yokoyama 2014[10]	Never married.	-

Supplementary Table 2: Risk of bias assessment of included studies

Study ID	Representativeness of cohort	Reliable exposure ascertainment	Reliable outcome ascertainment	Adjustment for confounders	Duration of follow up sufficient? (>5 years)	Loss to follow up <10%
Akimova 2014[35]	Yes, Russian cohort.	Yes, from survey and passport data.	Yes, mortality from the Tyumen committee registry.	Adjusted for age, systolic and diastolic blood pressure, BMI, total cholesterol, HDL, triglycerides, smoking, history of CAD, hypertension, education and profession.	Yes, 12 years of follow-up.	Yes, "the whole cohort was analysed".
Andersen 2011[11]	No, post-stroke Danish cohort.	Yes, from the Danish National Indicator Project database.	Yes, mortality from the Danish Central Person Registry.	Not adjusted for confounders.	No, 1 year of follow-up.	Yes, less than 0.2% were lost to follow-up.
Bell 2013[26]	No, post-stroke post-menopausal women.	Yes, from questionnaires.	Unclear.	Unclear what confounders adjusted for.	Yes, ranges from 12 to 17 years.	Unclear.
Consuegra-Sanchez 2015[6]	No, post-MI cohort.	Unclear.	Yes, mortality from medical records, local electronic registries or telephone contact.	Adjusted for age, sex, hypertension, diabetes mellitus, current smoker, dyslipidaemia, pre-existing MI, angina, heart failure, stroke, peripheral arterial disease, atrial fibrillation, cancer, chronic renal disease, chronic obstructive pulmonary disease, delay to presentation, type of MI, Killip class, heart rate, systolic blood pressure, glycaemia on admission, peak CK-MB, reperfusion including coronary revascularization and left ventricular ejection fraction.	Yes, median 6.1 years of follow-up.	Yes, 99.5% follow-up.
Dupre 2015[19]	No, participants were ever-married adults.	Yes, from Health and Retirement Study interviews.	Yes, CVD incidence from follow-up interviews every 24 months.	Adjusted for age, study cohort, race, ethnicity and geographic region, ever widowed, BMI, hypertension, diabetes, education, employment, income, health insurance, lives alone, no children, CES-D depressive symptoms, smoking status, alcohol use, physical exercise and all covariates.	Yes, 18 years of follow-up.	Yes, re-interview response rate were approximately 94%.
Dupre 2016[30]	No, post-MI cohort.	Yes, from Health and Retirement Study interviews.	Yes, mortality data from the National Death Index.	Crude results only.	Yes, 18 years of follow-up.	Yes, re-interview response rate were greater than 90%.
Eaker 2007[27]	Yes, Western cohort.	Yes, from questionnaires.	Unclear.	Adjusted for age, systolic blood pressure, BMI, smoking, diabetes, total/HDL cholesterol.	Yes, 10 years of follow-up.	Unclear.

Engstrom 2000[14]	No, females only cohort.	Yes, from National Census Registers.	Yes, CVD incidence from the Malmo Myocardial Infarction Register.	Adjusted for age, hypertension, diabetes, hyperlipidaemia, history of MI, and smoking.	Yes, average 10.7 years of follow-up.	Yes, 100% follow-up.
Engstrom 2004[28]	Yes, Western cohort.	Yes, from questionnaires.	Yes, stroke incidence from the Stroke Register in Malmo.	Adjusted for age.	Yes, over 10 years of follow-up	Unclear.
Engstrom 2006[20]	No, males only cohort.	Yes, from National Census Registers.	Yes, most strokes validated by review of hospital records and data from the Stroke register of Malmo Swedish. MI data from the Hospital Discharge register.	Adjusted for age, smoking, tobacco consumption, cholesterol, BMI, diabetes, systolic blood pressure, medication, log triglycerides, physical inactivity, alcohol consumption, angina, ceruloplasmin, alpha 1-antitrypsin, orosomucoid, haptoglobin, and fibrinogen.	Yes, average 18.7 years of follow-up.	Yes, 100% follow-up.
Floud 2014[13]	No, females only cohort.	Yes, from postal questionnaires.	Yes, IHD events from NHS Central Registers and GP records.	Adjusted for age, region, area deprivation, age left school, highest educational qualification, smoking, alcohol intake, strenuous exercise, BMI, hormone replacement therapy use, sleep duration, happiness, treatment for depression, parity, employment and participation in group activities.	Yes, average 8.8 years of follow-up.	Yes, "virtually complete" follow-up.
Gerward 2010[7]	Yes, Western cohort.	Yes, from the Swedish National Census.	Yes, mortality from National MI Register, death certificates autopsy and hospital records.	Adjusted for age at first coronary event and for date of first coronary event, systolic blood pressure, blood pressure medication, diabetes, cholesterol, log triglycerides, BMI, angina, smoking, physical inactivity, stressful work, problematic alcohol behaviour and occupation.	Yes, 21 years of follow-up.	Yes, 100% follow-up.
Ghosh-Swaby 2016[38]	No, post-MI and post-PCI cohort.	Unclear.	Unclear.	Adjusted for age, sex, race/ethnicity, prior history of smoking, hypertension, diabetes and heart failure.	No, 15 months of follow-up.	Unclear.
Golbourt 2010[36]	No, Israeli male only cohort.	Unclear.	Yes, mortality from National Death Registry.	Adjusted for socio-economic status index, BMI, blood pressure, smoking habits, family size, baseline prevalence of diabetes and CHD.	Yes, 34 years of follow-up	Unclear.
Hadi 2012[8]	No, post-ACS cohort.	Unclear.	Unclear.	Unclear what confounders adjusted for.	No, 1 year of follow-up.	Unclear.
Ikeda 2009[17]	No, Japanese cohort.	Yes, from questionnaires.	Yes, CHD incidence and mortality from medical records and the National Vital Statistics respectively.	Adjusted for age, public health centre area, stress, smoking, alcohol, physical activity, BMI.	Yes, median 11 years of follow-up.	Yes, greater than 90% follow-up.
Janzon 2004[24]	No, females only cohort .	Yes, from the National Population Census database from Statistics Sweden.	Yes, MI incidence from the Malmo Myocardial register and the Swedish Myocardial Infarction register. Mortality from the Swedish Causes of Deaths register.	Adjusted for age, hormone replacement, BMI, hypertension, cholesterol, diabetes and occupation.	Yes, average 14 years of follow-up.	Yes, 100% follow-up.
Jayaram 2013[39]	No, post-MI cohort.	Unclear.	Unclear.	Crude results only.	No, 2 years of follow-up.	Unclear.
Kilpi 2015[16]	Yes, Western cohort.	Yes, from Statistics Finland.	Yes, MI incidence from hospital discharge records and mortality from the cause of	Adjusted for living arrangements, education, occupation, income, wealth and employment status.	Yes, 12 years of follow-up.	Unclear, "minimal loss

			death register.			to follow-up".
Kriegbaum 2008[15]	No, males only cohort.	Yes, from Statistics Denmark.	Yes, IHD from the National Patient Registry and Cause of Death Registry.	Adjusted for mother's marital status at birth, father's employment at birth, BMI, and educational attainment.	Yes, 12 years of follow-up.	Yes, "nearly complete" register-based follow-up.
Malyutina 2004[18]	Yes, Western cohort.	Yes, from questionnaires.	Yes, mortality from the medical death register and autopsy records. MI and stroke deaths were additionally validated against the MONICA 'hot pursuit' registers.	Adjusted for age, smoking, total cholesterol, systolic blood pressure, frequency of drinking, BMI and education.	Yes, average 10.3 years of follow-up.	Yes, 100% follow-up.
Maselko 2009[31]	No, aged 50 and above only cohort.	Yes, from telephone or in-person interviews.	Yes, stroke incidence based on self or proxy report of doctors' diagnoses and in deceased participants information obtained from their spouse or children.	Adjusted for age at baseline, Hispanic ethnicity, black race, Southern birth, father's occupation, mother's and father's education, years of education, and year of Health and Retirement Study enrollment, years of education, income, wealth, adult socioeconomic status variables, indicators for overweight, obesity, alcohol, smoking, hypertension, diabetes mellitus, and heart disease.	Yes, average 9.4 years of follow-up.	Unclear.
Matthews 2002[29]	No, males only cohort.	Yes, from questionnaires.	Yes, before February 1982, mortality identified from next-of-kin interviews, routine follow-up of missed clinic visits, responses to postcards sent to the usual care participants, searches of publicly accessible files of deceased persons and cause of death was assigned by a 3-member panel of cardiologists not associated with the MRFIT and unaware of the participants' group assignment. Since February 1982, mortality from National Death Index.	Adjusted for age, intervention group, educational attainment, occurrence of a nonfatal cardiovascular event during trial, smoking, blood pressure, alcohol consumption and serum cholesterol level.	Yes, 9 years of follow-up.	Yes, follow-up considered to be "essentially 100% complete".
Orth-Gomer 2000[32]	No, post-CHD and females only cohort.	Yes, from interview.	Yes, mortality from the community healthcare registers, the Swedish National Death Registry and death certificates.	Crude results only.	Yes, average 5 years of follow-up.	Yes, 100% follow-up.
Panagiotakos 2008[3]	No, post-ACS cohort.	Unclear.	Unclear.	Adjusted for age, sex, discharge diagnosis, smoking and eating habits, hypertension, hypercholesterolaemia, diabetes, previous CHD, family history of cardiac disease, physical activity and education status.	No, 30 days of follow-up.	Unclear.
Quinones 2014[33]	No, post-MI cohort.	Yes, from interview.	Yes, from the population registries and death certificate.	Adjusted for sex, age ≥60, recruitment day, reperfusion therapy, hyperlipidemia, angina pectoris, diabetes, stroke, hypertension, bundle branch block, pulmonary edema and cardiac arrest.	Yes, median 5.3 years of follow-up.	Yea, 100% follow-up.
Samanci 2004[12]	No, post-stroke cohort.	Unclear.	Unclear.	Not adjusted for confounders.	No, 1 year of follow-up.	No, 26.8% lost to follow-up.

Schultz 2017[34]	Yes, American cohort.	Yes, from interview.	Yes, telephone or medical chart abstraction. Adjudication by 3 blinded physicians.	Adjusted for sex, race, diagnosis of hypertension, diabetes mellitus, low- and high density lipoprotein levels, heart failure, history of MI, estimated glomerular filtration rate, body mass index, obstructive coronary artery disease, smoking history, medications, education, and employment status.	No, median 3.7 years follow-up.	Unclear.
Sorlie 2004[25]	Yes, American cohort.	Yes, from personal and telephone interview.	Yes, mortality from National Death Index.	Adjusted for age, sex, race, Hispanic status, region of country, rural/urban and adjusted income.	Yes, up to 11 years of follow-up.	Unclear.
Strand 2004[37]	Yes, Norwegian cohort.	Unclear.	Yes, mortality from the National Cause of Death Register.	Adjusted for age, education, smoking, physical activity, systolic and diastolic blood pressures, BMI and cholesterol.	Yes, average 23.6 years of follow-up.	Unclear.
Vujcic 2014[9]	No, post-MI cohort.	Yes, from questionnaires.	Yes, mortality from telephone follow-up yearly.	Not adjusted for confounders.	Yes, median 77 months of follow-up.	Yes, 100% follow-up.
Wolinsky 2009[40]	No, elderly only cohort.	Unclear.	Unclear.	Crude results only.	Yes, 12 years of follow-up.	Unclear.
Xie 2016[2]	No, Chinese cohort.	Yes, from questionnaires.	Yes, CVD incidence from re-survey of participants by face-to-face or telephone interviews.	Crude results only.	Yes, 10 years of follow-up.	Yes, 6.3% were lost to follow-up.
Yokoyama 2014[10]	No, post-MI, males only and Eastern cohort.	Unclear.	Unclear.	Adjusted for age, Killip IV and left ventricular ejection fraction at the acute phase.	No, average 1.7 years of follow-up.	Unclear.

BMI=body mass index, HDL=high density lipoprotein cholesterol, CAD=coronary artery disease, MI=myocardial infarction, CK-MB=creatinine kinase – MB isoenzyme, CVD=cardiovascular disease, CES-D=Center for Epidemiologic Studies Depression Scale and CHD=coronary heart disease.

Supplementary Table 3: Crude results from included studies

Study ID	Study ID	Outcomes	Event rate
Akimova 2014[35]	Akimova 2014[39]	Incident CVD death in general population.	No crude results.
Andersen 2011[11]	Andersen 2011[15]	Mortality post-ischaemic stroke.	Mortality at 30 days: single 1,060/11,651 vs married/cohabiting 694/14,465. Mortality at 1 year: single: 2493/11,651 vs married/cohabiting 1620/14,465.
Bell 2013[26]	Bell 2013[30]	Mortality post-stroke.	Mortality in not married 576/1,500 vs currently married 527/1,656.
Consuegra-Sanchez 2015[6]	Consuegra-Sanchez 2015[8]	Mortality post-MI.	No crude results.
Dupre 2015[19]	Dupre 2015[23]	Incident acute MI in general population.	No crude results.
Dupre 2016[30]	Dupre 2016[34]	Mortality post-MI.	Mortality in never married 28/52 vs continuously married 460/915 vs remarried 208/441 vs divorced 148/271 vs widowed 374/518.
Eaker 2007[27]	Eaker 2007[31]	Incident CHD and mortality in general population.	No crude results.
Engstrom 2000[14]	Engstrom 2000[18]	Incident cardiac event in general population.	Incident cardiac events: married 71/6,639 vs single 33/2616.
Engstrom 2004[28]	Engstrom 2004[32]	Incident stroke in general population.	No crude results.
Engstrom 2006[20]	Engstrom 2006[24]	Incident coronary events and stroke in general population	Coronary event in married 436/4,705 vs never married 70/637 vs divorced 97/684 vs widowed 10/49. Stroke in married 168/4,705 vs never married 25/637 vs divorced 34/684 vs widowed 2/49.
Floud 2014[13]	Floud 2014[17]	Incident IHD and IHD mortality in general population.	IHD in women: partnered 23,816/594,675 vs not partnered 6,931/139,951 IHD mortality in women: partnered 1,442/594,675 vs not partnered 706/139,951
Gerward 2010[7]	Gerward 2010[10]	Mortality post-coronary event.	Mortality at 21 years in men: married 486/2,091 vs never married 147/362 vs divorced 161/434 vs widowed 16/45. Mortality at 21 years in women: married 66/343 vs never married 11/31 vs divorced 28/104 vs widowed 9/25.
Ghosh-Swaby 2016[38]	Ghosh-Swaby 2016[42]	Mortality post-MI.	Mortality in married/common law and living together 32/1,519 vs never married 6/223 vs separated/divorced/widowed 14/358. MACE in married/common law and living together 250/1,519 vs never married 44/223 vs separated/divorced/widowed 63/358. MI in married/common law and living together 126/1,519 vs never married 20/223 vs separated/divorced/widowed 31/358. Stroke in married/common law and living together 12/1,519 vs never married 4/223 vs separated/divorced/widowed 2/358.
Golbourt 2010[36]	Golbourt 2010[40]	Incident stroke mortality.	No crude results.
Hadi 2012[8]	Hadi 2012[11]	Mortality post-ACS.	In-hospital mortality: married 247/5,024 vs single 4/100 vs widowed 34/210. 30-day mortality: married 385/5,024 vs single 5/100 vs widowed 41/210. 1 year mortality: married 503/5,024 vs single 7/100 vs widowed 55/210.
Ikeda 2009[17]	Ikeda 2009[21]	Incident CHD and mortality in general	CHD in men alone 18/1,343 vs spouse 114/8,309 CHD mortality in men alone 10/1,343 vs spouse 57/8,309

		population.	All-cause mortality in men alone 193/1,343 vs spouse 1,152/8,309. CHD in women alone 14/2,281 vs spouse 27/9,804 CHD mortality in women alone 15/2,281 vs spouse 19/9,804, All-cause mortality in women alone 162/2,281 vs spouse 540/9,804.
Janzon 2004[24]	Janzon 2004[28]	Cardiac events in general population.	Cardiac events in married 157/7,579 vs unmarried 69/2,937.
Jayaram 2013[39]	Jayaram 2013[43]	Mortality post-MI.	Mortality at 2 years: unmarried 273/2,009 vs married 247/2,844.
Kilpi 2015[16]	Kilpi 2015[20]	Incident MI and MI mortality in general population.	MI events in men: marital partner 3,694/99,468 vs cohabitation 531/12,882 vs living with other 674/15,435 vs living alone 1,017/20,208. MI events in women: marital partner 967/99,894 vs cohabitation 130/11,552 vs living with other 214/18,553 vs living alone 321/21,289.
Kriegbaum 2008[15]	Kriegbaum 2008[19]	Incident IHD in general population.	IHD in men: cohabitant 160/3,882 vs never cohabitant 34/942 vs broken partnership 186/3541.
Malyutina 2004[18]	Malyutina 2004[22]	All-cause, CVD, CHD and stroke death in general population.	All-cause mortality in men: married 747/5,860 vs non-married 85/625 vs single 24/266 vs divorced 42/279 vs widowed 19/80. CVD mortality in men: married 349/5,860 vs non-married 43/625 vs single 9/266 vs divorced 23/279 vs widowed 11/80. CHD mortality in men: married 203/5,860 vs non-married 29/625 vs single 6/266 vs divorced 15/279 vs widowed 8/80. Stroke mortality in men: married 92/5,860 vs non-married 9/625 vs single 1/266 vs divorced 29/625 Not ma 7/279 vs widowed 1/80. All-cause mortality in women: married 145/3,750 vs non-married 81/1,173 vs single 11/265 vs divorced 25/489 vs widowed 45/415. CVD mortality in women: married 81/3,750 vs non-married 47/1,169 vs single 4/265 vs divorced 13/489 vs widowed 30/415. CHD mortality in women: married 37/3,750 vs non-married 22/1,169 vs single 3/265 vs divorced 6/489 vs widowed 13/415. Stroke mortality in women: married 28/3,750 vs non-married 16/1,169 vs single 0/265 vs divorced 4/489 vs widowed 12/415.
Maselko 2009[31]	Maselko 2009[35]	Incident stroke in general population.	Men and incident stroke: married 819/8,361 vs divorced/separated 74/782 vs never married 30/279 vs widowed 105/613. Women and incident stroke: married 619/7,856 vs divorced/separated 126/1,423 vs never married 53/412 vs widowed 546/3,092.
Matthews 2002[29]	Matthews 2002[33]	All-cause, CVD and MI death in general population.	Nonfatal CV events: married 2,099/9,817 vs separated 126/513 vs divorced 126/574.
Orth-Gomer 2000[32]	Orth-Gomer 2000[36]	Coronary events post-ACS.	Recurrent coronary events at average 5 years of follow up: single 4/24 vs widowed 3/18 vs divorced/separated 17/52 vs cohabiting 57/198.
Panagiotakos 2008[3]	Panagiotakos 2008[3]	Mortality and CVD post-ACS.	Mortality at 30 days: married 34/1711, unmarried 4/102, divorced/widowed 14/277. CVD at 30 days: married 120/1711, unmarried 4/102, divorced/widowed 25/277.
Quinones 2014[33]	Quinones 2014[37]	Mortality post-MI.	Mortality: married 388/2854 vs 145/912.
Samanci 2004[12]	Samanci 2004[16]	Mortality post-stoke.	Mortality at 1 year: single/widowed 20/41 vs married 15/106.

Schultz 2017[34]	Schultz 2017[38]	Mortality, CVD death, CVD death and MI in post-cardiac catheterisation or CHD.	Mortality: married 681/4088, unmarried 404/1963, divorced/separated 153/842, widowed 184/670. Cardiovascular death: married 412/4088, unmarried 276/1963, divorced/separated 102/842, widowed 126/670. Cardiovascular death and MI: married 506/4088, unmarried 336/1963, divorced/separated 135/842, widowed 142/670.
Sorlie 2004[25]	Sorlie 2004[29]	Out-of-hospital all-cause and CHD death in general population.	Total deaths in not married 23,899 vs married 35,135.
Strand 2004[37]	Strand 2004[41]	IHD death in general population.	No crude results.
Vujcic 2014[9]	Vujcic 2014[12]	Mortality post-MI.	No crude results.
Wolinsky 2009[40]	Wolinsky 2009[44]	Incident stroke in elderly population.	Stroke: lives alone 213/2039, widowed 256/2260, divorced/separated 22/276, never married 27/165, married 234/2756.
Xie 2016[2]	Xie 2016[2]	Incident CVD in general population.	CVD: spouse 157/1515 vs no spouse 33/224.
Yokoyama 2014[10]	Yokoyama 2014[13]	Mortality post-MI.	Mortality: married 39/328 vs unmarried 7/36.

MI=myocardial infarction, ACS=acute coronary syndrome, CHD=coronary heart disease, IHD=ischaemic heart disease, CV=cardiovascular, CVD=cardiovascular disease, PCI=percutaneous coronary intervention

Supplementary Table 4. Risk of adverse outcomes considering marital status in general population that differ when studies with unclear marital status ascertainment were excluded

Outcome	Marital status and subgroups	Studies	No. of participants (Not applicable, [NA] for studies with no crude result available)	Risk Ratio [95% CI]	Overall effect, P value	Heterogeneity, I^2	Subgroup differences between men only and women only (P value, I^2)
CHD death	Unmarried vs married						
	All	4	>766272 (1 NA)	1.49 [1.32, 1.69]	<0.001	50%	
	Men only	2	16137	1.27 [0.86, 1.89]	0.23	0%	0.50, 0%
	Women only	3	750135	1.54 [1.04, 2.28]	0.03	49%	
	Men and women	1	NA	1.60 [1.50, 1.71]	<0.001	-	
	Divorced vs married						
	All	3	>10378 (1 NA)	1.46 [1.00, 2.14]	0.05	0%	
	Men only	2	>6139 (1 NA)	1.46 [0.92, 2.32]	0.11	21%	0.98, 0%
	Women only	1	4239	1.44 [0.49, 4.25]	0.51	-	
	Widowed vs married						
	All	1	10105	0.90 [0.44, 1.86]	0.78	0%	
	Men only	1	5940	0.77 [0.24, 2.46]	0.66	-	0.78, 0%
	Women only	1	4165	1.00 [0.40, 2.50]	1.00	-	
Stroke death	Unmarried vs married						
	All	1	11404	1.29 [0.70, 2.37]	0.41	0%	
	Men only	1	6485	1.19 [0.56, 2.51]	0.65	-	0.71, 0%
	Women only	1	4919	1.52 [0.53, 4.34]	0.43	-	
Stroke events	Unmarried vs married						
	All	3	>16908 (2 NA)	1.08 [0.87, 1.34]	0.47	56%	
	Men only	3	>8640 (2 NA)	1.01 [0.81, 1.26]	0.93	41%	0.21, 35%
	Women only	1	8268	1.27 [0.87, 1.34]	0.47	-	
	Divorced vs married						
	All	3	>23811 (1 NA)	1.17 [1.03, 1.32]	0.01	58%	

	Men only	3	>14532 (1 NA)	1.22 [1.02, 1.46]	0.03	46%	0.47, 0%
	Women only	2	>9279 (1 NA)	1.09 [0.86, 1.39]	0.47	77%	
	Widowed vs married						
	All	3	>24676 (1 NA)	1.13 [1.06, 1.21]	<0.001	0%	
	Men only	3	>13728 (1 NA)	1.16 [1.03, 1.29]	0.01	0%	0.69, 0%
	Women only	2	>10948 (1 NA)	1.12 [1.04, 1.22]	0.004	0%	

Supplementary Table 5. Risk of adverse outcomes considering marital status in specific groups of participants that differ when studies with unclear marital status ascertainment were excluded.

Outcome	Marital status and subgroups	Studies	No. of participants (Not applicable, [NA] for studies with no crude result available)	Risk ratio [95% CI]	Overall effect, P value	Heterogeneity, I^2	Subgroup differences between men only and women only (P value, I^2)
Mortality post stroke	Unmarried vs married						
	All	1	3156	0.95 [0.77, 1.17]	0.62	-	
	Women only	1	3156	0.95 [0.77, 1.17]	0.62	-	
Mortality post MI	Unmarried vs married						
	All	5	>7560 (2 NA)	1.37 [1.02, 1.84]	0.03	86%	
	Men only	2	>2453 (1 NA)	1.76 [1.24, 2.49]	0.001	80%	0.56, 0%
	Women only	2	> 374 (1 NA)	1.38 [0.67, 2.86]	0.38	61%	
	Men and women	3	>4733 (1 NA)	1.10 [0.75, 1.62]	0.62	77%	
	Divorced vs married						
	All	2	4158	1.52 [0.97, 2.40]	0.07	89%	
	Men only	1	2525	1.91 [1.50, 2.43]	<0.001	-	0.95, 0%
	Women only	1	447	1.87 [1.04, 3.36]	0.04	-	
	Men and women	1	1186	1.09 [0.96, 1.23]	0.17	-	
	Widowed vs married						
	All	2	3937	1.45 [1.33, 1.57]	<0.001	0%	
	Men only	1	2136	1.49 [0.77, 2.89]	0.24	-	0.31, 2.3%
	Women only	1	368	2.74 [1.03, 7.28]	0.04	-	
	Men and women	1	1433	1.44 [1.32, 1.57]	<0.001	92%	

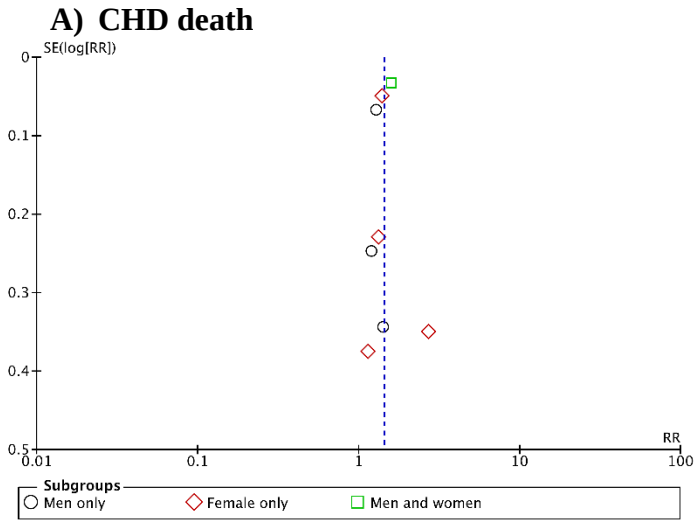
Supplementary Table 6. Risk of adverse outcomes considering marital status in general population that differ when studies with crude results and unadjusted results were excluded.

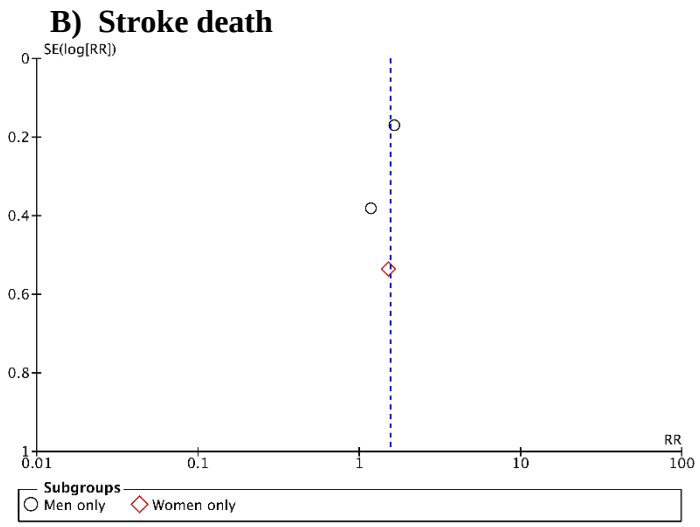
Outcome	Marital status and subgroups	Studies	No. of participants (Not applicable, [NA] for studies with no crude result available)	Risk Ratio [95% CI]	Overall effect, P value	Heterogeneity, I^2	Subgroup differences between men only and women only (P value, I^2)
Stroke event	Unmarried vs married						
	All	3	>16908 (2 NA)	1.08 [0.87, 1.34]	0.47	56%	
	Men only	3	>8640 (2 NA)	1.01 [0.81, 1.26]	0.93	41%	0.21, 35%
	Women only	1	8268	1.27 [0.95, 1.69]	0.10	-	
	Divorced vs married						
	All	3	>23811 (1 NA)	1.17 [1.03, 1.32]	0.01	58%	
	Men only	3	>14532 (1 NA)	1.22 [1.02, 1.46]	0.03	46%	0.47, 0%
	Women only	2	>9279 (1 NA)	1.09 [0.86, 1.39]	0.47	77%	
	Widowed vs married						
	All	3	>24676 (1 NA)	1.13 [1.06, 1.21]	<0.001	0%	
	Men only	3	>13728 (1 NA)	1.16 [1.03, 1.29]	0.01	0%	0.69, 0%
	Women only	2	>10948 (1 NA)	1.12 [1.04, 1.22]	0.004	0%	

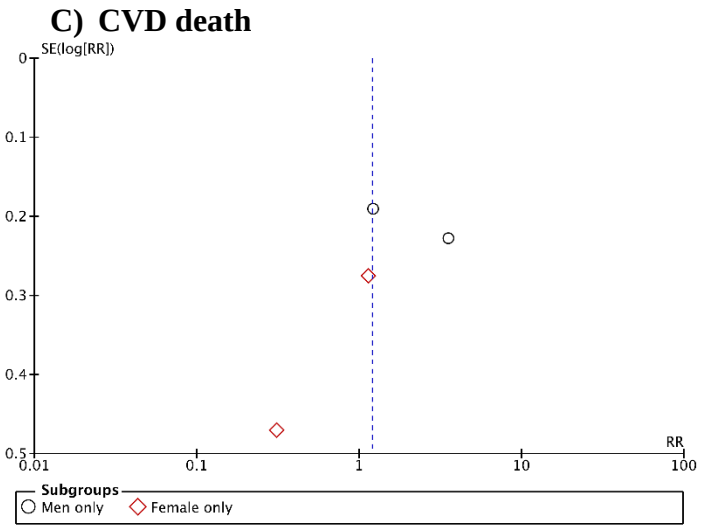
Supplementary Table 7. Risk of adverse outcomes considering marital status in specific groups of participants that differ when studies with crude results and unadjusted results were excluded.

Outcome	Marital status and subgroups	Studies	No. of participants (Not applicable, [NA] for studies with no crude result available)	Risk ratio [95% CI]	Overall effect, P value	Heterogeneity, I^2	Subgroup differences between men only and women only (P value, I^2)
Mortality post stroke	Unmarried vs married						
	All	1	3156	0.95 [0.77, 1.17]	0.62	-	
	Women only	1	3156	0.95 [0.77, 1.17]	0.62	-	
Mortality post MI	Unmarried vs married						
	All	8	>15636 (2 NA)	1.42 [1.06, 1.89]	0.02	86%	
	Men only	2	>2453 (1 NA)	1.76 [1.24, 2.49]	0.001	80%	0.56, 0%
	Women only	2	> 374 (1 NA)	1.38 [0.67, 2.86]	0.38	61%	
	Men and women	6	>12809 (1 NA)	1.31 [0.81, 2.10]	0.27	86%	
	Divorced vs married						
	All	2	>2972 (1 NA)	1.50 [0.93, 2.44]	0.10	70%	
	Men only	1	2525	1.91 [1.50, 2.43]	<0.001	-	0.95, 0%
	Women only	1	447	1.87 [1.04, 3.36]	0.04	-	
	Men and women	1	NA	0.84 [0.47, 1.50]	0.56	-	
	Widowed vs married						
	All	3	>7738 (1 NA)	1.85 [1.12, 3.06]	0.02	89%	
	Men only	1	2136	1.49 [0.77, 2.89]	0.24	-	0.31, 2.3%
	Women only	1	368	2.74 [1.03, 7.28]	0.04	-	
	Men and women	2	>5234 (1 NA)	1.82 [0.91, 3.65]	0.09	96%	

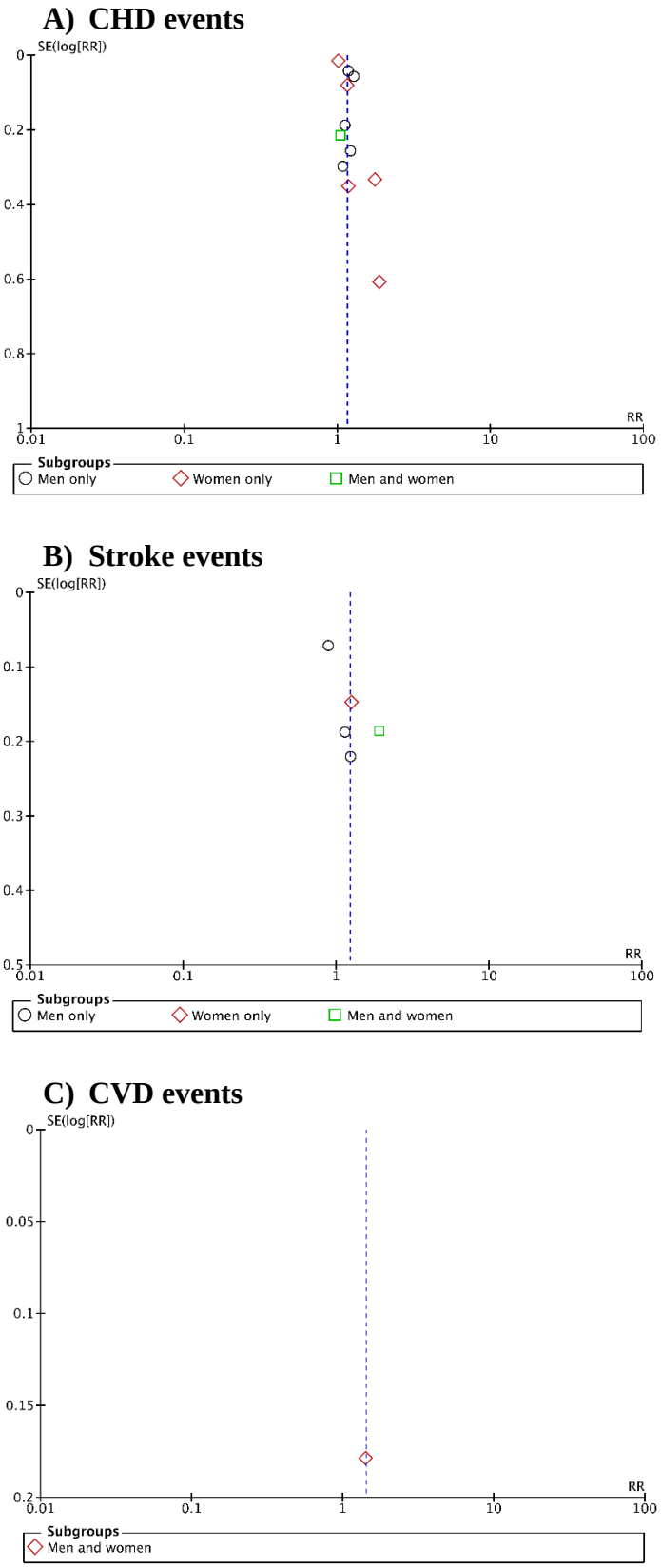
Supplementary Figure 1. Funnel plot of CHD, stroke and CVD deaths in unmarried vs married in general population.





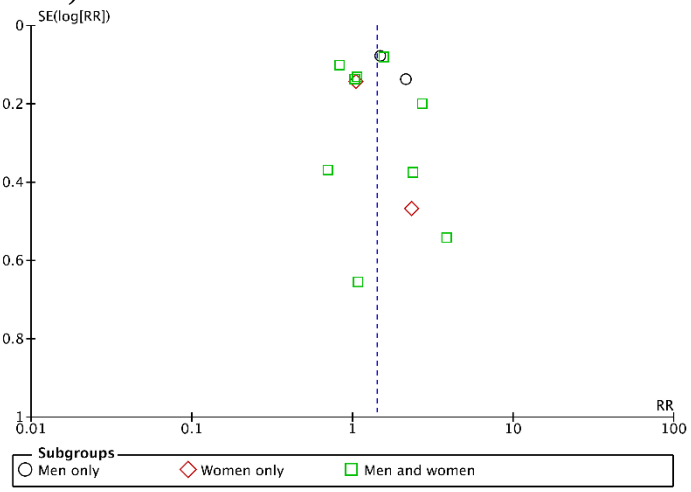


Supplementary Figure 2. Funnel plot of CHD, stroke and CVD events in unmarried vs married in general population.

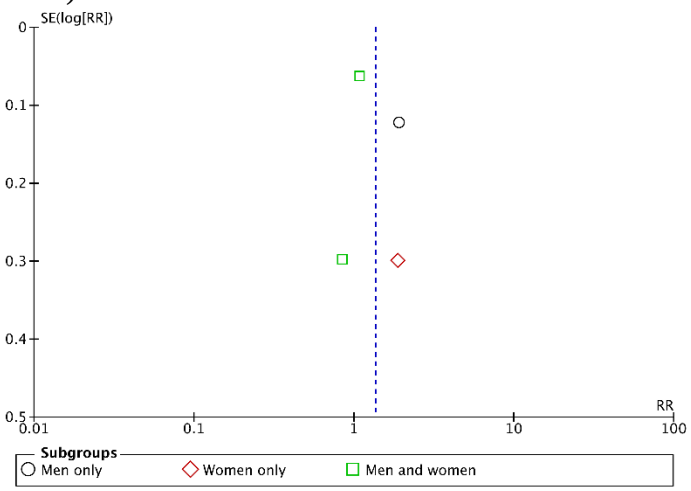


Supplementary Figure 3. Funnel plot of post MI mortality by marital status.

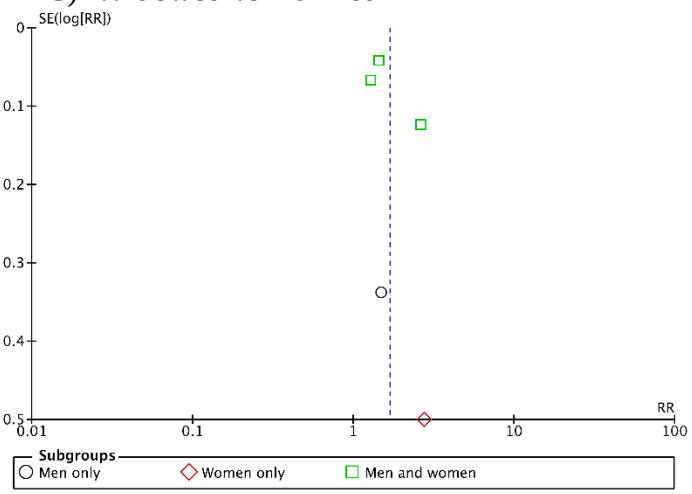
A) **Unmarried vs married**



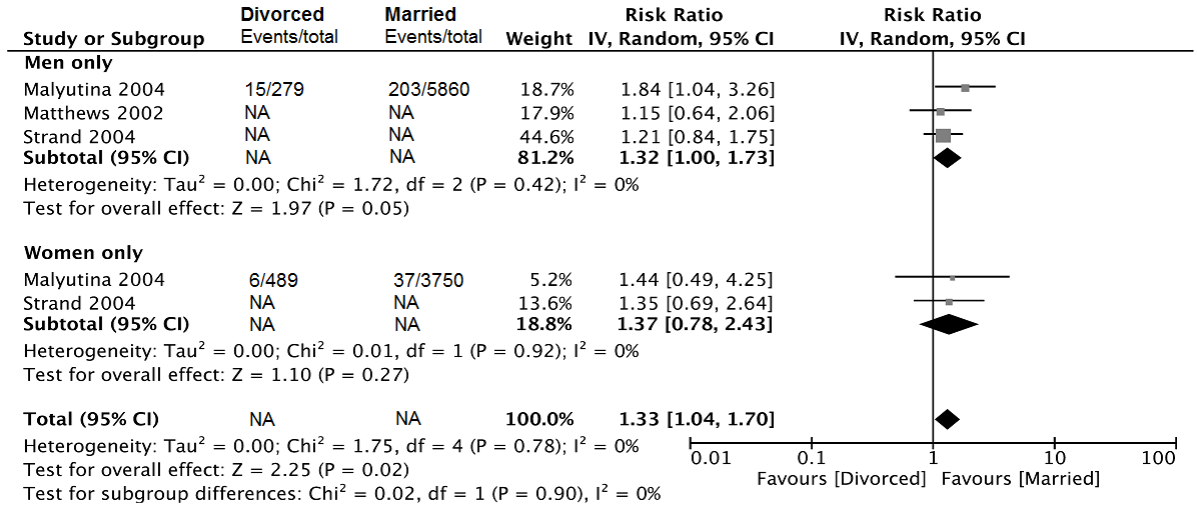
B) **Divorced vs married**

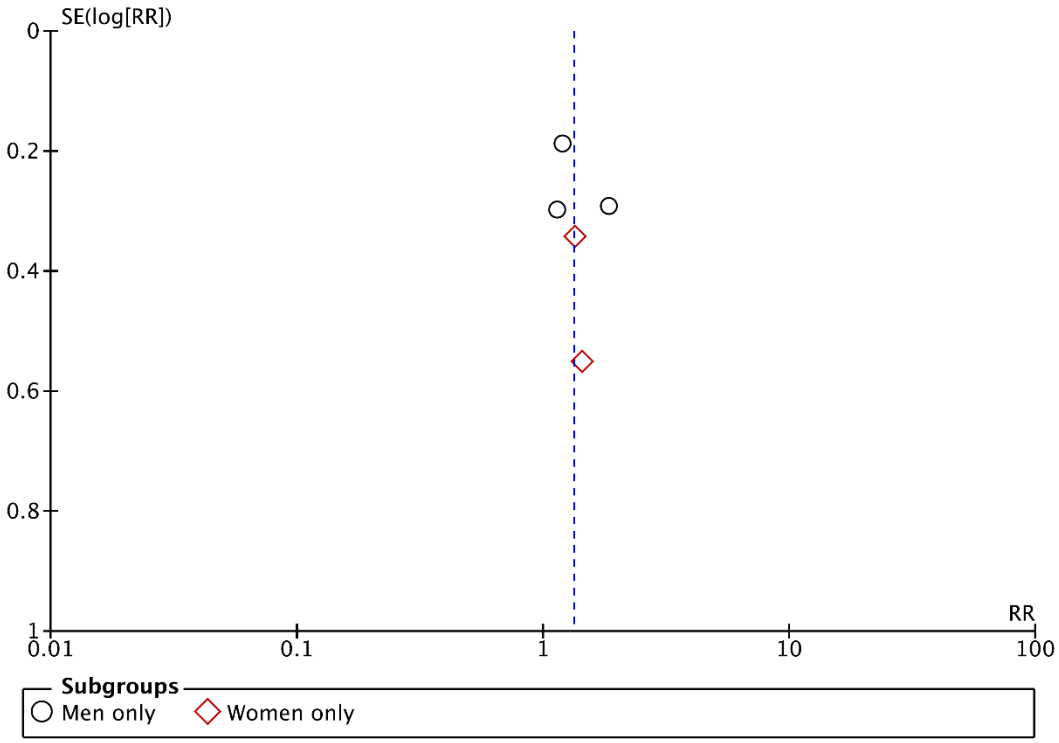


C) **Widowed vs married**

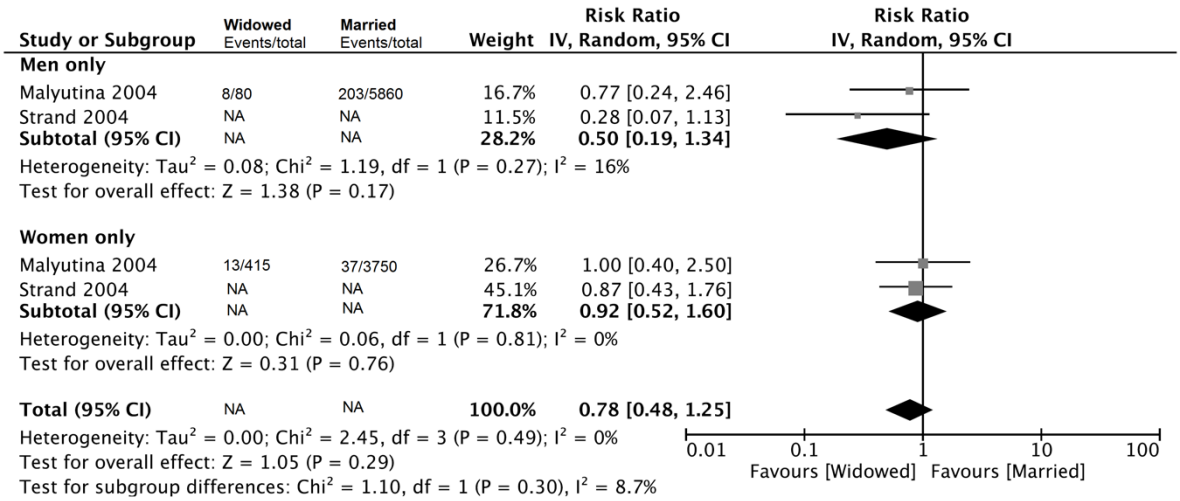


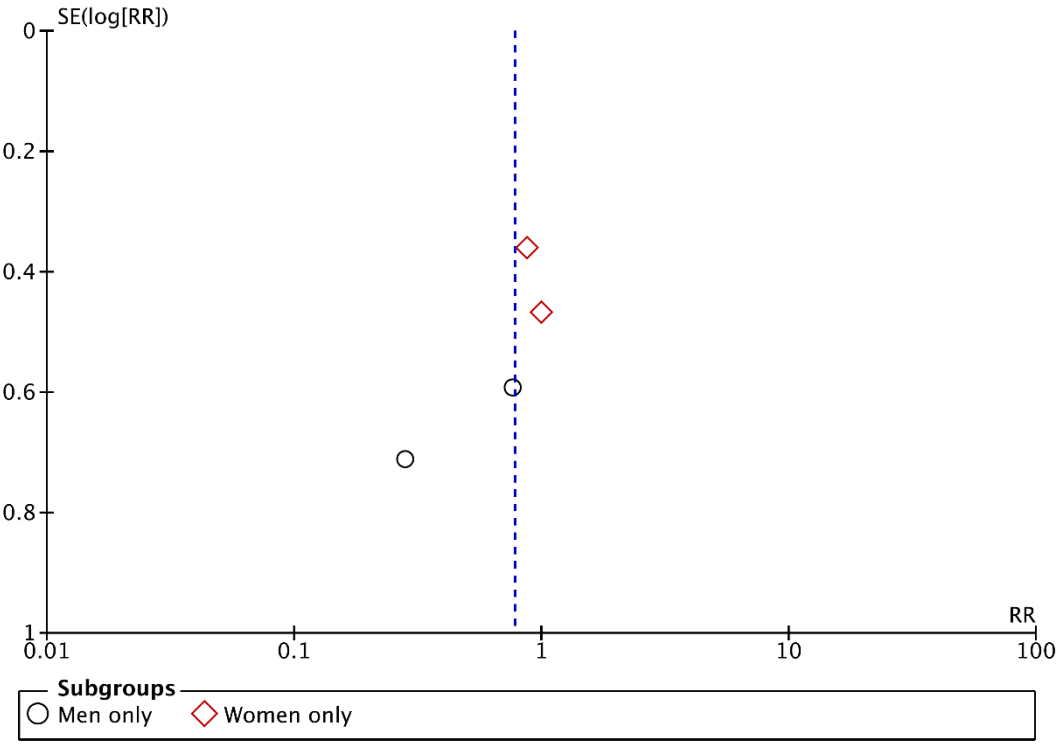
Supplementary Figure 4. Forest plot of CHD death in divorced vs married in general population and funnel plot.



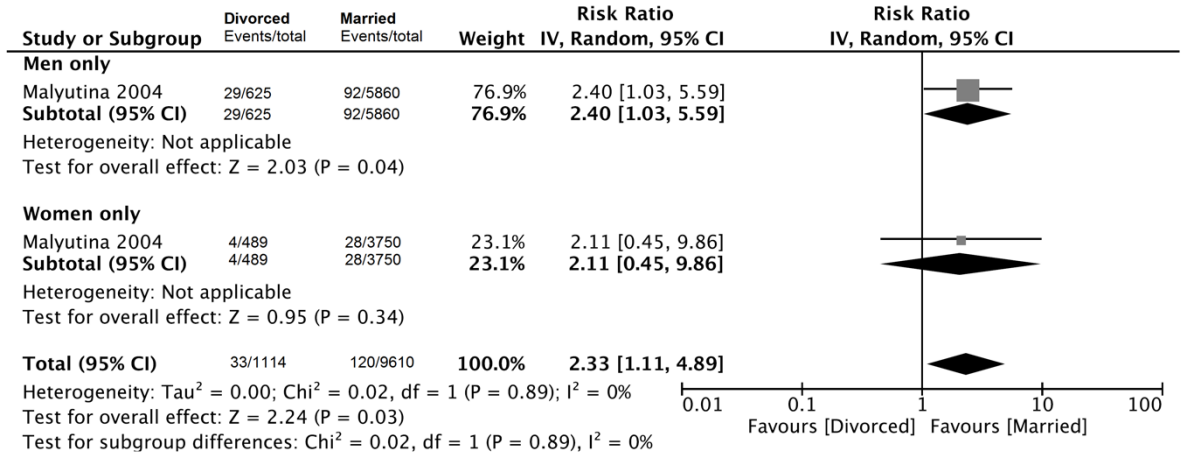


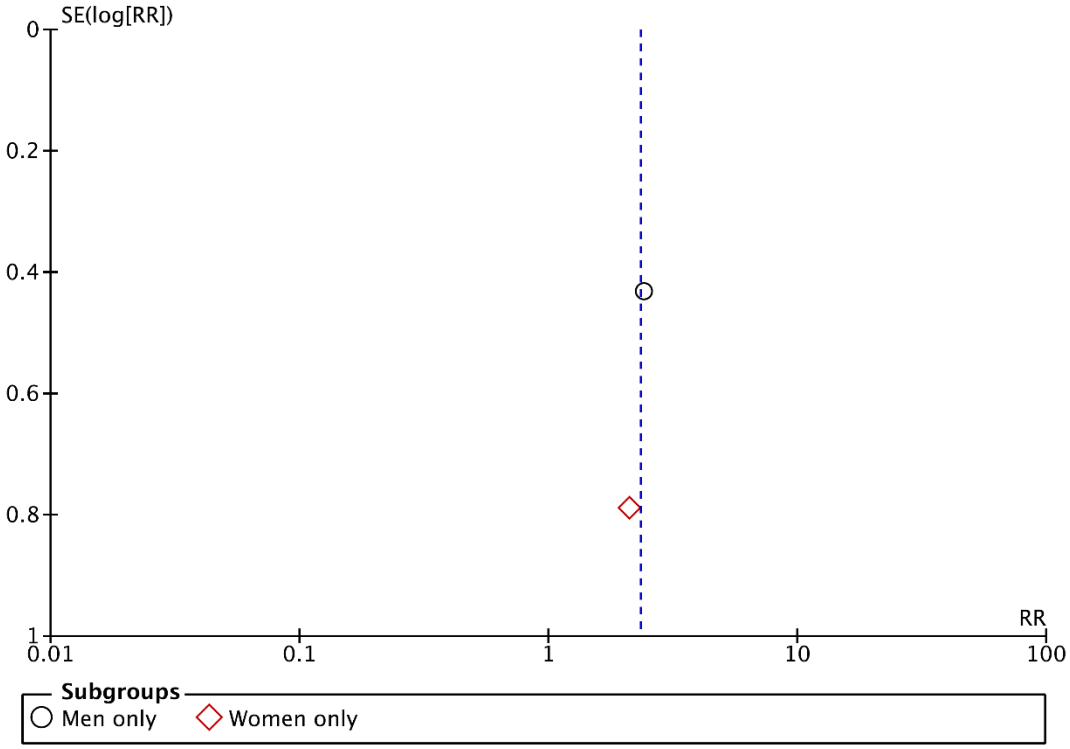
Supplementary Figure 5. Forest plot of CHD death in widowed vs married in general population and funnel plot.



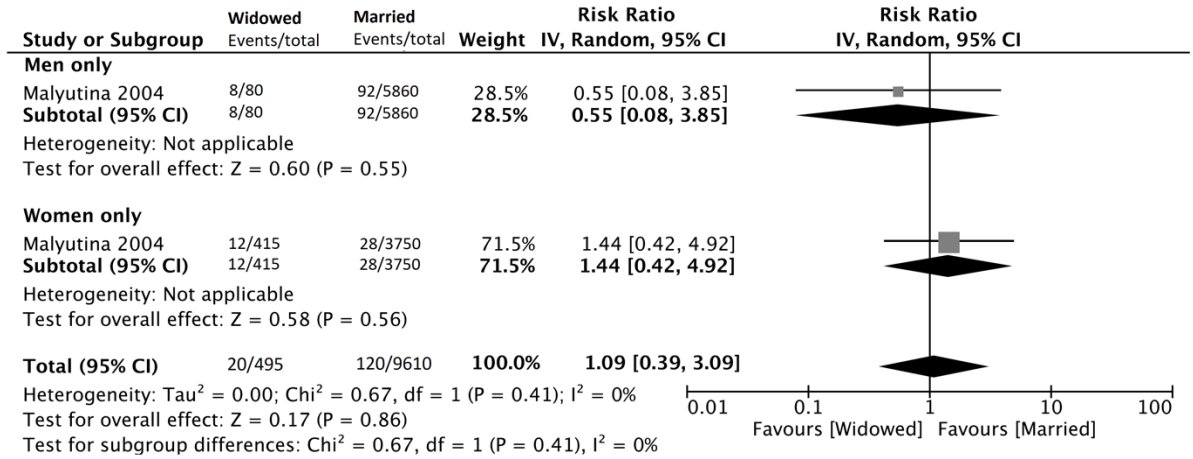


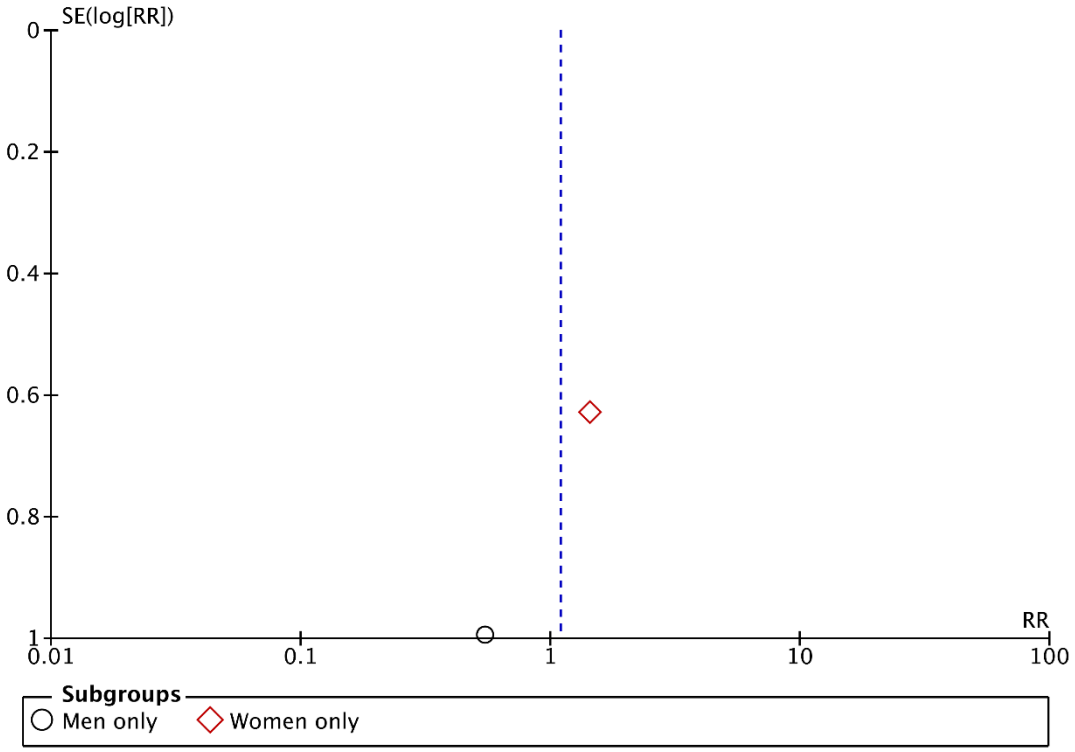
Supplementary Figure 6. Forest plot of stroke death in divorced vs married in general population and funnel plot.



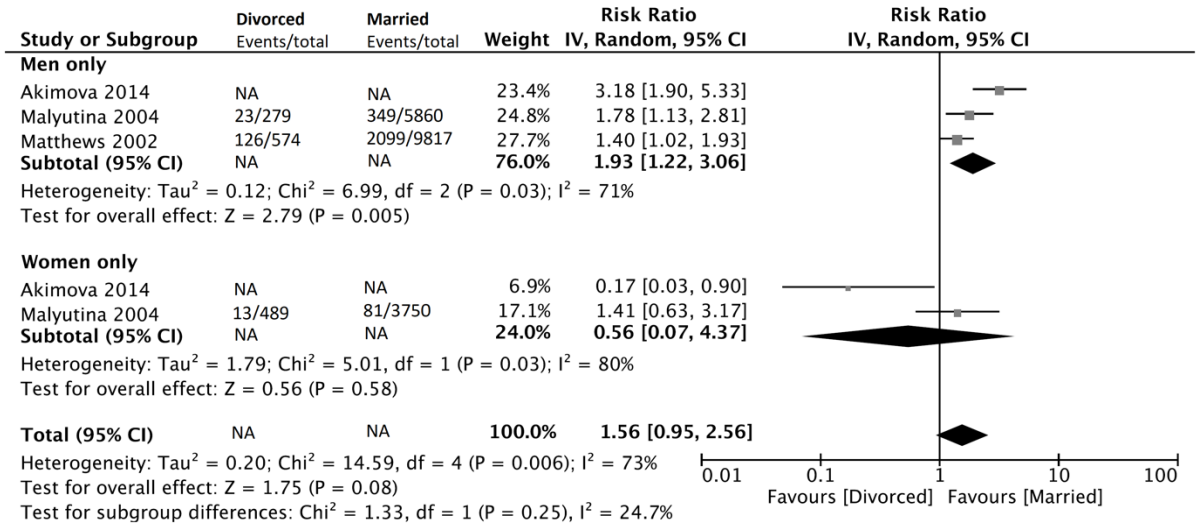


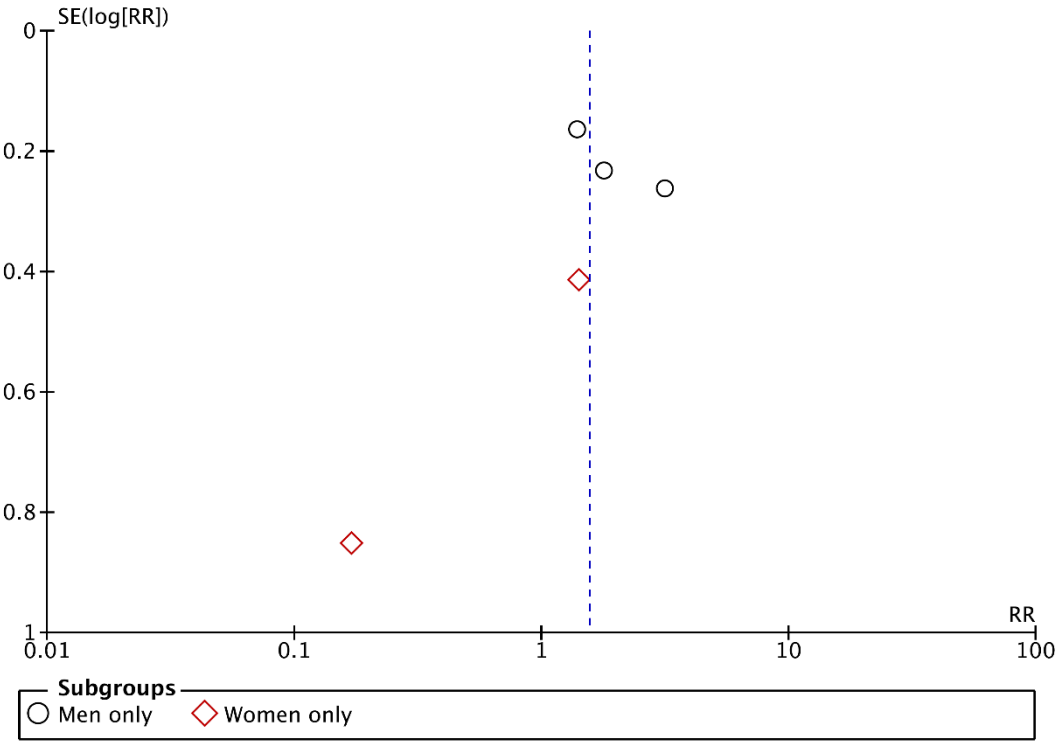
Supplementary Figure 7. Forest plot of stroke death in widowed vs married in general population and funnel plot.



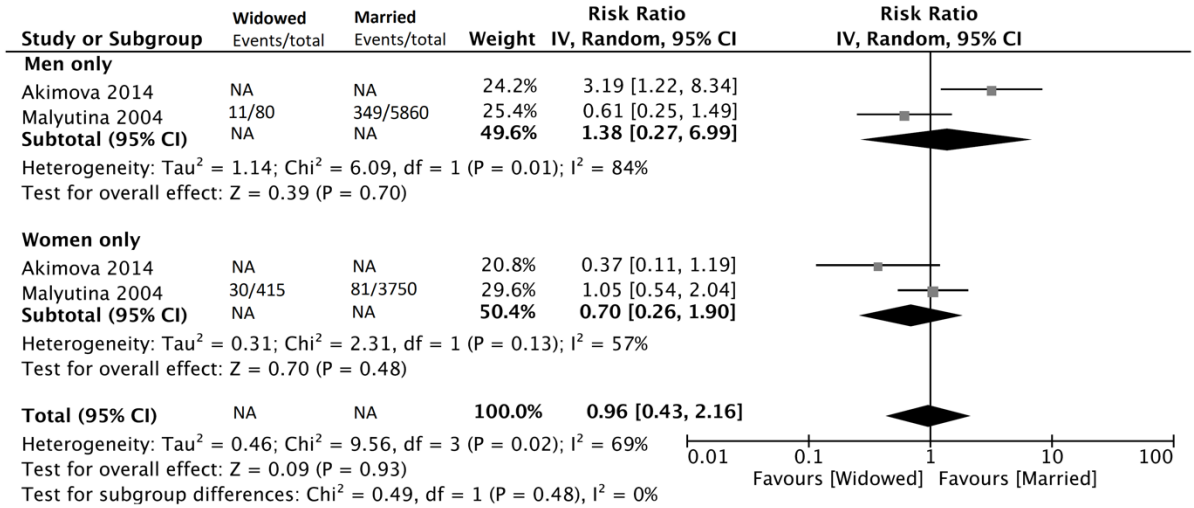


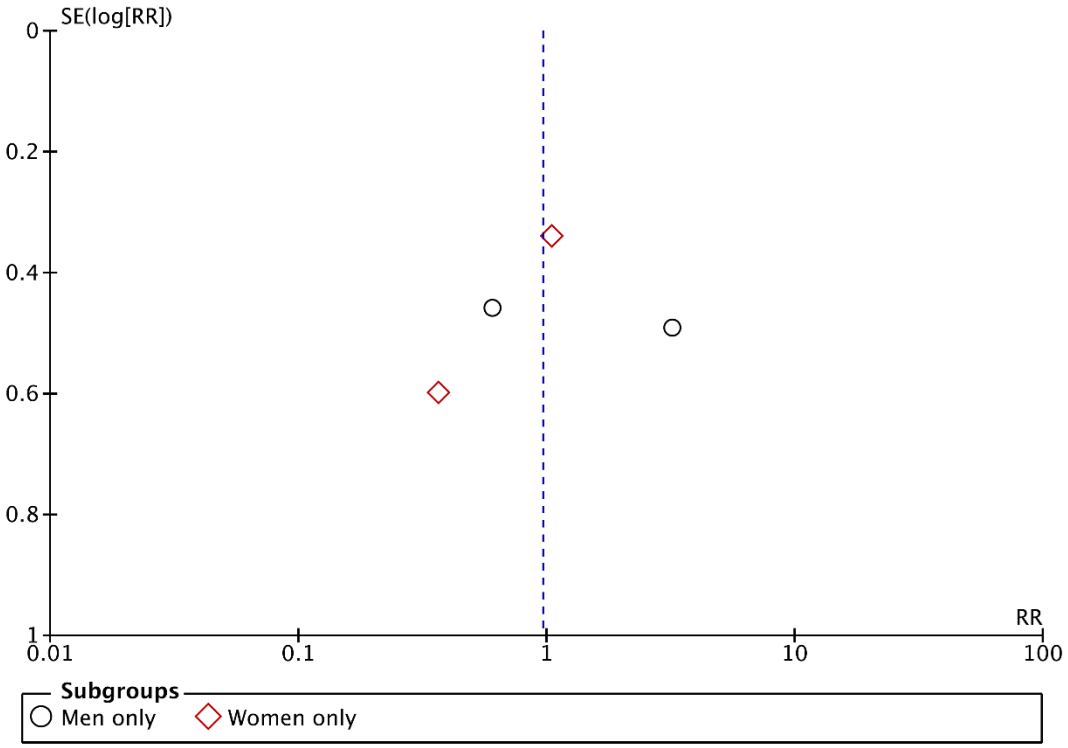
Supplementary Figure 8. Forest plot of CVD death in divorced vs married in general population and funnel plot.



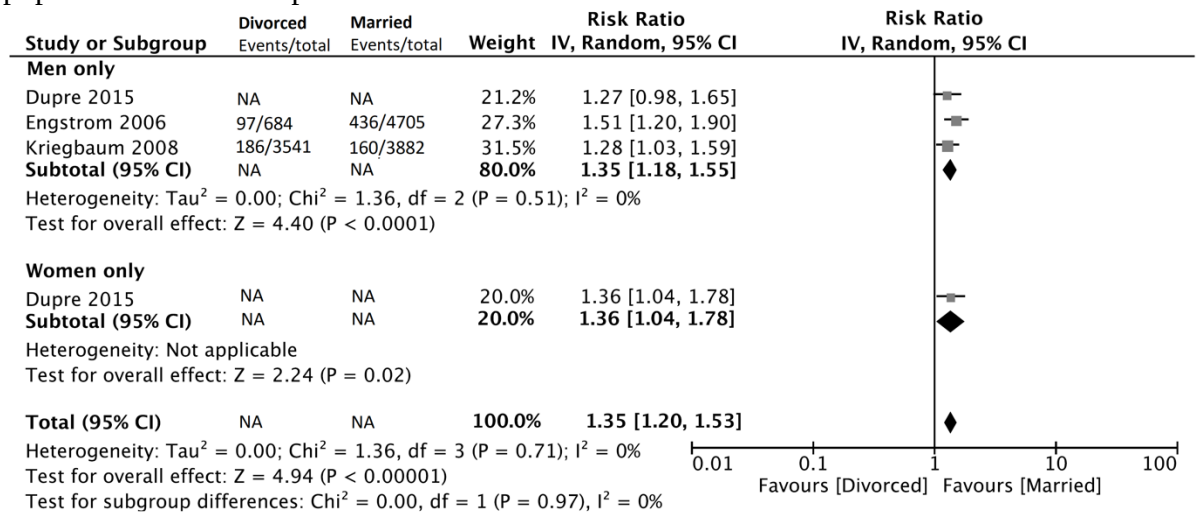


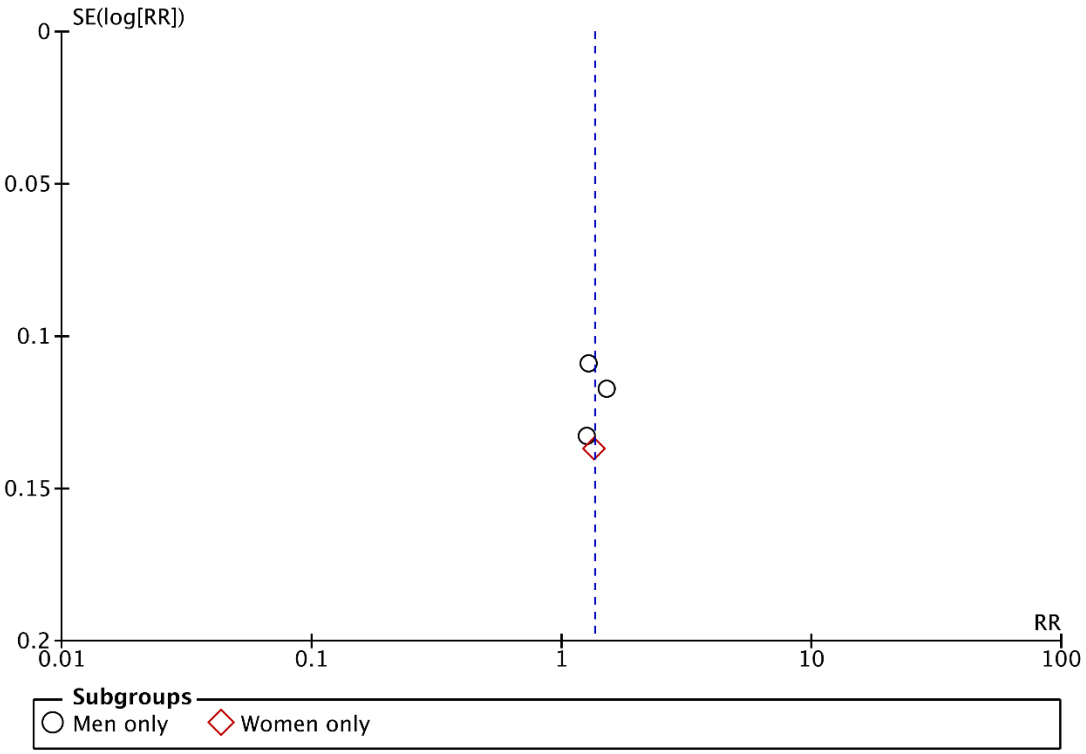
Supplementary Figure 9. Forest plot of CVD death in widowed vs married in general population and funnel plot.



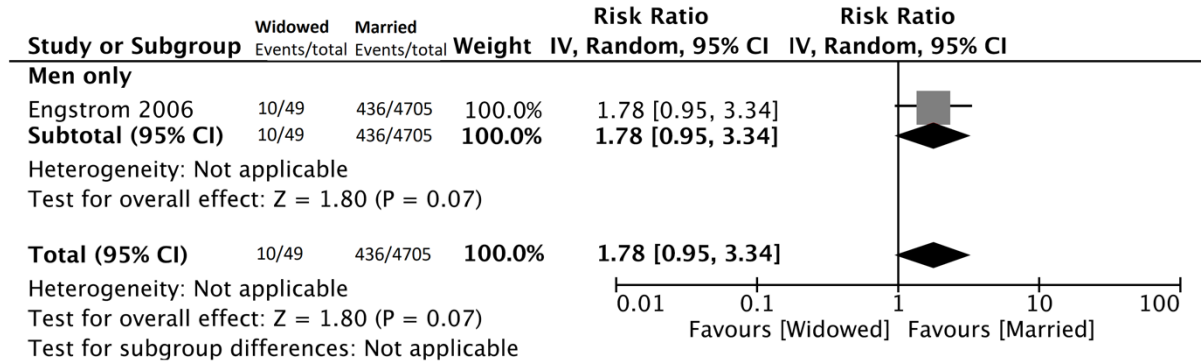


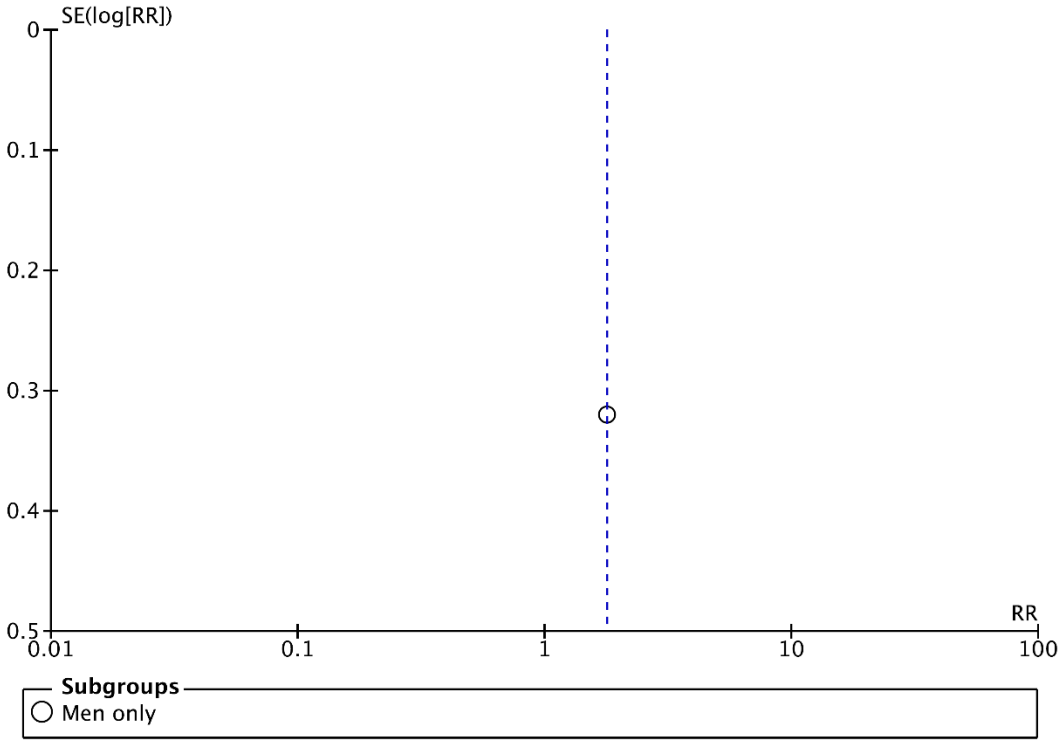
Supplementary Figure 10. Forest plot of CHD events in divorced vs married in general population and funnel plot.



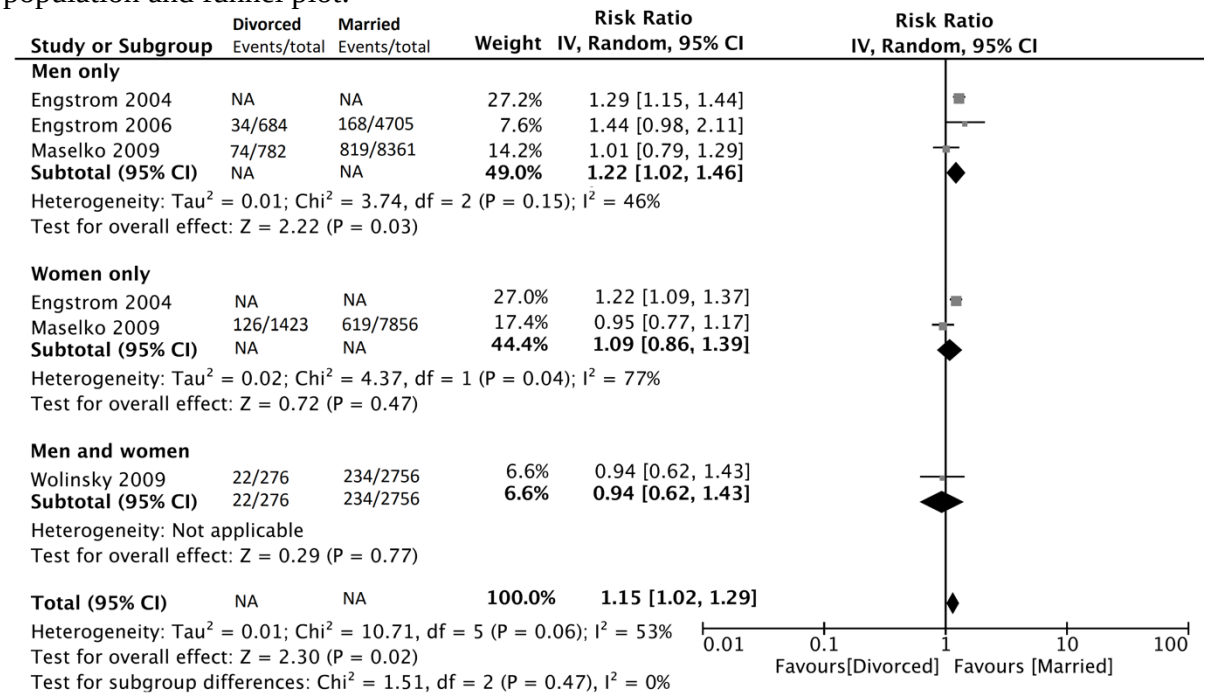


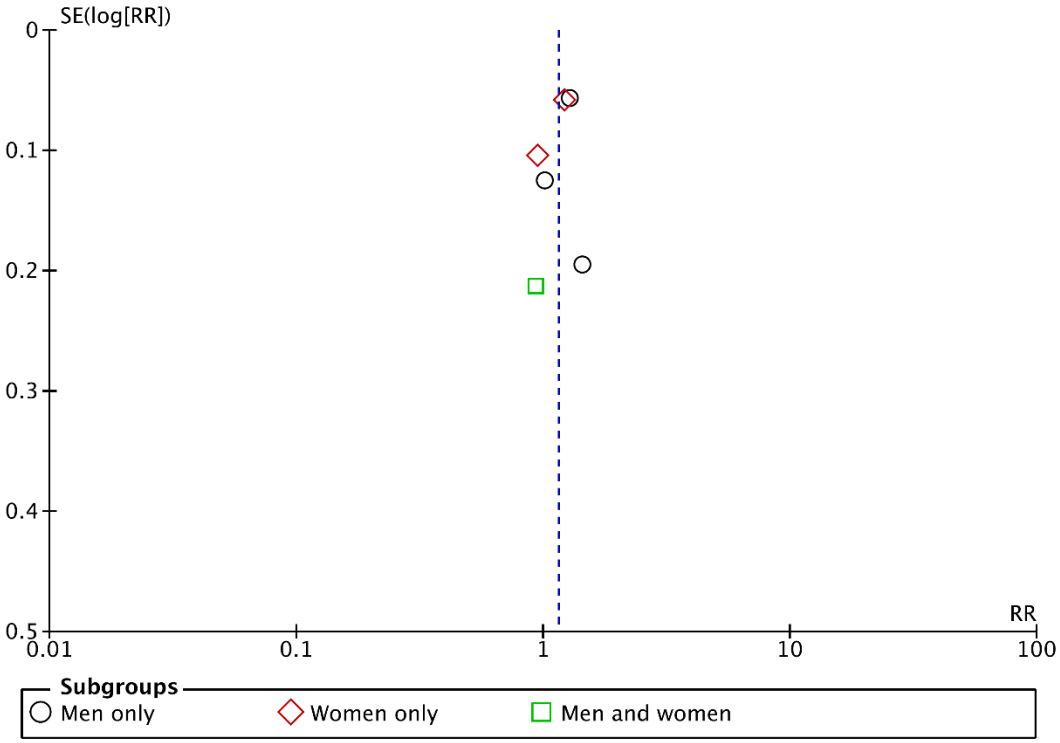
Supplementary Figure 11. Forest plot of CHD events in widowed vs married in general population and funnel plot.



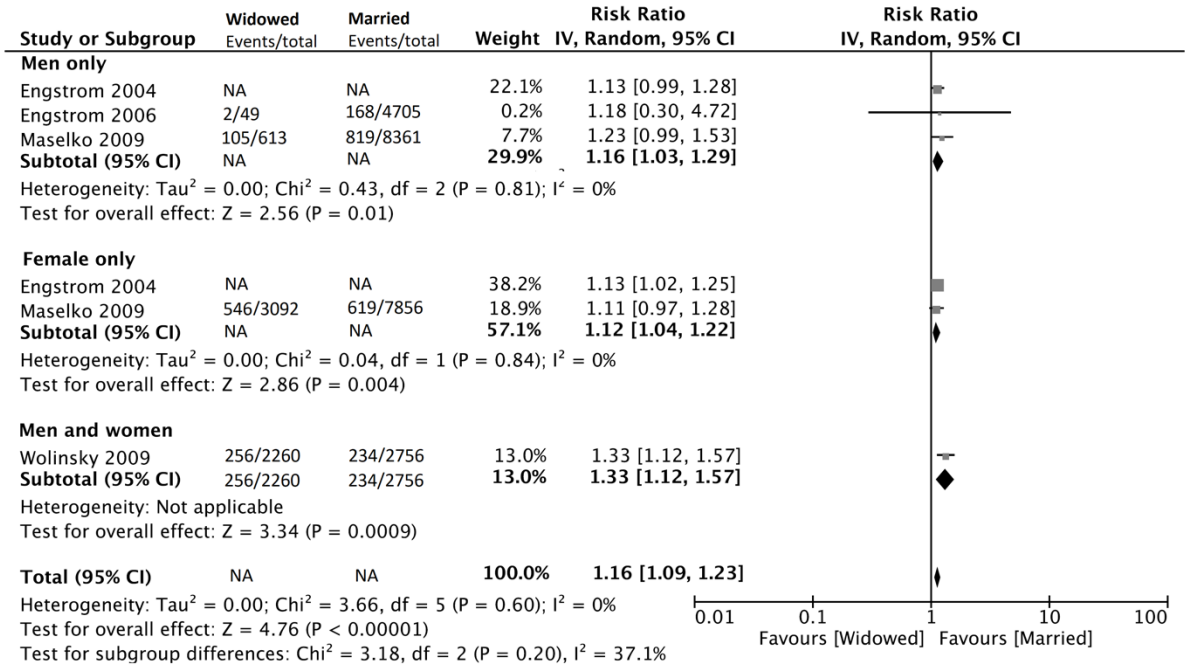


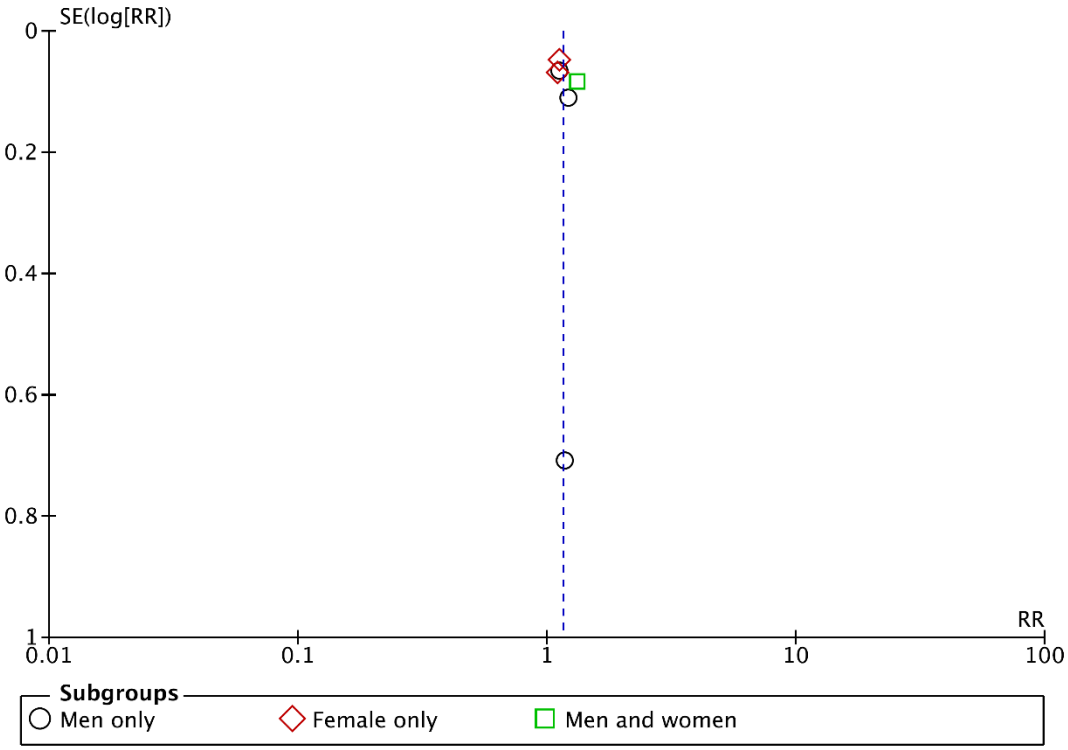
Supplementary Figure 12. Forest plot of stroke events in divorced vs married in general population and funnel plot.





Supplementary Figure 13. Forest plot of stroke events in widowed vs married in general population and funnel plot.





Supplementary Figure 14. Forest plot of post stroke death in unmarried vs married and funnel plot.