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New anti-depressant utilization pre and post bereavement: a population based study of partners and adult children

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Abstract

Purpose: Bereavement is associated with increased morbidity and mortality, but few studies examine the specific timing of depression onset. This study examines risk of developing new onset depression in adult children and partners by month one year before and after death.

Methods: Using population-based registers in Denmark, we assembled a cohort of 236,000 individuals who died a natural death (2010–2016). Partners and adult children of the deceased were identified and demographic and prescription data were collected. GEE logistic regression was used to model whether the bereaved received a new antidepressant prescription around the death of their loved one across 24 time intervals (12 months before and after death).

Results: Male and female partners had an increase in receipt of new antidepressant prescriptions in the 11 months after the death of their partner, with a peak increase two or three months after death. Partners also increased new antidepressant prescription use two months before death. Characteristics of the decedents including cause of death were not associated with new antidepressant prescription in the surviving partner. Adult children did not have increased odds of being prescribed new antidepressants at any time.

Conclusion: Both male and female partners have increase in new antidepressant utilization before and after the death of their partner. Our work points to the importance of supporting partners not only after the death of their partner, but also in the period before death when families may be actively engaged in caregiving for the seriously ill.

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Keywords

Bereavement; Depression; Antidepressant; Family

Background

The death of a spouse or partner is an incredibly stressful life event which is known to increase morbidities and put the bereaved at increased risk of mortality [1–3]. While minor depressive symptoms are common and expected after loss, complicated or prolonged grief and depressive symptoms can require medical intervention and treatment for some bereaved individuals [4]. Increased risk of suicide, self-harm, and psychiatric illness have been documented for at least 10 years after loss in bereaved families [5]. Psychotropic medications, e.g. anti-depressants, are commonly prescribed to bereaved partners (17.9%) within one year of bereavement [6]. In one study, the incidence rate of new prescriptions for antidepressants was 87% higher in bereaved partners compared to age and sex matched partnered non-bereaved controls [7].

The vast majority of research on the health outcomes of bereavement in the general population has focused on the period after death, especially on the challenging experience of loss of a spouse [8, 9]. The period before death is more often studied in the context of caregiving for a specific illness (e.g., cancer or dementia) when families may be dealing with stressful tasks such as symptom management and decision-making regarding nursing home entry and use of life-sustaining treatments [10], and may be experiencing stress associated with high out-of-pocket health-related spending [11]. While we know that caregivers who are providing care to family in the last years of life are vulnerable to symptoms of depression and anxiety in the post-death period [12, 13] and related emotional, physical, and financial challenges [14], we know less about the mental health of family members in the general population before and after death. Furthermore, specificity of timing of symptoms relative to loss is an important factor. Kristiansen et al. [15] in a recent meta-analysis found significant variation in prevalence of depression among widows over time peaking at 38% 1 month after death and decreasing to 10% up to 5 years after death. Although specificity of timing of mental health outcomes around bereavement would be beneficial for the targeting of caregiving and bereavement support, most studies are unable to capture detailed time intervals around bereavement [16, 17].

The majority of studies on bereavement have focused on the widowhood experience for partners or spouses [6, 15, 18–21], despite the fact that many individuals do not have partners at the time of death, and most family caregivers who are actively caring for individuals at the end of life are adult children [22]. The limited studies on mental health outcomes in bereavement that include adult children have focused on caregivers [16, 17, 23–25]. These research studies conclude that higher levels of caregiving are associated with more psychological distress during bereavement [25] and that, in general, bereaved partners experience more psychological distress than adult children [17, 24]. While these studies expand our knowledge on the health impacts of caregiving they do not elucidate how bereavement affects the mental health of partners and adult children within a population.

Understanding the experience of bereavement and its effects on mental health within the context of the general population, regardless of caregiving tasks, remains a major gap in the literature. Finally, while females are far more likely to be treated for depression than men [26, 27], it is not clear how these gender differences play out around bereavement. Female caregivers experience higher levels of grief and more help-seeking behaviors than males [25], although studies of bereaved caregivers and spouses are inconsistent. [6, 28, 29]

Understanding the mental health risks for families before and after death is an important step in supporting them through the bereavement process. Therefore, the purpose of this study is to examine the effects of bereavement on the odds of developing new onset depression in partners and adult children in the general population, both in the year before and the year after the death of a family member. Using population-based registers in Denmark, we examined the odds of receiving a new prescription for an antidepressant in each of the 12 months before and 12 months after the death of a partner or parent after adjusting for characteristics of the decedent and the bereaved. We hypothesized that utilization would increase before death and that effects would be highest among female partners.

Methods

Data sources

This study was conducted using population-based registers in Denmark with data collected between January 1, 2009 and December 31, 2016. In Denmark, all citizens with permanent residences are assigned a personal identification number (PIN) at birth or upon immigration. This PIN facilitates linkage of data between the Danish Civil Registration System, which includes data on date of birth, country of origin, civil status, and family identification number [30], the Danish Register of Causes of Death, which includes date, location, and cause of death of all residents who died in Denmark beginning in 1970 [31], the Danish National Patient Register, which includes data on non-psychiatric hospital admissions, outpatients contacts, and emergency room visits since 1995 [32], and the National Prescription Register, which contains information on all redeemed prescriptions since 1995 [33]. Because the healthcare system in Denmark is tax-financed and provides universal health access for all citizens with permanent residence, these registers capture the vast majority of billable health encounters among Danish citizens. Statistics Denmark provided additional demographic data including educational level, income, residential address, geographical region, and municipality services. The study was approved by the Danish Data Protection Agency (record number 17/9058). According to Danish law, ethical review board approval or informed consent from subjects are not required for purely register-based studies. The study was also reviewed by the Program for the Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai and was considered exempt.

Study population and timing

To define the study population, we identified all adult (≥ 18 years) Danish permanent residents who died due to natural deaths (excluding homicides, suicides, accidents, or acts of war) between January 1, 2009 and December 31, 2016 according to the Danish Registry of Causes of Death. Using the Danish Civil Registration System, decedents were linked to their

partners and children. Cohabiting partners were identified using the residential address information from Statistics Denmark. All decedents who were partnered and/or had 1 adult (> 18 years) children at the time of their death were included in the study. Bereaved individuals could be linked to multiple decedents (if, for example, they had multiple parents die over the study period). Similarly, all adult children for each decedent were included in the analysis. The time periods in this study were anchored to the date of death (day 0). The days immediately before and after the death were designated days -1 and 1 respectively. Each 30 day period one year before and after death was aggregated into month intervals. In order to avoid capturing underlying depressive disorders unrelated to the death of the parent or partner, individuals who received any antidepressant prescription in the 36–12 months before the death of the parent or partner were excluded.

Measures

The primary outcome examined was depression in bereaved partners and adult children in the 12 months before and after death, measured by new antidepressant prescriptions (Anatomical Therapeutic Chemical Classification System codes N06A) collected in the Danish National Prescription Registry [33]. These included non-selective monoamine reuptake inhibitors, selective serotonin reuptake inhibitors, type A monoamine oxidase inhibitors, non-selective monoamine oxidase inhibitors and unspecified antidepressants [34]. We obtained information from the prescription register from 2007 to June 2017, therefore we restricted the study population to adults dying from January 2010 until June 2016.

The information about the decedent collected included age at death, gender, use of municipal services (including personal or nursing care) in the last month of life, whether or not they lived with another person, income (in DKK), underlying cause of death (cancer, heart disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), dementia, and other), and country region (Capital Region, Region of Zealand, Region of Southern Denmark, Central Denmark Region, and North Denmark Region). The national patient register was used to determine dementia diagnosis and construct the Charlson comorbidity index [35] (categorized into five groups with a score of 0, 1–2, 3–4, or 5 and above).

The information collected about bereaved partners and adult children included age, marital status (married, partnered, or unmarried), gender, income, education (primary school, skilled worker, short theoretical, meaning 1–2 years of education, long theoretical, meaning 3–4 years of education, academic meaning 5 or more years of education), Charlson comorbidity index (categorized into five groups as above), employment status (employed vs. unemployed, pensioner, or missing employment data), and country region.

The dataset had few missing values and only 1.6% of individuals had missing data in either education level or income. Missing information on educational level was imputed as basic school education and missing information on income was imputed as no income. None of the other variables had missing information. On average, individuals with missing data on educational level or income were older than those without missing data.

Statistical Analysis

Generalized estimation equation (GEE) logistic regression modeling was used to account for non-independence of observations over time [36]. The number of months before or after death was the primary unit of analysis. The 12th month prior to the death was used as the referent month. Each analysis was conducted across three models to fully account for key characteristics of the bereaved and the decedent. Model 1 adjusted for age of decedent (18–49 vs. 50–59, 60–69, 70–79, 80–89, or 90 or older) and decedent's year of death. Model 2 additionally adjusted for characteristics of the bereaved including whether the bereaved was married or partnered, the bereaved's age, education level, Charlson comorbidity index and employment status. For adult children, a variable was also included to indicate whether or not they had siblings (no sibling vs. one or more siblings). Model 3 adjusted for all of the variables included in Model 2 and information about the decedent including cause of death, dementia diagnosis, Charlson comorbidity index, whether they needed municipality services (in home personal care services) 1 month before death, and the country region. All covariates were examined for multi-collinearity. Interactions of each time period by gender and relationship type were tested.

Sensitivity analyses

Two sensitivity analyses were performed. First, to ensure validity of prescription drug use as a proxy for clinical depression, we only included two or more prescriptions for antidepressants started during the 12 months before or after the death as our outcome. Second, as individuals may experience more than one death over the study follow up period, we conducted an additional analysis in which we only included the first death experienced by an individual (e.g., first parent death only).

Results

Characteristics of decedents and bereaved partners and children

Our sample included a total of 302,436 adults who died between January 1, 2010 and June 30, 2016. The median (IQR) age of the decedents was 78 (69–85) and 47% of the decedents were female. The most commonly identified underlying cause of death was cancer (35.5%). The next most common causes of death were ischemic heart disease (8.5%), cerebrovascular disease (6.8%), COPD (7.2%), and dementia (6.0%).

Of the 302,436 decedents who died between January 1, 2010 and June 30, 2016, 236,911 had a total of 129,678 partners that did not have a previous prescription for antidepressants, 65.5% of whom were female. The median age of partners was 72 years of age (IQR: 64–79). 67.0% of the bereaved partners were pensioners and 18.5% were still employed. The majority of bereaved partners had a primary school education (47.1%) and had a Charlson comorbidity index score of 0 (64.7%). Characteristics of decedents and bereaved partners (stratified by gender) are reported in Table 1.

Among decedents, we identified a total of 407,567 adult children that did not have a previous prescription for antidepressants, 46.5% of whom were female. The majority, 83.1% of the adult children had at least one living sibling. The median age of bereaved children was

48 years of age (IQR: 41–54). (Characteristics of bereaved adult children and decedents are reported in Table 2).

New anti-depressant prescriptions among the bereaved

A total of 24,391 (4.5%) of partners and adult children were prescribed a new antidepressant at any point during the 24 month study period. After bereavement, 7,780 adult children (1.9%) and 7,674 partners (5.9%) were prescribed a new antidepressant.

Interactions for month and relationship to decedent (adult child or partner) were statistically significant ($p < 0.0001$). There was a statistically significant interaction between gender and time among partners, but not among adult children. We therefore stratified all analyses of the bereaved into the following 3 groups: (1) female partners; (2) male partners; and (3) adult children.

Bereaved female partners were significantly more likely to receive a new antidepressant prescription starting two months prior to the death of their partner compared to 12 months prior to the death of their partner. While female partners remained significantly more likely to receive a new antidepressant prescription up to 12 months after the death of their partner in all of the models, the highest odds of receiving a new antidepressant prescription were seen three months after the death of their partners (odds ratio [OR] (95% confidence interval [CI]): 2.84 (2.45–3.28)). Among bereaved female partners, other factors associated with new antidepressant prescription included younger age, lower educational level, more comorbidities, and unemployment (Table 3). Characteristics of the decedent including cause of death, having a dementia diagnosis, the decedent's Charlson comorbidity index score, and the decedent's age were not significantly associated with increased risk of the bereaved being prescribed antidepressants (Table 3). Use of municipality services in the month before death was significantly associated with new antidepressant prescription (OR (95% CI): 1.09 (1.04–1.14)).

Bereaved male partners had significantly higher odds of receiving a new antidepressant prescription starting one month prior to the death of their partner. They had the highest odds of receiving a new antidepressant prescription in the second month after the death of their partners (OR (95% CI): 2.82 (2.31–3.45)) (Table 3) with a steady decline over 1 year. Observed characteristics of the decedents had no association with increased anti-depressant utilization other than use of municipality services before death.

Among bereaved adult children timing relative to death was not associated with new antidepressant prescription use before death. There was no increase utilization after death. Beginning in month 9 after death, we observed a decreased odds in prescriptions relative to 12 months before death. Decedent characteristics such as cause of death, dementia diagnosis, and Charlson comorbidity index score were not associated with increased odds of being prescribed antidepressants. Decedent's receipt of municipality services in the month prior to death was associated with increased odds of bereaved adult children being prescribed antidepressants (OR (95% CI): 1.06 (1.03–1.10)). Older age of decedent was inversely associated with the odds of bereaved adult children being prescribed

antidepressants among decedents between the ages of 80–89 and 90 or older (OR (95% CI): 0.74 (0.64–0.85) and 0.72 (0.62–0.84), respectively) (Table 3).

Sensitivity analysis

In a sensitivity analysis, which used receipt of at least two antidepressant prescriptions as the outcome, the results did not change materially. Similarly, 6.4% of bereaved children and 0.2% bereaved spouses experienced multiple deaths during study follow up. When we limited our analysis to the first bereavement only for those individuals who experienced multiple deaths, we continued to find the same prescription pattern around bereavement for male partners, female partners and children. (Results not shown).

Discussion

Our results suggest that bereaved partners have higher odds of developing new onset depression not only in the year after the death of their partner, but also in the two months preceding their death. Our findings regarding increased depression for bereaved partners after death are consistent with other studies [5, 6, 17, 25]. While caregiving studies in the context of terminal illness have shown that there is an increase in depression as death approaches for families up to 6 months before death, [7, 24] we only detected a significant increase in antidepressant prescriptions for bereaved partners two months prior to death. This difference is likely a reflection of the longer illness preceding the death of terminally ill patients compared to our study which included all natural deaths in a population. Our findings point to the importance of supporting partners not only around bereavement but also in the period before death. Given challenges in prognostication around time until death, palliative care and other supportive services for the family of individuals with serious illnesses is essential [37].

Despite well-known differences in gender and antidepressant utilization [27], male and female partners had similar increased risk of new utilization around the death of their partner. Lack of significant gender differences in new mental health risk after bereavement have been previously reported [5], and suggest we need to make sure widowers and other male bereaved caregivers receive appropriate mental health support. This may be especially important as men are increasingly taking on caregiving roles [38], many without support of other family [39]. We did find small but remarkable differences that emerged in timing of depression by gender. Male partners had greater increases in depression more immediately after death (one month) whereas females began to increase after two months. Such differences should be studied further and may suggest a need to tailor interventions for male partners closer to the time of death.

Unlike bereaved partners, bereaved adult children had no detectable increases in antidepressant utilization before or after their parent's death. These results are consistent with previous research [5, 17] which also did not find increased depression for adult children around bereavement. Our study, in fact, found that children had lower odds of being prescribed antidepressants starting nine months after the death of their parent. While researchers have suggested that for some individuals, trauma and stress may have positive effects as their attempts to find meaning in the traumatic event helps them to refocus their

purpose in life and identity [40, 41], further research is required to better understand this finding in adult children.

We included measures of cause of death, decedent comorbidity level, dementia status and use of in home personal care services (supported by the local municipality in Denmark) to approximate end-of-life care needs. Cause of death and level of comorbidity were not associated with more depression for family members. This was surprising as family members may have worse outcomes when they are more physically or emotionally or even financially burdened by their loved one's illness. We also did not find any impact of dementia status on depression despite the well-established unique stressors of caring for individuals with dementia, particularly at the end of life [42]. Previous research suggested that shorter duration of illness in the deceased may be associated with higher grief intensity in bereaved children, although this effect was not seen in bereaved partners [25]. The only decedent characteristic that was associated with increased odds of depression in both adult children and partners was the decedent's use of municipal services in the month before their death, likely a better indicator of caregiving intensity before death. Decedents who utilized municipal services in the month prior to their death are more functionally impaired (requiring assistance with personal care, wound care, etc.) and therefore may have been in more need of direct caregiver support with activities of daily living. Other studies have found that higher caregiving support is associated with increased likelihood of developing complicated grief [24, 25].

There are some limitations to this study. While antidepressant prescription is a frequently used proxy for depression diagnosis [6, 43] and has been shown to be a moderately reliable indicator of depression (area under the ROC curve 0.72) [44], we cannot definitively determine that everyone who was prescribed an antidepressant had a new depression diagnosis. Antidepressants may be prescribed for mental health disorders other than depression including anxiety disorders, compulsive disorders, phobias, post-traumatic stress disorder and bulimia. Tricyclic antidepressants are also sometimes prescribed for chronic nerve pain and inflammation from inflammatory bowel disease [45, 46]. Furthermore, people with depression who remain untreated or are treated without psychotropic medication will not be captured within this study. However, research indicates that prescriptions of antidepressants follow a similar trend to diagnoses of depression [47]. Most studies examining depression around bereavement focus on the measurement of depressive symptoms via symptom instruments such as the Center for Epidemiologic Studies Depression Scale (CESD) [48], Texas Revised Inventory of Grief (TRIG) [49], and the Prolonged Grief Questionnaire [50]. While these measures are useful in examining complicated grief or depression symptomatology, the same response rate and representativeness of the population is not possible using survey measures. By using antidepressant prescriptions as a proxy for depression diagnosis, we are able to examine the effect of bereavement on mental health in a wider proportion of the population, while still limiting the study to those who are likely to have a diagnosis of depression. Furthermore, there was no direct measure of caregiving in this study. Although use of municipality services in the month prior to death may be an indicator of increased need or care in the decedent, it does not provide any indication of who is providing that care. This study only included bereaved partners and adult children, which may exclude major sources of

caregiving and support for the decedents. Our analyses only focus on the 12 month periods before and after death. Future work should examine longer time frames around death as others have reported sustained increased in depression for longer time periods [15]. Finally, while the large sample size helps to increase the generalizability of these results, caution must still be used in applying these results to other populations. Denmark is a relatively small and culturally homogenous country with a nationalized healthcare system, and thus it may be difficult to apply these results worldwide.

Despite these limitations, this study has a number of strengths including that it is able to capture antidepressant medication prescription with monthly timing specificity for the bereaved in the period before and after the death of their partner or parent. Our study included all natural deaths in a population, not just individuals with diagnosed terminal illness. Additionally, as a population-based study using data that are estimated to include 99% of all Danish citizens and residents [29–31], we are able to reduce potential response bias that may be an issue in many studies of bereavement. Furthermore, the fact that Denmark has a nationalized healthcare system may mean that more individuals who could benefit from mental health treatment have access to it, as compared to other Western countries including the United States where mental health treatment is not available and often not accessed by those who need it. This study is also one of the few studies to simultaneously examine a population of bereaved partners and children to definitively compare their bereavement experiences. Finally, this study examines both factors associated with the bereaved and the decedent, allowing for a more nuanced understanding of the factors that may be associated with grief leading to clinical depression. Future work using these data, for example, can examine interactions in comorbidity level and timing of depression onset among the bereaved.

Conclusion

In conclusion, this research suggests that both male and female partners are at greater risk of depression in the two months before and 11 months after the death of their partner. This effect is not seen among the adult children of deceased parents. This research may be useful in guiding clinicians working with bereaved families to determine which family members are most likely to need additional mental health support. In particular, our work suggests that providing support to male and female partners who are caring for individuals at the end-of-life is essential, as increases in depression begin prior to death.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Prior A, et al., Bereavement, multimorbidity and mortality: a population-based study using bereavement as an indicator of mental stress. *Psychol Med*, 2018 48(9): p. 1437–1443. [PubMed: 28851470]
2. Allegra J, et al., Population-level impact of loss on survivor mortality risk. *Qual Life Res*, 2015 24(12): p. 2959–61. [PubMed: 26081295]
3. Taylor DH Jr., et al., The effect of spousal caregiving and bereavement on depressive symptoms. *Aging Ment Health*, 2008 12(1): p. 100–7. [PubMed: 18297484]
4. American Psychiatric Association, Depressive Disorders, in *Diagnostic and statistical manual of mental disorders* (5th ed.), A.P. Association, Editor. 2013, American Psychiatric Association: Arlington, VA.
5. Guldin MB, et al., Risk of suicide, deliberate self-harm and psychiatric illness after the loss of a close relative: A nationwide cohort study. *World Psychiatry*, 2017 16(2): p. 193–199. [PubMed: 28498584]
6. Shah SM, et al., Initiation of psychotropic medication after partner bereavement: a matched cohort study. *PLoS One*, 2013 8(11): p. e77734. [PubMed: 24223722]
7. King M, et al., Mortality and medical care after bereavement: a general practice cohort study. *PLoS One*, 2013 8(1): p. e52561. [PubMed: 23372651]
8. Stroebe M, Schut H, and Stroebe W, Health outcomes of bereavement. *Lancet*, 2007 370(9603): p. 1960–73. [PubMed: 18068517]
9. Stroebe M, et al., Grief is not a disease but bereavement merits medical awareness. *Lancet*, 2017 389(10067): p. 347–349. [PubMed: 28137681]
10. Institute of Medicine, *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life*. 2014, Washington, DC: The National Academies Press 630.
11. Kelley AS, et al., Out-of-Pocket Spending in the Last Five Years of Life. *J Gen Intern Med*, 2012.
12. Pottie CG, et al., Informal caregiving of hospice patients. *J Palliat Med*, 2014 17(7): p. 845–56. [PubMed: 24992371]
13. Pinquart M and Sorensen S, Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. *Psychol.Aging*, 2003 18(2): p. 250–267. [PubMed: 12825775]
14. Wolff JL, et al., End-of-life care: findings from a national survey of informal caregivers. *Arch Intern Med*, 2007 167(1): p. 40–6. [PubMed: 17210876]
15. Kristiansen CB, et al., The association of time since spousal loss and depression in widowhood: a systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol*, 2019 54(7): p. 781–792. [PubMed: 30887075]
16. Romero MM, Ott CH, and Kelber ST, Predictors of grief in bereaved family caregivers of person's with Alzheimer's disease: a prospective study. *Death Stud*, 2014 38(6–10): p. 395–403. [PubMed: 24666146]
17. Nielsen MK, et al., Predictors of Complicated Grief and Depression in Bereaved Caregivers: A Nationwide Prospective Cohort Study. *J Pain Symptom Manage*, 2017 53(3): p. 540–550. [PubMed: 28042073]
18. Thompson L, et al., The Effects of Late-Life Spousal Bereavement Over a 30-Month Interval. *Psychology and Aging*, 1991 6(3): p. 434–441. [PubMed: 1930760]
19. Egerod I, et al., Spousal bereavement after fibrotic interstitial lung disease: A qualitative study. *Respir Med*, 2019 146: p. 129–136. [PubMed: 30665511]
20. Shah SM, et al., The mental health and mortality impact of death of a partner with dementia. *Int J Geriatr Psychiatry*, 2016 31(8): p. 929–37. [PubMed: 26833866]
21. Asai M, et al., Impaired mental health among the bereaved spouses of cancer patients. *Psycho-Oncology*, 2013 22(5): p. 995–1001. [PubMed: 22550042]
22. Ornstein KA, et al., A National Profile Of End-Of-Life Caregiving In The United States. *Health Aff (Millwood)*, 2017 36(7): p. 1184–1192. [PubMed: 28679804]

23. Schulz R, et al., Preparedness for death and adjustment to bereavement among caregivers of recently placed nursing home residents. *J Palliat Med*, 2015 18(2): p. 127–33. [PubMed: 25469737]
24. Tang ST, et al., Course and predictors of depressive symptoms among family caregivers of terminally ill cancer patients until their death. *Psychooncology*, 2013 22(6): p. 1312–8. [PubMed: 22836818]
25. McLean S, Gomes B, and Higginson IJ, The intensity of caregiving is a more important predictor of adverse bereavement outcomes for adult-child than spousal caregivers of patients who die of cancer. *Psychooncology*, 2017 26(3): p. 316–322. [PubMed: 27139519]
26. Gorman JM, Gender differences in depression and response to psychotropic medication. *Gen Med*, 2006 3(2): p. 93–109. [PubMed: 16860269]
27. Wilkinson S and Mulder RT, Antidepressant prescribing in New Zealand between 2008 and 2015. *N Z Med J*, 2018 131(1485): p. 52–59. [PubMed: 30408818]
28. Nielsen MK, et al., Predictors of complicated grief and depression in bereaved caregivers: a nationwide prospective cohort study. *J Pain Symptom Manage*, 2016.
29. Masterson MP, et al., Psychosocial Health Outcomes for Family Caregivers Following the First Year of Bereavement. *Death Stud*, 2015 39(10): p. 573–8. [PubMed: 25651502]
30. Schmidt M, Pedersen L, and Sorensen HT, The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*, 2014 29(8): p. 541–9. [PubMed: 24965263]
31. Helweg-Larsen K, The Danish Register of Causes of Death. *Scand J Public Health*, 2011 39(7 Suppl): p. 26–9.
32. Lyng E, Sandegaard JL, and Rebolj M, The Danish National Patient Register. *Scand J Public Health*, 2011 39(7 Suppl): p. 30–3. [PubMed: 21775347]
33. Kildemoes HW, Sorensen HT, and Hallas J, The Danish National Prescription Registry. *Scand J Public Health*, 2011 39(7 Suppl): p. 38–41. [PubMed: 21775349]
34. Mayo Clinic Staff. Antidepressants: Selecting one that's right for you. 2019 [cited 2019 8/14/2019].
35. Charlson ME, et al., A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*, 1987 40(5): p. 373–83. [PubMed: 3558716]
36. Kleinbaum D and Klein M, Logistic Regression for Correlated Data: GEE, in *Logistic Regression. Statistics for biology and Health 2010*, Springer: New York, NY.
37. Ornstein KA, Schulz R, and Meier DE, Families Caring for an Aging America Need Palliative Care. *J Am Geriatr Soc*, 2017 65(4): p. 877–878. [PubMed: 28221667]
38. 2015 Report: Caregiving in the U.S 2015, National Alliance for Caregiving and the AARP Public Policy Institute.
39. Ornstein KA, et al., Spousal Caregivers Are Caregiving Alone In The Last Years Of Life. *Health Aff (Millwood)*, 2019 38(6): p. 964–972. [PubMed: 31158025]
40. Hibberd R, Meaning reconstruction in bereavement: sense and significance. *Death Stud*, 2013 37(7): p. 670–92. [PubMed: 24520967]
41. Kim Y, et al., Finding benefit in bereavement among family cancer caregivers. *J Palliat Med*, 2013 16(9): p. 1040–7. [PubMed: 23905875]
42. Vick JB, et al., Does Caregiving Strain Increase as Patients With and Without Dementia Approach the End of Life? *J Pain Symptom Manage*, 2018.
43. Guldin MB, et al., Healthcare utilization of bereaved relatives of patients who died from cancer. A national population-based study. *Psychooncology*, 2013 22(5): p. 1152–8. [PubMed: 22745052]
44. Trinh NH, et al., Using electronic medical records to determine the diagnosis of clinical depression. *Int J Med Inform*, 2011 80(7): p. 533–40. [PubMed: 21514880]
45. Uses. Antidepressants 2018 [cited 2019 8/5/2019].
46. Urits I, et al., Off-label Antidepressant Use for Treatment and Management of Chronic Pain: Evolving Understanding and Comprehensive Review. *Curr Pain Headache Rep*, 2019 23(9): p. 66. [PubMed: 31359175]

47. Bramesfeld A, Grobe T, and Schwartz FW, Prevalence of depression diagnosis and prescription of antidepressants in East and West Germany: an analysis of health insurance data. *Soc Psychiatry Psychiatr Epidemiol*, 2010 45(3): p. 329–35. [PubMed: 19452107]
48. Van Dam NT and Earleywine M, Validation of the Center for Epidemiologic Studies Depression Scale--Revised (CESD-R): pragmatic depression assessment in the general population. *Psychiatry Res*, 2011 186(1): p. 128–32. [PubMed: 20843557]
49. Montano SA, et al., Reliability generalization of the Texas Revised Inventory of Grief (TRIG). *Death Stud*, 2016 40(4): p. 256–62. [PubMed: 26678274]
50. Pohlkamp L, et al., Psychometric properties of the Prolonged Grief Disorder-13 (PG-13) in bereaved Swedish parents. *Psychiatry Res*, 2018 267: p. 560–565. [PubMed: 29982112]

Figure 1.

Odds of being prescribed a new antidepressant by month (adjusted* odds ratios and 95% confidence intervals) in the 12 months before and after the death of a partner (stratified by gender) or parent

*Adjusted for decedent age, months before or after death, bereaved information on married vs partners, bereaved education level, bereaved Charlson comorbidity index, and bereaved socioeconomic status plus decedent information on cause of death, dementia, decedent Charlson comorbidity index, municipality services 1 month before death, and region.

Table 1Characteristics of decedents and bereaved partners from January 1, 2010 to June 30th 2016

Characteristic	Partners Male N (%) N= 44,796	Partners Female N (%) N= 84,882
Characteristics of Decedents* N=129,678		
Gender		
Female	160 (0.3)	95 (99.9)
Male	44,636 (99.6)	84,787 (0.1)
Age, median (IQR)	71 (63–79)	75 (67–82)
Age groups		
18 — 49	2,358 (5.3)	2,178 (2.6)
50 — 59	5,646 (12.6)	6,625 (7.8)
60 — 69	12,345 (27.6)	19,149 (22.6)
70 — 79	13,920 (31.1)	27,592 (32.5)
80 --- 89	9,113 (20.3)	24,037 (28.3)
90+	1,414 (3.2)	5,301 (6.3)
Region		
Capital Region of Denmark	12,109 (27.0)	23,423 (27.6)
Region Zealand	7,861 (17.6)	15,173 (17.9)
Region of Southern Denmark	10,206 (22.8)	19,134 (22.5)
Central Denmark Region	9,387 (21.0)	17,517 (20.6)
North Denmark Region	5,233 (11.7)	9,635 (11.4)
Income, median (IQR)	128,933 (93,937–177,299)	159,174 (124,586–220,706)
Underlying cause of death		
Cancer	21,323 (47.6)	34,114 (40.2)
Heart disease	2,375 (5.3)	8,284 (9.8)
Cerebrovascular Disease	2,731 (6.1)	5172 (6.1)
COPD	3,168 (7.1)	4,919 (5.8)
Dementia	1,973 (4.4)	3,305 (3.9)
Other	13,226 (29.5)	29,088 (34.3)
Charlson Comorbidity index		
0	4,630 (10.3)	9,247 (10.9)
1–2	15,559 (34.7)	27,960 (32.9)
3–4	9,355 (20.9)	20,934 (24.7)
5+	15,252 (34.1)	26,741 (31.5)
Dementia diagnosis		
None	41,632 (92.9)	78,503 (92.5)
Diagnosed	3,164 (7.1)	6,379 (7.5)

Characteristic	Partners Male N (%) N= 44,796	Partners Female N (%) N= 84,882
Receipt of in home municipality services last month of life		
None	20,927 (46.7)	42,990 (50.7)
Received	23,869 (53.3)	41,892 (49.3)
Characteristics of Bereaved		
Marital status		
Married	35,672 (79.6)	66,965 (78.9)
Partnered	9,124 (20.4)	17,917 (21.1)
Age years, median (IQR)	73 (65–81)	71 (63–78)
Age groups		
18 — 49	2,107 (4.7)	4,212 (5.0)
50 — 59	4,611 (10.3)	10,025 (11.8)
60 — 69	11,174 (24.9)	23,473 (27.7)
70 — 79	13,691 (30.6)	29,250 (34.5)
80 --- 89	10,891 (24.3)	16,137 (19.0)
90+	2,322 (5.2)	1,785 (2.1)
Region		
Capital Region of Denmark	12,041 (26.4)	23,793 (28.0)
Region Zealand	7,853 (17.5)	14,986 (17.7)
Region of Southern Denmark	10,223 (22.8)	19,003 (22.4)
Central Denmark Region	9,435 (21.1)	17,508 (20.6)
North Denmark Region	5,244 (11.7)	9,592 (11.3)
Income, median (IQR) (DKK)	170,310 (130,660–245,101)	137,241 (97,157–191,888)
Education		
Primary school	18,376 (41.0)	42,668 (50.3)
Skilled Worker	18,154 (40.5)	26,642 (31.4)
Short theoretical (1–2 years)	1,480 (3.3)	2,094 (2.5)
Long theoretical (3–4 years)	3,800 (8.5)	10,103 (11.9)
Academic (5+ years)	2,989 (6.7)	3,375 (4.0)
Charlson Comorbidity index		
0	26,154 (58.4)	57,714 (68.0)
1–2	13,083 (29.2)	21,127 (24.9)
3–4	3,942 (8.8)	4,250 (5.0)
5+	1,617 (3.6)	1,791 (2.1)
New antidepressant use		
12 months before death	1,575 (3.5)	3,160 (3.7)
12 months after death	2,616 (5.8)	5,058 (6.0)
Never	40605 (90.6)	76664 (90.3)

IQR - interquartile range.

Table 2;Characteristics of Decedents and Bereaved Adult Children from January 1, 2010 to June 30th 2016

Characteristic	Adult Children N (%) N= 407,567
Characteristics of Decedents N=407,567	
Gender	
Female	188,739 (46.3)
Male	218,828 (53.7)
Age, median (IQR)	77 (69–84)
Age groups	
18 — 49	3,785 (0.9)
50 — 59	24,504 (6.0)
60 — 69	75,107 (18.4)
70 — 79	132,683 (32.6)
80 --- 89	137,066 (33.6)
90+	34,422 (8.5)
Lives alone	
Alone	221,174 (54.3)
With others	186,393 (45.7)
Region,	
Capital Region of Denmark	103,515 (25.4)
Region Zealand	67,984 (16.7)
Region of Southern Denmark	95,701 (23.5)
Central Denmark Region	90,992 (22.3)
North Denmark Region	49,375 (12.1)
Income, median (IQR)	158,508 (128,732—195,522)
Underlying cause of death	
Cancer	148,067 (36.3)
Heart disease	75,067 (18.4)
Cerebrovascular Disease	27,508 (6.8)
COPD	30,820 (7.6)
Dementia	23,449 (5.8)
Other	102,656 (25.2)
Charlson Comorbidity index	
0	48,778 (12.0)
1–2	146,180 (35.9)
3–4	97,990 (24.0)
5+	114,619 (28.1)

Characteristic	Adult Children N (%) N= 407,567
Dementia diagnosis	38,196 (9.4)
Receipt of in home municipality services last month of life	234,921 (57.6)
Characteristics of Bereaved	
Gender	
Female	189,613 (46.5)
Male	217,954 (53.5)
Marital status	
Married	229,343 (56.3)
Partnered	178,224 (43.7)
Living Siblings	
0	68,920 (16.9)
1 or more	338,647 (83.1)
Age years, median (IQR)	48 (41–54)
Age groups	
18 — 49	223,514 (54.8)
50 — 59	158,255 (38.8)
60 — 69	24,517 (6.0)
70 +	1,281 (0.3)
Region	
Capital Region of Denmark	120,649 (29.6)
Region Zealand	64,348 (15.8)
Region of Southern Denmark	88,021 (21.6)
Central Denmark Region	91,166 (22.4)
North Denmark Region	43,383 (10.6)
Income, median (IQR) (DKK)	246,139 (184,722–315,200)
Education	
Primary school	92,966 (22.8)
Skilled Worker	158,546 (38.9)
Short theoretical (1–2 years)	27,971 (6.9)
Long theoretical (3–4 years)	67,652 (16.6)
Academic (5+ years)	60,432 (14.8)
Charlson Comorbidity index	
0	363,071 (89.1)
1–2	38,963 (9.6)
3–4	3,344 (0.8)
5+	2,189 (0.5)
New antidepressant use	
12 months before death	8,393 (2.1)

Characteristic	Adult Children N (%) N= 407,567
12 months after death	7,780 (1.9)
Never	210,724 (96.7)

IQR - interquartile range

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Table 3:

Adjusted * Odds of the bereaved being prescribed an anti-depressant during the 12 months before and after the death of a loved one

Characteristic Total N=523,146	Female Partners Odds Ratio (95% CI)	Male Partners Odds Ratio (95% CI)	Adult Children Odds Ratio (95% CI)
Characteristics of Bereaved			
Gender			
Male	-	-	Ref
Female	-	-	1.47 (1.42–1.52)
Age groups			
18 — 49	Ref	Ref	Ref
50 — 59	0.82 (0.73–0.92)	0.98 (0.80–1.20)	0.92 (0.88–0.96)
60 — 69	0.57 (0.50–0.64)	0.80 (0.65–0.97)	0.67 (0.61–0.73)
70 — 79	0.70 (0.62–0.79)	0.89 (0.72–1.09)	0.49 (0.34–0.68)
80 --- 89	0.89 (0.78–1.01)	1.20 (0.98–1.48)	-
90+	1.00 (0.84–1.19)	1.27 (1.01–1.61)	-
Employment Status			
Employed	Ref	Ref	Ref
Unemployed	2.09 (1.65–2.65)	2.02 (1.47–2.77)	2.46 (2.31–2.62)
Pensioner	1.37 (1.25–1.50)	1.47 (1.29–1.66)	1.77 (1.70–1.85)
Missing	0.75 (0.68–0.84)	0.65 (0.55–0.77)	1.99 (1.56–2.52)
Education			
Primary school	Ref	Ref	Ref
Skilled Worker	0.94 (0.89–0.99)	1.05 (0.98–1.12)	0.86 (0.83–0.90)
Short theoretical (1–2 years)	0.76 (0.65–0.90)	1.03 (0.87–1.24)	0.63 (0.58–0.68)
Long theoretical (3–4 years)	0.77 (0.71–0.84)	0.89 (0.79–1.01)	0.68 (0.64–0.72)
Academic (5+ years)	0.69 (0.60–0.80)	0.84 (0.73–0.98)	0.52 (0.49–0.56)
Charlson Comorbidity index			
0	Ref	Ref	Ref
1–2	1.41 (1.34–1.48)	1.56 (1.45–1.68)	1.65 (1.58–1.73)
3–4	1.74 (1.60–1.90)	1.90 (1.72–2.10)	1.96 (1.72–2.23)
5+	2.13 (1.88–2.41)	2.84 (2.50–3.23)	3.03 (2.64–3.47)
Characteristics of Decedents			
Age Group			
18 — 49	-	-	Ref
50 — 59	-	-	1.09 (0.95–1.26)
60 — 69	-	-	0.99 (0.87–1.14)
70 — 79	-	-	0.87 (0.76–1.00)
80 --- 89	-	-	0.74 (0.64–0.85)
90+	-	-	0.72 (0.62–0.84)

Characteristic Total N=523,146	Female Partners Odds Ratio (95% CI)	Male Partners Odds Ratio (95% CI)	Adult Children Odds Ratio (95% CI)
Underlying cause of death			
Cancer	Ref	Ref	Ref
Heart disease	0.94 (0.88–1.00)	1.00 (0.90–1.10)	1.03 (0.98–1.08)
Cerebrovascular Disease	0.95 (0.86–1.05)	0.96 (0.83–1.09)	0.96 (0.89–1.03)
COPD	0.98 (0.89–1.08)	1.02 (0.90–1.15)	1.08 (1.01–1.15)
Dementia	1.03 (0.90–1.17)	1.02 (0.86–1.21)	0.99 (0.91–1.08)
Other	0.91 (0.86–0.97)	1.01 (0.92–1.10)	1.03 (0.99–1.08)
Charlson Comorbidity index			
0	Ref	Ref	Ref
1–2	1.03 (0.95–1.12)	1.02 (0.91–1.14)	1.05 (0.99–1.11)
3–4	0.98 (0.90–1.07)	0.97 (0.86–1.09)	1.07 (1.00–1.13)
5+	0.99 (0.91–1.08)	0.96 (0.84–1.08)	1.04 (0.98–1.10)
Dementia diagnosis			
No Dementia Diagnosis	Ref	Ref	Ref
Dementia Diagnosis	0.99 (0.90–1.08)	1.07 (0.95–1.22)	1.00 (0.94–1.07)
Receipt of in home municipality services last month of life	1.09 (1.04–1.14)	1.08 (1.01–1.16)	1.06 (1.03–1.10)

IQR - interquartile range; COPD – chronic obstructive pulmonary disease

* Also adjusted for months before and after death (–12 to 12), year of death, whether the bereaved children had siblings, the region of the country where the decedent lived, and whether or not the partners were married to the decedent