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ORIGINAL RESEARCH

Bereavement and Prognosis After a First Acute Myocardial Infarction: A Swedish Register-Based Cohort Study

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BACKGROUND: Despite accumulating evidence suggesting that bereavement is associated with increased risks of cardiovascular morbidity and mortality, the association between bereavement and prognosis after acute myocardial infarction (AMI) has not been well documented. We investigated the association by using Swedish register data.

METHODS AND RESULTS: We studied 266 651 patients with a first AMI included in the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) quality register from 1991 to 2018. We obtained information on bereavement (ie, death of a partner, child, grandchild, sibling, or parent), on primary (nonfatal recurrent AMI and death attributed to ischemic heart disease) and secondary outcomes (total mortality, heart failure, and stroke) and on covariates from several national registers. The association was analyzed using Poisson regression. The bereaved patients had a slightly increased risk of the primary outcome; the corresponding risk ratio (RR) was 1.02 (95% CI, 1.00–1.04). An increased risk was noted any time bereavement occurred, except if the loss was in the year after the first AMI. The association was strongest for the loss of a partner, followed by the loss of a child, grandchild, sibling, or parent. We also observed increased risks for total mortality (RR, 1.14 [95% CI, 1.12–1.16]), heart failure (RR, 1.05 [95% CI, 1.02–1.08]), and stroke (RR, 1.09 [95% CI, 1.05–1.13]) following bereavement.

CONCLUSIONS: Bereavement was associated with an increased risk of poor prognosis after a first AMI. The association varied by the relationship to the deceased.

Key Words: acute myocardial infarction ■ bereavement ■ prognosis ■ recurrent events ■ stress

Bereavement is a severe life event that affects most individuals several times in their lives. Increasing evidence suggests that bereaved people are at an increased risk of mental disorders,[1] mortality,[1] and cardiovascular disease (CVD), including acute myocardial infarction (AMI),[2–7] stroke,[8] atrial fibrillation,[9,10] and heart failure.[11]

Because of the increasing number of patients who survive CVD[12] and their advanced age,[12] bereavement in patients with CVD is common.[13] Nevertheless, few studies have investigated the association between bereavement and the prognosis of CVD,[3,14,15] although psychological distress is known to play a role in the progression of CVD.[16] The findings of these earlier studies have been mixed, possibly because of the differences in studied CVDs, study designs, and definitions of exposures and outcomes.[3,14,15] To our knowledge, only our earlier study investigated the link between bereavement and prognosis in patients with AMI based on the data from the Stockholm Heart Epidemiology Program.[13] However, the lack of detailed information on bereavement and the low statistical power limited our

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CLINICAL PERSPECTIVE

What Is New?

- Patients with acute myocardial infarction (AMI) who lost a close family member 1 year before or from the second year after the first AMI had an increased risk of both fatal and nonfatal recurrent events.
- The death of a partner had the strongest association with poor prognosis in AMI, followed by the loss of a child, grandchild, sibling, and parent.

What Are the Clinical Implications?

- Bereaved patients with AMI may benefit from increased social support and medical attention after AMI.

Nonstandard Abbreviations and Acronyms

IHD	ischemic heart disease

possibilities to investigate several important questions, namely (1) whether the association is present also in case of loss after AMI and (2) whether the association differs according to the type of bereavement (eg, relationship to the deceased, relative's cause of death, the time of loss), time since loss, sociodemographics, or secondary prevention measures.

In this large-scale study, we investigated whether the death of a close family member, that is, partner, sibling, child, grandchild, or parent, was associated with post-AMI prognosis and whether the association differed according to the type of loss, time since loss, characteristics of study participants, and secondary prevention measures.

METHODS

The data supporting the findings in this study were obtained from the Swedish National Board of Health and Welfare and Statistics Sweden but cannot be shared publicly because of ethical considerations and the Swedish relevant laws and regulations. The data are available from the aforementioned data holder authorities for researchers who fulfill specific requirements.

Study Population and Design

We conducted a population-based cohort study including patients with a first AMI recorded in the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) quality register from 1991 to 2018. The SWEDEHEART includes several quality registers for coronary heart diseases among others the RIKSHIA (Register of Information and Knowledge About Swedish Heart Intensive Care Admissions) and SEPHIA (National Registry of Secondary Prevention). The RIKSHIA has collected information on AMI in several Swedish counties since the early 1990s and became nationwide in 1995.[17] The SEPHIA was added to RIKSHIA in 2005 and has collected follow-up information on rehabilitation and secondary prevention surveillance at 6 to 10 weeks and 12 to 14 months after discharge for patients who were hospitalized for AMI and were aged <75 years.[17]

For each study participant, we identified parents, siblings, children, and grandchildren in the Swedish Multi-Generation Register and spouses or partners in the Swedish Total Population Register. Linkage to biological relatives was performed through the unique personal identification number assigned to each Swedish resident. Linkage was possible if the index individual was born in 1932 or later, was alive in 1961, and if family members were Swedish residents at some point since 1947 (when the personal identification number was introduced in Sweden).[18] We identified spouses or partners using the algorithm developed by Statistics Sweden and described in Data S1. We identified fathers for 46.1%, mothers for 48.5%, siblings for 41%, children for 82.2%, grandchildren for 72.4%, and spouses or partners for 56.2% of the study participants during the year before the AMI. In the analysis, we only included patients who had at least 1 live family member 1 year before the first AMI (n=266 651; the flowchart of the study is shown in Figure S1).

The study was approved by the Regional Ethics Review Board in Stockholm (2016/288–31/1). Informed consent is not needed for register-based studies in Sweden.

Exposure

We defined exposure as the death of a partner, child, grandchild, sibling, or parent 1 year before the first AMI or later. Information on these family members' date and cause of death was obtained from the Swedish Cause of Death Register. In cases of multiple losses during the observation period, we regarded the first loss as the index exposure. Exposure was further classified according to (1) the relationship to the deceased, (2) the cause of death (CVD, other natural death, and unnatural death), and (3) the timing of loss in relation to the AMI (the year before the first AMI and 0–1, 2–5, or >5 years after the AMI). We used the *International Statistical Classification of Diseases and Related*

Health Problems, Eighth Revision (*ICD-8*), *Ninth Revision* (*ICD-9*) and *Tenth Revision* (*ICD-10*) codes shown in Table S1 to categorize the relatives' causes of death.

Outcomes

Our primary outcome was the combination of nonfatal recurrent AMI and death attributed to ischemic heart disease (IHD). In addition, we studied total mortality, heart failure, and stroke as secondary outcomes. Nonfatal recurrent AMI was defined as the first hospital visit with a primary diagnosis of AMI 28 days after the first AMI. We identified the outcomes in the Patient Register and the Cause of Death Register using the *ICD*-8, *ICD*-9, and *ICD-10* codes shown in Table S1. Follow-up started on the date of the first AMI and ended at the first occurrence of the outcome, emigration, death, or December 31, 2018, whichever came first.

Covariates

We retrieved information on sex, age, and country of birth from the Total Population Register and on income from the Income and Taxation Register and LISA (Longitudinal Integration Database for Health Insurance and Labor Market Studies). We used data on income from the year before the first AMI. In case this information was missing, we used data from the year closest to the AMI during the 5 years preceding the event. We categorized income into 3 groups by the tertile distribution of each year. We retrieved information on the highest educational attainment from LISA. We obtained data on the history of psychiatric disorders and CVD as well as their partner and family (i.e., parents, siblings, children, and grandchildren) histories of psychiatric disorders and CVD from the Patient Register and the Cause of Death Register.

We retrieved information on type of infarction and diabetes at baseline as well as on regular cardiovascular medications and participation in secondary prevention programs at 6 to 10 weeks and 12 to 14 months after discharge from SWEDEHEART (Table S2).

Statistical Analysis

We estimated rate ratios (RRs) and 95% CIs for the association between bereavement and prognosis after AMI using Poisson regression. We treated exposure as a time-dependent variable, that is, bereaved patients contributed person-time from study entry until the loss to the unexposed group and to the exposed group afterward. Nonbereaved patients contributed person-time only to the unexposed group. We performed analyses with any loss and with loss categorized according to the cause of death, the relationship to the deceased, and the timing of loss in relation to the AMI. In our main models, we adjusted for age and calendar year at follow-up as time-dependent variables (with a yearly split), sex, country of birth, highest education, income and diabetes at baseline, having a spouse/partner, number of live children, number of live grandchildren, number of live siblings, number of live parents, and personal and family histories of psychiatric disorders and CVD 1 year before the first AMI as time-fixed variables. We studied the association between the death of a spouse/partner and the outcomes among those who were married, lived in a registered partnership, or had a cohabitant at 1 year before the first AMI. Similarly, we restricted the analyses corresponding to the death of other types of relatives, that is, child, grandchild, sibling, or parent, to those who had at least 1 alive corresponding relative at 1 year before the first AMI. Covariates adjusted in each relative-specific model are shown in the footnote of Figure 1.

To visualize the time-varying effect of bereavement on the primary outcome, we reran the main model after splitting the follow-up for the exposed group as 0 to 1 year, 2 to 5 years, 6 to 10 years, and >10 years. We also performed stratified analyses by sex, country of birth, age at AMI diagnosis (≤65 and >65 years), year of diagnosis, education, income, and type of infarction. Because bereaved individual's mental and cardiovascular health may benefit from cardiovascular medication and other secondary prevention measures,[19,20] we performed stratified analyses by relevant cardiovascular medications (Table S3) and participation in secondary prevention programs.

We performed statistical analyses with SAS 9.4.

RESULTS

A total of 64 053 (24.2%) patients experienced the loss of a close family member during the year before the AMI or later (Table S4). Compared with their unexposed counterparts, bereaved patients were younger, more likely to have the index AMI in earlier years and to be born in Sweden, and less likely to have diabetes, psychiatric disorders, and CVD at baseline. Furthermore, the exposed group was more likely to have a higher income and a family history of psychiatric disorders and CVD at baseline than the unexposed group (Table 1).

During the median follow-up of 4.4 years, 91 783 patients experienced the primary outcome, that is, nonfatal recurrent AMI or death attributed to IHD, 123 985 died, 48 414 had heart failure, and 25 858 had a stroke. Loss of a close family member was associated with modestly increased risks of nonfatal recurrent AMI or death attributed to IHD (RR, 1.02 [95% CI, 1.00–1.04]), total mortality (RR, 1.14 [95% CI, 1.12–1.16]), heart failure (RR, 1.05 [95% CI, 1.02–1.08]), and stroke (RR, 1.09 [95% CI, 1.05–1.13]) (Table 2). The associations were

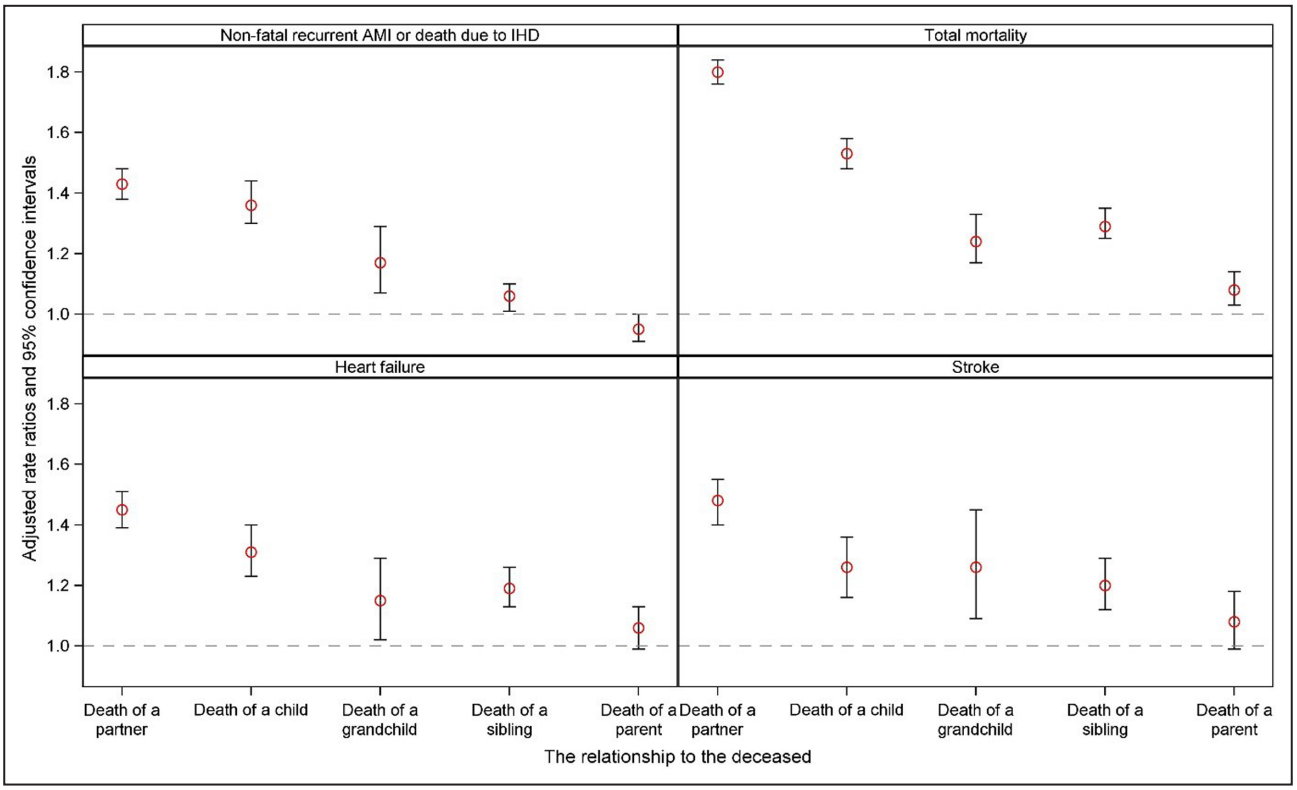

Figure 1. Adjusted rate ratios and 95% CIs for the association between type of deceased relative and prognosis after AMI. Each relative-specific analysis was performed among those who had at least 1 of the studied family members alive 1 year before the first AMI. For the death of a partner, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, personal and partner's histories of psychiatric disorders, and cardiovascular disease 1 year before the first AMI. For the death of a child, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live children, and personal and family histories of psychiatric disorders and cardiovascular disease 1 year before the first AMI. For the death of a grandchild, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live grandchildren, and personal and family histories of psychiatric disorders and cardiovascular disease 1 year before the first AMI. For the death of a sibling, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live siblings, and personal and family histories of psychiatric disorders and cardiovascular disease 1 year before the first AMI. For the death of a parent, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live parents, and personal and family histories of psychiatric disorders and cardiovascular disease 1 year before the first AMI. AMI indicates acute myocardial infarction; and IHD, ischemic heart disease.

similar across different causes of death of the relative (cardiovascular, other natural, and unnatural death) and were strongest for the loss of a partner, followed by the loss of a child, grandchild, sibling, and parent (Figure 1). The association with the death of a partner or a child was observed consistently in both the short- and long-term after the loss (Figure S2).

There was a positive association between bereavement and the risk of the primary outcome any time the bereavement occurred, except if the loss was in the year after the first AMI (Figure 2).

We observed slightly stronger associations between any loss and the primary outcome among older (>65 years) than younger patients, foreign born than Swedish born, and those with low compared with high income (Table S3). There was a trend toward a weaker association among those using statins or other lipid-lowering drugs at the time of the SEPHIA assessments as well as among those participating in a physical training program (Table S5). The association between bereavement and the primary outcome did not differ substantially according to other studied potential effect modifiers.

DISCUSSION

We found that patients with AMI who lost a close family member during the year before the AMI or later had modestly increased risks of the combination of nonfatal recurrent AMI and death attributed to IHD, all-cause mortality, heart failure, and stroke. The associations were strongest for the loss of a partner, followed by

Table 1. Characteristics of Study Participants According to Exposure to Bereavement

Variables	Exposure status	
	Unexposed (n=202 598)	Exposed (n=64 053)
Age at diagnosis, y, mean (SD)	71.3 (12.2)	65.7 (11.6)
Year of diagnosis, n (%)		
1991–1999	28 040 (13.8)	10 902 (17.0)
2000–2009	84 807 (41.9)	33 289 (52.0)
After 2009	89 751 (44.3)	19 862 (31.0)
Sex, n (%)		
Male sex	129 462 (63.9)	41 297 (64.5)
Female sex	73 136 (36.1)	22 756 (35.5)
Country of birth, n (%)		
Sweden	168 593 (83.2)	57 823 (90.3)
Other country	34 005 (16.8)	6230 (9.7)
Highest education, n (%)		
0–9 y	92 132 (45.5)	27 904 (43.6)
10–14 y	88 025 (43.4)	30 237 (47.2)
≥15 y	17 363 (8.6)	5296 (8.3)
Missing	5078 (2.5)	616 (1.0)
Income at baseline, n (%)		
Low tertile	67 166 (33.2)	18 778 (29.3)
Middle tertile	70 298 (34.7)	17 801 (27.8)
High tertile	64 881 (32.0)	27 434 (42.8)
Missing	253 (0.1)	40 (0.1)
Diabetes at baseline, n (%)		
No	162 211 (80.1)	54 372 (84.9)
Yes	37 600 (18.6)	8893 (13.9)
Missing	2787 (1.4)	788 (1.2)
Type of infarction, n (%)		
No infarction	150 (0.1)	51 (0.1)
STEMI	39 069 (19.3)	9945 (15.5)
NSTEMI	65 541 (32.4)	15 688 (24.5)
Missing	97 838 (48.3)	38 369 (59.9)
History of CVD 1 y before the first AMI, n (%)		
No	109 412 (54.0)	43 018 (67.2)
Yes	93 186 (46.0)	21 035 (32.8)
History of psychiatric disorders 1 y before the first AMI, n (%)		
No	177 267 (87.5)	57 470 (89.7)
Yes	25 331 (12.5)	6583 (10.3)
Number of family members alive 1 y before the first AMI, mean (SD)	6.4 (4.1)	7.5 (4.3)
Number of children alive 1 y before the first AMI, mean (SD)	2.0 (1.3)	2.0 (1.3)
Number of grandchildren alive 1 y before the first AMI, mean (SD)	2.9 (3.0)	2.6 (3.1)
Number of siblings alive 1 y before the first AMI, mean (SD)	0.8 (1.3)	1.6 (1.9)
Number of parents alive 1 y before the first AMI, n (%)		
0	179 143 (88.4)	37 309 (58.2)
1	17 075 (8.4)	19 430 (30.3)
2	6380 (3.1)	7314 (11.4)
Family history of CVD 1 y before the first AMI, n (%)*		
No	87 104 (43.0)	16 400 (25.6)
Yes	115 494 (57.0)	47 653 (74.4)
Family history of psychiatric disorders 1 y before the first AMI, n (%)*		
No	119 311 (58.9)	33 334 (52.0)
Yes	83 287 (41.1)	30 719 (48.0)
Having a spouse or partner 1 y before the first AMI, n (%)		
No	87 427 (43.2)	17 705 (27.6)
Yes	115 171 (56.8)	46 348 (72.4)
Partner's history of CVD 1 y before the first AMI, n (%)		
No	77 765 (67.5)	29 935 (64.6)
Yes	37 406 (32.5)	16 413 (35.4)
Partner's history of psychiatric disorders 1 y before the first AMI, n (%)		
No	105 112 (91.3)	41 984 (90.5)
Yes	10 059 (8.7)	4364 (9.5)

AMI indicates acute myocardial infarction; CVD, cardiovascular disease; NSTEMI, non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.

*Family members include parents, siblings, children, and grandchildren.

the loss of a child, grandchild, sibling, and parent, but were similar for different causes of death of the relative.

Comparison With Earlier Studies

Findings from the present study are consistent with those of our earlier investigation from the Stockholm Heart Epidemiology Program,[13] to our knowledge the only previous investigation regarding the role of bereavement in prognosis after AMI. In that study, we followed 1732 patients with a first AMI in 1992 to 1994 for a median of 14 years and found that the self-reported loss of a relative or close friend during the year before AMI was not related to AMI prognosis; however, the loss of a partner was associated with an increased risk of the combined outcome of nonfatal recurrent AMI and death attributed to IHD.[13] The availability of the extensive, prospectively collected information on family members' death through the Swedish Multi-Generation Register, the Total Population Register, and the Cause of Death Register and the possibility to link these data to the SWEDEHEART allowed us to extend this earlier work in several ways. Information on specific relatives and their date and cause of death made it possible to investigate the importance of the cause of death, the relationship to the deceased, the timing of the loss

Table 2. Adjusted RRs and 95% CIs for the Association Between Bereavement and Prognosis in Acute Myocardial Infarction

Exposure	Primary outcome*			Total mortality			Heart failure			Stroke		
	No. of events	Rate†	Multivariable RR‡ (95% CI)	No. of events	Rate†	Multivariable RR‡ (95% CI)	No. of events	Rate†	Multivariable RR‡ (95% CI)	No. of events	Rate†	Multivariable RR‡ (95% CI)
Unexposed	78773	64.6	Reference	99660	70.7	Reference	40094	31.1	Reference	20548	15.2	Reference
All deaths	13010	36.2	1.02 (1.00–1.04)	24325	56.0	1.14 (1.12–1.16)	8320	21.2	1.05 (1.02–1.08)	5310	13.0	1.09 (1.05–1.13)
Cause of death of the deceased												
Death attributed to CVD	5281	35.6	1.03 (1.00–1.06)	9440	52.5	1.14 (1.11–1.17)	3303	20.3	1.05 (1.01–1.10)	2100	12.4	1.09 (1.04–1.15)
Other natural deaths	7055	36.3	1.01 (0.99–1.04)	13612	57.8	1.14 (1.12–1.16)	4580	21.5	1.04 (1.01–1.08)	2914	13.2	1.09 (1.04–1.14)
Unnatural causes	674	41.5	1.04 (0.96–1.12)	1273	65.1	1.12 (1.05–1.18)	437	24.8	1.07 (0.97–1.18)	296	16.2	1.17 (1.04–1.32)

CVD indicates cardiovascular disease; and RR, rate ratio.

*The primary outcome was the combination of nonfatal recurrent acute myocardial infarction and death attributed to ischemic heart disease.

†Per 1000 person-years.

‡Adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, having a spouse/partner, number of live children, number of live grandchildren, number of live siblings, number of live parents, and personal and family histories of psychiatric disorders and CVD 1 year before the first acute myocardial infarction.

in relation to the AMI, and the time since the loss. Furthermore, the large sample size and the extensive sociodemographic and clinical data allowed us to investigate effect modification by relevant sociodemographic variables, type of infarction, and whether secondary prevention measures may modify the studied association. Our findings are also consistent with those of several, although not all, studies reporting a link between bereavement and incident CVD or cardiovascular death.[2–4,6,7,9–11] Furthermore, our results corroborate previous findings that psychological stress or stress-related disorders are associated with poor prognosis in IHD.[16,21–23] Nevertheless, the effect estimates of any loss on the prognosis of AMI were relatively small in the present study, possibly attributed to the fact that the death of a parent or sibling in old age—events in line with our expectations about the life cycle—accounted for >60% of the losses.

Several classification systems of sources of stress rate the death of a spouse or child as the most stressful life event one can experience.[24,25] Adults with an age range similar to that of our cohort members are likely to have the closest emotional ties with their partner, followed by children, grandchildren, siblings, and parents. The death of a partner deprives bereaved patients of a strong emotional bond and source of support, but may also lead to adverse changes in their life situation and in their finances.[26,27] In addition to the partner, children are also an important source of support in old age. We indeed found that the association was stronger in the case of the loss of a spouse or child compared with the loss of other family members, in line with a meta-analysis reporting a dose–response relation between psychological distress and death attributed to CVD.[28]

An increased medical attention, social support, and high socioeconomic status may attenuate the potential harmful effects of bereavement on AMI prognosis. The active surveillance during the year after AMI may identify patients who lost a close family member, possibly leading to further increased attention from health professionals.[13] In line with this hypothesis, we found that patients with AMI who lost a close family member during the year after the first AMI had a lower risk of the primary outcome than their nonbereaved counterparts. Furthermore, we observed a trend toward a weaker association among patients on statins or other lipid-lowering drugs and among those participating in a physical training program up to 14 months after the first AMI, although the statistical precision was low in these stratified analyses. In addition, the finding that the association was stronger among foreign-born than among Swedish-born patients and in groups with low than with high socioeconomic status may be supportive of the hypothesis that social and economic and education-related resources may somewhat buffer the

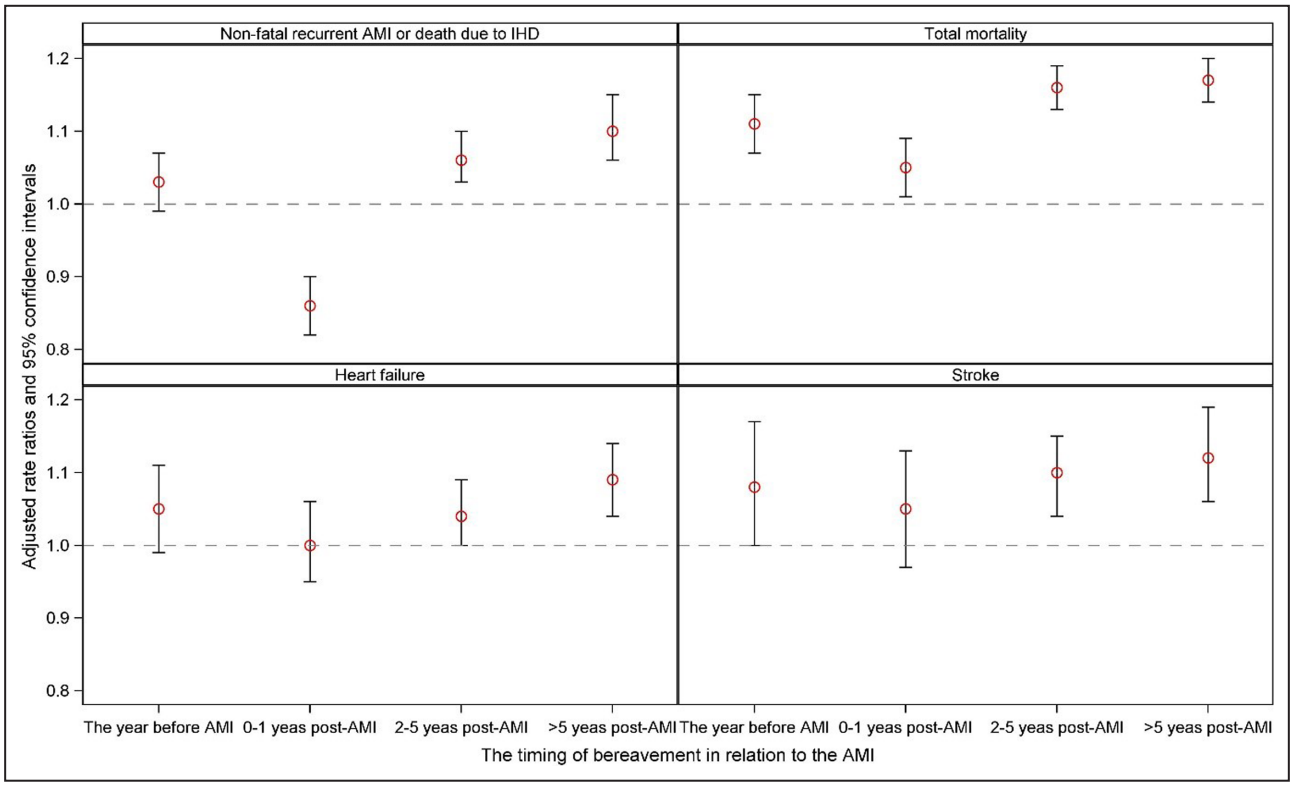

Figure 2. Adjusted rate ratios and 95% CIs for the association between bereavement and prognosis after AMI according to the timing of bereavement in relation to the AMI.
We adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, having a spouse/partner, number of live family members, number of live children, number of live grandchildren, number of live siblings, number of live parents, and personal and family histories of psychiatric disorders and cardiovascular disease 1 year before the first AMI. AMI indicates acute myocardial infarction; and IHD, ischemic heart disease.

effect of bereavement on AMI prognosis. Studies are needed to explore these questions further.

Potential Underlying Mechanisms

The 2 major explanations for the link between bereavement and CVD discussed in the literature concern confounding by cardiovascular risk factors clustered in the family and the adverse changes in finances, mental health, social support, lifestyle, level of stress-related cardiometabolic biomarkers, and compliance with medication.[1,2,9,11] The fact that the associations between bereavement and prognosis after AMI persisted after adjusting for a wide range of confounders and that the associations were generally similar between deaths attributed to CVD and other natural or unnatural deaths (the latter being unlikely to be strongly affected by familial confounders)[2,9,11] may support stress-related mechanisms as explanations of the observed associations.

Bereavement stress may affect prognosis in both the short- and long-term. In the short-term, bereavement may induce acute psychological and behavioral reactions such as depressive symptoms, anxiety, anger, sleep disturbance, heavy smoking, and alcohol abuse,[29–38] which may precipitate another infarction or lead to other adverse cardiovascular events or death. Bereavement can also activate the hypothalamic–pituitary–adrenal axis and the autonomic nervous system, which may induce acute changes in the neuroendocrine, metabolic, hemostatic, and cardiovascular activity, subsequently triggering the second infarction or other cardiovascular events.[16] Furthermore, the compliance with cardiac care and medications may diminish because of bereavement.[39] In the long run, negative emotions (eg, depression, anxiety) and unhealthy behaviors (eg, alcohol abuse, smoking, physical inactivity) may also mediate the association. Previous studies have indeed reported an increased risk of depression, anxiety, sleep problems, and loneliness several years after bereavement,[40–44] which are all well-known prognostic factors in AMI.[21,22,45,46]

Strengths and Limitations

The strengths of this study include the population-based study design, the large sample size, the long-term follow-up, the high-quality information on exposure and outcomes collected independently of each

other, and the availability of data on a large number of confounders. Some limitations, nevertheless, should be noted. First, although we adjusted for a wide range of confounders, the possibility of residual confounding by lifestyle factors, for example, physical activity, alcohol consumption, and diet, cannot be excluded. Second, because of the lack of longitudinal data, we could not test the mechanisms underlying the associations. Third, the generalizability of our findings may be limited to countries with a universal health care system and a culture similar to that of Sweden.

CONCLUSIONS

We found that bereavement was associated with an increased risk of poor prognosis in AMI. The associations were strongest for the loss of a partner, followed by the loss of a child, grandchild, sibling, and parent. Bereaved patients with AMI may benefit from increased social support and medical attention after AMI. Further studies are needed to confirm our findings and analyze the underlying mechanisms.

ARTICLE INFORMATION

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Disclosures

Dr Ljung is employed at the Swedish Medical Products Agency, Uppsala, Sweden. The views expressed in this article do not necessarily represent the views of the government agency. The remaining authors have no disclosures to report.

Supplemental Material

Data S1
Tables S1–S5
Figures S1–S2

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Supplemental Material

Data S1.

Supplemental Methods

The algorithm used by Statistics Sweden to identify spouses/partners

We defined study participants' marital status by linkage to their spouse/partner one year before the index acute myocardial infarction and by using information on their recorded marital status (married, in registered partnership, or cohabiting) for that year. The definitions of and the time periods with information on spouse/partner are described below:

- During 1968-1989, only information on spouses was available. Information on spouses was obtained from the Total Population Register for married Swedish residents.
- During 1990-2010, information on spouse, partner (since 1995) or cohabitant, the later defined based on common children, was available from the Total Population Register for individuals whose marital status was married/in partnership or cohabitant. A condition for the link to spouse/partner and to the cohabiting co-parent was registration on the same address.
- During 2011-2018, information on spouse/partner or cohabitant was retrieved from the Apartment Register for individuals whose marital status was married/in partnership or cohabiting. A condition for the linkage to spouses/partners was residence under the same address. Cohabitants were defined as two individuals of different sex, living under the same address, who are not close relatives and who had an age difference less than 15 years.

Table S1. The International Statistical Classification of Diseases and Related Health Problems codes used to identify the diagnoses and the causes of death.

Medical conditions or causes of death	ICD codes
Medical condition	
Acute myocardial infarction	ICD-9: 410
	ICD-10: I21, I22
Stroke	ICD-9: 430, 431, 434, 436
	ICD-10: I60, I61, I63, I64
Heart failure	ICD-9: 428
	ICD-10: I11.0, I13.0, I13.2, I50
Cardiovascular diseases	ICD-8: 390-458
	ICD-9: 390-459
	ICD-10: I00-I99
Psychiatric disorders	ICD-8: 290-315
	ICD-9: 290-319
	ICD-10: F00-F99
Cause of death	
Death due to ischemic heart diseases	ICD-9: 410-414
	ICD-10: I20-I25
Death due to cardiovascular diseases	ICD-9: 390-459
	ICD-10: I00-I99
Unnatural death	ICD-9: 798, 800-999, E800- E999
	ICD-10: R95, R96, R98, V01- Y98
Other natural deaths	All other codes

ICD=International Classification of Diseases.

Table S2. Data sources for the present study.

Register	Information	Period covered
SWEDEHEART		
RIKS-HIA	Information on patients with myocardial infarction at baseline (date, ICD code, type of infarction, revascularization during hospital stay, diabetes)	Regional register during 1990-1994 Nationwide register during 1995-2018
SEPHIA	Information on patients who were younger than 75 years and hospitalized for acute myocardial infarction at 6-10 weeks and 12-14 months after discharge: revascularization after discharge, regular cardiovascular medications (angiotensin-converting enzyme inhibitor, angiotensin II inhibitor, beta blocker, digitalis, diuretics, nitroglycerin, oral anticoagulants, lipid lowering drugs), as well as participation in cardiac rehabilitation program, stress management program, physical training program, and diet course.	2004-2018
Multi-Generation Register	Linkage to relatives	1961-2018*
Total Population Register	Linkage to partner†	Marriage: 1968-2018 Registered partnership: 1995-2018‡ Cohabiting: 2011-2018
Cause of Death Register	Date and cause of death	1952-2018
Patient Register	Information on inpatient and specialized outpatient care (diagnosis, date)	Inpatient care: 1969-2018 Hospital-based outpatient care: 2001-2018

Register of Incomes and Taxes	Personal disposable income	1968-1989
LISA	Personal disposable income, education	1990-2018

SWEDEHEART=The Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies; RIKS-HIA=The Register of Information and Knowledge About Swedish Heart Intensive Care Admissions; SEPHIA=the Swedish Heart Surgery Registry and the National Registry of Secondary Prevention; ICD=International Classification of Diseases; LISA=the Longitudinal Integration Database for Health Insurance and Labor Market Studies.

*Individuals born from 1932 onwards and alive on January 1, 1961 or later in Sweden are included as index persons in the Multi-Generation Register.

†We identified study participants' spouse/partner according to marital status (including marriage, registered partnership, and cohabiting) and linkage to the spouse/partner one year before the first acute myocardial infarction.

‡There were no new registered partnerships from May 1, 2009 when a gender-neutral marriage law entered into force in Sweden.

Table S3. Number of study participants according to the main exposure categories.

Exposure	N (%)
Unexposed	202,598 (76.0)
All deaths	64,053 (24.0)
According to the cause of death of the deceased	
Death due to cardiovascular disease	24,833 (9.3)
Other natural deaths	36,334 (13.6)
Unnatural deaths	2886 (1.1)
According to the time of the loss	
The year before AMI	9439 (3.5)
0-1 years post-AMI	8776 (3.3)
2-5 years post-AMI	23,759 (8.9)
>5 years post-AMI	22,079 (8.3)
According to the relationship to the deceased	
Death of a partner	18,954 (7.1)
Death of a child	5084 (1.9)
Death of a grandchild	1541 (0.6)
Death of a sibling	15,620 (5.9)
Death of a parent	22,854 (8.6)

AMI=acute myocardial infarction.

Table S4. Adjusted rate ratios and 95% confidence intervals for the association between bereavement and the combination of non-fatal recurrent acute myocardial infarction and death due to ischemic heart diseases in stratified analyses.

Subgroups	Events/N	Rate*	Multivariable RR† (95% CI)
Sex			
Men	56,004/170,759	52.7	1.03 (1.00-1.06)
Women	35,779/95,892	69.5	1.01 (0.97-1.05)
Country of origin			
Non-Sweden	11,560/40,235	47.5	1.10 (1.03-1.18)
Sweden	80,223/226,416	60.1	1.01 (0.99-1.03)
Age at diagnosis (years)			
≤65	24,019/94,088	31.4	1.00 (0.96-1.03)
>65	67,764/172,563	83.3	1.05 (1.02-1.08)
Calendar year of diagnosis			
1991-1999	20,753/38,942	60.0	1.05 (1.01-1.10)
2000-2009	47,748/118,096	54.9	1.05 (1.02-1.08)
After 2009	23,282/109,613	64.3	0.93 (0.89-0.98)
Education (years)			
≤9	48,354/120,036	70.6	1.05 (1.02-1.08)
10-14	34,632/118,262	47.2	1.00 (0.96-1.03)
≥15	5632/22,659	39.7	0.96 (0.87-1.05)
Income			
Low tertile	34,387/85,944	83.1	1.08 (1.04-1.12)
Middle tertile	32,021/88,099	67.2	1.03 (0.99-1.08)
High tertile	25,333/92,315	36.9	0.96 (0.93-1.00)
Type of infarction			
STEMI	11,454/49,014	59.7	0.96 (0.90-1.03)
NSTEMI	18,460/81,229	60.4	0.95 (0.90-1.00)

RR=rate ratio; CI=confidence intervals; STEMI=ST segment elevation myocardial infarction; NSTEMI=non-ST segment elevation myocardial infarction.

*Per 1000 person-years.

†Adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, having a spouse/partner, number of live children, number of live grandchildren, number of live siblings, number of live parents, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction.

Table S5. Adjusted rate ratios and 95% confidence intervals for the association between bereavement and the combination of non-fatal recurrent acute myocardial infarction and death due to ischemic heart diseases according to secondary preventive measures.

Subgroups	Events/N	Rate*	Multivariable RR*(95% CI)†
Regular cardiovascular medications prescribed in secondary prevention			
ACE inhibitor			
Missing‡	79,859/192,500	66.0	1.04 (1.02-1.07)
No	4406/27,602	33.4	0.94 (0.86-1.04)
Yes	7518/46,549	23.4	0.95 (0.89-1.02)
A2 inhibitor			
Missing‡	79,866/192,538	66.0	1.04 (1.02-1.07)
No	8776/54,287	31.0	0.95 (0.89-1.02)
Yes	3141/19,826	37.7	0.94 (0.84-1.05)
Beta blocker			
Missing‡	79,863/192,486	66.0	1.04 (1.02-1.07)
No	1011/7206	33.1	0.93 (0.76-1.14)
Yes	10,909/66,959	32.5	0.95 (0.90-1.01)
Diuretics			
Missing‡	79,864/192,519	66.0	1.04 (1.02-1.07)
No	9000/60,103	30.2	0.95 (0.89-1.02)
Yes	2919/14,029	42.8	0.94 (0.84-1.05)
Nitroglycerin			
Missing‡	79,876/192,557	66.0	1.04 (1.02-1.07)
No	10,625/69,023	31.0	0.95 (0.89-1.01)
Yes	1282/5071	54.5	0.94 (0.79-1.12)
Oral anticoagulants			
Missing‡	79,859/192,466	66.0	1.04 (1.02-1.07)
No	1542/9168	28.8	0.90 (0.77-1.05)
Yes	10,382/65,017	33.1	0.96 (0.90-1.02)
Lipid lowering drug			
Missing‡	79,859/192,472	66.0	1.04 (1.02-1.07)
No	457/2259	40.4	1.04 (0.79-1.37)
Yes	11,467/71,920	32.3	0.94 (0.89-1.00)
Statin			

Missing‡	79,865/192,495	66.0	1.04 (1.02-1.07)
No	516/2520	40.1	1.04 (0.80-1.34)
Yes	11,402/71,636	32.2	0.94 (0.89-1.00)
Early revascularization (within the year after the first AMI)			
Missing‡	78,535/187,532	65.9	1.04 (1.02-1.07)
No	10,241/64,325	30.7	0.94 (0.88-1.00)
Yes	3007/14,794	57.8	1.00 (0.88-1.14)
Participation in a stress management program			
Missing‡	79,874/192,560	65.9	1.04 (1.02-1.07)
No	11,222/70,562	32.5	0.94 (0.89-1.00)
Yes	687/3529	32.6	1.09 (0.87-1.36)
Participation in cardiac rehabilitation program			
Missing‡	79,891/192,711	65.9	1.04 (1.02-1.07)
No	6650/39,953	33.3	0.98 (0.91-1.05)
Yes	5242/33,987	31.6	0.92 (0.84-1.00)
Participation in diet course			
Missing‡	81,963/214,817	65.9	1.03 (1.01-1.06)
No	8223/44,478	29.2	0.98 (0.92-1.05)
Yes	1497/7356	30.9	0.93 (0.78-1.09)
Participation in physical training program			
Missing‡	79,876/192,597	65.9	1.04 (1.01-1.07)
No	7111/41,539	33.7	1.00 (0.93-1.07)
Yes	4796/32,515	30.9	0.88 (0.81-0.97)

ACE inhibitor=Angiotensin-converting enzyme inhibitor; A2 inhibitor=angiotensin II inhibitor; AMI=acute myocardial infarction; RR=rate ratio; CI=confidence intervals.

*Per 1000 person-years.

†Adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, having a spouse/partner, number of live children, number of live grandchildren, number of live siblings, number of live parents, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction.

‡ The individuals with missing follow-up information are those 1) who experience the outcome event or were censored before the first follow-up visit, 2) who were older than 75 years, 3) who were diagnosed with their first acute myocardial infarction before 2005 when the National Registry of Secondary Prevention (SEPHIA) was established, or (4) who were hospitalized for their first acute myocardial infarction in a hospitals that did not take part in SEPHIA (15 out of 75 Swedish hospitals).

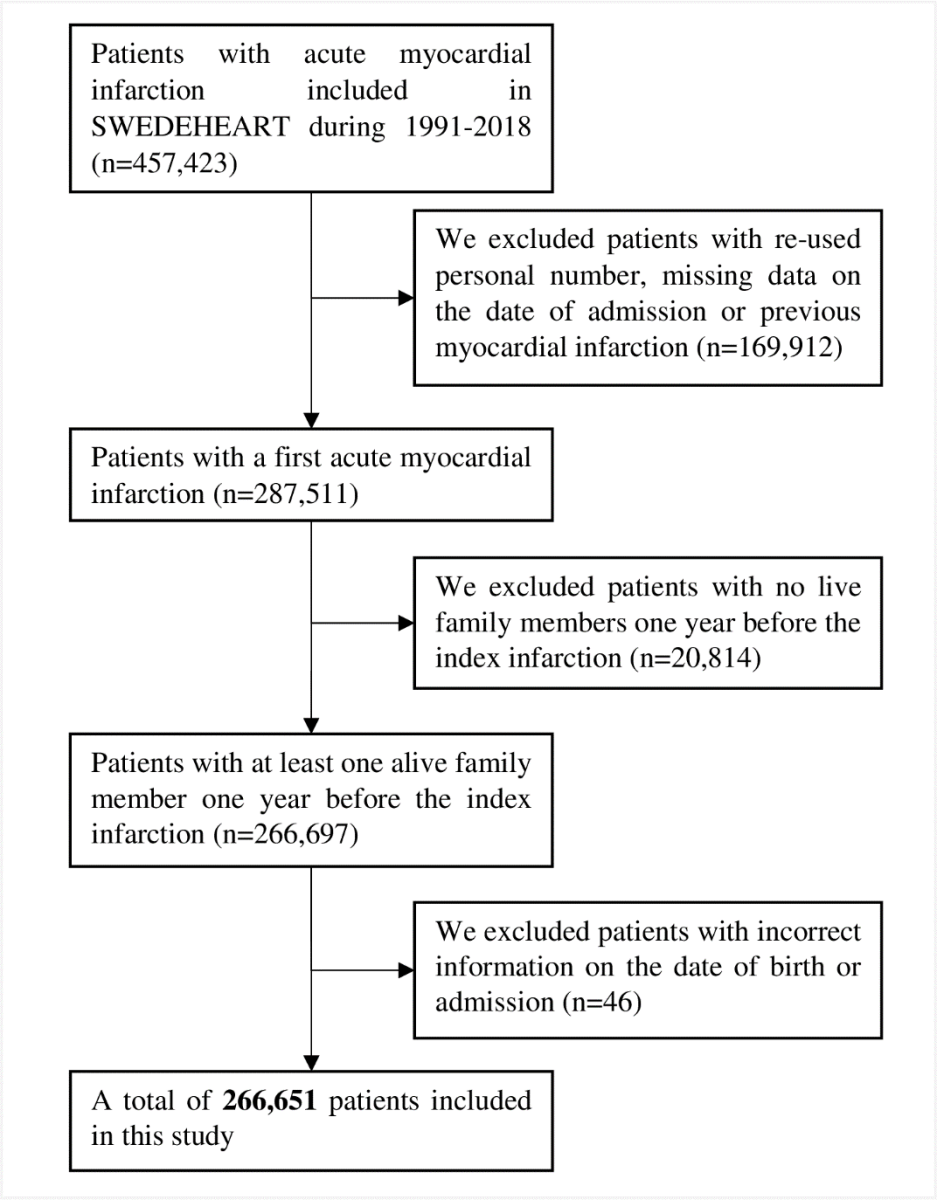

Figure S1. Flowchart of the study participants.

SWEDEHEART= the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies

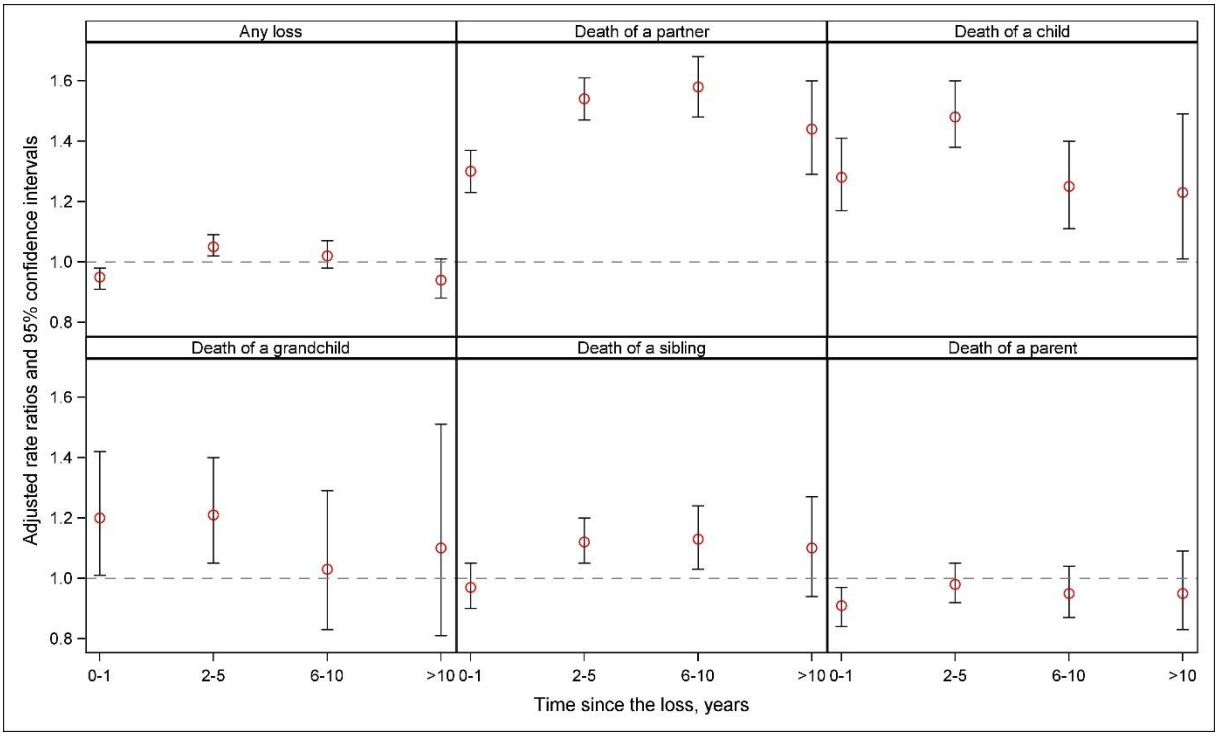

Figure S2. Adjusted rate ratios and 95% confidence intervals for the association between any loss and loss classified according to the relationship to the deceased and the risk of the combination of non-fatal recurrent acute myocardial infarction and death due to ischemic heart diseases, according to the time since the loss

Each relative-specific analysis was performed among those who had at least one of the studied family members alive one year before the first acute myocardial infarction. For *any loss*, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, having a spouse/partner, number of live family members, number of live children, number of live grandchildren, number of live siblings, number of live parents, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction. For the death of a *partner*, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, personal and partner's history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction. For the death of a *child*, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live children, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction. For the death of a *grandchild*, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live grandchildren, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction. For the death of a *sibling*, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live siblings, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction. For the death of a *parent*, we adjusted for age and calendar year of follow-up, sex, country of birth, highest education, income and diabetes at baseline, number of live family members, number of live parents, personal and family history of psychiatric disorders and cardiovascular diseases one year before the first acute myocardial infarction.