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Suicidal behavior in the older patient with schizophrenia

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Abstract

Little is known about treating elderly suicidal patients with schizophrenia. The purpose of this article is to review the literature dealing with this population and to discuss what is required to advance this field. Most available studies from middle-aged and older individuals suggest that risk factors include hopelessness, lower quality of life, past traumatic events, depressive symptoms, lifetime suicidal ideation and past attempts; it is not clear whether these findings are generalizable to geriatric populations. Although little treatment research has been performed in older suicidal patients with schizophrenia, an integrated psychosocial and pharmacologic approach is recommended. In addition, one recent study augmented antipsychotic treatment with an SSRI (i.e., citalopram) in a sample of middle-aged and older individuals with schizophrenia with subsyndromal depression; in that study, serotonin selective reuptake inhibitor augmentation reduced depressive symptoms and suicidal ideation. More research is required to better understand suicidal behavior in older patients with schizophrenia.

Keywords

antidepressant; antipsychotic; depression; elderly; geriatric; risk factor; schizophrenia; SSRI; suicide; treatment

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The assessment and treatment of suicidal behavior in patients with schizophrenia involves many challenges for clinicians. Compared to the general population, these patients hold an 8.5-fold greater risk of suicide.

Much less is known regarding suicidal behavior in the elderly patient with schizophrenia.

The purpose of this article to review the literature dealing with the assessment and treatment of older at-risk patients with schizophrenia and to discuss what studies are required to advance this field.

Most studies that are available for examining suicidal behavior in this subject population involve mixed samples of individuals who are middle-aged and older. It is not clear whether the findings from these mixed samples can be generalized to purely geriatric populations.

Patients with schizophrenia have higher rates of premature death due to various causes including cancer, cardiovascular disease and suicide [1]. Suicide is one of the leading causes of premature death among people with schizophrenia [2,3]. Compared with the general population, these patients hold an 8.5-fold greater risk of suicide [4]. A total of 4–13% eventually complete suicide [5–9]. Most completed suicides in patients with schizophrenia appear to occur early in the disease process [10–12] although the risk of suicidal behaviors in patients with schizophrenia is lifelong [13]. Evenson and colleagues found that patients with schizophrenia had the following age-specific mortality rates of suicide: 209/100,000 for ages 20–29 years; 220/100,000 for ages 30–39 years; patients over age 60 years had the lowest rates (40/100,000 for ages 60–69 years and 0/100,000 for ages over 70 years) [14]. In addition, a psychologic autopsy series of completed suicides of individuals with schizophrenia in Finland determined that approximately one third of patients were 45 years and older. Thus the risk of suicidal behavior is lower in older members of this population but is not insignificant.

Suicidal behavior in the elderly in general is a public health problem. In 2005, the elderly made up 12.4% of the population in 2004 and accounted for almost 16.6% of all suicides. The rate of suicide for the elderly for 2005 was 14.7 per 100,000 [15].

The purpose of this article is to review the literature that is available for older suicidal patients with schizophrenia and to provide suggestions for future research, which will be needed in order to improve our knowledge base of this problem and better manage this population of patients as well as to develop effective interventions.

Theoretical models

A discussion of current theoretical models of suicidal behavior in patients with schizophrenia is included with suggestions of how these may be adapted to the older suicidal patient with schizophrenia.

There are few theoretically driven, empirically testable models of psychological mechanisms that can explain suicidal behavior in general [15] and more specifically, for explaining suicidal behavior in people with schizophrenia [16]. A theoretical model for the older suicidal patient with schizophrenia is needed; however, much of the research required to develop a model is lacking. Currently available models that could be adapted to the older suicidal patient with schizophrenia include the ‘Cry of Pain’ model, the Schematic Appraisal Model of Suicide (SAMS) and the Interpersonal Theory of Suicidal Behavior.

The Cry of Pain model is based on an evolutionary approach to suicidal behavior. There are seven elements: stressors are present; stressors have been appraised along with their

consequences, within a context of defeat; perceptions of entrapment are magnified; this is coupled with inflexible negative perceptions of oneself, of others, and to the current circumstances; the individual continues to experience intractable feelings of entrapment owing to arrested flight; the individual has feelings of social isolation due to the perception that no rescue factors are available; and the individual possesses an awareness of imitation models along with accessibility to current methods of suicide [16,17].

Strengths of the Cry of Pain model include: the empirical basis for the components of defeat and entrapment is strong; there is a good evolutionary basis to the constructs of defeat and entrapment; cognitive factors affecting perceptions of defeat and entrapment are well identified; the origins to differing responses to stress are suggested; the role of emotions leading to suicidal behavior is emphasized; the model appears to explain both suicidal behavior and completed suicide; and the model has led to the development of treatment interventions. However, there are limitations of the model, including the fact that the concepts utilized are not mutually exclusive nor parsimonious. Much of the evidence for many of the components' involvement in suicidal behaviors especially in schizophrenia is only indirect. This applies especially to the role of cognitive biases and cognitive deficits.

Johnson *et al.* propose a modification of the Cry of Pain model and call the revised model the SAMS [18]. These authors incorporate additional issues on negative information-processing bias, the presence of suicide schema and an appraisal system. A third model of suicide is the 'Interpersonal Theory of Suicide' [19,20]. This theory postulates that suicidal behavior results from two interpersonal constructs, thwarted belongingness and perceived burdensomeness (which includes hopelessness). With this model, the capability to engage in suicidal behavior is separate from the desire to engage in suicidal behavior. The capability for suicidal behavior emerges, via habituation and opponent processes as a result of repeated exposure to painful and/or fear-inducing experiences. One of the strengths of the interpersonal theory is that it can provide explanations for difficult to explain epidemiological facts regarding suicide. This includes the gender distribution issue (i.e., male suicides outnumber female suicides worldwide, yet more women than men are engaging in nonlethal suicidal behavior) [21].

All of these theoretical models require further refinement to incorporate older populations with schizophrenia. Several issues associated with aging appear to be compatible with some of the elements of the various models. For instance, the 'Interpersonal' theory explains why males outnumber females; this is a characteristic of suicide in the elderly in general; however, it is not known whether this gender difference applies to elderly patients with schizophrenia since no consistent gender differences have been demonstrated in the elderly. Furthermore, much research needs to be performed to determine whether the Cry of Pain model and its revised model, the SAMS, are applicable to older patients with schizophrenia.

One important question that needs to be addressed through research is whether suicide in elderly people with schizophrenia results from factors that affect the elderly such as bereavement and chronic and deteriorating health conditions. On the other hand, does suicide occur in the older patient with schizophrenia from schizophrenia-related factors such as psychotic phenomena? Alternatively, could there be an interaction between age-related and schizophrenia-related factors? Future testing could address this and adapt aspects of the Cry of Pain, the Interpersonal Theory of Suicide and the SAMS model directed towards an older population with schizophrenia.

The role of depression

Many models of suicide are related to depressive symptoms. Both the Cry of Pain model and SAMS are derived from models of suicide in which depression is an important component.

Up to 50% of individuals with psychotic symptoms report one or more major depressive episodes [22–25]. As much as 50% of individuals with schizophrenia report suicidal ideation. Suicidal ideation and planning are thought to be precursors to completed suicide so it is important to address suicidal ideation as early as possible.

The prevalence of depressed mood at first hospital admission for schizophrenia can be as high as 83% [26] and depression in the residual phase has also been found to be predictive of suicide completion in schizophrenia [27]. Suicidal behaviors could be due to the effect of comorbid depression or an associated symptom such as hopelessness.

While depression is often present with suicidal behavior in people with schizophrenia it is not always invariably a component. For instance, a recent study using psychological autopsy methods indicated that 73% of people with schizophrenia who completed suicide did not experience depressed mood nor anhedonia within the weeks prior to death [28]. Thus, the risk of suicidal behavior should not be underestimated in those with schizophrenia in the absence of depressive symptoms.

Empirical findings

The various studies from mixed middle-aged and older samples suggest that risk factors in middle-aged and older individuals include hopelessness, lower quality of life, past traumatic events, depressive symptoms and lifetime suicidal ideation and past attempts.

Risk factors for suicidal behavior in patients with schizophrenia

In order to decrease suicide among people with schizophrenia, researchers have focused on risk factors so as to more effectively implement targeted interventions. This risk-based approach has its limitations in that it identifies a large sample of people, many of whom will not attempt or complete suicide. Thus, it is limited in that it may identify too many false positives and thus may not be helpful both theoretically and clinically. Risk factors in general include previous attempts, greater lethality of attempts, depression, hopelessness and psychotic symptoms [10,13,29–36]. In addition, the risk of suicide is higher in Caucasian patients with schizophrenia, although rates of suicide in the general population are highest among Caucasians, Native Americans and elderly males [37].

Duration of illness is another important risk factor. A recent study by Barrett *et al.* examined the prevalence and characteristics of suicidality in patients with a first episode of psychosis in two time intervals: prior to study entry and in the period of untreated psychosis [38]. Approximately 26% of the patients attempted suicide prior to study entry and 14% made suicide attempts during the period of untreated psychosis. Of patients who had experienced suicidal ideation or attempts, 70% were suicidal during the period of untreated psychosis. Suicide attempts during untreated psychosis were also associated with a younger age at illness onset and longer duration of untreated psychosis.

For individuals with more severe cases of schizophrenia, the risk of suicide is increased. Severity of illness can be exemplified by more frequent hospitalizations and longer durations of index hospitalizations. Severity can also be marked by numerous relapses, younger age of onset or the need for higher doses of antipsychotic medications [5,32,34,36,39–45].

Poor adherence is also a risk factor [41] as is family history of suicide [5,10,13,32–36,39,46,47]. Social support has been shown to serve as a mediator of suicide risk where higher risk is associated with lower levels of social support [10,11,30,40].

Spirituality is an important factor that appears to mediate the risk for suicide in various populations. Spirituality is an important part of resilience. As stated by Shulman, resilience occurs when coping leads to transformation, and/or being able to overcome obstacles while becoming more capable in the process [48]. Essentially, a level of spirituality or philosophical strength often anchors one's worldview; the belief in something greater can help people cope with challenges and bring meaning to their lives.

As mentioned, recent reviews found worsening psychosis as well as depression is consistently associated with completed suicides in patients with schizophrenia [41,46]. The data that examines whether there is a relationship between suicide and the presence of command hallucinations or delusions in people with schizophrenia are inconclusive [34,36,49,50]. For example, Zisook *et al.* investigated clinical and research records from 106 patients with schizophrenia who were reported to have auditory hallucinations, 43% of whom experienced command hallucinations [51]. No significant differences emerged between patients who did report command hallucinations and those who did not with regard to histories of violent and/or impulsive acts or prior suicide attempts. However, during the study, two patients committed suicide, both of whom were from the command hallucination group.

Demographic factors

Men with schizophrenia complete suicide more frequently than women with schizophrenia [5,11,33,52]. The mean age of patients with schizophrenia who kill themselves is approximately 33 years [8,53] with one study noting the greatest risk occurring between 20 and 39 years [54]. This is not to say that elderly people with schizophrenia are not vulnerable, since they commit suicide as well (see below) [13,55].

Psychosis & substance abuse

Makara-Studzinska and Kořlak reviewed the literature with regards to the influence of positive symptoms on the incidence of suicide attempts made in schizophrenia [56]. These authors stated that it is not clear whether positive or negative symptoms can influence suicidal behavior. There are studies of Schennach-Wolff *et al.* who assessed levels of suicidal behavior before and at the time of admission in patients with schizophrenia [57]. Suicidal patients (22%) scored significantly higher on the positive and negative syndrome scale (PANSS) negative subscore at admission and at discharge. Furthermore, Hocaoglu and Babuc reported on a sample of 120 patients with schizophrenia and suicidal ideation in which approximately one third had suicidal ideation [58]. Negative symptoms were higher in this group compared with those without suicidal ideation. However, there are other studies that are not consistent with these findings [56].

The connection between suicide, schizophrenia and substance abuse is also important [12,13,44,59]. Bolton *et al.* reviewed this issue recently [16]. Impulsivity is considered a feature of suicidal behavior and this may be heightened in those with a dual diagnosis of substance misuse [12,60]. Substance abuse and alcoholism can reduce inhibitions, and as a result, lead to impulsive behavior, and impaired judgement with increased social isolation, all of which can increase the likelihood of suicidal behaviors. In addition, difficulties in thinking styles related to substance misuse may reflect dysfunctional coping styles in these individuals as managing negative affect in people with schizophrenia [12,60–62]. In view of the changing patterns of the epidemiology of schizophrenia when considering those patients who have comorbid substance use/abuse, it becomes important that clinicians obtain accurate drug-use history in order to detect and promptly treat drug use/abuse [63].

In two cohort studies in the USA, significantly more comorbid substance abuse was found among people with schizophrenia who were suicidal, particularly among younger patients [64,65]. Harris and Barraclough performed a meta-analysis on suicide as outcome in mental disorders and determined the standardized mortality ratio for suicide of users to be higher than those of nonusers in all groups [4]. In subjects with alcohol dependence and abuse it was six-times higher, in opioid dependence and abuse 14-times and in cannabis users four-times. In this meta-analysis, suicide risk among patients with schizophrenia was 8.5-times greater than among patients without schizophrenia [4].

What do we know about risk factors in older patients with schizophrenia?

Very few studies have examined suicidal risk factors in older patients with schizophrenia. First of all, geriatric age starts at 65 years of age and most available studies come from mixed samples of individuals who are middle-aged and older. Thus, it is not clear whether the findings from these mixed samples can be generalized purely to the geriatric populations. One case-control study examined suicidal behavior in patients aged 60 and older, with a mean age of 67.5 ± 5.3 years [45]. Over a 10-year period, the authors examined computerized admission records in an Israeli hospital of inpatient admissions with schizophrenia who had attempted suicide. A comparison group consisted of the next two admissions of patients with schizophrenia who did not attempt suicide. Of 1066 patients, 49 suicide attempts were documented, which comprised 4.6% of the admissions. One third of these patients made a subsequent suicide attempt on a 10-year follow-up. In total, ten patients had attempted suicide more than once. Other than a history of suicide attempts, no other variables tested were associated with risk for suicidal behaviors.

Using an age cut-off of 55 years or greater, Cohen *et al.* recruited a sample of outpatients with early onset schizophrenia and compared them to a community sample of older persons [66]. Older persons with schizophrenia had a higher prevalence of lifetime suicidal thoughts (43 vs 6%) and suicidal attempts (30 vs 4%). In addition, 42% of the patients with schizophrenia who exhibited depression had a history of prior suicide attempts. The data also demonstrated that depression in this older group of patients is as strongly associated with prior suicide attempts as it is in younger populations [41,53,67]. Furthermore, they also found that past traumatic events were associated with suicidal behavior.

Montross *et al.* examined the prevalence and correlates of current suicidal ideation and past suicide attempts in a sample of 132 patients aged ≥ 40 years [68]. Suicidal ideation and past suicide attempts in this sample were prevalent. Nearly one half of the sample reported having attempted suicide once or more in their lifetime, similar to rates reported by Cohen *et al.* [66]. Using regression analysis, the authors determined that only past suicide attempts and hopelessness accounted for current suicidal ideation. Furthermore, having current suicidal ideation did not differ by diagnosis, race/ethnicity, marital status, living situation, age, education or severity of medical illness. Kasckow *et al.* examined suicidal behavior in a group of patients with schizophrenia and subsyndromal depressive symptoms ($n = 146$) aged 40 years or older [69]. The proportion of subjects 55 years and older was 29% and 7% were those greater than 65 years. A total of 36% of the sample had Intersect Suicide Scale scores >0 . Age was not associated with scores of suicidality. Furthermore, logistic regression revealed that quality of life scores were predictive of suicidal ideation; however, neither age- nor performance-based measures of everyday functioning, social functioning or medication management were predictive.

Heila *et al.* reported on a series of 92 completed suicides assessed by psychological autopsy methods [13]. The results were part of the nationwide National Suicide Prevention Project in Finland. In this study, all suicides of individuals with Diagnostic and Statistical Manual 3rd Edition, Revised (DSM-III-R) schizophrenia were investigated over a 12-month period by

using the psychological autopsy method. The mean age of the suicide victims with schizophrenia was 40.0 ± 13.2 years (range: 16–77 years; 26% women; 74% men). The mean age of the women did not differ significantly from the men. The authors divided their sample into a young (16–32 years; $n = 32$), middle (33–44 years; $n = 30$) and old (45–77 years; $n = 30$) group so that they could examine any variation in clinical characteristics among suicide in victims of different ages. These groups did not differ significantly in gender distribution. The use of violent suicide methods was greatest among the young, which included hanging, jumping from a high place, shooting a firearm, cutting, burning and jumping under a vehicle. Drug overdose was most common among middle-aged men and older women. Depressive syndromes were present among the young and old men, but occurred more frequently in the young and middle-aged women. The authors noted that owing to the number of women represented in this case series being small, the findings of age and gender specificity are only suggestive.

Although several studies suggest that most suicides in patients with schizophrenia tend to occur relatively early in the course of illness [70], they can occur over a large range of ages and illness durations. Furthermore, the high-risk group of young suicide completers among persons with schizophrenia characterized in previous studies [32–34,36,53] was very similar to the youngest group in the Heila *et al.* study in terms of mean age, proportion of men, depressive symptoms and violent suicide methods [13]. In summary, the limited literature on risk factors in elderly patients with schizophrenia mostly consists of mixed samples of middle-aged and older individuals. This available literature suggests that past attempts, low quality of life, depression, hopelessness and exposure to trauma are likely risk factors throughout the age continuum.

Treatment

Although little treatment research has been performed in older suicidal patients with schizophrenia, an integrated psychosocial and pharmacologic approach is recommended.

Assessment & initial management

Patients with schizophrenia and schizoaffective disorder require thorough assessment for the presence and nature of suicidal ideation or behavior, suicide risk and factors contributing to the suicidal symptoms. Once accomplished, a clinical decision must be made as to what would be the appropriate setting for treatment (i.e., either inpatient or outpatient). To maximize the probability of preventing suicide, the goals of treatment are to improve psychotic and depressive symptoms, alleviate patients' sense of demoralization and despair, encourage hope, assess social support and feasibility of their current living situation and if present, address substance abuse and anxiety disorders [70]. Thoughtful consideration needs to be made for the full range of treatments available in order to address these issues [71]. There are limited data supporting both psychosocial and pharmacologic approaches for suicidal patients with schizophrenia in general [72]; as a result, clinicians often follow guidelines that are associated with management of the suicidal patient with affective disorders [70]. Clearly, following discharge from a hospitalization, it is important for clinicians to set up psychosocial programs as part of after-care programs to complement or augment pharmacologic treatment.

Psychosocial modalities

A variety of psychosocial interventions have been shown to help patients with schizophrenia [73]. An integrated approach using several psychosocial modalities is regarded as standard practice [74–77] and these approaches include supportive employment, family intervention, psychoeducation, assertive community treatment, social skills training and cognitive

behavioral treatment; the latter appears to improve insight, positive symptoms, depressive symptoms and also suicidal behavior [78–82]. An important aspect of managing suicidal patients with schizophrenia involves empathic support [83]. Providers need to acknowledge the patients' degree of despair, losses and troubles with daily life and to engage patients in establishing realistic goals [5,50,82]. Sensitivity in addressing subjective distress and hopelessness is also important, since despair is known to be a risk factor for completed suicide [52,72,84].

One other important aspect to consider is whether patients develop a demoralization syndrome [85]. As patients become aware of their illness and its consequences they may develop a state of hopelessness. This, in turn, can accentuate depression and suicidal behavior. Enhancing adherence to psychiatric follow-up and maintaining social support are important components of care [86,87]. In addition, maintaining adherence to antipsychotic drug treatment is a critical component for suicide prevention efforts in general [88]. Poor adherence with medication has been shown to be associated with suicidal risk [41,89].

The role of recovery

It is likely that patients actively involved with recovery may have a lower suicide risk. In patients with schizophrenia, recovery extends beyond symptom remission and achievement of psychosocial milestones; it includes subjective perceptions of how persons with schizophrenia appraise their lives and the degree to which they can see themselves as meaningful individual in the world. Lysaker *et al.* indicated that psychotherapy can be transformed to assist people with schizophrenia in order to help them perceive and experience their lives as richer and to also see clearly their strengths, challenges, losses and hopes [90]. In addition, these authors suggest that psychotherapy could focus on assisting psychotic persons to think more about themselves and others in a more appropriate complex and flexible way.

Clearly more research is needed to determine whether implementing such a recovery program in people with schizophrenia will reduce suicidal behavior. This is especially important in the older suicidal patient with schizophrenia, in which a hopeful and optimistic point of view may likely show promise in elevating these individuals' quality of life.

Cognitive behavioral approaches for treating suicidal behavior

For elderly suicidal patients with schizophrenia more than 65 years of age, there are no psychosocial studies available examining suicidal thinking in patients with schizophrenia. There is one study with a mixed middle-aged and elderly cohort, which determined that cognitive behavioral social skills training can be helpful for a variety of outcomes [91]. Although suicidal behavior was not an outcome observed in this study, patients' social functioning improved, and they achieved significantly greater cognitive insight, more objectivity in reappraising psychotic symptoms and greater skill mastery. It would be of interest to examine this approach directly on suicidal behavior in a geriatric cohort.

A recent review by Tarrier *et al.* [92] indicated that cognitive behavioral therapies (CBTs) are effective at reducing suicidal behavior. A total of 123 potential articles of interest were found; of these, 28 met the entry criteria [92]. Studies were included if, first, they were published in a refereed journal, and second, they included a treatment group with a form or substantial component of cognitive, behavioral, or CBT, a control group as a comparison and any kind of self-harm or suicidal behavior as an outcome measure. Studies were excluded if they were only case studies, clinical descriptions, reviews or discussion articles. They were also not included if they did not include a control group, if they were published before 1980, or if they were not in English.

One recent trial by Tarrier *et al.* included patients with schizophrenia ($n = 278$) with suicidal behavior [79]. Patients with recent onset schizophrenia received CBT, supportive counseling or treatment as usual. Thus, this patient sample included a younger group with an average age of between 20 and 30 years. Treatment was delivered in the hospital over a 5-week period and participants were assessed at baseline, 1.5, 3 and 18 months. All groups improved but there were no beneficial or adverse effects of psychological treatment on suicidal behavior that were significantly different between the groups. The authors stated that CBT may need to be modified to directly target other suicidal behavior and its antecedents to significantly reduce risk. Since there was a significant but low correlation between reductions in suicidal behavior and reductions in psychotic and depressive symptoms, the authors wondered whether CBT may have a modest effect on reducing suicidal behavior by reducing psychotic and depressive symptoms. Future studies will need to address this.

Of all the studies reviewed by Tarrier *et al.* which examined CBT in suicidal people, the mean duration of treatment was 19.52 weeks (standard deviation = 24.77) [92]. There were six interventions greater than 12 months in duration, which included therapies focusing on dialectic behavior therapy (DBT) while the majority of interventions ($n = 20$) were brief (i.e., ≤ 6 months). Furthermore, there was a great deal of variability across the studies in terms of how the methods and treatment techniques were used and in how they were implemented. Interventions were either solely CBT or included CBT as a significant part. The most frequently used standardized treatment program was DBT, which was a manualized treatment combining strategies from behavioral, cognitive and supportive psychotherapies. In addition, treatment was delivered by a range of professions with varying levels of professional training and experience. Outcome measures included: satisfaction with life scale, hopelessness; suicidal ideation; suicidal attempts or plans; probability of suicide; and suicide threats.

Effect of treatment

There was a highly significant effect for CBT in reducing suicide behavior. Subgroup analysis indicated a significant treatment effect for adult (but not adolescent) samples, for individual (but not group) treatments and for CBT when compared with minimal treatment or treatment as usual. However, there were no positive effects when compared with another active treatment. Cognitive therapy had an overall positive effect on the outcome variables (combined Hedge's g : -0.59 ; z : -5.26 ; $p < 0.0001$; 95% CI: -0.811 to -0.371). Both DBT and general CBT demonstrated highly significant effects. Studies in which one-to-one CBT was included show a very significant effect, but studies involving groups alone were not significant. The effect sizes for CBT and DBT were large and comparable (respectively, combined Hedge's g : -0.562 ; z : -4.244 ; $p < 0.0001$; 95% CI: -0.825 to -0.302 ; combined Hedge's g : -0.697 ; z : -3.057 ; $p < 0.0001$; 95% CI: -1.143 to -0.250).

Developing cognitive behavioral approaches to treat the older suicidal patient with schizophrenia

A modified form of CBT may help treat suicidal behavior in the older suicidal patient with schizophrenia. As mentioned, there is no current intervention that is effective in suicidal younger adults with schizophrenia. If an effective intervention could be developed, then a revised version would need to be developed for the older suicidal adult with schizophrenia. Already several psychosocial interventions have been shown to be effective for the older adult with depression, including CBT, problem-solving therapy, supportive psychotherapy and interpersonal therapy. When integrated into primary care systems, there is evidence that

interpersonal therapy [93] and problem-solving therapy [94] can help reduce suicidal behavior.

An ideal intervention would need to incorporate additional components that are important in treating older individuals in general. This would include providing careful consideration of managing patients' medical comorbidities, especially those involving cerebrovascular comorbidities. In addition, consideration needs to be provided for normal cognitive deficits associated with aging, which could compound already existing cognitive deficits in patients with schizophrenia. It is also possible that these patients could have other developing cognitive deficits, such as early degenerative dementias. In addition, in this population of older adults, there are other issues which may also need to be addressed, such as a potential sedentary lifestyle, overeating, smoking and other forms of substance abuse/dependence [95–97].

Importantly, any intervention needs to be available within the context of an integrated approach toward treating this patient population. Studies, such as Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT), which have targeted suicidal depressed elderly in primary care, have indicated that collaborative care offered at the primary-care setting has superior outcomes compared with usual care [93,98]. Of course, another important issue to consider concerns access to care and delivery. One of the greatest limitations in the treatment of later-life mental disorders concerns diagnostic accuracy and treatment access; this is often more important than ensuring treatment efficacy. For example, in one study examining depressed high utilizers of primary care treatment, only 11% were found to receive adequate antidepressant treatment [99].

Pharmacologic approaches

With exceptions, medication studies that have examined suicidal behaviors as an outcome in patients with schizophrenia have primarily been performed with trials designed instead to treat the psychotic and/or depressive symptoms of the disorder. Furthermore, we cannot assume that if depression is targeted then suicidal thoughts and feelings will also improve. Ideally in intervention studies, the suicidal thoughts and behaviors should be addressed directly. Most pharmacologic approaches fail to do this; however, we will report below what pharmacologic evidence can be gathered to help assess the issue of suicidal behavior in patients with schizophrenia and will include what limited literature is available to address this in the suicidal older patient with schizophrenia.

First-generation antipsychotic medications

Even though first-generation antipsychotics are successful in treating positive symptoms, this is not necessarily associated with a decreased suicide risk in general in patients with schizophrenia. The rates determined in 1975 [100] and in 1992 [101] indicate that there was no appreciable change; this was at a time when use of antipsychotics was increasing. One review investigating the effects of first-generation antipsychotics on suicide rates demonstrated a modest advantage in patients with schizophrenia [102]. However, in considering this in the elderly, there is a concern of a higher rate of extrapyramidal, anticholinergic and sedating side effects which could arise with these agents in this population [103]. In studies examining individuals of all ages, extrapyramidal side effects have been associated with dysphoria, worsening subjective distress, agitation and suicidal behavior [104,105]. In general, the literature on the effects of first-generation antipsychotic drugs is inconsistent in determining whether these agents are helpful with the suicidal patient [70].

Ernst and Goldberg point out many of the methodological limitations of the investigations utilizing first-generation antipsychotic medications [103]. They state that many results appear to be confounded by retrospective study design, treatment assignments lacking randomization, recall bias, varying medication regimens and lack of control for comorbid psychiatric diagnoses. The reviewers also highlighted that many of the studies did not control other factors known to influence suicide in schizophrenia patients, such as previous suicide attempts, substance abuse, demographic factors, degree of insight, recent hospitalizations, poor premorbid functioning and adverse life events.

Palmer and colleagues point out that a further complicating factor in determining whether antipsychotics help improve suicidal behaviors [102] is that severely ill, symptomatic patients are likely to receive the highest doses of antipsychotic drugs. Therefore, rather than there being a linear relationship between suicidal behavior and neuroleptic dose, there might be a biphasic association. Suicide rates may be higher with very low doses (i.e., when the doses are ineffective) as well as very high doses (i.e., when there are more side effects or more severe illness). Thus, no clear dose–effect relation with suicidal behavior has been found for first generation antipsychotic medications for patients in general. Furthermore, it is not known how the benefits, if present, might generalize to the geriatric suicidal patient with schizophrenia.

Second-generation antipsychotic medications

Compared to first-generation antipsychotic agents, the second-generation agents may be more effective in reducing suicidal risk. This is especially true for clozapine, although clozapine as an agent for geriatric patients is limited owing to its side-effect profile. Studies examining second-generation agents such as risperidone and olanzapine on nongeriatric suicidal patients have been mixed [106–110]. Two meta-analyses examined rates of suicide attempts or completed suicide from randomized, double-blind, placebo-controlled studies involving either risperidone, quetiapine or olanzapine treatment: no differences were noted [111,112].

One of these meta-analyses by Khan *et al.* involved a total of 10,118 individuals participating in clinical trials with three new second-generation antipsychotics – either risperidone, olanzapine or quetiapine; 26 patients committed suicide and 22 patients did this while receiving a new antipsychotic; three patients committed suicide while receiving haloperidol, and one committed suicide while on a placebo [111]. These differences were not statistically significant ($\chi^2 = 0.99$; $df = 2$; $p = 0.6$). There were 51 suicide attempts in 51 patients; 43 of them attempted suicide while receiving either risperidone, olanzapine or quetiapine, seven were taking haloperidol, and one was taking placebo. The differences in suicide-attempt rates between these groups did not approach statistical significance ($\chi^2 = 0.21$; $df = 2$; $p = 0.7$).

Of seven pivotal studies with the three second-generation antipsychotics there were a total of 1926 patients; 1203 (62.5%) received one of the three new antipsychotic; 261 (13.6%) received haloperidol; and 462 (24.0%) received placebo. Among the 1203 patients receiving a new antipsychotic, the mean decrease in total Brief Psychiatric Rating Scale (BPRS) score at last observation carried forward (week 6) was 16.6%; among the 261 patients receiving an established antipsychotic, 17.3%; and among the 462 patients receiving placebo, 1.1%. Based on observation cases, for 839 patients considered at week 6, the mean decrease in total BPRS was 32.3% among the 575 patients continuing either quetiapine, olanzapine or risperidone; 29.5% among the 108 patients continuing haloperidol; and 22.4% among the 156 patients continuing the placebo. In terms of patient study completion rates, six out of seven favored a new antipsychotic and one favored an established antipsychotic.

There are very few studies that have specifically examined second-generation antipsychotics in elderly patients with schizophrenia. One 8-week double-blind study compared risperidone to olanzapine in older patients [113]; 175 patients with schizophrenia or schizoaffective disorder over 60 years of age were tested in a variety of settings (i.e., outpatients, hospital inpatients and residents of nursing or boarding homes). Median doses used were 2 mg/day of risperidone and 10 mg/day of olanzapine. According to a random-coefficient model, PANSS total scores were significantly reduced in both treatment groups at week 1 and all subsequent timepoints ($F [1169] = 89.9$; $p < 0.0001$). No significant between-treatment differences were noted ($F [1738] = 0.01$; $p = 0.959$). Clinical improvement, defined as a 20% reduction in PANSS total score, was achieved by 58% of patients in the risperidone group and 59% in the olanzapine group. Eight patients in the risperidone group (9.2%) and 14 in the olanzapine group (15.9%) reported extrapyramidal symptoms-related adverse events; the between-treatment difference was not significant. There were no outcomes assessing suicidal behaviors.

Metabolic syndrome and cardiovascular diseases are important causes of morbidity and mortality among patients with schizophrenia. Second-generation antipsychotics are associated with obesity and other components of metabolic syndrome, particularly abnormal glucose and lipid metabolism. Thus these potential side effects need to be carefully considered when prescribing these agents [114].

Clozapine

Clozapine was first reported to reduce rates of suicidality in a study among 88 treatment refractory patients with schizophrenia or schizoaffective disorder [115]. In that trial, 2 years prior to initiation of clozapine therapy, 22 suicide attempts were reported while 2 years after the start of clozapine treatment, the rate of suicide decreased by 88%. The International Suicide Prevention Trial (InterSePT) was a multicenter international prospective study which compared the effects of olanzapine and clozapine on suicidal behavior over 2 years [109]. Using an open-label design, this trial recruited patients with schizophrenia or schizoaffective disorder at high risk for suicidal behavior in having previous suicide attempts or current suicidal ideation. They were randomized to either clozapine (300–900 mg; $n = 479$) or olanzapine (10–20 mg; $n = 477$). Subjects were followed at the same intervals in both groups; clinical ratings were performed by blinded raters. Improved outcomes were observed with clozapine. This included improvements in suicidal behavior, suicide attempts, numbers of required hospitalizations, interventions needed to prevent suicide and the use of adjunctive antidepressants as well as anxiolytics.

Using a Cox proportional hazards regression model, which included treatment, number of previous suicide attempts, active substance or alcohol abuse, country, sex and age group at baseline, there was a 26% reduction in risk for suicide attempt or hospitalization to prevent suicide for those randomized to clozapine versus those randomized to olanzapine. The hazard ratio was 0.74 (95% CI: 0.57–0.96). Furthermore, a significant reduction in the 2-year event rate at the end of the study (olanzapine, 32.2% vs clozapine, 24.0%; 95% CI: 0.02–0.14; number needed to treat: 12) and a delay in time to event were demonstrated for clozapine-treated patients.

The InterSePT excluded patients 65 years of age and older. Thus, we do not know whether we can extrapolate the benefits of this trial to geriatric patients. Data on clozapine use in the elderly is limited. Furthermore the ‘Consensus Guidelines for the use of Antipsychotic Medication in the Elderly’ recommend caution when using clozapine in the elderly [103].

Treating depressive symptoms in patients with schizophrenia

Treating depression in the suicidal patient with schizophrenia is important since depressive symptoms are risk factors for suicidal behavior in patients with schizophrenia [41,116]. Of course, when evaluating depression in older patients with schizophrenia, reversible causes of depressive symptoms, such as abuse of and withdrawal from illicit drugs or the dysphoria and akathisia secondary to antipsychotic drugs should be carefully considered [70]. In addition, when depression is present, clinicians can augment pharmacologic approaches with psychosocial treatments, although there has been little research examining this practice in individuals at all ages or specifically in the elderly [117].

The 1999 expert treatment guidelines for schizophrenia recommended that in patients with schizophrenia and postpsychotic depression, SSRIs should be first-line agents [118]. The guidelines state that if an antidepressant is started then it is recommended that clinicians try these agents for at least 6 months. The evidence base supporting the use of antidepressants in treating depressive symptoms in patients with schizophrenia is strongest for SSRIs and very recently, more evidence has become available that supports the use of the SSRI, citalopram, as augmenting agents for antipsychotics as a way to help treat suicidal symptoms [119].

SSRIs in treating depressive symptoms in patients with schizophrenia

Except for one trial, the peer-reviewed, published, double-blind, placebo-controlled trials examining SSRIs for the treatment of depressive symptoms in patients with schizophrenia are limited by small sample size [120,121]. One larger study examined SSRI augmentation with citalopram; however, this was a mixed sample of middle-aged and elderly participants (age range: 40–75 years) with a mean age of 52.5 ± 7.1 years. Patients with schizophrenia or schizoaffective disorder who also had subsyndromal depressive symptoms [122] were included. In the intent to treat analysis, which included 198 patients randomized to citalopram augmentation versus placebo augmentation, the group with citalopram showed more improvement in depressive symptoms. The number needed to treat for improvement of depressive symptoms was six. No difference in adverse events occurred between participants receiving citalopram and placebo. Furthermore, linear regression determined there were no significant interactions between drug group and age with regards to depressive symptoms, quality of life and functioning, and adverse events did not differ with age [123].

In the same trial, the investigators examined the response of suicidal behaviors to citalopram treatment [119]. In total, 21% of the sample expressed suicidal ideation at baseline based on the Clinical Global Impression – Suicide Scale (CGI-SS). At 12 weeks, adding citalopram was associated with participants having significantly lower scores on the Beck Hopelessness Scale (i.e., 4.21 vs 4.98; $p < 0.05$), lower scores on the Intersect Scale for Suicidal Ideation (ISST; 17.7 vs 38.7%; $p < 0.005$) and item three of the HAMD, which assesses suicidality (14.4 vs 22.6%; $p < 0.05$) compared with placebo augmentation. Among the subset of 114 participants who exhibited no suicidal ideation at baseline, there were no differences between the two groups with regard to emergent ideation at the end of treatment. However, in the 55 participants with suicidal ideation at baseline, fewer participants treated with citalopram augmentation had end point suicidal ideation on the ISST (28.6 vs 66.7%; $p < 0.05$). Furthermore, 75% of depression responders who exhibited baseline suicidal ideation exhibited no suicidal ideation at the final visit on the ISST compared with 31.4% of nonresponders ($p < 0.05$). Using the CGI-SS scale, 84% of depression responders had no suicidal ideation at end point based on the CGI-SS compared with 31.3% of the nonresponders ($p < 0.05$). In those with baseline suicidal ideation, antidepressant treatment reduced suicidal ideation, especially in those whose depressive symptoms respond to treatment. Thus, this study suggests there may be a possible antisuicidal role for

antidepressant medication in this population of patients. However, since this was a study that included middle-aged and geriatric patients with schizophrenia, studies examining the use of SSRIs in older suicidal patients with schizophrenia need to be replicated in a geriatric sample.

Conclusion

Clearly much more research is required to better understand suicidal behavior in older patients with schizophrenia. Research focusing on assessing and treating the older suicidal patient with schizophrenia is currently very limited. This is important since prevalence estimates suggest that up to 50% of individuals experience suicidal ideation. The assessment and treatment of elderly suicidal patients with schizophrenia initially involves careful consideration of risk factors. Much of this evidence is derived from samples that include middle-aged patients in addition to geriatric patients; thus the generalizability of these findings to geriatric populations is not known. There are no theoretical models that can sufficiently explain suicidal behavior in older patients with schizophrenia. It is possible that the models currently available could be adapted for the older suicidal patient with schizophrenia. The formulation of a comprehensive safety plan involving bio-psychosocial interventions is always important when treating suicidal patients with schizophrenia. It is not clear which psychosocial interventions are helpful in the elderly patient since the literature is very limited with regards to this. There is evidence that CBT helps reduce suicidal behavior in people without schizophrenia. Whether this can be adapted to the patient with schizophrenia, especially the older patient, is not clear.

Clinicians' approaches for management are derived by extrapolating from studies in younger patients. In line with this issue, it is not known whether first- and/or second-generation antipsychotics are protective; it is also not clear whether clozapine is helpful in the elderly; there is the concern that factors that limit its use in younger populations may be worse in the elderly given their enhanced sensitivity to side effects. The benefit of clozapine in younger suicidal patients with schizophrenia appears to outweigh the side-effect risks [124] but whether this is still the case in the elderly remains unknown. Finally, antidepressant augmentation of the suicidal patient with schizophrenia and depression with SSRIs appears to be helpful in terms of reducing depressive symptoms and suicidal ideation. However, since these studies included middle-aged and older patients, it is not clear whether these positive findings would apply for patients aged 65 years and older.

Future perspective

At the current stage of research with older suicidal patients with schizophrenia, we are unfortunately left with more questions than answers. Clearly a great deal of research is required to address these important questions. Theoretical models applicable to this patient population need to be created and these models need to be empirically tested. A starting point with this avenue of investigation could include adapting the existing models such as the Cry of Pain, Schematic Appraisal Model of Suicide and Interpersonal Theory of Suicide to this population and then testing whether these revised models are useful. Another important question which needs to be addressed is whether suicide in elderly people with schizophrenia results from factors that affect the elderly, or does suicide occur from schizophrenia-related factors, such as psychotic phenomena? In addition, could there be an interaction between age-related and schizophrenia-related factors? Future testing needs to address this and could also help integrate the findings with models of suicide.

Further investigation to assess risk factors in samples of patients that are purely geriatric is needed to remove concerns regarding generalizability from previous studies derived from

mixed samples of middle-aged and geriatric individuals. The same approach is also needed with regards to intervention development. Newer psychosocially oriented approaches to treatment are needed. For instance, cognitive behavioral approaches could be adapted to this population and then tested to determine whether they can improve outcomes. In addition, telehealth-related monitoring systems could be tested in this population to establish whether they are feasible and if so, whether telehealth systems improve outcome. Also, pharmacologically based interventions need to be tested in geriatric individuals. The elderly are often more sensitive to psychotropic medications. Dosing regimens need to be well established by implementing well-designed clinical trials. Once risk factors are established and we determine which treatments will work, then clear guidelines for the assessment and treatment can be produced so that clinicians can best help this population of patients.

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Executive summary

- Studies indicate that risk factors for suicide in older persons with schizophrenia include a past history of suicide, depressive symptoms and past traumatic events.
- There is some evidence suggesting that suicidal ideation in mixed samples of middle-aged and older patients with schizophrenia improves when antipsychotic treatment is augmented with citalopram. However, future research needs to determine whether citalopram improves suicidal ideation in pure geriatric samples.
- Much research is needed to determine how psychosocial interventions can help treat the older suicidal patient with schizophrenia.
- Theoretical models applicable to the older suicidal patient with schizophrenia need to be developed and tested. A starting point could be to adapt the Cry of Pain, Schematic Appraisal Model of Suicide and Interpersonal Theory of Suicide.