Published in final edited form as:

J Epidemiol Community Health. 2018 June ; 72(6): 526–531. doi:10.1136/jech-2017-210114.

Gender differences in the use of anti-infective medications before and after widowhood: a register-based study

Adriana Santacroce¹, Jonas W Wastesson², Andreas Höhn^{3,4}, Kaare Christensen^{3,5,6}, and Anna Oksuzyan⁴

¹Dipartimento di Scienze Statistiche, Sapienza Università di Roma, Rome, Italy

²Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden

³Department of Epidemiology, Biostatistics and Biodemography, University of Southern Denmark, Odense C, Denmark

⁴Max Planck Institute for Demographic Research, Rostock, Germany

⁵Max-Planck Odense Center on the Biodemography of Aging, University of Southern Denmark, Odense C, Denmark

⁶Danish Aging Research Center, Odense C, Denmark

Abstract

Background—Recent findings suggest that bereavement due to spousal loss is associated with a decline in general immune functions, and thus to increased susceptibility to infections among widowed individuals. The present study aims to investigate whether spousal loss weakens immune defences more among men than among women using a 5% random sample of the total Danish population, and anti-infective medication use as a proxy for immune response.

Methods—We followed 6076 Danish individuals (67% women) aged 50 from 5 years before and up to 5 years after widowhood to examine changes in prescriptions of anti-infectives for systemic use.

Results—Women used more anti-infective drugs both before and after spousal loss (women: OR= 1.31; 95% CI 1.21 to 1.42). The age-related changes in the use of anti-infective medications in the period before widowhood were similar to that in the period after widowhood among both men and women. Also, age-related changes in the use of anti-infective medications were similar in both genders.

Correspondence to: Adriana Santacroce, Sapienza Università di Roma; adriana.santacroce@uniroma1.it.

Contributors AO and KC conceived the study. AS, AO, JWW and KC designed the study. AS analysed the data. AH provided support to run the programme code. AS and AO drafted the report. All authors critically revised the report and approved the final version of the report.

Competing interests None declared.

Patient consent No patients were involved in the study, but only secondary data analysis of existing register data approved by the Danish Data Protection Agency.

Ethics approval The study involves secondary data analysis of existing register data approved by the Danish Data Protection Agency.

Provenance and peer review Not commissioned; externally peer reviewed.

Conclusions—The present study shows that individuals are more likely to use anti-infective medication after being widowed than before being widowed, but this change is likely to be related to increasing age and it is similar in both genders.

INTRODUCTION

Widowhood is a common life experience that is more likely to occur with increasing age, and among women than among men. The female preponderance in widowhood is attributable to women having a lower average age at marriage¹ and a higher life expectancy than men.² It has been suggested that widowhood affects the mortality and the health of the surviving spouse. Adverse effects of spousal loss have been found for mortality,^{3–7} for physical disabilities and mental health,⁸ and for the risk of institutionalisation.⁹

Findings on the gender-specific effects of widowhood on mortality and health disadvantages have provoked controversy. Some studies have suggested that the effects of widowhood on mortality, as well as on all-cause medication and primary health-care use after spousal loss, are similar among men and women.^{5,10} Other studies have demonstrated that levels of excess mortality due to spousal loss are higher among widowers than among widows.^{4,6,8,11–14} The factors that appear to underlie the adverse effects of widowhood on health and mortality^{14–17} include the loss of social, material and task support, and changes in health behaviours, such as intensified smoking and alcohol consumption, having a less healthy diet, and having fewer interactions with healthcare services.^{14–16} The main physiological mechanism that appears to underlie the negative consequences of spousal loss for health and survival is an elevated secretion of the stress hormone cortisol,^{18,19} which can in turn compromise immune system function.²⁰ Bereavement due to spousal loss has been associated with a decline in general immune functions, such as neutrophil function,²¹ and with a reduction in the effectiveness of peripheral blood lymphocytes. These findings suggest that stress related to spousal loss may compromise immune modulation,²² and may therefore increase the susceptibility of widowed individuals to infections. However, the research evidence on gender differences in the effect of spousal loss on changes in immune defences is less extensive. To help fill this gap, the present study investigates gender differences around spousal loss in anti-infective medications, used as a proxy for immune system defences.

The existing research points to a higher degree of stress reactivity to cortisol among men than among women,²³ and to a female advantage in immune protection,^{24,25} mainly due to the immunosuppressive effects of progesterone and testosterone, and to the immunoenhancing effects of oestrogens.^{26,27} The incidences of many bacterial, viral, parasitic and fungal infectious diseases have been found to be substantially higher, and some infectious diseases have been shown to be more severe among men than among premenopausal women.²⁷ Studies have found that autoimmune diseases are more common, and that immune responses to vaccinations are often stronger, in women than in men.^{27,28} It has also been shown that women use more prescription antibiotics than men, and that most of the antibiotics women are prescribed are intended to treat respiratory tract infections (RTIs), bronchitis or urinary tract infections (UTIs).²⁹ In light of research evidence indicating that men have lower levels of immunocompetence than women,³⁰ and that the effects of widowhood on health and mortality are greater among widowers than among

widows, we hypothesised that the immune defences of widowers are more compromised than the immune defences of their female counterparts. If men are more susceptible to infections than women, we would expect to find that the use of anti-infective medications increases more after spousal loss among men than among women. In light of previous research findings indicating that levels of all-cause medication use¹⁰ and antibiotic use, particularly for RTIs and UTIs, are higher among women than among men,²⁹ we would expect to observe higher levels of anti-infective medication use among women than among men both before and after widowhood.

METHODS

Data

The study is based on a 5% random sample of the total Danish population identified through the Central Personal Register (CPR) and linked to the Danish National Prescription Registry (DNPR).³¹ Each resident in Denmark is assigned a unique personal identification number, which makes it possible to link registers with different types of information. The CPR has been collecting information on demographic characteristics since 1968, while the DNPR contains information about prescribed medications, including the date of prescription and the type of drug, based on the Anatomical Therapeutic Chemical (ATC) classification system, which has been in use since 1995.^{31,32} From the 5% sample, we selected residents of Denmark who were at least 50 years old by 1 January 1996, were married by 1 January 1995, and were widowed between 1 January 2000 and 31 December 2007. This observation period was chosen to ensure the availability of the DNPR data (from 1 January 1995 to 31 December 2012) at least 5 years prior to and up to 5 years after widowhood.

Health measures

Prescriptions for the following anti-infectives for systemic use were considered: antibacterials (J01), antimycotics (J02), antimycobacterials (J04), antivirals (J05), and immune sera and immunoglobulins (J06). Anti-infective medication use was defined as having a prescription or not having a prescription in each year (0 vs 1). The dispensation of anti-infective drugs was considered a proxy measure for immune system defences. Denmark has a relatively low level of antibiotic use compared with other European countries,³³ suggesting that the anti-infective medications are likely prescribed in response to real individual health needs. Hence, the use of anti-infective medications is likely to reflect the presence of an infectious disease and compromised immune system function.

Statistical methods

First, we calculated the proportions of men and women who were prescribed anti-infective medications for each of the 5 years before and after the index year (year of spousal loss or widowhood) by the age at widowhood in 10-year age groups (the number of individuals with an anti-infective medication prescription divided by the total number of individuals in the corresponding age group at widowhood and time to/after widowhood, by gender).

We then fitted a generalised linear mixed model for longitudinal data with a binary response to examine the likelihood of having a prescription for anti-infective medications for systemic

use. Each individual was followed from 5 years before widowhood until 5 years after widowhood or death, whichever came first. To overcome the correlation between time-dependent predictors and individual effects,³⁴ we divided the time-dependent covariate age into between and within components,^{34,35} by applying the QP decomposition.³⁵ Following this approach, we separated the variable *age* into its cross-sectional dimension (to estimate *cohort* effect), which represents the effect of losing a spouse at different ages on anti-infective medication use, and into its deviation from the cross-sectional dimension (to estimate *age* effect), which represents the effect of becoming older on anti-infective medication use.³⁶ To differentiate the period before from the period after widowhood, we included a dummy variable (widowhood indicator), assuming a value of 0 for the period before widowhood and a value of 1 otherwise. We interacted this variable with age to allow the slope of age before spousal death to differ from the slope following spousal death. This interaction tests whether there is a disjuncture in anti-infective medication use after widowhood, that is, whether there is widowhood effect on the use of anti-infective medications. We performed these analyses for the total population (model 1) and in sex-specific samples (model 2 for men and model 3 for women). To examine gender differences in the effect of widowhood on anti-infective medication use, we compared sex-specific estimates for age and the interaction between age and widowhood indicator in the period after widowhood, with the CIs obtained from the model performed on the total population. To test statistically gender differences in the effect of widowhood on anti-infective medication use, we also added three-way interaction to the model for the total population interacting gender, age and widowhood indicator.

It is possible that widowed who died within 1–3 years following spousal loss were less healthy than those who survived 5 years following spousal loss, and were more sensitive to stress related to spousal bereavement. Therefore, we reran the analysis among individuals who survived 1, 3 and 5 years after becoming widowed to examine whether the effect of spousal loss on the use of anti-infective medications differs across these subpopulations. We also excluded individuals who became widowed at ages 90+, as strategies for prescribing medications in this very old population have been found to differ from the strategies applied in the younger population.³⁷ All analyses were performed using Stata (Version 15).

RESULTS

In total, we identified 72 524 individuals (87% of the initial population aged 50 and older) who were at least 50 years old and had been married by 1 January 1996. During the observation period from 1 January 2000 to 31 December 2007, 6076 individuals (67% of whom were women) became widowed. Most of the individuals (66%) became widowed between ages 60 and 79 (table 1).

Figure 1 shows the proportion of ATC-J users within 5 years before and up to 5 years after widowhood, by gender and age at widowhood.

In general, a higher proportion of women than of men were using anti-infective medications (our results are driven by antibacterial prescriptions) both before and after becoming widowed, and the proportion tended to increase with advancing age.

Results from the total population (model 1, table 2) indicate that the odds of anti-infective medication use were higher for women than for men (women: OR=1.31; 95% CI 1.21 to 1.42). Men and women who became widowed at age 70 or older had higher odds of anti-infective medication use than their counterparts who became widowed at ages 50–59. In addition, each 1-year increase in chronological age in the period before spousal loss was related to an increase in anti-infective medication use (OR 1.07; 95% CI 1.05 to 1.10). The interaction between age and widowhood indicator was significant (OR=0.96; 95% CI 0.94 to 0.99), indicating that the age-related increase in the use of anti-infective medications was slightly smaller in the period after than in the period before widowhood. In sex-specific samples, however, the interaction between age and widowhood indicator was not significant in both genders, indicating that the age-related increase in the anti-infective medication use was similar in the period before and the period after widowhood. In sex-specific models, CIs of age before widowhood (men: OR=1.08; 95% CI 1.04 to 1.12; women: OR=1.07; 95% CI 1.04 to 1.10) and after widowhood (men: OR=1.04; 95% CI 0.95 to 1.12; women: OR=1.04; 95% CI 0.98 to 1.10) overlap with those obtained from the analysis of the total population. Similarly, we found overlapping CIs for the interaction between age and widowhood indicator in sex-specific models with that in the model for the total population. These findings indicate that the age-related changes in anti-infective medication use are similar among men and women both before and after widowhood. To test whether widowhood effect on the use of anti-infective medications differs between men and women, we further interacted gender, age and widowhood indicator (see online supplementary appendix). None of the interactions reached statistically significant level.

Additional sensitivity analyses considering only those individuals who survived at least 5 years after widowhood and excluding individuals who were widowed at age 90 or older (table 3 for men and table 4 for women) yielded similar results. The use of anti-infective medications was higher in the period after widowhood than in the period before widowhood across all four subpopulations. The interaction between age and widowhood indicator was not significant in any of these subsamples, both men and women, suggesting that the increase in the use of anti-infective medications after widowhood is age-related.

DISCUSSION

In the present study, we hypothesised that after the loss of a spouse, the immune defences of men would be more compromised than those of women, and that the use of anti-infective medications following spousal loss would increase more among widowers than among widows. Our results indicate that the use of anti-infective medications is consistently higher among women prior to and after spousal loss. Our findings also show that both men and women use more anti-infective medications after than before widowhood, and that this change in the use of anti-infective medications is related to increasing age rather than the effect of spousal loss.

Similar results are obtained when the analysis is restricted to the individuals who survived at least 1, 3 and 5 years since spousal loss. However, it might still be possible that widowhood effect is time-dependent, with the negative effects declining over time. Indeed, the estimates of widowhood period in the sensitivity analysis suggest that the ATC-J use is higher after

widowhood than before in all subpopulations (men and women), but its intensity declines for those who survive longer than those who die closer to spousal loss.

Our finding that women used more anti-infective medications before and after widowhood than men is likely a reflection of a general tendency for women to take more medications and use more primary healthcare services than men,¹⁰ and of higher incidences of the most common infections, and especially of RTIs and UTIs, among women than among men.²⁹ Previous studies conducted in Denmark have shown that women tend to take more all-cause medications and visit general practitioners more frequently than men.¹⁰ These patterns may be partially explained by a greater reluctance among men than among women to seek medical advice in a timely manner.^{10,38} A study that examined a subsample of the elderly population in Italy found that the overall drug prescription rate was slightly higher among women than among men.³⁹ A comparison of healthcare use in 34 European countries showed that, on average, women have a greater propensity to seek primary healthcare than men, and that the gender gap tends to be smaller for serious symptoms and larger for minor complaints.⁴⁰

The results of the present study support the findings of a previous register-based study in Denmark, which found little support for gender-specific differences in all-cause and system-specific medication use from 1 year before up to 5 years after a conjugal loss.¹⁰ With the present longitudinal analysis, we were able to investigate whether there is a disruption in age-related changes in the use of anti-infective medications in the period after widowhood compared with the period before widowhood, and whether this disruption is gender-specific. We were able also to capture the effect of widowhood on the use of anti-infective medications, and to disentangle the age-related changes by distinguishing between the within-individual changes over time (age effects) and the between-individual changes that were present at the beginning of the study, and that persisted over time (cohort effects).

A major strength of the present study is that our analysis was register-based: that is, our sample size was large and almost all of the individuals examined were followed up. Thus, the chances of individuals being selected into or dropping out of the study for reasons other than death or emigration from the country were very low. Previous research has shown that DNPR has high levels of completeness and reliability, and is therefore a valid data source for empirical research.³¹

In most previous studies, the immune system function was measured using biological markers of health, an approach that involves invasive procedures and is very expensive to do on a large scale. The use of anti-infective medications as a proxy measure for immune system defences in epidemiological research substantially increases the study sample size with little costs. In Denmark, anti-infective medications are prescription-only drugs that are tracked by pharmacies for reimbursement purposes.³¹ According to the European Centre for Disease Prevention and Control, the average consumption of anti-infective medications in Denmark in 2015 was 17.1 daily defined dose per 1000 inhabitants/day. Compared with other European countries, Denmark is in the 77th lower percentile of anti-infective medication use, with Greece having the highest value (38.9) and the Netherlands having the lowest value (12.3). Dispensation of anti-infective medications based on prescriptions and

the relatively low levels of antibiotic use in Denmark suggest that the anti-infective medications taken in Denmark are likely prescribed in response to real individual health needs. Nevertheless, the use of anti-infective medications as a proxy measure for immune defences may still be limited. It is likely to capture only the changes in the immune defences that result in substantially increased susceptibility to various infections, whereas weakening of the immune defences to a smaller extent that does not result in an infection requiring treatment with anti-infective medication would not be captured. Future large-scale studies using biological markers of health may be able to reveal sex-specific declines in the immune defences after spousal loss.

It is possible that men tend to delay or avoid seeking medical treatment for infectious diseases unless the condition becomes severe and requires hospital treatment. We were unable to examine this issue using our data due to the small number of hospital admissions for infectious diseases in Denmark in the 1995–2012 period. Furthermore, because of the small number of admissions, we were unable to perform a similar analysis for different groups of anti-infective medications. In general, however, our results were driven by antibacterial prescriptions (ie, 97% of the anti-infective drugs prescribed to men and women 1 year after bereavement were antibacterials) for the treatment of common infections. Our results are consistent with the findings of a recent systematic review of gender differences in the use of antibiotics, which indicated that women are more likely than men to be prescribed antibiotics in their life course.²⁹

In conclusion, the present study has demonstrated that individuals use more anti-infective medications after becoming widowed than before becoming widowed, but this change is likely to be related to the increasing age and is similar among widowers and widows.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding KC received support from the US National Institutes of Health (P01AG031719, 2P01AG031719) and the VELUX Foundation. AO received support from the Max Planck Society within the framework of the project, 'On the edge of societies: New vulnerable populations, emerging challenges for social policies and future demands for social innovation. The experience of the Baltic Sea States (2016-2021)'. The funders had no role in the design of the study; or in the collection, analysis or interpretation of the data or the results.

References

1. Bozon M. Women and the age gap between spouses: an accepted domination? *Popul.* 1991; 3:113–48. [PubMed: 12157912]
2. Barford A, Dorling D, Davey Smith G, et al. Life expectancy: women now on top everywhere. *BMJ.* 2006; 332:808. [PubMed: 16601021]
3. Lichtenstein P, Gatz M, Berg S. A twin study of mortality after spousal bereavement. *Psychol Med.* 1998; 28:635–43. [PubMed: 9626719]
4. Martikainen P, Valkonen T. Mortality after the death of a spouse: rates and causes of death in a large Finnish cohort. *Am J Public Health.* 1996; 86:1087–93. [PubMed: 8712266]
5. Schaefer C, Quesenberry CP, Wi S. Mortality following conjugal bereavement and the effects of a shared environment. *Am J Epidemiol.* 1995; 141:1142–52. [PubMed: 7771452]

6. Moon JR, Kondo N, Glymour MM, et al. Widowhood and mortality: a meta-analysis. *PLoS One*. 2011; 6:e23465. [PubMed: 21858130]
7. Shor E, Roelfs DJ, Curreli M, et al. Widowhood and mortality: a meta-analysis and meta-regression. *Demography*. 2012; 49:575–606. [PubMed: 22427278]
8. Stroebe M, Schut H, Stroebe W. Health outcomes of bereavement. *Lancet*. 2007; 370:1960–73. [PubMed: 18068517]
9. Nihtilä E, Martikainen P. Institutionalization of older adults after the death of a spouse. *Am J Public Health*. 2008; 98:1228–34. [PubMed: 18511726]
10. Oksuzyan A, Jacobsen R, Glaser K, et al. Sex Differences in Medication and Primary Healthcare Use before and after Spousal Bereavement at Older Ages in Denmark: Nationwide Register Study of over 6000 Bereavements. *J Aging Res*. 2011; [Epub ahead of print 10 Aug 2011]. doi: 10.4061/2011/678289
11. Bowling A. Mortality after bereavement: a review of the literature on survival periods and factors affecting survival. *Soc Sci Med*. 1987; 24:117–24. [PubMed: 3551087]
12. Goldman N, Korenman S, Weinstein R. Marital status and health among the elderly. *Soc Sci Med*. 1995; 40:1717–30. [PubMed: 7660185]
13. Mineau GP, Smith KR, Bean LL. Historical trends of survival among widows and widowers. *Soc Sci Med*. 2002; 54:245–54. [PubMed: 11824929]
14. Stroebe M, Stroebe W, Schut H. Gender differences in adjustment to bereavement: An empirical and theoretical review. *Review of General Psychology*. 2001; 5:62–83.
15. Eng PM, Kawachi I, Fitzmaurice G, et al. Effects of marital transitions on changes in dietary and other health behaviours in US male health professionals. *J Epidemiol Community Health*. 2005; 59:56–62. [PubMed: 15598728]
16. Kassel JD, Stroud LR, Paronis CA. Smoking, stress, and negative affect: correlation, causation, and context across stages of smoking. *Psychol Bull*. 2003; 129:270–304. [PubMed: 12696841]
17. Stroebe MS, Stroebe W. Who suffers more? Sex differences in health risks of the widowed. *Psychol Bull*. 1983; 93:279–301. [PubMed: 6844474]
18. Vitlic A, Khanfer R, Lord JM, et al. Bereavement reduces neutrophil oxidative burst only in older adults: role of the HPA axis and immunosenescence. *Immun Ageing*. 2014; 11:13. [PubMed: 25191511]
19. Richardson VE, Bennett KM, Carr D, et al. How Does Bereavement Get Under the Skin? The Effects of Late-Life Spousal Loss on Cortisol Levels. *J Gerontol B Psychol Sci Soc Sci*. 2015; 70:341–7. [PubMed: 24259378]
20. Glaser R, Kiecolt-Glaser JK. Stress-induced immune dysfunction: implications for health. *Nat Rev Immunol*. 2005; 5:243–51. [PubMed: 15738954]
21. Khanfer R, Lord JM, Phillips AC. Neutrophil function and cortisol:DHEAS ratio in bereaved older adults. *Brain Behav Immun*. 2011; 25:1182–6. [PubMed: 21420485]
22. Gerra G, Monti D, Panerai AE, et al. Long-term immune-endocrine effects of bereavement: relationships with anxiety levels and mood. *Psychiatry Res*. 2003; 121:145–58. [PubMed: 14656449]
23. Kudielka BM, Kirschbaum C. Sex differences in HPA axis responses to stress: a review. *Biol Psychol*. 2005; 69:113–32. [PubMed: 15740829]
24. Bird CE, Rieker PP. Gender matters: an integrated model for understanding men's and women's health. *Soc Sci Med*. 1999; 48:745–55. [PubMed: 10190637]
25. Waldron I. Sex differences in human mortality: the role of genetic factors. *Soc Sci Med*. 1983; 17:321–33. [PubMed: 6344225]
26. Bouman A, Heineman MJ, Faas MM. Sex hormones and the immune response in humans. *Hum Reprod Update*. 2005; 11:411–23. [PubMed: 15817524]
27. Giefing-Kröll C, Berger P, Lepperdinger G, et al. How sex and age affect immune responses, susceptibility to infections, and response to vaccination. *Aging Cell*. 2015; 14:309–21. [PubMed: 25720438]
28. Whitacre CC. Sex differences in autoimmune disease. *Nat Immunol*. 2001; 2:777–80. [PubMed: 11526384]

29. Schröder W, Sommer H, Gladstone BP, et al. Gender differences in antibiotic prescribing in the community: a systematic review and meta-analysis. *J Antimicrob Chemother.* 2016; 71:1800–6. [PubMed: 27040304]
30. Schooling CM. Could androgens be relevant to partly explain why men have lower life expectancy than women? *J Epidemiol Community Health.* 2016; 70:324–8. [PubMed: 26659456]
31. Kildemoes HW, Sørensen HT, Hallas J. The Danish National Prescription Registry. *Scand J Public Health.* 2011; 39:38–41. [PubMed: 21775349]
32. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health.* 2011; 39:22–5. [PubMed: 21775345]
33. Goossens H, Ferech M, Vander Stichele R, et al. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet.* 2005; 365:579–87. [PubMed: 15708101]
34. Neuhaus JM, Kalbfleisch JD. Between- and within-cluster covariate effects in the analysis of clustered data. *Biometrics.* 1998; 54:638–45. [PubMed: 9629647]
35. Krishnakumar, J. Time Invariant Variables and Panel Data Models: A Generalised Frisch–Waugh Theorem and its Implications. In: Baltagi, BH., editor. *Panel Data Econometrics: Theoretical Contributions and Empirical Applications.* Elsevier; 2006. p. 119-32.
36. Diggle, PJ., Heagerty, PJ., Liang, K-Y., et al. *Analysis of longitudinal data.* Oxford University Press; 2002. p. 1-18.
37. Wastesson JW, Parker MG, Fastbom J, et al. Drug use in centenarians compared with nonagenarians and octogenarians in Sweden: a nationwide register-based study. *Age Ageing.* 2012; 41:218–24. [PubMed: 22130561]
38. Juel K, Christensen K. Are men seeking medical advice too late? Contacts to general practitioners and hospital admissions in Denmark 2005. *J Public Health.* 2008; 30:111–3.
39. Nobili A, Franchi C, Pasina L, et al. Drug utilization and polypharmacy in an Italian elderly population: the EPIFARM-Elderly Project. *Pharmacoepidemiol Drug Saf.* 2011; 18:1150–7.
40. van Loenen T, van den Berg MJ, Faber MJ, et al. Propensity to seek healthcare in different healthcare systems: analysis of patient data in 34 countries. *BMC Health Serv Res.* 2015; 15:465. [PubMed: 26453459]

What is already known on this subject?

- ▶ Adverse effects of spousal loss have been found for mortality, for physical disabilities, for mental health and for the risk of institutionalisation.
- ▶ Recent findings suggest that bereavement due to spousal loss is associated with a decline in general immune functions, and thus to increased susceptibility to infections among widowed individuals.
- ▶ Empirical evidence on the gender-specific effects of widowhood on mortality and health is controversial.

What this study adds?

- ▶ Danish men and women aged 50+ use more anti-infective medications after becoming widowed than before becoming widowed. This increase in the use of anti-infective medications after widowhood is likely to be related to increasing age rather than the effect of losing a spouse.
- ▶ The age-related increase in the use of anti-infective medications is similar among men and women.

Figure 1.

Anti-infective medication use 5 years before and 5 years after widowhood for women and men, stratified by age at widowhood. ATC, Anatomical Therapeutic Chemical.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Age distribution according to age at widowhood by gender

Age group	Men		Women		Total	
	n	%	n	%	n	%
50-59	84	4	176	4	260	4
60-69	445	22	1212	30	1657	27
70-79	747	37	1624	40	2371	39
80-89	639	32	961	24	1600	26
90+	105	5	83	2	188	3
Total	2020	100	4056	100	6076	100

Table 2

Anti-infective medication use before and after widowhood, mixed effect logistic regression model

	Total population (model 1)	Men (model 2)	Women (model 3)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (ageing effect)	1.07 (1.05 to 1.10)	1.08 (1.04 to 1.12)	1.07 (1.04 to 1.10)
Women (reference: men)	1.31 (1.21 to 1.42)		
Age at widowhood (reference: 50–59)			
60–69	1.13 (0.93 to 1.39)	1.57 (1.10 to 2.24)	0.98 (0.77 to 1.25)
70–79	1.42 (1.16 to 1.73)	2.15 (1.52 to 3.03)	1.18 (0.93 to 1.49)
80–89	1.77 (1.45 to 2.17)	2.48 (1.75 to 3.50)	1.53 (1.20 to 1.96)
90+	1.97 (1.50 to 2.60)	2.97 (1.94 to 4.54)	1.59 (1.11 to 2.29)
Period after widowhood (reference: period before)	1.47 (1.29 to 1.68)	1.62 (1.27 to 2.07)	1.40 (1.19 to 1.63)
Period after widowhood × age (ageing effect)	0.96 (0.94 to 0.99)	0.96 (0.91 to 1.00)	0.97 (0.94 to 1.00)
Constant	0.15 (0.12 to 0.19)	0.13 (0.09 to 0.19)	0.31 (0.25 to 0.39)
AIC	72 776	22 781	49 988
BIC	72 866	22 852	50 066
Number of persons	6076	2020	4056
Number of observations	61 761	19 704	42 057

AIC, Akaike information criterion; BIC, Bayesian information criterion.

Table 3

Anti-infective medication use before and after widowhood among individuals who survived at least 1, 3 or 5 years after widowhood, and excluding individuals widowed at ages 90+, mixed effect logistic regression model—men

	Survived at least 1 year after widowhood	Survived at least 3 years after widowhood	Survived at least 5 years after widowhood	Excluding 90+
Men	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (ageing effect)	1.06 (1.02 to 1.10)	1.06 (1.02 to 1.11)	1.05 (1.00 to 1.10)	1.08 (1.04 to 1.12)
Age at widowhood (reference: 50–59)				
60–69	1.53 (1.08 to 2.18)	1.50 (1.05 to 2.14)	1.42 (0.99 to 2.05)	1.57 (1.10 to 2.24)
70–79	2.05 (1.45 to 2.90)	1.94 (1.37 to 2.74)	1.77 (1.23 to 2.53)	2.14 (1.52 to 3.02)
80–89	2.24 (1.58 to 3.18)	2.11 (1.47 to 3.01)	1.86 (1.28 to 2.72)	2.47 (1.75 to 3.49)
90+	2.76 (1.74 to 4.40)	2.61 (1.56 to 4.38)	1.69 (0.83 to 3.44)	
Period after widowhood (reference: period before)	1.62 (1.26 to 2.07)	1.47 (1.12 to 1.92)	1.40 (1.05 to 1.87)	1.60 (1.24 to 2.05)
Period after widowhood × age (ageing effect)	0.98 (0.93 to 1.03)	0.98 (0.93 to 1.04)	0.99 (0.93 to 1.05)	0.96 (0.91 to 1.00)
Constant	0.14 (0.1 to 0.19)	0.13 (0.10 to 0.19)	0.15 (0.10 to 0.21)	0.14 (0.1 to 0.19)
AIC	21 095	18 298	15 430	15 430
BIC	21 165	18 368	15 498	15 498
Number of persons	1806	1501	1253	1915
Observations	18 420	16 137	13 783	18 869

AIC, Akaike information criterion; BIC, Bayesian information criterion.

Table 4

Anti-infective medication use before and after widowhood among individuals who survived at least 1, 3 or 5 years after widowhood, and excluding individuals widowed at ages 90+, mixed effect logistic regression model—women

	Survived at least 1 year after widowhood	Survived at least 3 years after widowhood	Survived at least 5 years after widowhood	Excluding 90+
Women	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (ageing effect)	1.06 (1.03 to 1.09)	1.05 (1.02 to 1.08)	1.04 (1.02 to 1.07)	1.07 (1.04 to 1.09)
Age at widowhood (reference: 50–59)				
60–69	0.97 (0.76 to 1.23)	0.97 (0.76 to 1.24)	0.94 (0.74 to 1.21)	0.98 (0.77 to 1.25)
70–79	1.14 (0.90 to 1.45)	1.12 (0.88 to 1.42)	1.08 (0.84 to 1.38)	1.18 (0.93 to 1.49)
80–89	1.49 (1.16 to 1.90)	1.42 (1.11 to 1.83)	1.33 (1.03 to 1.73)	1.53 (1.20 to 1.96)
90+	1.58 (1.09 to 2.28)	1.51 (0.99 to 2.29)	1.22 (0.74 to 1.98)	
Period after widowhood (reference: period before)	1.38 (1.17 to 1.62)	1.29 (1.09 to 1.52)	1.20 (1.01 to 1.42)	1.37 (1.17 to 1.61)
Period after widowhood × age (ageing effect)	0.98 (0.95 to 1.01)	0.99 (0.96 to 1.02)	1.00 (0.97 to 1.03)	0.97 (0.94 to 1.00)
Constant	0.32 (0.25 to 0.40)	0.32 (0.25 to 0.40)	0.33 (0.26 to 0.42)	0.31 (0.25 to 0.40)
AIC	48 615	45 442	41 172	49 058
BIC	48 693	45 519	41 248	49 127
Number of persons	3882	3553	3185	3973
Observations	41 010	38 540	35 035	41 336

AIC, Akaike information criterion; BIC, Bayesian information criterion.