Substance use disorder and suicide-related behaviour around dates of parental death and its anniversaries: a register-based cohort study

Hiyoshi, Ayako; Berg, Lisa; Saarela, Jan; Fall, Katja; Grotta, Alessandra; Shebehe, Jacques; Kawachi, Ichiro; Rostila, Mikael; Montgomery, Scott

Substance use disorder and suicide-related behaviour around dates of parental death and its anniversaries: a register-based cohort study

Ayako Hiyoshi, Lisa Berg, Jan Saarela, Katja Fall, Alessandra Grotta, Jacques Shebehe, Ichiro Kawachi, Mikael Rostila, Scott Montgomery**

Summary

Background Parental death and its anniversaries, including anticipation of these dates, might cause distress and increase the risk of substance use disorder and suicide-related behaviour in bereaved adolescents and young adults. We examined whether the risk of substance use disorder and suicide-related behaviour increases around the date of parental death and subsequent anniversaries.

Methods Using Swedish national registers, we conducted a cohort study of individuals aged 12–24 years. We included individuals aged 12–24 years between Jan 1, 2001, and Dec 31, 2014, whose parents were alive at entry (n=1 858 327) and followed up with them until the end of age 24 years. We excluded individuals with a half-sibling, a history of emigration, a previous record of the outcome events, a parental death before study entry, two parental deaths on the same day during the follow-up, or missing data for relevant variables. Follow-up ended on the day of an outcome event or on Dec 31, 2014; at age 25 years, emigration, or death; or a year before the second parental death. We studied substance use disorder and suicide-related behaviour outcomes separately and included non-fatal and fatal events in both outcomes. We used Cox regression to estimate hazard ratios (HRs), controlling for baseline psychiatric, demographic, and socioeconomic characteristics. Parental death was modelled as a time-varying exposure over 72 monthly periods, starting from 1 year before the parental death to the fifth year and later after the death. Unmeasured confounding was also addressed in within-individual comparisons using a case-crossover design.

Findings During follow-up (median 7·5 [IQR 4·3–10·6] years), there were 42 854 substance use disorder events, with a crude rate of 3·1 per 1000 person-years. For suicide-related behaviour, there were 19 827 events, with a crude rate of 1·4 per 1000 person-years. Most of the events studied were non-fatal. In the month of parental death, the HR for substance use disorder risk was 1·89 (95% CI 1·07–3·33) among male participants, and, for suicide-related behaviour, was 3·76 (1·79–7·89) among male participants and 2·90 (1·61–5·24) among female participants. In male participants, there was an increased risk around the first anniversary (substance use disorder: HR 2·64 [95% CI 1·56–4·46] during the anniversary month; 2·21 [1·25–3·89] for the subsequent month; and for suicide-related behaviour: 3·18 [1·32–7·66] for the subsequent month). Among female participants, an increased risk of substance use disorder recurred around every year consistently in the month before the anniversary of the death and there was an increased risk for suicide-related behaviour in the months of the first and second anniversaries.

Interpretation Although effect sizes were large in this cohort study, the number of individuals who had the outcomes was small. Nevertheless, adolescents and young adults, especially women and girls, who had the death of a parent showed increased risk of substance use disorder and suicide-related behaviour around the first few death anniversaries. Adolescents and young adults, especially women and girls, who had the death of a parent could benefit from preventive measures to reduce distress around the first few years of death anniversaries.

Funding Swedish Research Council.

Clinical Epidemiology and Biostatistics, School of Medical Sciences, Örebro University, Örebro, Sweden (A Hiyoshi PhD, Prof K Fall PhD, J Shebehe MD, Prof S Montgomery PhD); **Department of Public Health Sciences, Stockholm University, Stockholm, Sweden** (A Hiyoshi, L Berg PhD, A Grotta PhD, Prof M Rostila PhD); **Centre for Health Equity Studies, Karolinska Institutet and Stockholm University, Stockholm, Sweden** (L Berg, A Grotta, Prof M Rostila); **Department of Epidemiology and Public Health, University College London, London, UK** (A Hiyoshi, Prof S Montgomery); **Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, Osaka, Japan** (A Hiyoshi); **Demography Unit, Åbo Akademi University, Vaasa, Finland** (Prof J Saarela PhD); **Integrative Epidemiology, Institute of Environmental Medicine** (Prof K Fall), **and Clinical Epidemiology Division** (Prof S Montgomery), **Karolinska Institutet, Stockholm, Sweden; Harvard TH Chan School of Public Health, Boston, MA, USA** (Prof I Kawachi PhD)

Correspondence to:
Dr A Hiyoshi, Clinical Epidemiology and Biostatistics, School of Medical Sciences, Örebro University, Örebro 703 62, Sweden
ayako.hiyoshi@oru.se

Introduction

The death of a parent early in life is a distressing life event for a child. About 3·4% of children in Sweden aged younger than 18 years,[1] and 3–5% of children aged younger than 16 years in the UK[2] and the USA,[3] have had the death of a parent.

An increased risk of substance use disorder and suicide-related behaviour for several years after parental death has been documented among bereaved children.[4–12]

A recent meta-analysis found that parental death by suicide was associated with a two-fold higher risk of suicide attempts and a three-fold higher risk of suicide in bereaved individuals.[13]

However, to the best of our knowledge, no study has examined whether the risk of substance use disorder and suicide-related behaviour increases around the time of parental death and its anniversaries among adolescents and young adults. Traumatic experiences, such as a

Research in context

Evidence before this study

Parental death and the anniversaries following the death can cause substantial distress in adolescents and young adults. We searched PubMed articles published from database inception to Nov 30, 2021, on the risk of substance use disorder and suicide-related behaviour in bereaved offspring. We used the medical subject headings terms "adolescent" or "young adult", "substance-related disorders" or "suicide", and "parental death", together with text searches for relevant terms in the title and abstract, such as "drug", "alcohol", "parental death", "death of a parent", and "loss of (a) parent(s)". We also searched Google with similar keywords. We found 107 studies, including a systematic review for substance use and suicide and a review for parental death in adolescence. Although an increased risk of substance use and suicide-related behaviour for several years after a parental death in individuals has been documented, we found no quantitative study focusing on how the risk of substance use disorder and suicide in young people changes over time after a parental death. Furthermore, we found no study that examined risk around the date of death anniversaries in offspring.

Added value of this study

Compared with adolescents and young adults who had not had the death of a parent, adolescents and young adults with the death of a parent showed a higher risk of substance use disorder and suicide-related behaviour around the date of parental death. The risk of substance use disorder and suicide-related behaviour was mostly driven by non-fatal events. The pattern of the anniversary effect differed by sex. Male participants showed an increased risk of these outcomes only around the first anniversary, but not subsequently. Female participants had an increased risk of substance use disorder across all four anniversaries examined, consistently in the month before the anniversary and less often during the anniversary month or the subsequent month. Female participants had an increased risk of suicide-related behaviour until the second anniversary.

Implications of all the available evidence

These findings suggest that bereaved individuals, especially women and girls, might benefit from preventive measures to reduce distress related to anniversaries, including preceding anticipation, of the death of a parent.

parent's death and its anniversaries, can cause acute responses among adolescents because they are less cognitively and socially developed than adults and might have difficulty in controlling impulsive reactions.[14]

The time preceding the death of the parent can also be challenging because of potential stress related to the anticipation of death.[15–17] Grief-related distress often decreases with time,[6,7] but some individuals experience even more intense distress than the initial grief by triggers such as the anniversary of a death.[18–20] Anniversary reactions have been conceptualised as psychological, somatic, and behavioural reactions to temporal triggers of an anniversary of a substantial past event.[20,21] The reaction might occur on the day or month of the anniversary of an important event,[20] but it might also precede the anniversary date because of anticipation.[22] The weeks after the death of the parent or anniversary can also represent a period of increased risk for events relating to psychological distress.[23] Individuals might revisit memories of their deceased parent and have intensified emotion when rituals and meetings around the time of death and anniversaries have ended.

We aimed to assess the risks for substance use disorder and suicide-related behaviour around the date of parental death and its anniversaries. We focused on young individuals (aged 12–24 years) because the early death of a parent, a major attachment figure, can be particularly devastating and cause substantial distress.[17,24] We also examined whether the associations differ by the sex of the child and age of the child at parental death because reactions to adverse childhood events have been found to differ by these characteristics.[25,26]

Methods

Study design and participants

In this Swedish register-based cohort study, we used data from linked national registers (the Total Population Register, the Multi-Generation Register, Population and Housing Censuses, the Patient Register, the Cause of Death Register, and the Longitudinal Database of Health, Insurance and Labour Market Studies), which included almost all children born in Sweden during 1976–2000. We included individuals who were aged between 12 and 24 years from Jan 1, 2001, to Dec 31, 2014. Study entry was on Jan 1, 2001 (the date that outpatient diagnoses were first available in the Patient Register), or at age 12 years, whichever occurred later. Follow-up ended on the day of an outcome event or when an individual reached age 25 years, at emigration, at death, a year before the second parental death, or on Dec 31, 2014 (the final date of observation in our data), whichever occurred first.

We excluded individuals with a half-sibling, a history of emigration, a previous record of the outcome events (ie, substance use disorder or suicide-related behaviour), a parental death before study entry, two parental deaths on the same day during the follow-up, or missing data for relevant variables. The follow-up ended 1 year before a second parental death to avoid the potential impact of the second death on the estimates. Individuals who had half-siblings were excluded as it was more likely that the parents did not live in the same household and, thus, have reduced contact or weaker connections with their offspring. Since we aimed to examine the incidence of the study outcomes around the time of parental death and anniversaries among individuals aged 12–24 years,

and given the availability of outpatient data from 2001, we excluded individuals with an outcome event or parental death before the start of follow-up.

This study was part of a research project investigating the health consequences of childhood bereavement. The specific research questions were not prespecified and were developed through the research process. A list of the registers and brief descriptions are included in the appendix (p 1). According to the Swedish Ethical Review Act, no consent from participants was required for register-based research. The Swedish Ethical Review Authority approved the use of registers for this study (2019–04143).

Procedures

To examine risk of substance use disorder and suicide-related behaviour around the date of parental death and its anniversaries, parental death was modelled as a time-varying exposure variable. We split follow-up time into approximately 30·5 day intervals (appendix p 3). The split started a year before the parental death, creating 12 monthly periods before the death. Follow-up from the date of parental death to the day before the fifth anniversary was also split into monthly intervals. Combining pre-death and post-death splits, there were 72 monthly periods in total. Follow-up time from the date of the fifth anniversary to the end of the study was included in the last category (period 73). We used non-bereaved person-year observations as a reference, which included data of individuals who never had parental death during the follow-up and data until a year before the parental death for those who had a parental death. An anniversary month was defined as a 1 month period starting 1 year from the date of the death and then recurring each subsequent year.

We also investigated the role of sex of the participant (male or female) and age of the participant at the parental death as potential effect modifiers in the relationship between parental death and anniversaries and our outcomes.

The following variables were identified as potential confounders for the associations between parental death and study outcomes: sex of offspring (male or female), birth order (first, second, or third or later born), and birth year (1976–82, 1983–88, 1989–94, or 1995–2000). Because our data included socioeconomic information for approximately every fifth year, we used the year closest to the individual's birth between 1976 and 2000 to identify the highest level of parental education (≤9, 10–12, or >12 years of education), the most advantageous parental occupational social class (professional, intermediate, or working class, based on an approximation of a three-category version of the European Socioeconomic Classification),[27] and the total disposable income of the two parents (year-specific quartiles). Furthermore, we identified the presence of any psychiatric diagnosis before study entry (ie, yes or no) using the International Classification of Diseases (10th version; ICD-10) F0–F98, excluding F10–16 and F18–F19. See the appendix (p 1) for more details.

Outcomes

We investigated two outcomes: substance use disorder and suicide-related behaviour. The incident date of each outcome was defined as the earliest date when any of the relevant ICD-10 codes were recorded in the Patient Register (including both inpatient and outpatient care) or Cause of Death Register.[28] We focused on the primary diagnosis or the underlying cause of death. Substance use disorder was defined using F10–F19, excluding F17 for tobacco dependency,[29] and suicide-related behaviour was defined using codes for intentional self-harm (X60–X84).[30] Substance use disorder and suicide-related behaviour were not mutually exclusive. Fatal and non-fatal events were combined, but also analysed separately. To assess the robustness of our findings in relation to the definition of the outcome, we did sensitivity analyses by extending the definitions to include accidental poisoning (X40–X42 and X45)[31] for substance use disorder and undetermined intent (Y10–34) for suicide-related behaviour. ICD (8th and 9th revision) codes were also used to exclude individuals who had these outcomes before the study entry (appendix p 1).

Statistical analysis

We summarised the characteristics of the participants by frequencies, proportions, and crude rates. For the descriptive analysis, individuals who had a parental death during the follow-up period were classified as bereaved and those who had not had a parental death during the follow-up were classified as non-bereaved. Median follow-up was calculated using observed follow-up times for all participants.

We fitted Cox proportional hazard regression models estimating hazard ratios (HRs; 95% CIs). To adjust for age effectively, we used age of participants as the time scale.[32] We modelled parental death as a time-varying exposure using the variable with monthly split. The proportional hazard assumption was assessed through both Schoenfeld residual tests and graphical assessments. We presented two models, one age-adjusted only (model 1) and another adjusted for all available potential confounders (modelled as categorical variables; model 2). To assess whether the consequences of bereavement differed by sex, we conducted likelihood ratio tests comparing models with and without interaction terms between the variable for monthly split and sex. We examined the differences of associations by the participants' age at parental death using Schoenfeld residual tests, which assessed whether the relative risks of the outcomes for the monthly periods were constant at any point of age (which is the time scale in this study).

We did several sensitivity analyses. First, we excluded individuals with a history of psychiatric diagnoses. Second, we separated non-fatal or fatal events. Third, we included the extended outcome definitions for non-fatal or fatal events, combined and separately.

Individuals who had a parental death at a young age might have familial and environmental characteristics

	All individuals			Male participants		Female participants	
	Total	Non-bereaved	Bereaved	Non-bereaved	Bereaved	Non-bereaved	Bereaved
Substance use disorder							
Total sample size, n	1 858 327	1 814 661	43 666	933 455	22 550	881 206	21 116
Substance use disorder during follow-up							
No	1 815 478 (97·7%)	1 772 742 (97·7%)	42 736 (97·9%)	910 931 (97·6%)	22 007 (97·6%)	861 811 (97·8%)	20 729 (98·2%)
Yes	42 849 (2·3%)	41 919 (2·3%)	930 (2·1%)	22 524 (2·4%)	543 (2·4%)	19 395 (2·2%)	387 (1·8%)
Non-fatal	42 844 (100·0%)	..	..	..	..	..	..
Fatal	5 (0·0%)	..	..	..	..	..	..
Suicide-related behaviour							
Total sample size, n	1 860 809	1 816 655	44 154	935 419	22 952	881 236	21 202
Suicide-related behaviour during follow-up							
No	1 840 982 (98·9%)	1 797 274 (98·9%)	43 708 (99·0%)	929 085 (99·3%)	22 782 (99·3%)	868 189 (98·5%)	20 926 (98·7%)
Yes	19 827 (1·1%)	19 381 (1·1%)	446 (1·0%)	6334 (0·7%)	170 (0·7%)	13 047 (1·5%)	276 (1·3%)
Non-fatal	19 123 (96·4%)	18 700 (96·5%)	423 (94·8%)	5818 (91·9%)	151 (88·8%)	..	..
Fatal	704 (3·5%)	681 (3·5%)	23 (5·2%)	516 (8·1%)	19 (11·2%)	..	..

Data are in n (%) unless specified. Data not shown if sample sizes were too small. Individuals who ever had a parental death during the follow-up were classified as bereaved individuals and the remaining individuals were classified as non-bereaved. For substance use disorder, there was no individual who attended or was admitted to hospital and died on the same day. For suicide-related behaviour, there were 34 individuals who attended or were admitted to hospital and died on the same day, and these individuals were included as fatal events.

Table 1: Distribution of substance use disorder and suicide-related behaviour by bereavement during the follow-up, in the whole population and stratified by the sex of individuals

underlying both parental death and the outcomes observed. To account for this confounding when identifying the anniversary-specific risks, we did secondary analyses using a case-crossover design among participants who had a parental death.[33] We estimated odds ratios (ORs) through within-individual comparisons using conditional logistic regression, where participants who had the outcome event were self-matched and served as their own control. The odds of a event occurring during the anniversary months were compared to the odds of an event occurring during non-anniversary months (appendix p 3).[34] Although anniversary events were considered to reflect temporal triggers, unrelated to biological and social factors,[21] we did analyses over 1 year at a time to avoid influences of potential confounding due to within-individual changes over time.[34] We also assessed whether associations change over the years from the first to the fourth anniversaries by comparing models with and without interaction terms between the variables for anniversary periods and year.

In all regression analyses, we accounted for clustering by sibling group using the cluster sandwich estimator, which gives robust SEs. The analyses were done using Stata (version 15/SE and 17/MP).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to submit the paper for publication.

Results

Of 2 527 933 individuals who were older than 12 years in 2001 or reached 12 years during the study period, we excluded 500 472 (19·8%) with a half-sibling, 83 155 (3·3%) with a history of emigration, 46 966 (1·9%) with a parental death before study entry, 151 (<0·1%) with two parental deaths on the same day during the follow-up, and 32 727 (1·3%) with missing data for relevant variables. We also excluded individuals with a previous record of the outcome events before study entry (6135 [0·2%] with a record of substance use disorder and 3653 [0·1%] with a record of suicide-related behaviour). After these exclusions, 1 858 327 individuals were included in the analysis for substance use disorder and 1 860 809 for suicide-related behaviour.

43 666 (2·3%) participants for the substance use disorder analysis and 44 154 (2·4%) participants for the suicide-related behaviour analysis had a parental death during the follow-up period (table 1). Bereaved individuals were more likely to be of third or later birth order and to have more socioeconomically disadvantaged parents than non-bereaved individuals (appendix p 16).

When we examined the proportional hazard assumption using Schoenfeld residual tests, there were some violations for potential confounders. In graphical assessments of log–log plots, the assumption was not satisfactorily met for sex, birth year, and history of psychiatric diagnoses (appendix pp 4–5). Therefore, these three variables were included as stratification variables to allow baseline hazards to vary for each category, and the rest of the variables were included in the model.

During the median follow-up of 7·5 years (IQR 4·3–10·6; in total 13 666 832 person-years), we identified 42 844 non-fatal and five fatal substance use disorder events (table 1). The crude rate of substance use disorder, combining both fatal and non-fatal events, was small at 3·1 per 1000 person-years (appendix p 17). Age-adjusted HRs were significantly higher for male participants than for female participants, for younger siblings than for first-born siblings, and for individuals with less advantageous parental socioeconomic circumstances.

For substance use disorders, HRs for each month over the 72 monthly periods were similar between the age-adjusted model (model 1) and the model adjusting for all potential confounding factors (model 2; appendix p 18). HRs from model 2 are shown in the appendix (p 6).

There was evidence of effect modification by sex of the offspring (likelihood ratio test p=0·0051); therefore, we stratified analyses by sex for substance use disorder. The distribution of data and the crude rates over 72 monthly periods for male and female participants are shown in the

appendix (p 19). When the parent died, male participants had an increased risk for substance use disorder in the month of death (HR 1·89 [95% CI 1·07–3·33]) and the second month (2·46 [1·51–4·02]), whereas female participants had an increased risk only in the second month of death (1·96 [1·09–3·54; table 2 and figure 1). For all four anniversaries during subsequent years, female participants showed an increased risk of substance use disorder in the month preceding the anniversary (1·61 [1·04–2·49]) for the first, the second (2·73 [1·51–4·92]), the third (2·38 [1·19–4·75]), and the fourth (3·64 [1·96–6·77]) years, but less often in the second month after the anniversary and not in the month of the anniversary. For male participants, there was an increased risk of substance use disorder during or just after the first anniversary (for the anniversary month 2·64 [1·56–4·46] and for the subsequent month 2·21 [1·25–3·89]), but no raised risk after these months. In male participants, but not female participants, there was an increased risk (1·56 [1·30–1·88]) across the period from the fifth anniversary to the end of follow-up (appendix p 19), which was a median of 2·1 (IQR 1·0–3·8) years. When we combined two anniversary years (first plus second and third plus fourth) the pattern of findings remained similar (appendix p 20). In both male and female participants, the proportional hazard assumption for substance use disorder was not violated for most of the 72 monthly periods, indicating that these HRs did not differ by age (appendix pp 21–22).

During follow-up, with a median of 7·6 years (IQR 4·3–10·6; in total 13 771 728 person-years), 19 827 suicide-related behaviour events were observed, of which 19 123 events were non-fatal and 704 were fatal (table 1). 13 154 (68·8%) of 19 123 events of suicide-related behaviour that were not fatal occurred in female participants, whereas 535 (76·0%) of 704 suicides (fatal events) were in male participants. The crude rate combining fatal and non-fatal events was small and equal to 1·4 per 1000 person-years (appendix p 23). In contrast with the results for substance use disorder, female participants had a higher risk of suicide-related behaviour than male participants (2·19 [2·13–2·26]). Age-adjusted HRs for suicide-related behaviour were higher for individuals with more disadvantaged parental socio-economic characteristics (appendix p 23), and the effect sizes were higher than those observed for substance use disorder.

HRs for each of the 72 months were similar in the age-adjusted model for suicide-related behaviour (model 1) and the fully adjusted model (model 2; appendix p 7, 24). Since the likelihood ratio test indicated that the associations differed by sex of the offspring (p=0·023), we stratified analyses by sex. The distribution of data and crude rates are shown in the appendix (p 25). In male participants, apart from the increased risk of suicide-related behaviour in the month of parental death (HR 3·76 [95% CI 1·79–7·89]) and the second month after the first anniversary (3·18 [1·32–7·66]), there was

	Substance use disorder		Suicide-related behaviour	
	Male participants	Female participants	Male participants	Female participants
Non-bereaved individuals (reference)	..	..	..	..
Month of parental death	1·89 (1·07–3·33)	0·73 (0·27–1·94)	3·76 (1·79–7·89)	2·90 (1·61–5·24)
Second month after the parental death	2·46 (1·51–4·02)	1·96 (1·09–3·54)	2·10 (0·79–5·59)	1·81 (0·86–3·80)
Month preceding the first anniversary	1·37 (0·88–2·13)	1·61 (1·04–2·49)	1·25 (0·52–2·99)	1·24 (0·67–2·32)
First anniversary month*	2·64 (1·56–4·46)	1·09 (0·45–2·61)	1·31 (0·33–5·24)	2·90 (1·51–5·57)
Second month after the first anniversary	2·21 (1·25–3·89)	1·91 (0·99–3·68)	3·18 (1·32–7·66)	1·56 (0·65–3·76)
Month preceding the second anniversary	1·50 (0·71–3·14)	2·73 (1·51–4·92)	1·51 (0·38–6·05)	1·12 (0·36–3·47)
Second anniversary month*	1·54 (0·73–3·23)	1·27 (0·53–3·05)	1·56 (0·39–6·23)	3·83 (2·06–7·12)
Second month after the second anniversary	1·30 (0·58–2·88)	0·75 (0·24–2·31)	NA	2·27 (1·02–5·06)
Month preceding the third anniversary	1·30 (0·54–3·12)	2·38 (1·19–4·75)	NA	0·46 (0·06–3·25)
Third anniversary month*	1·33 (0·55–3·20)	1·83 (0·82–4·07)	2·90 (0·94–9·00)	0·95 (0·24–3·79)
Second month after the third anniversary	1·04 (0·39–2·77)	1·20 (0·45–3·19)	1·91 (0·48–7·65)	1·87 (0·70–4·99)
Month preceding the fourth anniversary	0·64 (0·16–2·56)	3·64 (1·96–6·77)	NA	0·58 (0·08–4·11)
Fourth anniversary month*	0·99 (0·32–3·07)	0·37 (0·05–2·66)	1·23 (0·17–8·77)	1·20 (0·30–4·80)
Second month after the fourth anniversary	1·30 (0·49–3·46)	2·59 (1·23–5·43)	1·23 (0·17–8·72)	1·19 (0·30–4·76)

Data are in HR (95% CI). The estimates were adjusted for age, birth order, parental education, income, social class, year of birth, psychiatric diagnosis before entry, and data clustering by sibling. Estimates for all periods are shown in the appendix (pp 19, 25). HR=hazard ratio. NA=not available. *Day of anniversary to 1 month after anniversary.

Table 2: Adjusted hazard ratios for the risk of substance use disorder and suicide-related behaviour occurring on the specified months, stratified by the sex of individuals

no increased risk (table 2 and figure 2). In female participants, in addition to the month of parental death (2·90 [1·61–5·24]), the month of the first anniversary (2·90 [1·51–5·57]) and month of the second anniversary (3·83 [2·06–7·12]) showed increased risks. The estimates combining the first and second anniversary years, as well as the third and fourth, showed patterns consistent with the main findings for suicide-related behaviour (appendix p 26). No association was observed among male participants, but among female participants, HRs for the month of anniversary (3·32 [2·12–5·21]) and the subsequent month (1·89 [1·04–3·41]) for the first and second anniversaries combined showed an increased risk of suicide-related behaviour. However, no association was observed in the third and fourth years combined.

In both male and female participants, the proportional hazard assumption was not violated for most of the 72 months, indicating that there was little evidence that these HRs differed by age (appendix pp 27–28).
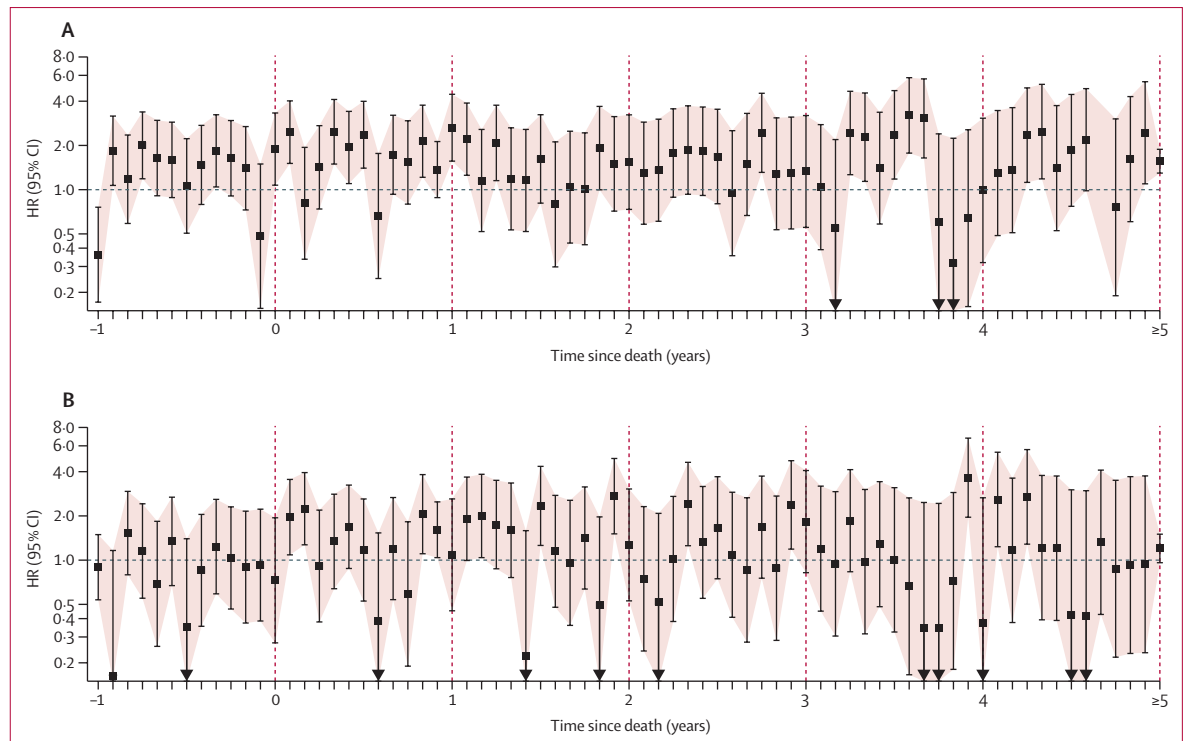
***Figure 1:* Risk of substance use disorder stratified by the sex of participants**
(A) Male participants. (B) Female participants. Non-bereaved individuals (ie, individuals without the death of a parent) were used as a reference. Lower CIs were truncated at 0·15. Estimate at –1 year is for a 1 month period starting from the date of a year before the parental death. Estimate at 0 years is for a 1 month period starting from the date of the parental death. Years 1, 2, 3, and 4 are 1 month periods starting from the date of the first, second, third, and fourth anniversary of the parental death. ≥5 years includes from the date of the fifth anniversary to the end of the follow-up period. The estimates were adjusted for age, birth order, parental education, income, social class, year of birth, psychiatric diagnosis before the entry, and data clustering by sibling. The HRs and CIs are reported numerically in the appendix (p 19). HR=hazard ratio.

For the first sensitivity analysis, we excluded 37 071 (2·0%) individuals for substance use disorder and 40 373 (2·2%) individuals for suicide-related behaviour with a history of psychiatric diagnoses. In analyses for both substance use disorder and suicide-related behaviour, and in analyses for both male and female participants, there were no notable deviations from the patterns observed in the main analyses (appendix pp 8–9, 29–80). For the second sensitivity analysis that separated non-fatal and fatal events, the results of non-fatal events were similar to the main analysis combining non-fatal events and fatal events (appendix pp 10–11). Detailed analyses of fatal events for substance use disorder and suicide were not feasible because there were too few outcome events. For the third sensitivity analysis in which we extended the definition of substance use disorder to include accidental poisoning and extended suicide-related behaviour to include undetermined intent, the distribution of data is shown in the appendix (p 31). For substance use disorders including accidental poisoning, there was no notable deviation from the patterns found in the main analyses (appendix pp 12, 32). The associations remained similar in the analysis focused on non-fatal events (appendix pp 13, 33). For analyses using suicide-related behaviour including undetermined intent, in male participants, the

CIs became narrower and HRs tended to attenuate compared with estimates from the main analyses. Only the month of parental death showed an association with increased suicide-related behaviour and not any anniversaries (appendix pp 14–15, 34–35). In female participants, there was no notable deviation from the patterns observed in the main analysis. Analyses focusing on fatal events were not feasible.

For the case-crossover analysis of anniversary-specific risk among individuals who had parental death, only those with a variation in the outcome were included in the analysis, thus the various models were restricted to analysing data for 11–110 individuals (appendix p 36). For both substance use disorder and suicide-related behaviours, the overall pattern of risk was mostly similar to that observed in the main analyses using Cox regression analysis, with generally larger effect sizes but wider CIs (figure 3). As in the main analysis, male participants had an increased risk for substance use disorder around the first anniversary, but not after, and female participants had an increased risk before the anniversary months in all four anniversaries examined and less consistently in the month of the anniversary or the subsequent month. There was evidence that the associations for substance use disorder differed over the years in male (p=0·048) but not
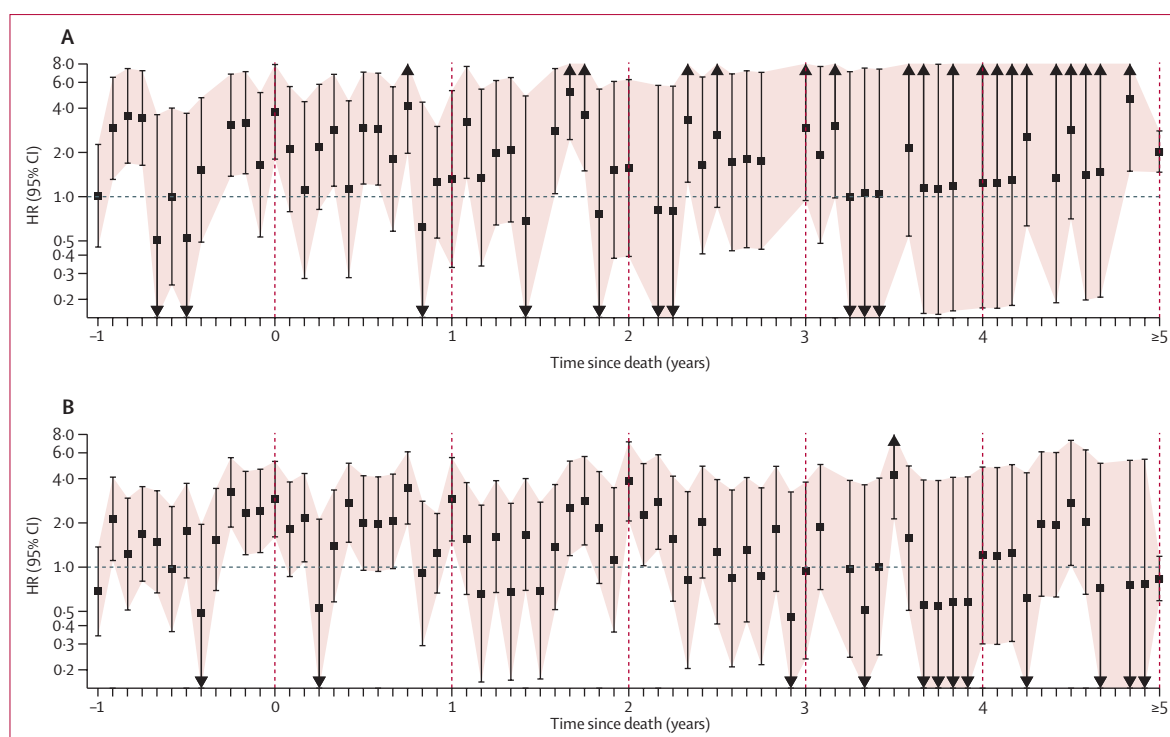
Figure 2: Risk of suicide-related behaviour stratified by the sex of participants
(A) Male participants. (B) Female participants. Non-bereaved individuals (ie, individuals without the death of a parent) were used as a reference. Upper CIs are truncated at 8·0 and the lower CIs at 0·15. Estimate at –1 year is for a 1 month period starting from the date of a year before the parental death. Estimate at 0 years is for a 1 month period starting from the date of the parental death. Years 1, 2, 3, and 4 are 1 month periods starting from the date of the first, second, third, and fourth anniversary of the parental death. ≥5 years includes from the date of the fifth anniversary to the end of the follow-up period. The estimates were adjusted for age, birth order, parental education, income, social class, year of birth, psychiatric diagnosis before the entry, and data clustering by sibling. The HRs and CIs are reported numerically in the appendix (p 25). HR=hazard ratio.

in female (0·70) participants. For suicide-related behaviour, male participants had a heightened risk only around the first anniversary. In female participants, the increased risk of suicide-related behaviour was primarily observed in the first 2 years. There was no evidence that the associations differed by year in male (p=0·24) or female (p=0·44) participants.

Discussion

In this cohort study of adolescents and young adults, we examined whether there was an increased risk of substance use disorder and suicide-related behaviour in bereaved individuals around the month of parental death and its anniversaries. Most of the observed events, in particular for substance use disorder, were non-fatal, and associations were driven by non-fatal events. The pattern of anniversary associations differed by sex. Male participants showed an increased risk of substance use disorder and suicide-related behaviour only around the month of parental death and the first anniversary, but not subsequently. Female participants had an increased risk of substance use disorder across all four anniversaries examined, consistently in the month before the anniversary and less often during the anniversary month or the subsequent month. Among female participants, we

observed an increased risk of suicide-related behaviour during the month of the first and second anniversaries.

To the best of our knowledge, this is the first study with large-scale data to investigate the risks of substance use disorder and suicide-related behaviour around the parental death and its anniversaries among adolescents and young adults. Only qualitative studies have described potential anniversary reactions for young individuals.[35] Among adults, increased risk of mortality around the death anniversaries has been observed among mothers who had a death of a child[21] and of substance use disorder in individuals who had a death of a parent.[36] Anticipatory anniversary effects have been suggested[22] because emotions can be more intense during anticipation than during retrospection,[37] but little research has been done. We observed increased risks at times around parental death and its anniversaries, even anticipation of the anniversary, similar to what has been suggested in adults by other studies.[21,22,36]

We observed some increased risks around the time of parental death and its first four anniversaries. However, some other months also showed increased risks, and estimates might have been confounded by unmeasured confounding. To address these concerns, we did case-crossover analysis and observed consistent patterns of
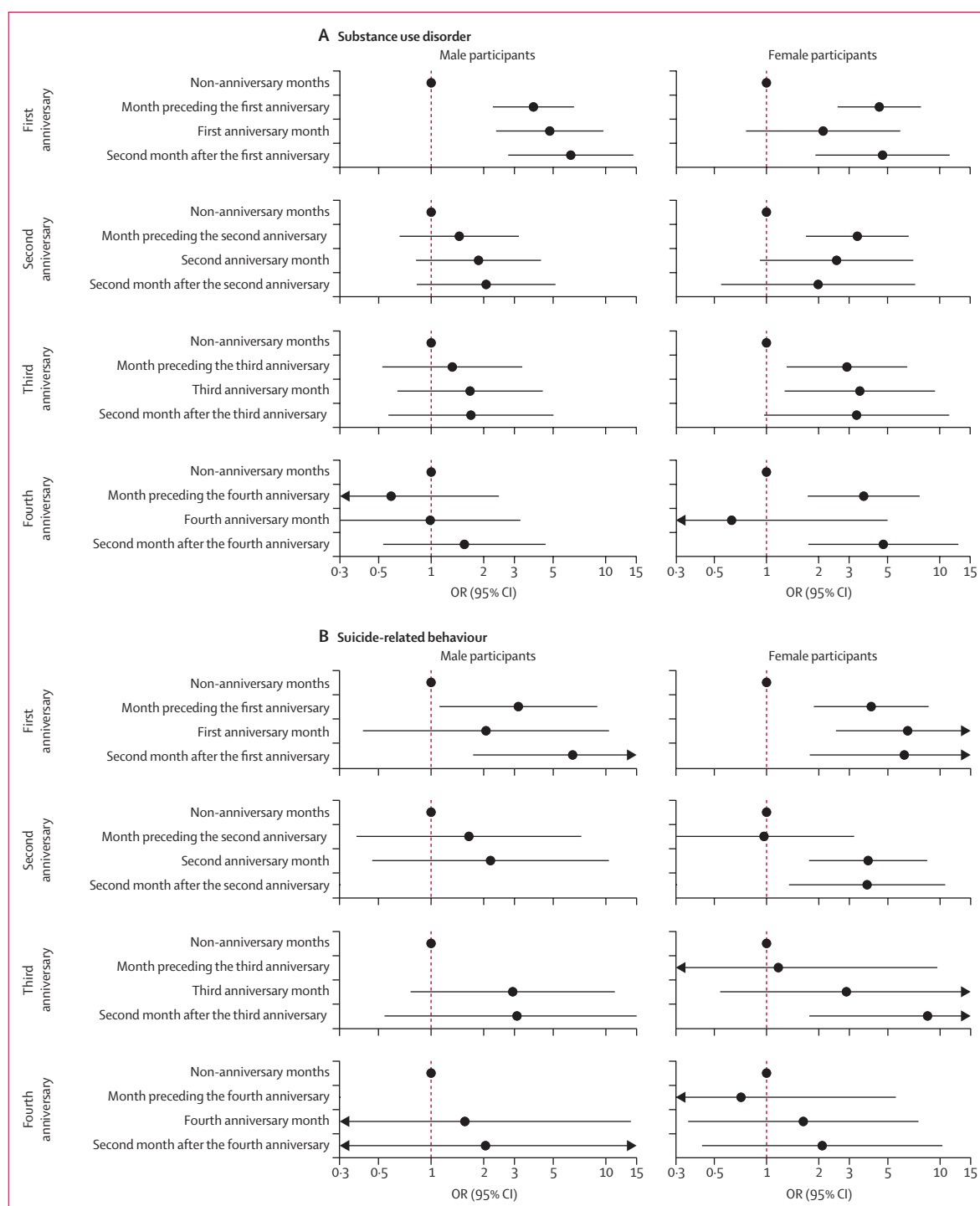
Figure 3: Case-crossover analysis using within-individual comparison for the risk of substance use disorder and suicide-related behaviour in the months around the anniversary of parental death, stratified by the sex of participants
(A) Substance use disorder. (B) Suicide-related behaviour. For each year analysed, the month of anniversary (a 1 month period starting from the date of parental death anniversary), a 1 month period preceding the anniversary, and 1 month period after the anniversary month were compared with non-anniversary months (reference). We used conditional logistic regression. The estimates were adjusted for data clustering. Lower CIs were truncated at 0·3 and the upper CIs at 15·0. The ORs and 95% CIs in this graph are reported numerically in the appendix (p 36) and a schematic figure is also shown in the appendix (p 3). OR=odds ratio.

increased risk of both substance use disorder and suicide-related behaviours for the target months, which was in line with the results of the main analysis (see appendix p 1 for additional discussion).

For bereaved male participants, the risk of both substance use disorder and suicide-related behaviour remained in the final period (from the fifth anniversary date to the end of follow-up). Such observations are consistent with studies showing that the increased risk of suicide[9,13] and substance use[38] lasts for many years for individuals with an early parental death. Although our study found specific periods that were potentially important for preventive measures, it does not dismiss the importance of addressing the needs of bereaved young individuals at other times.

We observed some months with increased risk even before the parental death, but the pattern was inconsistent between substance use disorder and suicide-related behaviour. Due to the absence of data, we were unable to discern when the condition of parents deteriorated before death. If seeing parents suffer causes the individual distress, the risks for both outcomes could increase towards the date of parental death. Alternatively, living circumstances (eg, poverty and a hazardous environment) or psychiatric or behavioural characteristics in parents associated with their early death might predispose offspring to a higher risk of substance use disorder and suicide-related behaviour. Given the inconsistent patterns, residual confounding, rather than pre-death anticipatory risks, might explain the increased risks during this period.

Male and female participants showed different patterns of associations. Our findings in female participants were consistent with a previous study that showed anniversary reactions in women who had a death of a child.[21] In suicide-related behaviour, there was a sex difference in the underlying rates of fatal and non-fatal events. However, the patterns of associations were mostly similar in both substance use disorder and suicide-related behaviour in analyses restricted to non-fatal events, although the increased risk of suicide-related behaviour for male participants around the first anniversary diminished. Therefore, the differences in rates of fatal and non-fatal suicide-related behaviour by sex alone might not explain our findings. Although inconclusive,[39] time perspectives have been reported to differ by sex and women might have more past-orientated perspectives than men.[40]

It should be noted that, although the magnitude of effect sizes was generally large, the number of individuals who had the outcomes was relatively small. In the first anniversary month, the number of events for substance use disorder in bereaved male participants was 9·5 per 1000 person-years, compared with an average of 3·2 events per 1000 person-years for non-bereaved male participants. Similarly, the number of events of suicide-related behaviour for bereaved female participants was 6·5 per 1000 person-years, compared with 2·0 per 1000 person-years for non-bereaved female participants. Therefore, in combination with the low incidence of early parental death, the absolute number of outcomes for the associations that we investigated was not large at a population level.[41] However, the development of a mental health problem at a young age might affect an individual's entire life.[42,43] We are not aware of any preventive measures considering anniversaries, including anticipating them as triggers of mental health problems. Brief interventions, such as group discussion to share experiences and counselling targeting the bereaved offspring or the remaining parent, can help prevent mental health problems or traumatic grief.[44] Therefore, preventive actions and support, targeting periods leading up to and around anniversaries, might help to decrease risk.

This study has some limitations. First, we identified outcomes on the basis of information on hospital care and death records, thus there might have been a degree of misclassification in our study outcomes. The Cause of Death Register records all deaths reported to authorities in Sweden[45] and the Patient Register has recorded inpatient care in Sweden since 1987 and outpatient care since 2001,[46] but individuals who did not seek health care or were treated at primary care were not identified in our study.[47,48] Accurate ascertainment of whether death was due to intentional suicide or was unintentional is challenging.[49,50] Studies from Australia and Brazil have shown that administrative data recorded using ICD-10 codes capture about 78% of suicides and 85% of non-fatal suicidal behaviour.[49] The rate of suicide recorded is also influenced by changes in the rate of post-mortem analyses done. For example, a 1% decrease in the post-mortem rate has been associated with a small decline in the suicide rate identified in the population.[51] The post-mortem rate in Sweden declined during our study period.[52] If such misclassification is non-differential (ie, unrelated to the exposure), our estimates are likely to underestimate the true associations; however, if differential, it could result in overestimations. However, in analyses in which we included undetermined intent in the definition of suicide-related behaviour, the pattern of associations remained similar. Second, because we examined risks on a monthly basis, the number of events per time unit was low and CIs were wide. Therefore, large effect sizes need to be interpreted cautiously, as ratio estimates tend to be of higher magnitude when the outcome is rare.[41] Third, the risk of substance use disorder and suicide-related behaviour might differ by the cause of parental death, and the anticipatory risk before the parental death might differ depending on whether the parent died suddenly or from a disease that developed over time. However, since we did not have data on the cause of parental deaths or disease characteristics before death, we could not assess potential differences resulting from the cause, or other characteristics, of parental death. Fourth, we studied individuals aged 12–24 years, excluded individuals with a half-sibling or a parental death before study entry, and followed up until

2014. These restrictions can affect the extent to which these findings can be generalised. For example, due to the focus on individuals aged 12–24 years, the results might not be generalisable to other age groups because, with increasing age, relationships with parents change and individuals might mature and cope with bereavement differently. Due to the exclusions and absence of data more recent than 2014, our study population might not be fully representative of the wider and more recent population. Additionally, associations between death anniversaries and the outcomes might be different for children with a parent who lives in another household. However, we believe that the impact of highly stressful events on mental health among younger individuals would not be markedly different in more recent birth cohorts from the cohort we studied. Fifth, as the risk associated with a first parental death can be different from the second parental death or parents dying on the same day, we did not study the risk associated with these more complex patterns of parental death. Sixth, our study investigated death anniversaries, but other anniversaries, such as for birthdays, holidays, or when the offspring reaches the age when the parent died, might also be relevant to anniversary reactions.[20,21,35] Finally, it needs to be stressed that, although we did not correct for multiple testing,[53] this study involved several tests, some of which might have resulted in chance findings. However, estimates from conditional logistic regression (producing fixed-effect estimates), where statistical power was reduced, provided estimates consistent with the main findings from the Cox regression models;[32,54] and consistency in patterns across the outcomes indicates that chance findings are unlikely to explain our results.

The strengths of our study include the accuracy of the date of the parental death and the prospectively recorded variables derived from registers, providing large data covering the entire Swedish population from ages 12–24 years during 2001–14.

In this study of adolescents and young adults, the risk of substance use disorder and suicide-related behaviour, mostly driven by non-fatal events, increased around the date of parental death and its first anniversary in both male and female participants. Whereas male participants did not show an increased risk after the first anniversary, female participants had an increased risk of substance use disorder around all four anniversaries examined, consistently during the month before the anniversary, and less often during the anniversary month itself or the subsequent month. Furthermore, in female participants, we observed an increased risk of suicide-related behaviour during the month of the first and second anniversary. Although the number of individuals who had the outcomes was small, these findings suggest that bereaved individuals, especially women and girls, could benefit from preventive measures to reduce distress related to anniversaries of the death of a parent.

References
1 Hjern A, Berg L, Arat A, et al. Children as next of kin in Sweden. 2017. https://anhoriga.se/globalassets/media/dokument/publicerat/publikationer-barn-som-anhoriga/rapporter/children_as_next_of_kin.pdf (accessed July 1, 2022).

2 Stripe N. How many children experience the death of their mother? UK Office for National Statistics. Feb 22, 2019. https://blog.ons.gov.uk/2019/02/22/how-many-children-experience-the-death-of-their-mother/ (accessed June 9, 2022).

3 Schonfeld DJ, Demaria T. Committee on Psychosocial Aspects of Child and Family Health, Disaster Preparedness Advisory Council. Supporting the grieving child and family. *Pediatrics* 2016; **138:** e20162147.

4 Cerel J, Fristad MA, Verducci J, Weller RA, Weller EB. Childhood bereavement: psychopathology in the 2 years postparental death. *J Am Acad Child Adolesc Psychiatry* 2006; **45:** 681–90.

5 Kaplow JB, Saunders J, Angold A, Costello EJ. Psychiatric symptoms in bereaved versus nonbereaved youth and young adults: a longitudinal epidemiological study. *J Am Acad Child Adolesc Psychiatry* 2010; **49:** 1145–54.

6 Brent D, Melhem N, Donohoe MB, Walker M. The incidence and course of depression in bereaved youth 21 months after the loss of a parent to suicide, accident, or sudden natural death. *Am J Psychiatry* 2009; **166:** 786–94.

7 Pham S, Porta G, Biernesser C, et al. The burden of bereavement: early-onset depression and impairment in youths bereaved by sudden parental death in a 7-year prospective study. *Am J Psychiatry* 2018; **175:** 887–96.

8 Wilcox HC, Kuramoto SJ, Lichtenstein P, Långström N, Brent DA, Runeson B. Psychiatric morbidity, violent crime, and suicide among children and adolescents exposed to parental death. *J Am Acad Child Adolesc Psychiatry* 2010; **49:** 514–23.

9 Guldin MB, Li J, Pedersen HS, et al. Incidence of suicide among persons who had a parent who died during their childhood: a population-based cohort study. *JAMA Psychiatry* 2015; **72:** 1227–34.

10 Syer S, Clarke M, Healy C, et al. The association between familial death in childhood or adolescence and subsequent substance use disorder: a systematic review and meta-analysis. *Addict Behav* 2021; **120:** 106936.

11 Hua P, Bugeja L, Maple M. A systematic review on the relationship between childhood exposure to external cause parental death, including suicide, on subsequent suicidal behaviour. *J Affect Disord* 2019; **257:** 723–34.

12 Guzzo MF, Gobbi G. Parental death during adolescence: a review of the literature. *Omega (Westport)* 2021; published online July 29. https://doi.org/10.1177/00302228211033661.

13 Calderaro M, Baethge C, Bermpohl F, Gutwinski S, Schouler-Ocak M, Henssler J. Offspring's risk for suicidal behaviour in relation to parental death by suicide: systematic review and meta-analysis and a model for familial transmission of suicide. *Br J Psychiatry* 2022; **220:** 121–29.

14 Dawes MA, Mathias CW, Richard DM, Hill-Kapturczak N, Dougherty DM. Adolescent suicidal behavior and substance use: developmental mechanisms. *Subst Abuse* 2008; **2:** 13–28.

15 Bonanno GA, Wortman CB, Lehman DR, et al. Resilience to loss and chronic grief: a prospective study from preloss to 18-months postloss. *J Pers Soc Psychol* 2002; **83:** 1150–64.

16 Sweeting HN, Gilhooly ML. Anticipatory grief: a review. *Soc Sci Med* 1990; **30:** 1073–80.

17 Alvis L, Zhang N, Sandler IN, Kaplow JB. Developmental manifestations of grief in children and adolescents: caregivers as key grief facilitators. *J Child Adolesc Trauma* 2022; published online Jan 28. https://doi.org/10.1007/s40653-021-00435-0.

18 Andriessen K, Krysinska K, Rickwood D, Pirkis J. "It changes your orbit": the impact of suicide and traumatic death on adolescents as experienced by adolescents and parents. *Int J Environ Res Public Health* 2020; **17:** 17.

19 Renvoize EB, Jain J. Anniversary reactions. *Br J Psychiatry* 1986; **148:** 322–24.

20 Gabriel MA. Anniversary reactions—trauma revisited. *Clin Soc Work J* 1992; **20:** 179–92.

21 Rostila M, Saarela J, Kawachi I, Hjern A. Testing the anniversary reaction: causal effects of bereavement in a nationwide follow-up study from Sweden. *Eur J Epidemiol* 2015; **30:** 239–47.

22 Chow AYM. Anticipatory anniversary effects and bereavement: development of an integrated explanatory model. *J Loss Trauma* 2010; **15:** 54–68.

23 Turnbull E, Dorahy M, Britt E, Hanna D. Exploring an anniversary effect three years after the February 2011 Christchurch earthquake. *Australas J Disaster Trauma Stud* 2020; **24:** 117–23.

24 Hayslip B Jr, Pruett JH, Caballero DM. The "how" and "when" of parental loss in adulthood: effects on grief and adjustment. *Omega (Westport)* 2015; **71:** 3–18.

25 Schilling EA, Aseltine RH Jr, Gore S. Adverse childhood experiences and mental health in young adults: a longitudinal survey. *BMC Public Health* 2007; **7:** 30.

26 Herzog JI, Schmahl C. Adverse childhood experiences and the consequences on neurobiological, psychosocial, and somatic conditions across the lifespan. *Front Psychiatry* 2018; **9:** 420.

27 Rose D, Harrison E. The European socio-economic classification: a new social class schema for comparative European research. *Eur Soc* 2007; **9:** 459–90.

28 Althouse AD. Basic principles of survival analysis with composite endpoints: why you must use the "first" event, not the "worst" event. *Int J Cardiol* 2015; **201:** 319–20.

29 Giordano GN, Ohlsson H, Kendler KS, Sundquist K, Sundquist J. Unexpected adverse childhood experiences and subsequent drug use disorder: a Swedish population study (1995–2011). *Addiction* 2014; **109:** 1119–27.

30 Rostila M, Saarela J, Kawachi I. Suicide following the death of a sibling: a nationwide follow-up study from Sweden. *BMJ Open* 2013; **3:** 3.

31 Leifman H. Drug-related deaths in Sweden: estimations of trends, effects of changes in recording practices and studies of drug patterns. June 1, 2017. https://www.emcdda.europa.eu/document-library/drug-related-deaths-sweden-%E2%80%93-estimations-trends-effects-changes-recording-practices-and-studies-drug-patterns_en (accessed June 20, 2022).

32 Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. *Am J Epidemiol* 1997; **145:** 72–80.

33 Fang F, Fall K, Mittleman MA, et al. Suicide and cardiovascular death after a cancer diagnosis. *N Engl J Med* 2012; **366:** 1310–18.

34 Mostofsky E, Coull BA, Mittleman MA. Analysis of observational self-matched data to examine acute triggers of outcome events with abrupt onset. *Epidemiology* 2018; **29:** 804–16.

35 Fox SS. Children's anniversary reactions to the death of a family member. *Omega (Westport)* 1984; **15:** 291–305.

36 Bunch J, Barraclough B. The influence of parental death anniversaires upon suicide dates. *Br J Psychiatry* 1971; **118:** 621–26.

37 Van Boven L, Ashworth L. Looking forward, looking back: anticipation is more evocative than retrospection. *J Exp Psychol Gen* 2007; **136:** 289–300.

38 Otowa T, York TP, Gardner CO, Kendler KS, Hettema JM. The impact of childhood parental loss on risk for mood, anxiety and substance use disorders in a population-based sample of male twins. *Psychiatry Res* 2014; **220:** 404–09.

39 Usunier JC, Valette-Florence P. The time styles scale—a review of developments and replications over 15 years. *Time Soc* 2007; **16:** 333–66.

40 Ely R, Mercurio A. Time perspective and autobiographical memory: individual and gender differences in experiencing time and remembering the past. *Time Soc* 2011; **20:** 375–400.

41 Noordzij M, van Diepen M, Caskey FC, Jager KJ. Relative risk versus absolute risk: one cannot be interpreted without the other. *Nephrol Dial Transplant* 2017; **32** (suppl 2): 13–18.

42 Schulte MT, Hser YI. Substance use and associated health conditions throughout the lifespan. *Public Health Rev* 2014; **35:** 35.

43 Reinherz HZ, Tanner JL, Berger SR, Beardslee WR, Fitzmaurice GM. Adolescent suicidal ideation as predictive of psychopathology, suicidal behavior, and compromised functioning at age 30. *Am J Psychiatry* 2006; **163:** 1226–32.

44 Bergman AS, Axberg U, Hanson E. When a parent dies—a systematic review of the effects of support programs for parentally bereaved children and their caregivers. *BMC Palliat Care* 2017; **16:** 39.

45 Brooke HL, Talbäck M, Hörnblad J, et al. The Swedish cause of death register. *Eur J Epidemiol* 2017; **32:** 765–73.

46 Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011; **11:** 450.

47 Tøllefsen IM, Helweg-Larsen K, Thiblin I, et al. Are suicide deaths under-reported? Nationwide re-evaluations of 1800 deaths in Scandinavia. *BMJ Open* 2015; **5:** e009120.

48 Fazel S, Långström N, Hjern A, Grann M, Lichtenstein P. Schizophrenia, substance abuse, and violent crime. *JAMA* 2009; **301:** 2016–23.

49 Swain RS, Taylor LG, Braver ER, Liu W, Pinheiro SP, Mosholder AD. A systematic review of validated suicide outcome classification in observational studies. *Int J Epidemiol* 2019; **48:** 1636–49.

50 Björkenstam C, Johansson LA, Nordström P, et al. Suicide or undetermined intent? A register-based study of signs of misclassification. *Popul Health Metr* 2014; **12:** 11.

51 Kapusta ND, Tran US, Rockett IR, et al. Declining autopsy rates and suicide misclassification: a cross-national analysis of 35 countries. *Arch Gen Psychiatry* 2011; **68:** 1050–57.

52 Rosendahl A, Mjörnheim B, Eriksson LC. Autopsies and quality of cause of death diagnoses. *SAGE Open Med* 2021; **9:** 20503121211037169.

53 Perneger TV. What's wrong with Bonferroni adjustments. *BMJ* 1998; **316:** 1236–38.

54 Hill TD, Davis AP, Roos JM, French MT. Limitations of fixed-effects models for panel data. *Sociol Perspect* 2020; **63:** 357–69.