The Effect of Losing the Twin and Losing the Partner on Mortality

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Several studies have explored the impact of marital bereavement on mortality, while increasing emphasis has recently been placed on genetic factors influencing longevity — in this paper, we study the impact of losing the spouse and losing the co-twin, for twins aged 50 to 70. We use data from the Danish Twin Registry and the Population Register of Denmark for the period 1968 through 1999. Firstly, we use survival analysis to study mortality after the death of the spouse or the co-twin. We find that the risk of dying is highest in the first year after the death of the spouse, as well as in the second year after the death of the co-twin. We then use event history analysis techniques to show that there is a strong impact of the event 'losing the co-twin' even after controlling for age, sex and zygosity and that this effect is significantly higher in the second year of bereavement. The effect is similar for men and women, and it is higher for monozygotic twins. The latter confirms the influence of genetic factors on survival, while the mortality trajectory with a peak in the second year after the death of the co-twin is consistent with the existence of a twin bereavement effect.

Writers and poets have suggested that it is possible to die of grief. This idea has been carried on by epidemiologists who started to study the effects of death on the survivors. Consequently a considerable body of research has focused on the effects of losing selected members of the social network (bereavement) on an individual's mortality (Bowling, 1987; Bowling, 1994; Helsing & Szklo, 1981; Jones & Goldblatt, 1987; Lillard & Waite, 1995; Mellstrom et al., 1982; Schaefer et al., 1995; Stroebe & Stroebe, 1983). Usually these studies analyse the death rates among bereaved persons and compare them with the non-bereaved, finding an increase of mortality after bereavement, especially in people with previous health disorders. The majority of the research done on bereavement has focused on the loss of the spouse since this has more effect on the daily life of the survivor and it is easier to catch from both vital statistics and survey data. The magnitude of the marital bereavement effect on mortality seems to vary with age and sex. The relative risk of mortality has been found to be higher for widowed males than for females, and to be higher for younger widowed persons than for the older widowed.

The differences found in epidemiological studies on marital bereavement are mainly due to the differences in the research design (case-control studies, retrospective analysis, cohorts of widows and widowers) and to differences in how individual characteristics are taken into account (duration of marriage, length of widowhood, incidence of remarriage) and the cultural changes in the population over time. Several methodological issues arise from the kind of data available for the study. The use of vital statistics data (like death certificates) allows a larger sample size, longer periods of observation, and causes of death, but it does not usually allow one to control for several variables that might partially explain the higher mortality of widowed people (such as previous marital status history, previous health problems, risky behaviours, financial situation). In the case of longitudinal surveys, more information is available on individual life course, but the sample size is typically much smaller, and the individual characteristics are recorded only at the beginning of the period considered (Lillard & Waite, 1995). Another approach based on longitudinal data focuses on the transition from marriage to widowhood, and then on the analysis of subsequent mortality. This is the approach that has been followed in this paper. It is then important, for our purposes, to analyse the timing of the impact of bereavement.

Another line of research has its focus on the influence of genetic factors on longevity. The first non-censored and population-based twin study that could provide an estimate of the magnitude of genetic influences on lifespan was conducted by McGue et al. (1993). A total of 600 Danish twin pairs born between 1870 and 1880 was included. Path analysis yielded a heritability of 0.22, with genetic influences being mainly non-additive. Later this study was expanded by Herskind et al. (1996) to include more than 2 800 twin pairs with known zygosity born between 1870 and 1900. These cohorts were followed from age 15 years to death. This study confirmed that approximately a quarter of the variation in lifespan in this population could be attributed to non-additive genetic factors, while the remaining three-quarters were due to non- shared environmental factors. Ljungquist et al. (1998) studied the

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1886–1900 Swedish twin cohorts and concluded that a maximum of one third of the variance in longevity is attributable to genetic factors.

Hence, it seems to be a rather consistent finding in the Nordic countries that approximately 25% of the variation in lifespan is caused by genetic differences. It is interesting that animal studies have revealed similar estimates for a number of species not living in the wild (Curtsinger et al., 1995; Finch & Tanzi, 1997). Several authors have proposed other theories in order to explain the similar trajectories in mortality for twins. The hypothesis is that they reflect a twin bereavement effect (which may be comparable in a way to the marital bereavement effect). Segal and Bouchard (1993) and Segal and Ream (1998) suggest that the grief intensity increases with increasing genetic relatedness to the deceased (kinship genetic principle). Some qualitative studies (Woodward, 1998) show the psychological effects in later life for twins who have lost their co-twin. This might suggest that, in addition to a correlation between life spans due to genetic factors, there is interdependence between the deaths of the two twins. Nevertheless, there are very few studies dealing with mortality following any bereavement other than the conjugal loss (Tomassini et al., 2001). Losing a sibling has probably been considered to have less impact than the death of a spouse, child or parent, since adult siblings normally do not live together and often do not have regular contacts. In contrast to this view, some studies have pointed out that the sibling bond has particular characteristics, which are different from their common relationship to their parents (Krupnick, 1984).

Based on this we hypothesised two possible scenarios explaining the twin correlation:

Hypothesis 1: Impact of time-constant factors only. If the correlation in lifespan between the twins is due solely to time-constant common factors (genetic or environmental), we would expect to observe a correlation between the two survival times only (see Figure 1).

The shorter the distance between the deaths of the twins, the higher is the correlation between the two events is. We would expect to observe a higher risk of mortality for survivor A after the death of co-twin B,

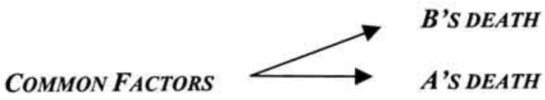

Figure 1

Impact of time-constant factors only.

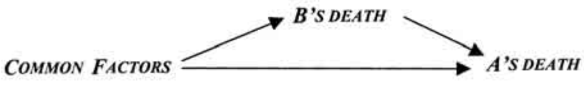

Figure 2

Bereavement effect.

Hypothesis 2: Bereavement effect. If there is also an effect of the co-twin's death (similar to the death of a spouse), we would expect to observe interdependence between the events (see Figure 2).

If there is interdependence, we should find a certain time lag before the event "death of a co-twin" has an impact on the risk of dying of the survivor. The existence of the time lag is due to the fact that the death of the co-twin needs a lag of time to produce some consequences on the survivor's risk of dying.

According to these two hypotheses, we tested if, controlling for age, the mortality risk of the surviving twin increases after the death of the co-twin. In particular, we tested whether there is a significant time lag between the death of the co-twin and the peak in the risk of dying, and if the effect of the co-twin's death depends on (or interacts with) sex and zygosity.

Materials and Methods

Study Population

The Danish Twin Registry is a population-based register of twins born in Denmark between 1870 and 1996, with the collection of information taking place in several steps. It was established in 1954 as the first nation-wide twin register in the world, and more than 60 000 twin pairs are included.

In this study we focused on death and bereavement in the age range 50 to 70 years, so we used twins from birth cohorts 1918–1949 and followed them through the period 1968–1999. Twins from these cohorts were identified by two different methods. The oldest cohorts born before 1931 were ascertained by scrutinising birth registers in every parish in Denmark, including pairs with both twins surviving to age 6 years. Only same-sexed twins from the cohorts 1911–1930 are included in the register. The later birth cohorts have been ascertained during the last 10 years with the Danish Civil Registration System as the primary source of identification. Twins from the birth cohorts 1931–1952 were identified based on the fact that almost always twins in a pair are born on the same date and in the same parish, and are given the same surname. From the Danish Civil Registration System all sets of persons fulfilling these criteria were extracted and their twin status was confirmed by either mailed questionnaires to living persons or verification in birth registers in case of death or emigration (Kyvik et al., 1996; Skytthe, 2000).

The zygosity of same-sexed twins was determined by the questionnaire method using the same method for the two cohorts. Based on four questions about the similarity of the twins the pair was assigned as either monozygotic, dizygotic or uncertain zygosity. The method has been proved to determine zygosity correctly in approximately 95% of the twin pairs (Hauge 1981).

The Danish Civil Registration System was introduced in April 1968 and encompasses persons, who have lived in Denmark since 2 April 1968 and have registered with the national registration offices. Every person alive at or born after April 2, 1968 has been assigned a unique identifier, the personal identification number. Information on date of birth and vital status (alive, death, emigration) is available, and changes in the marital status of a person (single, married, divorced, widowed) can be followed. Vital status and marital status of the monozygotic and dizygotic same sex twins are followed from the age of 50 years until the age of 70 years. Death of the spouse is indicated when the marital status changed to widowhood. No other change in marital status has been considered as an event.

For each twin identified to have lost his/her co-twin (1679 individuals) a group of 2 "control-twins" were found via the twin register (a total of 3358 control twins). Each control-twin was matched with respect to age, sex and zygosity. A control-twin was eligible only if he/she came from a twin pair in which both twins were alive the day the case-twin lost his/her co-twin. A control-twin was still eligible even if he/she lost his/her co-twin during the follow-up time. In this way we could compare directly the survival of twins who had just lost their co-twin to those who had not, without confounding due to age, sex, zygosity or selection in the twin register.

Analyses

Two sets of analyses were performed, nonparametric survival analysis and parametric event history analysis. (Readers that are not familiar with survival or event history analysis could consult the introductory texts of Allison, 1984, or Collett, 1994).

Nonparametric Survival Analysis

For the first analyses we selected all twins that had experienced the death of the spouse (*n* = 2145) or the death of the co-twin (*n* = 1679), when they were between 50 years and less than 70 years of age before the 1st January 2000. We then estimated, using the life-table method, hazard rates in the 36 months following the death of the spouse and the death of the co-twin, controlling for sex and zygosity.

In Figure 3, a Lexis diagram describing the periods and cohorts under study is shown: the area A refers to the periods and cohorts studied, while the B area refers to periods subject to right-censoring, (i.e., our observation is terminated at 1st January 2000 before the death of the surviving twin or the death of the spouse occurs.

Parametric Event History Analysis

In a second approach we performed a longitudinal analysis which considers the risk of dying of twins. Twins enter the risk set at wave 1, when they are aged between 50 and 70. We included the death of the co-twin (when occurring) as a time dependent covariate. We tested whether there is a significant increase in the mortality risk in the transition from the state 'co-twin alive' to the state 'co-twin dead', controlling for sex, age and zygosity. For this purpose we used discrete-time event history analysis models, with month as the time unit.

We estimated three models. The simplest one (model A) includes time-constant variables and a time-dependent variable of the status of the co-twin. In the second model (model B) the effect of the death of the co-twin is considered to be time-dependent itself, in order to pick up the existence of a time lag between the cause (death of the co-twin) and the possible effect (death of the surviving twin). In the third model (model C), the interaction between sex and zygosity with the time-dependent variable is included, in order to test if there is a different effect of losing the co-twin among men and women, as well as among monozygotic and dizygotic twins.

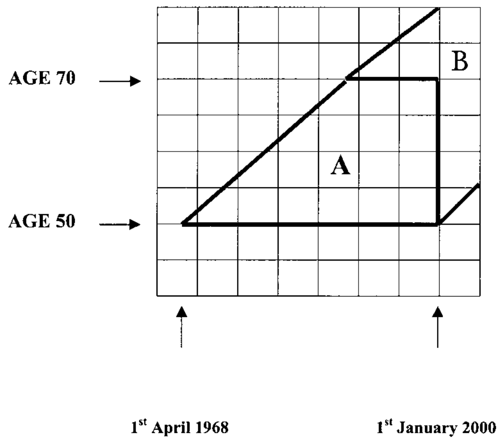

Figure 3

Lexis diagram describing the periods and cohorts under study. The area A refers to the window where death of spouse and co-twins is observed, while the B area refers to periods subject to right censoring.

To run this set of models we considered the survival of a randomly selected twin from each pair that reaches age 50 (*N* = 8309) after the 2nd of April 1968 (starting date of the Register) and we studied his/her mortality, with censorship at age 70 or at 1st of January 2000 for those younger at that date. A study by Simmons et al. (1997) shows that this procedure does not lead to substantial biases even at ages above 80.

The formulation of models A and B are reported below (equations 1 and 2), while model C is obtained by just adding the interaction terms.

Model A

$$\mathrm{logit}(\lambda_{it}) = \alpha + \beta X_i + \eta I_{(\tau_i,\infty)} \qquad (1)$$

Where *t* is the survival time, measured in months, starting from the 50th birthday. λ_{it} is the probability of death of individual *i* in month *t*, given that *i* was alive at month *t-1*.

X_i are the time constant covariates (age, sex, zygosity) of the individual i, and β their coefficients to be estimated. The constant variables includes age (four 5 year age groups, the oldest compared with youngest 50–54), sex (women compared to men), zygosity (*zygosity* = 1 when the twin is monozygotic).

I(*a*, *b*) is an indicator variable, assuming the value 1 if *t* is included in the interval (a, b), and 0 otherwise. τ_i is the time at death of the co-twin. The indicator then expresses the "status of the co-twin" that is 0 if the co-twin is alive and 1 if the co-twin is dead and η its coefficient.

Model B (time-dependent effect)

$$\mathrm{logit}(\lambda_{it}) = \alpha + \beta X_i + \eta_1 I_{(\tau_i,\tau_i+11)} + \eta_2 I_{(\tau_i+12,\tau_i+23)} + \eta_3 I_{(\tau_i+24,\infty)} \qquad (2)$$

Where in contrast to Model A the effects of the time-dependent variable that compare having lost the co-twin one year, (η_1) two years (η_2) and more than two years before (η_3), with not having lost the co-twin is included.

Results

Nonparametric Survival Analysis

We show estimated hazard rates in figures 4, 5, and 6 and tables 1, 2, and 3. We performed two separate analyses for mortality after the death of the spouse and after the death of the co-twin, respectively for men and women. The graphs show average annual hazard rates in the first, second and third year of bereavement. The starting point on the graph is the death of the spouse and the death of the co-twin. We should bear in mind that at this stage we do not control by age, so that the increase of both trajectories after the third year is likely to be due to an age effect as also indicated by the trajectory of the control group mortality shown in Figure 6. In tables 1, 2, and 3 we indicate for men, women, and zygosity respectively, the sample sizes, the mean ages, the monthly hazard rates (that are shown in the figures), and their confidence limits.

Figure 4 shows the two 'bereavement' effects for men: both have similar intensity (although the effect of losing the co-twin is consistently higher than the effect of losing the wife despite similar mean age), but they have different timing. The hazard rate after the death of the wife is higher in the first year, and then it tends to fall, as demonstrated in previous studies. The hazard rate seems to be higher in the second year after the death of the co-twin. Figure 5 shows the results for women: the intensity of the two effects is as expected lower than the male one, but the timing pattern is similar.

We estimated also hazard rates specific for zygosity (with men and women together): the results are showed in Figure 6. The hazard rates for monozygotic twins are higher compared to same sex dizygotic twins, and the peak in the second year after the loss of the co-twin is more distinct. The trajectory for the control group (that has not lost the co-twin) is also drawn and show the expected mortality trend with an increase due to age.

Parametric Event History Analyses

The results obtained in the event history analysis with the models B and C are shown in Table 4. The obtained results are in agreement with the results from the survival analyses and support the hypothesis of interdependence between the deaths of twins that we presented in hypothesis 2. The mortality risk increases significantly after the death of the co-twin, even after controlling for age. The highest point of the mortality risk is in the second year after the death of the co-twin. The interaction with sex or zygosity is not significant, so the timing effect of the loss seems not to depend on either sex or zygosity. The mortality is in general slightly lower for monozygotic twins (the principal effect is negative for mortality and the odds ratio is 0.80 compared to the dizygotic twins) and the interaction between having lost the co-twin and zygosity is strongly positive (the odds ratio is 2.56). The results confirm the trajectories obtained using survival analysis, with the peak in mortality in the second year after the death of the co-twin.

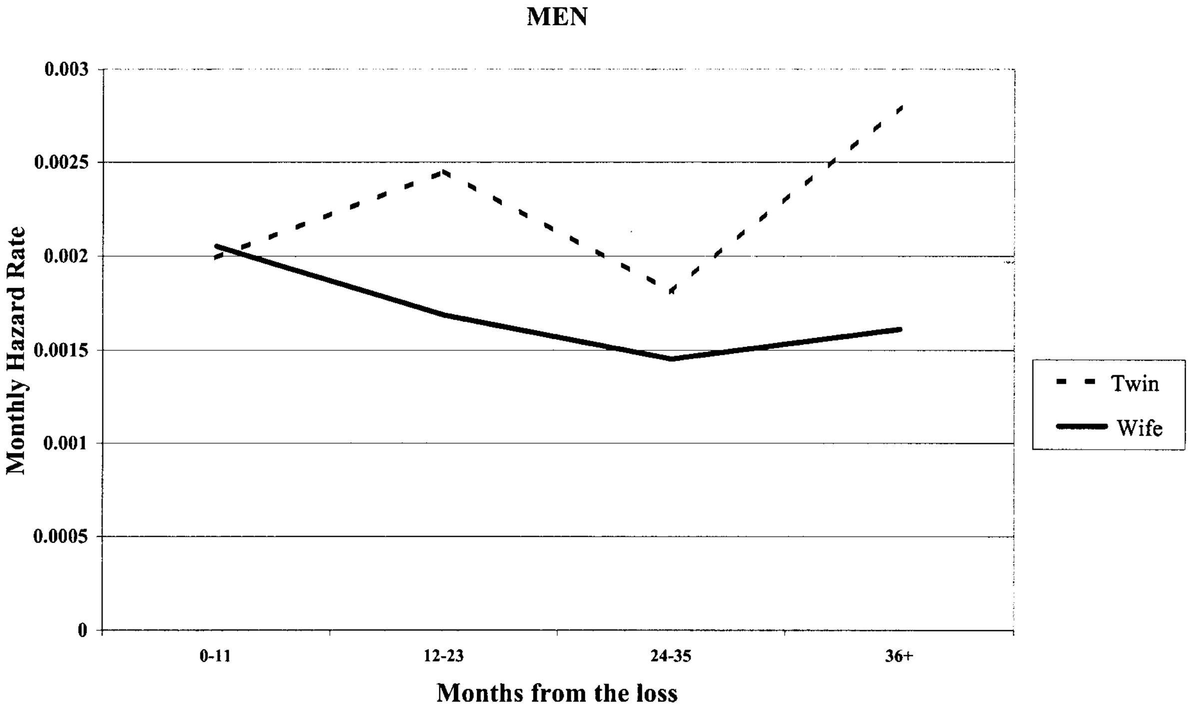

Figure 4

Comparison between survival after the death of the wife (full line) and the co-twin (dashed).

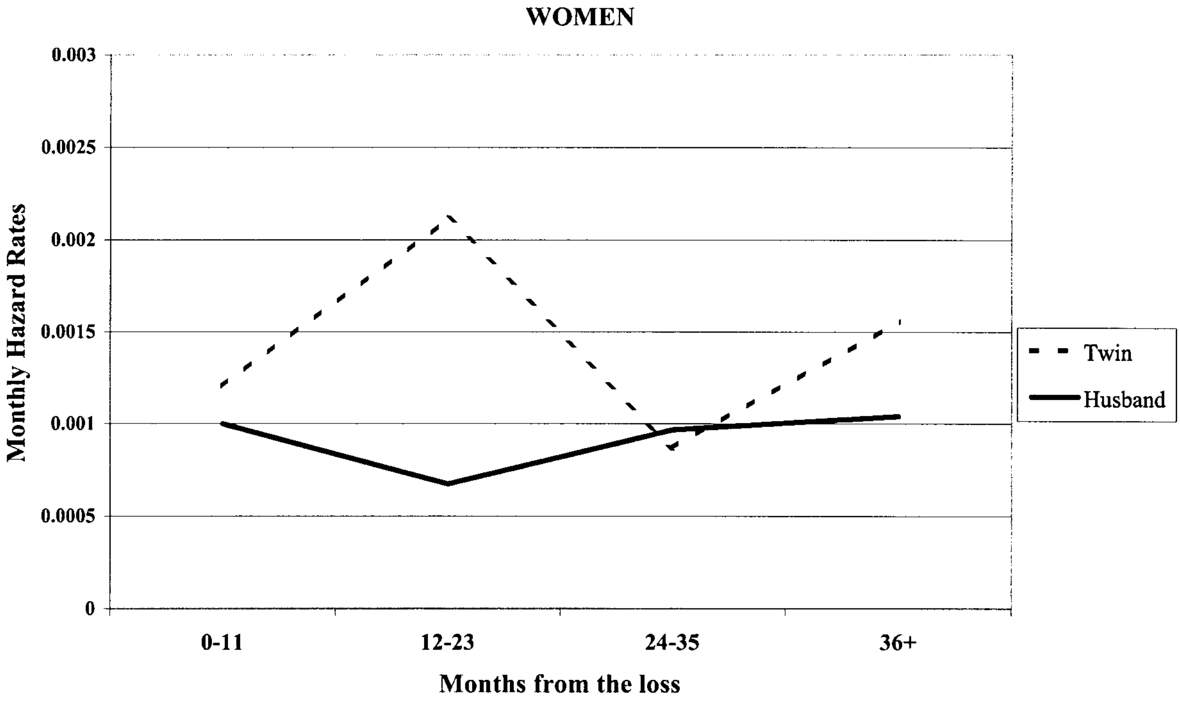

Figure 5

Comparison between survival after the death of the husband (full line) and the co-twin (dashed).

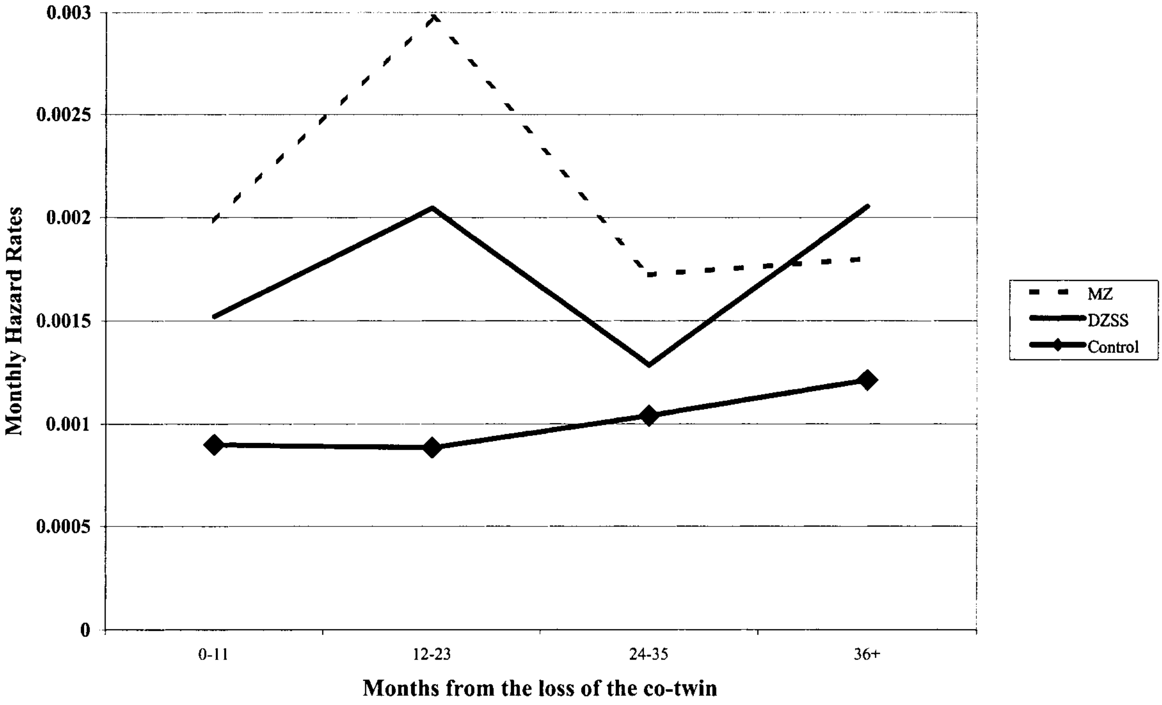

Figure 6

Comparison between survival after the death of the dizygotic same sex co-twin (full line) and the monozygotic co-twin (dashed).

Table 1

Monthly Hazard Rates and 95% Confidence Limits after the Death of the Wife and after the Death of the Co-twin — MEN

	Loss of the wife			Loss of the co-twin		
Months	Monthly hazard (10^{-2})	Hazard Lower 95% Conf.Lim.	Hazard Upper 95% Conf.Lim.	Monthly hazard (10^{-2})	Hazard Lower 95% Conf.Lim.	Hazard Upper 95% Conf.Lim.
0–11	0.21	0.09	0.32	0.20	0.12	0.28
12–23	0.17	0.06	0.28	0.25	0.15	0.34
24–35	0.15	0.04	0.25	0.18	0.09	0.27
36+	0.16	0.04	0.28	0.28	0.17	0.39
	N = 506	Mean age = 59.6		*N* = 958	Mean age = 59.4	

Table 2

Monthly Hazard Rates and Standard Errors after the Death of the Husband and after the Death of the Co-twin — WOMEN

	Loss of the husband			Loss of the co-twin		
Months	Monthly hazard (10^{-2})	Hazard Lower 95% Conf.Lim.	Hazard Upper 95% Conf.Lim.	Monthly hazard (10^{-2})	Hazard Lower 95% Conf.Lim.	Hazard Upper 95% Conf.Lim.
0–11	0.10	0.06	0.15	0.12	0.05	0.20
12–23	0.07	0.03	0.11	0.21	0.11	0.32
24–35	0.10	0.05	0.14	0.09	0.02	0.16
36+	0.10	0.05	0.16	0.16	0.06	0.25
	N =1639	Mean age = 59.2		*N* = 721	Mean age = 60.4	

Table 3

Monthly Hazard Rates and Standard Errors after the Death of the Co-twin — (NMZ = 485, NDZSS = 1194)

	Loss of the MZ co-twin			Loss of the DZSS co-twin		
Months	Monthly hazard (10^{-2})	Hazard Lower 95% Conf.Lim.	Hazard Upper 95% Conf.Lim.	Monthly hazard (10^{-2})	Hazard Lower 95% Conf.Lim.	Hazard Upper 95% Conf.Lim.
0–11	0.20	0.08	0.32	0.15	0.09	0.22
12–23	0.30	0.15	0.45	0.20	0.13	0.28
24–35	0.17	0.05	0.29	0.13	0.06	0.19
36+	0.28	0.12	1.22	0.21	0.12	0.29
	NMZ = 485			NDZSS = 1194		

Discussion

In this paper we studied the mortality trajectories after the death of the spouse and the death of the co-twin. We showed that mortality increases in the first year after the death of the spouse (a result that has been established in several previous studies). We have also provided new evidence of the existence of the twin 'bereavement effect' and its action on the mortality of the surviving twins. This effect appears to be stronger in the second year after the death of the co-twin. The event history model shows that this effect is significant even after controlling for age and sex. The interaction with sex is not significant, so the bereavement effect is similar for men and women. The interaction with zygosity is not significant either, so the timing effect is also similar for monozygotic and dizygotic same sex twins. The consistently higher mortality among monozygotic compared to dizygotic twins who had lost their co-twin provides evidence for the influence of genetic factors. However, the time pattern with a peak in the second year for both monozygotic and dizygotic twins indicates the existence of a twin bereavement effect.

We would like to stress that our analysis is conditioned by survival to age 50, and from 50 to 70, so the results that we have obtained are restricted to the age group considered and not to the entire life course. The model time origin is reaching the 50th birthday, and the event studied is twin mortality between age 50 and age 70. There is therefore no left censoring, while we have the common right censoring if the twin is alive at age 70 or, if younger than 70, is alive in January 2000.

In order to explain the higher mortality of those recently widowed, several factors are mentioned in the literature: stress from bereavement that may accelerate the appearance of physical or mental disorders, lack of social support after the death of the partner, a change in the

Table 4

Results from the Event History Models with the Loss of the Co-twin as a Time Dependent Covariate

	Model B			Model C		
	Odds Ratio	95% Wald Confidence Limits		Odds Ratio s	95% Wald Confidence Limits	
Sex (reference: male)						
Female	0.67**	0.59	0.76	0.68**	0.59	0.77
Age (reference: 50–54)						
55–59	1.49**	1.22	1.82	1.50**	1.23	1.82
60–64	2.78**	2.30	3.35	2.78**	2.31	3.35
65–69	3.90**	3.22	4.72	3.91**	3.23	4.73
Zygosity (reference: dizygotic)						
Monozygotic	0.81**	0.70	0.93	0.80**	0.69	0.92
Status of the co-twin (reference: co-twin alive)						
First year after co-twin's death	5.54**	2.55	12.02	5.54**	2.56	12.03
Second year after co-twin's death	8.93**	5.28	15.08	8.61**	4.12	18.03
Third year (or later) after co-twin's death	1.36**	1.10	1.68	1.36**	1.10	1.68
Interactions						
Second year*Female				0.45	0.14	1.46
Second year*Monozygotic				2.56	0.82	7.97

Note: Model C Sample size = 8309. –2*LL 10494.946.
* $p < 0.05$, ** $p < 0.01$.

family roles due to the sudden deprivation of spousal help in daily activities (especially for older men), the loss of the family's income producer (especially for older women), the lack of control that could lead to more risky behaviours regarding smoking and drinking. Other explanations refer to artefacts of the analyses, including selection effects (the healthier and wealthier people are more likely to remarry), the impact of homogamy (people in poor health tend to marry each other), and shared unfavourable environment.

While the immediate increase in death rates after bereavement is understandable in terms of stress (that accelerates the appearance of physical or mental disorders, that precipitates or aggravates illness, lack of social support, change in role, change in risky behaviours), the consequences beyond the first year are less clear. A long and intense grieving period has related consequences in the years thereafter. Furthermore the psychological disorders and the social withdrawal that follow the loss of a close relative could lead to severe distress later in life both in health and social relations. In addition to that, Klerman and Clayton (1984) suggest that "failure to cope adequately during the usual bereavement period predisposes a person to late psychiatric and medical problems".

The literature on bereavement effects of sibling loss is very sparse compared to the spouse bereavement literature. However, several factors can influence the tie between siblings: shared childhood environment and experiences, critical life events and geographical proximity. Sibling relations become closer later in life, when they share the care responsibilities of their parents (especially sisters). In this perspective losing a sibling can have important consequences on the mortality of the survivor, especially at older ages, since the anxiety may provoke an escalation in the fear of one's own death. All these relations could be enhanced for twins, who represent a unique sibling relationship.

The one-year incidence rate of bereavement for first-degree relatives in the general population is estimated to range from 5 to 9 per cent. In the 1999 Longitudinal Study of Ageing Danish Twins, for twins older than 70, it has been found that 13.4% of them had lost their spouse in the last five years, 15.3% the co-twin and 40.9% another sibling. In general, bereavement can predispose people to physical and mental diseases, can worsen existing illness, can lead to risky behaviours, and can alter the use of health services.

The results on the effect of losing the partner and its rapid effect on the mortality of the surviving spouse have been widely discussed in the previous studies on marital bereavement. The effect of losing the co-twin on mortality has been explained so far mainly in terms of genetic factors. Our finding that there is a stronger impact of the death of the co-twin in the second year after the death, suggests that there is a sort of twin bereavement effect on mortality, and this is occurring for both MZ and DZSS twins. It is possible that while the loss of the spouse has immediate consequences on daily life (mainly with the lack of the most important source of support), the loss of the twin could be felt more later on. Adult twins have normally separate lives and separate families, so that it is possible that when they lose their co-twin, their primary network (spouse and children) can help them cope with the grief immediately and therefore "postpone" the effect.

Future analysis including causes of death (available through the Danish Central Death Registry) may offer possible explanations for the different timing of the two bereavement effects.

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