Age-Related Response to Redeemed Antidepressants Measured by Completed Suicide in Older Adults: A Nationwide Cohort Study

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Objective: *To examine if the suicide rate of older adults prescribed antidepressants varies with age and to assess the proportion of older adults who died by suicide that had recently been prescribed antidepressants.* **Methods:** *A population-based cohort study using a nationwide linkage of individual-level records was conducted on all persons aged 50+ living in Denmark during 1996–2006 (1,215,524 men and 1,343,568 women). Suicide rates by treatment status were calculated using data on all antidepressant prescriptions redeemed at pharmacies.* **Results:** *Individual-level data covered 9,354,620 and 10,720,639 person-years for men and women, respectively. Men aged 50–59 who received antidepressants had a mean suicide rate of 185 (95% confidence interval [CI]: 160–211) per 100,000, whereas for those aged 80+ the rate was 119 (95% CI: 91–146). For women, the corresponding values were 82 (95% CI: 70–94) and 28 (95% CI: 20–35). Logistic regression showed a 2% and 3% decline in the rate for men and women, respectively, considered in treatment with antidepressants, with each additional year of age. An opposite trend was found for persons not in treatment. Fewer persons aged 80+ dying by suicide had received antidepressant prescriptions during the last months of life than younger persons.* **Conclusion:** *An age-dependent decline in suicide rate for antidepressant recipients was identified. One reason could be that older adults respond better to antidepressants than younger age groups. Still, the increasing gap with age between estimated prevalence of depression and antidepressant prescription rate in persons dying by suicide underscores the need for assessment of depression in the oldest old.* (Am J Geriatr Psychiatry 2014; 22:25–33)

Key Words: Aged, elderly, oldest old, suicide, antidepressant

On a worldwide level, suicide rates are highest in later life.[1] It has been emphasized that older adults are a diverse population, and suicidal behavior should not be examined as a unitary phenomenon among those over age 65.[2] Although antidepressants are indicated treatment for major

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depression in mid- and late life and major depression is a strong risk factor for suicide,[3–6] little is known about their impact on rate of suicide in older adults. Research indicates a complex association between antidepressants, age, and suicide. A meta-analysis of 372 double-blinded, randomized trials found a higher relative risk of suicidal ideation and behavior for participants under age 25, no effect for those aged 25–64, and reduced risk for those aged 65 and over when comparing antidepressant treatment with placebo.[7] This finding is partially supported by other studies.[8–11] Nevertheless, the indication of benefit with respect to suicide risk in older adults warrants further examination.

Although the rate of major depression in the general population seems to decrease with age,[12] more than 7% of older adults have been found to present clinically significant symptoms of depression.[13,14] In several developed countries, antidepressants are prescribed more frequently to older adults than to younger age groups.[15–18] Still, depression is widely under-treated in older adults.[19–21] Furthermore, the proportion of suicides with major depression seems to increase with age into later life.[22] Moreover, a substantial share of older adults dying by suicide are considered to suffer from an unidentified and untreated depression.[23] As a means of reducing suicide-related morbidity and mortality in older adults, detection and treatment of depression has been heavily emphasized.[24,25]

It is striking contrast that older adults are more likely to be treated with antidepressant medications than younger people despite their lower prevalence of affective disorder. The increasing population share of older adults underlines the importance of examining suicide risks associated with antidepressant medications, particularly when considering suicide's close association to depression and the fact that suicide rates increase with age. Also, is relevant to estimate how large a proportion of older adults dying by suicide are not in treatment with antidepressants.

Our primary objective was to examine whether the relationship between antidepressant exposure and suicide differs as a function of age. Second, we examined if the proportion of persons redeeming antidepressants during the last months before dying by suicide varied by age. Danish linkage records allowed us to address these questions using nationwide longitudinal data.

METHODS

Register records on all persons living in Denmark during January 1, 1996, through December 31, 2006, were assessed. In Denmark, a unique personal identifier enables linkage on an individual level of various administrative registers, such as the Centralized Civil Register and the Registry of Causes of Death.

An open and dynamic cohort study design was applied by including all persons aged 50 years and over. People who reached the age of 50 years after January 1, 1996, entered the study sample on the date of their 50th birthday. Persons migrating in or out of the country were left- or right-hand truncated at the date of the respective event. Similarly, persons dying by causes other than suicide were censored on the date of death. The observation period ended on December 31, 2006. The event of interest, death by suicide, was defined as deaths recorded as suicide according to the 10th revision of the *International Classification of Diseases and Related Health Problems*[26] or where the manner of death was stated as suicide.

Measures

Information on all antidepressants handed out at pharmacies, including date, drug type, and number of pills, is available since January 1, 1995 in the Register of Medicinal Product Statistics. Antidepressants are only available on prescription in Denmark. Pharmacies, furthermore, deliver medication to the homes of people with limited mobility. Drugs were grouped into tricyclic antidepressants (N06AA), selective serotonin reuptake inhibitors (SSRI: N06AB), and other types of antidepressants (N06AF, N06AG, and N06AX).

Using these data, it is possible to follow prescription patterns over time for each individual and form consecutive treatment periods. A person was considered in treatment with antidepressants from the date when a second prescription in a consecutive series was handed in at a pharmacy. The second prescription was preferred over the first because a substantial proportion of people discontinue treatment with antidepressants after having redeemed only one prescription.[27] In addition, 4 weeks of treatment is likely to show evidence of improvement in those who will respond to treatment,[28] a period that in many cases is equivalent to the length of the first prescription. Based on number of pills dispensed, we

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