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Review

Suicidal Behavior in Mild Cognitive Impairment and Dementia in the Old Adults: A Systematic Review and Meta-Analysis

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Abstract

Objectives: To address the prevalence and risk factors of suicidal outcomes in people with mild cognitive impairment or dementia. **Methods:** Four databases were searched for studies reporting data on the prevalence or the risk of a suicidal event, in people with a clinical diagnosis of MCI or dementia. The research was conducted according to PRISMA guidelines. A narrative synthesis was used to report the main findings. A random effect model was used across all analyses to calculate the prevalence and the odds ratio of suicidal outcomes in people with dementia. **Results:** Fifty-nine studies were included. The pooled prevalence of suicidal outcomes in people with dementia were as follows: suicidal ideation: 9.7% (95%CI 6.7-13.9), suicide attempt: 0.8% (95%CI 0.3-2.4), and suicidal death: 0.2% (95%CI 0.1-0.4). People with dementia had an increased risk of suicidal ideation (OR 1.87, 95%CI 1.21-2.88) and suicide attempt (OR 2.4, 95%CI 1.24-4.65) but no significant increase in the risk of suicidal death. The heterogeneity was high for each outcome. The risk factors for suicidal death in dementia were younger age, recent diagnosis, previous mental health disorder, and frontotemporal dementia. The prevalence of suicidal ideation in MCI ranged from 5 to 17.6%, with a moderate increase in suicide attempts (HR 1.34, 95%CI 1.09-1.65) and no increase in suicidal death. **Conclusions:** People with dementia frequently have suicidal thoughts and are at an increased risk of suicide attempts. Clinicians should be careful to identify those at higher risk in order to offer them supportive care and restrict their access to lethal means.

Keywords

suicide, Alzheimer's disease, dementia, mild cognitive impairment, MCI, neurocognitive disorder

Summary

The prevalence of suicidal events such as suicidal ideation, suicide attempt, or suicidal death is high in the elderly, including in people with dementia and mild cognitive impairment (MCI). This meta-analysis showed a high prevalence of suicidal ideation which occurred in about 1 of 10 people with dementia, whereas the prevalence of suicide attempts was lower, but substantial, in about 0.8% of cases. The prevalence of death by suicide was 0.2%. Compared to people without dementia, people with dementia had roughly twice the risk of suicidal ideation or suicide attempt but no significant increase in the risk of suicidal death. Clinicians should be particularly careful to identify those with a higher risk of suicidal death, for example younger patients, those with a recent diagnosis, a

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previous mental health disorder, or a diagnosis of frontotemporal dementia.

Introduction

Suicide is a major public health concern. The prevalence of suicide differs greatly by region or country and is the highest in Europe, with a crude rate of 12.4/100 000 in the year 2021.[1] The suicide rate is approximately twice as high for men as for women. However, these crude figures mask a much more complex reality, in which many factors such as age, socioeconomic status, access to health care, and mental and physical health, influence the risk of suicidal behavior or death by suicide. In high income countries, the suicide rate remains high in the elderly and often higher than middle-aged people.[2] For example, the crude rate in France in 2019 was 16.7/100 000 in the 65-74 years of age group, 28.6 in the 75-84 years group, and 28.2 in the ≥85 years group compared to ≤20 in the less than 65 years group.[1] Moreover, it is estimated that for 1 suicidal death, there are 20 suicide attempts and approximatively 200 people with suicidal ideation.[3] Suicide attempts by the elderly are more often fatal than those by younger people. Suicide is generally the consequence of a precipitating factor or a situational stressor in a vulnerable individual with predisposing factors. Older adults have both common and distinct risk factors for suicidality compared to younger subjects. Depression and other mental disorders are strong risk factors in all age groups. Specific risk factors for the elderly include chronic physical illness, chronic pain, disability and functional impairment, bereavement, widowhood, loneliness and lack of social support, and cognitive impairment such as impaired decision making and cognitive inhibition.[4] The actual prevalence of suicide among older adults is likely underestimated due to misclassification and social stigma.[5]

Neurological diseases that cause dementia or mild cognitive impairment are chronic conditions that are highly prevalent among older adults.[6] These diseases have a poor prognosis and lead to progressive functional impairment. They are also often responsible for behavioral and psychological symptoms.[7] The prevalence of depression in people with dementia range from 20% to 37% with a mean prevalence of 25% compared to 13% in the general community.[8] Receiving a diagnosis of Alzheimer's disease or another related disease can be considered a stressful event. Considering the aforementioned risk factors for suicide in the elderly, we can hypothesize that individuals with dementia or mild cognitive impairment are at an increased risk of suicide. Considering the growing public health burden of cognitive disorders and dementia in an ageing population, it is important to gather evidence about the prevalence and risk factors of suicidal events in people with cognitive impairment and dementia.[9] Suicidal events can be classified as passive (thoughts about wanting to be dead) or active (thoughts about killing oneself) suicidal ideation, suicide attempt, and completed suicide or suicidal death.[10]

A previous systematic review of suicide and Alzheimer's disease (AD) published in 2016, including 21 studies (8 were case reports), concluded that AD is associated with a moderate risk of suicide and that more prospective studies are needed to clarify the association between AD and suicidality.[11] The authors did not conduct a meta-analysis. Another systematic review of suicide and dementia published in 2020, including 47 studies published until 31st December 2018 (37 studies included in meta-analysis), reported a trend toward suicidal events, especially suicide attempts in dementia.[12] The effect size of the association of dementia and suicidal outcomes was non-significant for suicidal ideation (OR 1.37, 95% CI 0.78-2.39) and suicidal death (OR 1.28, 95% CI 0.77-2.14) but was significant for suicidal attempt (OR 2.24, 95% CI 1.01-4.97). Those diagnosed with dementia at a younger age were at a higher risk for suicidal thoughts. However, most of the studies included in this review had a cross-sectional or a case-control design that limited interpretation about causal relationships between dementia and suicide. All studies reported in these previous reviews included subjects at the dementia stage of AD or dementia of other or unspecified etiology. Both reviews included papers that used the psychological autopsy method, which means that the diagnosis of AD was made at the autopsy and the clinical data were collected from informants or medical records after the death of the subjects. There is a need for large, prospective studies that address the risk of suicidal behavior in individuals with mild cognitive impairment or dementia of various etiologies.

The dissemination of scientific knowledge about AD and related disorders to the general population likely increases awareness of the issue and potentially leads to earlier diagnoses. The development of new diagnostic criteria and the use of biomarkers allow for an earlier and more accurate diagnosis of neurocognitive disorders at the stage of mild cognitive impairment (MCI) or mild neurocognitive disorder.[13,14] These diagnostic criteria of prodromal AD or MCI due to AD are now widely used in routine practice.[15] The diagnosis of AD is usually disclosed to the patient earlier, probably at a younger age and more often than in the past. Considering the fact that some previous studies suggested that the risk of suicide was higher in younger subjects or at an early stage of AD compared to a late stage,[16] these changes in clinical practice could increase the prevalence of suicidal *events* in cognitively impaired subjects. To the best of our knowledge, there is not yet a systematic review on suicide and MCI. Therefore, we aimed to conduct a new systematic literature review to update previous reviews and synthetize

the data about this topic by also including people with cognitive impairment at a milder stage and reviewing recent studies conducted with larger cohorts, for which the clinical diagnosis of MCI or dementia was based on the most recent validated criteria. Overall, the aim of this systematic review was to answer: What is the prevalence and what are the risk factors of suicidal ideation, suicide attempt, or suicidal death in cognitively impaired people whether they are at the MCI or the dementia stage? Our goal is to more precisely evaluate the possible causal relationship between mild cognitive impairment (MCI) or dementia and the risk of suicidal behavior. We hope to identify possible risk factors for suicidal behavior in subjects suffering from MCI or dementia. Identifying these factors is crucial to the development of an effective prevention strategy.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 statement[17] was followed during the entire process of this research. A protocol was developed and registered on the Open Science Framework website prior to conducting the work (https://osf.io/8ru7k/?view_only=a35cdcd695a04f438bd872aca0106ffd).

Eligibility Criteria

We included (i) any observational studies (transversal, case control, prospective, or retrospective cohorts), (ii) published in a peer-reviewed journal, (iii) reporting original effect size (incidence, prevalence, odds ratio, risk ratio, relative risk) on suicide (suicidal ideation/thoughts, suicidal behavior/attempt, or suicide death), (iv) in people with a clinical diagnosis of MCI or dementia, due to AD or another disease or of unspecified etiology with or without a comparison to a control group, without restriction of setting or population, from any country of origin. We excluded papers about (i) cognitively unimpaired subjects (undergoing "predictive" tests or risk factor assessment such as APOE genotype) or autopsy series without clinical diagnosis, (ii) assisted suicide or euthanasia, (iii) suicide in caregivers, (iv) case reports, review papers, opinion papers, editorials, comments, (v) papers not written in English or French,[18] or (vi) papers exclusively dedicated to Huntington's disease.

Information Sources and Search Strategy

Our literature search was conducted in April 2023 in the following electronic databases: PubMed (NCBI), Embase (Elsevier), Scopus (Elsevier, Netherlands), and PsycINFO (ProQuest), with no limitation of time. The search strategy combined the use of the following MeSH terms and keywords: dementia, mild cognitive impairment, major neurocognitive disorder, mild neurocognitive disorder, Alzheimer's disease AND suicide or suicidal, or suicidality. The search strategy was established by consulting experts in the field. Moreover, the search team was composed of people from 4 different fields of expertise: neurology (EM), psychiatry (DJ), geriatrics (MdSH), and public health and epidemiology (CB). The detailed search strategy for each database is reported in Supplemental File 1. The reference lists of selected studies and of previous reviews were manually screened to identify additional papers. Experts in the field were contacted to identify any potential missing reference.

Selection Process

The results of our literature search were imported to reference manager software (EndNote20). After removing duplicates, references were imported to the Rayyan web platform to proceed with the screening and the first selection. Titles and abstracts were independently screened by 2 reviewers (EM, DJ). Any disagreement was resolved through discussion. In cases of unsolved disagreements, they were resolved by discussion with a third reviewer (MdSH). The full texts of the selected papers were again assessed independently by the same 2 reviewers (EM, DJ) for eligibility. In cases of discrepancy, consensus was reached after discussion and, if necessary, with the input of a third reviewer (MdSH).

Data Collection Process

The data were independently and manually extracted from selected studies by EM and DJ, using a data extraction form (Supplemental File 2) and encoded in a Microsoft Excel file. Any disagreement was resolved through discussion. The extracted data concerned the following domains: design of the study and methods, sample size, study population and control group (country, setting, demographic data, etiology, severity of cognitive impairment, risk factors), outcomes (type of event, measurement scale, measurement of effect sizes), main and additional results, general conclusion of the authors, limitations and biases, conflicts of interest, and sources of funding. We had 3 outcomes of interest: suicidal ideation or suicidal thoughts (SI), suicide attempts (SA), and death by suicide (SD). For these outcomes, we recorded data about prevalence by either extracting the raw number of subjects with the outcome compared to the whole sample or by extracting the proportion/percentage reported by the authors. The risk of an outcome compared to a control group without neurocognitive disorder (with the highest level of adjustment if several levels of adjustment were available)

was extracted as odds ratios (OR), hazard ratios (HR), or other effect sizes reported by the authors and their 95% confidence intervals (CI). Raw numbers of the outcomes in the study samples and the control groups were also extracted to calculate "crude" OR and perform meta-analyses. In cases of incomplete or unclear data, the study's authors were contacted by email to obtain missing data or explanation. For studies reporting different follow-up outcome results, we extracted the results of the most relevant period from a clinical point of view.

Study Risk of Bias Assessment

The Mixed Methods Appraisal Tool (MMAT; version 2018) was used during the quality appraisal of each included study.[19] The MMAT allows 1 to appraise the quality of the methodology of 5 different categories of empirical studies. The MMAT consists of questions about the clarity of the research question(s), the adequacy of the data to answer the research question, the representativeness of the target population, the validity and accuracy of the measurements, the completeness of the outcome data, the account of confounding factors and the risk of nonresponse bias, the change of the status of the participants that could influence the outcome, and the relevance of the statistical analysis.

Two reviewers (EM, DJ) performed the quality and risk of bias appraisal independently. Any disagreement was resolved through discussion. In cases of unsolved disagreement, they were resolved by discussion with a third reviewer (MdSH). Detailed scoring of the selected papers is reported in Supplemental File 3. We included all studies regardless of their quality.

Data Synthesis and Statistical Analysis

Results from selected papers are reported in 2 overview tables (Table 1 for people with dementia, Table 2 for people with MCI). A narrative synthesis of the main results regarding prevalence and identified risk factors of the 3 different outcomes (SI, SA, or SD) is provided. For studies that reported quantitative data or effect sizes that could be pooled, meta-analyses were performed to provide a quantitative estimate of the effects. Different meta-analyses were run, including meta-analyses on prevalence of the 3 outcomes in people with dementia, and meta-analyses assessing the risk of theses outcomes in people with dementia compared to controls. Considering the low numbers of studies of people with MCI, no meta-analysis was performed for this population.

Heterogeneity between studies was anticipated. Therefore, a random effect model was used across all analyses. Heterogeneity was evaluated with Cochrane Q statistics and quantified with I^2. Two studies reported only a combined outcome of suicidal ideation and suicide attempt in people with dementia, identified as suicidal behavior (SB) without data of the exact number of each component of the outcome. The data of these 2 studies were included in both meta-analyses of prevalence of SI and prevalence of SA in dementia. Subgroup analyses by outcomes and by study design were run to further explore the heterogeneity.

A publication bias analysis was performed, using a visual inspection of the funnel plot and Begg and Egger's regression tests. A leave-one-out analysis was performed to test the robustness of the statistical models. All analyses were performed in R Software and appropriate packages (Meta, Metafor).

Results

Summary of Search Results

A total of 3931 studies were identified in 4 databases. After removing 1537 duplicates, 2394 records were screened by title and abstracts and 77 were selected for full-text assessment. Six additional studies were identified through manual search of the reference list of retrieved full texts and previous reviews. A list of the excluded studies is provided in Supplemental File 4. A total of 59 studies were included in this review (Figure 1). Among these, there were 2 studies that reported data exclusively on people with MCI,[20,21] 3 studies of people with MCI or dementia,[22-24] and 54 studies involving people with dementia.[25-78] There were 26 cross-sectional studies, 22 cohort studies, 9 case-control studies, and 2 double-blind randomized controlled trials (RCTs). A summary of the selected studies of people with dementia or MCI is presented respectively in Table 1 and Table 2. Countries of origin of included studies were mainly located in Europe (n = 28) or North America (n = 16). The other studies were located in Asia (n = 9), Australia (n = 3), Mexico (n = 1), and Argentina (n = 1). We found 1 multi-site study worldwide. The sample size ranged from 18 to 7 300 395 participants. These studies were conducted in various settings: outpatient clinical services, emergency departments, geriatric or psychiatric hospitals, nursing homes, or population-based record linkages (outpatient or inpatient care) in regional or national databases. Inclusion criteria were heterogenous with age ≥60 years in most cases. The etiology of dementia was AD or other dementias in 16, AD in 9, frontotemporal dementia (FTD) in 5, Lewy body dementia (LBD) in 2, vascular dementia (VD) in 1, semantic dementia in 1, and unspecified in 23 studies. The etiology of MCI was AD in 1, various in 1, and unspecified in 3 studies. The studied outcomes were SI in 32, SA in 23, SD in 16 studies of dementia and SI in 3, SA in 1, and SD in 2 studies of MCI. Some studies reported data on 2 different outcomes. The quality of selected studies was

Table 1. Studies in People With Dementia Included in the Review.

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Rubin H 1989	Cross-sectional	68 83	72.1 (5) 71.6 (4.9)	54.4% 51%	Outpatients aged 64 to 81 y. USA	AD	Prevalence of SI in mild dementia: 15% according to collateral source and significantly higher than control (1%).
Ballard C 1996	Cross-sectional	124 0	79.6 (5.9)	73%	>65 y outpatients, mild or moderate dementia. UK	AD/VD/LBD/U	Prevalence of SI: 14.5%.
Forsell Y 1997	Cross-sectional	969	84.2 (4.3)	76.7%	≥75 y registered in the parish of Kungsholm (Stockholm). Sweden	U	Prevalence of SI: 23.6% in dementia vs 11% if no dementia, $P < 0.001$. No active SI.
Forsell & Winblad, 1997	Cross-sectional	253	92.3 (2.0)	79.4%	≥90 y, born before 1903, registered in the district of St Göran (Stockholm). Sweden	U	Prevalence of SI: 21% in dementia vs 22.3% if no dementia, NS.
Weiner MF 1997	Cross-sectional	30 0	68.8 (7.8)	NA	Outpatients. USA	AD	Prevalence of SI: 13.3%. No relation between HAM-D scores and MMSE
Bellini M 1998	Cross-sectional	18 16	95.1 (3.4) 98.1 (3.2)	55.6% 47.3%	Born in 1905 or before. Italy	U	OR of SI: 1.09 (95% CI 0.92-1.29) No difference in MADRS total score or item score.
Draper B 1998	Cross-sectional	221 0	71.6 (8.3)	57%	Consecutive referrals in a memory clinic. Australia	AD/VD/U	Prevalence of SI: 9.5%. Prevalence of SA: 0%. Significant correlation between SI and other depressive symptoms only in AD. No correlation between SI and age, insight or severity of dementia.
Shah A 1998	Cross-sectional	74	83 (65-99)	62%	Consecutive admissions in a continuing care geriatric ward. UK	U	Prevalence of SI: 29% (95% CI 15-43) in 41 subjects with dementia
Barak Y 2002	Cross-sectional	16 16	80.1 (8.1) 80.4 (7.1)	12% 12%	>65 y admitted in a psychiatric hospital. Israel	AD	Prevalence of SA: 7.4%. Lower cognitive impairment and higher rate of previous SA or affective disorder in SA subjects compared to 16 AD control without SA.
Harwood D G 2002	Cross-sectional	91 0	71.7 (7.9)	7.7%	Memory clinic and psychogeriatric unit. USA	AD	Prevalence of SI: 9.7%. Patient with hopeless ideation have increased symptoms of anxiety and depression and better insight into their cognitive deficits.
Gräsbeck A 2003	Cohort	96 0	64.6 (32-85)	59%	Psychiatric and psychogeriatric hospital. Sweden	FTD	Prevalence of SI: 9.4%. SI are associated with longer survival. If presence of SI before diagnosis: HR of mortality = 0.36 (95% CI 0.13-1.01) $P = 0.05$.

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Moretti R 2006	Cohort	231 0	75.9 (7.7)	45%	65-80 y outpatients with MMSE > 13. Italy	VD	Prevalence of SI: 9.1% at baseline, 6.9 % at 24 months. SI more frequent in multi-infarct dementia compared to subcortical VD.
Starkstein SE 2007	Cross-sectional	278 45	NA 69.2 (9.6)	63% 67%	Consecutive referrals, outpatients' dementia clinic. Argentina	AD	Prevalence of SI: 9.7%. No association between SI and the prevalence of dangerous behaviours.
Barca ML 2008	Cross-sectional	933 226	84.4 (7.9) 83.9 (9.1)	73% 68.1%	All patients in 26 nursing homes. Normay	U	Prevalence of SI: 10.9% vs 8.4% in controls (P = 0.474). No significative difference according to CDR score. Patients with dementia have more depressive symptoms.
Chan SSM 2008	Cross-sectional	520	NA	NA	≥60 y with very mild or mild dementia (CRD 0.5 or 1). China	U	Prevalence of SI: 2.5% (2.7% in CDR 0.5 and 1.6% in CDR 1). Clinically significant depressive symptoms: 1.7 % in CDR 0.5 and 5.9% in CDR 1.
Dombrovski A 2008	Case-control	32 32	70.2 (9) 71.5 (7.1)	53% 62%	≥60 y, major depression, SA within 3 m, MMSE ≥ 18. USA	U	Dementia in 2/32 suicidal vs 1/32 non suicidal depressed subjects. Elderly depressed patients with SA have poorer performance in executive functions than non-suicidal depressed subjects.
Erlangsen A 2008	Cohort	21 394 2 467 539	NA	60.1% 54.2%	Population-based record linkage, >50 y living in Denmark from 1990 to 2000.	AD/VD/U	Risk of SD in people diagnosed with dementia during 11 y study period: men 50-69 y RR 8.5 (95% CI 6.3-11.3), men ≥70 y RR 4.7 (95% CI 3.4-6.7), women 50-69 y RR 10.8 (95% CI 7.4-15.7), women ≥70 y RR 3.4 (95% CI 2.4-5.0). Higher risk of SD within 6 m after diagnosis (RR>13), if presence of mood or other psychiatric disorders, in AD compared to VD, if living with someone for older men.
Liu I C 2009	Case-control	43 43	75.5 (8.7) 78.6 (7.9)	NA NA	≥60 y attending emergency ward after SA. Taiwan	U	Dementia in 16.3% in SA group and 9.3% in controls, NS after adjustment for age and level of education.
Rosness TA 2010	Cross-sectional	221 0	58.6 (5.2)	51%	Dementia onset <65 y Memory clinic. Norway	AD/FTD/VD/U	Prevalence of SI: 13.1%. MADRS total score 10.2 (SD 7.1). 65% patients had some degree of depression.
Wiktorsson S 2010	Case-control	103 408	79.7 (5.3) NA	55% NA	≥70 y attending emergency ward after SA. Sweden	U	SA not associated with dementia. OR 1.04 (95% CI 0.5-2.4) in dementia vs no dementia. Factors associated with SA included being unmarried, living alone, lower education level, history of psychiatric treatment or SA, major and minor depression, feelings of loneliness.

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Engedal K 2011	Cross-sectional	112 0	83 (7.9)	69.6%	Geriatric hospitals and nursing homes. Norway	AD	Prevalence of SI: 11.6%. Depression in 34.8% to 53.5% according to 3 different diagnostic criteria.
Qin P 2011	Case-control	21 169 423 128	NA NA	35.4% 35.4%	Population-based record linkage, suicide in Denmark from 1981 to 1997	U	AIRR of SD = 3.4 (95% CI 2.4-43) in men and 5.7 (95% CI 4.3-7.5) in women. Dementia increased risk of suicide at the lowest level compared to other psychiatric disorders. AIRR higher in dementia subjects 36-60 y compared to dementia subjects >60 y.
Seyfried L 2011	Cohort study	294 952 0	NA	2.8%	VA databases, ≥60 y dementia diagnosis from 2001 to 2005. USA	U	Prevalence of SD: 0.09%. Most suicide occurred in newly diagnosed patients. Increased risk with white race (OR 1.49, 95% CI 1.14-1.95) depression (OR 2.04, 95% CI 1.45-2.85) history of psychiatric hospitalisation (OR 2.31, 95% CI 1.54-3.46) prescription of antidepressants (OR 2.11, 95% CI 1.57-2.84) or anxiolytics (OR 1.98, 95% CI 1.48-2.65). Lower risk with nursing home admission (OR 0.33, 95% CI 0.14-0.75).
McCarthy JF 2013	Cohort study	281 066	70.1 (12.4)	3.2%	Patients discharged from VA nursing home during fiscal years 2002 to 2008. USA	U	HR 0.66 (95% CI 0.37-1.19) for suicidal death in dementia vs no dementia, NS. SMR for SD: 2.4 (95% CI 2.0-2.9) for the whole group (dementia and no dementia) compared to VA general patient population.
Sabodash V 2013	Cross-sectional	25 111	62.4 (6.7) 61.3 (8.3)	56% 53%	Memory clinic. USA	Semantic dementia	Prevalence of SI or SA: 20% in semantic dementia vs 0.9% in AD, $P < 0.001$.
Kim SY 2014	Double blind RCT	66 0	55-85	63.6%	55-85 y outpatients, MMSE 14-26, included in a phase 2 trial. South Korea	AD	Screening of SI or SA as part of the safety assessment at every visit during 12 weeks (crossover, placebo-controlled study, 2 6-week treatment periods). Prevalence of SI: 6.1%. Prevalence of SA: 0%.
Waldö ML 2014	Cohort	97 0	58 (30-84)	52.6%	Memory clinic. Sweden	FTD	Prevalence of suicidal behaviour (SI or SA): 17.5%. Presence of depressive traits in 38.1%. In 9 patients, suicidal behaviour without any signs of depressive traits
Mormont E 2014	Cohort	100 0	77 (6.7)	69%	Memory clinic, MMSE >15/30, GDS = 3-4. Belgium	AD	No SA during 3 months follow-up after diagnosis disclosure. No significant change in depressive symptoms and improvement of anxiety.

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Fonseca L 2014	Cross-sectional	59 59	68 (45-81) NA	51% 51%	Memory clinic database. Portugal	FTD	SA in 17% of FTD patients, OR 3.81 (no CI available).
Randal JR 2014	Case-control	10 741 32 223	NA NA	55.8% 55.6%	All SA or SD cases in Manitoba administrative database from 1995 to 2009 Canada	U	OR of SD: 1.30 (95% CI 0.95-1.77). OR of SA: 1.44 (95% CI 1.14-1.80). Higher risk of SD or SA during the first year after diagnosis. After 1 year, no increased risk of SD but risk of SA remains significant. OR of SD 1 to 90 days after diagnosis: 2.17 (1.03-4.58), 91 to 364 days: 3.14 (1.66-5.94), > 364 days: 1.06 (0.74-1.51). OR of SA 1 to 90 days after diagnosis: 2.61 (1.36-4.98), 91 to 364 days: 2.84 (1.85-4.37), > 364 days: 1.29 (1.01-1.64).
Koyama A 2015	Cross-sectional	634 0	NA	61.8%	Outpatients' dementia clinic. Japan	AD/VD/LBD/FTD	Prevalence of SI: 10.1%. Higher NPI total score in SI+. Depression without SI in 21%. Higher caregiver burden if SI+.
Borges G 2015	Cross-sectional	2003 0	74.3	NA	≥65 y, survey at the home of the participants. Mexico	U	2-week prevalence of SI: 8.3% in dementia vs 4.2% in whole sample, PR 2.14 (95% CI 1.16-3.96). PR 0.82 non-significant in adjusted model that include anxiety and depression.
Mitchell R 2017	Cross-sectional	427 11 684	NA NA	46,6% 56.8%	Population-based record linkage, 50 y, hospitalized for intentional self-harm from 2003 to 2012. Australia	U	Age-standardized incidence rate of hospitalization for self-harm: 72.2/100 000 (95% CI 61.3-83.1) for subjects > 60 y with dementia vs 37.5/100 000 (36.5-38.6) without dementia. Age-adjusted 12 m mortality rate: 25.8% (95% CI 19.5-33.4) for dementia vs 15.4% (95% CI 14.7-16.1) for no dementia $P <$ 00 001.
Morgan C 2018	Case-control	2454 48 921	NA NA	59.6% 59.6%	Population-based record linkage, ≥65 y, self-harm recorded in general practitioner files from 2001 to 2014. UK	U	PR of dementia before SA vs controls: 2.47 (95% CI 2.19-2.80). PR of dementia after SA vs controls: 1.54 (95% CI 1.39-1.70). Increased risk of SD in self-harm whole cohort compared to no self-harm: HR 145.43 (95% CI 53.91-392.29).
Eliasen A 2018	Case-control	8974 89 740	41.5 (15.6) 41.5 (15.6)	63% 63%	>20 y, recorded in national database for self-poisoning with suicidal intent from 2006 to 2013. Denmark	AD, other	Increased risk of SA by self-poisoning in AD: OR 4.8 (95% CI 3.1-7.5). AD who committed SA were younger (mean age of 58.7 y, SD 16.0) than expected.

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Lai AX 2018	Cohort	56 296 0	79.7 (8.9)	2%	VA databases, ≥50 y, 2012 or 2013 and at least once in fiscal year 2008-2011. USA	AD/VD/MD/FTD/LBD	2-year prevalence of SI or SA: 3.89% in FTD, 2.79% in VD, 1.69% in LBD, 2.57% in MD and 0.83% in AD. For the whole population, 873 cases of SI and 69 cases of SA.
Chen R 2018	Cohort	91 126 364 504	NA NA	47.8% 47.8%	Population-based record linkage. Taiwan	AD/VD/other	People with dementia less likely to be hospitalized due to SA, HR 0.67 (95% CI 0.530-0.848) but more likely due to unintentional injury compared to no dementia.
Annor FB 2019	Cohort	141 592 0	NA	64.9%	Population-based record linkage. USA	U	Crude suicide mortality rate among persons with dementia: 9.3/100 000 person-years (95% CI 7.1-11.5). Higher risk if male (OR 4.8, 95% CI 2.7-8.4), if age < 65 y (OR 3.3, 95% CI 1.7-6.4) or 65-74 y (OR 2.3, 95% CI 1.4-4.0), if time since diagnosis ≤12 m (OR 6.0, 95% CI 3.5-10.4) or 12-24 m (OR 3.9, 95% CI 2.0-7.7).
Armstrong M J 2019	Cross-sectional	524	NA	NA	Online survey of caregivers of people with LBD who died in the in the past 5 y. USA	LBD	SD reported in 4 cases (0.8%).
Egan MF 2019	Double blind RCT	653 0	72.4 (7.6)	54.2%	55-85 y, MMSE 15-26, included in a phase 3 trial of verubecestat. 21 countries	AD	Screening of SI or SA as part of the safety assessment at every visit. In the placebo group, incidence of SI: 3.2%, of SA: 0.2%, during 78w follow-up. Higher risk if previous history of psychiatric disorder or SI.
Zucca M 2019	Cross-sectional	35 25	70.1 (6.3) 68.1 (7.4)	48.6% 68%	Memory clinic, MMSE > 23. Italy	FTD	Prevalence of SI: 40% vs 8% in controls (P = 0.009). Prevalence of SA: 11.4% vs 0% in controls (P = 0.006). Subjects with SA are younger and have a longer duration of disease than subjects with only SI.
An JH 2019	Cohort	5909 0	NA	65.8%	56 outpatient's clinics, from 2005 to 2013. South Korea	AD/VD/other	Prevalence of SD: 0.44%. SMR 0.98 (95% CI 0.71-1.31) for whole sample, NS. SMR in AD: 1.04 (95% CI 0.64-1.59), in VD: 0.75 (0.16-2.21), in other dementia: 1.23 (0.67-1.47), NS. Higher risk if unemployment: HR 3.71 (95% CI 1.54-8.95).
Korhonen T 2020	Cohort	75 83	65 (38-85) 66.4 (54-77)	42.7% 56%	Outpatients' memory clinic, retrospective chart review. Finland	FTD	Prevalence of "suicidality" any time before diagnosis: 10.7% in FTD vs 0% in AD.

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Erlangsen A 2020	Cohort	7 300 395 0	NA	50.1%	Population-based record linkage, ≥15 y living in Denmark from 1980 to 2016.	AD or U	AIRR of SD: 0.8 (95% CI 0.7-0.9) for dementia and 0.2 (0.2-0.3) for AD. AIRR of SD during first month after diagnosis of dementia: 3.0 (95% CI 1.9-4.6) and not significant > 3 months. Higher IRR in the period 1980-1999 compared to 2000-2016. Prevalence of SD in dementia: 0.2%.
Choi j W 2021	Cohort	36 541 36 541	NA NA	70% 70%	Population-based record linkage, newly diagnosed dementia from 2004 to 2012, ≥60 y, MMSE≤26 CDR≥1 or GDS≥3. South Korea	AD/VD/other	HR of SD during the first year: 2.57 (95% CI 1.49-4.44) for any dementia, 2.50 (90% CI 1.14-4.44) for AD and 0.94 (95% CI 0.22-4.04) NS for VD. SD in 113 subjects (0.31%) during 9 y follow-up. Higher rate during first year. Higher risk of SD for age 60-74 y compared to >74 y and if mental disorder diagnosed before dementia.
Armstrong MJ 2021	Cohort	95 0	72 (68-76)	26.3%	Movement disorder clinic, retrospective review of all files between 2010 and 2020. USA	LBD	Prevalence of SI at least once during 2 y follow-up: 18.9% (95% CI 12.3-28.0). Persistent SI (reported ≥ 2 visits) in 9.1%. No subject with SI reported a desire or a plan to kill themselves.
Sexton A 2021	Cohort	107 0	NA	NA	Neurogenetic clinic, retrospective review of all files of early onset (<65 y) FTD over the past 5 y. Australia	FTD	SD in 1 subject = 0.93%. SD rate 934/100 000 ≈ 10x higher compared to general population (10/100 000).
Holmstrand C 2021	Cohort	1163 0	83 (79-87)[1]	62.9%	65 y outpatients at risk of moving to nursing home within 6 months. 8 European countries	AD/VD/MD/ FTD/LBD/ other	Prevalence of SI at baseline: 14.27% (mild or intermittent in 10% and severe in 4%). At 3 m: 63 % stable without SI, 9% persisting or newly developed SI, improvement in 7%. Prevalence highest in The Netherlands and lowest in Spain. Prevalence higher in moderate stage of dementia compared to mild stage, if presence of other depressive symptoms or delusion, if anti-dementia medication.
Ortner M 2021	Cross-sectional	157 0	73.3 (11.4)	55.4%	University hospital, CDR 2 or 3. Germany	AD/FTD/VD/ other	Prevalence of SI: 9% in the last month, 28% at some time after symptoms onset. No difference in SI between early and late onset dementia. SA in 2 subjects (1.3%). Higher prevalence of SI in AD compared to FTD and in subjects with more severe BPSD.

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Moon S 2021	Cohort	62 282 0	NA	72.5%	Population-based record linkage, ≥60 y judged to need long-term care services. South Korea	U	Suicide mortality rate: 25.94/100 000 person-years. SD in 0.19% of the cohort. Lower risk in female HR 0.40 (95% CI 0.27-0.57) $P < 0.001$ and in fully dependant subjects HR 0.29 (95% CI 0.14-0.58) $P < 0.001$.
Günak MM 2021	Cohort	63 255 63 255	74.7 (10.3) 74.7 (10.3)	2.6% 3.1%	VA databases, ≥50 y VA health care user in 2008-2011 and 2012-2013. USA	U	Prevalence of SA: 0.6% vs 0.4% in controls. HR 1.23 (95% CI, 1.05-1.44), $P = 0.005$. HR if recent (<2 y) diagnosis: 1.44 (95% CI 1.17-1.77), $P < 0.001$. Prevalence of SD: 0.1% vs 0.2% in controls, HR 0.71 (95% CI 0.53-0.94) $P = 0.02$. Reduced risk of SD in dementia restricted to patients with ancient (>2 y) diagnosis with HR 0.65 (95% CI 0.46-0.89).
Naismith H 2022	Cross-sectional	18 252 0	81.4 (8.3)	61.4%	Population-based record linkage, diagnosis of dementia between 2007 and 2021. UK	AD/VD/MD/LBD	Prevalence of SI in a 12 m period around the diagnosis in the whole sample 15.1%, AD 15.9%, VD 13.1%, MD 14.5%, DLB 19.9%. After adjustment, SI more frequent in LBD and subjects with depression and less frequent in VD and if more impaired in ADL.
Novilla-Surette E M P 2022	Case-control	869 354 098	76.6 (7.1) 83.2 (8.2)	24.7% 53%	Population-based record linkage, ≥65 y, death between 2011 and 2015. Canada	U	SD vs other cause of death: OR 1.72 (95% CI 1.06-2.79) $P = 0.0277$ for recent (<2 y) diagnosis of dementia but OR 0.31 (95% CI 0.22-0.45) $P < 0.0001$ for all dementia cases. Risk of SD in dementia higher "early" <2 y after diagnosis and lower >2 y.
Alothman D 2022	Case-control	14 515 580 159	47.4 (36.0-59.7)[1] 81.6 (72.0-88.4)[1]	25.3% 50.1%	Population-based record linkage, ≥15 y, SD from 2001 to 2019. UK	U	No overall significant association between dementia and SD: AOR 1.05 (95% CI 0.85-1.29) but increased risk if < 65 y: AOR 2.82 (95% CI 1.84-4.33), in first 3 m after diagnosis: AOR 2.47 (95% CI 1.49-4.09), if psychiatric comorbidity: AOR 1.52 (95% CI 1.21-1.93). Highest risk if < 65 y AND within 3 m of diagnosis: AOR 6.69 (95% CI 1.49-30.12).

(continued)

Table 1. (continued)

First author year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Etiology	Main findings
Schmutte T 2022	Cohort	2 667 987 0	NA	62.2%	Population-based record linkage, ≥65 y, new dementia diagnosis from 2012 to 2015. USA	AD/VD/LBD/ FTD/U	SD rate = 26.42/100 000 person-years (0.03%). SMR for suicide = 1.53 (95% CI 1.42-1.65). Higher risk of SD among subjects aged 65 to 74 y with SMR = 3.4 (95% CI 2.94-3.86), within 3 m of diagnosis, in FTD compared to unspecified dementia (HR 2.91, 95% CI 1.67-5.05), if rural residence, if low income, if mental disorder comorbidity, if substance use, if chronic pain. Rate of suicidal event (SI or SA) = 726.46/ 100 000 person-years (0.73%). HR of suicidal event (SI or SA) = 0.83 (95% CI 0.81-0.86) in AD and 1.08 (95% CI 1.02-1.13) in VD compared to unspecified dementia.
Alipour-Haris G 2022	Cross-sectional	125 38 0	68.3 (1.0) to 77.4 (0.6) according to various aetiology	52.8%	Population-based record linkage, hospitalization of patients with dementia related to SI or SA from 2016 to 2018. USA	AD/VD/LBD/ FTD/MD	Among subjects with dementia hospitalized, prevalence of SI in AD = 0.7%, VD = 1.8%, LBD = 1.0%, FTD = 2.2%, MD = 2.3%. Prevalence of SA in AD = 0.1%, VD = 0.2%, LBD = 0.2%, FTD = 0.4%, MD = 0.2% Compared to AD, risk of SI or SA higher in VD (OR 1.85, 95% CI 1.69-201), in FTD (OR 1.35, 95% CI 1.13-1.62), in MD (OR 2.27, 95% CI 2.02-2.54). Risk of SI or SA higher if psychiatric comorbidities and lower in female (OR 0.77, 95% CI 0.73-0.81) and older subjects (per 5 y older: OR 0.85, 95% CI 0.85-0.87).
Jonson M 2023	Cohort	2438	86.6 (6.1)	71.2%	≥79 y, population-based samples in Gothenburg between 1986 and 2015. Sweden	U	Prevalence of SI in the past month: 13.98% in dementia vs 8.9% if no dementia, $P = 0.007$. Participants who reported a wish to die had the lowest survival.

Age = mean (SD or range) except [1] = median (IQR).

Abbreviations: AD = Alzheimer's disease, ADL = activities of daily living, AIRR = adjusted incidence rate ratio, AOR = adjuster odd ratio, BPSD = behavioural and psychological symptoms of dementia, FTD = frontotemporal dementia, GDS = global deterioration scale, HAM-D = Hamilton rating scale for depression, HR = hazard ratio, IQR = interquartile range, LBD = Lewy body dementia, m = month(s), MADRS = Montgomery-Asberg depression rating scale, MD = mixed dementia, MMSE = mini mental state examination, NA = non-available or not reported, NS = not significant, OR = odd ratio, PR = prevalence ratio, SA = suicide attempt, SD = suicidal death, SI = suicidal ideation, SMR = standardized mortality ratio, U = unspecified, VA = department of Veterans Affairs Health Care System, VD = vascular dementia, vs = vs, w = week, y = year(s).

NB. For HR, OR and RR, values are presented with the highest adjustment whenever possible.

Table 2. Studies in People With MCI Included in the Review.

First author Year	Design	N subjects N controls	Age subjects Age controls	Gender % Female	Participant characteristics, setting and location	Main findings
Rubin H 1989	Cross-sectional	41 83	73.9 (5.2) 71.6 (4.9)	44% 51%	Not reported USA	Prevalence of SI at the time of diagnosis: 5%. No significant difference compared to control.
Plamer K 2007	Cohort	47 185	NA NA	NA NA	Longitudinal population-based study, 75-95y Sweden	Prevalence of SI: 17.6% in amnestic-MCI (P = 0.006) and 16.7% in multidomain-MCI (P = 0.002), significantly higher than controls (3.2%).
An J H 2019	Cohort	4260 0	NA	NA	56 outpatients' clinics, all participants with cognitive impairment, 2005 to 2013 Korea	Prevalence of SD: 0.42%. SMR = 0.93 (95% CI 0.55-1.47), NS. Lower risk of SD if higher education, HR 0.90 (95%CI 0.81-0.99), P < 0.05.
Günak M M 2021	Cohort	21 085 63 255	74.7 (10.4) 74.7 (10.3)	3.1% 3.1%	VA databases, ≥50 y VA health care user in 2008-2011 and 2012-2013 USA	Prevalence of SA: 0.7% in MCI vs 0.4% in controls. HR 1.34 (95% CI 1.09-1.65), P = 0.005. HR if recent (<2 y) diagnosis: 1.73 (95% CI 1.34-2.22), P < 0.001. Prevalence of SD: 0.2% in MCI vs 0.2% in controls. HR 0.96 (95% CI 0.66-1.39), P = 0.82.
Rymo I 2023	Cross-sectional	286 182	74.8 (5.6) 72.5 (4.7)	79.4% 63.7%	Population based survey at home or in residential care Sweden	Prevalence of SI in the year before diagnosis: 16% in MCI vs 1.1% in controls. OR 16.99 (95% CI 4.07-70.98), P < 0.001. Increase in SI only significant for passive SI, not active SI. Prevalence of lifetime SI: 35.7% in MCI vs 14.8% in controls, OR 3.18 (95% CI 1.98-5.12), P < 0.001.

Age = mean (SD).
Abbreviations: CI = confidence interval, HR = hazard ratio, MCI = mild cognitive impairment, NA = non-available or not reported, NS = not significant, OR = odd ratio, SI = suicidal ideation, SA = suicide attempt, SD = suicidal death, SMR = standardized mortality ratio, U = unspecified, VA = department of Veterans Affairs Health Care System, y = years.

highly heterogenous, ranging from very poor to high (see Supplemental File 3).

Studies of Dementia

Prevalence Analyses. Twenty-eight studies, including 3 805 208 participants, reported data on the prevalence of SI that ranged from 1.1% to 40%. The pooled proportion of SI was 9.7% (95% CI 6.7-13.9), with a high level of heterogeneity (I^2 = 100%). See Figure 2(A). In our subgroup analysis according to outcome, no difference in terms of effect size was found between studies for which the outcome was SI (k = 26) or suicidal behavior that combined SI and SA (k = 2), P = 0.34. In subgroup analysis according to study design, a significant difference was found between subgroups, with a pooled prevalence of 12.2% (95% CI 8.2-17.7) in cross-sectional studies (k = 18), 7.1% (95% CI 3.2-15.3) in cohort studies (k = 8), and 3.5% (95% CI 2.4-5.1) in RCTs (k = 2), P < 0.01. The heterogeneity remained high for cross-sectional and cohort studies (I^2 = 100%) and was low for RCTs (I^2 = 28%). For additional forest plots, see Supplemental File 5.

Fifteen studies, including 3 936 449 participants, reported data on the prevalence of SA that ranged from 0.1% to 17.5%. The pooled proportion of SA was 0.8% (95% CI 0.3-2.4), still with a very high level of heterogeneity (I^2 = 100%). See Figure 2(B). In subgroup analysis, no difference in terms of effect size was found between studies for which the outcome was SA (k = 13) or suicidal behavior that combined SI and SA (k = 2), P = 0.24, and between cross-sectional studies (k = 7), cohort studies (k = 6), or RCTs (k = 2), P =

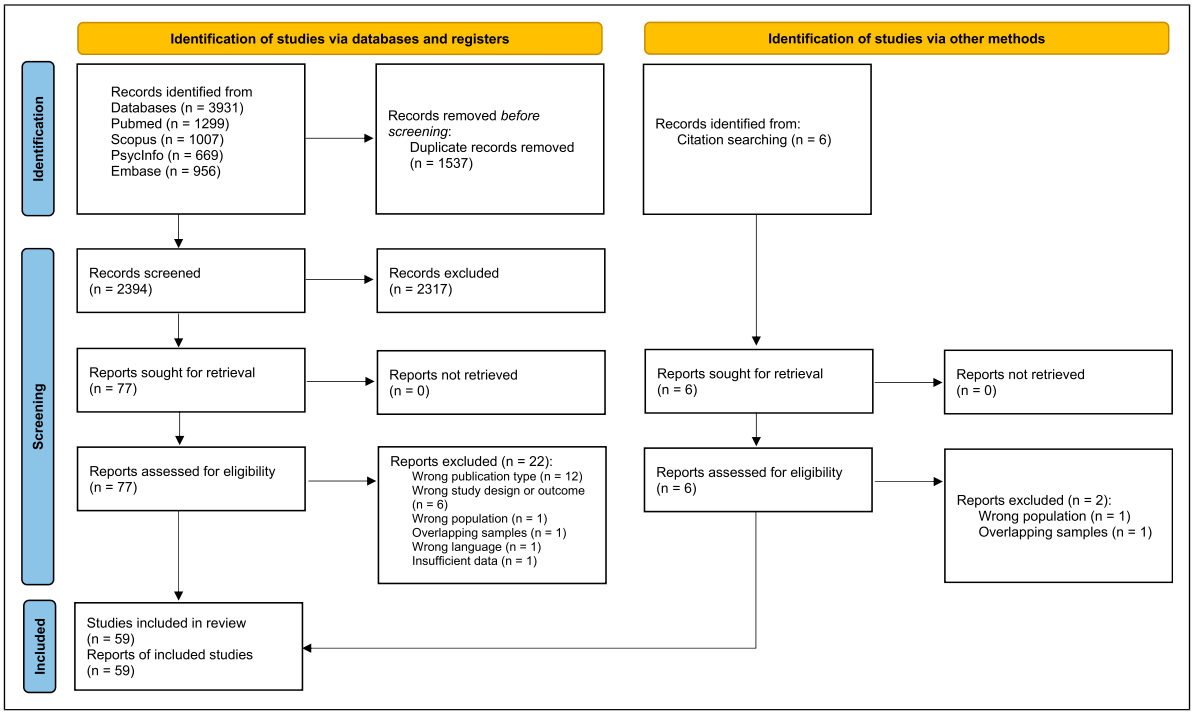

Figure 1. Flow diagram of study selection adapted from PRISMA 2020.

0.17. The heterogeneity remained high for cross-sectional and cohort studies (I^2 = 99%) and was null for RCTs (I^2 = 0%). For additional forest plots, see Supplemental File 5.

Twelve studies, including 3 537 701 participants, reported data on the prevalence of SD that ranged from 0% to 1.5%. The pooled proportion of SD was 0.2% (95% CI 0.1-0.4), with a high level of heterogeneity (I^2 = 100%). See Figure 2(C). In subgroup analysis according to study design, a significant difference was found between subgroups, with a pooled prevalence of 0.2% (95% CI 0.1-03) similar to the global model in cohort studies (k = 10) and a pooled prevalence of 0.9 % (95% CI 0.4-2.0) in cross-sectional studies (k = 2), $P < 0.001$. The heterogeneity remained high for cohort studies (I^2 = 100%) and was null for cross-sectional studies (I^2 = 0%). For additional forest plots, see Supplemental File 5.

A leave-one-out analysis was performed for each outcome and confirmed that the effect size was not determined by a single study. See Supplemental File 5.

Risk Analyses. Six studies that involved 1797 participants with dementia and 3230 controls were pooled and showed a significantly higher proportion of subjects with dementia, reporting SI with an OR of 1.87 (95% CI 1.21-2.88), I^2 = 68%. See Figure 3(A). In our subgroup analysis according to study design, no significant difference was found between cohort studies (k = 1) and cross-sectional studies (k = 5), $P = 0.52$. The heterogeneity remained moderate for cross-sectional studies (I^2 = 74%). For additional forest plots, see Supplemental File 5.

Ten studies that involved 157 852 participants with dementia and 609 780 controls were pooled and showed a significantly higher proportion of subjects with dementia, reporting SA with an OR of 2.40 (95% CI 1.24-4.65), I^2 = 98%. See Figure 3(B). In subgroup analysis according to study design, a significant difference was found between subgroups, with a pooled effect size nonsignificant for cohort studies (OR 1.03, 95% CI 0.43-2.43, k = 2) but significant for case-control studies (OR 3.08, 95% CI 1.51-6.29, k = 6) and cross-sectional studies (OR 4.26, 95% CI 1.25-14.5, k = 2), $P = 0.084$. The heterogeneity remained high for cohort and case-control studies (I^2 = 97%) and was null for cross-sectional studies (I^2 = 0%). For additional forest plots, see Supplemental File 5.

Nine studies, involving 587 723 participants with dementia and 11,019,567 controls, were pooled and showed no significant increase of SD in subjects with dementia, with an OR of 1.13 (95% CI 0.51-2.46), I^2 = 99%. See Figure 3(C). In subgroup analysis according to study design, no significant difference was found between cohort studies (k = 5) and case-control studies (k = 4), $P = 0.97$. The heterogeneity remained high for both subgroups (I^2 = 99% and 100%, respectively). For additional forest plots, see Supplemental File 5.

A leave-one-out analysis was performed for each outcome and confirmed that the effect size was not determined by a single study. See Supplemental File 5.

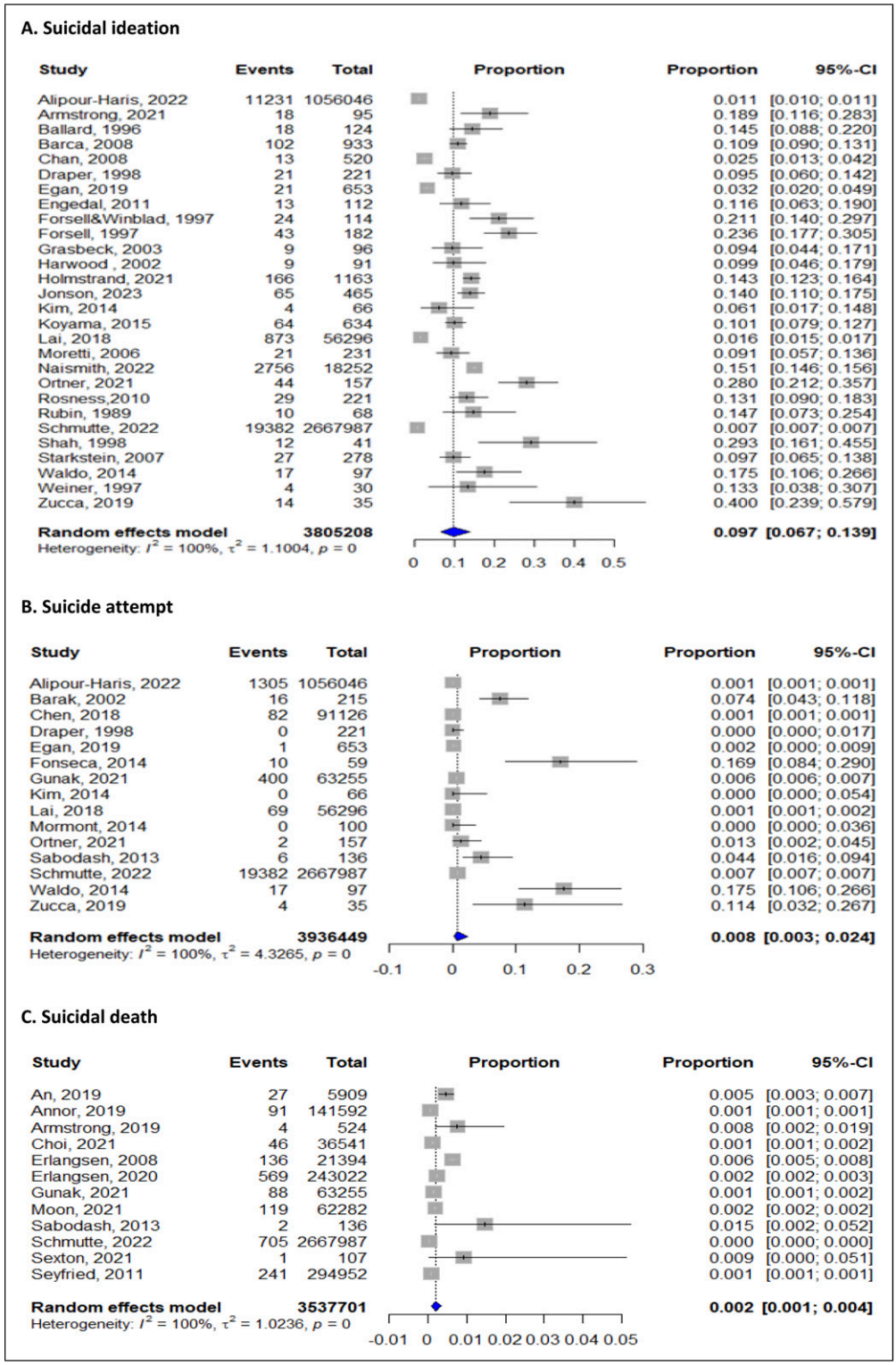

Figure 2. Forest Plots of prevalence of suicidal events in dementia.

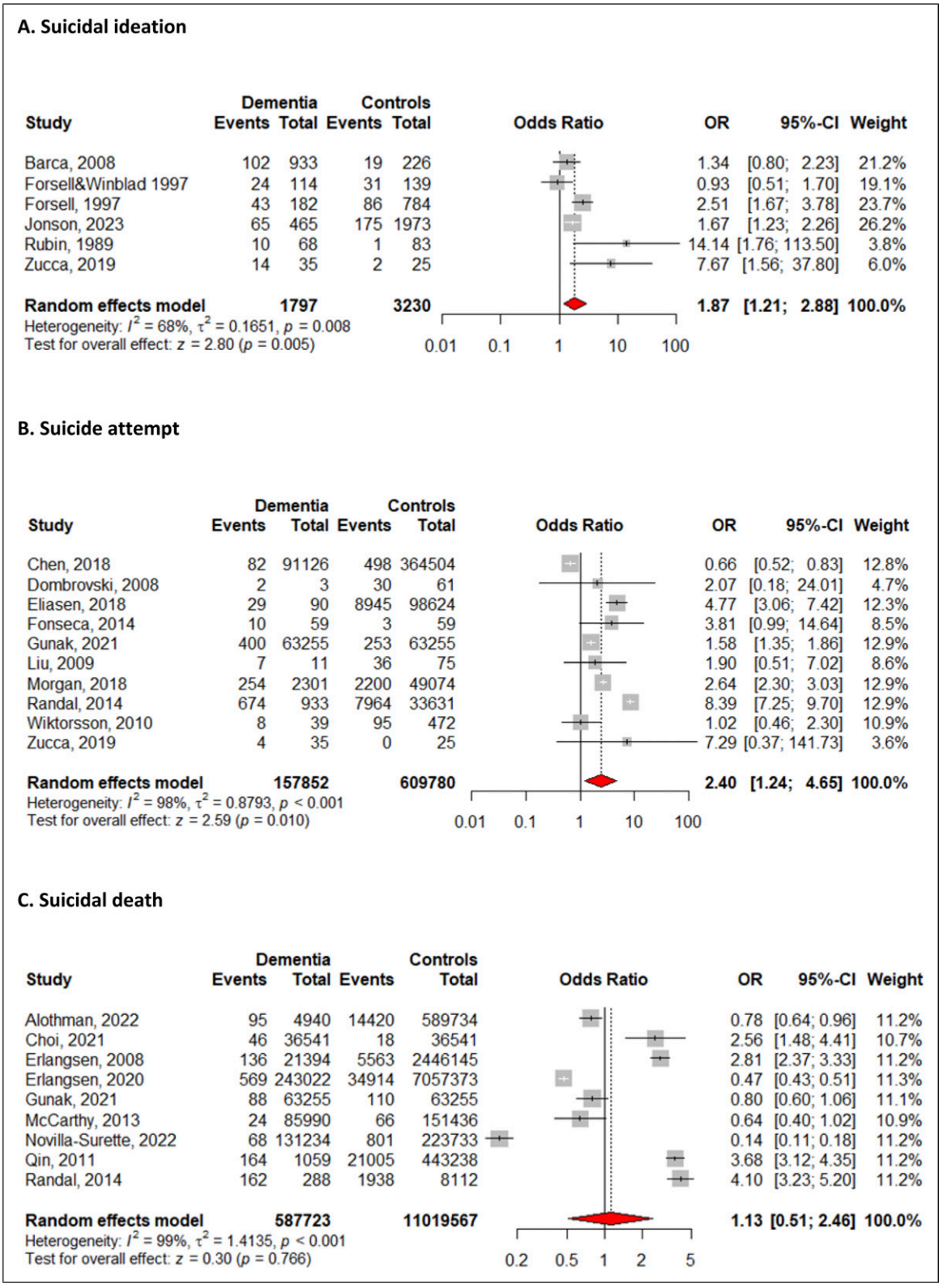

Figure 3. Forest Plots of risk analyses of suicidal events in dementia.

Risk Factors

Sex. One study[54] reported a higher prevalence of SI in women, while another study[25] reported a lower prevalence of hospitalization for suicidal behavior (SI or SA) in women. The risk of SD was found to be higher in women in 1 study[44] and higher in men in 2 studies.[27,59]

Age. Four studies found no correlation between age and SI[39,49,54] and no difference in the prevalence of SI in early onset dementia (<65 years) compared to late-onset dementia.[65] In 1 study, people with AD who committed SA by self-poisoning were younger than expected.[41] In another study, the risk of SA was higher in young FTD participants compared to older ones.[78] Five studies found a significantly higher risk of SD in younger participants compared to older ones, although the cut-off between young and old varied from study to study, between 65 to 75 years old.[26,27,37,44,70] One study found no relation between age and SD.[23] One study found a higher prevalence of SD in participants aged 60 to 69 years, though the difference was not statistically significant in a multivariate logistic regression model.[27]

Severity of Dementia. In 4 studies, the prevalence or the risk of SI was unrelated or not correlated to the severity of cognitive impairment.[32,39,49,54] One study found a higher prevalence of SI in the moderate stage of dementia compared to the mild stage,[50] while another study found a lower prevalence of SI in participants more impaired on activities of daily living.[63] One study found no relationship between the MMSE score and the risk of SD.[23]

Type of Dementia. SI was more frequent in multi-infarct VD compared to subcortical VD[60] and in semantic dementia compared to AD.[69] One study found no difference in the prevalence of SI in different types of dementia (AD, VD, LBD, or FTD).[54] One study found a higher prevalence of SI or SA in FTD compared to other types of dementia,[55] whereas another study found a higher prevalence of SI in AD compared to FTD.[65] In 1 study, the prevalence of SI was higher in LBD and lower in VD compared to AD.[63] One study found a higher prevalence of hospitalization for suicidal behavior (SI or SA) in VD, FTD, and MD compared to AD.[25] In 1 study, the rate of suicidal behavior (SI or SA) was higher in VD and lower in AD compared to unspecified dementia, whereas the risk of SD was higher in FTD compared to unspecified dementia.[70] One study found a lower risk of SD in VD compared to AD.[44]

Time since Diagnosis. Two studies found an increased risk of SA during the first year[67] or the first 2 years[24] after diagnosis of dementia. All the 10 studies that evaluated the risk of SD according to 'time since diagnosis' found a higher risk in the earlier period compared to a longer delay. The cut-off between a short delay or a recent diagnosis compared to a longer delay or an older diagnosis varied widely between studies. It was set respectively at 1 month,[43] 3 months,[26,70] 6 months,[44] 1 year,[37,67] or 2 years[24,27,64] after diagnosis. One study reported that the majority of suicides occurred by patients who were newly diagnosed.[72] However, in this study, a new diagnosis was defined as a first diagnosis of dementia occurring during the study period that lasted 5 years.

Studies of MCI

The prevalence of SI in people with MCI at the time of interview or during the preceding year ranged from 5% to 17.6%. In 1 study, there was no significant difference between the MCI group and the control group.[22] In 2 studies, the prevalence of SI was significantly higher among people with MCI than among control subjects.[20,21] Rymo et al[21] showed an increased risk only for passive SI, not for active and thus more severe SI. Only 1 study[24] reported data on the prevalence of SA that indeed was significantly increased in participants with MCI (0.7%) compared to participants with no cognitive impairment (0.4%), with an adjusted hazard ratio (AHR) of 1.34 (95% CI 1.09-1.65). The risk was higher if the diagnosis was recent (<2 years), with an AHR of 1.73 (95% CI 1.34-2.22). In the same study, the risk of SD was the same among MCI participants (0.2%) and controls (0.2%), with an AHR of 0.96 (95% CI 0.66-1.39). In a cohort of 4260 MCI participants without a control group, with a mean follow-up of 6.4 years, the prevalence of SD was 0.42%.[23] The standardized mortality ratio in this MCI group was 0.93 (95% CI 0.55-1.47) and was not different than the general Korean population. The risk of SD was lower in MCI participants with a higher education level.

Publication Bias

A visual inspection of the funnel plot and Begg and Egger's regression tests revealed a potential publication bias only for studies on the prevalence of SI in dementia. See Supplemental File 5.

Discussion

This meta-analysis showed a high prevalence of SI, occurring in about 1 out of 10 people with dementia, whereas the prevalence of SA was lower, but substantial, in about 0.8%. The prevalence of SD was 0.2%. Compared to people without dementia, people with dementia had roughly twice the risk of SI (OR 1.87, 95% CI 1.21-2.88) or SA (OR 2.4, 95% CI 1.24-4.65), but there was no significant increase in the risk of SD (OR 1.13, 95% CI 0.51-2.46). A previous meta-analysis published in 2020[12]

also showed an increased risk of SA in people with dementia of the same magnitude (OR 2.24, 95% CI 1.01-4.97) and no increase in the risk of SD but in contrast to our study, no increase in SI. A more recent meta-analysis[79] published in 2024, after we conducted our systematic literature search, also concluded that people with dementia had an increased risk of SI (OR 1.62, 95% CI 1.17-2.24) and no risk of SD (OR 1.13, 95% CI 0.81-2.10). However, in contrast to our data, the authors found no significant increase in the risk of SA. This difference is probably explained by the difference in selected studies about attempted suicide (7 out of 10 studies in common in both papers). Nevertheless, their results from the pooled prevalences of SI (10%), SA (0.8%), or SD (0.1%) were similar to our study. No meta-analysis was performed for studies conducted in people with MCI because of the small number of included studies. However, the available data suggested that SI can be highly prevalent in MCI up to 17.6% and higher than in controls. One study showed a moderate increase in SA (AHR = 1.34), while 2 studies showed no increase in SD in MCI.

The risk of suicidal events (SI, SA, or SD) is modulated by many factors like depression and other mental diseases, previous SA, chronic diseases with loss of functional ability, stressful life events, and socio-economic factors.[3,80,81] In this review, it was impossible to address all these factors due to the heterogeneity or the insufficiency of the collected data. Concerning the influence of sex or gender, the type of dementia or the severity of dementia per the risk of any suicidal event, the data were too scarce or conflicting to draw firm conclusions even if suicidal events seemed more frequent in FTD. A systematic review and meta-analysis performed by the same research group as the study of Desai et al.[79] on the same dataset analysed the risk of suicidality in the different dementia subtypes and compared rarer subtypes with AD.[82] They found that people with VD and LBD were more likely to experience SI and that people with VD, FTD or MD were more likely to attempt suicide while people with FTD or MD were no more likely to report SI than people with AD. There was no difference in SD between AD and VD. These heterogeneous results suggest that the risk of suicidal behavior vary from 1 dementia subtype to another. We need to be particularly vigilant with people with FTD or MD, who appear to be at higher risk of SD even though they may be less likely to express SI.

Younger people with dementia seemed to have a higher risk of SA or SD than older subjects. The delay between diagnosis and evaluation also appeared to be an important risk factor. Ten studies showed a significantly elevated risk of SA and SD shortly after a diagnosis of dementia compared to a longer delay, whatever the cut-off between short and long delay was, ranging from 1 month to 2 years. All of these 10 studies relied on administrative databases or population-based record linkages without data about the severity of dementia/cognitive impairment, although 1 can expect that subjects were less cognitively impaired sooner after diagnosis than later. The disclosure of a diagnosis of dementia can be perceived as a stressful life event for the patient.[83] Also, 1 can assume that in an early stage of the disease, the patients may have more insight and greater abilities to understand the consequences of their disease and to anticipate future loss and progressive burdensomeness. Perceived burdensomeness is often considered a major factor leading to suicide.[84] Later in the evolution, the loss of executive functions can impair the ability to plan and commit suicide. People with more advanced dementia are also probably more supervised, with reduced access to lethal means.

Depression or depressed mood and mental health comorbidities have significantly increased the risk of SI, SA, or SD in general populations[3,66] and in dementia.[26,37,61,67,70] The same research group that conducted the study by Desai et al.[75] performed a third systematic review and meta-analysis on the same dataset. They analysed the risk of suicidality in people with dementia according to the presence of comorbid mental health conditions.[85] This review revealed that those people with a general psychiatric comorbidity were at an increased risk of dying by suicide. The presence of depression or anxiety increased the risk of all suicide outcomes: SI, SA or SD. Comorbid personality disorder was associated with an increased risk of SA while substance use was associated with an increased risk of SD. The prevalence of depression in dementia is high,[7] but also in MCI.[86] The relationship between depression and cognitive impairment is complex. It can be difficult to determine whether depression is an independent condition that precedes dementia (and thus an independent risk factor) or whether it is a consequence of dementia. As a result, it may be difficult to determine if depression and other psychiatric comorbidities are independent variables that affect the risk of suicidal events in people with cognitive impairment and if they need to be considered in variable-adjustments in statistical models. This can have a significant impact on the results. For example, in Erlangsen et al.,[43] the adjusted (for period, sex, age group) incidence rate ratio (IRR) of SD in dementia was 2.2 (95% CI 2.1-2.4), yet the fully adjusted IRR was 0.8 (95% CI 0.7-0.9), with adjustment for psychiatric hospitalization or deliberate self-harm prior to dementia diagnosis. The authors acknowledged that adjusting for pre-existing mental disorders could be viewed as over-adjusting.

This study had several limitations. The quality of included studies was highly variable. Some studies had very small sample sizes and obvious recruitment bias. The population-based record linkage studies had the advantage of collecting very large population samples, but many

important clinical data were missing per demographic factors, etiology, or severity of dementia, which limited the subgroup analysis and the appraisal of the accuracy of the clinical diagnosis. Also, the definition of suicidal outcomes and the validity of the scales or instruments used to address them varied by study. Assessing for SI in cognitively impaired subjects is challenging. Language impairments and loss of memory can reduce the ability of patients to accurately report SI or SA, and informant-based questionnaires can be problematic. Some studies[32,42] included a significant proportion of subjects with severe cognitive impairment (a CDR score of 3 or MMSE<10). We assume that it is more difficult for the caregiver to interpret the state of mind or the mood of patients with severe dementia. In studies that used Veteran Affairs databases,[24,55,57,72] the population was composed of more than 96% male subjects, thus was the sample non-representative of the general population. The prevalence of some outcomes may have been underestimated. The subjects may have been reluctant to report directly about SI and feared stigmatization. Suicidal death may be under-reported and miss-classified as accidental death or of undetermined cause.[87] In some studies, the data on SA were limited to events that resulted in hospital-based care.[25,70]

There was very high heterogeneity in the meta-analysis of the OR estimates of SA and SD and the prevalence estimates of SI, SA, and SD during dementia. The heterogeneity was moderate in the estimate of the prevalence of SI. As our subgroup analysis demonstrated, this heterogeneity could not be explained solely by the design of the studies. A variety of factors must be considered, including geographical location, cultural differences, settings of the studies (outpatients vs hospitalization vs long-term care), age of subjects, severity and etiology of dementia, definition and tools to assess outcomes, and length of follow-up. The time period when the study was conducted can also influence the results. For example in Denmark, dementia and especially AD was recently associated with lower rates of suicide,[43] while an earlier study based on the same data source showed an increased risk of suicide.[44] The authors suggested that the implementation of support programs for dementia after 1995 might have prevented some suicides.

Conclusions

People with MCI or dementia frequently have suicidal thoughts and are at an increased risk of suicide attempts. Although the pooled risk of suicidal death was not increased in people with dementia, clinicians should be particularly careful to identify those at higher risk, for example younger patients (<65 years) and those with a recent diagnosis (especially immediately after the diagnosis), a previous mental health disorder, or a diagnosis of FTD. These patients should be offered supportive care and should have restricted access to lethal means (eg, drugs, weapons). More research is needed to better quantify the risk factors and identify patients at risk of suicide, especially during MCI. We also recognized a need to standardize and validate tools and scales to assess suicidal events of people with cognitive impairment. Overall, future research should focus on the prevention of suicide and management of suicidal behavior in people with cognitive impairment.

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