

Original Investigation

Increased Risk of Acute Cardiovascular Events After Partner Bereavement

A Matched Cohort Study

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IMPORTANCE The period immediately after bereavement has been reported as a time of increased risk of cardiovascular events. However, this risk has not been well quantified, and few large population studies have examined partner bereavement.

OBJECTIVE To compare the rate of cardiovascular events between older individuals whose partner dies with those of a matched control group of individuals whose partner was still alive on the same day.

DESIGN, SETTING, AND PARTICIPANTS Matched cohort study using a UK primary care database containing available data of 401 general practices from February 2005 through September 2012. In all, 30 447 individuals aged 60 to 89 years at study initiation who experienced partner bereavement during follow-up were matched by age, sex, and general practice with the nonbereaved control group (n = 83 588) at the time of bereavement.

EXPOSURES Partner bereavement.

MAIN OUTCOMES AND MEASURES The primary outcome was occurrence of a fatal or nonfatal myocardial infarction (MI) or stroke within 30 days of bereavement. Secondary outcomes were non-MI acute coronary syndrome and pulmonary embolism. All outcomes were compared between the groups during prespecified periods after bereavement (30, 90, and 365 days). Incidence rate ratios (IRRs) from a conditional Poisson model were adjusted for age, smoking status, deprivation, and history of cardiovascular disease.

RESULTS Within 30 days of their partner's death, 50 of the bereaved group (0.16%) experienced an MI or a stroke compared with 67 of the matched nonbereaved controls (0.08%) during the same period (IRR, 2.20 [95% CI, 1.52-3.15]). The increased risk was seen in bereaved men and women and attenuated after 30 days. For individual outcomes, the increased risk was found separately for MI (IRR, 2.14 [95% CI, 1.20-3.81]) and stroke (2.40 [1.22-4.71]). Associations with rarer events were also seen after bereavement, including elevated risk of non-MI acute coronary syndrome (IRR, 2.20 [95% CI, 1.12-4.29]) and pulmonary embolism (2.37 [1.18-4.75]) in the first 90 days.

CONCLUSIONS AND RELEVANCE This study provides further evidence that the death of a partner is associated with a range of major cardiovascular events in the immediate weeks and months after bereavement. Understanding psychosocial factors associated with acute cardiovascular events may provide opportunities for prevention and improved clinical care.

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Bereavement has long been recognized as a risk factor for increased mortality, particularly from cardiovascular disease,¹ with grief leading to potential adverse physiological responses.² A large literature on the relationship between bereavement and mortality from numerous countries^{3,4} uses a range of data sources and methods that have consistently shown higher rates of mortality in bereaved individuals. These findings have been summarized in 2 recent meta-analyses,^{5,6} one of which estimated a 41% increase in mortality in the first 6 months after the death of a spouse.⁵ Specific associations with cardiovascular mortality have been found, although studies have generally lacked statistical power to produce precise estimates of the risk within the first few months.^{7,8} A recent case crossover analysis of patients hospitalized with myocardial infarction (MI) reported a striking 21-fold elevated risk of nonfatal MI within 24 hours of the death of a significant person,⁹ but few of these deaths represented partner bereavements.

Bereavement is one of several psychosocial factors associated with acute cardiovascular events.^{2,10} Unlike anger or anxiety, the effect of bereavement is thought to persist for weeks and months.⁵ In addition, bereavement may be an exemplar for a range of adverse acute life events, such as unemployment or divorce, for which effects may persist. However, very few studies have attempted to examine the effect of bereavement across a range of life-threatening acute cardiovascular events. This dearth of studies may reflect in part the large sample size needed to examine spousal bereavement and the lack of information on nonfatal cardiovascular events in administrative data sources usually used in bereavement studies. In this report, we used a large primary care database from the United Kingdom to provide the first examination, to our knowledge, of the incidence of fatal and non-fatal MI, stroke, acute coronary syndrome (ACS), and pulmonary embolism (PE) in the months after the death of a partner.

Methods

Data Source

The Health Improvement Network (THIN) is an established primary care database that collects anonymized data from UK general practices.¹¹ The database includes a full record of diagnoses and prescriptions and has been shown to be demographically representative of the United Kingdom.¹² A feature of the THIN database is the family number, which allows practices to identify patients who live in the same household.¹³

Identification of Couples

We included 401 practices participating in the THIN database from January 1, 2005, through December 31, 2008, and used historical patient files to identify the household composition for a cohort of patients 60 years or older ($n = 672\,543$) on the earliest available date during this period. This date for each practice ranged from February 3, 2005, to November 4, 2008.

We developed an algorithm, described in detail elsewhere,¹⁴ to identify 171 720 different-sex couples with an age difference of 10 years or less. Couples among whom either

partner had any record of residence in a nursing home or other communal establishment were excluded. In a previous study,¹⁴ we confirmed the validity of our algorithm by comparison with national representative surveys in England, which verified that 99.4% of couples who were selected using our criteria identify themselves as married or cohabiting.

Bereavement

Couples were followed up in the primary care record from the specified date for their practice (study initiation date) to their last practice data collection date no later than September 17, 2012. The timing of bereavement was identified through the record of death in the deceased partner's primary care record. Of the study population, 35 872 individuals (20.89% of couples) experienced bereavement during follow-up.

Eligible Individuals

From the 35 872 bereaved individuals, we selected those who fulfilled the following criteria: (1) their practice had the potential for at least 6 months of follow-up data from their bereavement date; (2) they were aged 60 to 89 years at study initiation; and (3) they remained registered for at least 1 day after the bereavement. This method identified 31 427 individuals with partner bereavements from 2005 through 2012.

For our main comparison, we identified a control group of nonbereaved individuals matched for age (in 5-year bands), sex, and practice from couples who were registered on the date of bereavement of their matched set (the index date). As many as 3 nonbereaved controls ($n = 83\,588$) were identified for each bereaved individual. Only bereaved individuals (30 447 [96.88%]) with at least 1 matched control were included in the analysis.

We also created 2 additional sets of controls for analyses stratified by preexisting cardiovascular disease and medication (described below). The first additional controls were matched on the occurrence of a code for any coronary heart disease or cerebrovascular disease before the start of follow-up in addition to sex, age, and practice. This process identified 81 848 matched controls suitable for analysis. The second set of additional controls were matched by the receipt of any cardiovascular medication¹⁵ in the year before study initiation, and 82 232 matched controls were identified. Altogether, 32 814 patients appear as controls in all 3 matched cohorts.

Identification of Cardiovascular Events

Identification of events was achieved by electronically searching for Read codes on the patient record. We identified the following distinct events: MI, ACS without mention of MI, stroke, and PE. We chose to include PE because it has been linked recently to psychosocial factors such as stress.¹⁶ We did not include deep vein thrombosis with PE, because we focused on acute, life-threatening events that were less likely to be subject to identification bias.

The primary outcome was the occurrence of an MI or a stroke within 1 month (30 days) of bereavement. A priori we also chose to report on events occurring within 3 months (90 days) and 1 year (365 days) after bereavement. Multiple events were counted, but events occurring within 30 days of each other were counted as a single event.

Statistical Analysis

Conditional Poisson models were used to estimate the incidence rate ratios (IRRs) for all outcomes between bereaved and nonbereaved individuals during the prespecified periods (using the `xtpoisson` command in Stata, version 12.0 [StataCorp]). These models have been used extensively in matched cohort studies¹⁷ and produce risk ratios that are conditioned on the matched sets. A robust variance estimator was used to account for the outcome being a poor fit to the Poisson distribution.¹⁸ The IRRs were adjusted for age at bereavement (a continuous variable that provides additional adjustment beyond the age match), smoking status (at study initiation), history of chronic disease recorded more than 30 days before bereavement (coronary heart disease, cerebrovascular disease, diabetes mellitus, and hypertension), and the Townsend deprivation index.¹⁹ The Townsend deprivation index is a composite small-area ecological measure of deprivation that was assigned according to subject postcode and were summarized as quintiles based on national ranking. In brief, the Townsend deprivation index combines 4 measures of deprivation from the 2001 census (unemployment, access to a car, home ownership, and overcrowding) for small geographic areas in the United Kingdom into a standardized score. We included missing data for smoking status and Townsend deprivation index in the models as a separate category. For the PE outcome, we also adjusted for history of PE or deep vein thrombosis.

Analyses were also stratified by sex, age at bereavement, preexisting cardiovascular disease, and receipt of cardiovascular medication. The latter 2 analyses used the alternate match sets that additionally matched on cardiovascular disease or receipt of cardiovascular medication at study initiation.

Results

Characteristics of Groups

The age, sex, disease history, and smoking status among the bereaved individuals and their matched controls are summarized in **Table 1**. In crude unmatched comparisons, the bereaved group tended to be older (mean age at bereavement, 76.1 vs 75.2 years) and to include more women (64.44% vs 62.53%) than the overall controls, because matching was less complete for older bereaved women. However, these imbalances introduced by partial matching are accounted for in our conditional analysis. Bereaved individuals were more likely to have deregistered from the practice (2.70% vs 1.08%) or died (2.25% vs 1.60%) in the first 6 months after bereavement.

Cardiovascular Events

Table 2 summarizes the occurrence of cardiovascular events that were entered in the patient record in the first year after the bereavement index date. Within 30 days of their partner's death, 50 bereaved (0.16%) and 67 nonbereaved (0.08%) individuals had experienced an MI or a stroke, whereas at 1 year, 390 bereaved individuals (1.28%) had experienced an MI or a stroke compared with 927 nonbereaved controls (1.11%). The number of individuals with multiple events during the first year

Table 1. Characteristics of Bereaved Individuals and Their Matched Nonbereaved Controls

Characteristic	No. (%) of Patients ^a	
	Bereaved (n = 30 447)	Nonbereaved (n = 83 588)
Sex		
Female	19 620 (64.44)	52 270 (62.53)
Male	10 827 (35.56)	31 318 (37.47)
Age at bereavement, y		
60-69	6 410 (21.05)	19 755 (23.63)
70-79	13 443 (44.15)	39 371 (47.10)
≥80	10 594 (34.79)	24 462 (29.26)
Comorbidity 30 d before bereavement		
CHD ^b	5 672 (18.63)	14 243 (17.04)
Cerebrovascular disease ^c	2 804 (9.21)	7 331 (8.77)
CHD ^b or cerebrovascular disease ^c	7 608 (24.99)	19 397 (23.21)
Diabetes mellitus	3 880 (12.74)	10 183 (12.18)
Hypertension	15 559 (51.10)	41 688 (49.87)
PE or DVT	1 278 (4.20)	3 368 (4.03)
Smoking status at study initiation		
Never	14 100 (46.31)	41 867 (50.09)
Former	11 554 (37.95)	30 819 (36.87)
Current	3 955 (12.99)	8 773 (10.50)
Missing/unknown	838 (2.75)	2 129 (2.55)
Follow-up status, 6 mo after bereavement		
Died	684 (2.25)	1 336 (1.60)
Deregistered	823 (2.70)	905 (1.08)
Still registered	28 940 (95.05)	81 347 (97.32)

Abbreviations: CHD, coronary heart disease; DVT, deep vein thrombosis; PE, pulmonary embolism.

^a Percentages have been rounded and might not total 100.

^b Includes ischemic heart disease, myocardial infarction, and angina.

^c Includes stroke and transient ischemic attack.

was small (9 bereaved [0.07%] and 19 nonbereaved [0.06%]). Among all individuals during the first 30 days, relatively few non-MI ACS events (11 for both groups) and PEs (12 for both groups) occurred.

The IRRs for bereaved compared with nonbereaved patients for our main outcome and individual cardiovascular events during different periods after bereavement are shown in **Table 3**. In the first 30 days after bereavement, the occurrence of an MI or a stroke was more than twice as likely for bereaved patients (IRR, 2.20 [95% CI, 1.52-3.15]). The risk attenuated from 31 to 90 days (IRR, 1.35), falling to unity for the remainder of the first year (1.00). Consequently, overall differences were smaller when comparisons were made during the first 90 days (IRR, 1.59 [95% CI, 1.29-1.97]) or during the first year (1.14 [1.02-1.28]).

The increase in risk during the first 30 days was consistent when MI (IRR, 2.14) or stroke (2.40) was considered separately and for a composite outcome including ACS and PE (2.20). For non-MI ACS and PE, too few events occurred in

the first 30 days to obtain a reliable estimate separately; however, the IRRs were raised for both during the first 90 days (eg, 2.37 [95% CI, 1.18-4.75] for PE) or during the first year (eg, 1.39 [1.00-1.94] for PE). An alternative analysis with the matched set that was additionally matched on preexisting cardiovascular disease at study initiation gave similar overall results, with an IRR for MI or stroke at 30 days of 1.97 (95% CI, 1.34-2.88).

Table 2. Summary of Cardiovascular Events Recorded in the First Year After Bereavement or Index Date

Type of Event, Period	No. (%) of Patients	
	Bereaved (n = 30 447)	Nonbereaved (n = 83 588)
MI or stroke		
Within 30 d	50 (0.16)	67 (0.08)
Within 90 d	117 (0.38)	222 (0.27)
Within 365 d	390 (1.28)	927 (1.11)
MI		
Within 30 d	27 (0.09)	38 (0.05)
Within 90 d	54 (0.18)	102 (0.12)
Within 365 d	175 (0.57)	384 (0.46)
Stroke		
Within 30 d	23 (0.08)	31 (0.04)
Within 90 d	63 (0.21)	123 (0.15)
Within 365 d	216 (0.71)	553 (0.66)
Non-MI ACS		
Within 30 d	11 (0.04)	11 (0.01)
Within 90 d	25 (0.08)	36 (0.04)
Within 365 d	69 (0.23)	147 (0.18)
PE		
Within 30 d	12 (0.04)	12 (0.01)
Within 90 d	25 (0.08)	32 (0.04)
Within 365 d	71 (0.23)	151 (0.18)
Any of the above		
Within 30 d	71 (0.23)	90 (0.11)
Within 90 d	161 (0.53)	285 (0.34)
Within 365 d	515 (1.69)	1186 (1.42)

Abbreviations: ACS, acute coronary syndrome; MI, myocardial infarction; PE, pulmonary embolism.

Effect Modification by Sex, Age, Preexisting Disease, and Receipt of Cardiovascular Medication

Table 4 summarizes the IRRs for MI or stroke stratified by sex, age at bereavement, prior cardiovascular disease, and receipt of cardiovascular medication. Although no results of formal tests for heterogeneity were statistically significant during the first 30 days after bereavement, possibly owing to lack of power, trends toward differences were found for some groups. A larger relative association for any MI or stroke in the first 30 days after bereavement was seen in bereaved women (IRR, 2.93 [95% CI, 1.71-5.02]) compared with bereaved men (1.65 [0.96-2.84]); however, the IRRs were very similar when calculated during the first year after bereavement. Analyses based on alternative control groups that additionally matched on prior cardiovascular disease or receipt of cardiovascular medication suggested that the relative effect of bereavement may be higher in bereaved patients who had not received such a diagnosis or had not been prescribed such a drug at study outset. Further investigation of effect modification by expectation of bereavement or living alone after bereavement was not possible owing to a lack of statistical power.

Discussion

In our study, we found a marked increase in the incidence of cardiovascular events in older individuals in the months after the death of their partner. This association was found separately for MI, stroke, ACS, and PE.

Strengths and Weaknesses

We believe that our matched cohort study is the first to examine the occurrence of a range of cardiovascular events after partner bereavement. The study is based on a large contemporary cohort representative of bereaved older couples in the United Kingdom. Our study, in common with most large epidemiological studies of bereavement, does not attempt to examine individual psychological reactions to bereavement or the severity of grief. However, the death of a partner, in itself, is widely recognized as an important negative life event, and our design is free of any recall bias.

Table 3. Adjusted IRRs for Cardiovascular Events After Bereavement Compared With Nonbereaved Controls

Event Type	Days After Bereavement or Index Date, IRR (95% CI) ^a				
	1-30	31-90	91-365	1-90	1-365
MI or stroke	2.20 (1.52-3.15)	1.35 (1.03-1.76)	1.00 (0.88-1.15)	1.59 (1.29-1.97)	1.14 (1.02-1.28)
MI	2.14 (1.20-3.81)	1.19 (0.69-2.06)	1.11 (0.87-1.42)	1.47 (1.01-2.13)	1.20 (0.98-1.48)
Stroke	2.40 (1.22-4.71)	1.30 (0.87-1.93)	0.89 (0.73-1.10)	1.52 (1.09-2.11)	1.02 (0.85-1.22)
Non-MI ACS	... ^b	1.91 (0.84-4.30)	1.19 (0.79-1.79)	2.20 (1.12-4.29)	1.38 (0.97-1.96)
PE ^c	... ^b	2.01 (0.85-4.77)	1.17 (0.80-1.72)	2.37 (1.18-4.75)	1.39 (1.00-1.94)
Any	2.20 (1.53-3.15)	1.35 (1.03-1.76)	1.00 (0.88-1.15)	1.59 (1.29-1.97)	1.14 (1.02-1.28)

Abbreviations: ACS, acute coronary syndrome; ellipses, not calculated; IRR, incidence rate ratio; MI, myocardial infarction; PE, pulmonary embolism.

^a Includes 114 035 patients. The IRRs are adjusted for age at bereavement (continuous variable), Townsend deprivation index,¹⁹ history of chronic disease (cardiovascular disease, cerebrovascular disease, diabetes mellitus,

and hypertension recorded 30 days before bereavement or index date), and smoking status (at study initiation).

^b Too few events occurred for a reliable estimate to be made.

^c Additionally adjusted for history of deep vein thrombosis or PE.

Table 4. Adjusted IRRs for MI or Stroke After Bereavement Stratified by Sex, Age, and History of Cardiovascular Disease and Receipt of Medication

Stratified Group	Total No. of Patients	MI or Stroke Events Within 30 d			MI or Stroke Events Within 90 d	MI or Stroke Events Within 365 d
		No. (%) of Patients	IRR (95% CI) ^a	P Value for Heterogeneity ^b	IRR (95% CI) ^a	IRR (95% CI) ^a
Women						
Bereaved	19 620	28 (0.14)	2.93 (1.71-5.02)	.14	1.70 (1.26-2.29)	1.11 (0.94-1.30)
Nonbereaved	52 270	30 (0.06)	1 [Reference]		1 [Reference]	1 [Reference]
Men						
Bereaved	10 827	22 (0.20)	1.65 (0.96-2.84)	.49	1.51 (1.10-2.06)	1.17 (0.99-1.39)
Nonbereaved	31 318	37 (0.12)	1 [Reference]		1 [Reference]	1 [Reference]
Age 60-75 y at bereavement						
Bereaved	14 072	18 (0.13)	2.74 (1.35-5.56)	.49	1.42 (0.96-2.10)	1.03 (0.83-1.28)
Nonbereaved	42 035	21 (0.05)	1 [Reference]		1 [Reference]	1 [Reference]
Age >75 y at bereavement						
Bereaved	16 375	32 (0.20)	2.05 (1.34-3.14)	.17	1.74 (1.35-2.25)	1.19 (1.04-1.37)
Nonbereaved	41 553	46 (0.11)	1 [Reference]		1 [Reference]	1 [Reference]
No history of CHD or cerebrovascular disease at study initiation ^c						
Bereaved	23 753	35 (0.15)	2.52 (1.55-4.09)	.17	1.50 (1.11-2.02)	1.05 (0.89-1.24)
Nonbereaved	65 627	41 (0.06)	1 [Reference]		1 [Reference]	1 [Reference]
History of CHD or cerebrovascular disease at study initiation ^c						
Bereaved	6399	16 (0.25)	1.38 (0.69-2.78)	.10	1.07 (0.67-1.70)	0.98 (0.79-1.21)
Nonbereaved	16 221	29 (0.18)	1 [Reference]		1 [Reference]	1 [Reference]
No cardiovascular drug prescribed in year before study initiation ^d						
Bereaved	10 556	15 (0.14)	3.23 (1.38-7.58)	.10	1.95 (1.19-3.21)	1.23 (0.94-1.62)
Nonbereaved	29 123	16 (0.05)	1 [Reference]		1 [Reference]	1 [Reference]
Cardiovascular drug prescribed in year before study initiation ^d						
Bereaved	19 601	36 (0.18)	1.44 (0.92-2.26)	.10	1.06 (0.80-1.41)	1.00 (0.86-1.16)
Nonbereaved	53 109	65 (0.12)	1 [Reference]		1 [Reference]	1 [Reference]

Abbreviations: CHD, coronary heart disease; IRR, incidence rate ratio; MI, myocardial infarction.

^a Adjusted for age at bereavement (continuous variable), Townsend deprivation index,¹⁹ history of chronic disease (CHD, cerebrovascular disease, diabetes mellitus, and hypertension recorded 30 days before bereavement or index date), and smoking status (at study initiation).

^b Calculated as test between stratified groups (1-30 days only).

^c Based on alternative matchset (30 152 bereaved patients and 81 848 controls) matched by age, sex, practice, and history of CHD or cerebrovascular disease at study initiation.

^d Based on alternative matchset (30 157 bereaved and 82 232 controls) matched by age, sex, practice, and receipt of any cardiovascular drug in the year before study initiation.

We have used the same database to show 25% higher mortality in the first year after partner bereavement in older couples, with a peak in the first 3 months.¹⁴ The recording of the date of death in the THIN database has been validated,²⁰ with approximately 95% entered within 1 day of the actual date via a Read code on the medical record. The small proportion of deaths (about 9% in our couples) that were ascertained through deregistration flags tended to be given a date a few weeks later than the actual date of death.²⁰ Thus, for a few bereaved patients, we may not have assigned the date of bereavement accurately. However, this misclassification would lead to an underestimate of any early effect of bereavement, especially during the first month.

Our selection of controls, based on 3:1 matching when possible, produced a group who was slightly younger and less likely to have smoked and who had less comorbidity. Although we attempted to adjust for such differences, the

bereaved may still be marginally at a greater risk of cardiovascular events throughout follow-up, but this would not explain the raised 30-day effect and subsequent attenuation of risk. Indeed, the essentially similar risks of cardiovascular events between the bereaved individuals and nonbereaved controls in the last 9 months of the first year suggest that our results cannot be explained by uncontrolled confounders or selection bias and are truly attributable to an acute effect of bereavement.

One strength of our study is that we were able to include a range of nonfatal cardiovascular outcomes and not just associated mortality, which has been used by many other studies that are based on administrative or census data. Approximately 85% of our cohort who experienced an event within 30 days was still alive at 6 months. However, our outcomes relied on the general practice record alone, without any external linkage to hospital records or diagnosis.

Bereavement is unlikely to have influenced the recording of cardiovascular events in the general practice record, so the probable effect of absent diagnoses would be to bias estimates toward the null. Clinical misdiagnosis of cardiovascular disease owing to psychosomatic symptoms, such as an anxiety attack, may occur in bereaved patients, but cardiovascular disease is unlikely to be classified as an MI, which requires objective electrocardiographic and cardiac marker changes, or as a stroke, which presents as a clear clinical syndrome. Recording of MIs in UK primary care has been incentivized as part of the Quality and Outcomes Framework since 2004, and evidence suggests that this incentive has resulted in better recording of chronic disease within the scheme.²¹ Recently, the positive predictive value of recorded MIs in primary care has been estimated as extremely high (>90%).²²

Related Literature

Excess death from cardiovascular causes in the postbereavement period has long been identified,¹ with estimates of the increase in cardiovascular mortality risk due to bereavement reported in large population cohorts in the United States,^{23,24} Scotland,⁷ Sweden,^{25,26} and Finland.^{8,27} Some of these studies also reported associations of bereavement with cerebrovascular deaths.^{7,8,23} The Renfrew/Paisley Study⁷ and the Finnish study of census records²⁷ suggested that bereavement of a spouse produced a raised risk within the first 6 months for mortality from coronary heart disease and stroke. An earlier study of widowed persons in Finland in the 1970s showed increased relative risks for death from ischemic heart disease in the first week (2.3 for men and 3.5 for women).⁸ We are not aware of any large population cohort that has examined fatal and nonfatal cardiovascular events as we did.

The recent case-crossover analysis by Mostofsky et al⁹ estimated a pronounced 21-fold (95% CI, 13.1-34.1) increase in the risk of MI in the immediate 24 hours after bereavement. However, this specific risk estimate was derived from only 19 bereavements. Further, less than 5% of bereavements in their study were identified as involving a spouse, with most relating to a distant relative or friend.

We are not aware of any studies that have linked bereavement to an increase in the risk of PE. A Swedish study found that men with persistent stress had increased risk of PE,¹⁶ whereas a case study in Japan found an increase in PE after a catastrophic earthquake²⁸ in which the physical and psychological stress combined with prolonged immobilization were thought to be contributing factors. Some bereaved spouses may dramatically reduce their level of activity in the postbereavement period. However, our findings are based on small numbers and require further validation.

Although we had limited power to assess effect modification, we found a suggestion that the relative increase in the risk of MI or stroke in the first month after bereavement may be higher in women and in individuals without cardiovascular disease or medication at study initiation. Many studies have suggested that men are at greater risk during the first 6 months after bereavement,^{27,29,30} with one recent meta-analysis⁵ estimating a larger overall relative risk for a bereavement effect

in men vs women (1.23 vs 1.04) and another⁶ estimating a larger hazard ratio (1.27 vs 1.15). However, recent work from Sweden^{25,26} has found higher mortality from MI and stroke among women who had lost a sibling.

The finding of a possible greater relative increase in cardiovascular events in bereaved patients without preexisting disease extends our previous finding from the same cohort of couples, among whom the effect of bereavement on mortality was greater in those with no comorbid conditions.¹⁴ The suggestion of a greater vulnerability for this group may be explained by less use of medications such as statins or antiplatelet agents in those without diagnosed cardiovascular disease, and our analysis stratified on prebereavement use of cardiovascular medications is consistent with this hypothesis. Other authors³¹ have suggested that such medication may protect individuals from the adverse cardiovascular consequences of psychological stress. Unfortunately, our analysis is underpowered to resolve whether this possible protection results from medication use, history of disease, or other unmeasured factors. However, we have recently shown that bereaved patients have poorer medication coverage before and immediately after bereavement,³² so our findings may also reinforce the importance of adherence to a medication regimen in reducing the health impact of bereavement.

Interpretation and Implications

Our study confirms the potential of major life events, such as bereavement, to lead to marked short-term increases in the risk of cardiovascular events. Although our study cannot describe the exact time course of this increased risk in the first month after bereavement, other evidence suggests a marked rise in the days after bereavement that attenuates.⁹ A number of physiological mechanisms for psychosocial triggers of acute cardiovascular events have been postulated,^{2,10} and some are supported by results of small empirical studies in individuals who experience bereavement. These mechanisms include short-term changes in blood pressure,³³ cortisol levels,³⁴ heart rate variability,³⁵ platelet activation, and clotting factor levels.³⁶ Our novel findings on PE further support the hypothesis that bereavement predisposes individuals to a prothrombotic state.³⁷

During the period around the death of a loved one, patients may neglect their own health care needs,³⁸ which may place them at greater risk of adverse cardiovascular events. We have previously shown that prescribing medication to lower lipid levels, antiplatelet medication, and drugs acting on the renin-angiotensin system fall in the immediate peribereavement period in patients at high risk of cardiovascular disease.³² Longer-term behavioral changes affecting lifestyle factors, such as smoking and alcohol consumption, may also eventually contribute.²⁷

The absolute contribution of bereavement to overall cardiovascular event rates is likely to be small, because partner bereavement is usually a nonrepeated event for an individual, and the higher risk is relatively short-term. A recent review¹⁰ attempted to calculate population-attributable fractions for a range of possible MI triggers. Although cocaine use produced the greatest relative risk, the authors estimated the

greatest population-attributable fraction (7%) for air pollution from traffic exposure because most of the population will be exposed on multiple occasions. By contrast, anger or negative emotions only contributed population-attributable fractions of 1% to 2%. Although the subsequent analysis by Mostofsky et al⁹ reported a marked risk increase in the 24 hours after bereavement, this increase applied to fewer than 1% of the patients with MI in their study.³⁹ This finding suggests that bereavement may only account for a small proportion of major cardiovascular events.

Nevertheless, for bereaved individuals, the increased risk of cardiovascular events is important and one element of a range of poor health outcomes after bereavement. At present, there is limited evidence on whether intervention would be effective or appropriate to reduce cardiovascular risk after acute triggers such as bereavement. Other authors³¹ have suggested a range of strategies for “triggered acute risk preven-

tion,” and, of these, the most appropriate and feasible seems to be ensuring good long-term management of cardiovascular risk among individuals before and after bereavement through lifestyle modification and medication. This approach will also provide benefit outside the bereavement period and has the merit of not medicalizing bereavement.

Conclusions

We have described a marked increase in cardiovascular risk in the month after spousal bereavement, which seems likely to be the result of adverse physiological responses associated with acute grief. A better understanding of psychosocial factors associated with acute cardiovascular events may provide opportunities for prevention and improved clinical care.

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