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Is marital status a protective factor for cardiovascular diseases? A review of the evidence

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Abstract:	Background: There is evidence showing that marital status (MS) and marital disruption (i.e., separation, divorce, and being widowed) is associated with poor physical health outcomes, including for all-cause mortality. We evaluated the available evidence on the association between MS and cardiovascolar (CV) diseases, outcomes and CV risk factors. Methods: All relevant papers, including the MeSH term 'marital status' in their title, were searched using the PubMed database. Moreover, the crossed search terms were: "cardiovascular diseases", "acute myocardial infarction", "acute coronary syndrome", "coronary artery disease", "cardiac arrest", "heart failure", "heart diseases", "cardiovascular mortality", "cardiovascular risk factors", "hypertension", "cholesterol", "obesity", "smoking", "alcohol", "fitness and/or physical activity", "health". Case- reports, comments, discussion letters, abstracts of scientific conferences, articles in other than English language, and conference abstracts or proceedings were excluded. Results: In total, 817 references were found and, according to the inclusion criteria, 35 studies (accounting for a total of 1 245 967 subjects) were considered suitable for analysis. In particular, 23 studies dealt with 'cardiovascular diseases' and 12 with 'cardiovascular risk factors'. Conclusions: The great majority of studies showed better outcomes for married persons compared with single, divorced or widowed persons. Males





Is marital status a protective factor for cardiovascular diseases? A review of the evidence

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Running title: Marital status and cardiovascular diseases

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ABSTRACT

Background: There is evidence showing that marital status (MS) and marital disruption (i.e., separation, divorce, and being widowed) is associated with poor physical health outcomes, including for all-cause mortality. We evaluated the available evidence on the association between MS and cardiovascolar (CV) diseases, outcomes and CV risk factors.

Methods: All relevant papers, including the MeSH term 'marital status' in their title, were searched using the PubMed database. Moreover, the crossed search terms were: "cardiovascular diseases", "acute myocardial infarction", "acute coronary syndrome", "coronary artery disease", "cardiac arrest", "heart failure", "heart diseases", "cardiovascular mortality", "cardiovascular risk factors", "hypertension", "cholesterol", "obesity", "smoking", "alcohol", "fitness and/or physical activity", "health". Case-reports, comments, discussion letters, abstracts of scientific conferences, articles in other than English language, and conference abstracts or proceedings were excluded. **Results:** In total, 817 references were found and, according to the inclusion criteria, 35 studies

(accounting for a total of 1 245 967 subjects) were considered suitable for analysis. In particular, 23 studies dealt with 'cardiovascular diseases' and 12 with 'cardiovascular risk factors'. *Conclusions:* The great majority of studies showed better outcomes for married persons compared

with single, divorced or widowed persons. Males generally had the poorest outcomes.

Key words (journal's list): cardiovascular health – health disparities

Other MeSH terms:

Ó marital status – mortality – cardiovascular diseases – cardiovascular risk factors – health – gender

Introduction

Previous studies observed that, in hospitalized subjects, marital status (MS) represented independent risk factor for some important outcomes.¹ In fact, admission severity of illness was higher in unmarried than married patients, and moderate or high severity was significantly different from unmarried and married patients (40 vs. 32%, respectively).¹ Moreover, the results from a study conducted in the United States showed that current marriage was associated with longer survival.² Independent of demographic and socioeconomic characteristics, the death rate for unmarried subjects was significantly higher than for married subjects. Although the effect was significant for all categories of unmarried persons, it was greatest for those who had never married, and significantly stronger for men than for women.² Support was obtained from a comprehensive review and meta-analysis of 53 studies, including more than 250 000 subjects.³ The overall relative risk (RR) for married vs non-married individuals (including widowed, divorced/separated, and never married) was 0.88, independent of gender and geographical area. In particular, compared with married individuals, the widowed, divorced/separated and never married persons had increased RRs of death (1.11, 1.16, and 1.11, respectively).³

The aim of the present study was to evaluate the available scientific evidence on the association between MS and cardiovascular (CV) diseases outcomes, CV risk factors as well.

Methods

All relevant papers, including the MeSH term 'marital status' in their title, were searched across the PubMed database. Moreover, the crossed search terms were: "cardiovascular diseases", "acute myocardial infarction", "acute coronary syndrome", "coronary artery disease", "cardiac arrest", "heart failure", "heart diseases", and "cardiovascular mortality". Again, other crossed search terms were: "cardiovascular risk factors", "hypertension", "cholesterol", "obesity", "smoking", "alcohol", "fitness and/or physical activity", "health". Systematic reviews, meta-analyses, controlled trials, cohort studies and case-control studies were considered for inclusion. Case-reports, comments,

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discussion letters, abstracts of scientific conferences, articles in other than English language, and conference abstracts or proceedings were excluded.

Results

In total, 817 references containing the title word "marital status" were found. After elimination of duplicates, and according with inclusion criteria, 35 studies (accounting for 1 245 967 subjects) were considered suitable for this study. We decided to include all the eligible studies, independent of their sample size, since sometimes studies with smaller samples deal with particular diseases, such as heart transplantation. Of course, these smaller studies could not have an equal weighting when evaluating their results. For simplicity, we decided to roughly split all these studies into two main general topics: (i) cardiovascular diseases and (ii) cardiovascular risk factors. Table 1 summarizes reports from studies dealing with CV diseases. In total, 23 studies were included (9 from the United States, 3 from UK, 2 each from Greece and Japan, 1 each from China, Germany, Middle East, Netherlands, Spain, Sweden and UK), accounting for 923 722 subjects in total. The lowest number of cases per study was 136 and highest 734 626. As for main topic, 19 dealt with mortality and/or survival, e.g., CV diseases, myocardial infarction and coronary ischemic disease, heart failure, heart transplantation, 2 dealt with risk and occurrence, i.e., cardiac arrest,

myocardial infarction, and 2 dealt with outcome, i.e., percutaneous coronary intervention (PCI), and heart failure.

Table 2 summarizes reports from studies dealing with CV risk factors. In total, 12 studies were included (4 from the United States, 2 each from Korea and Sweden, 1 each from Finland, Greece, Hong Kong, and Japan), accounting for 322 245 subjects in total. The lowest number of cases per study was 325 and highest 127 545. As for main topic, 7 dealt with risk factors, e.g., smoking, obesity, hypertension, 1 with dietary habits, 2 with fitness and physical activity, and 2 with health and health behavior.

In total, 18 out 33 studies provided separate analysis for subgroups by sex (55%), with similar distribution both for CV diseases (11/21, 52.3%) and CV risk factors (7/12, 58.3%).

Discussion

At least to the best of our knowledge, this is the first paper systematically collecting all the available evidence on the impact of MS on CV diseases. It seems to be strongly confirmed that MS plays an important role also in CV diseases and risk factors. The great amount of data deserves a brief detailed report of results.

CV diseases

Mortality and/or survival

(i) CV diseases (in general)

Mendes de Leon et al. screened middle-aged men in Holland, and found that non-married had higher risk for coronary mortality than the married ones.⁴ Ebrahim et al investigated the effect of MS on mortality among \geq 7 000 middle-aged British men. Single (never-married) men had a higher risk of CV disease mortality, but divorced/separated men had not. Moreover, men who divorced during the follow-up period were at increased risk of CV disease mortality, whereas those who became widowed were not.⁵ More recently, in a large Japanese study on \geq 94 000 patients, never married men compared with married men showed an increased risk of mortality from CV disease. Divorced and widowed women showed moderately increased risks of mortality married row disease, compared with married women.⁶ In a Scottish study, the risk of CV mortality was greatest in single, never married men and separated/divorced women compared with those that were married in gender stratified models.⁷ In separately adjusted models, the most important were behavioral factors, metabolic dysregulation, and psychological distress, that explained, respectively, up to 33%, 16%, 10% of the relative change in the hazard ratios between MS and CV mortality. In particular, behavioral factors had a particular relevance for the relationship between being separated/divorced

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and CV mortality in both men and women.⁷ Even in particular subgroups of patients, such as those in hemodialysis, patients who were single had higher risk than married patients for mortality from CV disease, and divorced/widowed patients had higher risk than married (HR=1.73).⁸ In a US study on 10-year coronary heart disease incidence and mortality, even after adjusting for classical risk factors, married men were almost half as likely to die during follow-up compared with the unmarried.⁹

<u>Brief summary remarks</u>: Married subjects generally had a lower risk of mortality compared with other conditions.

(i) Acute myocardial infarction, acute coronary syndrome and coronary artery disease Acute myocardial infarction (AMI). A study conducted in the US in the early '80s, reported an adjusted in-hospital case fatality rate for AMI of 19.7% and 26.7%, respectively, for married and unmarried males.¹⁰ Similar finding were confirmed also for married and unmarried females (23.3% and 37.4%, respectively). A 10-year follow-up of subjects discharged alive also confirmed a better survival rate for married compared with unmarried males and females.¹¹ More recently, in Spain the condition of widow, compared with married, was independently associated with higher all-cause death (HR=1.29) in contrast to single (HR 1.04) and divorced (HR=0.84), and gender did not show interaction with MS.¹² In Germany, overall MS showed an insignificant protective HR of 0.76. However, stratified analyses revealed strong protective effects only among men and women aged < 60 years and diagnosed with hyperlipidemia. Interestingly, the same protective effect (HR: 0.52) was confirmed also for subjects with co-habitation status.¹³

Acute coronary syndrome (ACS). In a national cohort study in the UK, Cox analysis comparison of MS and mortality showed lower mortality rates for married (OR=0.863), widowed (OR=0.959) and unmarried (OR=0.973) compared with single patients. Moreover, divorced patients had significantly \uparrow mortality rate compared to single patients (OR=1.068).¹³ Two Greek studies focused on ACS, with very similar results. Panagiotakos et al. found that never-married patients had 2.8-times and 2.7-times higher risk of dying during hospitalization and during the first 30-days

following hospitalization, respectively, compared with married patients.¹⁴ Notara et al. reported that married patients had approximately 1/3 lower risk of ACS mortality compared with single, widowed or divorced patients¹⁵ Results from a large study conducted in Middle East countries found that MS was an independent predictor for in-hospital mortality and, in particular, widowed marital status was associated with worse CV risk profile, and both in-hospital and 1-year outcome.¹⁶ Also in Sweden, unmarried status in men, but not in women, was significantly associated with increased risk of suffering a coronary event in men, but not in women. Moreover, unmarried status was also related with an increased case fatality rate (1st day) in both gender.¹⁷ In a large study in the UK on \geq 700 000 women, those who were married or living with a partner had a similar risk of a first ischemic heart disease event as women who were not, but a significantly lower risk of mortality.¹⁸

<u>Brief summary remarks</u>: Married subjects generally had lower mortality rates compared with other conditions, and in studies with separate analysis by gender there were not important differences.

(i) Dilated cardiomyopathy, heart failure and heart transplantation

In patients with idiopathic dilated cardiomyopathy, MS was a statistically significant independent predictor of survival, with single patients having a poorer survival than those who were married.¹⁹ As for heart failure (HF), married patients experienced longer event-free survival than nonmarried ones.²⁰⁻²¹ However, when medication adherence entered in the model, MS was not a significant predictor of event-free survival, demonstrating a strong mediation effect on the relationship of MS to survival.²¹ Once again, also in subjects with orthotopic heart transplantation, it was reported an improved 5-year survival for married patients compared with unmarried patients.²² <u>Brief summary remarks</u>: Even if smaller, these studies deserve attention since they are the only available for these kinds of diseases. Hence, married subjects had longer survival.

(i) Risk and outcome

Results from a cohort of $\geq 2\ 000$ subjects with out-of-hospital cardiac arrest showed that cases were more likely to be unmarried than the controls (30.2 vs 21.0%), defined as being separated or

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divorced, single or widowed. Unmarried participants had a higher risk of sudden cardiac arrest (OR 1.53).²³ As for clinical outcome of patients survived to an in-hospital cardiac arrest, females, especially those without living spouse, had worse neurological outcomes than males.²⁴ A Chinese study showed that also after adjustment for age, sex, BMI, psychosocial factors, lifestyle, and other risk factors, the OR for AMI associated with being single was 1.51 overall (1.19 in men and 2.00 in women, respectively).²⁵ MS has been found to impact also on outcome of percutaneous coronary intervention (PCI), both urgent and elective. Compared with unmarried, married patients exhibited a lower prevalence of hypertension, diabetes, smoking, and a higher prevalence of hypercholesterolemia and family history of coronary artery disease. Married patients had superior short- and long-term outcomes up to 1 year when compared with unmarried patients, and these benefits persisted after adjustment for multiple traditional CV risk factors.²⁶ There are also contrasting results for HF patients. On one hand, results from a small US study found that MS was not a significant variable for in-hospital death or for time to readmission.²⁷ On the other, another small study conducted in Singapore showed that being unmarried independently predicted mortality with ORs very near to that of New York Heart Association class (2.20 and 2.41, respectively).²⁸ Brief summary remarks: Although in the presence of limited evidence, being married is associated with a lower risk of cardiac arrest and with a better outcome of PCI.

CV risk factors

Smoking. In large Korean population, smoking rates were higher for unmarried subjects compared with their married ones.²⁹ The results showed that MS had a stronger protective influence on smoking in women than men, contrary to the gender pattern previously reported in western countries. The authors hypothesized that these findings could be explained by cultural tradition discouraging married women from smoking, but liberating divorced women.²⁹ In Sweden, never-married and divorced subjects showed a significantly higher prevalence of daily smoking than married/cohabitating respondents ³⁰ and, in Finland, living without a spouse was associated with daily smoking and higher nicotine dependence.³¹

Obesity. In a sample of workers in Sweden, obesity was associated with an increased incidence of coronary events and deaths in all diverse occupational groups. However, being single significantly increased the CV risk associated with obesity.³² On the other hand, in Greece, a higher risk of obesity was found in married men and women than in the unmarried subjects.³³

Hypertension A different blood pressure pattern has also been related to MS. Married subjects showed greater odds of dipping compared with nonmarried ones, and a lower nighttime systolic blood pressure.³⁴ Moreover, single/divorced subjects had greater odds of being unaware and uncontrolled blood pressure levels than married subjects.³⁵

CV risk factors A Japanese study compared lifestyle and risk factors between men who were married and those who had never married.³⁶ Never married men were more likely to skip breakfast, had higher smoking rates, average values of diastolic blood pressure, serum total cholesterol and fasting plasma glucose. The proportion of participants with three or more risk factors, i.e., smoking, hypertension, hypercholesterolemia and hyperglycemia was higher in the never married as well.³⁶ Interestingly, MS is also an important factor for cholesterol screening. In fact, the highest percentages of people screened for cholesterol were widowed men and women (75 and 81%, respectively), in contrast with only 26% and 38% for single men and women, respectively.³⁷ *Dietary habits* In a study performed in Hong Kong, single women had lower consumption of vegetables and fish, compared with married women. Single men had a better CV risk factor profile, including diastolic blood pressure, triglycerides and cholesterol/high-density lipoprotein ratio, and lower body mass index.³⁸

Physical activity and fitness MS represents important determinant for physical activity participation among older adults. Compared with single counterparts, married men reported higher median levels of exercise participation and married women reported higher levels of total activity.³⁹ In a sample of $> 8\ 000\ US$ subjects, the transitions to being married (from single to married or from divorced to remarried) was associated with a modest reduction, while divorce was associated with a modest increase in fitness levels in men.⁴⁰

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Health behavior The results of a study on > 120 000 US subjects showed that, regardless of any population subgroup or health indicator, married adults were generally found to be healthier than adults in other MS categories. MS differences in health were found in each of the three age groups studied (18-44, 45-64, and 65 years and over), but were most striking among adults aged 18-44 years.⁴¹ The one negative health indicator for which married adults had a higher prevalence was overweight or obesity. Married adults, particularly men, had high rates of overweight or obesity relative to adults in other marital status groups across most population subgroups studied. Never married adults were among the least likely to be overweight or obese.⁴¹ In a Korean population of middle-aged adults, it was shown that subjects living with partners were more likely to have healthier behavior than living without a partner, and the association between MS and health behaviors differed by sex.⁴²

<u>Brief summary remarks</u>: As a general observation, being married is associated with lower risk factors (with the exception of contrasting results for obesity) and a better health status. However, many confounding effects, such as different sample size and weighting among studies, different ethnicity and cultural habits, including diet and smoking, may significantly influence the final results especially in consideration of implications by gender.

The possible relationship between MS and mortality from various causes has been the object of many studies. In a large US series of > 280 000 subjects, as for the group of people aged 45-64 years, non-married subjects showed a statistically significant higher risk of mortality for various causes compared with married counterparts. Younger age groups showed higher relative risk than older age groups, and the higher risk in non-married was comparable for both females and males.⁴³ In a cohort of British women, being single was significantly associated with higher all-cause mortality (HR=1.45), whereas being divorced or widowed showed no excess mortality risk ⁴⁴ More recently, also in a Chinese population (approximately 50 000 subjects), unmarried and widowed women had an increased all-cause mortality risk (+11% and +10%, respectively), but never married

women showed the greatest excess (+46%). As for mortality for CV disease, divorce and not being married were associated with elevated risk (+47% and +65%, respectively) in men⁴⁵ Other European studies confirmed these findings as well. In a wide population study in Norway (> 800) 000 subjects), divorced, never married and widowed subjects (with respective decreasing odds) had significantly higher mortality for most causes of death compared with married ones. Among the non-married subjects, the excess mortality among the non-married was higher for men than for women.⁴⁶ In most studies, a gender difference seems to be evident. Robust confirmation derives from the largest available study, including near 2.5 million subjects in Switzerland.⁴⁷ The benefit of being married was stronger for men than for women, although adjustments for living arrangements showed different impact. In fact, in men, mortality risks were highest for 45-64-year-old divorced and single (HR 1.72 and 1.67, respectively) who lived alone. In women of the same age, the highest risk (HR 1.70) was present in single and in those were living with a partner.⁴⁷ Gender differences have been reported also in the effect of MS on dementia and Alzheimer disease.⁴⁸ and even on frailty. A recent Italian study found that unmarried men were at higher risk of frailty, while widowed women carried a lower risk of becoming frail than married women.⁴⁹ CV risk factors have been shown to exhibit differences by gender as well. Diet represents a critical factor to health. and it can play a role in these differences by gender. Results from an important longitudinal study on middle-age and older adults in UK showed that unhealthy changes to diet, evaluated with the 4 indicators of healthy eating, e.g., fruit quantity and variety, and vegetable quantity and variety, that accompanied divorce, separation and becoming widowed were more common among men than women.⁵⁰ Mood may contribute to poor metabolic control. It has been recently reported that women, who had higher prevalence of depression than men, showed also significant associations with metabolic risk factors, e.g., high fasting blood glucose and high glycohemoglobin.⁵¹ Finally, a very recent US study opened up a novel possible explanation regarding telomeres.⁵² Telomeres are DNA-protein structures, located at the ends of chromosomes, that serve to maintain DNA integrity during cell division. ⁵³ They shorten with successive cell divisions, and gradual

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shortening of telomeres after each cell division eventually can lead to a loss of cellular division capacity and cell death.⁵⁴ Thus, telomere length has come to be viewed as a biomarker of cellular aging and as a potential biomarker for factors that contribute to aging and age-related diseases.⁵⁴ Wishman et al. studied a population of > 3000 subjects performing telomere length assay on DNA extracted from saliva samples, and found that separated or divorced persons had shorter salivary telomeres than those who were continuously married or had never been married. ⁵² The association between marital disruption and telomere length, with no differences by gender, remained statistically significant also after multiple adjustments. Interestingly, currently married adults with a history of divorce evidenced shorter telomeres than people who were continuously married or never married.52

Previous evidence is available showing that MS and marital disruption, i.e., marital separation, divorce, is associated with a wide range of poor mental and physical health outcomes, including increased risk for all-cause mortality. The present study, collecting the available evidence, seems to add confirmation also for CV diseases and CV risk factors. Most studies show better outcomes for married persons, and men who were single generally had the poorest results. It is possible that persons who are married may have lower mortality because of protective effects of marriage or even selection of healthy individuals into marriage. This could maybe explain why most studies have shown evident different effects by gender, and generally unfavourable for males. On the other hand, accelerated cellular aging could also be one pathway through which marital disruption is associated with morbidity and mortality. Further studies are needed to investigate possible underlying mechanisms, to favor preventative strategies.

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Table 1. Marital status and cardiovascular diseases: available evidence from most relevant studies.

Disease	Author, year,	Main findings
CVD	Tanno, 2013 Japan, 1064	In hemodialysis patients, subjects single and divorced/widowed had \uparrow risks than married for mortality from CV disease (HR=1.68 and 1.73, respectively.
CVD	Molloy, 2009 Scotland, 13889	The risk of CV mortality was \uparrow in single, never married M and separated/divorced W compared with married. Behavioural factors had particular relevance for the relationship between being separated/ divorced and CV mortality in both M and W.
CVD	Ikeda, 2007 Japan, 94062	Compared with married M, never-married M showed \uparrow risk of mortality from CV disease (RR=3.05). For never- married W, there was a smaller but significant \uparrow risk of mortality from all causes (RR=1.46). Divorced and widowed M showed moderately \uparrow risk of mortality from CV disease, compared with married M.
CAD	Eaker, 2007 USA, 3682	Married M, compared with unmarried, showed a significantly lower risk of dying during follow-up (HR=0.54).
CVD	Mendes De Leon, 1992 Netherlands, 3365	Nonmarried M, never married and widowed had significantly \uparrow RR for coronary mortality than married (2.2, 2.9, 2.9, respectively). Not being married \uparrow the risk for fatal and total reinfarction (RR=3.6 and 2.5).
CVD	Ebrahim, 1995 UK, 7735	Single (never-married) M had \uparrow risk of CV disease mortality (RR=1.5). Divorced/separated M were not at \uparrow risk of mortality. M who divorced during the follow-up period were at \uparrow risk of CV disease mortality (RR=1.9), but not those who became widowed.
AMI	Consuegra- Sanchez, 2015 Spain, 7408	Patients widowed were significantly older, in higher proportion W, and showed \uparrow prevalence of CV risk factors. Compared to the other subgroups, widowed showed \uparrow mortality. At multivariate analysis, being widowed, compared to married, was independently associated with \uparrow all-cause death (HR=1.29) in contrast to single (HR 1.04) and divorced (HR=0.84). Gender did not show interaction with MS.
AMI	Quinones, 2014 Germany, 2854	Overall MS did not show significant protective effect, but stratified analyses found strong protective effects for M and W $<$ 60 years with hyperlipidemia (HR=0.27 and 0.43 for 2-year to 10-year survival, respectively).
AMI	Hu, 2012 China, 2909	After adjustment (age, sex, BMI, psychosocial factors, lifestyle), the ORs for AMI associated with being single was 1.51 overall (1.19 in M, 2.00 in W).
AMI	Chandra, 1983 USA, 1401	IH case fatality rate was 19.7% and 26.7% (p<0.05) in married and unmarried M, and 23.3% and 37.4% (p<0.05) in married and unmarried W, respectively. A 10-year follow-up of subjects discharged alive also showed a better survival rate for married compared to unmarried M and W (p<0.0001 and p<0.025, respectively).
ACS	Hayes, 2016 UK, 25287	Cox analysis comparison of MS and mortality showed statistically significant \downarrow mortality rates for married (OR=0.863), widowed (OR=0.959) and unmarried (OR=0.973) compared to single patients. Divorced patients had significantly \uparrow mortality rate compared to single patients (OR=1.068)
ACS	Notara, 2015	Married patients had $29\% \downarrow$ risk of ACS mortality compared with single, widowed or divorced.

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Greece, 2172 Middle East, 2334 MS was an independent predictor for IH mortality. Widowed patients had ↑ IH, 30-day and 1-year mortality rates Middle East, 5334 ACS Panagiotakos, 2008 IH mortality rate was higher in W than in M (3.2% and 5.7%, respectively, p=0.009). Never-married patients had, Greece, 2172 ACS Panagiotakos, 2008 IH mortality rate was higher in W than in M (3.2% and 5.7%, respectively, p=0.009). Never-married patients had, compared with married, 2.8- and 2.7-times ↑ risk of dying during hospitalization and during the first 30-days following hospitalization, respectively (p<0.01). IHD Floud, 2014 W married or living with a partner had a similar risk of a first IHD event as W who were not (RR=0.99), but a significantly ↓ risk of mortality (RR=0.2, 2, 0.001), independent of socio-economic groups or lifestyle. Coronary event Gerward, 2010 Ummarried married (HR=1.10, 1.42, 1.77 for never married, divorced and widowed, respectively. In both gender, unmarried was also related with ↑ case fatality rate (1st day) compared with married (M: OR=2.14, 1.91, 1.49; W: OR=2.32; 1.87, 2.74 for never married, divorced and widowed, respectively. Cardiac arrest Empana, 2008 USA, 2119 Ummarried participants had ↑ risk of sudden cardiac arrest (OR: 1.53), after adjustment for risk factors. Consistent findings were found according to sex, age >70 years, earlier coronary heart disease, presence of clinical depression. Ummarried patients showed ↓ prevalence of hypertension (86 vs 88%), diabetes (34 vs 38%), smoking (19 vs 25%), and ↑ prevalence of hypertenesimi and family history of CAD. Married patients, compared with			
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statistically significant independent predictor of survival, with single patients having a poorer survival than	cardiomyopathy	USA, 138	59.0% among single patients, and 80.0 and 71.2% among married patients. In multivariable analysis, MS was
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Heart failure Watkins, 2013 MS was not a significant variable for ischemic heart disease (HR=0.71), or for time to readmission for heart	Heart failure	Watkins, 2013	MS was not a significant variable for ischemic heart disease (HR=0.71), or for time to readmission for heart
$\frac{\text{USA, 357}}{\text{failure (HR=1.16)}}$		USA, 357	failure (HR=1.16).
Heart failure Chung, 2009 Married patients had longer event-free survival than unmarried (p=0.009).	Heart failure	Chung, 2009	Married patients had longer event-free survival than unmarried (p=0.009).
USA, 166 Heat feilure We 2012 Condise court free consistences in conservation to the increase of User and User and the test of	II. and failure	USA, 166	Condise must fire empired and in a many mind activate them in must id. Here wind activate many must bill also
Heart failure wu, 2012 Cardiac event-free survival was worse in unmarried patients than in married patients were more likely	Heart failure	WU, 2012	Cardiac event-free survival was worse in unmarried patients than in married. Unmarried patients were more likely
medication adherence in the model. MS was not a significant predictor of event free survival		USA, 130	medication adherence in the model MS was not a significant predictor of event free survival
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transplantation USA 260 vear survival (n=0.02)	transplantation	1311, 2011 USA 260	vear survival ($p=0.02$)
Abbreviations: ACS=acute coronary syndrome: AMI=acute myocardial infarction: CAD=coronary artery disease: CVD=cardiovacular disease: HR=bazard	Abbreviations: A	CS=acute coronary syr	your surviver (p. 0.02).

ratio; IH=in-hospital; M=men; IHD=ischemic heart disease; MACE=major adverse cardiac event; MS=marital status; PCI=percutaneous coronary intervention; nterven RR=relative risk; W=women;

Table 2.	Marita	l status and	cardiovascula	risk factors:	available evidence	from most relevant studies.

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2			
4	Table 2. Marita	l status and cardiova	ascular risk factors: available evidence from most relevant studies.
5			
6 7	Risk factor	Author, year, country, n of cases	Main findings
8 9	Cardiovascular	Kamon, 2008 Japan, 1582	Never married M were more likely to skip breakfast, and had ↑ smoking rates, average diastolic BP values, serum total cholesterol and fasting plasma glucose compared with married M.
10 11	Hypertension	Causland, 2014 USA, 325	Married subjects had \uparrow adjusted OR of dipping (2.26) compared with nonmarried. Being married was associated with \downarrow nighttime systolic BP (-2.4 mmHg), especially for M vs W (-3.1 vs1.7 mmHg).
12 13	Obesity	Tzotzas, 2010 Greece, 17341	↑ risk of obesity in married M (OR=2.28) and married W (OR=2.31) than unmarried.
14 15 16 17	Obesity	Hedblad, 2002 Sweden, 20099	Being single significantly \uparrow the risk associated with obesity. The multivariate-adjusted RR of coronary events and deaths was, respectively, 1.91 and 2.54 (manual workers) and 4.79 and 3.80 (self-employed workers), compared with those who were cohabitants.
18 19	Smoking	Pennanen, 2014 Finland, 1746	Living without a spouse was associated with daily smoking and \uparrow nicotine dependence.
20 21	Smoking	Lindstrom, 2010 Sweden, 27757	The ORs of daily smoking for middle-aged subjects, and unmarried and divorced subjects were significantly \uparrow than the reference groups.
22 23 24	Smoking	Cho, 2008 Korea, 110015	Smoking rates were \uparrow for unmarried M and W compared to married. The gap in smoking rates between unmarried and married W was much greater than that between unmarried and married M. MS had a stronger protective influence on smoking in W than M.
25 26	Dietary habits	Woo, 1999 Hong Kong, 1010	Single W had \downarrow consumption of vegetables and fish, compared with married W. Single men had a better cardiovascular risk factor profile (\downarrow diastolic BP, triglycerides, cholesterol/HDL ratio, BMI)
27 28	Fitness	Ortega, 2011 USA, 8871	Compared with control groups (single, married, divorced), transitioning from single to married was associated with \downarrow in fitness in W; divorce with \uparrow in fitness in M; and remarriage with \downarrow in fitness in M.
29 30 21	Physical activity	Pettee, 2006 USA, 3420	Compared with single subjects, married M had \uparrow median levels of exercise participation and married W reported \uparrow levels of total activity.
32 33 34	Health behavior	Yim, 2012 Korea, 2522	The risk of undergoing health screening (OR=0.53) and having regular breakfast (OR=0.50) were \downarrow in M living without a partner than with a partner. W living without a partner had \uparrow smoking and alcohol consumption risk (OR=2.27 and 5.33) than the counterparts.
35 36	Health	Schoenborn, 2004 USA, 127545	Married adults were healthier than adults in other MS categories. MS differences in health were present in all age groups. Married adults: ↑ prevalence of overweight or obesity.

Abbreviations: BMI=body mass index; BP=blood pressure; HR=hazard ratio; M=men; MS=marital status; OR=odds ratio; RR=relative risk; W=women

