

Widowhood and immune system: register-based study of anti-infective medication use in Denmark, 1995-2012

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Abstract

Spousal loss is a major life event that has negative implications with respect to health and mortality for the outliving spouse. In general, health disadvantages are found to be more pronounced for widowers than for widows and recent researches suggest that spousal loss compromises the immune defense among older individuals. However, it remains to be investigated whether the decline in the immune defense has a sex-specific pattern and, consequently, may contribute to the excess male mortality after widowhood. The aim of this study is to examine the changes in the immune system after widowhood and whether these changes are sex-specific. The register data available of the 5% sample of the total Danish population was used to address this research question. Drugs classified as Anti-Infectives for Systemic Use in the Anatomical Therapeutic Chemical Classification System (ATC- J) were used as a proxy of immune system. The study included a case-cohort comparison (widowed vs married individuals). Descriptive results show that women have a higher use of ATC-J drugs compared to men and this difference is more pronounced among widowed than among married controls. The ATC-J medication use increases after widowhood, and this increase is similar in men and women. Preliminary conclusions find no support for higher decline of immune system in widowers.

Introduction

Spousal loss is a major stressful life event that becomes more prevalent as individuals age. Widowhood is likely to change many aspects of daily life that, in turn, may be reflected on individual health and wellbeing.

Studies of health consequences after spousal loss suggest excess mortality after widowhood (Kaprio et al., 1987; Lichtenstein et al., 1998; Manor & Eisenbach, 2003) that has been found to be greater for men than for women (Martikainen et al., 1996; Erlangsen et al., 2004; Stroebe et al., 2007). Recent studies suggest that spousal loss compromises the immune defense among older individuals (Khanfer et al., 2011), and bereaved adults have a transiently increased risk of atrial fibrillation (Graff et al., 2016). However, it remains to be investigated whether the decline in the immune defense has a sex-specific pattern and, consequently, may contribute to the excess male mortality after widowhood. The aim of this study is to examine the changes in the immune system (using Anti-Infective medications as a proxy) after widowhood and whether these changes are sex-specific.

Data and method

Data from a 5% sample of the total Danish population register were used. All Danes alive and married by January 1, 1995 and widowed in the period from January 1, 1996 to December 31, 2011 who did not migrate outside Denmark were selected from Central Personal Register and linked to the Prescription Medicine Register (n= 47,042). Drugs classified as Anti-Infectives for Systemic Use in the Anatomical Therapeutic Chemical Classification System - named ATC-J - were used as proxy of immune system. The proportion of ATC-J users was calculated for one

year before and one year after the day of widowhood. Married individuals in the period from January 1, 1995 to at least one year after the age at bereavement of the widowed were randomly selected and matched on sex and age with every widowed person. The matching age was +/- 1 age at bereavement of the case group. Among this married sample 43% of the individuals (controls) become widowed afterwards (at least 1 year after their “hypothetical” widowhood). After a preliminary matching 26 individuals (18 women and 8 men) were without controls. These women were 8 in the age group 90-94 (0.52% of this age group) and 10 in age group 95+ (6.90% of this age group). The 8 men without controls were in age group 95+ (2.23% of this age group). All these cases still had no controls when the criteria were changed to +/- 2 years. The analysis of the medication use before and after widowhood with or without these 26 controls provided similar results so they were excluded from the analysis. The sample has 47,042 married individuals that were compared with 47,042 widowed individuals. Chi-square tests were used to examine sex differences in the prevalence of anti-infective drugs for systemic use both before and after widowhood, for cases and controls. The age at widowhood was categorized in 5-year age groups: 50-54, ..., 95+.

Preliminary results

In total, 47,042 bereaved individuals (67.04% women) and 47,042 married are included in the analysis. Figure 1 shows the percentage of men and women - both widowed and married sample-taking anti-infectives for systemic use 1 year before and 1 year after widowhood.

For the widowed sample the percentage of ATC-J increases with advancing age for both men and women. The proportion of ATC-J users increases after widowhood and this increase is similar for both men and women. Women have higher percentage of ATC-J use compared to men. The sex differences among widowed are statistically significant in all age groups except for

the youngest one year before and one year after the widowhood, and the oldest age group one year before the widowhood.

For the married sample the pattern is less clear. Table 1 shows the change in ATC-J use before and after widowhood. For the widowed sample there is an increase in anti-infectives use for both men and women. For the married sample this increase is not found.

Figure 1. Percentage of ATC-J users 1 year before and 1 year after the widowhood. Widowed and married sample.

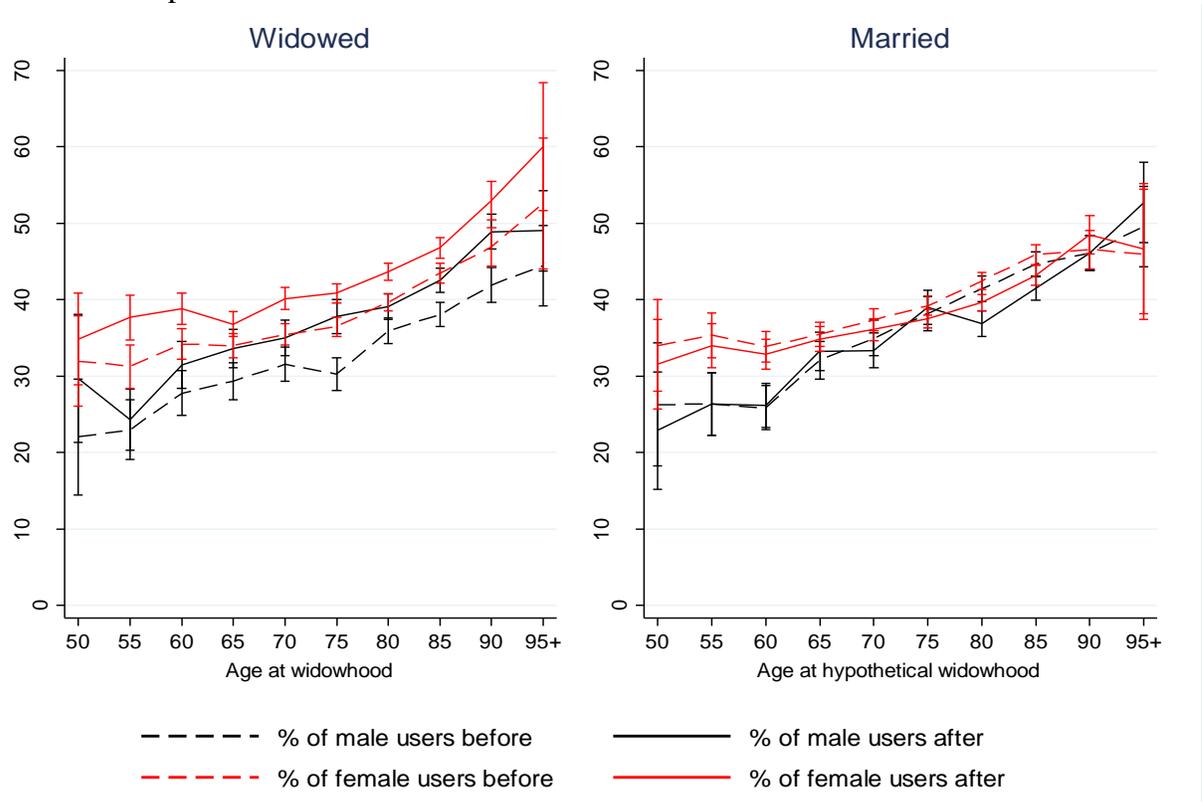


Table 1. Differences in the proportion of ATC-J users 1 year before and 1 year after widowhood

Age at widowhood	Widowed		Married	
	Men % (SE)	Women % (SE)	Men % (SE)	Women % (SE)
50-54	7.6 (4.8)	2.9 (3.7)	-3.4 (4.7)	-2.5 (3.7)
55-59	1.4 (2.5)	6.4 (1.8)	0.0 (2.6)	-1.4 (1.7)
60-64	3.7 (1.9)	4.6 (1.3)	0.3 (1.8)	-1.0 (1.2)
65-69	4.3 (1.5)	2.8 (1.0)	1.2 (1.6)	-0.6 (1.0)
70-74	3.5 (1.4)	4.7 (0.9)	-1.6 (1.4)	-1.3 (0.9)
75-79	7.5 (1.3)	4.4 (0.7)	0.8 (1.4)	-1.7 (0.8)
80-84	3.1 (1.0)	4.0 (0.7)	-4.5 (1.1)	-2.9 (0.7)
85-89	4.5 (1.0)	3.3 (0.8)	-3.2 (1.0)	-2.7 (0.9)
90-94	7.0 (1.4)	6.1 (1.5)	0.0 (1.5)	1.9 (1.6)
95+	4.6 (3.2)	7.4 (5.5)	3.1 (3.1)	0.7 (5.4)

Preliminary conclusions

Preliminary descriptive results suggest that the ATC-J medication use increases within a year after widowhood and the increase is similar in men and women. The study supports previous findings that the immune defense decline after spousal loss. Contrary to our initial hypothesis, these results suggest that the decline in immune defense is similar in both genders.

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