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ORIGINAL ARTICLE

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A unique bond: Twin bereavement and lifespan associations of identical and fraternal twins

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Abstract

Analyses of twin mortality often use models with dependent unobserved frailty terms capturing genetic and childhood environmental determinants. This ignores that mortality rates can be co-dependent due to bereavement effects, that is, to a causal effect of the loss of the co-twin on the mortality rate of the surviving twin. We develop a novel approach based on a model incorporating both types of dependence. We prove identification and we estimate models with Danish register data on twin pairs. Among men, losing an identical co-twin at age 75 causally reduces the remaining lifetime on average by more than a year. This bereavement effect is less severe among non-identical twins. The results are relevant for the assessment of the economic component of bereavement effects in general. Furthermore, estimates of correlations between the frailty terms by zygosity and the ensuing relative importance of genetic determinants are highly dependent on whether bereavement effects are ignored.

KEYWORDS

frailty, genetic determinants, hazard rate, identification, loss of co-twin, Mortality

1 | INTRODUCTION

Twin mortality has been an important research topic since many decades. First and foremost, the comparison of the association of lifetimes of identical twins with the association of lifetimes of fraternal twins is informative on the role of genetic mortality determinants. This extends to

cause-specific mortality and rates at which illnesses occur. In the literature, the most elaborate approach involves the estimation of bivariate survival models with unobserved mortality determinants called 'frailty terms'. The latter terms are individual specific but may be stochastically related among twins, and the correlation is allowed to depend on the zygosity of the twin pair (e.g. see Hougaard et al., 1992a,b; Wienke et al., 2001; Yashin & Iachine, 1995a). Frailty terms allow for a convenient interpretation as a summary measure of the effects of the underlying genetic predisposition and childhood environmental determinants. In bivariate models with frailty terms, the association of lifetimes of twins is driven by the correlation of their frailty terms. If frailty terms are more strongly correlated among identical twins then this indicates that genetic background is important.

However, there is a second major reason for why twin lifetimes can be correlated, and this concerns causal bereavement effects of the loss of the co-twin on the mortality rate of the surviving twin. Due to the unique bond that twins share, the loss of the co-twin can have severe effects on the surviving twin. Studies of bereaved twins document that the loss of the co-twin causes psychological stress that can also lead to a health deterioration.[1] Ultimately this may lead to a higher mortality rate. Of course one may think of other events in the adult life of twins that affect the association of their lifetimes, but bereavements are particularly relevant for the analysis of mortality because by definition bereavements mostly occur in the age span where mortality rates are high, that is, at high ages. This is why bereavements are potentially important drivers of lifetime associations especially among the elderly. Ignoring bereavement effects in twin mortality analysis may lead to biased results. To see this, note that bereavement effects may be present even if genetic and early-life environmental characteristics are irrelevant. In that case, the association of twins' lifetimes may be wrongly attributed to those characteristics. What is more, in real life, bereavement effects may be stronger among identical twins because of how their social environment reacts to the loss, and this strengthens the association of their lifetimes, which in turn may lead to incorrect inference on the effects of genes on mortality.[2]

Adverse bereavement effects on mortality are of interest in their own right. They involve health care costs and they may inspire policymakers to design treatments to ameliorate their size. Twin bereavement effects on mortality have been analysed by, for example, Tomassini et al. (2001, 2002) and Hougaard et al. (1992a). However, these and other existing empirical studies on this topic base their results on the estimation of univariate survival models for one member of each twin pair, where an indicator of the realized mortality of the co-twin is included as an exogenous time-dependent covariate. Clearly, this ignores longevity dependence due to correlated unobserved individual characteristics. This drawback is the mirror image of the above-mentioned limitation of the frailty approach, namely that one of the two types of dependence of lifetimes is

[1]Segal et al. (1995, 2002), Segal and Ream (1998) and Woodward (1988) document how the loss of the co-twin can cause severe emotional stress. Besides feelings of despair, depersonalization (numbness, shock), rumination (preoccupation with the deceased) and loss of control, bereaved twins also show symptoms such as loss of appetite and vigour and other physical symptoms (Segal & Blozis, 2002). Chronic stress due to bereavement is a major cause of disease; see for example, Stroebe and Stroebe (1987), Stroebe et al. (1993), Sanders (1980, 1999) and Selye (1936, 1955).

[2]One could claim that stronger bereavement effects among identical twins are to some extent due to genetic similarity. However, this stretches the range of what constitute genetic effects and this would limit the usefulness of twin studies to assess the contribution of genetic factors in the population as a whole. A different connection between genes and bereavement is studied in a recent study by Schultze-Florey et al. (2012). They find that the size of bereavement effects on circulating levels of inflammatory markers is affected by the genotype. Prolonged exposure to high levels of these markers has adverse health effects. This suggests that the effect of bereavement on health is to some extent affected by genetic determinants, although it is not clear to what extent this translates into mortality effects. We return to the potential importance of this mechanism in the final section of the paper.

ruled out by construction.[3] As already pointed out by Hougaard et al. (1992a), this may bias the results.

In her discussion of Hougaard et al. (1992a), Flournoy (1992) argues that a super-model is needed that accounts both for a bereavement effect and for the influence of unobserved correlated factors. Along these lines, we introduce a bivariate survival model for twin lifetimes which incorporates bereavement effects as well as unobserved frailty terms that may capture genetic and childhood effects. As seen from a single twin, the model includes mortality of the co-twin as a time-dependent covariate. In addition, each of the twins' own mortality rates is allowed to depend on an individual-specific frailty term that may be correlated with the co-twin's frailty term. This accounts for the endogeneity of the co-twin's mortality as a covariate.

In the paper we formally prove that with minimal covariate variation between twin pairs, all components of the model are identified from the observable joint distribution of twin lifespans conditional on observed covariates. This includes the identification of the bereavement effect and the joint distribution of the frailty terms. Identification does not require covariate values to differ by twin within the twin pair, and it does not require functional-form assumptions on the force of mortality or the distribution of the frailty terms. In general, in the estimation of models with unobserved confounders, identification is a valuable property, as it implies that the results are not driven by such functional-form assumptions. Our identification result extends to cause-specific mortality.

We estimate the model with data on 9,270 twin pairs in the Danish Twin Registry born in Denmark between 1873 and 1930. This includes 2,808 identical (monozygotic) and 6,462 fraternal (dizygotic) pairs. For our purposes, a major advantage of these cohorts is that right-censoring of lifetimes due to end-of-study is relatively rare. Indeed, 81% of the twins are observed to die before 2004. In the data, the observed covariates do not vary within same-sex twin pairs.[4]

We also examine whether the estimated correlation of the twins' frailty terms is sensitive to whether bereavement is taken into account or not, for each zygosity. More in general, we show how estimated effects change when one of the two sources of lifetime dependence is ignored.

Our study has a number of relevant implications which can each be related to an existing strand of literature. First, as already discussed above, there is the literature on bivariate survival models with unobserved frailty terms, including applications to twin mortality, to which we contribute. In the twin context, this literature has adjusted standard gene/environment decomposition methods, in order to deal with mortality outcomes (we turn to this in Section 5 below). Second, there is the wider literature on bereavement effects on mortality. Most of this literature concerns conjugal bereavement (e.g. see Bowling, 1987; Lichtenstein et al., 1998; Lindeboom et al., 2002; Manor & Eisenbach, 2003; Van den Berg et al., 2011). These studies tend to find sizeable effects, reflecting both economic loss and emotional hardship. In contrast to spouses, most adult twins have separate families and separate economic support systems, so that twin bereavement effects can be expected to mostly reflect emotional hardship. This suggests that by comparing the magnitudes of conjugal and twin bereavement effects, we may identify the relative importance of the emotional component in the total conjugal effect. Or, at the very least, if the emotional component in the conjugal effect exceeds the effect among twins, this enables

[3]Tomassini et al. (2002, 2001) match each bereaved twin to two unbereaved twins based on zygosity, age and sex and compare the two resulting mortality rates after the age when bereavement takes place. This ignores the endogeneity of the time of bereavement caused by shared genetic factors, or in other words, the dependence of the underlying frailty terms.
[4]The majority of the data comprises same-sex twin pairs, since collection of their records had priority in the early years of the Twin Registry which is the first ever nationwide twin register in the world.

us to bound the economic component of the conjugal effect. Assessments of the extent to which conjugal bereavement captures economic effects may need to take this into account.[5]

The outline of the paper is as follows. In Section 2 we introduce the mortality model with bereavement effects and we prove identification. Section 3 presents the twin dataset from the Danish Twin Registry while Section 4 discusses the estimation method. Subsequently, the estimation results are in Section 5. Section 6 concludes.

2 | MODEL AND IDENTIFICATION RESULT

In this section we introduce a new bivariate model for twin lifespans. Each twin is exposed to the risk of dying at every age $t \in [0, \infty)$, given that he has reached that age. Since we are interested in measuring the causal effect of the end of one lifespan on the subsequent residual lifespan of the other (the bereavement effect), we specify the mortality rate (or 'hazard') of each twin $j = 1, 2$ conditional on the realization of the lifespan of the co-twin $T_k = t_k$. In addition, we condition on observable characteristics x of the twin pair and the realization of frailty terms V_j.

Model 1 The hazard rates of $T_1|(T_2 = t_2, x, V_1)$ and $T_2|(T_1 = t_1, x, V_2)$ are given by

$$\theta(t|T_2 = t_2, x, V_1) = \lambda(t)\phi(x)\delta(t, t_2, x)^{I(t>t_2)}V_1$$
$$\theta(t|T_1 = t_1, x, V_2) = \lambda(t)\phi(x)\delta(t, t_1, x)^{I(t>t_1)}V_2,$$

where the bereavement effect function $\delta(t, t_k, x)$ has the property that it can be expressed as $\delta(t, t_k, x) = \delta_a(t - t_k)\delta_b(t_k, x)$.

The function $\lambda(t)$ captures the dependence of the mortality hazard on age while $\phi(x)$ incorporates the effect of covariates. $I(t > t_k)$ denotes the indicator function that is equal to one when the loss of the co-twin has occurred and zero otherwise. As long as both twins are alive, each twin j faces the mortality hazard $\lambda(t)\phi(x)V_j$. Once the co-twin has died, the mortality hazard of the surviving twin is rescaled by $\delta_a(t - t_k)\delta_b(t_k, x)$, reflecting the bereavement effect. Here, the first multiplicative term δ_a describes the dependence of the bereavement effect on the time passed since the loss occurred, while δ_b accounts for the dependence on the age at the time of bereavement and covariates x.[6]

[5] A third relevant implication of our study concerns the identification of bivariate duration models that contain causal effects as well as unobserved heterogeneity. In the so-called timing-of-events approach, the realization of some event (say, a treatment) may causally affect the hazard rate of some duration outcome variable, where the former is only observed if it occurs before the latter. The timing-of-event model postulates mixed proportional hazard specifications (see e.g. Van den Berg, 2001) for each of the two hazard rates, where the unobserved determinants of the hazard rates may be mutually dependent. Abbring and van den Berg (2003) prove identification without functional-form assumptions. However, this requires observed covariates to have different effects on each of the two hazard rates of the individual. In applications of their model, it generally does not make sense to expect covariate effects on treatment and outcome to be identical. In contrast, in our current setting, same-sex twins may have identical covariate values and the two hazard rates naturally have symmetric specifications as functions of their determinants. The timing-of-events approach has been used to study conjugal bereavement effects on mortality, where there is no compelling reason to impose symmetry restrictions across the male and female mortality rates, and where covariate values differ across spouses within couples (see Gourieroux & Lu, 2015; Lu, 2017; Van den Berg et al., 2011).

[6] The identification result below can be straightforwardly extended to cases where the bereavement effect function differs between the two durations. Thus, if the two spells can be distinguished in the data, it is possible to identify two separate bereavement effects $\delta_1(t, t_2, x)$ and $\delta_2(t, t_1, x)$.

Conditional on observed twin pair characteristics x, Model 1 allows for two types of dependencies between lifespans T_1 and T_2. The first is introduced through the joint distribution of V_1 and V_2 capturing similarities in genetic makeup and childhood experiences of the two twins. The second is introduced through the function $\delta(t, t_k, x)$ reflecting the effect of bereavement. Note that conditional on x and V, the only dependence between lifespans T_1 and T_2 comes from the bereavement effect function $\delta(t, t_k, x)$. Consequently, this function can be given a causal interpretation as the effect of the end of one lifespan on the remaining length of the other.

The bereavement effect in Model 1 can be said to generate a local dependence between T_1 and T_2, as it only affects the hazard rate of the surviving twin after the loss has occurred. In contrast to this, the time-constant unobserved factors V give rise to a global dependence. This reflects the fact that genetic dispositions and characteristics shaped during childhood influence the mortality hazard of the two twins over their whole lifespan. The difference between global and local dependence is key to the identification of our model.

The local nature of the bereavement effect in Model 1 rules out anticipatory effects. In particularly, it rules out a scenario in which a twin anticipates the future date of death of his co-twin and is affected by this knowledge to the degree that his own mortality hazard today is affected. Furthermore, the unobservable influences V are assumed to be time constant, thus ignoring twin-pair-specific unobservable shocks, such as major events within the extended family. Notice that we do not require that x varies within twin pairs. As we shall see, in the 1873–1930 birth cohorts in our data, only pair-specific covariates are observed, with the exception of the twin's sex which is the same within the majority of twin pairs.

As prerequisites for identification of Model 1, we impose the following regularity assumptions:

Assumption 1 The vector x is k-dimensional with $1 \leq k < \infty$ and $\phi : \mathcal{X} \to U \subset (0, \infty)$. The set $\mathcal{X} \subset \mathbb{R}^k$ contains at least two values. For some a priori chosen x_0, the normalization $\phi(x_0) = 1$ holds.

Assumption 2 The function $\delta_a : [0, \infty) \to (0, \infty)$ is right-continuous. For $\delta_b : [0, \infty) \times \mathcal{X} \to (0, \infty)$ it holds that $\nexists\, c \in (0, \infty)$ s.t. $\delta_b(0, x) = c\phi(x)^{-1}\ \forall x \in \mathcal{X}$.

Assumption 3 The function $\lambda : [0, \infty) \to (0, \infty)$ is cadlag (right-continuous with left limits) and satisfies that for all $t \in (0, \infty)$, $0 < \lim_{s \uparrow t} \lambda(s) < \infty$. It has an integral $\Lambda(t) := \int_0^t \lambda(\tau) d\tau < \infty, \forall t \geq 0$. Furthermore,

$$\tilde{\Lambda}(t, s) := \int_s^t \lambda(\tau)\delta_a(\tau - s)d\tau < \infty, \quad \forall\{(t, s) \in [0, \infty)^2 : t > s\}.$$

For some a priori chosen t_0 and t_0^*, the normalizations $\int_0^{t_0} \lambda(\tau)d\tau = \int_0^{t_0^*} \lambda(\tau)\delta_a(\tau)d\tau = 1$ hold.

Assumption 4 V is an $\mathbb{R}_+^2$-valued time-invariant random vector $(V_1, V_2)'$ and is drawn from a distribution G which does not depend on x and has a finite positive mean. G is such that $P(V \in (0, \infty)^2) = 1$.

Assumption 5 $\exists$ an open set $\Psi \in (0, \infty)^2$ with $t_1 > t_2\ \forall\ (t_1, t_2) \in \Psi$ s.t. at all points $(t_1, t_2) \in \Psi$ the function $\Delta(t_1, t_2, x) = \tilde{\Lambda}(t_1, t_2)\delta_b(t_2, x)$ is continuously differentiable with respect to t_2.

For Assumption 1 a single dummy variable x suffices that does not need to vary across the two hazards, provided that it has an effect. In such a case, $\phi(x)$ takes on only two values on $\mathcal{X}$. Note that Assumption 3 does not rule out the piecewise constant case or most functional forms.

Furthermore, functional forms with $\lim_{s\downarrow 0}\lambda(s)=\infty$ such as the Weibull function are not ruled out. However, according to Assumption 2, the magnitude of the instantaneous bereavement effect must be finite, so functional forms of δ_a with $\lim_{s\downarrow 0}\delta_a(s)=\infty$ are excluded.

Proposition 1 *If Assumptions 1–4 are satisfied, then the functions λ, ϕ, δ_a, δ_b from Model 1 are non-parametrically identified from the distribution of $(T_1, T_2)|x$.*

The proof is in Appendix A.1 (for λ and ϕ) and Appendix A.2 (for δ_a and δ_b). Note that G remains undetermined in Proposition 1. This leads to:

Proposition 2 *If Assumptions 1–5 are satisfied, then Model 1, which is characterized by the functions G, λ, ϕ, δ_a, δ_b, is non-parametrically identified from the distribution of $(T_1, T_2)|x$.*

The proof is in Appendix A.3.

In the empirical analysis of models with unobserved confounders, non-parametric identification is a valuable property, as it implies that the results are not fully driven by ad hoc functional-form assumptions. If the model is not non-parametrically identified then the estimation of a model with parametric functions G, λ, ϕ, δ_a, δ_b may give a priori sensible point estimates but these would be fully driven by those parametric functional forms. In particular, estimation with a different set of parametric functions may lead to different estimates of the effects of interest.

We make two minor comments about the identification results. First, the results can be applied to the study of cause-specific mortality. The hazard rates then represent rates of mortality due to a specific cause. This requires that death due to other causes can be regarded as independent right-censoring of the duration until death to that particular cause. Second, the proofs of the propositions do not use the assumption that the marginal distributions of the frailty terms V_1 and V_2 are identical. Hence, this assumption is superfluous and may be used for a model specification test. It may be an interesting topic for further research to see if the overidentifying information can be used to identify models that are less restrictive in some other direction.

3 | THE DANISH TWIN REGISTRY

The Danish Twin Registry was first established in 1954 with the goal of following up on all same-sex twins who were born since 1870 and who survived as twins at least until the age of 6. We have access to data on cohorts from 1873 to 1930, implying that we observe uncensored lifespans for most individuals before 1 January 2004, when our window of observation ends. There is some selectivity in the very early cohorts, with twins who died young less likely to be included in the sample. Furthermore, covariates are barely observed if the pair did not survive as twins until 1 January 1943. Therefore, we restrict attention to twin pairs still alive at the latter date. While the registry contains some different-sex twin pairs, most effort was devoted to following up on same-sex and particularly monozygotic twin pairs. We refer to Skytthe et al. (2002) and Hauge et al. (1968) for detailed descriptions of the registry and the way in which it has been collected.

The resulting sample includes 2,870 monozygotic and 6,625 dizygotic twin pairs, 1,239 of which are different-sex twin pairs. Twins still alive on 1 January 2004 or who emigrated at a prior date have right-censored lifespans. Overall, the death date is observed for 81% of the individuals in our sample. For each twin pair, we observe zygosity, sex, region of birth and date of birth. The information on zygosity has been shown to be highly accurate, with a misclassification rate below 5% (see Holm, 1983; Lykken, 1978). We restrict attention to an indicator for being born in

TABLE 1 Summary statistics of 9495 Danish twin pairs

	Mean	Std. Dev.	Min.	Max.
Lifespan	75.50	11.95	14.39	105.47
Left-truncation age	33.62	13.86	12.01	70.03
Right-censored	0.19	0.39	0	1
Monozygotic	0.30	0.45	0	1
Male	0.48	0.5	0	1
Born in spring	0.26	0.44	0	1
Born in Copenhagen	0.13	0.34	0	1
Birth year	1908.90	13.85	1873	1930
N	18,990			

Copenhagen to distinguish between rural and urban areas in Denmark. Additional distinctions between small towns and rural areas outside of Copenhagen proved to be uninformative. Table 1 provides summary statistics of variables used in our empirical analysis.

In the Registry, each twin pair's two members are distinguished by labels 1 and 2. Since the data were manually copied from parish books, and since traditionally the first-born twin member was recorded first, it seems likely that twin 1 is the first born and twin 2 is the second born. However, there is no solid evidence for this and therefore this variable is typically not used in studies with the Registry (e.g. see Herskind et al., 1996; Hougaard et al., 1992b). In our sample, a Kolmogorov–Smirnov test for equality of distribution functions of T_1 and T_2 fails to reject the null hypothesis of equal distributions in our sample; they look essentially identical. Therefore, we do not use this variable in our analyses.

For our purposes it is important to point out that Denmark did not witness major epidemics between 1873 and 2004. Cross-national comparisons reveal that Denmark stands out as the country with the lowest excess mortality for the 1918/1919 worldwide influenza pandemic (see Ansart et al., 2009; Canudas-Romo & Erlangsen, 2008). Furthermore, Denmark remained neutral in both world wars, and despite being occupied by Germany during the Second World War, casualties were negligible compared to the rest of Europe.

4 | EMPIRICAL IMPLEMENTATION

In this subsection we explain how we estimate the model of Section 2 with the data of the Twin Registry. We choose flexible specifications for the model determinants λ, ϕ, δ and G and we estimate the various model versions with Maximum Likelihood.[7,8]

[7]This is in line with the econometric and biostatistical literature in which models with unobserved frailty terms or 'random effects' are estimated, in particular in the absence of spells in the data that are driven by shared unobserved determinants. In this literature it is uncommon to use non-parametric estimators based on constructive identification results, as the latter often only consider specific small subintervals of the outcome variables or the covariates. In any case, the proof of our identification result in Section 2 is not constructive as it relies on Elbers and Ridder (1982)'s non-constructive findings, so this does not lead to an estimation method anyway.

[8]As we explain later in this section, we are interested in allowing the model determinants λ and G to depend on specific covariates, and such features are straightforwardly incorporated in the empirical approach we adopt. They do not

The vector of frailties (V_1, V_2) for each twin pair is assumed to be drawn from a Cherian bivariate Gamma distribution. This family of distributions is often used for twin frailty terms in mortality models (e.g. see Wienke et al., 2001, 2002; Yashin & Iachine, 1995b) as it allows for the interpretation of the individual frailty term as the sum of a shared twin-pair-specific term $\tilde{V}_0$ and an individual-specific term $\tilde{V}_j$:

$$V_j = \tilde{V}_0 + \tilde{V}_j \quad \text{for } j \in 1, 2.$$

Here, each term $\tilde{V}_1$, $\tilde{V}_2$ and $\tilde{V}_0$ is independently drawn from Gamma distributions. With this structure, the bivariate Gamma distribution of $(V_1,\ V_2)$ has identical marginal distributions, which makes sense. Their mean is normalized to one, and consequently the joint distribution of $(V_1,\ V_2)$ can be fully described by two parameters: the variance σ^2 of V_j and correlation ρ of V_1 and V_2. The latter is computed as the ratio of the shared and total variation $\rho = \mathrm{Var}(\tilde{V}_0)/\mathrm{Var}(\tilde{V}_0 + \tilde{V}_j)$. Recall that our sample includes monozygotic (MZ) and dizygotic (DZ) twin pairs. Accordingly, we estimate separate parameters for both types of zygosity: σ^2_{MZ}, ρ_{MZ} and σ^2_{DZ}, ρ_{DZ}.[9]

For a twin pair with right-censored lifespans at t_1 and t_2 the bivariate survival function $S(t_1,\ t_2|x) = P(T_1 > t_1,\ T_2 > t_2|x)$ can now be expressed as

$$\begin{aligned} S(t_1, t_2|x) &= \begin{cases} S^*(t_1, t_1|x) - \int_{t_2}^{t_1} S_{t_2}(t_1, \tau|x)d\tau, & \text{for } t_1 \geq t_2 \\ S^*(t_2, t_2|x) - \int_{t_1}^{t_2} S_{t_1}(\tau, t_2|x)d\tau, & \text{for } t_1 < t_2 \end{cases} \\ \text{with } S^*(t_1, t_2|x) &= (1 + \sigma^2\phi(x)[\Lambda(t_1) + \Lambda(t_2)])^{-\frac{\rho}{\sigma^2}} \\ &\quad (1 + \sigma^2\phi(x)\Lambda(t_1))^{-\frac{(1-\rho)}{\sigma^2}} (1 + \sigma^2\phi(x)\Lambda(t_2))^{-\frac{(1-\rho)}{\sigma^2}} \end{aligned} \tag{1}$$

and with partial derivatives $S_{t_j}(t_1, t_2|x) = \frac{\partial S(t_1,t_2|x)}{\partial t_j}$ for $(j = 1, 2)$. For a few of the twin pairs the lifespan of one twin is right-censored while the co-twin is observed to live past this censoring point. Here, right-censoring may occur, for example, due to emigration. As a consequence, bereavement could have occurred any time between the censoring point and ∞. This is taken into account by taking the expectation over all possible times of bereavement.

Since our dataset only includes twin pairs for which both twins survive past 1 January 1943, this left-truncation has to be taken into account in the likelihood function. We denote the respective truncation age of twin j on 1 January 1943 by t^0_j. With this the survival function is

$$S(t_1, t_2|T_1 > t^0_1, T_2 > t^0_2, x) = S(t_1, t_2|x)S(t^0_1, t^0_2|x)^{-1}$$

For given functions $\phi, \lambda, \delta_a, \delta_b$, this leads to the following likelihood contribution of a twin pair:

$$\begin{aligned} L(t_1, t_2, c_1, c_2|x) = [&c_1c_2S(t_1, t_2|x) - c_1(1 - c_2)S_{t_2}(t_1, t_2|x) - (1 - c_1)c_2S_{t_1}(t_1, t_2|x) \\ &+ (1 - c_1)(1 - c_2)S_{t_1,t_2}(t_1, t_2|x)] \cdot S(t^0_1, t^0_2|x)^{-1}. \end{aligned} \tag{2}$$

invalidate the applicability of the identification proof, as long as one element of x satisfies the assumptions conditional on all other elements of x.

[9] A key assumption for the identification result in Section 2 is that G does not depend on covariates x. However, Propositions 1 and 2 can be applied to the separate samples of monozygotic and dizygotic twin pairs as long as x contains at least one additional element satisfying the assumptions. It follows that the two joint distributions G_{MZ} and G_{DZ} are then separately identified.

Here, c_1 and c_2 denote binary censoring indicators for T_1 and T_2 and $S_{t_1,t_2}(t_1,t_2|x) = \frac{\partial^2 S(t_1,t_2|x)}{\partial t_1 \partial t_2}$. The functional forms of S, S_{t_1}, S_{t_2} and S_{t_1,t_2} and details of the derivations are presented in Appendix A.4.

To proceed, we now discuss the specifications of the functions $\phi(x)$, $\lambda(t)$, $\delta_a(t-t_k)$ and $\delta_b(t_k,x)$. The baseline hazard (or force of mortality, or duration dependence) function $\lambda(t)$ is specified as $\lambda(t) = e^{\alpha_1 t+\alpha_2 t^2+\alpha_3 t^3}$. This generalizes the Gompertz function $e^{\alpha_1 t}$ which is commonly used in models for high-age mortality and is known to give a reasonably good fit across a wide range of ages. However, in our setting, it is particularly important to have a flexible functional form, since we aim to estimate the impact of an intermediate event later in life, and the estimate of that impact may be biased if the baseline hazard is misspecified. For this reason we do not impose $\alpha_2 = \alpha_3 = 0$. As a further precautionary measure against misspecification of λ, we allow it to vary across birth cohorts. Early-life health conditions improved over the birth years in our sample, and Gavrilov and Nosov (1985) show that the more recent cohorts faced disproportionally high gains in mortality reductions at higher ages. We therefore allow the parameter vector $(\alpha_1\ \alpha_2\ \alpha_3)$ to be different across three different birth cohort intervals: 1873–1899, 1900–1915 and 1916–1930.

Covariate effects enter the hazard through $\phi(x) = e^{\beta' x}$, as is common in proportional-hazard types of models.[10] The function $\delta_a(t-t_k)$ in the bereavement effect function is specified as a piecewise constant function of $t-t_k$. Specifically, $\log\ \delta_a(t-t_k) = \delta_q^t$, allowing for three time intervals for $t-t_k$, each represented by values $q \in \{1, 2, 3\}$: up to 1 year, 2 to 4 years and after 4 years. (Note that the notation δ_q^t should not be taken to suggest that δ_a depends on t rather than on $t-t_k$.) Furthermore, we take $\log\ \delta_b(t_k,x) = \delta_l^{age} + \delta^{x\prime}x$, where δ_l^{age} reflects how the bereavement effect depends on the age interval l in which t_k occurs. We allow for three age intervals for t_k, each represented by values $l \in \{1, 2, 3\}$: below 65, 66 to 79 and above 80.

We performed an extensive simulation study of the small-sample performance of the maximum likelihood estimation of the model. For parameter values close to those we estimate, the parameter estimates are very close to their true values for samples as small as 10,000 individuals, that is, in the range of our actual sample size (results available upon request). We also examined to what extent estimation results change if the rate of right-censored lifetimes increases. For this we artificially right-censor all lifetimes at age 90 in our actual data. This increases the censoring rate from 19% to 25%. The estimation results are virtually identical to those in the next section. The same applies if we artificially right-censor all lifetimes once they reach the calendar year 1995. This increases the censoring rate from 19% to 35% (details available upon request).

5 | EMPIRICAL ANALYSIS

5.1 | Estimation results

Parameter estimates are shown in Table 2. Four different model versions are estimated. Models I and II are restricted models estimated for the purpose of comparing our comprehensive approach to the two approaches used in the two strands of the twin mortality literature discussed in Section 1. In Model I, the only possible dependence between twin lifespans conditional on

[10]Following the line of reasoning in footnote 9, separate models can be envisaged for twins sharing a specific value of specific covariates, such as monozygosity. However, estimation of such models requires sufficiently large subsamples. For our moderate sample size, the scope for such analyses is limited. In our main analysis, we allow for full flexibility in the effect of zygosity on the bivariate frailty distribution, and we include zygosity in the covariate vector x as well, along with the other covariates. In Section 5.2 we discuss estimation results for separate models by gender.

TABLE 2 Estimation results: Twin mortality models

	(Model I)		(Model II)		(Model III)		(Model IV)	
	Bivariate Model with ber.effect		Corr. Frailty Model no ber.effect		Corr. Frailty Model with ber.effect		Corr. Frailty Model with ber.eff. (extended)	
Variable	**Estimate**	**St.Error**	**Estimate**	**St.Error**	**Estimate**	**St.Error**	**Estimate**	**St.Error**
Covariates:								
Male	0.3979 ***	(0.0164)	0.5856 ***	(0.0284)	0.5143 ***	(0.0291)	0.4954 ***	(0.0292)
log(birth year – 1872)	−0.1088 ***	(0.0239)	−0.245 ***	(0.0504)	−0.1808 ***	(0.0391)	−0.1806 ***	(0.0382)
Born in spring	0.0253	(0.0183)	0.0447	(0.0274)	0.0363	(0.0237)	0.0355	(0.0232)
Born in Copenhagen	0.0876 ***	(0.024)	0.1195 ***	(0.0357)	0.1073 ***	(0.0309)	0.1059 ***	(0.0304)
Dizygotic	0.1557 ***	(0.024)	0.0435	(0.0341)	0.1137 ***	(0.035)	0.1129 ***	(0.0346)
Bereavement effect:								
First year	0.517 ***	(0.0544)	–	–	0.4029 ***	(0.0768)	0.4303 ***	(0.0884)
Second to fourth year	0.5211 ***	(0.0398)	–	–	0.4037 ***	(0.0699)	0.4226 ***	(0.0824)
After 4 years	0.545 ***	(0.0328)	–	–	0.4184 ***	(0.0754)	0.3944 ***	(0.0878)
Dizygotic	−0.2798 ***	(0.036)	–	–	−0.2538 ***	(0.0737)	−0.2491 ***	(0.0776)
Male	–	–	–	–	–	–	0.0382	(0.036)
Age at ber. below 65	–	–	–	–	–	–	0.1077 ***	(0.0362)
Age at ber. above 80	–	–	–	–	–	–	−0.1087 **	(0.0479)
Corr. Gamma frailty:								
Variance monozygotic	–	–	0.4982 ***	(0.0598)	0.3287 ***	(0.0646)	0.3171 ***	(0.0658)
Dizygotic	–	–	0.4697 ***	(0.0581)	0.2748 ***	(0.0602)	0.2712 ***	(0.0619)
Correlation monozygotic	–	–	0.945 ***	(0.0638)	0.5957 ***	(0.1586)	0.5162 ***	(0.1826)
Dizygotic	–	–	0.4964 ***	(0.0532)	0.3452 ***	(0.1356)	0.1868	(0.1725)

Maximum likelihood parameter estimates based on Equation (2). All four estimations are based on 9,495 twin pairs. Standard errors in parentheses. Increasing numbers of stars indicate increasing values of the ratio of the coefficient and its standard error, suggesting a larger coefficient and/or a coefficient with a smaller standard error. (Formally, this corresponds to ranges of values of the Wald test statistic of the null hypothesis that the coefficient equals zero.)

covariates is generated by the bereavement effect. This model does not allow for systematic unobserved lifetime determinants of the twins. The diametrically opposite approach is represented by Model II which is a correlated frailty model that does not include a bereavement effect. Model III synthesizes Models I and II. Model IV simply extends Model III by allowing for a more extensive set of determinants of the bereavement effect.

When comparing the estimates of the correlated Gamma frailty distribution in Model II to those from Models III and IV, one sees considerably higher estimates of the variance and correlation parameters in Model II. This applies to monozygotic (σ^2_{MZ}, ρ_{MZ}) as well as dizygotic (σ^2_{DZ}, ρ_{DZ}) twin pairs. Clearly, the estimated correlations in Model II not only reflect the influence of shared genetic and environmental determinants but also reflect the causal dependence between twin lifespans due to a bereavement effect. If the correlations in Model II are interpreted as reflecting the influence of shared genetic and environmental determinants (i.e. if any role of bereavement effects is ruled out) then this leads to an overestimation of the importance of the joint genetic and childhood environmental characteristics as mortality determinants.

Even more importantly, the estimated correlation parameter decreases more strongly for monozygotic twins than for dizygotic twins, once we account for a bereavement effect. In the light of the rather small standard errors of the estimates of the correlation parameter, the inter-zygosity difference in the decrease is substantial. This suggests that studies based on correlated frailty models that ignore bereavement effects overestimate the importance of genetic factors in lifetime durations. Wienke et al. (2001) explain how zygosity-specific correlations of twin frailty terms can be used for ACDE decompositions, that is, can be used to decompose the total variation into genetic (additive A and due to dominance D) and environmental (shared C and non-shared E) factors. This framework is not straightforwardly applicable to our setting because the covariates x contribute to the shared environmental factors C as well, and because ACDE decompositions are not always identified from twin data (see e.g. Wienke et al., 2001). Nevertheless, the decompositions point at a strong reduction of the importance of genetic factors if bereavement effects are taken into account.[11] Recall that all of this concerns the decomposition of V and not of T itself and that all of this is conditional on covariates x. Therefore, the decompositions ignore the role of shared environmental factors embedded in x.

The results also show that bereavement effects should not be studied in isolation from unobserved twin-pair-specific confounders. In Model I, the estimated bereavement effects are dramatically large. For example, they imply that a monozygotic male twin who is 75 years old and has lost his co-twin at the age of 70 would die on average 2.2 years earlier compared to if he had never experienced this loss. In Models III and IV (which fit the data better due to the addition of a range of parameters that are all estimated to be relevant with small standard errors) we find considerably lower estimates (see Section 5.3 below).

We now turn to the other parameter estimates in Table 2. The covariate effects are fully in line with those in the literature, especially in studies using the Danish Twin Registry. We therefore refer to that literature (see Sections 1 and 3) for detailed discussions. As pointed out in that

[11] For example, consider ACE decompositions for Model II and IV. For Model II, we obtain that 90% of the total variation of the frailty term is due to genetic factors, 4% is due to shared environmental factors and 6% is due to non-shared environmental factors. In Model IV, the point estimates $\hat{\rho}_{MZ}$ and $\hat{\rho}_{DZ}$ of the correlation parameters are not compatible with an ACE decomposition because $\hat{\rho}_{MZ}$ exceeds $2\hat{\rho}_{DZ}$, albeit only slightly. By slightly increasing the value of ρ_{DZ} and slightly decreasing the value of ρ_{MZ}, a point is reached where the ACE decomposition is possible, attributing about 45% to genetic factors and about 55% to non-shared environmental factors.

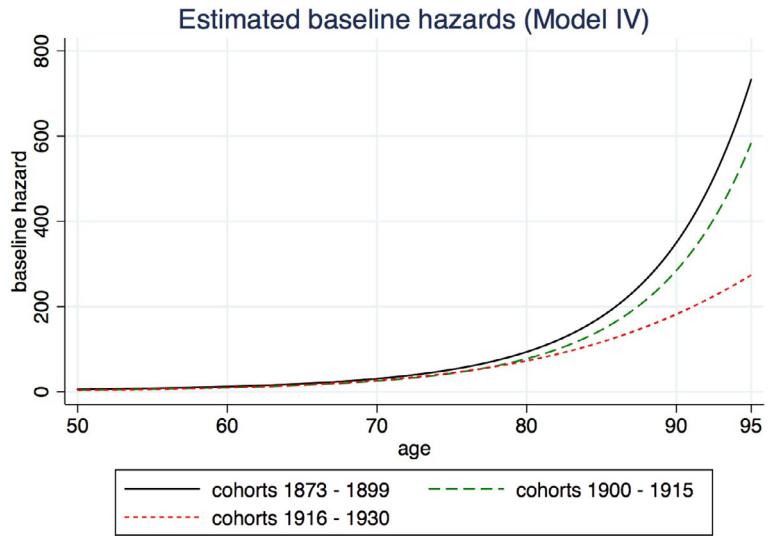

FIGURE 1 Baseline hazard functions based on estimates for Model IV of the baseline hazard: $\lambda(t) = \exp(\alpha_1 t + \alpha_2 t^2 + \alpha_3 t^3)$ where the parameter vector $(\alpha_1 \alpha_2 \alpha_3)$ varies by birth cohort interval and where we multiply $\lambda(t)$ by the constant term in the covariate effect function, that is, by $\exp(\beta_0)$ as well as by the birth-year covariate effect in β (evaluated at its interval-specific mean) [Colour figure can be viewed at wileyonlinelibrary.com]

literature, to some extent the estimated zygosity effect in β may be affected by disproportionately high early-life mortality selection among one or both members of MZ twin pairs.[12]

For sake of brevity we do not list all estimated parameters of the baseline hazard functions, but we give a graphical representation for Model IV in Figure 1, showing the shape of the functions for each of the three birth cohort intervals $c = 1, 2, 3$ (1873–1899, 1900–1915, 1916–1930). For expositional reasons, this includes the constant term in β as well as the effect of birth year in x (we take the effect at the mean of this covariate per birth cohort interval). Since few individuals reached ages above 95, the relevant age period is 50–95. Note that due to left-truncation and right-censoring at ages that vary across individuals, it is not informative to display raw mortality figures. The figure clearly shows that more recent cohorts have a considerably lower mortality hazard at higher ages compared to the earlier cohorts. In particular, the individual mortality rate among those born in the most recent birth cohort interval 1916–1930 increases much less steeply at ages above 85. This change in the ageing process over time is known as the late-life mortality deceleration (see Gavrilov & Nosov, 1985).

The bereavement effect in Model IV is piecewise constant in the time since bereavement, accounting for three successive time intervals. The three parameter estimates are all sizeable with small standard errors and they are of similar size, suggesting persistence of the effect. The size of

[12]We also estimated a model that imposes $\sigma_{MZ} = \sigma_{DZ}$ and $\beta_{DZ} = 0$ from the outset. Interestingly, the estimated frailty distributions do not differ much from those in Table 2, leading further credence to our inference regarding genetic decompositions. However, imposing $\beta_{DZ} = 0$ even though DZ twins in the data have a somewhat higher mortality rate leads to a positive estimated bereavement effect for DZ twins with a large coefficient (results available upon request). To understand this, note that in the restricted model, the only remaining mortality role for zygosity runs through the bereavement effect which affects observed mortality outcomes only for those whose co-twin is observed to die first. We view it as a challenge for further research to expand on this, notably by dealing with early-life mortality by using untruncated data.

TABLE 3 Residual life expectancies of twins in years by zygosity and sex. Based on estimated Model IV. The first column reports the current age. Subsequent columns report the corresponding residual life expectancies, given that bereavement is never experienced or occurs at ages 60, 70, 80 or 90. Covariates and frailty term are set to their average values

	Male					Female				
		Bereavement at age					Bereavement at age			
Age	No Bereav.	60	70	80	90	No Bereav.	60	70	80	90
Residual life expectancy for monozygotic twins										
65	14.5	11.46				17.73	14.46			
75	8.09	6.00	6.42			10.49	8.06	8.55		
85	3.57	2.45	2.66	2.89		4.99	3.55	3.83	4.13	
95	1.15	0.74	0.81	0.90	0.90	1.75	1.14	1.26	1.38	1.38
Residual life expectancy for dizygotic twins										
65	13.79	12.26				16.98	15.32			
75	7.59	6.53	6.97			9.92	8.69	9.2		
85	3.29	2.72	2.95	3.20		4.64	3.91	4.21	4.53	
	1.04	0.83	0.92	1.01	1.01	1.59	1.29	1.41	1.54	1.54

the estimated bereavement effect for dizygotic twin pairs is only half the size of that of monozygotic twin pairs. This is in line with findings in psychological studies (see Segal & Bouchard, 1993; Segal et al., 1995) based on survey data with bereaved twins. These studies construct measures of grief intensities and all find higher grief intensities for monozygotic twins. That bereavement effects are larger for monozygotic twins explains why the estimated frailty correlation parameter for monozygotic twins is so sensitive to whether bereavement effects are taken into account. To put this differently: ignoring that bereavement effects are larger for monozygotic twins leads to an overestimation of the importance of genetic drivers of mortality. Note that gauging the quantitative size of these effects is difficult due to the nonlinear nature of the models. Section 5.3 provides the corresponding effects on mean residual lifetimes which are arguably easier to comprehend.

In Model IV, the bereavement effect also depends on the age at bereavement. Evidently, there is a decrease in the bereavement effect in the age at which the loss occurs. In particular, the effect at age 85 of having lost the co-twin at age 80, compared to experiencing no bereavement, is relatively small, with an implied decrease in residual life expectancy of 0.68 years (Table 3: monozygotic males at age 85). This is also in line with findings from psychological studies with bereaved twins who find a negative correlation between grief intensities and the age at which bereavement is experienced (see Segal et al., 1995).

5.2 | Additional analyses

We performed a range of sensitivity analyses. First, we consider simple Gompertz functional form specifications for the baseline hazard λ as a function of t. We find that this specification is too restrictive to fit most model varieties, in the sense that some parameter estimates have implausible

values. Estimates for parameters of G are frequently at the boundary of the interval of admissible values. In addition, it appears that the estimates of the bereavement-effect parameters are sensitive to adopting the Gompertz specification, perhaps because the latter, while restrictive as a function of t, does allow for cohort-specific baseline hazards whereas the former are imposed to be common across cohorts. Perhaps not surprisingly, the imposition of an even more restrictive model with a Gompertz $\lambda(t)$ that is common across cohorts solves these issues to some extent. The ensuing bereavement effect estimates are close in size to those in the previous subsection. However, the parameters of G are sometimes still at the boundary of the interval of admissible values, which complicates their interpretation, and it remains difficult to allow for bereavement effects that depend on the age at bereavement (results available upon request). The fact that the parameters of the third-order polynomials of $\log \lambda(.)$ in the previous subsection are not close to zero and have small standard errors confirms that such a level of flexibility is warranted to obtain meaningful results.

One may also consider alternative specifications where the function $\lambda(t)$ is restricted to be common across cohorts but $\log \lambda(t)$ still is a third-order polynomial. The estimation results are in line with those of the previous subsection, although the estimated bereavement effects are slightly larger (results available upon request). Again, this confirms that the Gompertz specification is too restrictive. At the other extreme, one may relax the third-order polynomial specification for $\log \lambda(t)$. However, this leads to numerical instability where the values of the polynomial parameters can vary without affecting the fit of the model.

Note that the comparison of estimates with and without interactions of $\lambda(t)$ and the birth cohort indicator effectively informs us whether the results are sensitive to a departure of the proportionality assumption of the basic model. This is important because, as Balan and Putter (2019) demonstrate, in data with small clusters (such as twins), it is very difficult to disentangle frailty from non-proportionality. In other words, non-proportionality that is not taken account of may affect the estimates of the parameters of G. Our identification proof requires only one single covariate to have a proportional effect, and this gives us some leeway in allowing other observed covariates to act in a non-proportional way on the model determinants. As noted above, in addition to allowing the baseline hazard $\lambda(t)$ to depend on the birth cohort interval in a non-proportional way, we allow the frailty distribution to depend on zygosity.

To proceed, we attempt to estimate separate models by specific values of some covariates, effectively allowing for full interactions of such covariates with all model determinants. First, we tried to estimate the model separately by birth cohort intervals of 10 or 15 years but the resulting subsamples turned out to be too small for reliable inference. Moderate increases of the lowest ages at which lifetimes are left-truncated do not have important implications for the empirical findings. Similarly, if we take age 13 as the age at entry, that is, if we assume that V is independent of x at age 13, then the results are virtually identical to those reported. This extends to early prime ages.

Next, we tried to estimate separate models by gender, for same-sex twin pairs in the data. The resulting sample sizes are rather small (3938 male pairs and 4318 female pairs). It turned out that the point estimates within gender type were often very highly correlated with each other, suggesting that the balance between sample size and model flexibility was lost. This affected, in particular, coefficients of the frailty distribution and the baseline hazard. The results are therefore not particularly informative, and one would prefer to use larger samples with a larger number of covariates, possibly also covariates that can have different within-pair values. With this caveat in mind, the point estimates do tend to confirm key conclusions of the previous subsection, namely that the bereavement effects are sizeable and that the estimated genetic contribution to mortality decreases if bereavement effects are taken into account.

We also perform a few simulations to see how the estimation results depend on violation of the proportionality assumption for covariates. Specifically, we examine the implications if the baseline hazard function $\lambda(t)$ depends on whether the twin pair is born in Copenhagen or not, by assuming that the data-generating process is such that among the latter, α_1 is 0.8 of the value of among the former. Estimation is based on a model that ignores this. Most parameter estimates are close to those in the paper (results available upon request). The estimated correlation of frailty among dizygotic twins is now always larger than in the corresponding model in Table 2, but this does not invalidate the qualitative conclusions.

In summary, our results are robust with respect to a range of assumptions, while at the same time, we find that the adoption of more restrictive model specifications does not always lead to meaningful results.

5.3 | Residual life expectancies

One advantage of our modelling approach at the individual level is that it enables us to predict residual lifetimes as a function of preassigned ages at which the loss of the co-twin is experienced. Expected residual lifetimes are relevant for health care policy and are frequently calculated within the demographic and gerontological literature. For a twin j who lost his or her co-twin at age t_k, the expected residual lifetime at age s is computed as (see e.g. Lancaster, 1990)

$$\mu(s, t_k, x) = \frac{\int_s^\infty P(T_j > t | T_k = t_k, x) dt}{P(T_j > s | T_k = t_k, x)} \quad \forall t_k < s.$$

Expected residual lifetimes for monozygotic and dizygotic male and female twins, as implied by the estimated Model IV, are presented in Table 3. These numbers are calculated for individuals with mean values of V and with values of x (except zygosity and gender) that equal the average in the sample. Since the dependence of the bereavement effect on sex is very small and imprecisely estimated, we set this coefficient to zero in our calculations for Table 3. A male monozygotic twin who has reached the age of 75 and lost his co-twin at the age of 70 will live on average for 6.42 remaining years. If he never experiences twin bereavement, he will live on average for 8.09 years longer. A similar pattern is observed for female twins.

6 | CONCLUSION

Our analysis merges two types of models that previously have been used separately in studies analysing twin lifespans. This enables us to disentangle two effects of particular interest in this strand of literature, namely the causal effect of bereavement on the one hand, and the influence of genetic factors and early childhood experiences on the other. This has implications for both strands of literature. We find strong positive bereavement effects that decrease in magnitude with the age at bereavement and that are more pronounced in monozygotic twin pairs than in dizygotic pairs. If the influence of unobserved time-constant correlated factors is ignored, as in previous studies on twin bereavement, bereavement effects are severely overestimated.

Likewise, ignoring bereavement effects in twin mortality analysis leads to biased results. Our empirical results suggest that studies that aim to shed light on the importance of genetic and early-life environmental characteristics and that ignore bereavement effects tend to overestimate

the importance of those characteristics as mortality determinants. Moreover, they tend to overestimate the importance of genetic factors in lifetime durations. The latter is at least partly due to the fact that bereavement effects are larger among monozygotic twins.[13]

We view it as an interesting topic for further research to examine under which conditions models are identified that allow bereavement effects to vary with individual-specific unobserved characteristics. In particular, such characteristics may have genetic determinants, and this would imply that the individual magnitude of the bereavement effect has a genetic component. The study by Schultze-Florey et al. (2012) relates genetic features to levels of inflammation markers after bereavement and identifies a specific single nucleotide polymorphism (SNP) that influences how strong the levels of these markers increase after bereavement. It is an open question whether these interaction effects are quantitatively relevant for mortality. This depends on how common the relevant genotype is, the size of the effect of the SNP on inflammation after bereavement, and the size of the effect of the heightened inflammation after bereavement on subsequent mortality. For our purposes, in the twin setting, two additional issues need to be kept in mind. First, the extent to which such interaction effects influence twin lifespan analyses depends on the extent to which the relevant SNP affects the individual mortality rate in the absence of bereavement. Second, Schultze-Florey et al. (2012) examine spousal bereavement instead of twin bereavement. As discussed earlier in our paper, spousal bereavement typically involves major financial and economic changes as well as changes in the organization of the household. These changes may lead to larger interaction effects on inflammation and subsequent mortality, compared to the case of twin bereavement.

In this context, we also point out another implication of our study, namely, that bereavement effects on mortality that are mostly emotional are substantial. This in turn suggests that the economic component only covers a fraction of the conjugal bereavement effects on mortality found in the literature. A careful analysis of the magnitudes of these components is beyond the scope of this paper, and our data do not allow for this. In our view this constitutes an important topic for further research, with policy implications for the type of support that may help the bereaved to minimize effects on their own mortality.

As a methodological contribution, we prove identification of symmetric duration models with dependent unobserved determinants and a causal effect of one duration on the hazard, relying on only minimal covariate variation. Such models have a wider relevance, for the empirical study of parallel systems and networks.

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[13]It should be kept in mind that these findings are based on a model framework with multiplicative frailty terms. This is in line with most studies in the literatures that we build on. However, it would be an important topic for future research to examine whether the findings can be validated with different model frameworks.

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SUPPORTING INFORMATION

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APPENDIX

A.1. Identification of λ and ϕ

The survival function of $Z|x$ with $Z = \min\{T_1, T_2\}$ is derived as follows

$$\begin{aligned} P(Z > t|x) &= P(T_1 > t, T_2 > t|x) \\ &= \int_0^\infty \int_0^\infty P(T_1 > t|x, V_1) P(T_2 > t|x, V_2), dG(v_1, v_2) \\ &= \int_0^\infty \int_0^\infty e^{-\phi(x)\Lambda(t)(V_1+V_2)}, dG(v_1, v_2) \\ &= \int_0^\infty e^{-\phi(x)\Lambda(t)W}, dG_W(w) \quad \text{with } W = V_1 + V_2. \end{aligned} \tag{A1}$$

For the second equality we exploit that before the first death has occurred no bereavement effect is experienced yet. Consequently, conditional on x and V the events $(T_1 > t)$ and $(T_2 > t)$ are independent. We further use Assumption 4 which implies $G(v_1, v_2|x) = G(v_1, v_2)$.

The distribution of Z has a hazard rate of the mixed proportional form: $\theta_z(t|x, W) = \theta(t|T_2 \geq t, x, V_1) + \theta(t|T_1 \geq t, x, V_2) = \lambda(t)\phi(x)W$ with frailty $W = V_1 + V_2$ drawn from distribution G_W. The results by Elbers and Ridder (1982) (see also Lancaster, 1990; Van den Berg, 2001, for an overview) on the identification of the mixed proportional hazard model imply that, under Assumptions 1–4, the model in Equation (A1), characterized by the functions λ, ϕ and G_W, is identified. In particular, Assumption 1 assures sufficient covariate variation in form of at least one dummy variable.[14] Furthermore, we require the distribution of W to be independent of x and to have a positive and finite mean. Assumption 1 assures the independence of (V_1, V_2) and x. From this the independence of $W = V_1 + V_2$ directly follows. Similarly, as V_1 and V_2 are assumed to have finite positive mean, so does W.

A.2. Identification of δ_a and δ_b

We consider the following hazard rate,

$$\theta(t|T_k = 0, x, V_j) = \tilde{\lambda}_j(t)\tilde{\phi}_j(x)V_j \text{ with } \tilde{\lambda}_j(t) = \lambda(t)\delta_a, \quad \tilde{\phi}_j(x) = \phi(x)\delta_b(0, x), \tag{A2}$$

where the frailties V_j are drawn from $G_{V_j|T_k=0,x}$ for $j, k \in \{1, 2\}$ and $j \neq k$. This hazard rate can be said to have a mixed proportional form as it is proportional in t,x, and an unobserved frailty term.

We now demonstrate that the conditional frailty distribution $G_{V_j|T_k=0,x}$ does not depend on x. Its density is given by:

$$\begin{aligned} f(v_j|T_k = 0, x) &= \frac{\theta_k(0|x, V_j)S_k(0|x, V_j)f(v_j|x)}{\theta_k(0|x)S_k(0|x)} \\ &= \frac{\int_0^\infty \lambda(0)\phi(x)v_k \; dG(v_k|x, V_j)f(v_j|x)}{\int_0^\infty \lambda(0)\phi(x)v_k \; dG(v_k|x)} \\ &= \frac{E(V_k|x, V_j)f(v_j|x)}{E(V_k|x)}. \end{aligned} \tag{A3}$$

[14] See also Kortram et al. (1995) for the case of only two possible values for $\phi(x)$.

According to Assumption 4 (V_1, V_2) are independent of x. Therefore, Equation (A3) simplifies to

$$f(v_j|T_k = 0, x) = \frac{E(V_k|V_j)f(v_j)}{E(V_k)}. \tag{A4}$$

Note that the right-hand side of Equation (A4) does not depend on x. From Equation (A4) it also follows that the distribution of $(V_j|T_k = 0)$ for $j, k \in \{1, 2\}$ and $j \neq k$ has a positive and finite mean, since $G(v_1, v_2)$ has this property.

Assumption 2 states that the functions $\phi(x)$ and $\delta_b(0, x)$ are not proportional, assuring that the function $\hat{\phi}(x) = \phi(x)\delta_b(0, x)$ generates sufficient exogenous variation.

Thus, following Elbers and Ridder (1982), under Assumptions 1–4, the mixed proportional hazard model defined by $\{\tilde{\lambda}, \tilde{\phi}, G_{V_j|T_k=0,x}\}$ is identified. Since λ is known from Appendix A.1, this in turn identifies δ_a. Similarly, since ϕ is known from Appendix A.1, the function $\delta_b(0, x)$ follows as a function of x.

To identify $\delta_b(t, x)$ as a function of t and x, we consider the magnitude of the jump of the observed hazard rate of twin member j at the moment t that twin member k dies,

$$\begin{aligned}\frac{\lim_{s\downarrow t}\theta(s|T_k = t, x)}{\lim_{s\uparrow t}\theta(s|T_k = t, x)} &= \frac{\phi(x)\delta_b(t, x)\lim_{s\downarrow t}\delta_a(s - t)\lambda(s)E(V_j|T_j \geq s, T_k = t, x)}{\phi(x)\lim_{s\uparrow t}\lambda(s)E(V_j|T_j \geq s, T_k = t, x)} \\ &= \delta_b(t, x)\delta_a(0)\frac{\lambda(t)}{\lim_{s\uparrow t}\lambda(s)}.\end{aligned} \tag{A5}$$

Assumptions 2 and 3 ensure that $\delta_a(0)$ is finite and positive and ensure the existence of positive and finite values and limits of λ at t. Also, the model assumptions guarantee that the conditional frailty distributions at $s > t$ and at $s < t$ converge to the distribution at t as s approaches t, so that the conditional means vanish from the equation. Note that the left-hand side of Equation (A5) is observable for all $(t, x) \in (0, \infty) \times \mathcal{X}$. Since $\delta_a(0)$ and the function λ are identified in previous steps, we can trace out the function $\delta_b(t, x)$ over $(0, \infty) \times \mathcal{X}$.

Together, Appendix A.1 and Appendix A.2 therefore prove Proposition 1.

A.3. Proof of Proposition 2

Recall that the functions $\lambda, \phi, \delta_a, \delta_b$ in Model 1 are identified under Assumptions 1–4. The only function that remains undetermined is the bivariate frailty distribution G. For this we adopt the additional Assumption 5.

The observable density $f(t_1, t_2|x)$ for $t_1 > t_2$ can be expressed as follows

$$\begin{aligned}f(t_1, t_2|x) &= \int_0^\infty \int_0^\infty f(t_1|T_2 = t_2, x, V_1)f(t_2|x, V_2)\ dG(v_1, v_2) \\ &= c(t_1, t_2, x)\int_0^\infty \int_0^\infty V_1 V_2 e^{-\phi(x)(\Lambda(t_2)+\Delta(t_1,t_2,x))V_1} e^{-\phi(x)\Lambda(t_2)V_2}\ dG(v_1, v_2) \\ &= c(t_1, t_2, x)\partial^2_{s_1,s_2}\mathcal{L}_G\left(\phi(x)(\Lambda(t_2) + \Delta(t_1, t_2, x)), \phi(x)\Lambda(t_2)\right),\end{aligned}$$

with $c(t_1, t_2, x) = \lambda(t_1)\lambda(t_2)\phi(x)^2\delta_a(t_1 - t_2)\delta_b(t_2, x)$, $\Delta(t_1, t_2, x) = \tilde{\Lambda}(t_1, t_2)\delta_b(t_2, x)$ and bivariate Laplace transform $\mathcal{L}_G$ with cross derivative $\partial^2_{s_1,s_2}\mathcal{L}_G$.

Absolute monotonicity and complete monotonicity:

Definition 1 Let Ω be a nonempty open set in $\mathbb{R}^n$. A function $f : \Omega \to \mathbb{R}$ is absolutely monotone if it is nonnegative and has nonnegative continuous partial derivatives of all orders. f is completely monotone if $f \circ m$ is absolutely monotone, where $m : x \in \{\omega \in \mathbb{R}^n : -\omega \in \Omega\} \to -x$.[15]

This definition states that a function f is completely monotone if it is derivatives of all orders exist, and if these derivatives are continuous and have switching signs for each order (starting with a positive first derivative). It follows directly that if a function f is completely monotone then all derivatives of second order of f will also be completely monotone. Since the bivariate Laplace transform $\mathcal{L}_G(s_1, s_2)$ is known to be a completely monotone function, it directly follows from Definition 1 that the cross derivative of $\mathcal{L}$ given by $\partial^2_{s_1,s_2}\mathcal{L}_G(s_1, s_2) = \frac{\partial^2 \mathcal{L}_G(s_1,s_2)}{\partial s_1 \partial s_2}$ is also completely monotone.

Tracing out the Laplace transform: The function $f : \mathbb{R}^2_+ \to \mathbb{R}^2_+$ is given by $f(t_1, t_2) = (\phi(x)(\Lambda(t_2) + \Delta(t_1, t_2, x)), \phi(x)\Lambda(t_2))$. It maps the vector (t_1, t_2) on the vector of arguments of the Laplace transform (s_1, s_2), with $s_1 = \phi(x)(\Lambda(t_2) + \Delta(t_1, t_2, x))$ and $s_2 = \phi(x)\Lambda(t_2)$. In the following we will show that we can vary (t_1, t_2) on an open set such that $f(t_1, t_2)$ will also attain all values in a nonempty open set. Under Assumption 5 (with $t_1 > t_2 \; \forall \; (t_1, t_2) \in \Psi$) it holds that at all points (t_1, t_2) in the open set Ψ the first derivatives of f exist and are continuous and f has Jacobian

$$J_f(t_1, t_2) = \begin{bmatrix} \phi(x)\lambda(t_1)\delta(t_1, t_2, x) & \phi(x)\left(\lambda(t_2) + \frac{\partial\Delta(t_1,t_2,x)}{t_2}\right) \\ 0 & \phi(x)\lambda(t_2) \end{bmatrix}.$$

Note, that the determinant of J_f is given by $det(J_f(t_1, t_2)) = \phi(x)^2\lambda(t_1)\lambda(t_2)\delta_1(t_1, t_2, x)$, and since under Assumptions 1–4 the functions ϕ, λ, δ_a, δ_b can only attain strictly positive (and finite) values on Ψ, it follows that $det(J_f(t_1, t_2)) \neq 0 \; \forall \; (t_1, t_2) \in \Psi$. Assumption 5 assures that $\frac{\partial\Delta(t_1,t_2,x)}{t_2}$ exists and is continuous on Ψ. Therefore, on the nonempty open set Ψ the function $f(t_1, t_2)$ is continuously differentiable with invertible Jacobian J_f. Using the inverse-function theorem it follows that there exists an nonempty open set $\Upsilon \subset (0, \infty)^2$ such that the function $f(t_1, t_2)$ attains all values in Υ when t_1 and t_2 vary over $\Psi \subset (0, \infty)^2$.

A.4. Derivation of the likelihood function

In the following the functional forms of S, S_{t_1}, S_{t_2} and S_{t_1,t_2} are derived. We start with the survival function $S(t_1, t_2|x) = P(T_1 > t_1, T_2 > t_2|x)$:

$$S(t_1, t_2|x) = \begin{cases} S^*(t_1, t_1|x) - \int_{t_2}^{t_1} S_{t_2}(t_1, \tau|x)d\tau, & \text{for } t_1 \geq t_2 \\ S^*(t_2, t_2|x) - \int_{t_1}^{t_2} S_{t_1}(\tau, t_2|x)d\tau, & \text{for } t_1 < t_2 \end{cases}$$

Here, $S^*(t_1, t_2|x)$ denotes the survival function in the absence of a bereavement effect

$$\begin{aligned} S^*(t_1, t_2|x) &= \int\int_0^\infty P(T_1 > t_1|x, V_1)P(T_2 > t_2|x, V_2)\; dG(v_1, v_2) \\ &= \int\int\int_0^\infty e^{\phi(x)\Lambda(t_1)(\tilde{V}_0+\tilde{V}_1)}\; e^{\phi(x)\Lambda(t_2)(\tilde{V}_0+\tilde{V}_2)}\; dG(\tilde{v}_0)dG(\tilde{v}_1)dG(\tilde{v}_2) \end{aligned}$$

[15] For $n = 1$ this definition reduces to the familiar definitions in Widder (1946).

$$= \int_0^\infty \mathrm{e}^{\phi(x)[\Lambda(t_1)+\Lambda(t_2)]\tilde{V}_0}\, dG(\tilde{v}_0) \int_0^\infty \mathrm{e}^{\phi(x)\Lambda(t_1)\tilde{V}_1}\, dG(\tilde{v}_1) \int_0^\infty \mathrm{e}^{\phi(x)\Lambda(t_2)\tilde{V}_2}\, dG(\tilde{v}_2)$$
$$= (1+\sigma^2\phi(x)[\Lambda(t_1)+\Lambda(t_2)])^{-\frac{\rho}{\sigma^2}} (1+\sigma^2\phi(x)\Lambda(t_1))^{-\frac{(1-\rho)}{\sigma^2}} (1+\sigma^2\phi(x)\Lambda(t_2))^{-\frac{(1-\rho)}{\sigma^2}}.$$

The last three equalities follow from the assumption that $G(v_1, v_2)$ is a Cherian bivariate Gamma distribution, that is, the terms $\tilde{V}_0, \tilde{V}_1, \tilde{V}_2$ are independent and drawn from univariate Gamma distributions: $\tilde{V}_0 \sim \Gamma(\rho\sigma^{-2}, \sigma^{-2})$ and $\tilde{V}_1, \tilde{V}_2 \sim \Gamma((1-\rho)\sigma^{-2}, \sigma^{-2})$.

In the following S_{t_j} is derived. For this purpose we define the functions g_a, g_b and g_c

$$g_a(s_1, s_2, x) = 1 + \sigma^2\phi(x)[\Lambda(s_2) + \Delta(s_1|s_2, x)]$$
$$g_b(s_1, s_2, x) = 1 + \sigma^2\phi(x)[2\Lambda(s_2) + \Delta(s_1|s_2, x)]$$
$$g_c(s, x) = 1 + \sigma^2\phi(x)\Lambda(s).$$

with $\Delta(s_1|s_2, x) = \int_{s_2}^{s_1} \lambda(u)\delta_a(u - s_2)\delta_b(s_2, x)\, du$.

We can now derive $S_{t_j}(t_j, t_k|x) = \frac{\partial S(t_j,t_k|x)}{\partial t_j} = -P(T_j = t_j, T_k > t_k|x)$. Let $t_j \geq t_k$ with $j, k \in \{1, 2\}$, $j \neq k$

$$\begin{aligned} S_{t_k}(t_j, t_k|x) &= \int\int_0^\infty P(T_j > t_j|T_k = t_k, x, V_j) P(T_k = t_k|x, V_k)\, dG(v_j, v_k) \\ &= \phi(x)\lambda(t_k) \\ &\quad \times \int\int\int_0^\infty (\tilde{V}_0 + \tilde{V}_k)\, \mathrm{e}^{\phi(x)[\Lambda(t_k)+\Delta(t_j|t_k,x)](\tilde{V}_0+\tilde{V}_j)}\, \mathrm{e}^{\phi(x)\Lambda(t_k)(\tilde{V}_0+\tilde{V}_k)}\, dG(\tilde{v}_0)dG(\tilde{v}_j)dG(\tilde{v}_k) \\ &= \phi(x)\lambda(t_k) g_b(t_j, t_k, x)^{-\left(\frac{\rho}{\sigma^2}+1\right)} g_c(t_k, x)^{-\left(\frac{(1-\rho)}{\sigma^2}\right)} g_a(t_j, t_k, x)^{-\left(\frac{(1-\rho)}{\sigma^2}+1\right)} \\ &\quad \times [\rho g_a(t_j, t_k, x) + (1-\rho) g_b(t_j, t_k, x)]. \end{aligned}$$

This yields

$$S_{t_j}(t_j, t_k|x) = \begin{cases} \frac{\partial S^*(t_j,t_j|x)}{\partial t_j} + \int_{t_k}^{t_j} S_{t_1,t_2}(t_1, \tau|x) d\tau, & \text{for } t_j > t_k \\ \phi(x)\lambda(t_k) g_b(t_j, t_k, x)^{-\left(\frac{\rho}{\sigma^2}+1\right)} g_c(t_k, x)^{-\left(\frac{(1-\rho)}{\sigma^2}\right)} & \\ g_a(t_j, t_k, x)^{-\left(\frac{(1-\rho)}{\sigma^2}+1\right)} [\rho g_a(t_j, t_k, x) + (1-\rho) g_b(t_j, t_k, x)], & \text{for } t_j \leq t_k. \end{cases}$$

Finally, $S_{t_1,t_2}(t_1, t_2|x) = \frac{\partial^2 S(t_1,t_2|x)}{\partial t_1 \partial t_2} = P(T_1 = t_1, T_2 = t_2|x) = f^*(\max\{t_1, t_2\}, \min\{t_1, t_2\})$ with

$$\begin{aligned} f^*(t_j, t_k) &= \phi(x)^2 \lambda(t_j)\lambda(t_k)\delta_a(t_j - t_k)\delta_b(t_k, x) \\ &\quad \times g_b(t_j, t_k, x)^{-\left(\frac{\rho}{\sigma^2}+2\right)} g_a(t_j, t_k, x)^{-\left(\frac{(1-\rho)}{\sigma^2}+1\right)} g_c(t_k, x)^{-\left(\frac{(1-\rho)}{\sigma^2}+1\right)} \\ &\quad \times [\rho(\rho+\sigma^2) g_a(t_j, t_k, x) g_c(t_k, x) + \rho(1-\rho) g_b(t_j, t_k, x) g_c(t_k, x) \\ &\quad \times \rho(1-\rho) g_b(t_j, t_k, x) g_a(t_j, t_k, x) + (1-\rho)^2 g_b(t_j, t_k, x)^2]. \end{aligned}$$

In the estimation, the integrals $\int_{t_2}^{t_1} S_{t_2}(t_1, \tau|x) d\tau$ and $\int_{t_1}^{t_2} S_{t_1}(\tau, t_2|x) d\tau$ are evaluated using numerical integration methods.