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Perspective

Considerations for the assessment of suicidal ideation and behavior in older adults with cognitive decline and dementia

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Abstract

Introduction: Better understanding of suicide risk and its management in older adults with cognitive impairment and/or dementia remain significant unmet public health needs. Urgency to address them derives from concern that CNS treatments for dementia may impact suicide risk. Regulatory guidances requiring assessment of emergent suicidal ideation and behavior (SI/SB) at every clinical trial visit emphasize the need for understanding their prevalence.

Methods: The literature regarding SI/SB in older persons with cognitive impairment or dementia was reviewed by an Alzheimer's Association Taskforce with emphasis on epidemiology, classification, assessment, and regulatory requirements.

Results: Gaps in our knowledge were identified, challenges discussed and recommendations for future work provided.

Discussion: Currently available SI/SB data from geriatric persons with dementia do not provide adequate understanding of its epidemiology, identification, assessment, or management. The growing public health burden of this population requires greater attention from clinicians and researchers on tactics and assessment tools to meet these needs.

Keywords: Suicide; Suicide assessment; Dementia; Suicidality; Elderly; Suicidal ideation; Suicidal behavior; Suicide risk; Cognitive impairment

1. Introduction

Persons with Alzheimer's disease (AD) represent a rapidly expanding portion of the world's population. Its prevalence doubles every 5 years after age 65 years and its treatment accounts for an increasing proportion of national health care budgets. Finding safe treatments and better

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disease management is a global priority. One aspect of dementia care that has received limited focus is the identification and management of comorbid suicidal ideation (SI) and suicidal behavior (SB).

Older adults make up 12% of the US population but account for 18% of all suicide deaths. This is an alarming statistic, as the elderly are the fastest growing segment of the population. Furthermore, elder suicide may be underreported by ≥40% as "silent suicides," like deaths from overdoses, self-starvation, or dehydration, and "accidents" are often not reported as suicides [1]. SI and SB remain inadequately understood, under-recognized, and undertreated in this population [2]. Additional concerns that medications affecting the central nervous system (CNS) may increase the risk of SI/SB have led the US Food and Drug Administration (FDA) to take a position that SI/SB should be assessed at each visit during clinical trials when developing drugs for neurologic and psychiatric conditions. This includes clinical trials of drugs used to treat patients with AD and related dementias. This increases the urgency for knowing the background risk for SI/SB in various segments of this population. However, there is no consensus on how SI/SB is best assessed in patients with the cognitive impairment of dementia-spectrum disorders.

In this review article, the information gathered by the Task Force on Suicidal Ideation and Behavior in Persons with Dementia Spectrum Conditions as part of the Alzheimer Association Research Roundtable (AARR) (AARR Task Force members: Larry Alphs (Chair–SIB Task Force), Janssen Scientific Affairs; Robert Brashear, Janssen Alzheimer's Immunotherapy; Phillip Chappell, Pfizer; Yeates Conwell, University of Rochester; Sarah DuBrava, Pfizer; Dean Hartley, Alzheimer's Association; Ni Aye Khin, Food and Drug Administration (FDA); Nick Kozauer, FDA; David Miller, Bracket; Rachel Schindler, Pfizer (Chair of AARR); Eric Siemers, Eli Lilly & Co; Michelle Stewart, Pfizer; Kristine Yaffe, University of California San Francisco.) are summarized, gaps in our knowledge are identified, and directions to advance this research provided.

2. Methods

As part of its mission to overcome barriers to the development of safe and effective treatments for AD, the AARR convened a task force to discuss issues related to the assessment of SI/SB in AD clinical trials. Over a 2 year period, the task force met regularly to identify key considerations related to SI/SB risk in the healthy elderly and older persons in the dementia continuum. Concerns related to SI/SB nosology, classification, assessment, epidemiology, and regulatory science were identified. The relevant geriatric and dementia literature in these subject areas was reviewed, and consensus on its interpretation was obtained from experts on the task force. In addition, a survey was conducted to determine how SI/SB is currently being assessed in AD clinical trials [3]. The results of this work are summarized here.

3. Issues of definition, classification, and measurement

Clear, broadly accepted and carefully defined terminology is critical to understanding and effectively communicating information regarding the complexities of SI/SB in patients with mild-cognitive impairment (MCI) and dementia. Yet, refinement of definitional distinctions and development of a common vocabulary for SI/SB remain unmet goals.

Some data indicate that, even when active thoughts about taking one's life (SI) are absent, death ideation (defined as thoughts that life is not worth living or as the desire for one's own death) is associated with increased suicide risk [4]. Given the prevalence of death ideation among the elderly, it is important to distinguish death ideation from active SI (defined as thinking about self-harm with the intent to take one's life) and to understand the strength of any linkage to increased suicide risk. Furthermore, to reliably assess changes in SI/SB, distinctions must be drawn between passive and active SI, suicide attempts, suicide, and self-injurious behavior not associated with SI. Clinically meaningful and reliably identified gradations of SI and associated modulatory factors for suicide risk must be better studied; boundaries between suicidal thinking and normal end-of-life preparations for death must be defined, and terms such as method, plan, intent, and preparatory acts must be clearly distinguished. Conditions prevalent throughout the lifespan can also be seen in older persons. Thus, for this population too, nonsuicidal incidents of self-harm arising from cognitive disability or psychosis, or self-mutilation associated with personality disorders must be differentiated from behaviors whose intent is death. Although FDA guidance [5] calls for distinctions among preparations for suicide, aborted suicide attempts, and interrupted suicide attempts, in practice such distinctions are not readily apparent.

To better design and interpret studies that address outstanding questions, it is also important to distinguish among methodologic terms such as a suicide risk assessment that is performed with a scale or similar tool, population-based suicide risk that represents an observed risk based on a study of a defined population (often reported as an odds ratio or a hazard ratio), an individual's actual suicide risk (which can only be estimated), and a clinician-based suicide risk assessment that represents a clinician's best estimate of suicide risk.

3.1. Efforts toward standardization of terminology

Repeated efforts have been made to encourage widespread adoption of standardized definitions for SI/SB [6–9]. However, significant barriers remain. Acceptance of common terminology has also been impeded by the heterogeneous nature of SI/SB as manifested by its disparate cultural, demographic, and clinical subgroup meanings across the lifespan.

In 2002, the Institute of Medicine called for universally accepted definitions of suicide, suicide attempts, and SI

[10]. Several groups took up this challenge. Among these, investigators at Columbia University developed the Columbia Classification Algorithm for Suicide Assessment (C-CASA) to provide a broad classification of SI/SB categories [11]. The FDA subsequently established draft guidance [5] that recommended prospective collection and classification of SI/SB terms using this system or another well-qualified alternative during CNS drug development. In parallel, the Centers for Disease Control and Prevention partnered with the Veterans Administration (VA) to create the Self-Directed Violence Classification System [12]. This taxonomy is very similar to that of the C-CASA [13] and has been disseminated for use by the VA, the Department of Defense, and other health care delivery systems [14].

4. Epidemiology of suicidal ideation and behavior in older persons with cognitive decline and dementia

4.1. Risk for suicide in the elderly with mild-cognitive impairment/dementia

The overall risk for suicide is 0.011% per year in the general population, but this risk varies widely across the age, gender, geographic, and racial spectrum. Although the attempt rate for suicide is higher among younger adults than among middle-aged or older adults, the completion/attempt ratio is approximately 60-fold higher in older women than in younger women. Similarly, the rate of death by suicide is 5 times higher in very elderly white males than in the general population [15,16].

Although studies on the occurrence of SI/SB in people with dementia have been conducted for decades, they have been highly variable with regard to subject selection, definition of endpoints and methodologic rigor. Consequently, estimates for the prevalence of SI in this population vary from $<$1% to $>$42% [17,18]. Failure to use standardized definitions for terms associated with SI/SB has been particularly problematic for establishing relationships between dementia and suicide. In addition, failure to use well-validated tools to measure SI/SB or to report the severity of dementia has made results difficult to interpret [18]. Consequently, the available literature does not permit firm conclusions regarding the prevalence of SI/SB, or even whether rates are increased or decreased in persons with dementia. This represents an important deficit in knowledge as uncertain understanding of the background suicide risk makes it difficult to interpret the effects of treatment interventions on that risk.

In Denmark, Erlangsen et al [17] linked death records to a prospective nationwide registry database. The relative risk for suicide in persons aged 50 to 69 years with a dementia diagnosis was 8 times greater than it was for persons of the same age without dementia. For persons $\geq$70 years, the relative risk was 3 times higher. This finding persisted even after controlling for the presence of a mood disorder. The period shortly after the initial dementia diagnosis was the time of greatest relative risk for both men and women. The robustness of this result is supported by the fact that this study evaluated the entire population of Denmark and considered only patients with a clear diagnosis of dementia. It does not provide information on the effect of lesser degrees of cognitive impairment [16].

In contrast, a prospective 10-year US-based cohort study of older adults found no association between dementia-related cognitive impairment and suicide [19]. Another study reported that dementia was significantly less common among those who took their own lives than among those in a matched comparison group of older adults who died of natural causes [20]. In a similar study in Western Australia, Lawrence et al [21] linked hospital admission records with mental health service records to establish mortality data for persons aged $\geq$60 years. Although dementia was found not to be associated with increased risk of suicide, both men and women in this age group had significantly elevated rates of attempted suicide compared to the general population. A handful of controlled psychological autopsy studies have attempted to make retrospective diagnoses of dementia in older adults who died by suicide, comparing them with matched samples of older adults living in the community or older adults who died of natural causes [22]. One of these case-controlled studies found that dementia was less common among persons who died by suicide than in a control population of age-matched and sex-matched persons who died of natural causes [20]. Similar studies found no association between dementia and suicide [22].

A possible interpretation of these disparate findings is that death by suicide is more common early in the course of dementing illnesses, often before its diagnosis is formally documented. Suicide might represent a response to an AD diagnosis or to depression that is often comorbid with AD. Disinhibition, impaired problem solving, and poor decision making associated with cognitive decline could further contribute to suicide risk. In addition, behavioral and psychological symptoms of dementia can adversely affect employment, interpersonal relationships, and general health status thereby contributing to increased suicide risk [23,24]. Later in the course of dementia, when it is more likely to have been diagnosed, suicide risk may decrease because supervision is greater, access to lethal means is reduced, and the cognitive capacity required to plan and implement a lethal suicide attempt is diminished.

Some of the differences among these studies may be consequences of study methodology. Normal thoughts about dying may be confused with SI in persons near the end of life. Thus, differences in the definition of SI might have resulted in different SI rates. Additionally, AD goes undiagnosed in $>$50% of persons later found to have it. Death certificates often do not reflect AD as a contributor to death. Age-related increases in social isolation may also put older persons at increased risk of having their SI/SB overlooked.

Consequently, sampling techniques that differentially capture these subpopulations may account for some of the variance seen in published results.

4.2. Additional risk associated with depression

Depression is well established as a risk factor for suicide and is an important confounding condition for interpreting risk of suicide among elderly persons with dementia [25,26]. A recent review indicates that the prevalence of depression in persons with MCI is high, with a median occurrence of 44.3% and a range of 9%–83% in hospital-based studies and a median occurrence of 15.7% and a range of 3% to 63% in population-based studies [27].

Findings on the residual contribution of dementia to SI/SB after accounting for depression have been inconsistent. In one study [28], the association between SI and cognitive impairment disappeared after accounting for depression, but in another, it did not [29]. The complex relationship between dementia and depression, including differentiation among overlapping symptoms and the potential contribution of each to the etiology and presentation of the other, significantly contributes to the difficulty in unraveling interactions among dementia, SI, SB, and depression. All in all, risk of SI/SB in persons with dementia-spectrum illness cannot be ruled out.

5. Challenges in assessment of suicidal ideation and behavior in patients with dementia

5.1. General clinical considerations

At present, experience in the use of SI/SB assessments in patients with cognitive impairment or dementia is insufficient, and the tools that have been tested may not be adequate to capture important contributors to suicide risk in this population. Thus, we cannot be certain of the accuracy of our knowledge regarding actual suicide risk at any stage of dementia. Nor do we have knowledge of additional risk that pharmacologic agents contribute to background risk. As noted above, the greatest concern is probably for early stages of dementia. It would be most helpful to gather reliable information regarding these stages and determine how treatments applied during these stages impact suicide risk. In addition, even for older people who do not appear to be cognitively impaired, the assessor must consider their potential reluctance to speak directly about suicidal thoughts [30,31]. Frequency of contact with the clinician, stage of dementia, the patient's communication skills and their insight into their symptoms must all be considered. Because of increasing loss of memory for recent events, patients' estimates of the frequency or duration of subjective states may be particularly affected. Consequently, self-reports of SI and SB are likely to become less reliable as dementia progresses. Little research has been directed toward understanding the impact of these impairments on the ability of these patients to accurately report SI/SB.

5.2. Research considerations for clinical trials

SI/SB assessment in clinical trials raises a number of practical methodological questions. Recent FDA guidance recommends that SI/SB be assessed at every trial visit but does not suggest a particular trial visit frequency. The frequency of clinical trial visits has been an area of debate. Both the number of these visits and the number of assessments may represent a substantial burden for subjects and caregivers. To manage these challenges as cognitive impairment progresses, valid assessment of SI/SB may require that different approaches and instruments (or different versions of the same instrument) with simpler vocabulary and syntax be necessary. These might be conducted at the subject's home or by telephone/Internet. Many patients with MCI may be reliably assessed without input from a third party. On the other hand, input from a third party is likely essential for patients with moderate to severe dementia. For patients with more severe cognitive impairment, assessment of suicide risk may have to be based more on overtly observable behaviors than on self-reports. At end stage AD, SI/SB assessment may best be limited to SB evaluations.

5.3. Caregiver considerations for assessment of suicidal ideation and behavior

Various groups have stressed the importance of incorporating information from third parties, such as spouses, caregivers, and medical providers, when completing SI/SB assessments in patients with dementia. The 2012 draft FDA guidance specifically notes that an assessment "is not considered complete for any visit until information from all potential sources has been evaluated and integrated" into the overall assessment [5].

Caregivers may be able to report on a patient's observable behaviors and overt verbalizations, but they are not able to reliably report on a patient's internal experiences of SI. Increasing weight should be given to caregiver reports, based on the extent of the observer's contact with the patient. The different emphasis on patient versus caregiver input as dementia progresses is likely to affect the psychometrics of a scale across different levels of cognitive ability. This may necessitate different scoring approaches in later stages of dementia, when no reliable assessment of SI is possible and only observable behaviors can be rated. Also, given that treatment of a patient with MCI or AD extends over years, care may be provided by different persons over that interval. These caregivers may have highly variable insight into the patient's SI and SB. Indeed, they may be cognitively impaired or depressed themselves. This variability will affect the validity of the information obtained, and this should be considered when making assessments.

Little research is available regarding the reliability and validity of caregiver reports. In particular, no studies regarding SI/SB assessment have been conducted to determine who is qualified to provide third-party input, how third-party input can best be obtained, how discrepancies between patient and caregiver input should be handled, or at what level of cognitive impairment input from a third party should be systematically incorporated.

6. Review of suicidal ideation and behavior assessment instruments used in the elderly

The Task Force completed a comprehensive summary of assessment tools that may be used to collect information on SI/SB in geriatric populations. Brief descriptions of these instruments and their limitations are provided to assist researchers in identifying measures for assessing SI/SB for their clinical trial work. Table 1 describes the most commonly used instruments for suicide assessment, a subset of which have been used in the elderly. Table 2 summarizes important psychometric information about these scales. Only the Geriatric Suicide Ideation Scale has been specifically developed to assess the severity of SI/SB in older persons [36]. In practice, several instruments developed for use in younger populations have been used. Among these are the Columbia-Suicide Severity Rating Scale (C-SSRS) [54], the Beck Scale for Suicide Ideation [32,55], the Paykel Suicide Scale [38], and the Clinical Global Impression-Severity of Suicidality (CGI-SS) [33].

7. Survey of trialists of dementia studies

To better understand issues identified in this overview, the AARR convened a task force to conduct an online survey of trialists regarding experiences with SI/SB assessment in subjects with dementia. The goal of the survey was to identify the prevalence of SI/SB in persons with dementia-spectrum impairments who have participated in clinical trials and to understand the challenges encountered by investigators when conducting SI/SB assessments in this patient population [3]. An evaluable group of 204 trialists responded regarding their experience with nearly 10,000 patients. Although the incidence of SB identified from this research was low and appeared to decline with increasing severity of dementia [3], the results indicated that SI may occur more commonly in patients with MCI or dementia than was previously recognized. The survey results support the usefulness of prospective assessment of SI/SB in MCI and milder forms of dementia but raise important questions about the validity and reliability of SI/SB assessments in moderate to severe dementia. These results suggest a limited value for assessment of SI/SB in severe dementia because informant responses are regarded as unreliable. The survey results highlight the need to develop validated assessments that can be used to establish the epidemiology of SI/SB through the full course of dementia.

8. Regulatory considerations for the assessment of SI/SB in persons with mild cognitive impairment and Alzheimer's disease

In recent years, concerns regarding potential treatment-emergent SI and SB have arisen after a FDA-conducted meta-analyses of several clinical trial databases (viz., those for antiepileptic drugs and antidepressants) and from spontaneous reports regarding other drugs (e.g., retinoins, beta-blockers, reserpine, drugs for smoking cessation, or weight loss) [5]. The degree of risk suggested by these reports varies from product to product and within population subgroups.

Follow-up studies with more systematic assessments of safety are needed to better understand these relationships. To that end, the FDA has determined that prospective assessments for SI/SB should be included in pharmaceutical trials of drugs that have CNS effects, including those developed for cognitive impairment and dementia. The FDA guidance [5] recommends that assessment of SI/SB events be ascertained for every patient at every visit for most trials and that these events be classified using the C-CASA or an alternative system. This approach allows for aggregation and comparison of findings across drugs, drug classes, and patient populations. Prospective assessments also help ensure that patients experiencing suicidal thoughts or behaviors are recognized and adequately treated. This guidance acknowledges potential limitations to the reliability of assessments of SI/SB in patients with severe cognitive impairment and does not urge assessments in patients with severe dementia [5].

9. Future directions for clinical assessment of suicide

Several directions for developing a better understanding of and therapy for SI/SB in elderly persons with dementia-spectrum symptoms are suggested by this review. These include more standardization of nomenclature and classification related to SI/SB, better descriptive and epidemiologic characterization of SI/SB over the course of dementia; development of better assessment tools and improved psychometric characterization of those tools for use in clinical trials. Driving this need are growing numbers of clinical trials of investigational drugs for dementia for which safety data regarding possible induction of SI/SB must be collected.

To provide optimal individualized suicide risk assessment, an ideal SI/SB assessment tool would comprehensively capture a range of suicide risk factors and would be validated for the full course of dementia. It would be suitable for use in both clinical trial settings and in clinical practice with patients who are physically and technically challenged. In addition, such a tool would be easily understood and administered by new raters.

Establishing internal consistency, test–retest reliability, and convergent validity through the various stages of dementia is important for determining the value of any new

Table 1
Instruments used for the assessment of suicidal ideation and/or behavior

Instrument	Description
Beck Scale for Suicide Ideation (BSS/SSI)	The Beck Scale for Suicide Ideation (BSS) was developed in 1979 by Beck et al [32]. It consists of five screening questions. Fourteen additional items are scaled ordinally from 0 to 2 and measure the frequency, intensity, and subject's attitudes toward suicidal thoughts, feelings of control over them, and suicide plans. Two additional items address previous suicide attempts. The BSS is a patient-rated version of Beck's original, clinician-rated Scale for Suicidal Ideation (SSI). The BSS has high internal reliability with Cronbach alpha coefficients between 0.90 and 0.97. Its test–retest reliability is reported as moderate (r = 0.54) when used in psychiatric inpatients over a 1 week period.
Clinical Global Impression-Severity of Suicidality (CGI-SS)	The Clinical Global Impression-Severity of Suicidality was initially developed by Lindenmayer et al [33] for assessing severity of suicidal ideation and behavior in subjects at risk for suicide. It is a component of the ISST-Plus. This scale is a member of a family of clinical global impression scales that provide a global rating of overall severity of a subject's illness for specific illnesses, including schizophrenia, schizoaffective disorder, depression, bipolar disorder, and dementia. The CGI-SS is an ordinal scale with six levels of global severity for suicidality (0 = not at all suicidal, 1 = questionably suicidal, 2 = mildly suicidal, 3 = moderately suicidal, 4 = severely suicidal, and 5 = extremely suicidal). Detailed descriptors for each item to guide ratings are not provided.
Columbia-Suicide Severity Rating Scale (C-SSRS)	The Columbia-Suicide Severity Rating Scale (C-SSRS) [34] is a semistructured clinical interview designed to prospectively measure frequency and severity of SI/SB. It was developed for the National Institute of Mental Health Treatment of Adolescent Suicide Attempters Study. It is intended to assist clinicians in assessing and treating people at risk for suicide. Reliability and validity of this scale have been demonstrated with inter-rater reliability reported as high as 90%. Suicidal ideation is rated on a scale of 0 (no ideation present) to 5 (active ideation with plan and intent), and suicidal behavior is assessed as ranging from preparatory acts to suicide attempt. Aborted and interrupted suicide attempts are distinguished. Patient-rated and computer-based versions of the C-SSRS are available.
Columbia Classification Algorithm of Suicide Assessment (C-CASA)	The Columbia Classification Algorithm of Suicide Assessment (C-CASA) [11] was designed for retrospective classification of suicidal events in clinical trials. It has been used by the FDA for analyses of clinical trial data on antidepressants and antiepileptic agents. Definitions of suicidality are based on empirical findings from studies of the phenomenology of suicidality. Ratings include nine categories that distinguish SI/SB (codes 1–4), nonsuicidal events (codes 7, 8), and indeterminate but potential suicidal events (codes 5, 6, 9).
FDA-modified Columbia Classification Algorithm of Suicide Assessment (FDA-CASA)	This FDA modification of the C-CASA was published in 2012 [35]. It includes additional categories of SI and SB identified from the C-SSRS and removes categories that were not considered needful for prospective studies. Its 11 preferred categories are Suicidal ideation (Passive; Active: Nonspecific (no method, intent, or plan); Active: Method, but no intent or plan; Active: Method and intent, but no plan; Active: Method, intent, and plan) Suicidal behavior (Completed suicide; Suicide attempt; Interrupted attempt; Aborted attempt; Preparatory actions toward imminent suicidal behaviors) Self-injurious behavior, no suicidal intent
InterSePT Scale for Suicidal Thinking (ISST)	The InterSePT Scale for Suicidal Thinking (ISST) was developed by Lindenmayer et al [33] to assess severity of suicidal ideation in subjects with schizophrenia. The developers used factor analysis to guide deletion of items from the BSS that were redundant or correlated poorly with the total score and item descriptors were modified to facilitate rating. The remaining 12 items quantify conscious and overtly expressed suicidal thinking by assessing suicidal thoughts, desires, and related risk factors identified during a 20–30 minute semistructured, clinician-administered interview. Each item of the ISST is scored on an ordinal scale of increasing severity for suicidal ideation (0, 1, or 2). Results are summarized as a sum of the individual item scores.
InterSePT Scale for Suicidal Thinking—Plus (ISST-Plus)	The ISST-Plus, a modified version of the ISST, was developed by Alphs and Lindenmayer (unpublished data, 2009) to assess suicidal behaviors as well as ideation. The tool is grouped into three component scales. Part I adds an additional item to the original ISST. Otherwise, it is used identically to the original ISST. Part II includes 10 patient-reported items that address suicidal behavior as the prior ISST-Plus assessment. Part III contains a clinical global assessment of suicidal ideation and behavior. The instrument was developed for use in clinical trials and includes items that permit classification of information according to the C-CASA algorithm. It standardizes procedures for addressing missing visits. An optional narrative template is included to guide documentation of suicide behavior observed during a clinical trial. The ISST-Plus takes about 15–20 minutes to complete. High inter-rater reliability was found in a study of 22 inpatients with schizophrenia or schizoaffective disorder.
Geriatric Suicide Ideation Scale	A 31-item multidimensional assessment scale for suicide ideation and related factors in older adults developed by Heisel and Flett [36] Factor analysis supports a four-factor structure for the GSIS, with subscales assessing suicide ideation, death ideation, loss of personal and social worth, and perceived meaning in life. Psychometric analyses supports strong internal consistency and test–retest reliability. Construct and criterion validity for the GSIS and its subscales have been demonstrated by positive associations with measures of depression, hopelessness, and self-reported health problems and negative associations with life satisfaction and psychological well-being. The 10-item Suicide Ideation subscale has been able to discriminate psychiatric patients from nonpatients.
Geriatric Depression Scale (GDS)	A 15-item scale designed for elderly persons that includes a 5-item GDS subscale (GDS-SI) designed to screen for suicide ideation [37]. Exploratory factor analyses support a two-factor structure for the GDS-15 in elderly patients who are cognitively intact but functionally impaired. Component subscales assessing depression and positive affect have been shown to have moderate internal consistency reliability. A GDS cut score of 4 has been shown to maximize sensitivity and specificity for suicide ideation with optimal cut scores 5 for men and 3 for women. A GDS-SI cut score of 1 has been demonstrated to be an optimal cut score for identifying suicidal ideation in both men and women. A significant weakness of the scale is its low correlation with suicide attempt status.

(*Continued*)

Table 1
Instruments used for the assessment of suicidal ideation and/or behavior (*Continued*)

Instrument	Description
Paykel Suicide Scale	Paykel et al. [38–41] identified five interviewer-administered questions that assess increasing levels of intent: (1) "Have you ever felt that life was not worth living?" (2) "Have you ever wished you were dead?—for instance, that you could go to sleep and not wake up?" (3) "Have you ever thought of taking your life, even if you would not really do it?" (4) "Have you ever reached the point where you seriously considered taking your life or perhaps made plans how you would go about doing it?" (5) "Have you ever made an attempt to take your life?" These items may be used to assess suicidal ideation during the past week, month, year, or lifetime. Respondents answer each item "yes" or "no." Although these hierarchical questions were not initially designed as a scale, they have been scored on a scale from 0 to 5. Ratings are scored hierarchically according greatest magnitude of suicidal ideation endorsed.
SAD PERSONS Scale	The SAD PERSONS scale was originally developed by Patterson, et al [42]. It includes 10 risk factors for suicide (male sex, age <19 years or >45 years, depression, previous attempt, ethanol abuse, rational thinking loss, social supports lacking, organized plan, no spouse, and sickness), and each item scored '1' if present and '0' if absent. Subjects are categorized as at low, moderate, or high risk for suicide.
Modified SAD PERSONS Scale	The Modified SAD PERSONS scale (MSPS) [43] modifies the risk factors for suicide to be male sex, age <19 years or >45 years, depression or hopelessness, previous attempts or psychiatric care, excessive ethanol or drug use, rational thinking loss, single, divorced, or widowed, organized or serious attempt, no social supports, and stated future intent for suicide (items 3, 6, 8, and 10 are scored as '2' if present). Subjects are categorized as at low, moderate, or high risk for suicide.
Sheehan Suicidality Tracking Scale (S-STS)	The Sheehan Suicidality Tracking Scale (S-STS) [44] was designed to assist researchers assess SI/SB and self-harm in research and clinical settings. It is a 13-item scale, with each item scored on a 5-point Likert scale. Data are analyzed as individual item scores, a suicidal ideation subscale score, a suicidal behavior subscale score, and a total score. The S-STS was adapted from the Suicidality Module of the Mini International Neuropsychiatric Interview (MINI) Structured Diagnostic Interview for DSM-IV. It is first subject rated and then clinician rated. Discrepancies are addressed in a follow-up interview that provides a final rating. An alternative S-STS Clinically Meaningful Change Measure (CMCM) version has been developed (D. Sheehan M.D., personal communication). This version of the S-STS addresses domains not included in the current S-STS: suicide risk/protective factors, clinician's judgment of suicide risk, clinician's and patient's judgment of needed disposition/treatment, functional impairment from suicidality, quality of life related to suicidality, hopelessness, ability and willingness to cope and to stay safe, global severity of suicidality.
Suicide trigger scale version 3	The Suicide Trigger Scale version 3 (STS-3) is a 42-item self-report developed by Yaseen et al [45,46], It is an ordinal scale with 3 frequency categories (0 = not at all, 1 = somewhat, 2 = a lot). Unlike the other scales identified in this report, the STS-3 does not contain questions that are overtly related to suicide. The rationale is to avoid over-reliance on self-reported suicidal symptoms and reduces the possibility of over-reporting and under-reporting of such symptoms.
Other psychiatric instruments	Many rating scales designed to measure symptoms of specific psychiatric disorders also include one or more items to assess suicide ideation or behavior. Owing to the widespread use of and familiarity with these scales, several have been used as an outcome measure for SI/SB in clinical trials. Examples include the Schedule for Affective Disorders and Schizophrenia [47], Overt Aggression Scale [48], Montgomery-Asberg Depression Rating Scale [49], Hamilton Depression Rating Scale [50], and Beck Depression Inventory [51].

SI/SB assessment tool. Initially, most patients with MCI are able to reliably provide self-reports of SI/SB, with less need for caregiver input. Later, when patients reach a threshold of severe cognitive impairment, which might be defined by performance on a neuropsychological assessment battery, caregiver input might be required. In addition, weighting information, depending on the informant's knowledge base and the investigator's confidence in the information obtained, may be helpful when scoring such an instrument.

Requirements for validation to support such an instrument represent a significant commitment of time and resources. Although this work is frequently regarded as superfluous by funding agencies, its fundamental importance to valid epidemiologic and clinical data collection make it a priority.

A model for improving SI/SB assessment in patients with cognitive dysfunction has been provided by developers of the Quality of Life–Alzheimer's Disease scale [56,57]. Completion of that instrument is done by either the patient using a structured interview with Likert-type response options or the caregiver completing a similar questionnaire. Patients may provide their responses orally or in writing. Separate scores from the patient and the caregiver are then provided to a trained clinician rater who provides a final score. Such an approach allows for the scale's adaptive use in persons with varying levels of cognitive impairment.

The FDA's expectation that all CNS-active drugs be prospectively assessed in clinical trials for possible SI/SB potential has led to the accumulation of a significant body of information related to geriatric patients, including those with MCI and dementia. This includes valuable experience regarding both methodologic issues related to the collection of SI/SB information in this population and the effects of different pharmacologic agents on their suicidal thinking and behavior. Despite this accumulating database, the authors have been unable to identify a systematic review of this work. One solution to current gaps in our understanding would be to form a scientific consortium with the

Table 2
Properties and limitations of scales used for assessment of suicidal ideation and/or behavior

Instrument	Validation	Captures ideation	Captures behavior	Captures risk factors for suicide	Sensitive to rapid change in ideation	Captures global clinical judgment of risk	Limitations
Beck Scale for Suicide Ideation (BSS/SSI)	Standardized in inpatient and outpatient psychiatric patients populations, as well as diverse settings such as primary care, ER, and rehabilitation programs. During its development, BSS items were reviewed by clinicians and pilot tested among 50 psychiatric inpatient and outpatients (BSS manual) [32].	++	++	+	No	No	Minimally important change on the BSS has not been established. Captures only 3 levels of severity.
Clinical Global Impression-Severity of Suicidality (CGI-SS)	Strong correlation with ISST total scores ($r = 0.61$, $P < .0001$). Demonstrated a large but not statistically significant decrease in suicidal ideation in a trial of citalopram in 198 patients with schizophrenia or schizoaffective disorder [33].	+	+	−	Yes	Yes	Only a few published studies have evaluated this scale. Not specifically documented for use in or validated in an elderly population.
Columbia-Suicide Severity Rating Scale (C-SSRS)	Psychometrics (validity, internal consistency) reported in adolescent suicide attempters; depressed adolescents in a drug study; and adults seeking ER care for psychiatric reasons [34].	++	++	+	No	No	Definitions of certain terms/ categories are insufficient. Domains like "intent," "plan," "method" are neither mutually exclusive nor empirically derived. Other important domains of classification of possible suicide outcomes in clinical trials are missing. Not specifically validated in an elderly population.
InterSePT Scale for Suicidal Thinking–Plus	CGI-SS and recent suicidal attempts was excellent in 980 patients with schizophrenia or schizoaffective disorder and history of suicidal ideation. ISST total scores highly correlated with the CGI-SS and significantly differentiated the different levels of CGI-SS. Internal reliability was high, with overall Cronbach alpha coefficient of 0.88. High inter-rater reliability was found in a study of 22 inpatients with schizophrenia or schizoaffective disorder. [unpublished data, 2009]	++	−	−	No	No	Validation was performed only in patients with schizophrenia or schizoaffective disorder, who had a relatively low severity for each item. This does not address its sensitivity for intermediary amounts of suicidal thinking. Not specifically developed for use in or validated in an elderly population.

(*Continued*)

Table 2
Properties and limitations of scales used for assessment of suicidal ideation and/or behavior (*Continued*)

Instrument	Validation	Captures ideation	Captures behavior	Captures risk factors for suicide	Sensitive to rapid change in ideation	Captures global clinical judgment of risk	Limitations
ISST-Plus	45 patients from an emergency department and psychiatric inpatient unit who had a spectrum of suicidal ideation/behavior were interviewed and rated by separate, trained raters on the C-SSRS, the S-STS, and the ISST-Plus. Each of these ratings was mapped to the C-CASA and results were compared. [unpublished data, 2016]	++	++	−	No	Yes	Not specifically developed for use in or validated in an elderly population. Predictive validity has not been established.
Geriatric Suicide Ideation Scale	A 31-item scale that has been validated in a heterogeneous sample of 172 adults ≥65 years and in a sample of 107 heterogeneous elderly adults [36].	++	−	+	No	No	Predictive validity has not been established. Measures of suicide behaviors are very general.
Geriatric Depression Scale (GDS)	Validated in 960 functionally impaired, cognitively intact, community-dwelling primary care patients aged 65 years and older [37].	+	−	+	No	No	A measure focusing on depression rather than suicide ideation. A significant weakness of the scale is its low correlation with suicide attempt status.
Paykel Suicide Scale	Validated in studies of various patient populations [38–41] Reliability, concurrent validity and predictive validity have not been established.	++	+	−	No	No	Does not use currently accepted nomenclature [8,9]. Chiefly used as a screening tool; utility in clinical trials is not known. Not validated in an elderly population.
SAD PERSONS Scale	Only a few published studies have utilized this scale, with varying methodology and results [42]	−	−	++	No	No	A 6-month study of 4019 subjects showed low sensitivity and low positive predictive value [52]. Researchers concluded that these scales should not be used in isolation [53] or to screen self-harm patients presenting to general hospitals [52]. Not validated in an elderly population.
Sheehan Suicidality Tracking Scale (S-STS)	Adapted from Suicidality Module of the MINI, which has had extensive reliability and validity testing. Evaluated in two double-blind, placebo controlled trials. Demonstrated increased sensitivity over the rater administered HAM-D Item#3 for identifying suicidal ideation and behavior [44].	++	++	−	No	No	The generalizability of this validation study is limited by its small sample size. Subjects were limited to female subjects, with generalized anxiety disorder, and screening excluded subjects at significant risk for suicide. Not validated in an elderly population.

(*Continued*)

Table 2
Properties and limitations of scales used for assessment of suicidal ideation and/or behavior (*Continued*)

Instrument	Validation	Captures ideation	Captures behavior	Captures risk factors for suicide	Sensitive to rapid change in ideation	Captures global clinical judgment of risk	Limitations
Suicide Trigger Scale 3 (STS)-3	High internal consistency with a Cronbach alpha of 0.942. Total scores correlate with C-SSRS severity of ideation scores (r = 0.327). Predictive validity shown for postdischarge suicide attempts in high-risk psychiatric patients admitted for suicidal ideation or attempt [45,46].	−	−	++	No	No	Does not contain questions overtly related to suicide, to avoid response bias by those wanting to either hide or exaggerate their suicidality. Not validated in an elderly population.

NOTE. Symbols: −, not captured by scale; +, captured by scale to some extent; ++, well captured by scale.

mission of bringing accumulated experience and data together and exploring it for best practice in data collection and for identification of potential SI/SB risk factors. Such an output could deepen our cumulative understanding of SI/SB in older adults with cognitive decline and drive better studies for the future.

10. Summary

Characterization and management of the overall risk for SI/SB across the spectrum of dementia-related disorders remain poorly understood. Addressing these concerns is challenging because cognitive impairment in persons with dementing illnesses is progressive and affects the reliability of patient responses. Interpretation of the available literature is further complicated by divergent definitions of terms and inadequate population sampling techniques. Data generated by the AARR task force and by several epidemiologic studies suggest that the incidence of SB and completed suicide in dementia are low and decline with increasing severity of dementia. However, findings reported in the literature are disparate and conclusions from the limited studies that exist are conflicting. Thus, significant knowledge gaps remain.

Given the growing public health burden of dementia-related illnesses, the need to address questions regarding SI/SB in dementia is urgent and requires broad involvement from geriatricians, dementia researchers, the pharmaceutical industry, and regulators. Solutions will require broad collaboration among the relevant stakeholders and better clinical trial methodologies. Given our current state of knowledge, the introduction of improved SI/SB assessment tools and their more sophisticated use in this population is critical. The value of providing structured SI/SB monitoring in patients with cognitive decline or frank dementia remains uncertain. However, given the high rates of suicide in geriatric populations, such monitoring should be considered, particularly early in the course of the disease.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.trci.2016.02.001.

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