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Risk factors for suicidal behaviour in late-life depression: A systematic review

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Abstract

BACKGROUND

Suicide is a leading cause of preventable death worldwide, with its peak of maximum incidence in later life. Depression often puts an individual at higher risk for suicidal behaviour. In turn, depression deserves particular interest in old age due to its high prevalence and dramatic impact on health and wellbeing.

AIM

To gather integrated evidence on the potential risk factors for suicide behaviour development in depressive older adults, and to examine the effects of depression treatment to tackle suicide behaviour in this population.

METHODS

A systematic review of empirical studies, published from 2000 onwards, was conducted. Suicidal behaviour was addressed considering its varying forms (*i.e.*,

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wish to die, ideation, attempt, and completed suicide).

RESULTS

Thirty-five papers were selected for review, comprising both clinical and epidemiological studies. Most of studies focused on suicidal ideation (60%). The studies consistently pointed out that the risk was related to depressive episode severity, psychiatric comorbidity (anxiety or substance use disorders), poorer health status, and loss of functionality. Reduced social support and loneliness were also associated with suicide behaviour in depressive older adults. Finally, the intervention studies showed that suicidal behaviour was a robust predictor of depression treatment response. Reductions in suicidal ideation were moderated by reductions in risk factors for suicide symptoms.

CONCLUSION

To sum up, common and age-specific risk factors seem to be involved in suicide development in depressive older adults. A major effort should be made to tackle this serious public health concern so as to promote older people to age healthily and well.

Key Words: Late-life depression; Suicide behaviour; Disability; Chronic disease; Loneliness

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Core Tip: Suicide constitutes a global health concern. In this regard, suicide is one of the leading ten causes of death in five of the 21 Global Burden of Disease defined regions. Suicide mortality is more prevalent in older adults in comparison to younger adults, due to the cumulated influence of multiple risk factors over time. The role of depression in late-life suicide deserves particular interest due to its elevated prevalence and relationship with functional disability and chronic disease development. Results from this study may contribute to planning intensive assessment protocols in older adults with depression to target suicide, as well as to monitoring suicide behaviour as a key indicator of depression treatment success.

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INTRODUCTION

Over 700000 deaths are attributed to suicide every year, making it the second leading cause of preventable death across the world and a serious public health concern[1]. An increasing trend of suicide death has also been reported between 2000 and 2017, with the highest rate of completed suicide observed in men older than 85 years[2-5].

Suicide should be considered a multifactorial phenomenon, involving dreadful consequences at varying levels, such as medical, legal, psychological, and economic levels among others[6]. Furthermore, it should be noted that psychiatric patients are more likely to die by suicide than the general population individuals[7-9].

Major depression deserves particular attention in old age as over 16% of community-dwelling older adults may experience an episode of clinically-relevant depressive symptoms susceptible for a clinical diagnosis, although not all report suicidal symptoms[10,11]. Some authors claim for considering the distinctive features of depression in old age. In this sense, a greater burden of somatic symptoms (e.g., agitation, insomnia, and weight loss) may be evident in late-life depression[12]. Moreover, a higher risk of depressive episode onset may be observed among people with a history of depression in comparison to those who do not show any previous

episode. Since first episodes tend to appear from adolescence to middle age, late-life depression relapses may adopt more enduring statuses with a poorer prognosis in comparison to other life periods[13,14].

Besides, neurodegenerative and other ageing-related processes have to be taken into account in later life[15,16]. From this perspective, ageing-related frailty (*i.e.*, decreased physiological reserves, leading to adverse effects on health) and related disability have been extensively associated with poorer health status, including a higher rate of falls, increased health care service utilization, and mortality. Some studies have also linked limitations in activities of daily living with some somatic symptoms also seen in depression (*e.g.*, fatigue and agitation) as well as with risk factors for depressive symptom aggravation, such as reduced social participation and feelings of loneliness. On the other hand, the increased risk of showing metabolic diseases (*e.g.*, diabetes, hypercholesterolemia, and hypertension) and their daily management may decisively lead to emotional distress and depression development in late life[17,18]. Finally, the aging-related cognitive decline and its pathological evolution to dementia may be expected to increase the risk of late-life depression development[19].

Evidence is mixed regarding the contribution of aging-related factors (*e.g.*, increased metabolic and cognitive decline risk and loss of functionality) on the emergence of suicidal behavior symptoms in late-life depression[20-22]. Note that suicide behaviour should be understood more widely, comprising its varying forms (*i.e.*, wish to die, suicidal ideation, planning, attempt, and completed suicide) falling over the suicidality continuum. In this regard, it is relevant to mention that the strongest risk factors for death by suicide are the engagement in suicidal attempt and suicidal ideation[10].

Each suicidality form may have a distinctive way of expression[23]. Likewise, each form may be influenced by specific risk factors. For instance, suicidal ideation in old age was proven to be associated with sociodemographic factors (*e.g.*, lower educational attainment, living alone, and economic hassles) as well as some clinical factors, such as history of childhood abuse, poor self-perceived health, psychiatric comorbidity, and poorer social support (leading to loneliness and isolation) among others[2,24]. On the other hand, persistent suicidal ideation may be a major risk factor for suicide attempt, as well as other sociodemographic and clinical features, such as being White Caucasian, higher impulsivity levels, and suffering from chronic pain syndromes[21,25,26]. Unfortunately, inconsistencies have been described between the studies focused on suicide behaviour development and its related risk factors in depressive older adults.

This systematic review aimed to gather evidence on the risk of engaging in suicide behaviour among older adults with late-life depression. Moreover, it intended to investigate form-specific nuances of suicidality among older adults with depression, by studying the influence of sociodemographic, clinical, and psychological risk factors on suicidality form risk. Finally, we were interested in exploring the effect of interventions to reduce suicide behaviour on depressive symptoms.

MATERIALS AND METHODS

This study was conducted following the guidelines proposed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015) initiative[27,28]. Moreover, this systematic review was registered in PROSPERO platform (ID: CRD42021223897).

Article selection criteria

Studies were selected according to PICOS strategy in line with PRISMA-P 2015 guidelines. In this sense, the population criteria guided to select the following studies: Studies focused on human samples of older individuals (aged 65 years or higher) with a diagnosis of major depression disorder (MDD), according to a diagnostic manual of (mental) diseases. To satisfy intervention criteria, studies should assess suicide behaviour (by means of interviews, self-reports, or hospital/local or national records). Control criteria guided to select studies that comprised a control group of individuals who had been diagnosed with a MDD (and no suicide behaviour). In longitudinal studies, a baseline assessment of MDD patients would serve as a control condition. Regarding the outcome criteria, study should have a measure of suicide in its varying forms: Ideation, plan, attempt, and completed suicide. In addition, the passive wish to die was also considered as an outcome, as it can be understood as a passive form of suicidal ideation[29-31]. Composite scores derived from integrating multiple suicidality forms (*e.g.*, suicidality risk) were also considered. Finally, criteria on study

item were: Empirical studies published in scientific literature in Spanish or English, from 2000 onwards.

Search strategy

Papers were located following a two-way approach: An ascendant approach which involves scientific databases being consulted. The consulted databases were: Web of Science, PubMed, PsycInfo, and SCOPUS. The database search was conducted between November and December 2020. Queries were created combining three main key terms and their respective thesaurus (see the search queries in the [Supplementary Table 1](#)): Suicide (related MeSH terms: "Suicide, Attempted" and "Suicide, Completed"), depression (related MeSH terms: "Depressive Disorder", OR "Depressive Disorder, Treatment-Resistant" and "Depressive Disorder, Major"), and old age (exact MeSH term: 'Aged').

Articles were screened by a reviewer on an initial review of title, abstract, and keywords. Pre-selected papers were fully read by an independent reviewer to ratify the selection. A third peer reviewer approved the adequate selection of every paper to be included in this study. Discrepancies on paper selection were resolved by discussion.

Data extraction and bias assessment

Relevant data were extracted from each article using a coding manual by an independent coder (different from the reviewers who selected the article). Data from these variables were extracted: Age, sex, sample size, depression status, presence of a psychiatric comorbidity, chronic diseases, and disability; loneliness feelings, self-esteem, mental health treatment, follow-up length (longitudinal studies), and results of the study.

The Newcastle–Ottawa Quality Assessment Scale (NOQAS) was used to measure methodological quality of studies as a way to control for publication bias[32].

RESULTS

Database searches resulted in a total of 16431 hits retrieved. Over 64% ($n = 10495$) of them were duplicated records ([Figure 1](#)). A total of 5936 articles were excluded in the screening phase (*i.e.*, title, abstract, and keyword reading). A final sample size of 35 articles were reviewed after the full-text review phase.

The selected articles and their main features are displayed in [Table 1](#). Over 54% of articles were published in 2010 onwards. On the other hand, 42.86% of articles were led by United States research groups, far followed by studies conducted in the United Kingdom and Taiwan (8.57% of studies in both cases). Study sample size ranged from 24[33] to 654232[34], with a mean of 22211.77 (SD: 109023.38). Male/female ratio was also quite diverse across studies, with a percentage of female participants ranging from 0[2,35,36] to 74%[37]. Mean age fluctuated between studies from 69.51[38] to 84.37 years[39], with an overall mean age of 72.5 (SD: 0.5) years. Finally, the methodological quality of studies ranged from 2 to 9 ([Table 1](#)).

Most studies (60%) selected examined suicidal ideation outcome[3,10,20-22,25,36,38-52]. On the other hand, suicide attempt was assessed in 40% of studies[2,3,21,35,37,41,44,52-57]. Finally, nine studies (25.71%) addressed death by suicide[2,33,34,37,54,56], three (8.57%) assessed wish to die[22,39,58], two (5.71% of studies) focused on suicidality risk[59,60], and only one evaluated suicide planning[45]. The most commonly used scale to measure suicidal ideation was the Hamilton depression rating scale (HDRS)[61] in 23.81% of suicidal ideation studies; a clinical interview relied on the Diagnostic and Statistical Manual of Mental Disorders (DSM)[62], and the Beck scale for suicidal ideation (SSI)[63], both used in 14.29% of studies measuring suicidal ideation. In suicide attempt studies, most of studies collected data on attempts from either national or local registers (42.86% of these studies) due to hospital admission.

Regarding sociodemographic risk factors, Barnow *et al*[39] showed a relationship between increased levels of wish to die and age among German seniors. Moreover, some studies have highlighted a higher risk of suicidal behaviour in women[39,52] and White Caucasian[25]. In the same vein, Lohman *et al*[47] observed lower scores in the HDRS among older adults from ethnic minority groups. On the other hand, the study by Bartels *et al*[41] reported higher scores of suicidal ideation among older Americans from Asian ethnic groups (in comparison to those from the African ethnic group). These authors also found that suicidal ideation was associated with comorbid anxiety disorder, fewer social support, and more medical comorbidity. Moreover, the level of

Table 1 Summary of studies included in the review

Ref.	Sample size	Sex (% female)	Mean age (yr)	Methodological quality	Suicide outcome	Suicide assessment	Treatment study testing and result	Depression-related factors	Significant risk factors
Almeida <i>et al</i> [2], 2016	38170	0	72	5	Suicide attempt and completed suicide	National register			Chronic diseases (+)
Arslanoglou <i>et al</i> [20], 2019	63	73.02	80.52	4	Suicidal ideation	Scale: HDRS	Psychological: PATH. Better outcomes for the PATH intervention <i>vs</i> supportive care	Depressive episode onset (-)	Cognitive function, (+) disability, (-) and social factors (social support) (-)
Aslan <i>et al</i> [3], 2019	150	72.7	71.3	4	Suicidal ideation and suicide attempt	Clinical interview: DSM-IV			Education attainment, (-) anxiety symptoms (+)
Awata <i>et al</i> [40], 2005	1145	58.07	76.29	4	Suicidal ideation	Clinical interview: DSM-IV		Depressive symptoms (+)	Disability (+) and social factors (social support) (+)
Barak <i>et al</i> [53], 2006	202	58.41	76.55	5	Suicide attempt	Local/regional register		Antidepressant use (-)	
Barnow <i>et al</i> [39], 2004	516	48.1	84.37	4	Wish to die and suicidal ideation	Scale: HDRS, GMS-A			Age, (+) sex (female), (+) subjective health status (-)
Bartels <i>et al</i> [41], 2002	2240	23.9		5	Suicidal ideation and suicide attempt	Scale: PSS			Ethnic group (Asians), (+) ¹ medical diseases, (+) social factors (social support), (-) comorbid anxiety disorder (+)
Bakkane Bendixen <i>et al</i> [59], 2018	218	67	75.6	4	Suicidality risk	Scale: MADRS			Anxiety symptoms (+)
Bickford <i>et al</i> [42], 2021	88	62.5	71.5	4	Suicidal ideation	Scale: GSIS		Depressive symptoms (+)	Frailty and disability (+)
Bickford <i>et al</i> [10], 2020	225	64.9	71.4	4	Suicidal ideation	Scale: GSIS			Perceived stress (+)
Bonnewyn <i>et al</i> [58], 2017	68	59.29	73.87	5	Wish to die	Scale: SSI			
Brådvik and Berglund[54], 2009	1206			5	Suicide attempt and completed suicide	National register			
Bruce <i>et al</i> [43], 2004	412			6	Suicidal ideation	Scale: SSI	Pharmacological: PROSPECT. Reductions in suicidal ideation due to treatment		
Cole <i>et al</i> [44], 2006	113	63.4	79.2	5	Suicidal ideation and suicide	Clinical interview: DSM-IV		Major depression (+)	

					attempt				
Coupland <i>et al</i> [55], 2011	60746	66.7	75	6	Suicide attempt	Local/regional register	Pharmacological: Antidepressants. No effect of treatments on suicidal outcomes	Antidepressant use (+)	Self-harm (+)
Hwang <i>et al</i> [35], 2010	70	0	79.4	6	Suicide attempt	Clinical interview			Brain volume (<i>i.e.</i> , reductions in dorsal medial prefrontal cortex) (+)
Innamorati <i>et al</i> [56], 2014	331	24.4		4	Suicide attempt and completed suicide	Autopsy			Social factors: Widowhood, (+) loneliness, (+) social support. (-) Life stressors (+)
Jokinen and Nordström [37], 2008	99	73.73	73	5	Suicide attempt and completed suicide	National register			Dexamethasone suppression (-)
Kiosses <i>et al</i> [45], 2017	74	73.66	80.90	4	Suicidal ideation and plan	Scale: MADRS	Psychological: PATH. Better outcomes for the PATH intervention <i>vs</i> supportive care		Negative emotions, (+) cognitive function (-)
La Pia <i>et al</i> [46], 2001	36	55.55		4	Suicidal ideation	Scale: HDRS	Pharmacological: Fluoxetine. Suicidal ideation reductions as a robust predictor of response		
Lee <i>et al</i> [21], 2003	156	32.69	73.6	2	Suicidal ideation and suicide attempt	Scale: HDRS; Clinical interview: DSM-IV		Delusional symptoms, (+) depressive symptoms (+)	Cognitive function, (-) disability (+)
Liu <i>et al</i> [36], 2020	47	0	83.8	5	Suicidal ideation	Scale: SSI		Depressive symptoms (+)	Chemokines (MCP-2/CCL8) (+)
Lohman <i>et al</i> [47], 2016	112	69.6	76.5	6	Suicidal ideation	Scale: HDRS	Nurse-based: CAREPATH. Lower proportions (31.3%) of CAREPATH patients showing suicidal ideation at follow-up, <i>vs</i> TAU patients (63.6%)		Ethnic group (minorities), (-) disability, (+) burdensomeness (+)
Lutz <i>et al</i> [48], 2021	75	66	71.57	4	Suicidal ideation	Scale: GSIS	Psychological: 12-wk problem-solving therapy. Changes in functional disability predicted the changes in suicidal ideation		Disability (+)
Lynch <i>et al</i> [38], 2004	77	62.3	69.51	3	Suicidal ideation	Scale: ASIQ		Hopelessness (+)	Negative affect intensity and reactivity (+)
Mansour <i>et al</i> [25], 2020	5546	61.5	76.8	7	Suicidal ideation	Clinical Interview: ICD-10			Ethnic group (White) (+)
McIntyre <i>et al</i> [22], 2008	1763	28.59	73.68	4	Wish to die and suicidal ideation	Scale: GSIS			Subjective health status, (-) medical conditions, (+) disability, (+) health service utilization, (+) anxiety disorder (+)

Meeks <i>et al</i> [49], 2008	148	60	80.3	5	Suicidal ideation	Center admission record		Sleep difficulty (+)	Chronic pain, (+)
Morse and Lynch [50], 2004	65	69.2	70.3	4	Suicidal ideation	Scale: ASIQ			
Nishida <i>et al</i> [33], 2015	24	41.67	78.7	8	Completed suicide	Autopsy			Stroke severity (+)
Richard-Devantoy <i>et al</i> [57], 2012	40	62.5	76.5	9	Suicide attempt	Clinical interview: DSM-IV			Cognitive function (-)
Sacco <i>et al</i> [60], 2015	8480	52.97	75.91	5	Suicidality risk	Clinical Interview: ICD-10		Depressive symptoms (+)	Alcohol use disorder, (+) liver disease (+)
Szanto <i>et al</i> [51], 2003	395	72.91	71.4	4	Suicidal ideation	Scale: HDRS	Pharmacological and psychological: Paroxetine, nortriptyline with or without psychotherapy. Participants with a higher risk of suicidality needed a greater time for suicidal ideation reduction	Depressive episode onset, (-) number of episodes, (+) depressive symptoms, (+) recurrence of depressive episode (+)	Psychiatric inpatient (+)
Tan and Wong [52], 2008	80	69.1	72.7	5	Suicidal ideation and suicide attempt	Scale: BDI, SSI. Clinical interview (not specified)		History of suicide behavior (+)	Sex (female), (+) psychiatric inpatient treatment (-)
Zivin <i>et al</i> [34], 2007	654232			7	Completed suicide	National register			Substance use disorder, (+) PTSD (-)

¹In comparison to black participants.

The methodological quality of the studies was assessed by means of the Newcastle-Ottawa Quality Assessment Scale. The relationships between the depression-related and risk factors with the suicide outcome were positive (+), indicating the higher the level of the factor (or the presence of this condition), the higher the risk of the suicide outcome. An inverse relationship between the depression-related and risk factors with the suicide outcome was indicated by (-), with higher levels of the factor (or the presence of this condition) associated with a lower suicide outcome risk. ASIQ: Adult suicidal ideation questionnaire; DSM: Diagnostic and statistical manual of mental disorders; BDI: Beck depression inventory; GMS-A: Geriatric mental state examination; GSIS: Geriatric suicide ideation scale; HDRS: Hamilton depression rating scale; ICD: International classification of diseases manual; MADRS: Montgomery-Asberg depression rating scale; SSI: Beck scale for suicidal ideation.

education was negatively associated with a higher risk of suicide behaviour engagement (*i.e.*, suicidal ideation and attempt), as Aslan *et al*[3] reported.

In terms of depression features, the studies showed a higher risk of suicide in depressive episodes with earlier onset[20,51]. On the other hand, the use of antidepressants was associated with a lower risk of suicide behaviour[53], but results did not seem to be conclusive due to divergences with other studies. In this vein, Coupland *et al*[55] observed a higher probability to show suicide behaviour in patients under antidepressant treatment. Finally, the severity of depressive symptoms was strongly associated with higher suicide behaviour across studies[36,40,42,51,60]. Meeks *et al*[49] highlighted the relationship between sleep difficulty and suicidal ideation. More concretely, the study aimed to assess whether chronic pain would be associated with comorbidity, length of hospitalisation, suicidal ideation, and sleep duration in depressive geriatric inpatients. As a result, the authors found an elevated prevalence

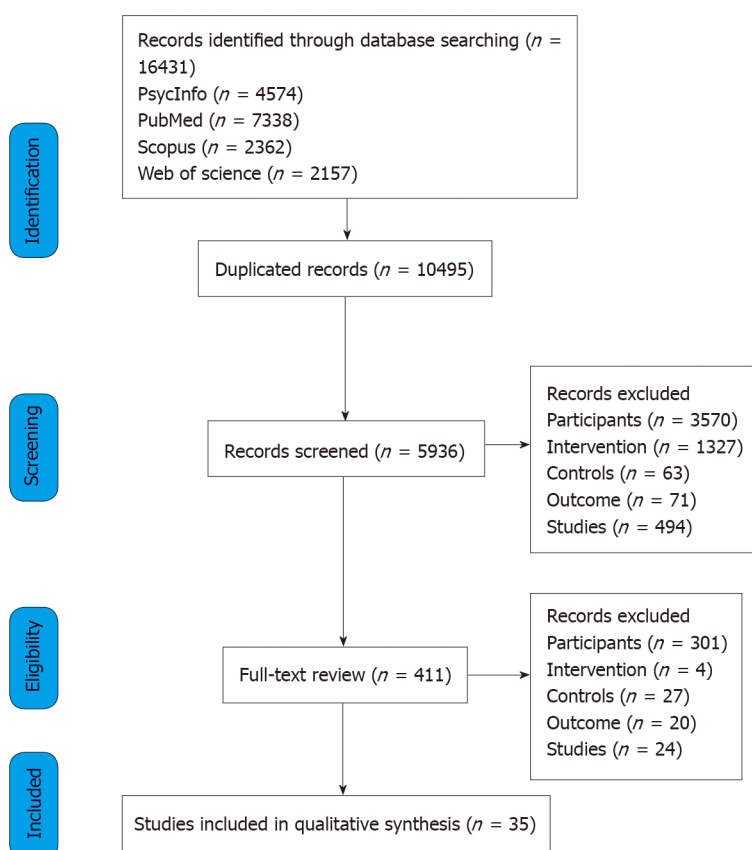


Figure 1 Flow diagram of study selection

of chronic pain among these patients (62% of patients). Moreover, patients with comorbid depression and chronic pain showed a higher risk of suicidal ideation than patients without chronic pain. Other factors associated with suicidal ideation in this study were the diagnosis of a personality disorder, more elevated medical burden, and total sleep time decrease.

The study by Lynch *et al*[38] provided some evidence in line with the well-known relationship between suicidal ideation and hopelessness. Finally, other studies point to a higher risk of suicidal behaviour in patient with both history of depressive episodes (*i.e.*, number of episodes and recurrence) and number of suicide episodes[51,52].

Regarding clinical factors, studies agree in highlighting the relationship between health status indicators and suicidality forms. First, some studies showed an increased risk of suicidality in psychiatric inpatients[34,52]. Moreover, mounting evidence has suggested a consistent relationship between anxiety (*i.e.*, comorbid anxiety disorder or elevated anxiety symptoms) and suicide, regardless of suicidality form[3,22,41,59]. Other studies focused on comorbidity with other psychiatric disorders. In this vein, Zivin *et al*[34] highlighted a reduced risk of death by suicide among veterans with comorbid depression and posttraumatic stress disorder. However, this result was moderated by age, as younger veterans did show a higher suicide rate than their older counterparts. Results were contradictory regarding personality traits. As aforementioned, Meeks *et al*[49] did find a positive relationship between suicidal ideation and a diagnosis of a personality disorder in depressive older adults with chronic pain. However, Morse and Lynch[50] failed to identify positive correlations between pathological personality traits (*i.e.*, paranoid, schizotypic, narcissistic, borderline, and avoidant) and suicidal ideation. On the other hand, the presence of co-occurring substance abuse disorder was associated with a higher suicide risk in this sample. Sacco *et al*[60] also found a significant relationship with alcohol use disorder. The association between cognitive decline and suicidal ideation seems to be evident as shown by Kiosses *et al*[45] and Richard-Devantoy *et al*[57], even though none of the studies addressing cognitive function included samples with either dementia or mild cognitive impairment.

Several studies showed an increased risk for suicidal behaviour with higher disability levels[20,22,40,42,47,48], poorer health status[22,39], and multimorbidity[41, 47]. Almeida *et al*[2] studied the relationship of multiple clinical factors with suicide

attempt and completed suicide among older men from Australia. The authors found that more than 57% of depressive men who completed suicide showed physical multimorbidity (*i.e.*, five or more health conditions). McIntyre *et al*[22] aimed at providing some evidence on the influence of comorbid anxiety on suicidal risk of depressive patients. The authors concluded that anxiety and depression co-occurrence may represent a gradient of clinical severity, leading to increasing levels of poorer self-reported health status, higher number of medical disorders, worse mental functioning, and greater use of emergency services. On the other hand, as aforementioned, chronic pain was associated with increased suicidal ideation[49]. Finally, the postmortem study by Nishida *et al*[33] revealed a clear relationship between stroke severity and completed suicide in older adults who had presented acute poststroke depression. More concretely, suicide victims were more likely to have shown progressive supranuclear palsy with argyrophilic grain disease.

In terms of psychosocial factors, the lack of social support has been systematically associated with suicidality across studies, particularly with suicidal ideation[20,40,41]. Innamorati *et al*[56] conducted a postmortem study comparing data from psychological interviews of patients who died by suicide and psychiatric outpatients who did not engage in suicide attempt. The study revealed higher levels of loneliness and lack of social support among suicide victims. Moreover, victims were more likely to be widowed and living alone before death. Finally, higher levels of stress were found among suicide victims. Bickford *et al*[42] also highlighted the relationship between perceived stress levels and suicidal ideation. Jokinen and Nordström[37] provided a piece of evidence connecting physiological stress response and suicide. The study analysed how the dexamethasone test (DST) may be useful to predict suicide attempt or death by suicide among depressed inpatients. A total of 24 patients (24.24% of sample participants) committed a suicide attempt and six patients died by suicide. The DST no-suppression was proven to be able to distinguish between suicide victims and survivors. On the other hand, Liu *et al*[36] explored how inflammatory factors and chemokines (the hypothalamus-pituitary-adrenal axis is involved in regulation of inflammatory factors) may distinguish between depressive men with and without suicidal ideation. As a result, participants with suicidal ideation showed higher levels of MCP-2/CCL8 chemokines than healthy controls and depressive men without suicidal ideation, as well as a higher number of depressive symptoms.

Finally, interventions to deal with depression and suicide behaviour deserve being mentioned. Eight studies analysed the effects of interventions to ameliorate depressive symptoms, targeting suicidal behaviour (*i.e.*, ideation and attempting). Three studies tested psychological interventions[20,45,48], and three were focused on pharmacological interventions[43,46,55]; the study by Lohman *et al*[47] analysed the effects of a nursing-based intervention (the CAREPATH). On the other hand, the study by Szanto *et al*[51] included data from two primary trials on antidepressant treatments (*i.e.*, paroxetine and nortriptyline) and another trial combining pharmacological and psychological treatment. The 12-wk problem adaptation therapy (PATH) programme was studied by Kiosses *et al*[45] and Arslanoglou *et al*[20]. The intervention was focused on providing emotion regulation skills. The PATH yielded reductions in suicidal ideation during the course of treatment, in comparison to supportive therapy. On the other hand, Lutz *et al*[48] evaluated factors related to suicide ideation due to a psychological treatment delivery (12-wk problem-solving therapy). As a result, they found that the changes in functional disability derived from the intervention predicted the reductions in suicidal ideation.

Regarding pharmacological interventions, results were mixed. First, Coupland *et al*[55] showed that the use of antidepressants (regardless of typologies: Tricyclic antidepressants or selective serotonin reuptake inhibitors) was associated with the presence of suicide attempts among the patients. However, Bruce *et al*[43] found beneficial effects of the use of antidepressants following the PROSPECT clinical algorithm (citalopram and psychiatric sessions, with training for clinicians to better manage late-life depression) on suicidal ideation. La Pia *et al*[46] studied the effect of fluoxetine on late-life depression. The authors found that suicidal ideation change was a robust predictor of treatment response. Szanto *et al*[51] pointed that symptom amelioration due to pharmacological intervention (with or without psychotherapy) was slower in depressive patients with a higher suicidality risk.

Lohman *et al*[47] analysed the effectiveness of the nurse-based depression management intervention (CAREPATH) in older adults with depression. The authors found a decreased risk of suicidal ideation in the CAREPATH group (only 31.3% of patients showing suicidal ideation in the 1-year follow-up), in comparison to controls (63.6% of them showing suicidal ideation). The decreased risk of suicidal ideation was associated with being an ethnic minority member, and lower limitations in instru-

mental activities of daily living and burdensomeness.

DISCUSSION

This systematic review aimed to gain insight into the risk factors for suicide behaviour development in older people with depression. From a lifelong perspective, suicide behaviour may reach its level of maximum incidence rate in late life[5,10]. Depression constitutes a main contributor to suicide behaviour development across the lifespan[8,64,65]. A total of 35 manuscripts were selected from our robust methodological approach, covering both clinical studies[20,33,55] and epidemiological studies[34]. Despite the wide heterogeneity observed between the studies, our review revealed that most papers focused on suicidal ideation, mainly using self-reported measures, followed by suicide-attempt studies. Very few studies addressed risk factors for early forms of suicidality, such as passive suicidal ideation (*i.e.*, wish to die ideation)[22,39,58], as well as completed suicide and its potential risk factors[2,33,56].

Our study focused on the role of four types of risk factors for suicide behaviour: Sociodemographic factors, factors related to depressive episodes (current episode and history of episodes), other clinical factors (both psychiatric and organic factors), and psychosocial factors. In addition, the effect of mental health interventions was studied. First, it highlighted the influence of some sociodemographic factors on suicidal ideation among depressive older adults: Being woman and White Caucasian[39,47,52]. According to the integrated motivational-volitional model (IVM)[23], the genetic, biologically-based vulnerabilities may put individuals at higher risk of particular suicidality forms. In this vein, findings derived from the studies reviewed suggest that sex (being woman) and ethnic factors may show an age-invariant effect on suicidal ideation among depressive individuals, in line with other studies across the lifespan [64,65]. Unfortunately, data exploring the relationship between sociodemographic factors and other suicidality forms (*i.e.*, attempt and completed suicide) were not available for late-life depression patients. The exception that proves the rule only comprises two studies. First, Aslan *et al*[3] found a relationship between elevated suicidal ideation and attempt, and lower education level. Innamorati *et al*[56] showed that widowhood may be associated with a higher risk of engaging in suicide attempt and death by suicide. Widowhood may make social networks and participation become limited, with the subsequent emergence of feelings of loneliness and other mediators of suicide behavior[23]. Difficulties in emotion regulation and disease management may be related with a lower education level in old age[17,66]. In other words, lower education level may therefore be associated with poorer coping strategies. In line with the IVM[63], deficits in coping strategies may increase motivational moderators of suicidal ideation (*i.e.*, feeling of defeat, hopelessness, humiliation, or entrapment). The difficulties in emotion regulation may also be seen in depressive older individuals with cognitive decline[67].

Some episode-related factors may be involved in the emergence of suicide behaviour symptoms. These factors may boost the influence of motivational moderators on suicidal ideation and may increase the probability of ideation turning into attempt subsequently. The history of recurrent depression deserves being mentioned. First, depressive older adults are very likely to show a history of previous episodes[13]. Moreover, a depressive episode tends to be associated with a poorer prognosis and enduring symptoms in late life[68,69]. The studies included in this review were quite consistent in highlighting an increased risk of suicidal ideation among people with more severe episodes (*i.e.*, episode with an earlier onset, more severe symptoms, and treatment resistance) and those with a history of depressive episodes[20,36,42,46,51,60]. Conversion of suicidal ideation into suicide attempt may be boosted by the history of self-harm and suicide episodes, due to habituation processes and increased physical pain tolerance[55]. In this vein, people may erroneously learn that the suicide attempt constitutes an optimal strategy to cope with hassles and problematic situations[63].

Other clinical factors highlighted in our study were the presence of either a comorbid anxiety disorder or a co-occurring substance use disorder. Both types of disorders have been strongly associated with suicide behaviour symptoms[70,71]. Of particular interest is the relationship found between comorbid depressive and anxious symptoms and suicide among community-dwelling older adults, even from earlier subclinical stages[72,73]. On the other hand, alcohol-related disorders are strongly associated with suicide, both at the individual level (*e.g.*, up to six times more likelihood to engage in suicide behaviour in alcohol abusers) and population (*i.e.*,

increasing population drinking trends are associated with raising suicide rates) level [74,75]. Conversely, the debate is still open on the relationship between pathological personality traits and suicide among depressive older adults, due to the low number of studies and mixed evidence obtained [49,50]. Some mediating factors (*e.g.*, impulsivity or emotion dysregulation) are very likely to play a relevant role in the relationship between personality and suicide [23].

Multimorbidity and poorer health status have been systematically associated with suicide behaviour symptoms across studies [2,41,47]. In the similar vein, disease burden and difficulties in activities of daily living have proven to put depressive older adults at higher risk of suicide behaviour, regardless of suicidality form [20,42,48]. Disability and chronic diseases have shown a main, independent association with suicide, apart from depression [76,77]. However, these results should be considered more cautiously due to the influence of multiple ageing-related processes (*e.g.*, inflammatory imbalance and metabolic dysregulation) on both depression and chronic disease development [78,79]. Anyway, disability and chronic disease management may be particularly challenging and stressful for older adults due to progressive functional losses, increased economic costs, and frequent hospital admission [80,81]. Elevated stress has also been associated with a higher risk of suicidality across the reviewed studies [10,56]. In line with the IVM, recurrent exposure to stressors and daily hassles may increase the salience and cognitive accessibility of suicide triggering individuals engaging in suicide attempt [23].

Regarding the psychosocial factors, the reviewed studies identified the lack of social support and increased feelings of loneliness as main contributors to suicide behaviour in depressive older adults [20,41,56]. Social participation and social support may buffer the impact of stress in late life. In turn, social resources may work as protective factors that prevent depressive symptom aggravation and suicide behaviour emergence [82,83]. On the other hand, social isolation and related emotional states (*i.e.*, loneliness) may lead to systematic deficient emotion regulation due to its impact on cognitive bias development (*e.g.*, selective retrieval of negative memories), as well as metabolic dysregulation due to loss of adherence to healthy lifestyle habits [84-86].

Finally, eight intervention papers were reviewed in our study. Some of the papers analysed the effect of targeted treatments on suicide behaviour [45,47], and others (pharmacological treatments, mainly) focused on wide depressive symptoms [46,51]. As a main conclusion of these studies, the reductions in suicidal behaviour (suicidal ideation) were moderated by changes in risk factors (*e.g.*, functional disability and burdensomeness) that may presumably involve deactivation of suicide-related cognitive mediators (*e.g.*, hopelessness and feelings of entrapment). Unfortunately, further studies should be done to support this speculation. On the other hand, it was found that a robust predictor of treatment response to antidepressants was the reduction of suicidal ideation. Some studies postulate the role of suicide ideation as a central symptom of depression whose amelioration may lead to improvement in other symptoms, due to contagion mechanisms [87,88]. Therefore, all these studies stress the key role of suicide behaviour in the maintenance of a depressive disorder in late life.

The present study comes from a robust framework to systematically review the risk factors of suicide behaviour emergence, maintenance, and remission in depressive older adults. Depression constitutes a highly prevalent mental disorder with a dreadful impact in late life [89,90]. Suicide behaviour has been consistently associated with depression, leading to worse outcome. Our study examined suicide in depressive older adults considering varying suicidality forms (*i.e.*, wish to die, suicidal ideation, attempt, and completed suicide). Moreover, a wide variety of risk factors were studied. On the other hand, the present study has some limitations that deserve mentioning. First, conclusions from this systematic review are essentially qualitative. Further studies should address the relationship between depression and suicide from a more analytical standpoint (*i.e.*, meta-analysis). Furthermore, our review was focused on recent literature covering the period from 2000 onwards. In this regard, the present study serves as an updated picture of the existing literature on depression and suicide in older adults. On the other hand, subthreshold depression was not addressed in this study. Some studies have demonstrated an evident relationship between subclinical depression statuses and suicide in old age [73,91,92]. In this regard, full-blown depressive disorders are related to a higher risk of negative outcomes and usually show a poorer prognosis in late life [89,93]. Finally, this study came from defining older adults as individuals who are 65 years or older. Our definition goes in line with that proposed by the World Health Organization [94]. Although we are aware that this definition might be narrowed, we decided to adopt a robust criterion for older age definition due to the huge variability of definitions across cultures [95].

CONCLUSION

Some clinical implications may be derived from our study. First, further research should be done to disentangle specific mechanisms involved in some forms of suicidality. In this vein, it is particularly relevant to gain insight into potential risk factors for dangerous suicidality forms (*e.g.*, suicide attempt and re-attempt) in a vulnerable population as older adults are. Second, policy makers may have a decisive role in tackling suicide in old age by promoting multicomponent prevention strategies, addressing both health-related and social factors (*e.g.*, strategies to promote social participation). Finally, suicide-targeted interventions should be developed and delivered on a wider basis to tackle the excess of mortality by suicide and to treat depression syndromes in older adults. In the same vein, suicide behaviour should be prioritised as a key therapeutic goal, even from its earliest forms (*i.e.*, wish to die).

ARTICLE HIGHLIGHTS

Research background

Suicide is one of the most relevant health hazards worldwide, particularly in old age with elevated rates of mortality by suicide. Depression constitutes the most prevalent mental health condition in old age, affecting almost one in five older adults at a community level. Depression is one of the most relevant risk factor for suicide behaviour in its multiple forms (*i.e.*, ideation, attempt, and completed suicide).

Research motivation

This study comes from the interest in reinforcing lines on research at community and clinical levels so as to improve the quality of life of older patients that may show severe mental health conditions: Older adults with depression and suicidal ideation and behaviour.

Research objectives

This study aimed to analyse the relationship between risk factors for suicide behaviour development and late-life depression, as well as to explore the effects of depression treatment on suicide behaviour.

Research methods

A systematic review was conducted covering the period from 2000 onwards, by selecting scientific papers on the relationship between late-life depression and suicide. The review was conducted following the guidelines proposed by the PRISMA-P 2015 statement.

Research results

Factors related to depressive episode severity, psychiatric comorbidity, poorer health status, and disability were highlighted to be related with the emergence of suicide behaviour among depressive older adults. Psychosocial factors were also involved in suicide behaviour emergence. Finally, suicidal behaviour was proven to be a key predictor of depression treatment response.

Research conclusions

Very few studies were focused on severe suicidal behaviour. For that reason, further research is needed to accurately disentangle the pathways involved in the transition between ideation and suicide attempt to prevent death by suicide. Changes in suicidal ideation seem to be decisive in terms of depressive disorder prognosis in late life.

Research perspectives

The results may help increase the awareness on the study of mechanisms involved in suicide from people at risk, as those with a depressive disorder, an actual lure in late life, taking into account its devastating impact in terms of mental health and wellbeing.

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