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Alcohol-related mortality following the loss of a child: a register based follow-up study from Norway

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Alcohol-related mortality following the loss of a child: a register based follow-up study from Norway

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Abstract

Objectives The death of one’s child is one of the most stressful events a person can experience. Research has shown that bereaved parents have a higher mortality than non-bereaved parents. This increased mortality might partly be caused directly by long-term stress. However, changes in health behaviour such as an increase in alcohol consumption might also play a role. This study examines the association between losing a child and alcohol-related mortality. In addition to Cox regression models using data covering the entire Norwegian adult population, we employ sibling fixed-effect models in order to partly control for genes and childhood experiences that might be associated with both losing a child and alcohol-related mortality.

Design A follow-up study between 1986 and 2015 based on Norwegian register data.

Setting Norway

Participants The entire Norwegian adult population.

Primary outcome measure Alcohol-related mortality.

Results An increased alcohol-related mortality rate was found among parents who had experienced the death of a child. The hazard ratio of alcohol-related mortality among those bereaved of a child was 1.59 (95% confidence interval (CI) 1.48-1.71), for women 2.04 (95% CI: 1.78-2.32) and for men 1.46 (95% CI 1.34-1.60). After including sibling-fixed effects, the hazard ratio of alcohol-related mortality among parents who had lost a child was 1.31 (95% CI 1.04-1.65).

Conclusions This study provides evidence that parents who have lost a child have a higher alcohol-related mortality than the general adult population. This result holds when adjusting for genetic predisposition for alcohol problems as well as childhood environment using sibling fixed-effect models.

Keywords: Epidemiology; Substance misuse; Public health
ARTICLE SUMMARY

Strengths and limitations of this study

- This study is based on high quality register data covering the entire Norwegian adult population
- This study employs sibling fixed-effects to partly control for genes and childhood characteristics
- There might still be residual confounding from genes and event not shared by siblings
INTRODUCTION

A number of studies have found an elevated parental mortality subsequent to the death of an underage or adult offspring \(^1-^4\). These studies argue that there might be a number of pathways from bereavement to mortality. Depression and grief may lead to suicides and possibly accidents. Stress might adversely affect health directly. Furthermore, bereavement might lead to changes in health behaviour, such as poorer diet, less exercise and an increase in smoking and alcohol consumption.\(^1^2\)

Alcohol can be used in an attempt to alleviate stress, reduce tension and cope with the mental distress following negative life events \(^5^6\).

So far, there has also been limited research into the link between bereavement and problematic alcohol consumption. Pilling and colleagues\(^7\) found that bereaved men displayed more problematic patterns of drinking behaviours two years post bereavement. They found no significant difference between non-bereaved men and men bereaved for less than two years or more than three years, nor between bereaved and non-bereaved women. This study did, however, only include participant who had lost a parent or a partner, and the vast majority (86 percent) had lost a parent. Although sad and stressful, this form of bereavement is more expected and part of the natural life cycle than losing a child.

A few studies have considered the relationship between widowhood and alcohol consumption. These studies have generally found higher levels of problematic alcohol consumption and elevated levels of alcohol-related mortality among widows and widowers\(^8^9\). In one study, 30 % of widows reported drinking alcohol to deal with the grief\(^8\).

Only a small number of studies have considered alcohol consumption following the death of a child.

A study concentrating on stillbirths, neonatal deaths and sudden infant death syndrome found that mothers who had experienced a stillbirth or lost an infant had a higher frequency of heavy drinking than non-bereaved mothers two months following the loss\(^10\). Two Danish register-based studies
using inpatient or outpatient treatment for a substance abuse disorder as the outcome, found that
bereaved parents had a higher risk of being admitted to treatment for substance abuse problems,
especially shortly after the loss of an underage child\textsuperscript{11,12}. These studies did, however, not distinguish
between treatment for alcohol problems and drug abuse.

This study fills a gap in the literature by focusing on alcohol-attributable deaths. It is of interest in and
by itself to know whether there is an excess alcohol-related mortality subsequent to the loss of a
child. Furthermore, the number of alcohol related deaths can be perceived is one indicator of
alcohol problems in general among the bereaved and therefore useful in a wider context. For the
purpose of studying also non-lethal alcohol related problems an alternative is surveys with questions
regarding alcohol use. However, getting a sufficient number of parents who have lost a child to
participate might be difficult. In addition, there might be underreporting of current drinking, and
reporting on alcohol use prior to the loss might be at risk of recall bias. Focusing instead on
treatment for alcohol use disorder also has its drawbacks. Only a minority of those with alcohol use
disorder are likely to seek treatment\textsuperscript{13,14,15}. There might also be a selection in who seeks help. For
example, earlier research has found that among those with an alcohol use disorder women are less
likely than men to seek treatment\textsuperscript{16}. Stigma is one of the most common reasons cited for not seeking
treatment for alcohol use disorder\textsuperscript{17} and a study found that married parents reported the highest
level of stigma attached to seeking substance abuse treatment\textsuperscript{18}. Alcohol-related mortality might be
less affected by selection than treatment for alcohol problems.

In this study, we consider the loss of not only underage children, but all offspring regardless of age.
Although the impact on the parent of losing a child might be smaller when the child is no longer co-
residing with the parent, earlier research has nonetheless found long-term associations between
losing a middle-aged child and parental mortality that were in line with or even higher that the
estimated effects of losing a teenager\textsuperscript{2}. 
In order to come closer to causality, we exploit the fact that using Norwegian register data we are able to link different generations, and thereby identifying siblings, which enables us to employ a within-family design. Models including sibling-fixed-effects take into account part of the genetic predisposition for alcohol abuse as well as factors in the childhood home that are shared by siblings and which might influence alcohol use later in life, such as parental drinking patterns, religiousness and parenting style. This type of design can mitigate problems caused by omitted variables concerning parental characteristics and early-life environment.

This study aims to add to the existing literature by analysing the link between parental bereavement and alcohol-related mortality using (1) Cox regression and controlling for adult socio-demographic characteristics such as education, marital status and number of children, (2) sibling fixed-effect models that control not only for observed characteristics but also unobserved childhood characteristics and part of the genetic makeup.

METHODS

Data

The study is based on data from a number of Norwegian administrative registers. We include all persons living in Norway on 1st January 1986 or later. The study population was then followed until time of death, emigration, or until December 31, 2015, whichever came first.

In the Norwegian Central Population Register, which includes every person resident in Norway for some time after 1960, each person is given a unique person identification number. This number enables individual record linkages between the different registers, as well as linking parents to their children. Through connecting parents and offspring, we are also able to link siblings. In our sibling sample we include only full biological siblings. However, we are only able to link those born after 1964 or living in the parental home in 1970 to their parents and therefore siblings.
Years of birth and dates of emigration were included from the Central Population Register along with information about marital status at the beginning of each year and number of children. Highest level of education was added from the National Education Database. The Cause of Death Register provided information about the date and the cause of death in accordance with the International Classification of Diseases (ICD), using the 9th revision from 1986-1995 and the 10th revision from 1996 to 2015.

Alcohol-related deaths were defined as ICD 9: 255.0, 265.2, 291, 292.2, 303, 3050, 357.5, 359.4, 425.5, 535.3, 571.0-571.3, 790.3, 980.0, 980.1, 980.9 and E860. ICD 10: F10, E24.4, E52, G31.2, G62.1, G72.1, I42.6, K29.2, R78.0, K70, K86.0, T51.1, T51.9, X45, X65 and Y15. We also include deaths where alcohol was a contributing cause of death, either alcohol-related disorders (F10), alcohol intoxication (T51, Y91) or alcohol in the blood (R78.0, Y90).

Model

Cox proportional hazard regression models were used to analyse whether losing a child is associated with alcohol-related mortality. The death of a child is a time-varying feature, which means that when a child dies, the parent changes status from non-bereaved to bereaved.

Given their importance as predictors of mortality, the following background variables are included in the analysis: Age, sex, education, marital status and number of children. Marital status is included as a time varying variable consisting of the categories never married, married, divorced and widowed. Education is included as a time varying variable and distinguishes those with missing information about the level of education, those with less than completed high school, high school, and a university degree. Calendar year and age are included as time-varying control variables in all models.

In the first model, we compare the alcohol-related mortality of those who have lost a child to the rest of the adult population. We show results for the both sexes combined, as well as for mothers and fathers separately, since earlier research has found that losing a child affects mothers and fathers differently. In the second model, we compare groups of siblings where at least one sibling has
lost a child. In these models each childhood family is allowed to have a different baseline hazard
function. In this analysis singletons, those who only have half-siblings and those whose mother or
father are not registered are dropped from the sample. Only siblings who are discordant for both
losing a child and alcohol-related death contribute to the estimates. Unfortunately, due to lack of
statistical power we were not able to do these analyses separately for mothers and fathers.

**Participant and public involvement**

The public or interest groups were not involved in the design and nor the choice of outcome measure
in this study. There are no plans to involve the public or interest groups in choosing a dissemination
strategy.

**RESULTS**

The exposure time and number of deaths by sex, bereavement status, education and marital status,
in the population, as well as in the sibling sample are shown in Table 1. Among the bereaved there
were 816 alcohol-related deaths during 2,063,214 years of follow-up, while there were 15,564
alcohol related deaths during 101,097,486 years of follow-up among the non-bereaved (Table 1). In
the sibling sample there were 203 alcohol-related deaths during 550,083 years of follow-up, while
there were 5,128 alcohol related deaths during 54,458,208 years of follow-up among the non-
bereaved.

In the general population, there were more than three times as many alcohol-attributable deaths
among men (12,852) than among women (3,537). However, the sex difference was much smaller
among those who had lost a child, where only about twice the number of men (560) compared to
women (256) died of alcohol-related causes.

Table 2 shows results from analyses examining the association between having lost a child and
alcohol-related mortality. When analysing men and women together, the hazard ratio for alcohol-
related mortality for bereaved versus non-bereaved individual was 1.59 (95% CI: 1.48-1.71) after
adjusting for sex, year, age, education, marital status and number of children. When running the analyses stratified by sex, the hazard ratio for bereaved mothers was 2.04 (95% CI: 1.78-2.32) and for bereaved fathers 1.46 (95% CI: 1.34-1.60).

In the final analysis, presented in Table 3, we include sibling-fixed effect in the model presented in Table 1, with men and women analysed together. Controlling for childhood characteristics that are shared by siblings and part of the genetic makeup, the hazard ratio was 1.31 (95% CI: 1.04-1.65).

**DISCUSSION**

This follow-up study using high quality register data covering the entire Norwegian population and spanning nearly 30 years, shows that losing a child is associated with a substantially higher alcohol-related mortality for both men and women. The link is particularly strong among women, where bereaved mothers had a hazard of alcohol-related mortality twice that of non-bereaved women.

Results from models including sibling fixed-effects confirm the results from the standard Cox model, that bereaved parents have a higher alcohol-related mortality than their non-bereaved siblings, suggesting a causal relationship.

Our results correspond with findings from previous research that show that parents who have lost a child have higher levels of entry into substance abuse treatment than their non-bereaved counterparts\(^{11,12}\).

We focus on causes of death that are directly attributable to alcohol consumption such as accidents that took place while under the influence of alcohol and long term consequences of heavy alcohol consumption such as liver cirrhosis. However, a number of other diseases are partly attributable to alcohol consumption, such as many forms of cancer and heart disease. This means that the true number deaths caused by alcohol is likely to be higher.
Our results suggest that the excess mortality from alcohol-related causes following the death of a child is higher among mothers than among fathers. This is consistent with findings from earlier studies focusing on health outcomes such as psychotropic medicine use and all-cause mortality which have found more adverse outcome of losing a child for mothers than fathers. In line with our findings, Li et al. find that compared to their non-bereaved counterparts, bereaved mothers have higher levels of psychiatric hospitalization for substance abuse than bereaved fathers.

Strengths and limitations

The main strength of this study is that it is based on high quality register data which means that there is little loss to follow-up and there are no problems caused by recall bias or non-response. Furthermore, having data covering the whole Norwegian population for multiple generations means that we can link siblings and apply a within-family design. Certain genetic predispositions and early-life characteristics might be associated with both losing a child and alcohol-related mortality. For example, the heritability of alcohol use disorder has been estimated to be between 50 and 70%. This study shows that even when taking childhood characteristics and the genetic heritage shared by siblings into account, bereaved parents have a heightened alcohol-related mortality.

However, despite the obvious strengths of the sibling fixed-effects design, the results from these models might still be confounded by childhood experiences that the siblings did not share or where the age at the time of the event matters. Furthermore, except for monozygotic twins, siblings only share parts of their DNA – 50 percent on average – which means that genetic predispositions for alcohol abuse could not be fully accounted for in the model. Finally, those who do not have full siblings are dropped from the analysis.

The findings from this study provide evidence that the heightened mortality among parents who have lost a child is at least partly caused by changes in health behaviour. This underpins the need for health and support services to monitor the alcohol use and other health behaviour among bereaved...
parents. In addition, early and customized help for bereaved parents might help prevent long-term changes in health behaviour. Earlier research has indicated that mothers may be particularly affected by the loss. For example they have a higher excess mortality\textsuperscript{1,2} and a higher use of psychotropic medication\textsuperscript{19} following the death of a child. They may therefore need extra support from health and bereavement services. As it contradicts usual gender norms, support services should be especially aware that women might use alcohol as a coping mechanism following the loss of a child.

Unfortunately, due to lack of statistical power we were not able to include sibling-fixed effect in the models stratified by the sex of the parent. This would be an interesting line of inquiry for future research. Another logical next step would be to quantify to what extent the heightened parental mortality following the loss of a child is caused by changes in health behaviour and to what extent it is directly attributable to the effects of stress on bodily functioning. Norway has strict alcohol policy with high taxes, a state monopoly on the sale of wine and spirits, as well as other measures to restrict alcohol consumption. The results from this study might not be directly transferable to settings with a different alcohol policy. Studies from countries with less strict alcohol policies would therefore be of interest.

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**Competing interest:** The authors have no competing interests to declare.

**Data sharing:** The data used in this study are available from Statistics Norway and the Norwegian Institute of Public Health. In order to obtain and link the data ethical approval is needed. Transfer of these data outside Norway’s borders is not allowed.

**Author Contribution:** SC formulated the study design, carried out the data analyses and drafted the paper. AR, KS-L and LJH participated in the interpretation and discussion of the findings and critically revised the paper.
**Ethical approval:** The Regional Committee for Medical and Health Research Ethics granted approval for the research project (REK 2014/1970). As the study utilised existing registry data, no written or verbal consent to participate was required.
Table 1 Descriptive statistics

|                                      | The whole population (N=5,633,387) | The sibling sample (N=2,598,002) |
|--------------------------------------|-----------------------------------|----------------------------------|
|                                      | Prevalence | Exposure time | Number of deaths | Prevalence | Exposure time | Number of deaths |
| Total exposure time                  |            | 103,160,700   | 16,380            |            | 55,008,291    | 5,331            |
| Not bereaved                         | 98%        | 101,097,486   | 15,564            | 99%        | 54,458,208    | 5,128            |
| Bereaved                             | 2%         | 2,063,214     | 816               | 1%         | 550,083       | 203              |

**Education**

|                                      | Less than high school |         | High school |         | University degree |         | Missing |         |
|--------------------------------------|-----------------------|----------------|-------------|-----------------|-----------------|----------------|----------------|
|                                      | 51%                   | 52,606,639 | 11,912      | 41%            | 22,553,399 | 3,798         |
|                                      | 24%                   | 24,307,663 | 2,575       | 31%            | 17,052,570 | 960           |
|                                      | 22%                   | 23,189,978 | 1,439       | 27%            | 14,852,239 | 494           |
|                                      | 3%                    | 3,056,420  | 454         | 1%             | 550,083    | 79            |

**Marital status**

|                                      | Married | Never married | Divorced | Widowed | Sex |
|--------------------------------------|---------|---------------|----------|---------|-----|
|                                      | 41%     | 45%           | 8%       | 6%      | Men | 49% | 51% |
|                                      | 52%     | 39%           | 8%       | 1%      |     | 52% | 48% |
|                                      | 28,604,311 | 21,453,233 | 4,400,663 | 550,083 |     | 28,604,311 | 26,403,980 |
Table 2 Hazard Ratios (and 95% confidence intervals) for the association between bereavement and alcohol-related mortality, parents who have lost a child compared to adults who have not lost a child, Norway, 1986-2015.

|                     | All    |          | Men    |          | Women  |          |
|---------------------|--------|----------|--------|----------|--------|----------|
|                     | Unadjusted | Adjusted | Unadjusted | Adjusted | Unadjusted | Adjusted |
| Having lost a child | 1.82 (1.69-1.95) | 1.59 (1.48-1.71) | 1.87 (1.72-2.04) | 1.46 (1.34-1.60) | 2.30 (2.02-2.61) | 2.04 (1.78-2.32) |

**Education**

|                     |        |        |        |        |
|---------------------|--------|--------|--------|--------|
| Less than high school | 1.76 (1.68-1.84) | 1.74 (1.66-1.83) | 1.71 (1.53-1.91) |
| High school         | 1      | 1      | 1      |
| University degree   | 0.63 (0.59-0.68) | 0.63 (0.59-0.68) | 0.60 (0.52-0.70) |
| Missing             | 1.59 (1.44-1.76) | 1.53 (1.37-1.71) | 1.75 (1.37-2.23) |

**Marital status**

|                     |        |        |        |        |
|---------------------|--------|--------|--------|--------|
| Married             | 1      | 1      | 1      |
| Never married       | 3.58 (3.39-3.79) | 4.62 (4.33-4.93) | 1.71 (1.53-1.92) |
| Divorced            | 10.00 (9.55-10.46) | 12.46 (11.82-13.13) | 4.95 (4.52-5.42) |
| Widowed             | 2.60 (2.44-2.78) | 3.22 (3.97-3.49) | 1.82 (1.63-2.04) |

|                     |        |        |        |        |
|---------------------|--------|--------|--------|--------|
| Number of children  | 0.90 (0.88-0.91) | 0.91 (0.90-0.93) | 0.80 (0.78-0.83) |
| Age                 | 1.03 (1.03-1.03) | 1.04 (1.04-1.04) | 1.01 (1.01-1.01) |
| Year                | 0.90 (0.89-0.90) | 0.91 (0.90-0.91) | 0.87 (0.85-0.88) |

**Sex**

|         |        |        |
|---------|--------|--------|
| Men     | 1      | -      |
| Women   | 0.21 (0.20-0.22) | - |
Table 3 Hazard Ratios (and 95% confidence intervals) for the association between bereavement and alcohol-related mortality, parents who have lost a child compared to their non-bereaved siblings, Norway, 1986-2015.

|                          | All          |
|--------------------------|--------------|
| Having lost a child      | 1.31 (1.04-1.65) |
| **Education**            |              |
| Less than high school    | 1.84 (1.64-2.08) |
| High school              | 1            |
| University degree        | 0.60 (0.50-0.71) |
| Missing                  | 2.05 (1.40-2.99) |
| **Marital status**       |              |
| Married                  | 1            |
| Never married            | 5.77 (4.92-6.76) |
| Divorced                 | 8.17 (7.13-9.36) |
| Widowed                  | 5.57 (4.24-7.33) |
| **Number of children**   | 0.83 (0.79-0.87) |
| **Age**                  | 1.08 (1.07-1.09) |
| **Year**                 | 1.01 (0.97-1.06) |
| **Sex**                  |              |
| Men                      | 1            |
| Women                    | 0.29 (0.26-0.32) |
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| Section/Topic             | Item # | Recommendation                                                                 | Reported on page # |
|--------------------------|--------|-------------------------------------------------------------------------------|------------------|
| Title and abstract       | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1                |
|                          |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 2                |
| Introduction             |        |                                                                                |                  |
| Background/rationale     | 2      | Explain the scientific background and rationale for the investigation being reported | 5                |
| Objectives               | 3      | State specific objectives, including any prespecified hypotheses                | 6                |
| Methods                  |        |                                                                                |                  |
| Study design             | 4      | Present key elements of study design early in the paper                         | 5-6              |
| Setting                  | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6                |
| Participants             | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | N/A              |
|                          |        | (b) For matched studies, give matching criteria and number of exposed and unexposed | N/A              |
| Variables                | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-7              |
| Data sources/measurement | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 6-7              |
| Bias                     | 9      | Describe any efforts to address potential sources of bias                         | 5-6              |
| Study size               | 10     | Explain how the study size was arrived at                                         | N/A              |
| Quantitative variables   | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 11               |
| Statistical methods      | 12     | (a) Describe all statistical methods, including those used to control for confounding | 7-8              |
|                          |        | (b) Describe any methods used to examine subgroups and interactions              | N/A              |
|                          |        | (c) Explain how missing data were addressed                                       | 7                |
|                          |        | (d) If applicable, explain how loss to follow-up was addressed                    | 6                |
|                          |        | (e) Describe any sensitivity analyses                                            | N/A              |
| Results | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | N/A |
|---------|-----|---------------------------------------------------------------------------------|------|
|         |     | (b) Give reasons for non-participation at each stage                              | N/A |
|         |     | (c) Consider use of a flow diagram                                               | N/A |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 12  |
|         |     | (b) Indicate number of participants with missing data for each variable of interest | 12  |
|         |     | (c) Summarise follow-up time (eg, average and total amount)                      | 12  |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time                   | 12  |
| Main results | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 13  |
|         |     | (b) Report category boundaries when continuous variables were categorized        | N/A |
|         |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | N/A |
| Discussion |      |                                                                                  |      |
| Key results | 18  | Summarise key results with reference to study objectives                         | 9   |
| Limitations |      |                                                                                  |      |
| Interpretation | 20  | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 9-11|
| Generalisability | 21  | Discuss the generalisability (external validity) of the study results            | 11  |
| Other information |      |                                                                                  |      |
| Funding | 22  | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 11  |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Alcohol-related mortality following the loss of a child: a register based follow-up study from Norway

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Alcohol-related mortality following the loss of a child: a register based follow-up study from Norway

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Abstract

Objectives The death of one’s child is one of the most stressful events a person can experience. Research has shown that bereaved parents have a higher mortality than non-bereaved parents. This increased mortality might partly be caused directly by long-term stress. However, changes in health behaviour such as an increase in alcohol consumption might also play a role. This study examines the association between losing a child and alcohol-related mortality. In addition to Cox regression models using data covering the entire Norwegian adult population, we employ sibling fixed-effect models in order to partly control for genes and childhood experiences that might be associated with both losing a child and alcohol-related mortality.

Design A follow-up study between 1986 and 2014 based on Norwegian register data.

Setting Norway

Participants The entire Norwegian adult population.

Primary outcome measure Alcohol-related mortality.

Results An increased alcohol-related mortality was found among parents who had experienced the death of a child. The hazard ratio of alcohol-related mortality among those bereaved of a child was 1.59 (95% confidence interval (CI) 1.48-1.71) compared to non-bereaved parents, for women 2.03 (95% CI: 1.78-2.32) and for men 1.46 (95% CI 1.34-1.59). After including sibling-fixed effects, the hazard ratio of alcohol-related mortality among parents who had lost a child was 1.30 (95% CI 1.03-1.64).

Conclusions This study provides evidence of an elevated alcohol-related mortality among parents who have lost a child compared to non-bereaved parents. Although strongly attenuated, there is still an association when adjusting for genetic predisposition for alcohol problems as well as childhood environment using sibling fixed-effect models.

Keywords: Epidemiology; Substance misuse; Public health
ARTICLE SUMMARY

Strengths and limitations of this study

- This study is based on high quality register data covering the entire Norwegian adult population
- This study employs sibling fixed-effects to partly control for genes and childhood characteristics
- There might still be residual confounding from factors not shared by siblings
INTRODUCTION

The death of a child is a devastating event with implications for parents’ mental health, sickness-absence and labour market attachment. During the last decades there has been a growing body of evidence of an association between parental bereavement and mortality. This study fills a gap in the literature by focusing on alcohol-attributable mortality subsequent to the loss of a child.

So far, there has been limited research into the link between bereavement and problematic alcohol consumption. Pilling and colleagues found that bereaved men displayed more problematic patterns of drinking behaviour two years post bereavement. They found no significant difference between non-bereaved men and men bereaved for less than two years or more than three years, nor between bereaved and non-bereaved women. That study did, however, only include participants who had lost a parent or a partner, and the vast majority (86 percent) had lost a parent. Although sad and stressful, this form of bereavement is more expected and part of the natural life cycle than losing a child.

A few studies have considered the relationship between widowhood and alcohol consumption. These studies have generally found higher levels of problematic alcohol consumption and elevated levels of alcohol-related mortality among widows and widowers. In one study, 30% of widows reported drinking alcohol to deal with the grief.14 15

Only a small number of studies have considered alcohol consumption following the death of a child. A study concentrating on stillbirths, neonatal deaths and sudden infant death syndrome found that mothers who had experienced a stillbirth or lost an infant had a higher frequency of heavy drinking than non-bereaved mothers two months after the loss. Two Danish register-based studies using inpatient or outpatient treatment for a substance abuse disorder as the outcome, found that bereaved parents had a higher risk of being admitted to treatment for substance abuse problems, especially shortly after the loss of an underage child. These studies did, however, not distinguish between treatment for alcohol problems and drug abuse.
The number of alcohol-related deaths can be perceived as one indicator of alcohol problems in
general among the bereaved and therefore useful in a wider context. For the purpose of studying
also non-lethal alcohol-related problems an alternative is surveys with questions regarding alcohol
use. However, it might be difficult to get a sufficient number of parents who have lost a child to
participate. In addition, there might be underreporting of current drinking, and reporting on alcohol
use prior to the loss might be at risk of recall bias. Focusing instead on treatment for alcohol use
disorder also has its drawbacks. Only a minority of those with alcohol use disorder are likely to seek
treatment. There might also be a selection in who seeks help. For example, earlier research has
found that among those with an alcohol use disorder women are less likely than men to seek
treatment. Stigma is one of the most common reasons cited for not seeking treatment for alcohol
use disorder and a study found that married parents reported the highest level of stigma attached
to seeking substance abuse treatment. Alcohol-related mortality might be less affected by
selection than treatment for alcohol problems.

Since the early paper by Li, et al. there has been growing evidence of an elevated mortality among
bereaved parents compared to non-bereaved parents. In these studies, mainly from the Nordic
countries, Israel and the US, the most consistent finding is a heightened mortality among mothers subsequent to the loss of a child. Valdimarsdóttir, et al. compared Icelandic cohorts born from 1800 to 1880 where 61.1% of parents lost at least one child, to cohorts born from 1931 to 1996 where 5.2% lost a child, found elevated mortality among bereaved mothers across most cohorts. Among fathers, there was only an elevated mortality post bereavement in the youngest cohorts. Most other studies examining fathers separately have found no or weak associations.

A heightened maternal mortality following the death of an infant has been found across studies. On the other hand, the evidence for an excess mortality following the death of a child between the ages of 1 and 18 is more mixed. Most studies have found a heightened mortality following
the death of an adult offspring. Rostila, et al. found a lowered mortality in the first three years subsequent to the death of an adult offspring, but a heightened mortality after eight years of follow-up. There is some evidence to suggest that mothers have a more elevated mortality following the death of an infant or very young child, whereas men’s mortality is more strongly associated with the death of an adult offspring.

Li, et al. found maternal mortality to be particularly high subsequent to the external cause death of a child, whereas parental mortality following the loss of a child due to a natural cause of death was elevated only in the long term.

The death of a child has been linked to parental suicide and external cause mortality in general. There is some evidence, albeit not unambiguous, that cancer incidence and cancer survival are associated with the loss of a child. An association with death from cardiovascular diseases are found in some but not all studies.

Earlier studies argue that there might be a number of pathways from bereavement to mortality. Depression and grief may lead to suicides and possibly accidents. Stress might adversely affect health directly. Furthermore, bereavement might induce changes in health behaviour, such as poorer diet, less exercise and an increase in smoking and alcohol consumption.

One problem facing research into the relationship between the loss of a child and parental mortality is that there is likely to be selection in who loses a child, which might confound the relationship between bereavement and mortality. It might be that those who lose a child have poorer health or more adverse health behaviours already prior to the loss.

Alcohol can be used in an attempt to alleviate stress, reduce tension and cope with mental distress following negative life events. However, parents who lose a child might have a higher level of alcohol consumption already prior to the loss. There are a number of reason why parents with a high alcohol consumption might be more at risk of losing a child. Both drinking during pregnancy and while having an infant is associated with increased risk of infant mortality.
during childhood is also associated with higher adult mortality in the offspring. The link between parental drinking and offspring’s alcohol-related mortality is particularly strong, probably stemming from transmission of alcohol problems, either through shared genes or environment. Children growing up in households with high alcohol consumption often also tend to be subject to other adverse experiences, which especially when taken together, predict premature mortality. Moreover, high levels of parental drinking during childhood are associated with a number of offspring health problems that are also linked to premature mortality, such as behaviour problems, attention deficit hyperactivity disorder, and mental illness. Finally, there might be clustering and intergenerational transmission of detrimental health behaviours that when combined are strong predictors of premature death.

One way to try to disentangle the effects of parental bereavement on alcohol use from alcohol consumption prior to the loss is to employ a sibling fixed-effect design. Siblings share, on average, 50% of their genetic material and such models will therefore partly control for the hereditability of alcohol use. Furthermore, these models control for shared early life family environment factors that might influence alcohol use later in life, such as parental drinking, low parental education, parental divorce and parental death. In order to come closer to causality, we therefore exploit the fact that using Norwegian register data we are able to link different generations, and thereby identify siblings, which enables us to employ a within-family design.

The elevated all-cause mortality among bereaved parents that have been found in population samples have recently been confirmed in studies employing a sibling comparison design as well as a twin study. This study aims to add to the existing literature by analysing the link between parental bereavement and alcohol-related mortality using (1) Cox regression and controlling for adult socio-demographic characteristics such as education, marital status and number of children, (2) models that take into account the age of the child at the time of death and the cause of death, (3) sibling fixed-effect
models that control not only for observed characteristics but also unobserved childhood
characteristics and part of the genetic makeup.

METHODS

Data

The study is based on data from a number of Norwegian administrative registers. We include all adults living in Norway on 1st January 1986 or later. The study population was then followed until time of death, emigration, or until 31st December, 2014, whichever came first.

In the Norwegian Central Population Register, which includes every person resident in Norway for some time after 1960, each person is given a unique person identification number. This number enables individual record linkages between the different registers, as well as linking parents to their children. Through connecting parents and offspring, we are also able to link siblings. In our sibling sample we include only full biological siblings. We are only able to link those born after 1964 or living in the parental home in 1970 to their parents and therefore siblings.

Years of birth and dates of emigration were included from the Central Population Register along with information about marital status at the beginning of each year and number of children. Highest level of education was added from the National Education Database. The Cause of Death Register provided information about the date and the cause of death in accordance with the International Classification of Diseases (ICD), using the 9th revision from 1986-1995 and the 10th revision from 1996 to 2014.

Alcohol-related deaths were defined as ICD 9: 255.0, 265.2, 291, 292.2, 303, 3050, 357.5, 359.4, 425.5, 535.3, 571.0-571.3, 790.3, 980.0, 980.1, 980.9 and E860. ICD 10: F10, E24.4, E52, G31.2, G62.1, G72.1, I42.6, K29.2, R78.0, K70, K86.0, T51.1, T51.9, X45, X65 and Y15. We also include deaths where alcohol was a contributing cause of death, either alcohol-related disorders (F10), alcohol
intoxication (T51, Y91) or alcohol in the blood (R78.0, Y90). These are deaths directly attributable to alcohol, either suicide and accidents that took place while under the influence of alcohol or long term consequences of harmful alcohol use. The Norwegian Cause of Death Register is generally regarded as having a high quality, with a coverage of 98% of deaths. However, there is likely to be underreporting of alcohol-related causes of death. Furthermore, coding changes might disrupt time trends in specific causes of death.

For deaths among offspring, we distinguish between deaths due to external causes of death – suicide, accidents and homicides (ICD9: E800 - E999 and ICD10: V01-Y89) and natural causes of death (all other codes). Norway has a low infant mortality rate and an average child mortality rate compared to other OECD countries.

Model

Cox proportional hazard regression models were used to analyse whether losing a child is associated with alcohol-related mortality. The death of a child is a time-varying feature, which means that when a child dies, the parent changes status from non-bereaved to bereaved.

We control for characteristics on which bereaved and non-bereaved parents have been shown to differ and that are also associated with alcohol-related mortality; marital status, education and number of children. Marital status is included as a time varying variable consisting of the categories never married, married, divorced and widowed. Education is included as a time varying variable and distinguishes those with compulsory education, high school, a university degree and missing education. Calendar year and age are included as time-varying control variables in all models.

In the first model, we compare the alcohol-related mortality of those who have lost a child to non-bereaved parents. We show results for both sexes combined, as well as for mothers and fathers separately, since earlier research has found that losing a child affects mothers and fathers differently.
the mode of death of the offspring – external causes of death and natural causes of death. Thirdly, we run models stratified by the age of the child at time of death. In the final model, we compare groups of siblings where at least one sibling has lost a child. In these models each childhood family is allowed to have a different baseline hazard function. In this analysis singletons, those who only have half-siblings and those whose mother or father are not registered are dropped from the sample. Only siblings who are discordant for both losing a child and alcohol-related death contribute to the estimates. Unfortunately, due to lack of statistical power we were not able to do this analysis separately for mothers and fathers.

**Participant and public involvement**

The public or interest groups were involved neither in the design nor in the choice of outcome measure in this study. There are no plans to involve the public or interest groups in choosing a dissemination strategy.

**RESULTS**

The exposure time and number of deaths by sex, bereavement status, education and marital status, in the population, as well as in the sibling sample are shown in Table 1. Among the bereaved there were 816 alcohol-related deaths during 2,063,214 years of follow-up, while there were 15,564 alcohol-related deaths during 101,097,486 years of follow-up among the non-bereaved (Table 1). In the sibling sample there were 203 alcohol-related deaths during 550,083 years of follow-up, while there were 5,128 alcohol-related deaths during 54,458,208 years of follow-up among the non-bereaved.

[TABLE 1 HERE]
In the general population, there were more than three times as many alcohol-attributable deaths among men (12,852) than among women (3,537). However, the sex difference was much smaller among those who had lost a child, where only about twice the number of men (560) compared to women (256) died of alcohol-related causes.

Table 2 shows results from analyses examining the association between having lost a child and alcohol-related mortality. When analysing men and women together, the hazard ratio for alcohol-related mortality for bereaved parents versus non-bereaved parents was 1.59 (95% CI: 1.48-1.71) after adjusting for sex, year, age, education, marital status and number of children. When running the analyses stratified by sex, the hazard ratio for bereaved mothers was 2.03 (95% CI: 1.78-2.32) and for bereaved fathers 1.46 (95% CI: 1.34-1.59).

(TABLE 2 HERE)

Table 3 shows results from analyses stratified by the cause of death of the child, as well as by the age of the child at the time of death. Alcohol-related mortality is higher among bereaved than non-bereaved parents regardless of whether the cause of death was external or natural. The alcohol-related mortality is, however, significantly higher following the death of a child due to external causes (HR 1.47 95% CI: 1.34-1.61) than following the loss of a child due to natural causes (HR 1.79 95% CI: 1.61-1.99). In the analyses stratified by gender, we find this difference between loss due to external and natural causes only among fathers. There is an elevated alcohol-related mortality subsequent to the loss of a child whether the child was an infant (HR 1.55 95% CI: 1.30-1.86), aged 1 to 18 (HR 1.54 95% CI: 1.32-1.80) or an adult offspring (HR 1.61 95% CI: 1.47-1.76). There is an elevated mortality among both fathers and mothers who have lost an offspring regardless of the age of the offspring. Mothers who have lost an infant (HR 2.52 95% CI: 1.86-3.43) have a higher alcohol-related mortality then fathers who have lost an infant (HR 1.27 95% CI: 1.01-1.59). Likewise, mothers
(HR 1.97 95% CI: 1.68-2.30) have a higher alcohol-related mortality than fathers (HR 1.52 95% CI: 1.36-1.69) subsequent to the loss of an adult offspring.

[ TABLE 3 HERE ]

In the final analysis, presented in Table 4, we include sibling-fixed effect in the model presented in Table 1, with men and women analysed together. Controlling for childhood characteristics that are shared by siblings and part of the genetic makeup, the hazard ratio was 1.30 (95% CI: 1.03-1.64).

[ TABLE 4 HERE ]

**DISCUSSION**

This follow-up study using high quality register data covering the entire Norwegian population and spanning nearly 30 years, shows that losing a child is associated with a substantially higher alcohol-related mortality for both men and women. The link is particularly strong for women, where bereaved mothers had a hazard of alcohol-related mortality twice that of non-bereaved mothers. There was an excess alcohol-related mortality among those who have lost a child regardless of whether the child was an infant, aged 1 to 18 or an adult offspring. The alcohol-related mortality was elevated among both parents who had lost a child due to external causes of death and to natural causes of death. Results from models including sibling fixed-effects confirm the results from the standard Cox model, that bereaved parents have a higher alcohol-related mortality than their non-bereaved siblings. The association between parental bereavement and alcohol-related mortality is, however, strongly attenuated by the inclusion of sibling fixed-effects in the model.
Our results correspond with findings from previous research that show that parents who have lost a child have higher levels of entry into substance abuse treatment than their non-bereaved counterparts. 2 3

We focus on causes of death that are directly attributable to alcohol consumption such as accidents that took place while under the influence of alcohol and long term consequences of heavy alcohol consumption such as liver cirrhosis. Alcohol plays a role in many accidental deaths, 77 suicides 78 and drug-related deaths 79 and is likely to be underreported as a contributing cause of death. 66

Furthermore, a number of diseases, such as many forms of cancer and heart disease, are partly attributable to alcohol consumption. 80 This means that the true number of deaths caused by alcohol is likely to be higher.

Our results suggest that the excess mortality from alcohol-related causes following the death of a child is higher among mothers than among fathers. This is consistent with findings from earlier studies focusing on health consequences such as psychotropic medicine use 81 and all-cause mortality 7 8, which have found more adverse outcomes of losing a child for mothers than for fathers. In line with our findings, Li et al. 2 find that compared to their non-bereaved counterparts, bereaved mothers have higher levels of psychiatric hospitalization for substance abuse than bereaved fathers.

Our findings show that among men, particularly those who have lost a child due to external causes of death have an elevated mortality from alcohol-related causes. Earlier research has found that parents who have been bereaved by violent causes of death have more adverse outcomes on measures such as being admitted to treatment for mental health problems, 3 sickness absence due to psychiatric problems 82 and higher levels of complicated grief. 83 As mental health problems and complicated grief 85 are linked to alcohol misuse, this might help explain the higher levels of alcohol-attributable deaths in this group.

Strengths and limitations
The main strength of this study is that it is based on high quality register data which means that there is little loss to follow-up and there are no problems caused by recall bias or non-response.

Furthermore, having data covering the entire Norwegian population for multiple generations means that we can link siblings and apply a within-family design. Certain genetic predispositions and early-life characteristics might be associated with both losing a child and alcohol-related mortality. For example, the heritability of alcohol use disorder has been estimated to be between 50 and 70\%.\(^{86}\)

This study shows that even when taking childhood characteristics and the genetic heritage shared by siblings into account, bereaved parents have a heightened alcohol-related mortality.

However, despite the obvious strengths of the sibling fixed-effects design, the results from these models might still be confounded by childhood experiences that the siblings did not share or where the age at the time of the event matters. There might also be other factors not shared by siblings that affect both alcohol use and the risk of losing a child. Furthermore, except for monozygotic twins, siblings only share parts of their DNA – 50 percent on average – which means that genetic predispositions for alcohol abuse could not be fully accounted for in the model. Finally, those who do not have full siblings are dropped from the analysis. Another limitation is that there might be underreporting of alcohol-related deaths\(^{66}\) and cultural differences in coding of alcohol-related deaths across countries\(^{87}\) might make comparisons difficult.

The findings from this study provide evidence that the heightened mortality among parents who have lost a child might be partly caused by changes in health behaviour. This underpins the need for health and support services to monitor the alcohol use and other health behaviour among bereaved parents. In addition, early and customized help for bereaved parents might help prevent long-term changes in health behaviour. Earlier research has indicated that mothers may be particularly affected by the loss. For example they have a higher excess mortality\(^{78}\) and a higher use of psychotropic medication\(^{481}\) following the death of a child. They may therefore need extra support from health
and bereavement services. As it contradicts usual gender norms, support services should be especially aware that women might use alcohol as a coping mechanism following the loss of a child.

Unfortunately, due to lack of statistical power we were not able to include sibling-fixed effect in the models stratified by the sex of the parent, the cause of death or the age of the child at the time of death. This would be an interesting line of inquiry for future research. Another logical next step would be to quantify to what extent the heightened parental mortality following the loss of a child is caused by changes in health behaviour and to what extent it is directly attributable to the effects of stress on bodily functioning. Norway has strict alcohol policy with high taxes, a state monopoly on the sale of wine and spirits, as well as other measures to restrict alcohol consumption. The results from this study might not be directly transferable to settings with a different alcohol policy. Studies from countries with less strict alcohol policies would therefore be of interest.

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**Competing interest:** The authors have no competing interests to declare.

**Data sharing:** The data used in this study are available from Statistics Norway and the Norwegian Institute of Public Health. In order to obtain and link the data ethical approval is needed. Transfer of these data outside Norway’s borders is not allowed.

**Author Contribution:** SC formulated the study design, carried out the data analyses and drafted the paper. AR, KS-L and LJH participated in the interpretation and discussion of the findings and critically revised the paper.

**Ethical approval:** The Regional Committee for Medical and Health Research Ethics granted approval for the research project (REK 2014/1970). As the study utilised existing registry data, no written or verbal consent to participate was required.
### Table 1 Descriptive statistics

|                          | The whole population (N=5,633,387) | The sibling sample (N=2,598,002) |
|--------------------------|-----------------------------------|----------------------------------|
|                          | Prevalence | Exposure time | Number of deaths | Prevalence | Exposure time | Number of deaths |
| **Total**                |            |              |                 |            |              |                 |
| Not bereaved             | 98%        | 103,160,700  | 16,380           | 99%        | 55,008,291    | 5,331            |
| Bereaved                 | 2%         | 52,606,639   | 5,331            | 2%         | 550,083       | 203              |
| **Education**            |            |              |                  |            |              |                  |
| Compulsory education     | 51%        | 51,097,486   | 15,564           | 99%        | 52,606,639    | 3,798            |
| High school              | 24%        | 24,307,663   | 816              | 1%         | 24,307,663    | 960              |
| University degree        | 22%        | 23,189,978   | 1,439            | 27%        | 23,189,978    | 494              |
| Missing                  | 3%         | 3,056,420    | 454              | 1%         | 3,056,420     | 79               |
| **Marital status**       |            |              |                  |            |              |                  |
| Married                  | 41%        | 42,295,887   | 11,912           | 41%        | 42,295,887    | 3,798            |
| Never married            | 45%        | 46,422,315   | 2,575            | 31%        | 46,422,315    | 960              |
| Divorced                 | 8%         | 9,284,463    | 5,441            | 8%         | 9,284,463     | 1,859            |
| Widowed                  | 6%         | 6,189,642    | 1,458            | 1%         | 6,189,642     | 160              |
| **Sex**                  |            |              |                  |            |              |                  |
| Men                      | 49%        | 50,548,743   | 12,844           | 52%        | 50,548,743    | 4,320            |
| Women                    | 51%        | 52,611,957   | 3,536            | 48%        | 52,611,957    | 1,011            |
Table 2 Hazard Ratios (and 95% confidence intervals) for the association between bereavement and alcohol-related mortality, parents who have lost a child compared to non-bereaved parents, Norway, 1986-2014.

|                          | All Unadjusted | All Adjusted | Men Unadjusted | Men Adjusted | Women Unadjusted | Women Adjusted |
|--------------------------|---------------|--------------|----------------|--------------|------------------|---------------|
| Bereaved parent          | 2.04 (1.89-2.19) | 1.59 (1.48-1.71) | 2.08 (1.91-2.27) | 1.46 (1.34-1.59) | 2.39 (2.10-2.72) | 2.03 (1.78-2.32) |
| Non-bereaved parent      | 1             | 1            | 1              | 1            | 1                | 1             |
| Childless                | 1.60 (1.54-1.65) | 1.11 (1.02-1.20) | 1.46 (1.40-1.52) | 1.09 (1.00-1.19) | 1.23 (1.13-1.34) | 1.16 (0.97-1.38) |

**Education**

- Compulsory education: 1.76 (1.68–1.84) (1.74 (1.66-1.83)) 1.71 (1.53-1.91)
- High school: 1 (1)
- University degree: 0.63 (0.59-0.68) (0.63 (0.59-0.68)) 0.60 (0.52-0.70)
- Missing: 1.58 (1.43–1.75) (1.52 (1.36-1.70)) 1.73 (1.35-2.20)

**Marital status**

- Married: 1 (1)
- Never married: 3.34 (3.09-3.61) (4.35 (3.98-4.75)) 1.56 (1.32-1.84)
- Divorced: 9.98 (9.54-10.45) (12.44 (11.80-13.11)) 4.95 (4.52-5.42)
- Widowed: 2.62 (2.45-2.80) (3.24 (2.99-3.52)) 1.84 (1.64-2.06)

**Number of children**

- 0.90 (0.88-0.91) (0.92 (0.90-0.94)) 0.81 (0.78-0.84)

**Age**

- 1.03 (1.03-1.03) (1.04 (1.03-1.04)) 1.01 (1.01-1.01)

**Year**

- 0.90 (0.89-0.90) (0.90 (0.90-0.91)) 0.87 (0.85-0.88)

**Sex**

- Men: 1
- Women: 0.21 (0.20-0.22)
Table 3 Hazard Ratios (and 95% confidence intervals) for the association between bereavement and alcohol-related mortality compared to non-bereaved parents, stratified by the age and cause of death of the offspring, Norway, 1986-2014.

| Cause of death of child | All         | Men         | Women       |
|-------------------------|-------------|-------------|-------------|
| Non-bereaved parent     | 1           | 1           | 1           |
| Natural causes          | 1.47 (1.34-1.61) | 1.33 (1.19-1.49) | 1.93 (1.64-2.28) |
| External causes         | 1.79 (1.61-1.99) | 1.66 (1.47-1.89) | 2.22 (1.82-2.72) |

| Age of child            | All         | Men         | Women       |
|-------------------------|-------------|-------------|-------------|
| Non-bereaved parent     | 1           | 1           | 1           |
| < 1                     | 1.55 (1.30-1.86) | 1.27 (1.01-1.59) | 2.52 (1.86-3.43) |
| 1 - 18                  | 1.54 (1.32-1.80) | 1.43 (1.19-1.71) | 1.91 (1.41-2.60) |
| > 18                    | 1.61 (1.47-1.76) | 1.52 (1.36-1.69) | 1.97 (1.68-2.30) |

Controlling for sex, age, education, marital status and number of children.
Table 4 Hazard Ratios (and 95% confidence intervals) for the association between bereavement and alcohol-related mortality, parents who have lost a child compared to their non-bereaved siblings, Norway, 1986-2014.

| Category                | Hazard Ratio (95% CI) |
|-------------------------|-----------------------|
| All                     | 1.30 (1.03-1.64)      |
| Bereaved parent         | 1                     |
| Non-bereaved parent     | 1                     |
| Childless               | 1.18 (0.99-1.40)      |
| **Education**           |                       |
| Compulsory education    | 1.84 (1.63-2.07)      |
| High school             | 1                     |
| University degree       | 0.59 (0.50-0.71)      |
| Missing                 | 2.03 (1.39-2.97)      |
| **Marital status**      |                       |
| Married                 | 1                     |
| Never married           | 5.39 (4.53-6.42)      |
| Divorced                | 8.16 (7.12-9.36)      |
| Widowed                 | 5.59 (4.25-7.34)      |
| **Number of children**  |                       |
|                         | 0.86 (0.81-0.91)      |
| **Age**                 |                       |
| Age                     | 1.08 (1.07-1.09)      |
| **Year**                |                       |
| Year                    | 1.01 (0.97-1.06)      |
| **Sex**                 |                       |
| Men                     | 1                     |
| Women                   | 0.29 (0.26-0.33)      |
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### STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies

| Section/Topic          | Item # | Recommendation                                                                 | Reported on page # |
|------------------------|--------|---------------------------------------------------------------------------------|--------------------|
| **Title and abstract** | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1                  |
|                        |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 2                  |
| **Introduction**       | 2      | Explain the scientific background and rationale for the investigation being reported | 5                  |
| **Objectives**         | 3      | State specific objectives, including any prespecified hypotheses                  | 6                  |
| **Methods**            | 4      | Present key elements of study design early in the paper                           | 5-6                |
| **Study design**       | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6                  |
| **Setting**            | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | N/A                |
|                        |        | (b) For matched studies, give matching criteria and number of exposed and unexposed | N/A                |
| **Participants**       | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-7                |
| **Variables**          | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 6-7                |
| **Data sources/ measurement** | 9  | Describe any efforts to address potential sources of bias                          | 5-6                |
| **Bias**               | 10     | Explain how the study size was arrived at                                         | N/A                |
| **Study size**         | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 11                 |
| **Statistical methods**| 12     | (a) Describe all statistical methods, including those used to control for confounding | 7-8                |
|                        |        | (b) Describe any methods used to examine subgroups and interactions               | N/A                |
|                        |        | (c) Explain how missing data were addressed                                       | 7                  |
|                        |        | (d) If applicable, explain how loss to follow-up was addressed                    | 6                  |
|                        |        | (e) Describe any sensitivity analyses                                             | N/A                |  

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### Results

| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | N/A |
|--------------|-----|-----------------------------------------------------------------------------------------------------------------|-----|
|               |     | (b) Give reasons for non-participation at each stage                                                             | N/A |
|               |     | (c) Consider use of a flow diagram                                                                                | N/A |

| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 12 |
|------------------|-----|----------------------------------------------------------------------------------------------------------------|-----|
|                  |     | (b) Indicate number of participants with missing data for each variable of interest                               | 12 |
|                  |     | (c) Summarise follow-up time (eg, average and total amount)                                                     | 12 |

| Outcome data | 15* | Report numbers of outcome events or summary measures over time                                                   | 12 |

| Main results  | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 13 |
|---------------|-----|-----------------------------------------------------------------------------------------------------------------|-----|
|               |     | (b) Report category boundaries when continuous variables were categorized                                        | N/A |
|               |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |

| Other analyses| 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses                     | N/A |

### Discussion

| Key results | 18  | Summarise key results with reference to study objectives                                                        | 9  |

### Limitations

| Interpretation | 20  | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 9-11 |
|----------------|-----|----------------------------------------------------------------------------------------------------------------|-----|
| Generalisability | 21  | Discuss the generalisability (external validity) of the study results                                          | 11  |

### Other information

| Funding | 22  | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 11  |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.