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ORIGINAL RESEARCH ARTICLE

Use of Psychoactive Medications and Risk of Suicide in Late Life (75+): A Total Population Study

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Abstract

Background Psychoactive medications play an important role for the mental health and risk of suicidal behaviour in the oldest segment of the population (75+). A better understanding of psychoactive medication use is advocated to prevent suicide in this age group.

Purpose We investigated the risk of suicide associated with the use of psychoactive medications in the total population aged ≥ 75 years, with and without exposure to antidepressants.

Method A national population-based register study, including all Swedish residents aged ≥ 75 years between 2006 and 2014 ($N = 1{,}413{,}806$). A nested case–control design was used to investigate psychoactive medications associated with suicide among users and non-users of antidepressants. Risk estimates were calculated in adjusted conditional logistic regression models for the entire cohort and by gender.

Results Suicide occurred in 1305 persons (907 men and 398 women). Among them, 555 (42.5%) were on an antidepressant at the time of suicide. Adjusted incidence rate ratio (aIRR) for suicide was increased in those who were on hypnotics in the total cohort (aIRR 2.05, 95% confidence interval 1.74 to 2.41), in both users and non-users of antidepressants and for both genders. Elevated suicide risk was observed in those who concomitantly used anxiolytics with antidepressants (1.51, 1.25 to 1.83). Decreased risk of suicide was observed among those who were on anti-dementia drugs, in the total cohort (0.33, 0.21 to 0.52) and in both users and non-users of antidepressants. Use of antipsychotics and mood stabilisers showed no effect on suicide risk.

Conclusion Use of hypnotics and concomitant use of anxiolytics with antidepressants was associated with increased risk of late-life suicide. Our findings suggest the need for careful evaluation of the benefit–risk balance of psychoactive medications as well as their availability as a possible suicide means. Future research should consider the indication of use of the psychoactive medications and the severity of psychiatric and medical illnesses of the patients.

Key Points

Risk of suicide was increased in older adults who were using prescribed sleep medications.

Concomitant use of anxiolytics and antidepressants was associated with heightened risk of suicide in older adults.

There is a need of careful monitoring of older adults prescribed psychoactive medication to reduce risk of suicide.

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1 Introduction

Suicide rates are the highest in the oldest population [1]. Older adults who die by suicide are often depressed, or have other psychiatric morbidities [2, 3]. Therefore, treatment of depression and other psychiatric conditions is a major suicide prevention strategy in this age group.

Psychoactive medications are widely prescribed to older adults to treat behavioural and psychological symptoms associated with increased risk of suicidal behaviour [4–6]. Among older adults aged 75+ in Sweden, about four out of ten are prescribed psycholeptic medications (antipsychotics, hypnotics or anxiolytics) and about one-fifth are on antidepressants [7]. Psychoactive medications are commonly used for suicide [8, 9]. Further, emergency department visits for self-harm involving prescribed medications are significantly more common in older adults [10]. Yet, some research has shown that antidepressants and lithium, may be protective of suicidal behaviour [11, 12]. Taken together, psychoactive medications play an important role for the mental health and risk of suicidal behaviour among older people.

Surprisingly, only a few pharmacoepidemiological studies have investigated how the use of psychoactive medications may impact the risk of suicide in older adults [11, 13–16]. None of these were conducted in the 75+ segment of the general population. Findings from research that includes "younger old" adults are not appropriate to extrapolate to the "older old" adult population (75+) as use patterns, treatment response and side effects of psychoactive medications differ with age due to higher levels of comorbidities and age-related physiological changes [17].

A better understanding of psychoactive medication use is advocated to prevent late-life suicide. Such knowledge will help to inform healthcare practitioners for a better monitoring of their older patients at risk and to contribute to improvement of the quality and safety of prescribing for a particularly sensitive and vulnerable age group with high consumption of psychoactive medications.

The availability of high-quality national registers in Sweden with full population coverage offers unique opportunities to examine with real-world big data how the use of psychoactive medications may affect the risk of late-life suicide with enough power, and without selection or recall bias. Gender-specific data are essential in this connection as older adult women consume more psychoactive medications [18] and show better adherence to suicide-preventive programmes [19], while suicide rates are far higher in men in this age group [20].

We recently conducted a large national study to investigate late-life suicidal behaviour among new users of antidepressants aged 75 years and older in Sweden [13]. We found an increased risk of suicidal behaviour among antidepressant users who concomitantly used anxiolytics, hypnotics or antipsychotics suggesting a need of close monitoring. Risk was decreased in those with anti-dementia medications while no significant effect was found in those on mood stabilisers. New users make up only a small proportion of all antidepressant users in this age group, as duration of antidepressant treatment tends to be long in older adults. We therefore aimed to investigate the risk of suicide associated with the use of psychoactive medications in the total population aged 75+, and with respect to treatment with antidepressants.

2 Methods

2.1 Study Design and Study Population

We conducted a population-based register study including all Swedish residents aged 75 and over between 1 January 2006 and 30 June 2014. All were followed from the time they fulfilled the eligibility criteria until 31 December 2014, or censored at migration or death occurring during the study period.

2.2 Data Sources

Data from multiple national registers were linked through the unique personal identity number [21]. Older adults aged 75 and over were identified from the total population register. The Swedish Prescribed Drug Register was employed to identify users of antidepressants and other psychoactive medications [22]. The register has full coverage of redeemed prescribed medications in outpatient care and in long-term care facilities. It contains information on the name of the dispensed medications, the Anatomic Therapeutic Class (ATC), the amount of medication dispensed, the prescribed daily dose, and the date of dispensing. The National Patient Register includes diagnoses for specialised inpatient and outpatient healthcare based on the International Classification of Diseases, 10th version (ICD-10) [23]. This register was used to identify individuals with an episode of non-fatal self-harm. It was also used to identify depression requiring specialised healthcare, considered as serious depression, since the common practice in Sweden is that milder forms of depression are treated within primary care and more serious cases are referred to specialised inpatient or outpatient services [24]. Data on the cause of death, including suicide, were collected from the Cause of Death Register [25]. Residents in long-term care facilities were identified from the National Care and Social Service

database. Sociodemographic data were collected from Statistics Sweden.

2.3 Use of Antidepressants and of Other Psychoactive Medications

Antidepressants were defined as substances included in the ATC N06A, with the exception of tricyclics (N06AA), as these medications are primarily prescribed to older adults for chronic pain conditions in Sweden. The other psychoactive medications were classified as: antipsychotics [N05A, except lithium (N05AN01), which is used as a mood stabiliser], anxiolytics (N05B), hypnotics (N05C), anti-dementia drugs (N06D) and mood stabilisers (N03AF01, N03AG01, N03AX09, N05AN01). To avoid an immortal bias, the use of antidepressants and other psychoactive medications was assessed within 90 days prior to the start of observation period and prior to the occurrence of suicide or study end. This period was chosen on the basis of the Swedish Pharmaceutical Benefits Scheme, by which patients can purchase 3 months' supply. For persons with multidose prescriptions, a period of 30 days was considered sufficient as these prescriptions are, in most cases, automatically renewed every 2 weeks. Concomitant use of an antidepressant and another psychoactive medication was assessed on the basis of the supply periods covered by both medications.

2.4 Study Outcome

Persons who died by suicide were identified from the Cause of Death Register on the basis of the ICD-10 codes: intentional self-harm (X60–X84) and harm of undetermined intent (Y10–Y34), as well as sequelae of intentional self-harm (Y87.0) and events of undetermined intent (Y87.2).

2.5 Covariates

Covariates found to be associated with both use of psychoactive medications and late-life suicide were considered: past-year episode of non-fatal self-harm and use of specialised care for depression, as a proxy for serious depression. We also considered sociodemographic characteristics: marital status, country of birth, residence in a long-term care facility, highest attained level of education and occupation category at retirement [27].

2.6 Statistical Analysis

The characteristics of those who were users and non-users of antidepressants at baseline were compared using chi-square tests. A nested case–control design was used to investigate the psychoactive medications associated with suicide in the total cohort and among users and non-users of antidepressants separately. Each person who died by suicide was matched with 50 living individuals of the same gender and age group. The nested case–control data were analysed using conditional logistic regression with each case and its controls forming a separate stratum. User status with regard to antidepressants and other psychoactive medications was considered at the time of suicide in the regression analysis. User status of all considered psychoactive medications was included in the adjusted models including all the covariates. Gender interaction was incorporated into the model. Analyses were stratified by gender. Owing to the rarity of suicide, estimated odds ratios may be considered incidence rate ratios (IRRs) [26]. *P* values and 95% confidence intervals (CIs) were reported. Data analyses were performed by SAS version 9.4 (SAS Institute Inc, NC, USA).

3 Results

Characteristics at baseline are presented in Table 1 for the total population aged 75+ ($N = 1{,}413{,}806$). The mean age was 80.5 years, and nearly six out of ten were women. One-fourth (26%) were users of antidepressants. Hypnotics were the most commonly prescribed psychoactive medications, used by about one-third of all older adults aged 75 and above (58.1% in users of antidepressants versus 26.9% in the non-users). Anxiolytics were used by about one-fourth of the cohort; about half of the antidepressant users and one-tenth in the non-users. Use of all psychoactive medications was more common in antidepressant users. Mood stabilisers were the least prescribed, used by about 2% of the total cohort.

Suicide occurred in 1305 persons (907 men and 398 women). Among them, 555 (42.5%) were on antidepressants at the time of suicide. Hanging was the most common method of suicide, followed by poisoning. Details of rates and methods of suicide in the total cohort and per gender, in users and non-users of antidepressants were previously reported [27]. At the time of suicide, more than half ($n = 690$) were on a hypnotic, about one-third ($n = 446$) were on an anxiolytic, and 1 out of 12 were on an antipsychotic ($n = 106$). Only 3% ($n = 39$) were on a mood stabiliser, and 1.8% ($n = 23$) were on an anti-dementia medication.

Use of hypnotics was associated with a two-fold increased risk of suicide in the total cohort (IRR 2.05, 95% CI 1.74–2.41), and in both users and non-users of antidepressants (Table 2). In the total cohort, risk of suicide was also increased in users of anxiolytics (IRR 1.34, 95% CI 1.16–1.55) but stratification by antidepressant use revealed increased risk in antidepressant users only (IRR 1.51, 95% CI 1.25–1.83). Use of anti-dementia medications was, however, associated a lower risk of suicide regardless of antidepressant use status. Use of mood stabilisers and antipsychotics did not have an effect on the risk of suicide.

Table 1 Characteristics of old adults aged 75+[a] users and non-users of antidepressants[b] and other psychoactive medications ($N = 1{,}413{,}806$)

Characteristics	All 75+ ($N = 1{,}413{,}806$) *n* (%)	Non-users of anti-depressants ($N = 1{,}004{,}641$) *n* (%)	Users of anti-depressants ($N = 373\ 661$) *n* (%)	*p*-value
Age category				
75–79	765,950 (54.2)	605,939 (60.3)	139,170 (37.2)	< 0.0001[c]
80–84	287,801 (20.4)	182,111 (18.1)	98,143 (2.36)	
85–89	220,091 (15.6)	130,342 (13.0)	84,983 (22.7)	
≥ 90	139,964 (9.9)	86,249 (8.6)	51,365 (13.7)	
Women	817,154 (57.8)	542,276 (54.0)	250,565 (67.1)	< 0.0001[d]
Men	596,652 (42.2)	462,365 (46.0)	123,096 (32.9)	< 0.0001[d]
Use of other psychoactive medications				
Hypnotics	487,993 (34.5)	270,732 (26.9)	217,261 (58.1)	< 0.0001[d]
Anxiolytics	338,795 (24.0)	157,233 (11.1)	181,562 (48.5)	< 0.0001[d]
Antipsychotics	86,573 (6.1)	40,610 (2.9)	45,963 (12.3)	< 0.0001[d]
Anti-dementia	70,798 (5.0)	31,127 (2.2)	39,671 (10.6)	< 0.0001[d]
Mood stabilisers	31,789 (2.2)	17,944 (1.3)	13,845 (3.7)	< 0.0001[d]
Previous episode of self-harm	1952 (0.1)	400 (0.04)	1524 (0.4)	< 0.0001[d]
Specialised care for depression	26,395 (1.9)	7406 (0.7)	18,075 (4.8)	< 0.0001[d]
Residence in a long-term care facility	120,949 (8.6)	39,310 (3.9)	79,797 (21.4)	< 0.0001[d]

[a]Residents in Sweden between 2006 and 2014

[b]Persons taking tricyclic antidepressants and no other type of antidepressant ($n = 35{,}504$) were excluded from the subgroup analysis

[c]The χ^2 test for variables with multiple categories to test for differences across categories

[d]The χ^2 test for dichotomous variable to establish if there are differences between users and non-users of antidepressants

Similar results were obtained for the associations between the use of psychoactive medications and suicide in the gender-stratified analyses (Table 2). However, for antipsychotics, a decreased risk of suicide was found in men not treated with antidepressants. The association between use of hypnotics and suicide was no longer significant in women without antidepressant treatment, but this finding should be interpreted with caution due to the relatively small number of suicide cases in the stratified analyses.

4 Discussion

In this national study of the total Swedish population aged 75 years and older, we found increased risk of suicide in those who used a hypnotic, as well as in persons on antidepressants who concomitantly used an anxiolytic. Use of anti-dementia medication was associated with a lower risk of suicide in persons both with and without antidepressants. Use of neither mood stabilisers nor antipsychotics was related to suicide risk.

Results of increased risk of suicide in users of hypnotics expand on the findings of our previous study conducted in new users of antidepressants aged 75+ [28], by demonstrating increased risk associated with hypnotics regardless of antidepressant use. One possible explanation for the observed risk increase may be that these drugs impair judgement, and may create behavioural confusion [29]. In our previous population-based research in which older adults took part in face-to-face psychiatric examinations, we have shown that sleep problems may be independent predictors of suicidality [30]. Toxicological studies conducted in mixed age groups found that modern hypnotics "Z-Drugs" were frequently taken before suicide deaths, often in combination with other sedatives or alcohol [31, 32]. However, there may be other mechanisms to explain this association, and this needs to be further explored. Steps for decreasing the risks of suicide when prescribing hypnotics have also been suggested [33].

Concomitant use of anxiolytics and antidepressants may indicate a more complex psychopathology, which could help to explain the finding of elevated suicide risk in older adults using both these drug types [34, 35]. Previous research has found that the occurrence of concomitant depression and anxiety is associated with more severe symptoms, poorer outcomes and a higher incidence of suicide [36–38]. Another consideration is that older adults from recent cohorts are less likely to abstain from alcohol compared with earlier-born cohorts [39], and possible interactions between these psychoactive medications and alcohol are to be considered [40].

Table 2 Incidence risk ratio of suicide in users of psychoactive medications in persons aged 75+, and in antidepressants users and non-users separately

Characteristics	All persons aged 75+			Non-users of antidepressants			Users of antidepressants		
	N case/control	Crude IRR (95% CI)	Adjusted IRR[a] (95% CI)	N case/control	Crude IRR (95% CI)	Adjusted IRR[a] (95% CI)	N case/control	Crude IRR (95% CI)	Adjusted IRR[a] (95% CI)
Total cohort									
Antipsychotic	106/9635	1.54*** (1.26–1.89)	0.98 (0.76–1.27)	32/2675	1.06 (0.74–1.52)	0.73 (0.46–1.14)	63/9225	1.24 (0.95–1.62)	1.07 (0.77–1.48)
Anxiolytics	446/40,867	1.82*** (1.62–2.04)	1.34*** (1.16–1.55)	156/11,807	1.26* (1.05–1.51)	1.07 (0.83–1.37)	257/33,559	1.75*** (1.48–2.07)	1.51*** (1.25–1.83)
Hypnotics	690/59,274	2.32*** (2.07–2.59)	2.05*** (1.74–2.41)	296/18,178	1.83*** (1.57–2.14)	1.87*** (1.34–2.6)	353/43,138	2.31*** (1.94–2.75)	2.12*** (1.74–2.58)
Anti-dementia	23/9303	0.32*** (0.21–0.49)	0.33*** (0.21–0.52)	13/2631	0.42** (0.24–0.73)	0.43** (0.23–0.8)	9/8916	0.16*** (0.08–0.31)	0.25*** (0.13–0.49)
Mood stabilisers	39/3593	1.43* (1.04–1.98)	0.88 (0.60–1.29)	14/1068	1.14 (0.67–1.95)	1.11 (0.61–1.99)	22/2626	1.47 (0.95–2.26)	0.74 (0.431–1.26)
Men									
Antipsychotic	56/4728	1.21 (0.92–1.60)	0.78 (0.56–1.08)	15/1713	0.67 (0.40–1.12)	0.42** (0.26–0.81)	37/4341	1.10 (0.78–1.56)	1.12 (0.76–1.66)
Anxiolytics	270/18,410	1.69*** (1.46–1.95)	1.33** (1.12–1.59)	104/7130	1.17 (0.94–1.46)	1.05 (0.78–1.42)	155/14,131	1.73*** (1.40–2.14)	1.55*** (1.22–1.97)
Hypnotics	439/27,620	2.16*** (1.90–2.47)	1.99*** (1.63–2.42)	207/11,132	1.76*** (1.47–2.10)	1.86** (1.25–2.76)	218/18,981	2.2*** (1.77–2.73)	2.03*** (1.59–2.58)
Anti-dementia	18/4709	0.37*** (0.23–0.59)	0.37*** (0.22–0.61)	11/1731	0.49* (0.27–0.90)	0.51 (0.26–1.02)	6/4229	0.17*** (0.08–0.38)	0.25*** (0.11–0.57)
Mood stabilisers	26/1963	1.32 (0.89–1.96)	0.95 (0.6 ; 1.487)	11/781	1.08 (0.59–1.97)	1.18 (0.60–2.3)	13/1361	1.25 (0.71–2.19)	0.74 (0.39–1.43)
Women									
Antipsychotic	50/4907	2.24*** (1.65–3.03)	1.54* (1.02–2.33)	17/962	2.26** (1.35–3.78)	1.73 (0.86–3.46)	26/4884	1.50 (0.98–2.27)	0.96 (0.53–1.74)
Anxiolytics	176/22,457	2.09*** (1.71–2.56)	1.31* (1.02–1.69)	52/4677	1.49* (1.07–2.08)	1.04 (0.65–1.65)	102/19,428	1.78*** (1.34–2.35)	1.46* (1.05–2.03)
Hypnotics	251/31,654	2.72*** (2.21–3.34)	2.20*** (1.64–2.96)	89/7046	2.09*** (1.53–2.86)	1.78 (0.93–3.42)	135/24,157	2.53*** (1.88–3.40)	2.30*** (1.63–3.26)
Anti-dementia	5/4594	0.22*** (0.09–0.52)	0.25** (0.10–0.62)	2/900	0.29* (0.06–0.97)	0.24 (0.06–1.03)	3/4687	0.15** (0.05–0.47)	0.26* (0.08–0.83)
Mood stabilisers	13/1630	1.73 (0.98–3.02)	0.90 (0.43–1.86)	3/287	1.45 (0.46–4.62)	0.88 (0.24–3.25)	9/1265	1.95 (0.99–3.86)	0.77 (0.30–1.98)

[a]Adjusted for age, use of specialised care for depression, residence in a long-term care facility : marital status, country of birth, highest attained level of education, occupation category at retirement and episode of non-fatal self-harm within 1 year preceding suicide or end of study

CI, confidence interval; IRR, incidence risk ratio; *N*, number

Alcohol use may intensify impulsive tendencies, thereby increasing risk of suicidal behaviour.

The lower risk of suicide among users of anti-dementia drugs is likely to be explained, at least in part, by confounding by indication. There is some evidence that clinical dementia is associated with lower risk of suicidal behaviour [3, 41, 42]. Further, a recent meta-analysis of clinical trials including persons with Alzheimer's disease suggested a beneficial effect of continuing anti-dementia medications on neuropsychiatric symptoms, including agitation, depression, delusions, hallucinations and sleep impairment [43]. These symptoms were previously found to be associated with increased risk of suicide. However, the evidence was moderate and future research should also consider the type and stage of dementia to better understand any effect of anti-dementia medications on occurrence of suicide. The degree of cognitive decline is important to consider here as research suggests that early-stage dementia is associated with elevated suicide risk [44, 45].

Antipsychotics did not have a significant effect on suicide in our cohort. Antipsychotics are used in late life for a wide variety of indications including psychotic disorders, bipolar depression and treatment-resistant depression. These medications are also used off-label for a large spectrum of behavioural symptoms in dementia [5, 46]. We were not able to adjust for indication and confounding by indication must be considered. Mood stabilisers were rarely used and did not have an effect on suicide risk in our cohort. We could not investigate lithium use due to the small number of persons using this medication, but we note that the authors of a recent meta-analysis that included randomised trials including adults of mixed ages found inconclusive results for an anti-suicidal effect of lithium [47].

4.1 Methodological considerations

The study is based on national register-based data, minimising the risk of selection or recall bias. While we adjusted our regression models for several known confounders, our study design did not allow investigating other factors, such as substance misuse and family history of psychiatric disorders, nor did we have details about the indication of use of a specific psychoactive medication. Therefore, indication biases are to be considered [48]. Moreover, while previous research showed that a high proportion of older adults aged 65+ who died by suicide had untreated mental disorders [49], our research approach did not allow for the identification of such cases, nor could we identify depressed patients with primary care contact only as they are not included in the National Patient Register. Even milder forms of depression may be associated with suicidal behaviour in older adults [50], and it is unclear whether odds ratios in our adjusted models might have been attenuated. Our data covered the period from the start of the Swedish Prescribed Drug Register to the end of 2014, and some prescribing practices may have changed. However, statistics indicate a stable proportion of 75+ users of psychoactive medications in recent years [7]. We did not use any analytical method to address the variation in exposure to psychoactive medications over time. Our approach to consider in the regression models the latest exposure status to each of the considered psychoactive medications to assess their association with risk of suicide allowed to consider those who either started or stopped medications after the start of the study. We did not consider specific use patterns such as switching or discontinuation of medications as that was beyond the scope of the study. The use of medications was based on dispensed data, and it was not possible to assess the effect of non-adherence to medications as the majority of persons aged 75+ in Sweden have this multidose prescribing, which automatically creates high refill adherence. Therefore, some individuals classified as users may not have taken their medications as prescribed.

While poisoning was a common method of suicide (25% of all suicides) [27], our data lacked detail on the specific agent. The lack of data on psychiatric and somatic comorbidities other than serious depression is a significant limitation. Previous research focusing on older adults aged 65+ showed increased risk of suicide in persons diagnosed with cancer, neurological disorders, pain, chronic obstructive pulmonary disease, liver disease, male genital disorders, arthritis/arthrosis [50] and stroke [51]. More research is needed on possible sociodemographic and clinical mediators influencing the association of use of psychoactive medications and suicide in the oldest segment of the population. Our study design did not enable identification of deaths due to indirect suicidal behaviour as such deaths are not classified as suicide in the National Cause of Death Register.

5 Conclusion

Our results underline the importance of careful evaluation of the benefit risk balance of anxiolytics and hypnotics as well as their availability as possible suicide means in older adults. Our findings may help to inform the prescribers about psychoactive medications associated with an increased risk of suicide and which may require a closer monitoring. Future research should consider the indication of use and the clinical characteristics of patients.

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Declarations

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Conflicts of Interest Khedidja Hedna (KH) and Margda Waern (MW) declare that they have no conflict of interest.

Data Sharing Statement The datasets generated during and/or analysed during the current study are not publicly available due to the sensitive nature. According to the Swedish Ethical Review Act, the Personal Data Act and the Administrative Procedure Act, data can be made available after legal review for researchers who meet the criteria for access to this type of sensitive and confidential data. For questions about this, please contact KH (Khedidja.hedna@neuro.gu.se). Aggregated data may be available from Statistics Sweden or from the National Board of Health and Welfare upon request.

Ethics Approval The study was approved by the Regional Ethical Review Board in Gothenburg (no. 111-15) in accordance with national regulations.

Consent to Participate No consent was required as no patients were recruited. The study is based solely on national register data. All data were matched by Statistics Sweden and anonymised before delivery.

Description of Authors' Roles KH designed and planned the study, organised data collection, participated in the analysis of data and interpretation of the results, and drafted the manuscript. MW is the principal investigator of the project. She acquired funding and contributed to data collection and interpretation, and she took part in the writing of the manuscript. Authors declare that they read and approved the manuscript prior to its submission.

References

1. Naghavi M. Global, regional, and national burden of suicide mortality 1990 to 2016: systematic analysis for the Global Burden of Disease Study 2016. BMJ. 2019;364: l94.
2. Hunt IM, Kapur N, Robinson J, et al. Suicide within 12 months of mental health service contact in different age and diagnostic groups: National clinical survey. BJPsych. 2006;188:135–42.
3. Harwood D, Hawton K, Hope T, Jacoby R. Psychiatric disorder and personality factors associated with suicide in older people: a descriptive and case–control study. Int J Geriatr Psychiatry. 2001;16:155–65.
4. Lenze EJ, Ajam OH. Antidepressant treatment for late-life depression: considering risks and benefits. J Am Geriatr Soc. 2019;67:1555–6.
5. McKean A, Monasterio E. Indications of atypical antipsychotics in the elderly. Expert Rev Clin Pharmacol. 2015;8:5–7.
6. Gerlach LB, Wiechers IR, Maust DT. Prescription benzodiazepine use among older adults: a critical review. Harv Rev Psychiatry. 2018;26:264–73.
7. Swedish National Board of Health and Welfare. Statistical database for medications 2008–2020. https://sdb.socialstyrelsen.se/if_lak/val.aspx. Accessed 30 Mar 2023.
8. Gibson CJ, Li Y, Jasuja GK, Keyhani S, Byers AL. Long-term psychoactive medications, polypharmacy, and risk of suicide and unintended overdose death among midlife and older women veterans. J Gen Intern Med. 2022;37:770–7.
9. Darke S, Duflou J, Torok M. Toxicology and circumstances of completed suicide by means other than overdose. J Forensic Sci. 2009;54:490–4.
10. Geller AI, Ehlman DC, Lovegrove MC, Budnitz DS. National estimates of emergency department visits for medication-related self-harm: United States, 2016–2019. Inj Prev. 2022;28:545–52.
11. Hedna K, Fastbom J, Jonson M, Wilhelmson K, Waern M. Psychoactive medication use and risk of suicide in long-term care facility residents. Int J Geriatr Psychiatry. 2022. https://doi.org/10.1002/gps.5684.
12. Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant medication use and rate of suicide. Arch Gen Psychiatry. 2005;62:165–72.
13. Hedna K, Andersson Sundell K, Hamidi A, Skoog I, Gustavsson S, Waern M. Antidepressants and suicidal behaviour in late life: a prospective population-based study of use patterns in new users aged 75 and above. Eur J Clin Pharmacol. 2018;74(2):201–8.
14. Erlangsen A, Bille-Brahe U, Jeune B. Differences in suicide between the old and the oldest old. J Gerontol B Psychol Sci Soc Sci. 2003;58:S314–22.
15. Erlangsen A, Agerbo E, Hawton K, Conwell Y. Early discontinuation of antidepressant treatment and suicide risk among persons aged 50 and over: a population-based register study. J Affect Disord. 2009;119:194–9.
16. Erlangsen A, Conwell Y. Age-related response to redeemed antidepressants measured by completed suicide in older adults: a nationwide cohort study. Am J Geriatr Psychiatry. 2014;22:25–33.
17. Reynolds CF III, Frank E, Kupfer DJ, Thase ME. Treatment outcome in recurrent major depression: a post hoc comparison of elderly "young old" and midlife patients. Am J Psychiatry. 1996;153:1288.
18. Swedish National Board of Health and Welfare. Statistics on Pharmaceuticals 2018. https://www.socialstyrelsen.se/statistik/statistikdatabas/lakemedel. Accessed 30 Mar 2023.
19. Lapierre S, Erlangsen A, Waern M, et al. A systematic review of elderly suicide prevention programs. Crisis. 2011;32:88–98.
20. Swedish National Board of Health and Welfare. Statistics on causes of death 2019. https://www.socialstyrelsen.se/statistik-och-data/statistik/alla-statistikamnen/dodsorsaker/. Accessed 30 Mar 2023.
21. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekbom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. Eur J Epidemiol. 2009;24:659–67.
22. Wettermark B, Hammar N, MichaelFored C, et al. The new Swedish prescribed drug register—opportunities for

pharmacoepidemiological research and experience from the first six months. Pharmacoepidemiol Drug Saf. 2007;16:726–35.
23. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. BMC Public Health. 2011;11:450.
24. Swedish National Board of Health and Welfare. National guidelines for care of depression and anxiety disorders 2021—Support for control and management. https://www.socialstyrelsen.se/kunskapsstod-och-regler/regler-och-riktlinjer/nationella-riktlinjer/riktlinjer-och-utvarderingar/depression-och-angest/. Accessed 30 Mar 2023.
25. Brooke HL, Talbäck M, Hörnblad J, et al. The Swedish cause of death register. Eur J Epidemiol. 2017;32:765–73.
26. King G, Zeng L. Estimating risk and rate levels, ratios and differences in case–control studies. Stat Med. 2002;21:1409–27.
27. Hedna K, Hensing G, Skoog I, Fastbom J, Waern M. Sociodemographic and gender determinants of late-life suicide in users and non-users of antidepressants. Eur J Public Health. 2020;30:958–64.
28. Carlsten A, Waern M. Are sedatives and hypnotics associated with increased suicide risk of suicide in the elderly? BMC Geriatr. 2009;9:20.
29. Kripke DF. Hypnotic drug risks of mortality, infection, depression, and cancer: but lack of benefit. F1000Research. 2016;5:918.
30. Fässberg MM, Östling S, Börjesson-Hanson A, Skoog I, Wærn M. Suicidal feelings in the twilight of life: a cross-sectional population-based study of 97-year-olds. BMJ Open. 2013;3: e002260.
31. Michel K, Arestegui G, Spuhler T. Suicide with psychotropic drugs in Switzerland. Pharmacopsychiatry. 1994;27:114–8.
32. Carlsten A, Waern M, Holmgren P, Allebeck P. The role of benzodiazepines in elderly suicides. Scand J Public Health. 2003;31:224–8.
33. McCall WV, Benca RM, Rosenquist PB, et al. Hypnotic medications and suicide: risk, mechanisms, mitigation, and the FDA. Am J Psychiatry. 2017;174:18–25.
34. Gorman JM. Comorbid depression and anxiety spectrum disorders. Depress Anxiety. 1996;4:160–8.
35. Sherbourne CD, Wells KB. Course of depression in patients with comorbid anxiety disorders. J Affect Disord. 1997;43:245–50.
36. Jeste ND, Hays JC, Steffens DC. Clinical correlates of anxious depression among elderly patients with depression. J Affect Disord. 2006;90:37–41.
37. Blazer DG. Psychiatry and the oldest old. Am J Psychiatry. 2000;157:1915–24.
38. Bartels SJ, Coakley E, Oxman TE, et al. Suicidal and death ideation in older primary care patients with depression, anxiety, and at-risk alcohol use. Am J Geriatr Psychiatry. 2002;10:417–27.
39. Waern M, Marlow T, Morin J, Östling S, Skoog I. Secular changes in at-risk drinking in Sweden: birth cohort comparisons in 75-year-old men and women 1976–2006. Age Ageing. 2013;43:228–34.
40. Smith JP, Randall CL. Anxiety and alcohol use disorders: comorbidity and treatment considerations. Alcohol Res. 2012;34:414–31.
41. Haw C, Harwood D, Hawton K. Dementia and suicidal behavior: a review of the literature. Int Psychogeriatr. 2009;21:440–53.
42. Erlangsen A, Stenager E, Conwell Y, et al. Association between neurological disorders and death by suicide in Denmark. JAMA. 2020;323:444–54.
43. Seibert M, Mühlbauer V, Holbrook J, et al. Efficacy and safety of pharmacotherapy for Alzheimer's disease and for behavioural and psychological symptoms of dementia in older patients with moderate and severe functional impairments: a systematic review of controlled trials. Alzheimer's Res Ther. 2021;13:131.
44. Alothman D, Card T, Lewis S, et al. Risk of suicide after dementia diagnosis. JAMA Neurol. 2022;79:1148–54.
45. Choi JW, Lee KS, Han E. Suicide risk within 1 year of dementia diagnosis in older adults: a nationwide retrospective cohort study. J Psychiatry Neurosci. 2021;46:e119–27.
46. Carton L, Cottencin O, Lapeyre-Mestre M, et al. Off-label prescribing of antipsychotics in adults, children and elderly individuals: a systematic review of recent prescription trends. Curr Pharm Des. 2015;21:3280–97.
47. Nabi Z, Stansfeld J, Plöderl M, Wood L, Moncrieff J. Effects of lithium on suicide and suicidal behaviour: a systematic review and meta-analysis of randomised trials. Epidemiol Psychiatr Sci. 2022;31: e65.
48. Grimes DA, Schulz KF. Bias and causal associations in observational research. Lancet. 2002;359:248–52.
49. Pompili M, Innamorati M, Masotti V, et al. Suicide in the elderly: a psychological autopsy study in a North Italy area (1994–2004). Am J Geriatr Psychiatry. 2008;16(9):727–35.
50. Fässberg MM, Cheung G, Canetto SS, et al. A systematic review of physical illness, functional disability, and suicidal behaviour among older adults. Aging Ment Health. 2016;20(2):166–94.
51. Pompili M, Venturini P, Lamis DA, et al. Suicide in stroke survivors: epidemiology and prevention. Drugs Aging. 2015;32(1):21–9.