Determinants of suicidal behavior in dementia: A Swedish national register-based study

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ABSTRACT

Objectives: To examine predictors of suicidal behavior (SB) in adults aged 75 years and above with dementia.

Design: Longitudinal national register-based study.

Participants and setting: Swedish residents aged ≥ 75 years with dementia identified in the Swedish Dementia Registry (SveDem) between 1 January 2007 and 31 December 2017 ($N = 59\ 042$) and followed until 31 December 2018. Data were linked with numerous national registers using personal identity numbers.

Measurements: Outcomes were nonfatal self-harm and suicide. Fine and Gray regression models were used to investigate demographics, comorbidities, and psychoactive medications associated with fatal and nonfatal SB.

Results: Suicidal behavior was observed in 160 persons after dementia diagnosis; 29 of these died by suicide. Adjusted sub-hazard ratio (aSHRs) for SB was increased in those who had a previous episode of self-harm (aSHR = 14.42; 95% confidence interval [CI] = 7.06–29.46), those with serious depression (aSHR = 4.33, 95%CI = 2.94–6.4), and in those born outside Sweden (aSHR = 1.53; 95% CI = 1.03–2.27). Use of hypnotics or anxiolytics was also associated with a higher risk of SB; use of antidepressants was not. Milder dementia and higher frailty score also increased risk of SB. Risk was decreased in those who received home care (aSHR = 0.52; 95%CI = 0.38–0.71) and in the oldest group (aSHR = 0.35; 95%CI = 0.25–0.49).

Conclusion: In addition to established targets for suicidal behavior prevention (improved identification and treatment of depression and previous self-harm), several new risk factors were suggested. There is a need for innovative public health strategies to meet the needs of older dementia patients with a foreign background. Home care may have a potential positive effect to prevent SB in people with dementia, but this needs to be further explored.

Key words: suicidal behavior, dementia, geriatrics, registries, longitudinal study

Introduction

Given population aging, dementia constitutes a growing healthcare burden (Winblad *et al.*, 2016). Behavioral and psychological symptoms affect up to 90% of patients with dementia (Aalten *et al.*, 2005; Cerejeira *et al.*, 2012), and patients with these symptoms have demonstrated an increased risk of suicide ideation (Koyama *et al.*, 2015).

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Perception of the disease and its course might increase hopelessness (Turnbull *et al.*, 2003); diminishing cognitive capacities might impair problem-solving skills, and social changes, such as activities of daily living and, particularly, perceived burdensomeness may further increase risk of suicidal behavior (SB) (Jahn and Cukrowicz, 2011; Van Orden *et al.*, 2010). A recent meta-analysis showed increased risk of nonfatal self-harm in persons with dementia (Álvarez Muñoz *et al.*, 2020). Results regarding suicide were inconclusive in that meta-analysis but there are several studies suggesting increased risk in persons recently diagnosed with dementia (Álvarez Muñoz *et al.*, 2020;

Alothman *et al.*, 2022; Choi *et al.*, 2021; Conejero *et al.*, 2018; Erlangsen *et al.*, 2008; Seyfried *et al.*, 2011). Given the high prevalence of dementia in late-life as well as the strong intent to die in older adults who self-harm (Wiktorsson *et al.*, 2022), the investigation of predictors of nonfatal self-harm and suicide in the oldest segment of population with dementia is warranted. Surprisingly, research in this field is scarce and factors related to SB are inadequately understood.

Thus far, research on SB in older adults with dementia has been mainly based on case reports (Baptista *et al.*, 2017; Nicholson, 2013), investigated risk factors for suicide ideation rather than suicidal actions (Holmstrand *et al.*, 2021; Kim and Hyun, 2013; Koyama *et al.*, 2015), or compared risk factors between suicide decedents with and without dementia (Purandare *et al.*, 2009). Some large studies focused on suicide in selected populations such younger older adults diagnosed with dementia during hospitalization (Erlangsen *et al.*, 2008), persons in contact with mental health services (Purandare *et al.*, 2009), through insurance claims (Annor *et al.*, 2019), or using data from a health system serving primarily men (Seyfried *et al.*, 2011). None examined predictors of SB in the oldest segment of the population, where suicide rates are particularly high.

The Swedish Dementia Registry (SveDem), which includes a large nationwide clinical dementia cohort, provides a useful context to study SB in the oldest adults with a large source population allowing sufficient power to investigate rare events such as SB (Religa *et al.*, 2015). It further offers the possibility to link data to other national demographic, clinical, and pharmacy claim resources. The current study aims to examine potential predictors of SB in Swedish adults aged 75 years and over with a diagnosis of dementia. Further, we conducted gender-specific analyses as we found different risk factors for nonfatal self-harm (Hedna *et al.*, 2020a), and suicide (Hedna *et al.*, 2020b) in men and women aged 75 + in our previous nationwide studies.

Methods

Study setting

We conducted a national register-based study including all Swedish residents aged 75 + diagnosed with dementia and registered in the SveDem registry from 1st January 2007 to 31st December 2017 and followed until 31st December 2018. Persons were censored if they died of causes other than suicide during the follow-up time.

Data sources

The SveDem registry is a national quality registry for monitoring the diagnosis, treatment, and care of people with dementia in Sweden (Religa *et al.*, 2015). It covers 100% of memory clinics and 75% of primary care units in Sweden (Uppsala Clinical Research Center, 2022). Once affiliated, the care unit agrees to report all newly diagnosed patients with dementia to SveDem for registration. There are no exclusion criteria, and any patient with newly diagnosed dementia can be registered. Patients are registered with the type of dementia disorder, information about living conditions, and performance on diagnostic tests. Global cognitive status is assessed by Mini-Mental State Examination (MMSE).

For the purpose of this study, data from SveDem were linked with other registers using each participant's unique national identifier number (Ludvigsson *et al.*, 2009). Medical conditions (other than dementia) within the 5 years prior to dementia diagnosis were extracted from the Swedish National Patient Register. This register contains prospectively collected data from all inpatient and specialized outpatient visits in Sweden. The coverage of inpatient discharges is >99% (Ludvigsson *et al.*, 2011). Medical diagnoses are classified according to the International Classification of Diseases, Tenth Revision (ICD-10). Information on dispensed medications was extracted from the Swedish Prescribed Drug Register (Wettermark *et al.*, 2007). This register contains patient-level records of prescriptions dispensed by Swedish pharmacies in outpatient care and in nursing homes and its coverage is >99%. Medications are classified using Anatomical Therapeutic Chemical (ATC) codes. Data on all-cause mortality, including suicide, were extracted from the National Cause of Death Register which covers 100% of deaths in Sweden (Brooke *et al.*, 2017). The above-mentioned registers are held by the National Board of Health and Welfare. Sociodemographic data for the study cohort were retrieved from Statistics Sweden.

Assessment of demographic, medical, and medication data

Demographic data at baseline included age, gender, and marital status. Living situation was also assessed: Living in long-term care facility, living at home alone vs. living at home with a co-resident. Recipients of home care were defined as getting care in their own residence, which could include not only practical assistance in daily living but also advanced healthcare by visiting medical personnel. Dementia diagnoses were set by clinicians and for the purpose

of this paper, a person with an MMSE score above 20 was considered to have "less severe" cognitive decline in line with the dementia severity cutoffs of Pernecsky and colleagues (Perneczky *et al.*, 2006). Dementia was classified as Alzheimer's disease, vascular dementia, unspecified dementia, and other dementia types. Medical doctors in Sweden generally use MacKeith criteria to diagnose Dementia with Lewy bodies (McKeith *et al.*, 2005), and the Lund-Manchester criteria for frontotemporal dementia (The Lund and Manchester Groups, 1994).

We retrieved diagnoses from specialized care to create a Charlson Comorbidity Index (CCI) Score (Charlson *et al.*, 1987) using the algorithm described by Quan *et al.* (Quan *et al.*, 2005) and adapted to the Swedish setting by Ludvigsson *et al.* (Ludvigsson *et al.*, 2021). We also assessed the Hospital Frailty Risk Score (HFRS) as follows: Low risk (<5), intermediate risk (5–15), and high risk (>15) (Gilbert *et al.*, 2018). Use of specialized healthcare for depression was considered as a marker of serious depression as in Sweden, milder forms of depression are treated within primary care while more serious cases are referred to specialized care (Swedish National Board of Health and Welfare, 2021).

Self-harm and suicide outcomes

The study outcomes were identified using the following ICD-10 codes: intentional self-harm (X60–X84) and harm of undetermined intent (Y10–Y32) from the Cause of Death Register (suicide) and from the National Patient Register (nonfatal self-harm).

Statistical analyses

Use of specified psychoactive medications was considered a time-varying exposure, assessed both at the time of dementia diagnosis and during the three-month window prior to the occurrence of SB or the study end. This window coincides with the dispensing of 3-months' worth of medication which is standard in Sweden. Medical diagnoses in specialized care, CCI and HFRS, were assessed both upon dementia diagnosis and within five years of the SB or end of study.

We used Chi-square tests to assess categorical differences between patients who had a nonfatal self-harm episode or died by suicide vs. all others with regard to demographics, comorbidities, mental conditions, and psychoactive medication use. Subsequently, considering the rarity of suicide and nonfatal self-harm events, a composite outcome of SB including both nonfatal self-harm and suicide was applied.

Fine and Gray regression models were used to identify potential predictors of SB including independent variables that showed significant associations in the univariate analyses. The Fine and Gray model is a time-to-event model, similar to the Cox proportional hazard model. The Fine and Gray model is developed for competing data and takes into account that participants may die of causes other than that of interest. This is of relevance considering the high age of the cohort. Multivariate models were adjusted for age and gender. Marital status was also included in the adjusted model as it was previously found to have divergent effects on risk of late-life nonfatal self-harm and suicide in men and women (Hedna *et al.*, 2020a, 2020b). Adjusted sub-hazard ratios (aSHRs) and 95% confidence intervals (95% CIs) were calculated for the occurrence of the SB in the total cohort and in men and women separately. In order to assess the robustness of our findings, we used Cox proportional hazards models to estimate the hazard ratios for cause-specific risk. A 0.05 significance level was used. Statistical analysis was performed using SAS, version 9.4 (SAS Institute Inc. Cary, NC).

We further conducted sensitivity analysis considering suicide as outcome and including either sociodemographics (model 1) or prescribed medications (model 2). We also investigated the risk of SB considering Alzheimer's disease and other types of dementia as differential risk of suicidal ideation by dementia subtype has been reported (Naismith *et al.*, 2022), and as it was thought that patients with non-Alzheimer dementia may be at increased risk due to the association of these subtypes with neuropsychiatric symptoms such as depression, hallucinations, and delusions (Armstrong *et al.*, 2021; Haw *et al.*, 2009).

Informed consent is not required upon registration in SveDem. Nevertheless, patients are informed orally and in writing about the registration and have the right to refuse participation or withdraw their data from the registry at any time. SveDem does not record the personal number of patients who refuse participation. All data were matched by Statistics Sweden and analyzed anonymously. The study was approved by the Swedish Ethical Review Authority (Dnr 2020-00040).

Results

We identified 59 042 persons aged 75 years and over diagnosed with dementia. The mean age was 83.4 (range: 75–105 years) at time of diagnosis and six out of ten were women (Table 1). One-tenth lived in a long-term care facility and one-third received

Table 1. Characteristics of adults aged 75 + diagnosed with dementia between 2007 and 2017 (N = 59 042)

CHARACTERISTICS	TOTAL COHORT (%)
Age categories	
75–84	35,099 (59)
85 +	23,943 (41)
Women	35,847 (61)
Marital status	
Married/having partner	25,272 (43)
Without partner	33,707 (57)
Country of birth	
Sweden	51,995 (88)
Outside Sweden	7047 (12)
Type of residence	
Living at home alone	27,935 (47)
Living at home with co-resident	25,942 (44)
Home care[1]	21,440 (36)
Living in a long-term care facility	5313 (9)
Possession of firearm	1516 (2.6)
Mini-Mental State Exam	
0–10	2040 (4)
11–20	22,106 (37)
21–25	21,958 (37)
26–30	8679 (15)
Missing	4259 (7)
Type of dementia disorder	
Alzheimer´s disease	28,653 (49)
Vascular dementia	11,952 (20)
Dementia with Lewy bodies	1045 (1.8)
Parkinson's disease dementia	663 (1.1)
Frontotemporal dementia	423 (0.7)
Unspecified	15,119 (26)
Other	1187 (2.0)
Comorbidities[2]	
Psychiatric conditions	
Mood disorder	3900 (6.6)
Depression	3719 (6.3)
Anxiety disorders	2144 (3.6)
Psychotic disorders	580 (1.0)
Previous self-harm episode	325 (0.6)
Bipolar disorder	290 (0.5)
Sleep disorders	43 (0.1)
Medical conditions	
Cancer	12,431 (21)
Cardiovascular disease	9930 (17)
Cerebrovascular disease	7788 (13)
Charlson comorbidity index[2]	
0	20,553 (34.8)
1–2	23,946 (40.6)
3–4	10,816 (18.3)
5–15	3727 (6.3)
Hospital Frailty Risk Score[2]	
0–<5	43,416 (74)
5–15	14,364 (24)
>15	1262 (2)
Number of prescribed medications. Mean (SD) [range]	5.0 (3.2) [0–44]
Use of psychoactive medications[3]	
Antidementia	32,640 (55)

Table 1. Continued

CHARACTERISTICS	TOTAL COHORT (%)
Acetylcholinesterase inhibitors	26,149 (44)
Analgesics	23,046 (39)
Opioids	8342 (14)
Antidepressants	19,762 (33)
SSRI	13,703 (23)
SNRI/NRI	7,835 (13)
Other	832 (1.4)
Hypnotics	15,051 (26)
Zopiclone	9909 (17)
Zolpidem	3278 (5.6)
Anxiolytics	10,364 (18)
Oxazepam	8706 (15)
Antipsychotics	5095 (8.6)
Risperidone	2951 (5.0)
Antiepileptics	2439 (4.1)
Medications to treat substance use disorders	61 (0.1)

SD: standard deviation; SSRI: Selective serotonin reuptake inhibitors; SNRI/NRI: Serotonin and norepinephrine reuptake inhibitors/Norepinephrine reuptake inhibitors.

[1] Getting care at own residence, which could include support in activities of daily living by home care assistants and/or advanced healthcare by visiting medical personnel.
[2] Within 5 years prior to dementia diagnosis. Diagnoses retrieved from the National Patient Register including specialized care services.
[3] Within the 3 months following dementia diagnosis. Based on refilled medications from the Swedish Prescribed Drug Register.

home care. Mean MMSE was 20.6 ± 5.0 points and 52% had MMSE >20. The mean CCI was 1.6 ± 1.5. The mean HFRS was 3.5 ± 4.1. The most common dementia type was Alzheimer's disease (49%), followed by vascular dementia (20%). One-fifth were diagnosed with cancer and a similar proportion with a cardiovascular disease. Overall, 6.3% had serious depression, and 0.6% had a registered episode of nonfatal self-harm within the 5 years prior to dementia diagnosis. One-eighth had a cerebrovascular disease. More than half used anti-dementia medications and one third were on antidepressants.

Older adults with dementia born outside Sweden were younger, received less home care, were less often users of antidepressants, and more often users of hypnotics compared to the native born (Supplementary Table S1). Further, 14% of those aged 85 + were residents in a long-term care facility, while this proportion was 7% in those aged 75–84 years (p-value <0.001). Home care was received by 49% of those aged 85 + and 28% of those aged 75–84 years (*p*-value <0.001).

The median follow-up time was 3.1 years (interquartile range: 1.8–4.8 years), and 59% died during the study period. Overall, 132 had ≥ 1 non-fatal self-harm episode after diagnosis of dementia (59 men and 73 women), yielding an incidence rate

Table 2. Methods of suicidal behavior in Swedish residents aged 75 + diagnosed with dementia between 2007 and 2017 (*N* = 59,042)

METHOD OF SELF-HARM	NON-FATAL SELF-HARM[1]			SUICIDE[2]		
	TOTAL COHORT *N* = 132	MEN *N* = 59	WOMEN *N* = 73	TOTAL COHORT *N* = 29	MEN *N* = 16	WOMEN *N* = 13
Poisoning	75	24	51	3	2	1
Sharp and blunt object	26	17	9	1	1	–
Jumping from high place	9	6	3	5	3	2
Moving object	8	5	3	–	–	–
Drowning and submersion	5	2	3	3	1	2
Smoke, fire and flame	5	2	3	3	–	3
Hanging, strangulation and suffocation	2	2	–	9	6	3
Other and unspecified	2	1	1	3	1	2

[1] Based on diagnoses from the National Patient Register.
[2] Based on diagnoses from the Cause of Death Register.

of 53 per 100 000 person-years for the total cohort (65 per 100 000 person-years in men and 47 per 100 000 person-years in women). Nonfatal self-harm episode occurred within a median time of 1.1 years (interquartile range: 0.5–2.3 years) after dementia diagnosis. About six out of ten used poisoning as a method of nonfatal self-harm (Table 2). One person with a nonfatal self-harm episode died by suicide later during the observation period.

Suicide was the cause of death for 29 individuals (16 men and 13 women), corresponding to an incidence rate of 12 per 100 000 person-years for the total cohort (18 per 100 000 person-years in men, and 8 per 100 000 person-years in women). The median time between dementia diagnosis and suicide was 1.7 years (interquartile range: 0.88–2.69 years). About one-third (10) of suicides occurred in the first year after dementia diagnosis. Eight out of ten used a violent suicide method (Table 2).

In the bivariate analysis (Table 3), younger age (75–84 years) and being born outside Sweden was more common in those with SB compared to the remainder of the cohort who did not self-harm. The non-SB group had higher rates of home care at the time of dementia diagnosis. A significantly greater number of those with SB had a previous episode of nonfatal self-harm or used specialized care for depression during the five years prior to dementia diagnosis. Nine out of ten of those who died by suicide had less severe cognitive decline compared to 6 out of ten in the non-SB group (*p* < .001). Notably, a larger proportion of those who had a nonfatal self-harm episode had intermediate to high risk of frailty score compared to those with no SB (HFRS ≥ 5; nonfatal self-harm group = 50% vs. no SB group = 40%; *p* = 0.02). Moreover, 55% of those with nonfatal self-harm episode were prescribed an antidepressant as compared to 44% of the no SB

group (*p* = 0.009). More than four out of ten of those with SB had been prescribed a hypnotic; this can be compared with 24% in the group with no SB (*p* < .001).

The results of the regression analysis are presented in Table 4. In the total cohort, the adjusted sub-hazard ratio for SB was elevated more than eleven-fold in those who had a previous episode of nonfatal self-harm, and fourfold in those who used specialized care for depression. Risk of SB was elevated in those born outside of Sweden, in those with a higher frailty score (HFRS ≥ 5) or with less severe cognitive decline (MMSE >20). Risk for SB was also increased in users of hypnotics or anxiolytics while it was not elevated in users of antidepressants. Lower risk for SB was, however, associated with older age (85 +), and risk was decreased by half in those who received home care.

Overall, findings of the Cox regression analysis (see Supplementary Table S2) were in accordance with the Fine and Gray models with the exception of MMSE >20 which was not associated with SB in the Cox regression.

In the gender-stratified analysis (Table 4), being born outside Sweden was associated with increased risk of SB in men. In women, a slight increase in the sub-hazard ratio was associated with a higher HFRS. The same applied to lower MMSE score. However, the confidence intervals of the Fine and Gray sub-hazard ratios overlapped considerably in the stratified analysis suggesting similar associations.

In the sensitivity analysis considering suicide only (See Supplementary Table S3), foreign country of birth, use of hypnotics, or anxiolytics were not associated with increased risk of suicide. However, results should be interpreted with caution considering the low number of suicides. Risk estimates of SB were similar in Alzheimer's and all other dementia subtypes (see Supplementary Table S4).

Table 3. Comparison of characteristics of adults aged 75 + diagnosed with dementia, by suicidal behavior status (*N* = 59,042)

Characteristics	NO SUICIDAL BEHAVIOR (*N* = 58,882)	NON-FATAL SELF-HARM (*N* = 132)		SUICIDE (*N* = 29)		ANY SUICIDAL BEHAVIOR[1] (*N* = 160)	
	n (%)	*n* (%)	*p*-value[2]	*n* (%)	*p*-value[2]	*n* (%)	*p*-value[2]
Age: 75–84 years[3]	20 742 (35)	80 (61)	<0.001	20 (69)	<0.001	99 (62)	<0.001
Women	35 761 (61)	73 (55)	0.20	13 (45)	0.08	114 (54)	0.07
Married/Having partner[3]	20 802 (35)	51 (39)	0.40	13 (45)	0.29	63 (39)	0.26
Born outside Sweden	7 016 (12)	25 (19)	0.01	7 (24)	0.04	31 (19)	0.02
Living alone[4]	27 856 (47)	66 (50)	0.54	13 (45)	0.79	79 (49)	0.6
Living in long-term care facility[3]	5 613 (9.5)	9 (7)	0.29	–	–	9 (6)	0.09
Home care[3,5]	42 781 (73)	77 (58)	<0.001	14 (48)	0.003	81 (51)	<0.001
Mini-Mental State Exam score >20[4]	30 536 (52)	86 (65)	0.10	26 (90)	<0.001	111 (69)	0.04
Alzheimer´s disease	28 574 (49)	68 (52)	0.49	11 (38)	0.25	79 (49)	
Depression[6]	3 540 (6.0)	34 (26)	0 < 0.001	11 (38)	<0.001	44 (28)	<0.001
Previous self-harm[6]	96 (0.2)	6 (4.5)	0 < 0.001	4 (14)	<0.001	9 (5.6)	<0.001
Charlson Comorbidity Index >1[6]	21 275 (36)	45 (34)	0.63	13 (45)	0.33	58 (36)	0.90
Hospital Frailty Risk Score ≥ 5[6]	23 648 (40)	66 (50)	0.02	14 (48)	0.37	79 (49)	0.01
Antidepressants[7]	25 927 (44)	73 (55)	0.009	15 (52)	0.40	87 (54)	0.008
Anxiolytics[7]	15 516 (26)	44 (33)	0.07	10 (34)	0.32	53 (33)	0.03
Hypnotics[7]	14 362 (24)	59 (45)	<0.001	12 (41)	0.03	70 (44)	<0.001
Antidementia[7]	25 077 (43)	62 (47)	0.31	9 (31)	00.21	70 (44)	0.77

[1] No fatal-self-harm or suicide identified during the study period.
[2] Chi^2-test for comparison between those who had a fatal or non-fatal SB with those with no suicidal behavior to establish if there are differences between categories.
[3] Last status recorded prior to the end of study.
[4] At time of dementia diagnosis.
[5] Defined as getting care at own residence, which could include support in activities of daily living by home care assistants and/or advanced healthcare by visiting medical personnel.
[6] Based on diagnoses in specialized care within 5 years prior to the end of follow-up.
[7] Refilled within three months prior to the end of follow-up.

Overall, most factors had a smaller effect on nonsuicide deaths compared to their effect on SB risk (see Supplementary Table S5).

Discussion

In this large national cohort including the oldest segment of the population with dementia, over a tenfold increased risk of SB was observed in those who had a previous episode of self-harm. Serious depression was associated with a fourfold risk. An increased risk of SB was also found in those born outside Sweden and in those aged 75–84 years. Use of hypnotics or anxiolytics, but not antidepressants, was related to increased risk of SB. Associations were observed between more severe frailty and SB, as well as for less severe cognitive decline, Comorbidity, as measured by the Charlson Comorbidity Index, was not found to increase risk.

Reduced risk was seen in those who received home care.

The large increased risk associated with a previous episode of self-harm prior to the dementia diagnosis might represent a period of cognitive decline prior to onset of clinical dementia and before its diagnosis is formally documented. Mild cognitive impairment was found to be common in older suicide attempters (Osvath *et al.*, 2005). Further, as anticipated (Haw *et al.*, 2009; Savva *et al.*, 2009; Seyfried *et al.*, 2011), depression was a strong risk factor for SB among persons with dementia. Because psychological symptoms, including those found in persons with major depression, are common and occur at early stages of dementia (Savva *et al.*, 2009), and early recognition, treatment, and management of these symptoms may help reduce risk for SB in older adults with dementia. Most persons with dementia are likely to have regular encounters with the healthcare system

Table 4. Fine and Gray Sub-hazard ratios for factors associated with suicidal behavior[1] in Swedish residents aged 75 + diagnosed with dementia between 2007 and 2017 (N = 59,042)

VARIABLES	TOTAL COHORT		MEN		WOMEN	
	UNIVARIATE REGRESSION SHR (95%CI)	MULTIVARIATE[2] REGRESSION SHR (95%CI)	UNIVARIATE REGRESSION SHR (95%CI)	MULTIVARIATE[2] REGRESSION SHR (95%CI)	UNIVARIATE REGRESSION SHR (95%CI)	MULTIVARIATE[2] REGRESSION SHR (95%CI)
Age 85 + (Ref: 75–84)	0.32 (0.23–0.44)***	0.35 (0.25–0.49)***	0.39 (0.24–0.62)***	0.42 (0.26–0.68)**	0.27 (0.18–0.42)***	0.31 (0.20–0.48)***
Gender women (Ref: men)	0.86 (0.62–1.17)	0.78 (0.56–1.09)	–	–	–	–
Unmarried/No partner (Ref: with partner)[3]	0.81 (0.59–1.12)	1.10 (0.79–1.53)	1.48 (0.93–2.35)	1.35 (0.85–2.16)	0.79 (0.49–1.28)	0.95 (0.60–1.49)
Born outside Sweden (Ref: Sweden)	1.67 (1.12–2.48)*	1.53 (1.03–2.27)*	2.01 (1.13–3.54)*	1.81 (1.02–3.2)*	1.43 (0.83–2.47)	1.38 (0.80–2.38)
Home care (Ref: no home care)[4]	0.53 (0.39–0.72)***	0.52 (0.38–0.71)***	0.48 (0.30–0.75)**	0.45 (0.28–0.71)**	0.57 (0.37–0.89)*	0.58 (0.38–0.9)*
Depression (Ref: no depression)[5]	5.36 (3.78–7.59)***	4.33 (2.94–6.4)***	3.74 (2.08–6.73)***	2.92 (1.53–5.59)**	6.81 (4.35–10.66)***	5.56 (3.38–9.17)***
Previous SH (Ref: no previous SH)[5]	30.37 (15.24–60.49)***	14.42 (7.06–29.46)***	19.44 (5.79–65.23)***	10.59 (3.09–36.26)**	42.95 (18.80–98.15)***	19.29 (8–46.48)***
HFRS ≥ 5 (Ref: HFRS <5)[5]	1.47 (1.08–2.01)*	1.46 (1.07–1.99)*	1.14 (0.72–1.8)	1.15 (0.73–1.82)	1.78 (1.17–2.72)**	1.79 (1.17–2.73)**
MMSE score >20 (Ref: MMSE ≤20)	1.62 (1.15–2.27)**	1.53 (1.08–2.15)*	1.34 (0.81–2.2)	1.29 (0.78–2.11)	1.87 (1.17–2.99)**	1.77 (1.10–2.83)*
Use of antidepressants (Ref: no use)[6]	1.18 (1.08–2.02)*	1.20 (0.99–2.05)	1.21 (0.86–2.29)	1.25 (0.89–2.36)	1.16 (0.87–2.12)	1.11 (0.90–2.21)
Use of anxiolytics (Ref: no use)[6]	1.36 (0.98–1.89)	1.43 (1.03–1.99)*	1.41 (0.86–2.29)	1.45 (0.89–2.36)	1.36 (0.87–2.12)	1.41 (0.93–2.23)
Use of hypnotics (Ref: no use)[6]	2.42 (1.77–3.31)***	2.21 (1.59–3.06)***	2.55 (1.61–4.05)***	2.51 (1.55–4.07)**	2.30 (1.5–3.54)**	1.95 (1.25–3.05)**

HFRS: Hospital frailty risk score; Ref: Reference group; SH: self-harm; SHR: Sub-hazard ratio, CI: confidence interval, MMSE: Mini mental state exam

[1] Non fatal-self-harm or suicide identified during the study period.
[2] Adjusted for all variables with significant associations in the univariate regression, as well as gender and marital status.
[3] Last status recorded prior to the end of study.
[4] Last status recorded at end of study. Defined as getting care at own residence, which could include advanced healthcare by visiting medical personnel.
[5] Based on diagnoses in specialized care within 5 years prior the end of study.
[6] Refilled within three months prior the end of study.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

considering their health condition Therefore, the increased risk of SB in those with previous episode of self-harm or with serious depression may indicate a missed opportunity for SB prevention.

We could not identify any study on SB in foreign-born older adults with dementia for comparison. Some possible explanations of the heightened SB risk could be due to the underuse of mental healthcare services, and the under treatment of mental illnesses in some groups of immigrants (Patel *et al.*, 2017), especially in those from lower socioeconomic position countries (Lindgren *et al.*, 2021) Barriers that may limit or delay seeking mental healthcare may include ethno-cultural prohibitions on exposing personal or family matters to outsiders (Rousseau and Frounfelker, 2018), the consideration of dementia as part of normal ageing, or as a shameful condition (Sagbakken *et al.*, 2018). The proportion of those who received home care was lower in those born outside Sweden. Foreign born persons might rely to a greater degree on relatives (Songur, 2021). Those with no family or those with families residing far away may risk further isolation after dementia diagnosis, contributing to a higher risk of SB. The increased risk of SB in the foreign-born older adults with dementia echoes our findings in the general 75 + population (Hedna *et al.*, 2020a, 2020b). The foreign-born seem to constitute a particular risk group for SB, and our results point to a need to improve mental healthcare for those with dementia. Older immigrants are however a heterogeneous group, and more research is needed to better elucidate associations with SB.

The lower risk of SB in those receiving home care was somewhat unexpected as elevated risk was reported in a retrospective study of older adult suicides and a population-based comparison group (Waern *et al.*, 2003). A more recent study suggests that receiving home care can make it possible for a person with dementia to stay in own home and to remain stable without suicidal ideation with the help of both formal and informal caregivers (Holmstrand *et al.*, 2021). The absence of home care may also be a marker of early dementia in our cohort, a period when the risk of SB was found to be the highest (Choi *et al.*, 2021; Seyfried *et al.*, 2011). Lower perceived availability of social support was found to be associated with a greater risk of suicidal ideation and behavior in adults aged 50 + years, including those with cognitive decline (Cui *et al.*, 2022). As a significant proportion of older adults with dementia live alone, receiving home care may present a window of opportunity to decrease loneliness, and to communicate clinical information to relevant healthcare professionals. This could result in optimized prescribing, improved management of side effects, as well as better medication adherence.

Antidepressant use was not associated with increased risk of SB. This finding differs from previous observations for the general population aged 75 years and above where nonfatal self-harm (Hedna *et al.*, 2020a) and suicide (Hedna *et al.*, 2020b) were more common in users of antidepressants, a finding that most likely reflected confounding by indication. Antidepressants are often prescribed into the course of dementia for conditions such as psychomotor agitation and pathological crying in dementia (Farina *et al.*, 2017). One meta-analysis found that depression remission rates in those with dementia favored antidepressants, but the evidence was of moderate quality (Dudas *et al.*, 2018). More research is needed to better understand the association between antidepressants and suicidal behavior in older adults taking into consideration indication, the specific molecules, and dosage. The elevated risk of SB in users of hypnotics may be explained by the possible role of these drugs in worsening depression, impairing judgement, and creating behavioral confusion, as well as through pharmacological overdose (W. Vaughn McCall *et al.*, 2017). The use of these drugs may indicate underlying sleep disorders, a common condition in those with dementia (Molano and Vaughn, 2014), found to be associated with increased risk of self-harm (Kay *et al.*, 2016). Use of anxiolytics could be seen as a proxy for anxiety symptoms, previously found to be independently associated with suicidality in older adults (Jonson *et al.*, 2012). The effects of psychoactive medications have not been tested in patients with dementia, and our results underline the importance of careful evaluation of such prescriptions in this population.

We found that severity of medical comorbidity did not impact SB risk. This was in line with the finding of Seyfried and colleagues (Seyfried *et al.*, 2011). One limitation of our current study design is that we could not assess the impact of disability resulting from medical comorbidities, which represents a potential mediator in the medical comorbidity–SB relationship.

Frailty was associated with SB in our cohort. We could not find another study conducted in older adults with dementia for comparison. A recent mini review found that frailty was associated with suicidality in older adults, including suicide ideation, suicide attempts, and completed suicides (Shah *et al.*, 2022). Cognitive frailty, characterized by the simultaneous presence of both physical frailty and cognitive impairment, was associated with increased risk of suicidal ideation among a cohort of Chinese adults aged 60 + years (Zhao *et al.*, 2021). Debilitating health problems and life-threatening conditions have previously been identified as important risk factors for suicide in older adults (Choi *et al.*, 2019; Waern *et al.*, 2003). More

evidence is needed to evaluate the causality between frailty and SB in older adults with dementia. The lower risk of suicidal behavior in those aged 85 + years may be partially explained by the higher proportion of the oldest group receiving home care or social services compared to the younger group. In our previous studies, risk of both nonfatal self-harm (Hedna *et al.*, 2020a) and suicide (Hedna *et al.*, 2020b) was lower in residents of long-term care facilities. This setting may offer greater monitoring from health professionals and less access to lethal means of self-harm. Another consideration is that persons in the oldest group may be less physically able to carry out a self-harm act.

While we expected that risk of SB would be greater in those with Alzheimer's disease (Conejero *et al.*, 2018), such an association was not found in our cohort. This may be partially explained by the categorization used in the dementia register. Some cases of Alzheimer's disease would be included in the mixed dementia group. Also, the proportion with unspecified dementia was relatively high in the SveDem register.

We did not find the anticipated gender differences for risk factors of SB. We could identify no other studies assessing risk factors of SB in older men and women with dementia for comparison. More research is needed to better elucidate any potential confounders in gender-stratified models.

Methodological considerations

The main strength of this research is the large cohort of older adults with dementia across Sweden. The identification of medical diagnoses, medications, and sociodemographic factors used national registers that were complete and allowed for follow-up of individuals which removed potential for attrition or recall bias. SveDem is a naturalistic nationwide clinical database, which facilitates the translation of research findings into clinical preventive recommendations. The lack of primary care data is a limitation as some milder psychiatric and medical diagnoses are underestimated. While the Swedish Prescribed Drug Register has full coverage of dispensed medications from pharmacies, it was not possible to determine actual medication intake. Medication exposure was considered as time-dependent, taking into account the change in prescribing patterns that occur after dementia diagnosis and thus more accurately reflective of medication use at the time of suicidal behavior. We cannot rule out the possibility of confounding by indication in the association between use of psychoactive medications and SB. It is also likely that people who were perceived to experience therapeutic benefit were more likely to be prescribed psychoactive medications for depression, anxiety, or other

behavioral symptoms of dementia. This was a correlational study, and we cannot make conclusions regarding causality. The associations of SB with sociodemographic factors (country of birth and age) are not prone to be bidirectional. However, the other factors (medications used, medical diagnoses, and place of residence) may be susceptible to a reverse causality although the related variables were collected before the occurrence of the suicidal behavior recorded during the observation period. Our results should be interpreted with this limitation in mind. Although we adjusted for a range of covariates, there are unknown factors that may affect the risk of SB. Due to the rarity of suicidal behavior, we also had to limit the number of variables in the regression models. Our findings in the gender-stratified analysis should be interpreted with caution due to the low number of cases.

Death certificates often do not reflect dementia as a contributor to death, and tools to assess suicidal behavior are not adapted for patients with cognitive impairment or dementia (Alphs *et al.*, 2016). Furthermore, older adults' suicide may be underreported as deaths from overdoses, self-starvation, dehydration, or "accidents" are often not reported as suicides (Kiriakidis, 2015). This issue is attenuated somewhat by the inclusion of uncertain SB in our study outcome. Another consideration is that our study includes only persons diagnosed with clinical dementia, and results may not apply to those with preclinical states, for whom SB might be construed as a dementia prodrome (Gujral *et al.*, 2021; Tu *et al.*, 2016). Finally, our findings cannot be extrapolated to other settings considering variations in sociodemographic characteristics, healthcare services, and differences in medico-legal death investigation systems.

Conclusions

Our findings provide an impetus to improve the quality of clinical and social care to prevent suicidal behavior in older adults with dementia. Several new correlates were suggested, in addition to established targets for suicidal behavior prevention such as improved identification and treatment of depression and previous self-harm. Since the majority of older adults with dementia have healthcare contacts, the increased risk of SB in those with comorbid depression, users of hypnotics, or with a previous episode of SB indicates a missed opportunity for healthcare to screen and monitor older adults at higher risk of SB. The increased risk of SB in those with foreign background requires further research to determine whether innovative public health strategies to meet the needs of this group might decrease risk of SB. Our observation of lower risk of SB in those who

received home care may indicate a potential positive effect of such service to prevent SB in this older adults with dementia, but more research is needed. Future research should explore variation in risk factors for SB among different dementia subtypes and degrees of frailty, as well as over the course of the disease.

Conflict of interests

None.

Description of authors' roles

K. Hedna designed and planned the study, organized data collection, participated in the analysis of data and interpretation of the results, and drafted the manuscript. R. Sigström and K. Johnell contributed to the interpretation of the results and participated in manuscript writing. M. Waern is the principal investigator of the project. She acquired funding and contributed to the design and planning of the study, in data collection and interpretation, and she took part in the writing of the manuscript. All authors declare that they have reviewed and approved the manuscript prior to its submission.

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Supplementary material

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