Antidepressant use before and after death of a family member: a cohort study

Helena Honkaniemi[1], Mikael Rostila[1], Maarit Kauppi[2], Pekka Virtanen[3], Liudmila Lipiäinen[4], Jaana Pentti[2], Mika Kivimäki[2,5], Jussi Vahtera[6]

[1] Department of Public Health Sciences and Centre for Health Equity Studies (CHESS), Stockholm University, Stockholm, Sweden; [2] Finnish Institute of Occupational Health, Turku, Finland; [3] Faculty of Social Sciences, School of Health Sciences, University of Tampere, Tampere, Finland; [4] School of Social Sciences and Humanities, University of Tampere; [5] Department of Epidemiology and Public Health, University College London Medical School, London, UK; [6] Department of Public Health, University of Turku, Turku, Finland

Correspondence to: Mikael Rostila, Department of Public Health Sciences and Centre for Health Equity Studies (CHESS), Stockholm University, 10691 Stockholm, Sweden, mikael.rostila@su.se, +468164416

Word count (text): 982

ABBREVATIONS

AD Antidepressants

ATC Anatomical Therapeutic Code

DDD Defined daily dose

SRH Self-rated health

Death in the family has been shown to influence the health of bereaved relatives [1]. Psychological symptoms caused by bereavement may be linked to the use of psychotropic medications such as antidepressants (AD), yet evidence on AD use patterns around bereavement is sparse [2]. The aim of this study is to describe trajectories of AD use around parental, child and spousal bereavement, and to examine whether these trajectories vary as function of individual risk factors preceding bereavement.

Data were drawn from linked records from national health registers and repeat surveys in a prospective cohort study of Finnish municipal service personnel [3]. Of the 106,243 eligible participants, 88,739 had register data available on all AD prescriptions and qualified for surveys in 2000/02, 2004/05 or 2008/09 inquiring into family death, with 65,604 (74%) responses. The final study population included 2,040 participants reporting at least one family death, with a complete history of AD prescriptions from two years before to two years after bereavement. Compared to the entire cohort, our study population was older and more likely to be female, with similar levels of education.

Occurrence and timing of death of a parent, child or spouse within the preceding 12 months were measured from a list of 16 life events [3]. Parental deaths were treated as one group (n=1,754). Due to few events, child and spousal deaths were combined into another (n=293). Child/spousal loss was measured in all waves. Parental loss was only measured in 2004/05 and 2008/09. We used the month of death as our index date.

The Finnish Prescription Register provided information on AD purchases, including dispensation date, WHO Anatomical Therapeutic Chemical (ATC) code [4], and quantity purchased as defined daily doses (DDDs; proxy for number of days treated). We extracted information on all AD purchases (ATC-code N06A) from two years before to two years after the index date, and used the dispensation date as the start of AD use, projecting the end date with total DDDs dispensed and combining consecutive and overlapping periods of medication as earlier [5]. The four years were divided into 16 consecutive three-month periods (eight before and eight after death), each with a dichotomous measure of AD use (at least one day of treatment).

Baseline characteristics were drawn from the survey before bereavement (in 1997/98, 2000/02 or 2004/05). This included self-rated health (SRH), classified as suboptimal (average/worse) or optimal (good/very good health); high distress, identified with a cut-off score of four in the 12-

item General Health Questionnaire [6]; high anxiety, categorized by a mean score in the highest quartile of the short Trait Anxiety Inventory [7]; and sleeping problems, reported for at least two to four nights a week in the Jenkins Scale [8]. Risk behaviours included heavy alcohol use, with a cut-off of 288 grams of absolute ethanol/week for men and 192 g/week for women [9]; current smoking; and physical inactivity (<2 Metabolic Equivalent of Task-hours/day). Further covariates included participants' age, sex, education (basic/intermediate or high), and presence of chronic conditions including diabetes, rheumatoid arthritis, asthma or coronary heart disease (acquired from the National Drug Reimbursement Register) or cancer (from the Finnish Cancer Registry).

Trajectory or latent class growth analysis [10] was applied to study patterns of dichotomous AD use over the 16 three-month periods from before to after bereavement, using the Expectation and Maximization algorithm to model parameter estimates and Bayesian information criteria to select the optimal number of trajectories. For both bereavement groups, three trajectories of AD use were identified (Figure): "low prevalence" for no use or persistently low use before and after bereavement; "increasing prevalence" for increased use from before to after; and "high prevalence" for persistently high use before and after. Among parentally bereaved, 10% belonged to increasing and 7% to high prevalence, while among child/spousally bereaved, 11% belonged to increasing and 6% to high prevalence. Within the increasing prevalence trajectories, the average number of annual treatment days rose from 244 before to 260 after parental loss, and from 213 before to 257 after child/spousal loss. For high prevalence, average annual treatment length remained relatively unchanged, at 314 days before and 319 after parental loss, and 325 before and 314 after child/spousal loss.

Baseline characteristics of the sample are given in Supplements. Multinomial logistic regression analysis was used to examine potential determinants of these trajectories, adjusting for age and sex, with low prevalence trajectory groups as references (Figure). Observations were weighted with the posterior probability of belonging to the chosen trajectory.

For parentally bereaved, belonging to the increasing prevalence trajectory was predicted by heavy alcohol use, high distress, high anxiety and sleeping problems before loss. High prevalence was predicted by suboptimal SRH, physical inactivity, high distress, high anxiety and sleeping problems. For child/spousal loss, increasing prevalence was observed among those with

suboptimal SRH, high anxiety and sleeping problems before loss. Along with heavy alcohol use, physical inactivity and high distress, these factors were also associated with high prevalence.

All associations remained significant after further adjustment for education and chronic conditions, with the exception of heavy alcohol use for child/spousal loss (Supplements).

In conclusion, we found similarly grouped trajectories in both cohorts. Prior health risks predicted the occurrence of increasing and high AD use trajectories over low trajectories. Despite our use of reliable, high coverage registers, our study had some limitations. We were unable to stratify our analyses by cause of death or by specific psychiatric diagnosis, which could have revealed altered trajectories of AD use. In lieu of actual dosages, our dichotomous measure of AD purchases may have overestimated the severity of grief. Finally, it is possible that AD use around bereavement may vary by international treatment practices, and should thus be explored in differing contexts.

Acknowledgements

This research was funded by the Swedish Research Council (Grant No. 2017-03266) and supported by NordForsk and the Academy of Finland (311492). The Ethics Committee of the Hospital District of Helsinki and Uusimaa approved this study.

REFERENCES

1 Rostila M, Saarela J, Kawachi I: Mortality in parents following the death of a child: a nationwide follow-up study from Sweden. J Epidemiol Community Health 2012;66:927-933.

2 Kravdal Ø, Grundy E: Health effects of parental deaths among adults in Norway: purchases of prescription medicine before and after bereavement. SSM Popul Healt 2016;2:868-875.

3 Vahtera J, Pentti J, Helenius H, Kivimäki M: Sleep disturbances as a predictor of long-term increase in sickness absence among employees after family death or illness. Sleep 2006;29:673-682.

4 WHO Collaborating Centre for Drug Statistics Methodology: Guidelines for ATC classification and DDD assignment. Oslo, Norwegian Institute of Public Health, 2017,

5 Lau HS, de Boer A, Beuning KS, Porsius A: Validation of pharmacy records in drug exposure assessment. J Clin Epidemiol 1997;50:619-625.

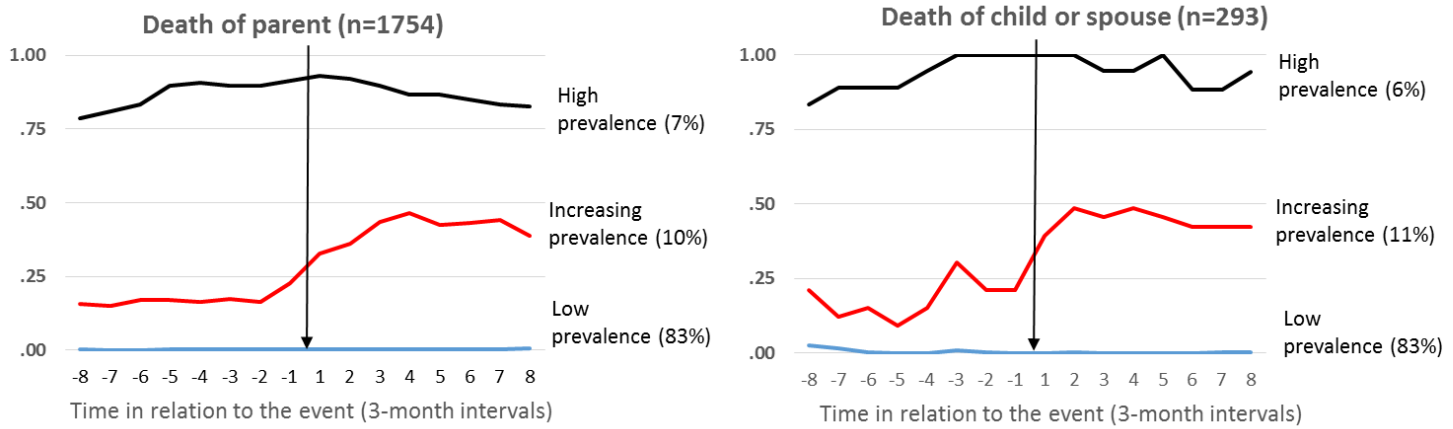
6 Goldberg D, Williams P: A user's guide to the General Health Questionnaire. Windsor, NFER-Nelson, 1988.

7 Marteau TM, Bekker H: The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). Br J Clin Psychol 1992;31:301-306.

8 Jenkins CD, Stanton B-A, Niemcryk SJ, Rose RM: A scale for the estimation of sleep problems in clinical research. J Clin Epidemiol 1988;41:313-321.

9 World Health Organization: International guide for monitoring alcohol consumption and related harm. Geneva, World Health Organization, 2000,

10 Nagin D: Analyzing developmental trajectories: a semiparametric, group-based approach. Psychol Methods 1999;4:139.



	Death of a parent (n=1,754)					Death of child or spouse (n=293)				
	Low use (n=1,455)	Increasing use (n=172)		High use (n=127)		Low use (n=242)	Increasing use (n=33)		High use (n=18)	
Predictor of AD use	OR	OR	95% CI	OR	95% CI	OR	OR	95% CI	OR	95% CI
Age (≥50 vs <50 yrs)	1.00	0.89	0.64 to 1.22	1.32	0.90 to 1.93	1.00	1.50	0.67 to 3.39	1.97	0.62 to 6.21
Sex (women vs men)	1.00	1.31	0.84 to 2.05	1.50	0.88 to 2.56	1.00	1.66	0.48 to 5.77	0.58	0.18 to 1.88
Education (low vs high)	1.00	1.06	0.77 to 1.46	0.82	0.56 to 1.19	1.00	0.84	0.40 to 1.76	0.48	0.18 to 1.31
Self-rated health (poor vs good)	1.00	1.37	0.91 to 2.07	4.04	2.64 to 6.21	1.00	2.81	1.09 to 7.27	3.51	1.09 to 11.4
Chronic conditions (yes vs no)	1.00	1.56	0.97 to 2.52	1.51	0.87 to 2.61	1.00	1.35	0.48 to 3.83	0.44	0.06 to 3.50
Heavy alcohol use (yes vs no)	1.00	2.39	1.42 to 4.04	1.80	0.97 to 3.33	1.00	1.52	0.39 to 5.90	3.85	1.05 to 14.1
Low physical activity (yes vs no)	1.00	1.04	0.67 to 1.63	1.80	1.16 to 2.77	1.00	1.88	0.74 to 4.79	3.27	1.07 to 10.0
Current smoking (yes vs no)	1.00	1.15	0.69 to 1.89	0.75	0.40 to 1.38	1.00	-	-	1.66	0.48 to 5.71
High distress (yes vs no)	1.00	2.05	1.39 to 3.04	3.03	1.99 to 4.62	1.00	1.51	0.58 to 3.92	3.53	1.14 to 10.9
High anxiety (yes vs no)	1.00	1.92	1.28 to 2.86	4.40	2.88 to 6.72	1.00	3.69	1.38 to 9.87	10.12	2.66 to 38.6
Sleeping problems (yes vs no)	1.00	1.96	1.32 to 2.91	2.62	1.68 to 4.08	1.00	3.75	1.18 to 12.0	12.11	1.53 to 95.9

Age- and sex-adjusted odds ratios (OR) with 95% confidence intervals (CI) estimated from multinomial logistic regression models using the trajectory of low AD use as a reference group. Information about predictors was drawn from national health registers and responses to an earlier survey before the family death.

Figure. Predictors of trajectories of antidepressant (AD) use (yes or no) in 3 month time periods from 2 years before to 2 years after the death of a family member