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Review article

# Risk of suicide in people living with dementia and comorbid mental health conditions: A systematic review and meta-analysis



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# ABSTRACT

*Background:* People with dementia (PwD) are more vulnerable to experiencing suicidal ideation than the general population. Within this group, certain risk factors such as being younger and male increase risk of death by suicide. However, currently little is known on whether comorbid mental health conditions in this population also elevate the risk of suicide outcomes. We aimed to determine if comorbid mental health conditions increased the risk of suicidal ideation, suicide attempts and death by suicide in PwD.

*Methods*: Five databases were searched from inception to July 2023. Peer-reviewed publications reporting data for suicide outcomes in PwD with a comorbid mental health condition were included. Random effects metaanalyses models were used to calculate the pooled effect sizes.

*Results*: 22 relevant studies were identified for inclusion 14 of which reported sufficient data to be included in the meta-analyses. In PwD, those with a general psychiatric comorbidity were at increased risk of death by suicide (OR = 2.61, [95%CI: 1.47; 4.63]). Those with comorbid depression or anxiety were at increased risk of all suicide outcomes (depression: ideation OR = 5.11, [95%CI:1.73;15.07], attempt OR = 7.75, [95%CI:2.68;22.41], death OR = 3.44 [95%CI:1.65;7.18]; anxiety: ideation OR = 3.69, [95%CI:1.41;9.66]; attempt OR = 2.27, [95% CI:1.08;4.78]; death OR = 2.36, [95%CI:2.02;2.75]). PwD and comorbid personality disorder and substance use were at increased risk of suicide attempt (OR = 4.60, [95%CI:1.36;15.55] and death by suicide (OR = 2.19, [95% CI:1.80;2.66] respectively.

*Conclusion:* Comorbid mental health conditions put PwD at increased risk of suicide outcomes. There is an urgent need for the assessment and monitoring of mental health in PwD in routine care to mitigate suicide risk.

#### 1. Introduction

Suicide is a global public health concern, with a range of contributing causes and widespread consequences. Despite the development of national and international suicide prevention strategies, the rate of suicide is not decreasing in England (National Health Service, 2023). Therefore, it is important to identify and understand risk factors for suicide to help inform the nature and type of suicide prevention efforts.

Suicide outcomes include suicidal ideation, attempted suicide, and

death by suicide. Suicidal ideation encompasses a range of thoughts, wishes or preoccupations with death and suicide, and can include intent and plans to act on such ideas (Harmer et al., n.d.); for the purposes of this study, the term excludes euthanasia or self-harm without suicidal intent.

Older adults appear to be particularly vulnerable to suicide outcomes, with some estimates indicating that older adults are eight times more likely to die by suicide in comparison to younger age groups (Bachmann, 2018). People with dementia (PwD) may present a

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particularly vulnerable group, although findings have not been consistent. A systematic review and meta-analysis found that a diagnosis of dementia conferred a higher risk of suicide attempts, but not of ideation or deaths (Muñoz et al., 2020). A more recent systematic review and meta-analysis (Desai et al., 2024) found that a dementia diagnosis conferred a higher risk of suicidal ideation (with a prevalence of up to 10 % in PwD), but did not find an increased risk of suicide attempts or deaths. There were significant levels of heterogeneity in the metaanalytic models of both papers, suggesting the potential existence of moderating variables that have not been accounted for.

The recent study (Desai et al., 2024) conducted a thorough review of factors in PwD which increased risk of suicide outcomes. This review highlighted that people with moderate dementia symptoms were more at risk of suicidal ideation than those with mild dementia symptoms. Men with dementia were more likely to attempt and die by suicide than women with dementia, and younger PwD were more likely to die by suicide than older PwD. However, one risk factor of note that was not included in the review was comorbid mental health problems.

Mental health is of particular interest because of its associations with suicide in the general population. A meta-review (Chesney et al., 2014) found strong links between mental health disorders and suicide mortality. Depression was found to have one of the highest suicide rates of all mental health problems. In line with this, a narrative review (Beghi et al., 2021) found a similar pattern for suicide deaths in older adults, and reported depressive disorders to be a strong risk factor for suicide attempts. The prevalence of comorbid depression in people with allcause dementia has been reported as up to 25.0 %, which is significantly elevated compared to healthy community controls (13.0 %) (Kuring et al., 2018). While the prevalence for comorbid anxiety and post-traumatic stress disorder were found to be 14.0 % and 4.4 % respectively, these were not significantly different to the prevalence in healthy controls. Psychotic symptoms occur in approximately one third to one-half of patients with Alzheimer's disease and may occur even more frequently in people with other forms of dementia (Fischer and Agüera-Ortiz, 2018). A large United States study found that for PwD, bipolar disorder had a prevalence of between 1.33 % and 5.67 %depending on dementia type; schizophrenia a prevalence of between 1.26 % and 3.81 %; substance use disorder a prevalence of between 0.32 % and 13.35% (Lai et al., 2018).

The presence of dementia plus a comorbid mental health condition may place an individual at elevated risk of suicide outcomes. However, this has not been adequately assessed. Given this gap in the literature, this study aimed to conduct a systematic review and meta-analysis to investigate whether comorbid mental health conditions are associated with increased suicide outcomes in PwD.

#### 2. Methods

The systematic review and meta-analysis was prospectively registered on PROSPERO (Ref: CRD42022328945) and conducted and written in accordance with PRISMA guidelines (Page et al., 2020).

#### 2.1. Search strategy and selection criteria

Five databases (Medline, Embase, PsycInfo, CINAHL Plus, and Web of Science) were searched from inception to July 2023. Search terms included those relevant to dementia (e.g., 'Alzheimer', 'frontotemporal dementia', 'Lewy body') and suicidality (e.g., 'suicide', 'suicidal ideation', 'life-threatening behaviour') (see Supplementary Information for full search terms). After deduplication of the search hits, the results were subject to a title and abstract screen. The remaining search hits were then subject to full text inspection to assess their eligibility for the current study. Studies were included if they were: peer reviewed; included a population of PwD (as defined by DSM or ICD criteria); reported data on the association of a mental health problem (as defined by DSM/ICD diagnosis or outcome on a standardised measure) with suicide outcomes; written in English or with an English translation. Studies were excluded if they were: review articles; case studies, qualitative studies or intervention studies; studies about euthanasia or self-harm without suicidal intent. In addition, all included studies were subject to forwards searches (citation searches) and backward searches (reference list searches) to identify additional relevant studies. One author (RM) conducted the screen at each stage with another author (EN) independently double rating 10 % of the articles at each stage. Consensus agreement was very good (>98 %) for all stages. Disagreements were resolved through discussion with a senior author (JS).

#### 2.2. Quality assessment

The Newcastle-Ottawa Scale (NOS) (Wells et al., 2000) was used to assess the quality of all included studies, based on three categories: case selection, comparability of cases to controls, and quality of exposure/outcome. Each study could score a total of 6, 8 or 9 depending on study design, and the percentage total indicates high, moderate or low quality. One author (RM) completed the quality assessment on all included studies, with another author (EN) independently double rating all studies. Consensus agreement was good at >90 % for all studies. Disagreements were resolved through discussion with a third author (AJ).

#### 2.3. Data extraction and analysis

Data on study characteristics (authors, year, location, sample size, design) and investigated variables (mental health condition, suicide outcomes) were extracted by one author (RM). Where a study reported frequency data, this was extracted and the odds ratio (OR) and 95 %confidence intervals (95 % CI) were calculated. Where raw data were not available, the OR and 95 % CI were extracted from the study directly. If effect sizes were reported in multiple models with different levels of adjustment, the effect size from the least adjusted model was extracted to allow for better consistency within models and to keep heterogeneity to a minimum. All data extractions were independently double checked by another two authors (RD, AJ). Disagreements were resolved through discussion. As some studies had used data from the same cohort of participants, each estimate was checked for sample overlap. If two study samples overlapped, priority was given to including the study that reported the largest sample size. In the situation where two studies reported the same sample size, priority was given to the study with the longest follow-up period. We conducted a metaanalysis when two or more effect sizes were available for a particular mental health condition and suicide outcome. A random effects model was used to calculate the pooled effect size using the inverse variance weighted method. For all models, heterogeneity was assessed using Cochran's *Q* statistic and the  $I^2$  statistic.

All analyses were run in RStudio (version 2022.12.0 + 353) using the metafor package (Viechtbauer, 2010).

In the situation where a study met inclusion criteria but did not report sufficient data to include in a meta-analysis, the study authors were contacted to request the raw frequency data.

#### 3. Results

#### 3.1. Study selection

A total of 8243 studies were identified from the database searches. After removing duplicates, 4983 studies were screened by title and abstract, of which 121 studies were identified for full text screen. Five additional studies were identified for full text screen through reference searches and forward citation screening of identified studies. In total, 22 studies were identified for inclusion in the current study (see Fig. 1). Of these, 14 had sufficient data to be included in meta-analyses and the remaining eight studies were summarised in a narrative review.

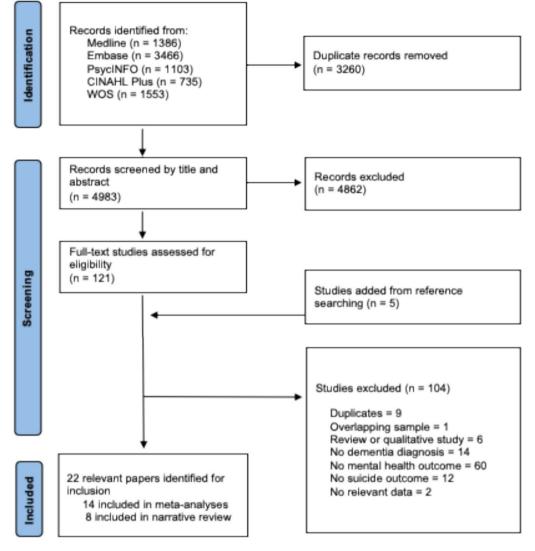


Fig. 1. Flow Diagram Depicting Study Selection Process.

# 3.2. Study characteristics

The study characteristics of 14 studies included in one or more metaanalysis are summarised in Table 1. Four studies (Alipour-Haris et al., 2022; Annor et al., 2019; Schmutte et al., 2021; Seyfried et al., 2011) were conducted in the USA, two (Alothman et al., 2022; Naismith et al., 2022) in the UK and two in Sweden (Hedna et al., 2023; Mo et al., 2023). One study was conducted in each of Germany (Heun et al., 2003), South Korea (Choi et al., 2021), Denmark (Erlangsen et al., 2020) and China (Ou et al., 2020); one across eight European countries (Holmstrand et al., 2021); and one study did not report a location (Osvath et al., 2005). Dementia sample sizes ranged from 65 to 2,667,987 participants. All studies measured either depression (n = 11) or general psychiatric comorbidity (n = 4), with one study (Schmutte et al., 2021) measuring both. Other mental health problems studies included anxiety (n = 5), substance use (n = 4), schizophrenia (n = 3) and personality disorders (n = 2). Studies measured outcomes of death by suicide (n = 8), attempted suicide (n = 3), and suicidal ideation (n = 4). Three studies were classified as longitudinal and six as cross-sectional.

# 3.3. Quality of studies

Ten studies included in the meta-analyses were rated as 'high' quality, and four as 'moderate'.

# 3.4. Meta-analyses

3.4.1. Risk of suicide in PwD with comorbid depression

Pooling data from four studies (N = 19,824 participants) indicated that PwD with comorbid depression were significantly more likely to report suicidal ideation than PwD without comorbid depression (OR = 5.11[95%CI = 1.73;15.07]). There were significant levels of heterogeneity in the model ( $\chi^2 = 76.65$ , df = 3, p < .001,  $I^2 = 96$ %). Pooling data from three studies (N = 2,680,663 participants) indicated that PwD and comorbid depression were significantly more likely to attempt suicide than PwD without comorbid depression (OR = 7.75[95%CI = 2.68;22.41]). There were significant levels of heterogeneity in the model ( $\chi^2 = 250.11$ , df = 2, p < .001,  $I^2 = 100$ %). Pooling data from five studies (N = 3,200,614 participants) indicated that PwD and comorbid depression were significantly more likely to die by suicide than PwD without comorbid depression (OR = 3.44[95%CI = 1.65;7.18]). There were significant levels of heterogeneity in the model ( $\chi^2 = 29.66$ , df = 4, p < .001,  $I^2 = 94$ %) (Fig. 2).

# 3.4.2. Risk of suicide in PwD with comorbid anxiety

Pooling data from two studies (N = 1496 participants) indicated that PwD and comorbid anxiety were significantly more likely to report suicidal ideation than PwD without comorbid anxiety (OR = 3.69[95% CI = 1.41;9.66]). There were significant levels of heterogeneity in the

#### Table 1

Characteristics of included studies.

Study (year)	Country and setting	Design	Sample	Comorbid Mental Health Condition	Suicide Outcome	Observation Window/ Follow-up	Quality Assessmen
(Alipour- Haris et al., 2022) *	USA Inpatients admitted for suicide attempts	Retrospective cross-sectional	N = 12,538 AD n = 5592 VaD n = 5035 DLB n = 578 FTD n = 370 MD n =	Condition: Depression, anxiety, substance use, personality disorder, bipolar disorder, PTSD, psychotic disorder Measure: ICD-10-CM codes	Outcome: Suicide attempt Measure: Algorithm compiled by the Veteran's Health Administration	2016–2018	High
Alothman et al., 2022) *	England Electronic health records from primary care, secondary care and the Office of	Case-control study	NB n = 963 N = 594,674 Dementia n = 4940	Condition: General psychiatric comorbidity Measure: ICD-10	Outcome: Death by suicide Measure: Death record	2001–2019 with median follow-up of 2.3 years	High
(Annor et al., 2019) *	National Statistics USA Dementia registry in Georgia	Retrospective of electronic records	N = 141,592	Condition: Depression Measure: ICD-10	Outcome: Death by suicide Measure: Georgia Vital Records and Georgia Violent Death Reporting	2013–2016 with median follow-up of 4.3 years	High
Armstrong et al., 2021)	USA Patients with DLB at a tertiary movement disorders clinic at the University of Florida	Retrospective cohort study	N = 95	Condition: Depression, anxiety, psychosis Measure: Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), psychosis item on Unified Parkinson's Disease Rating	System Outcome: Suicidal ideation Measure: Suicide item on the Beck Depression Inventory-II (BDI-II)	2010–2020	Low
Carey et al., 2023)	Australia Community-dwelling people living with dementia	Cross-sectional	<i>N</i> = 94	Scale (UPDRS) Condition: Depression Measure: Geriatric Depression Scale-15 (GDS- 15)	Outcome: Suicidal ideation Measure: Two self-report items (one adapted from the Patient Health Questionnaire-9 and one developed for the study)	2018–2020	Low
Choi et al., 2021) *	South Korea National Health Insurance Service data	Longitudinal (12 years)	N = 73,082 Dementia n = 36,541 AD $n =$ 26,936 VaD $n =$ 4326 NOS $n =$	Condition: Anxiety, substance use, schizophrenia, general psychiatric comorbidity Measure: ICD-10 diagnosis	developed for the study) Outcome: Death by suicide Measure: ICD-10 codes X60–X84	10 % random sample of the elderly population aged 60 years or older in 2002 were followed up for 12 years until 2013	High
Draper et al., 1998)	Australia Outpatients in a memory disorders clinic in Sydney	Cross-sectional	5279 N = 221 AD $n =$ 148 VaD $n =$ 24 Other $n =$ 49	Condition: Depression Measure: Clinician- administered Hamilton Depression Rating Scale-24 (HRDS-24)	Outcome: Suicidal ideation Measure: Suicide item on the HRDS-24	1985–1994	Moderate
Engedal et al., 2011)	Norway Patients with AD in nursing homes and geriatric psychiatric hospitals	Cross-sectional	N = 112	Condition: Depression Measure: PDC-dAD, DSM- IV-TR and ICD-10	Outcome: Suicidal ideation Measure: Suicide item on the Cornell Scale for Depression in Dementia	NR	High
Erlangsen et al., 2020) *	Denmark Population-based record linkage: civil, mortality and hospital records via personal ID number	Retrospective electronic health records (11 years)	N = 2,467,539 Dementia n = 21,394	Condition: Depression Measure: ICD-8 or ICD-10 diagnosis	(CSDD) Outcome: Death by suicide Measure: Registered cause of death as indicated on The Registry	1990–2000	High
					of Causes of Death		

# Table 1 (continued)

Study (year)	Country and setting	Design	Sample	Comorbid Mental Health Condition	Suicide Outcome	Observation Window/ Follow-up	Quality Assessment
	linked with numerous national registers	register-based study	VD n = 11,952 DLB n = 1045 PDD = 663 FTD n = 423 NOS n = 15,119 Other n = 1187	specialized healthcare for depression (which requires diagnosis)	Measure: ICD-10 coding of cause of death on the Cause of Death Register		
Heun et al., 2003) *	Germany In- and out- patients of the Department of Psychiatry of the Universities of Mainz and Bonn, with matched controls recruited from the general population	Cross-sectional	N = 185 Dementia n = 76	Condition: Depression Measure: Composite International Diagnostic Interview (CIDI) with diagnosis based on DSM III- R and ICD-10	Outcome: Suicidal ideation Measure: Composite International Diagnostic Interview (CIDI)	NR	Moderate
(Holmstrand et al., 2021) *	Eight European countries: Estonia, Finland, France, Germany, the Netherlands, Spain, Sweden and the UK Community-dwelling	Cross-sectional cohort study	N = 1163	Condition: Depression, anxiety Measure: Neuropsychiatric Inventory (NPI)	Outcome: Suicidal ideation Measure: Score of 1–2 on the suicide item on the Cornell Scale for Depression in Dementia	2010–2013 with 3- month follow-up	Moderate
(Koyama et al., 2015)	PwD Japan Dementia clinic outpatients with a diagnosis of dementia with a community- living carer able to participate in the study	Cross-sectional	N = 634	Condition: Depression Measure: Japanese version of the Neuropsychiatric Inventory (NPI)	Outcome: Suicidal ideation Measure: Assessed by caregiver interview using the Japanese version of the Neuropsychiatric	2007–2013	Moderate
Mo et al., 2023) *	Sweden Electronic Health records/registers	Longitudinal cohort study	N = 1,006,104 Dementia n =	Condition: General psychiatric comorbidity Measure: ICD-10	Inventory (NPI) Outcome: Death by suicide Measure: Death records	2007–2018 with median follow-up of 2.5 years	High
(Naismith et al., 2022) *	UK National Health Service Records from secondary care services in four South London boroughs	Cross-sectional	235,085 $N = 18,252$ $AD = 51.9$ % $VaD =$ $21.7 %$ $MD = 23$ % $DLB = 3.4$	Condition: Depression Measure: Health of the Nation Outcome Scales (HoNOS)	Outcome: Suicidal ideation Measure: Clinician records analysed using a natural language processing application	2007–2021	High
Ortner et al., 2021)	Germany Patients with advanced dementia at a hospital clinic and their carers	Cross-sectional	% N = 157 AD $n =$ 100 FTD $n = 40$ VaD = 4 Other = 13	Condition: Depression, anxiety Measure: Neuropsychiatric Inventory (NPI)	Outcome: Suicidal ideation, suicide attempt Measure: interview with caregiver using modified version of the Columbia- Suicide Severity Rating Scale (C-SSRS)	2017–2019	Low
Osvath et al., 2005) *	Country: NR Inpatients hospitalised in a psychiatric ward	Cross-sectional case-control	N = 214 Dementia n = 124	Condition: Depression Measure: DSM-IV diagnosis	Outcome: Suicide attempt Measure: Reason for	2001–2002	Moderate
Ou et al., 2020) *	after a suicide attempt China Outpatients of the Department of Neurology in West China Hospital of Sichuan University	Cross-sectional retrospective and case-control	N = 3733 Dementia n = 65 (CBS)	Condition: Depression, anxiety Measure: Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Rating Scale	hospitalisation Outcome: Suicidal ideation Measure: Chinese version of the HDRS, including items on death ideation, suicidal ideation or gestures, and suicide	2012-2019	Moderate
(Schmutte et al., 2021) *	USA National cohort of Medicare free-for-	Retrospective longitudinal cohort study	N = 2,667,987	Condition: Depression, anxiety, substance use, schizophrenia, general	attempts Outcome: Suicide attempt, death by suicide	2012–2015 following participants during	High 1 on next page

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#### Table 1 (continued)

Study (year)	Country and setting	Design	Sample	Comorbid Mental Health Condition	Suicide Outcome	Observation Window/ Follow-up	Quality Assessment
	service beneficiaries aged 65+ with newly diagnosed AD or related dementia linked to the National Death Index			psychiatric comorbidity, personality disorder Measure: ICD-9 or ICD-10 diagnosis	Measure: ICD-9 or ICD-10 code	first 12 months after a new dementia diagnosis	
(Seyfried et al., 2011) *	USA Department of Veterans Affairs healthcare records of veterans >60	National retrospective cohort study	N = 294,952	Depression, anxiety, substance use, schizophrenia, bipolar disorder, PTSD	Outcome: Death by suicide Measure: ICD-10 code	2001–2005	High
	years old with the diagnosis of dementia			Measure: ICD-9 diagnosis			
(Shah et al., 1998)	UK Patients from five acute and continuing care	Cross-sectional	N = 194 Dementia n = 42	Condition: Depression Measure: Depression scale	Outcome: Suicidal ideation	1995–1997	Moderate
	geriatric medicine wards in London			on the Brief Assessment Schedule (BAS-DEP)	Measure: Item on the Brief Assessment Schedule (BAS)		
(Zucca et al., 2019)	Italy Patients with behavioural variant	Cross-sectional	N = 60 Dementia n = 35	Condition: Depression, anxiety	Outcome: Suicidal ideation	NR	Moderate
	FTD (bvFTD) attending a memory clinic and healthy age- and education-matched controls		(bvFTD)	Measure: Hamilton depression rating scale (HDRS), Hamilton Anxiety Rating Scale	Measure: Semi-structured interview using the Scale for Suicide Ideations (SSI)		

Note. AD: Alzheimer's disease; VaD: Vascular dementia; DLB: Dementia with Lewy bodies; FTD: Frontotemporal dementia; MD: Mixed dementia; PDD: Parkinson's disease dementia; NOS: dementia not otherwise specified; CBS: Corticobasal syndrome; NR: Not Reported. PwD: People living with dementia.

Study included in meta-analysis.

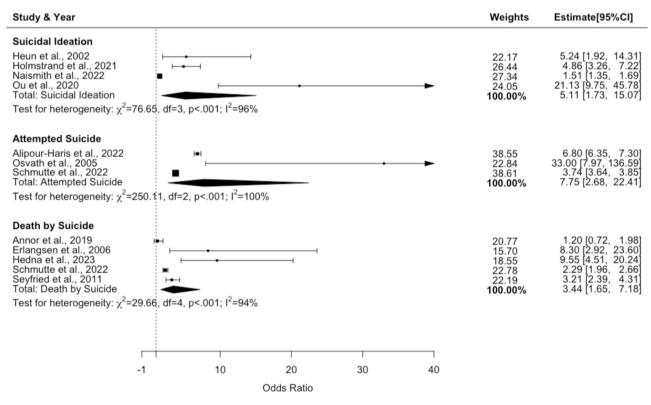


Fig. 2. Risk of suicide outcomes in PwD and comorbid depression.

model ( $\chi^2 = 9.28$ , df = 1, p < .001,  $I^2 = 89$  %). Pooling data from two studies (N = 2,680,525 participants) indicated that PwD and comorbid anxiety were significantly more likely to attempt suicide than PwD without comorbid anxiety (OR = 2.27[95%CI = 1.08;4.78]). There were significant levels of heterogeneity in the model ( $\chi^2 = 373.95$ , df = 1, p < .001,  $I^2 = 100$  %). Pooling data from three studies (N = 2,989,407

participants) indicated that PwD and comorbid anxiety were significantly more likely to die by suicide than PwD without comorbid anxiety (OR = 2.36[95%CI = 2.02;2.75]). The level of heterogeneity in the model was non-significant ( $\chi^2 = 0.88$ , df = 2, p = .64,  $I^2 = 0$ %) (Fig. 3).

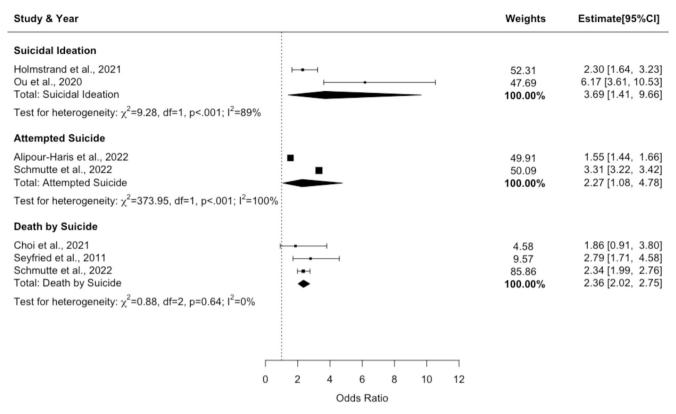


Fig. 3. Risk of suicide outcomes in PwD and comorbid anxiety.

# 3.4.3. Risk of suicide in PwD and other mental health comorbidities

Pooling data from four studies (N = 2,938,952 participants) indicated that PwD and a general psychiatric comorbidity were significantly more likely to die by suicide than PwD without a general psychiatric comorbidity (OR = 2.61[95%CI = 1.47;4.63]). There were significant

levels of heterogeneity in the model ( $\chi^2 = 54.93$ , df = 3, p < .001,  $I^2 = 95$  %). Pooling data from two studies (N = 2,680,525 participants) indicated that PwD and comorbid personality disorder were significantly more likely to attempt suicide than PwD without comorbid personality disorder (OR = 4.60[95%CI = 1.36;15.55]). There were

Study & Year					Weights%	Estimate[95%CI]
$\begin{array}{l} \textbf{General Psychiatric Comorbidity \& Death by Suicided Alothman et al., 2022 \\ Choi et al., 2021 \\ Mo et al., 2023 \\ Schmutte et al., 2022 \\ Total: General Psychiatric Comorbidity & Death by Su \\ Test for heterogeneity: \chi^2 = 54.93,  df = 3,  p < .001;  l^2 = 95\% \end{array}$	icide		-		26.80 21.37 24.62 27.21 <b>100.00%</b>	3.17 [2.61, 3.90] 1.70 (0.94, 3.08] 5.45 (3.70, 8.01] 1.55 [1.34, 1.81] 2.61 [1.47, 4.63]
Personality Disorder & Attempted Suicide Alipour-Haris et al., 2022 Schmutte et al., 2022 Total: Personality Disorder & Attempted Suicide Test for heterogeneity: $\chi^2$ =186.08, df=1, p<.001; l <sup>2</sup> =99	H∎H 		<b>⊢</b> ∎-1		49.85 50.15 <b>100.00%</b>	2.47 [2.12, 2.90] 8.55 [7.85, 9.32] 4.60 [1.36, 15.55]
Schizophrenia & Death by Suicide Choi et al., 2021 Schmutte et al., 2022 Seyfried et al., 2011 Total: Schizophrenia & Death by Suicide Test for heterogeneity: $\chi^2$ =5.58, df=2, p=0.06; l <sup>2</sup> =68%	1 I	_		1	27.35 40.22 32.43 <b>100.00%</b>	4.70 [1.38, 15.98] 0.96 [0.50, 1.84] 0.89 [0.33, 2.39] 1.44 [0.56, 3.75]
Substance Use & Death by Suicide Choi et al., 2021 Schmutte et al., 2022 Seyfried et al., 2011 Total:Substance Use & Death by Suicide Test for heterogeneity: $\chi^2$ =0.01, df=2, p=0.99; l <sup>2</sup> =0%	<u>↓</u> <u>↓</u>				── 0.94 85.98 13.08 <b>100.00%</b>	2.40 [0.32, 18.01] 2.18 [1.77, 2.69] 2.21 [1.29, 3.80] 2.19 [1.80, 2.66]
	0	5	10	15	20	
			Odds Ratio			

Fig. 4. Risk of suicide in PwD with other mental health comorbidities.

significant levels of heterogeneity in the model ( $\chi^2 = 186.08$ , df = 1, p < .001,  $I^2 = 99$  %). Pooling data from three studies (N = 2,982,683 participants) indicated that PwD and comorbid schizophrenia were not significantly more likely to die by suicide than PwD without comorbid schizophrenia (OR = 1.44[95%CI = 0.56;3.75]). The level of heterogeneity in the model was non-significant ( $\chi^2 = 5.58$ , df = 2, p = .06,  $I^2 = 68$  %). Pooling data from three studies (N = 2,982,446 participants) indicated that PwD and comorbid substance use were significantly more likely to die by suicide than PwD without comorbid substance use (OR = 2.19[95%CI = 1.80;2.66]). The level of heterogeneity in the model was non-significant ( $\chi^2 = 0.01$ , df = 2, p = .01,  $I^2 = 0$  %) (Fig. 4).

# 3.4.4. Narrative review

Eight studies did not contain sufficient data to include in the metaanalyses. Armstrong et al. (Armstrong et al., 2021) found that 66 % of individuals with dementia with Lewy bodies (DLB) died within five years, with 0.8 % dying by suicide. In their study, Carey et al (Carey et al., 2023) identified that 37 % of people with dementia (PwD) experienced depressive symptoms, with 6 % reporting suicidal ideation. Draper et al (Draper et al., 1998) found a moderate correlation between depressive symptoms and suicidal ideation (r = 0.35) in a cohort of people with Alzheimer's disease and vascular dementia. Similarly, Engedal et al (Engedal et al., 2011) reported depression in 53.5 % of people with Alzheimer's disease, with 27 % expressing suicidal thoughts. Koyama et al (Koyama et al., 2015) found depression in 21 % of their sample, with 10.1 % experiencing suicidal ideation, which was associated with depression severity. Ortner et al., 2021) found 28 % of people with advanced dementia had suicidal thoughts, and 1.3 % attempted suicide, again this was associated with depressive symptoms. Shah et al (Shah et al., 1998) reported 29 % of PwD had suicidal ideation, again associated with higher depressive symptoms. Finally, Zucca et al (Zucca et al., 2019) found 40 % of people with frontotemporal dementia reported suicidal ideation, with increased anxiety and depression correlating to a higher suicide risk.

#### 4. Discussion

We aimed to assess the risk of suicide outcomes in PwD with coexisting mental health conditions. The analyses indicated that the presence of general psychiatric comorbidity (defined as at least one co-morbid mental health condition) was associated with an increased risk of death by suicide in PwD. We found that PwD and comorbid depression were at elevated risk of suicidal ideation, suicide attempts, and death by suicide. A similar pattern of increased risk was observed in PwD with comorbid anxiety. However, the effect sizes for anxiety were smaller compared to those associated for depression. This suggests that depression may be a more significant risk factor for suicide outcomes in PwD than anxiety. This is in line with the clinical features of depression, as suicidal ideation is a common symptom of depression but not a core component of anxiety. When examining other mental health conditions, comorbid personality disorder was found to be positively associated with elevated risk of suicide attempt, and comorbid substance use was positively associated with elevated risk of death by suicide. However, this review did not find a similar pattern of increased risk in PwD who also have a diagnosis of schizophrenia.

This is the first review to specifically investigate the association of suicide outcomes in PwD and comorbid mental health conditions. The previous review conducted by Desai et al (Desai et al., 2024) found that prevalence of suicidal ideation in PwD was higher than in the general population (10 % vs 2 %). The authors also found that for PwD, certain characteristics were associated with elevated risk of suicide attempts and death by suicide; for example, younger people and men were at increased risk of dying by suicide than older people and women with dementia. The current review extends the review (Desai et al., 2024) by adding the risk factors of depression, anxiety, personality disorder and substance use to the list of factors which may make PwD more

vulnerable to suicide outcomes.

The findings from this review have significant clinical implications for the management of PwD and coexisting mental health conditions. Symptoms of anxiety and depression are commonly found in PwD, with some estimates putting the prevalence at 42 % for depressive symptoms and at 39 % for anxiety symptoms (Zhao et al., 2016). It is important to note the distinction between mental health conditions and neuropsychiatric symptoms (NPS), which encompass non-cognitive symptoms of dementia such as agitation, aggression and apathy (Lyketsos et al., 2011). While depression and anxiety symptoms are common within NPS, they appear to be associated with the neurodegenerative process itself (Lyketsos et al., 2011), whereas psychiatric disorders such as major depressive disorder may precede dementia onset (Onvike, 2016). It should be noted that it may not always be possible to differentiate between the two and NPS are also found to be associated with elevated risk of suicidal ideation (Koyama et al., 2015). However, clinically diagnosed comorbid mental health conditions may indicate additional vulnerability to suicidality beyond that found in PwD with NPS.

The elevated risk of all suicide outcomes, particularly among PwD with comorbid depression and anxiety, highlights the need for routine screening and proactive management of depression and anxiety in this population. Given that depression and anxiety are both prevalent in PwD and that these symptoms increase the risk for all suicide outcomes, clinicians should be aware of the importance of identifying and treating these symptoms in this population. Comprehensive psychiatric or psychological assessment may be important for differentiating mental health conditions from dementia-related symptomatology, to ensure appropriate interventions and suicide prevention strategies.

In addition, results showing that other mental health comorbidities also increase suicide risk (such as personality and substance use disorders) highlights the necessity for comprehensive mental health assessments in PwD, in order to identify and treat these comorbidities. A diagnosis of schizophrenia did not appear to increase the risk of death by suicide in PwD in this study. This null finding may be explained by a lack of power in the analyses as the numbers of PwD and comorbid schizophrenia were relatively low.

In healthcare, there has historically been an assumption that individuals with dementia are not at an increased risk of suicide, as dementia is often associated with cognitive decline and reduced selfawareness, which could potentially lower the risk of such thoughts and actions. This assumption may have led to the underestimation of suicide risk among people with dementia. This lack of awareness is reflected in current healthcare guidance as neither the World Health Organisation's guidelines (World Health Organization, 2017) nor the UK's National Institute for Health and Care Excellence (NICE) guidelines (NICE, 2018) include information about suicide outcomes in this population or address the increased vulnerability of PwD with comorbid mental health conditions. However, recent research (Desai et al., 2024) has challenged this notion and the current research provides further information on which co-morbid mental health conditions are important when assessing risk in this population.

The present study has many strengths including the fact that many of the studies reported data using large cohorts, making the statistical analyses particularly powerful. However, one limitation of the present study is that many of the meta-analytic models contained high and significant levels of heterogeneity. It was not possible to formally analyse this heterogeneity through meta-regression due to insufficient numbers of studies in each model. However, it is likely that some of the heterogeneity is explained by factors such as differences in how mental health outcomes and suicide outcomes were defined, and study design such as follow-up times. Another limitation to the present review is that not all the mental health conditions that PwD can experience were captured in this review due to a lack of available primary studies reporting on these outcomes. Therefore, it is not currently known how less common mental health conditions such as bipolar disorder impact the risk of suicide in PwD. Recent research has also identified that some dementia subtypes are more vulnerable to suicide outcomes than others (Nuzum et al., 2025). Furthermore, depression appears to be more frequent in rarer subtypes of dementia (Chiu et al., 2017). Future research could focus on mental health conditions comorbid with different dementia subtypes, to generate a comprehensive picture of the suicide risk profile in this group.

Overall, these results indicate that PwD with comorbid mental health conditions are at elevated risk of suicide outcomes. The results emphasise the importance of assessing and monitoring mental health in PwD, aiming to mitigate suicide risk through early detection, targeted interventions, and the integration of mental health care into routine dementia management. Addressing these risks may go some way to improving outcomes and quality of life for this vulnerable population.

# CRediT authorship contribution statement

Radvile Medeisyte: Writing - original draft, Methodology, Investigation, Formal analysis, Conceptualization. Eleanor Nuzum: Writing review & editing, Methodology, Investigation, Formal analysis, Data curation. Amber John: Writing - review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Anastasia Tsipa: Writing - review & editing, Methodology, Investigation, Data curation. Caroline Fearn: Writing - review & editing, Methodology, Investigation, Data curation. Georgina Charlesworth: Writing - review & editing. Sebastian J. Crutch: Writing - review & editing. Céline El Baou: Writing - review & editing, Methodology. Gavin R. Stewart: Writing - review & editing. Suman Kurana: Writing - review & editing, Investigation. Emilie V. Brotherhood: Writing review & editing. Katie Flanagan: Writing - review & editing, Investigation. Alberto Salmoiraghi: Funding acquisition. Amy Kerti: Funding acquisition. Joshua Stott: Writing - review & editing, Supervision, Conceptualization. Roopal Desai: Writing - review & editing, Methodology, Visualization, Supervision, Formal analysis, Conceptualization.

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For the purpose of open access, the author has applied a Creative Commons Attribution (CC BY) licence to any Author Accepted Manuscript version arising.

### Declaration of competing interest

I/We declare no competing interests.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.03.075.

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