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# Suicidal risk in patients with aggression in schizophrenia: a systematic review

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**Introduction:** Suicide represents the primary risk factor for mortality among individuals diagnosed with schizophrenia, with a mortality rate that is 10 times higher than that observed in the general population. In the study of individuals who have committed suicide, some exhibited a high risk of aggression and impulsivity, which permitted the consideration of these indicators as predictors of suicide risk. The extant literature contains a number of debates concerning diverse conceptualizations of aggression and impulsivity in the context of suicidal behavior. The present study examined the levels of verbal and physical aggression in individuals diagnosed with schizophrenia, finding that 43% exhibited verbal aggression and 24% physical aggression, levels that are significantly higher than those observed in the general population. Concurrently, an analysis of the psycho-emotional state of patients with suicidal behavior in the anamnesis reveals an indication that the suppression of emotions (including aggression) and the avoidance of harm may result in suicide. This finding is at odds with the previously mentioned results, and consequently, the present review sought to assess the impact of aggressive behavior on suicide risk in patients diagnosed with schizophrenia.

**Methods:** The search was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The literature search was conducted in PubMed, Cochrane Library, PsychINFO and Mendeley Data. The search terms used were “aggress\*” and “suicid\*” or “autoaggress\*” and “schizophrenia\*”. The search was limited to papers published between 2009 and 2024 (the last 15 years), and the search was continued until November 2024. This systematic review has been registered in PROSPERO (CRD42024628033).

**Results:** A total of 1,364 articles were identified, 295 of which were duplicates. Following a thorough review, 1,046 articles that did not align with the title and abstract were excluded from the analysis. During the literature search, 23 articles were read in full, of which eight studies met the inclusion criteria. A total of eight studies provided information on the effect of aggressive behavior on suicide in patients with schizophrenia. Of these, six studies demonstrated a positive association between aggression and suicidal behavior or employed a logistic regression model in which the risk of aggression increased the risk of suicide and vice versa. Conversely, two studies revealed no association between suicide risk and aggression.

**Conclusions:** Patients with a documented history of suicide attempts and aggressive behavior are considered to be at risk of suicide, thus emphasizing the necessity for preventive measures to be implemented for this cohort of patients. However, the conclusion regarding the influence of aggressive behavior on increased suicide risk may not be entirely accurate and may not reflect the true extent of the problem, due to the significant number of methodological inaccuracies and discrepancies in the design of the studies included in the review.

**Systematic review registration:** <https://www.crd.york.ac.uk/PROSPERO/view/CRD42024628033>, identifier CRD42024628033.

#### KEYWORDS

schizophrenia, aggression, suicide, suicide risk, aggressive behavior

## 1 Introduction

Suicide represents the primary risk factor for mortality among individuals diagnosed with schizophrenia, with a mortality rate that is 10 times higher than that observed in the general population (1). For instance, the suicide prevalence rate among individuals with schizophrenia is reported to be 352.2 per 100,000 person-years (95% CI 239.3–485.7 per 100,000 person-years) (2), with 44.3% of cases involving a documented suicide plan (3). It has been established that individuals diagnosed with schizophrenia are more likely to employ violent methods in the course of committing suicide, in comparison to the general population. The most prevalent methods include jumping from a height or drowning (4–6). It is estimated that between 50% and 60% of individuals who attempt suicide for the first time will ultimately succumb to their actions (7, 8), the occurrence of a suicide attempt has been demonstrated to result in an elevated risk of subsequent completed suicide (9–11). Risk factors for suicide in schizophrenia include poor compliance with medication, a history of suicide attempts, a sense of hopelessness, male gender, belonging to the white race, tobacco and alcohol use (12), childhood trauma (13–15) and demoralization (16). However, other studies have reported conflicting data on the impact of suicide risk factors such as low education and income, and ethnicity (13). The identification of markers of suicidal behavior in schizophrenia through the study of cognitive function represents a promising area of research. A review study has indicated that a better understanding of the course of the illness among patients, achieved through higher IQ, better executive functioning and higher levels of comprehension, may serve as a predictor of suicidal behavior (17). It is interesting to note that a set of these characteristics offers patients protection against aggressive behavior directed towards others. However, a previous review has already reported deficits in cognitive functions, such as impaired planning and reduced working memory, which contribute to suicidality in schizophrenia (18). The present study suggests that the analysis of a series of cognitive functions may offer a valuable

means of identifying individuals who are at risk of suicide. However, the available data are somewhat contradictory. Nevertheless, it is important to consider other risk factors for suicide, as low cognitive functioning is also a risk factor for natural mortality in schizophrenia (19, 20). Moreover, the necessity to ascertain risk factors for suicide is predicated on the objective of preventing it, as there are proven prevention methods for those at high risk, chiefly clozapine (21) and psychotherapeutic methods (22).

Research focusing on individuals who have committed suicide has indicated that some of them exhibit elevated levels of aggression and impulsivity, which can be regarded as indicators of suicide risk (23, 24). There is an ongoing debate in the literature about the different understandings of the terms aggression and impulsivity within the framework of suicidal behavior (25, 26). For instance, impulsivity is defined as “poorly thought out, prematurely expressed, unreasonably risky or inappropriate actions that often lead to undesirable outcomes” (27), whereas aggression is defined as behavior aimed at harming another person motivated to avoid harm (28), expressed verbally and physically (29). Aggression is the sole predictor of suicidal behavior. The prevalence of verbal aggression in individuals diagnosed with schizophrenia is 43%, while the prevalence of physical aggression is 24% (30), which significantly exceeds the figures observed in the general population (31). The etiology of aggressive behavior in schizophrenia has been linked to structural and functional changes in the brain (32, 33), and alleles of genes associated with an increased risk of aggression have been identified (34, 35). Furthermore, aggression is considered a likely predictor of suicidal behavior, as demonstrated in genetic (36–38), and neuroimaging studies (39–42). The relationship between aggression and suicidal behavior is supported by the fact that the same 5-HT receptors are involved in their pathogenesis: 5-HT1A, 5-HT2A, 5-HT2B, 5-HT2C (43–45). It is evident that individuals diagnosed with schizophrenia who exhibit suicidal tendencies and aggressive behavior constitute a distinct clinical entity. In this group, therapeutic and rehabilitative interventions are

likely to be ineffective, as patients with aggressive tendencies often disregard clinical interventions, violate treatment regimens, and evade drug therapy, thereby hindering the efficacy of psychotherapy (46, 47). Conversely, analysis of the psychoemotional state of patients with a history of suicidal behavior reveals evidence that the suppression of emotions (including aggression), and the avoidance of harm, can result in suicide (48–50).

## 2 Methods

### 2.1 Research question

The objective of the present review was to assess the impact of aggressive behavior on suicide risk in patients diagnosed with schizophrenia. We asked to research question:

What is the relationship between suicide risk and aggressive behavior in people with schizophrenia?

### 2.2 Search strategy

This research was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (51). The literature search was conducted by three researchers, who independently and separately searched the three databases: PubMed, Cochrane Library, PsychINFO and in the one secure cloud-based repository Mendeley Data. The search terms used were “aggress\*” and “suicid\*” or “autoaggress\*” and “schizophren\*”. The search was limited to works published between 2009 and 2024 (the last 15 years), and the search was continued until November 2024. The complete search terms can be found in [Appendix A](#). There were no restrictions on the language of the article. This systematic review was registered with PROSPERO (CRD42024628033).

### 2.3 Inclusion criteria

Inclusion and exclusion criteria are described using the PICOS strategy and displayed in the [Table 1](#).

### 2.4 Data extraction

The selection of research results will be conducted by three independent reviewers (BL, KM, KG), who will utilize the established inclusion/exclusion criteria to make their decisions. In all cases, data were extracted twice, once jointly and once separately by the two authors (BL and KM). The extracted data were then compared, and where discrepancies or disputes were identified, a third author was involved (KG).

Data extraction: the initial phase of this process will be the entry of the data into a standardized spreadsheet by one reviewer. This will be followed by two other reviewers who will then check the extracted data independently. The following data elements were to be extracted: the authors' names; the country in which the study was conducted; the date of publication; the title of the study; the total sample size; the mean age of the participants; the guidelines according to which a psychiatric diagnosis was made; the principle according to which the research sample was divided into subgroups; the characteristics of the subgroups (number, number of patients with suicidal and separately aggressive behavior); the methods for detecting suicidal and aggressive behavior (medical history data or use of scales); and, in the case of suicide and aggression risk scales, the mean and standard deviation for each group in separate studies.

### 2.5 Methodological quality assessment

The present study examined patients diagnosed with schizophrenia who exhibited either suicidal tendencies or

TABLE 1 Eligibility criteria.

|              | Inclusion                                                                                                                                                                                                          | Exclusion                                                                                                                                                                                                                                   |
|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Population   | Adult individuals (age, 18–60 years) diagnosed with schizophrenia according to the International Classification of Diseases (ICD-10), DSM-IV, DSM-IV-TR, DSM-IV-R                                                  | Children, adolescents, or older adults.<br>Patients with other major disorders, such as bipolar disorder or dementia.<br>Patients with limited physical activity (e.g., cardiopulmonary disease).<br>People with intellectual disabilities. |
| Intervention | Suicidal risk or suicidal behavior in the history (including completed suicide) and evidence of a relationship between suicidal behavior and aggression                                                            | With other mental disorders (depression, borderline personality disorder, and others)                                                                                                                                                       |
| Comparator   | Patients with schizophrenia without suicidal risk (thoughts, attempts), or patients with schizophrenia with suicidal risk without aggression, or patients with schizophrenia with aggression without suicidal risk | No comparison group                                                                                                                                                                                                                         |
| Outcomes     | Identified relationship between aggressive behavior and suicide risk directly using statistical analysis (logistic regression) or objective psychometric measures                                                  | No assessment of the relationship between aggressive behavior and suicide risk directly, indirect relationship through other indicators                                                                                                     |
| Study design | Non-randomized studies: case-control, cross-sectional, cohort studies                                                                                                                                              | Systematic reviews, meta-analyses, letter to the editor, abstracts                                                                                                                                                                          |

behaviors. The following characteristics were deemed essential in determining the suitability of a study for inclusion: Firstly, patients must be diagnosed with schizophrenia. Secondly, there must be documented history of suicide risk or suicidal behavior, including completed suicide. Thirdly, there must be evidence of an association between suicidal behavior and aggression. Studies were excluded from the review if they did not contain the following information: 1) incorrect description of the sample (missing data for inclusion in the study); 2) information about the study did not match the researchers' search query. The verification of diagnosis should be conducted in accordance with international clinical guidelines by multiple independent specialists (DSM or ICD criteria could be utilized); the assessment of suicide risk should be performed by a psychiatrist (one or more) according to the following variants: suicidal behavior, presence of suicidal thoughts, completed suicide) or by using psychometric instruments; and the assessment of aggressive behavior, both at the time of the study and of evidence of aggression in the medical history by the following methods: clinical interview or by using psychometric scales; establishment of an association between suicidal behavior and aggression in patients with schizophrenia by correlation or by using logistic regression.

A risk of bias (quality) assessment was conducted.

In accordance with the stipulated guidelines set out in the Cochrane Handbook, the reviewers proceeded to assess the risk of systematic error in each of the included studies. To this end, the ROBINS-E tool was utilized for the purpose of evaluating non-randomized trials. The ROBINS-E tool encompasses the following domains: bias due to confounding, bias due to measurement of exposure, bias in selection of study participants, bias due to post-exposure interventions, bias due to missing data, bias in measurement of outcome, and bias in selection of reported outcome. Each item was then evaluated as being either high risk, causing some concern, or low risk of systematic error. The ROBINS-E (Risk Of Bias In Non-randomized Studies - of Exposures) assessment tool was utilized to evaluate the risk of bias in the study (52). We used the standardized 7 domains to assess risk of bias: 1) risk of bias due to confounding, 2) risk of bias arising from measurement of the exposure, 3) risk of bias in selection of participants into the study (or into the analysis), 4) risk of bias due to post-exposure interventions, 5) risk of bias due to missing data, 6) risk of bias arising from measurement of the outcome, 7) risk of bias in selection of the reported result. Quality assessment was carried out separately by two authors (BL, KM), with a third author involved in the event of disagreement or dispute (KG).

The R package "Robvis" was employed for the purpose of plotting (53).

## 3 Results

### 3.1 Study selection

A total of 1,364 articles were identified, 295 of which were duplicates. Following a thorough review, 1,046 articles that did not

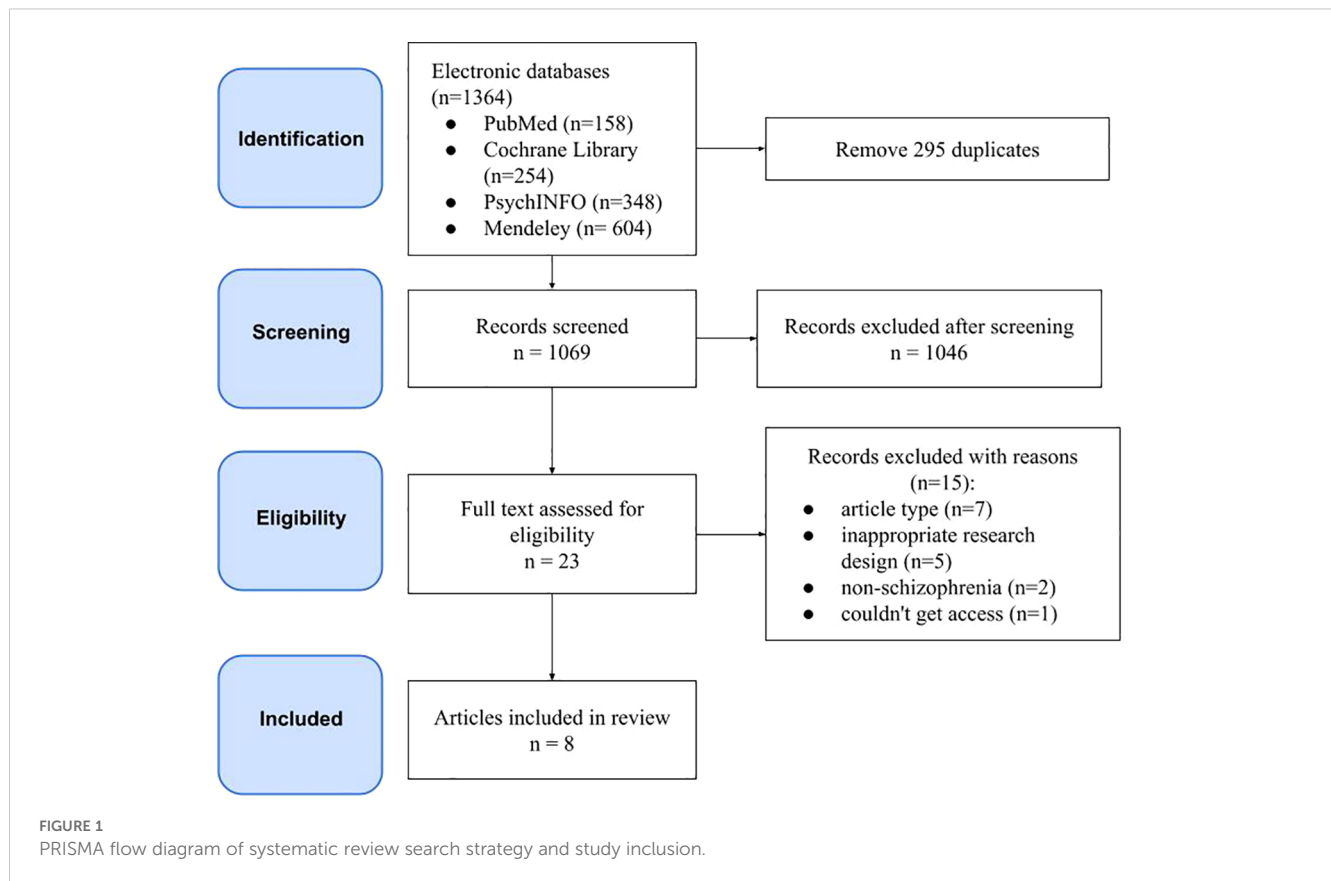
align with the title and abstract were excluded from further consideration. During the literature search, 23 articles were read in full, of which eight studies met the inclusion criteria. The results of the search and the rationale for exclusion are illustrated in Figure 1.

### 3.2 Sample characteristics

A total of eight studies were included in the analysis, providing data on 102,760 patients diagnosed with mental disorders, of whom 10,698 had been diagnosed with schizophrenia (54–61). Patients were recruited from hospitals in China, Canada, Germany, Turkey, Norway, Israel and France. The mean age of the study participants was reported in 5 articles (55, 57, 58, 60, 61) and was  $37.5 \pm 11.9$ , this indicator was not provided by the other studies (54, 56, 59). The total number of cases of schizophrenia and suicide in all eight studies was 624. In one article, however, the exact number of patients with suicidal behavior was difficult to calculate because the main group was considered to be patients with schizophrenia with only "inpatient suicide" and "suicide attempt (admission)" ( $n=47$ ), which were included in the total number of patients with schizophrenia and suicide (60). The total number of patients with aggressive behavior was extracted from four articles, yielding a total of 1,294 patients (54, 56, 59, 61). In three articles, the calculation of the number of aggressive patients was not possible due to the provision of only parametric indicators of the aggressiveness of the groups (55, 57, 58). In one study, the precise number of patients with aggressive behavior could not be ascertained, as it is possible for the same patients to be included in different groups, e.g. 'physical assault admission', 'physical assault inpatient', 'threatening behavior admission' or 'damage to property admission' (60). In one study, the precise number of patients with aggressive behavior could not be ascertained due to the inclusion of the same patients in different groups, e.g. 'lifetime suicide attempt', 'inpatient suicide attempt or suicidal ideation' and 'admission for physical assault', 'admission for physical assault inpatient', 'admission for threatening behavior' or 'admission for damage to property' (60). Three studies reported the number of patients with schizophrenia who exhibited suicidal behavior and aggression, constituting 62% ( $n=133$ ) of all patients with schizophrenia and suicide included in these studies (54, 56, 59).

### 3.3 Suicide assessment

Three studies utilized psychometric scales to evaluate suicide risk upon admission to hospital: Suicide Risk Assessment (SRS) (54, 57), Nurses' Assessment of Suicide Risk for Suicide (54), and The InterSePT Scale for Suicidal Thinking (ISST) (55). In three studies, suicidal behavior was assessed according to the following criteria: history of lifetime suicide attempts (58), suicidal behavior in hospital including completed suicide (60), and completed suicide only (59). However, it should be noted that in two studies, the circumstances and time of occurrence of suicidal thoughts and attempts remain unreported (56, 61).



### 3.4 Aggressive assessment

In the five articles, the following psychometric scales were utilized to evaluate the level of aggression at hospital admission: two articles employed the Overt Aggression Scale (OAS) (57, 58), in one study the Modified Overt Aggression Scale (54) was used, in another the Buss-Perry Aggression Questionnaire (BPAQ) (56) was employed, and in the last study a separate item on the scale was taken into account: Positive and Negative Syndrome Scale “Disordered regulation and control of action on inner urges/emotions” (G14) (55). In the other two articles, the assessment of aggressive behavior was conducted in accordance with two distinct methodologies. Firstly, the occurrence of aggression was gauged by examining episodes of aggression within the hospital setting and the individual’s medical history (60). Secondly, the assessment of aggressive behavior was undertaken 12 months prior to the occurrence of suicide (59). It is noteworthy that one study did not report the circumstances of the occurrence of aggression (61).

### 3.5 Design of the research and diagnosis verification

The extant literature on this subject comprises two case-control studies (54, 59), five cross-sectional studies (55–57, 60, 61), and one cohort study (58). The diagnoses were verified using the following diagnostic systems: ICD-10 (54, 60), DSM-IV (55, 56, 59, 61), DSM-IV-TR (57), DSM-IV-R (58). Patients were examined by a

psychiatrist and a psychologist (56, 58), a specialist and a psychiatric assistant (61), and two psychiatrists (57). The number of specialists (psychiatrists and psychologists) who confirmed the diagnosis, collected the anamnestic data and assessed the psychometric indicators was not indicated in (54, 55, 59, 60).

### 3.6 Studies on aggression and suicide in schizophrenia patients

A total of eight studies incorporated data pertaining to the impact of aggressive behavior on suicide in patients diagnosed with schizophrenia (see Table 2). In the study (56), aggressive behavior was found to be associated with suicidal behavior in 50% of patients with aggression ( $\chi^2 = 6.276$ ,  $p = 0.012$ ). Furthermore, a higher mean score on the OAS scale was observed in patients with a history of suicide attempts (58) when compared to those without (3 versus 1.8,  $p = 0.03$ ). The number of previous suicide attempts exhibited a positive correlation with the score on the OAS scale ( $p = 0.001$ ). The study (59) included patients diagnosed with schizophrenia who had completed suicide and whose history was studied retrospectively. The study found an association between suicide and aggressive behavior in 38% of cases ( $\chi^2 = 13.16$ ,  $p = 0.0003$ ).

The remaining studies used logical regression to analyses the association between different factors (including aggression and suicidal behavior) (54) found an association between overt aggression and some other sociodemographic and clinical-

TABLE 2 Study characteristics and main findings of included studies (N=8).

| Author, year (country)                   | Sample (n)                    | Diagnostic classification | Included diagnosis                                  | Age (mean SD) | Research groups (n)                                                                                                                                                  | Suicidal behavior/ attempts | Aggression         | Suicide assessment tool                                                       | Aggression assessment tool                                                                                             | Scale score                                                                                                                                                                                           | The relationship between aggression and suicide risk                                                             |
|------------------------------------------|-------------------------------|---------------------------|-----------------------------------------------------|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|--------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Lin Y. et al., 2023 (54)(China)          | 849 (schizophrenia n = 523)   | ICD-10                    | Schizophrenia, bipolar disorder, depression, others | –             | 1) Suicidal intention (n=270, with schizophrenia = 157), 2) Non-Suicidal intention (n=579, with schizophrenia = 366)                                                 | Psychometric scale          | Psychometric scale | Suicide Risk Assessment Scale, Nurses' Assessment of Suicide Risk for Suicide | Modified Overt Aggression Scale                                                                                        | –                                                                                                                                                                                                     | Overt aggression linked to suicidal behavior                                                                     |
| Tousignant M. et al., 2010 (59) (Canada) | 67                            | DSM-IV                    | Schizophrenia                                       | –             | 1) Suicide with schizophrenia - n=33, 2) Control group (schizophrenia without suicide) - n= 34                                                                       | Anamnestic data             | Anamnestic data    | –                                                                             | –                                                                                                                      | –                                                                                                                                                                                                     | Suicide was associated with aggressive behavior                                                                  |
| Neuner T. et al., 2011 (60) (Germany)    | 49257 (schizophrenia n= 8901) | ICD-10                    | Schizophrenia and other disorders                   | 40,4 ± 13,6   | 1) Suicidal behavior/ attempts with schizophrenia - n=47, 2) Control group (other mental illness with suicidal behavior/ attempts) - n= 216                          | Anamnestic data             | Anamnestic data    | –                                                                             | –                                                                                                                      | –                                                                                                                                                                                                     | Suicidal behavior or attempts were not associated with a history of violent behavior                             |
| Kösger F. et. al., 2016 (56) (Turkey)    | 68                            | DSM-IV                    | Schizophrenia                                       | –             | 1) Aggressive behavior in patients with schizophrenia - n=30 (with suicide = 15), 2) No aggressive behavior in patients with schizophrenia - n=38 (with suicide = 8) | Anamnestic data             | Psychometric scale | –                                                                             | Buss–Perry Aggression Questionnaire (BPAQ)                                                                             | BPAQ group with aggressive behavior - physical aggressive = 17.07 ± 11.18, verbal = 9.50 ± 4.46                                                                                                       | Aggressive behavior was associated with suicidal behavior                                                        |
| Mork E. et. al., 2013 (55) (Norway)      | 251                           | DSM-IV                    | Schizophrenia                                       | 30,1 ± 9,8    | 1) Suicide attempt and self-harm (SA + NSSH) - n=36, 2) Only suicide attempt (SA only) - n=52, 3) No suicide attempt and self-harm (NoSA) - n=163                    | Psychometric scale          | Psychometric scale | The InterSePT Scale for Suicidal Thinking (ISST)                              | Positive and Negative Syndrome Scale (PANSS) G14 (Disordered regulation and control of action on inner urges/emotions) | ISST - No current suicidality (0), n (%): SA + NSSH = 13 (36); SA only = 27 (53); NoSA = 117 (72); Low suicidality (0.1-1.0), n (%): SA + NSSH = 14 (39); SA only = 20 (39); NoSA = 41 (25); Moderate | Group pf Suicide attempt and self-harm had higher scores on current impulsive aggression and depressive symptoms |

(Continued)

TABLE 2 Continued

| Author, year (country)                   | Sample (n) | Diagnostic classification | Included diagnosis | Age (mean SD) | Research groups (n)                                                                                                                                                                                                                                                                                                 | Suicidal behavior/ attempts | Aggression         | Suicide assessment tool  | Aggression assessment tool   | Scale score                                                                                                                                                           | The relationship between aggression and suicide risk                                                                                                                                      |
|------------------------------------------|------------|---------------------------|--------------------|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|--------------------|--------------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                          |            |                           |                    |               |                                                                                                                                                                                                                                                                                                                     |                             |                    |                          |                              | to high (1.1-2.0), n (%): SA + NSSH = 2 (6); SA only = 6 (12); NoSA = 8 (5); PANSS G14 (median (min-max)): SA + NSSH = 2 (1-6); SA only = 1 (1-4); NoSA = 1 (1-4)     |                                                                                                                                                                                           |
| Iancu I. et al., 2010 (57) (Israel, USA) | 68         | DSM-IV-TR                 | Schizophrenia      | 39,4 ± 12,17  | 1) Low impulsivity (n=35) (with suicide = 9), 2) high impulsivity (n=33) (with suicide = 15)                                                                                                                                                                                                                        | Psychometric scale          | Psychometric scale | Suicide Risk Scale (SRS) | Overt Aggression Scale (OAS) | OAS for low impulsivity group = 5.5183.40, for high impulsivity group = 7.2483.61; SRS for low impulsivity group = 8.7784.49, for high impulsivity group = 11.6484.24 | Older age and higher rates of aggression, impulsivity and general psychopathology on the PANSS subscale had significant contribution to the explained variance in predicting suicide risk |
| Lejoyeux M. et al., 2013 (58)(France)    | 100        | DSM-IV-R                  | Schizophrenia      | 41,9 ± 13,1   | The authors of the study did not divide the patients into subgroups. However, an analysis of the baseline data presented in the study did allow for the identification of suicidal behavior in the sample. The following division of the sample was revealed: 1) Suicide with schizophrenia - n=53, 2)Control group | Anamnestic data             | Psychometric scale | –                        | Overt Aggression Scale (OAS) | OAS with suicide group 3 ± 3, without suicide = 1.8 ± 2.4                                                                                                             | Patients with a history of suicide attempts had higher scores on the Overt Aggression Scale (OAS)                                                                                         |

(Continued)

TABLE 2 Continued

| Author, year (country)       | Sample (n) | Diagnostic classification | Included diagnosis | Age (mean SD) | Research groups (n)                                                                                                                                                                                                           | Suicidal behavior/ attempts | Aggression tool | Suicide assessment tool | Aggression assessment tool | Scale score | The relationship between aggression and suicide risk                                                      |
|------------------------------|------------|---------------------------|--------------------|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------|-------------------------|----------------------------|-------------|-----------------------------------------------------------------------------------------------------------|
| Yildiz M., 2010 (61)(Turkey) | 720        | DSM-IV                    | Schizophrenia      | 35,5 ± 11,0   | (schizophrenia without suicide) - n= 47<br>Suicide with schizophrenia - n=199, second group (schizophrenia without suicide) = 521; aggression with schizophrenia = 341, second group (schizophrenia without aggression) = 379 | Anamnestic data             | Anamnestic data | -                       | -                          | -           | The presence of physically aggressive behavior is associated with suicidal thoughts and suicidal attempts |

dynamic factors with the risk of suicidal behavior in patients with severe mental illness (including schizophrenia) (OR = 2.008, 95% CI: 1.410, 2.861) (55) also included cases of self-harm without the intention to die in the group with suicidal behavior. Patients with suicidal behavior and self-harm without intent to die had higher scores for current impulsive aggression and depressive symptoms than patients with schizophrenia without suicidal behavior, but statistical analysis did not reveal significant differences (57) developed a predictive model and found that older age and higher rates of aggression, impulsivity and general psychopathology on the PANSS subscale made a positive and significant contribution to the explained variance in predicting suicide risk ( $\text{Exp(B)} = 0.67$ ,  $\beta = 0.36$ ,  $p < 0.001$ ) (61) also predicted suicide risk. The presence of physically aggressive behavior has been found to be associated with the following variables: suicidal thoughts and attempts ( $\chi^2 = 33324$ ,  $p = 0.001$ ), suicide attempts ( $\chi^2 = 8253$ ,  $p = 0.004$ ), and a criminal record ( $\chi^2 = 22410$ ,  $p = 0.001$ ). The findings indicate that suicidal thoughts and attempts significantly elevate the risk of physically aggressive behavior, with a reported threefold increase ( $\beta = 3.17$ ) (60). However, a separate report states that suicidal behavior or attempts are not associated with a history of violent behavior (OR 4.584,  $p = 0.145$ ). However, difficulties arose during the interpretation of results due to the fact that the primary group with suicide in schizophrenia included only patients who had committed or attempted suicide in hospital. The logistic regression was carried out on 5241 patients, taking into account the suicide sign on admission to hospital, which was indicated for a larger number of patients than in the study group (60).

3.7 Quality assessment

The results are demonstrated in Figures 2 and 3.

The quality assessment identified 4 studies with a high risk of bias and 4 studies with some concern about bias. The high risk was primarily attributable to ambiguity in the measurement of exposure or an absence of data. For instance, in the study conducted by Tousignant et al. (2011), it was not possible to ascertain the severity of indicators of aggression and suicidal risk in relation to the completed suicide of the primary group (data on the presence of aggressive behavior, suicide attempts in the history were obtained from the words of relatives) (60). The absence of psychometric averages and the presence of gaps in the analyzed data are notable. The analysis was conducted on a different number of subjects, and the data lacked psychometric indicators and separation into groups. However, it did indicate the number of patients with schizophrenia who had both suicidal attempts and aggressive behavior. The study (54) demonstrates an absence of average indicators in terms of socio-demographic, clinical, dynamic and psychometric indicators. Concurrently, the presence of comorbid disorders (e.g., alcoholism, surfactant dependence) was not consistently considered, potentially introducing a high risk of bias. In the remaining articles, concerns regarding risk of bias were identified, stemming from the inability to assess the researcher’s bias in measuring outcomes, particularly in the context of data presented in medical records and the collection of anamnestic

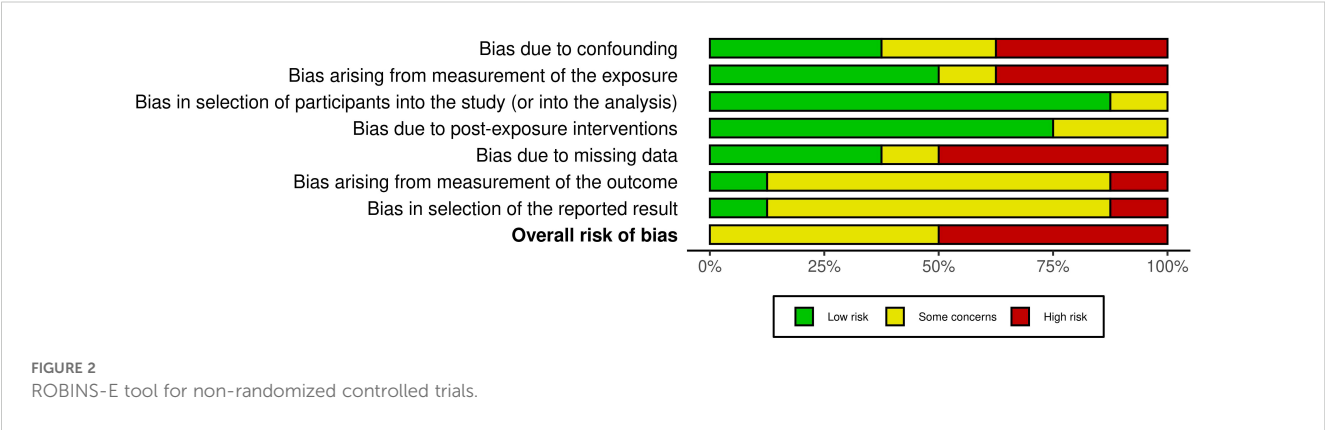


FIGURE 2 ROBINS-E tool for non-randomized controlled trials.

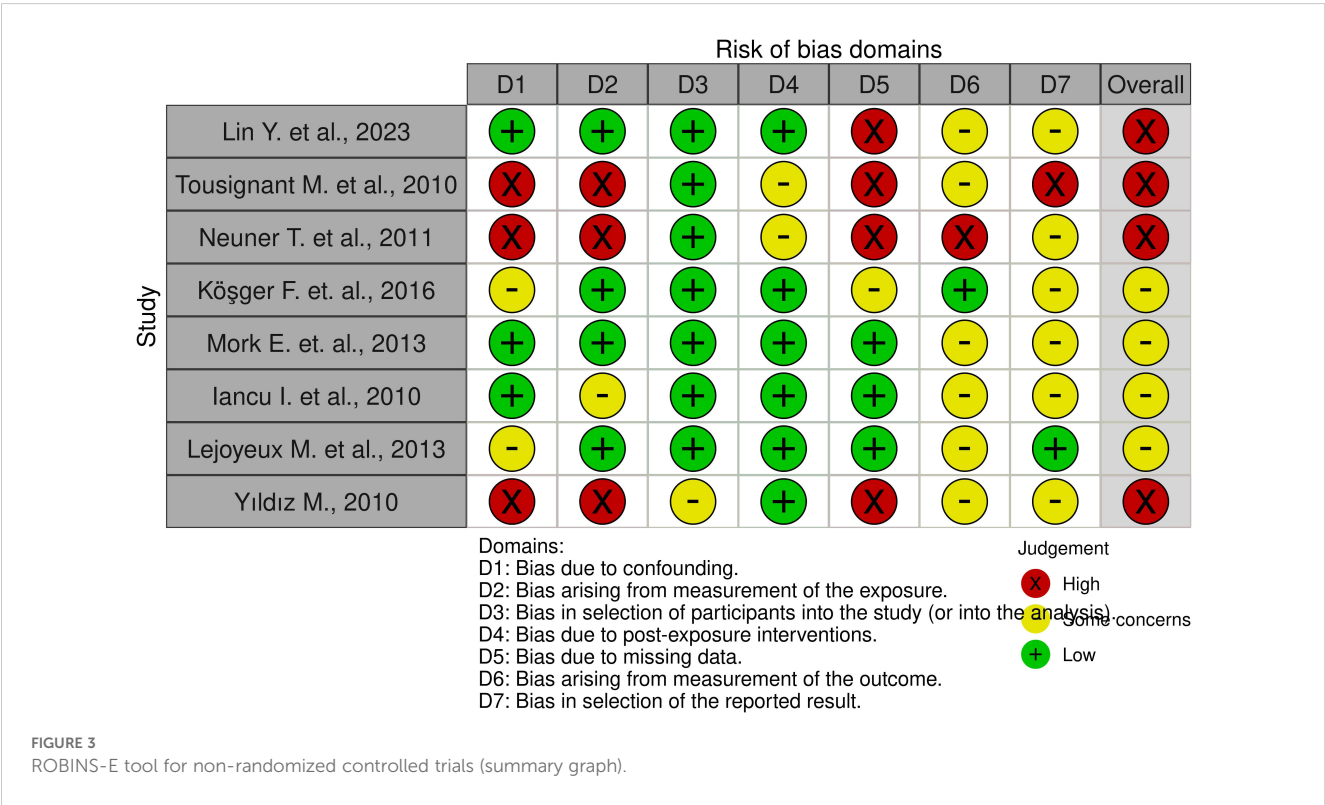


FIGURE 3 ROBINS-E tool for non-randomized controlled trials (summary graph).

data from relatives. The principal outcome of the risk of bias assessment was an understanding of the impossibility of performing a meta-analysis for the studies selected in the systematic review.

#### 4 Discussion

This review presents evidence on the association between suicide risk and aggressive behavior in patients diagnosed with schizophrenia. The majority of studies indicate a correlation between aggression and suicidal behavior (55–59, 61), with this relationship manifesting in various forms. A study of the history of patients who have committed suicide (59) demonstrated that suicidal behavior is associated with elevated levels of mental vulnerability, including aggressive behavior.

When discussing aggressive behavior in schizophrenia, it is imperative to address its comorbidity with other psychiatric disorders, as evidenced by the fact that up to 47% of patients also suffer from concomitant substance dependence (46), which in itself increases the risk of aggression (62, 63). Furthermore, it is imperative to acknowledge that depression, a common comorbidity in schizophrenia, is present in 50% of cases (64), and has been demonstrated to heighten the risk of suicidal behavior (65, 66). Furthermore, a study (58) revealed that patients with a history of suicidal behavior exhibited higher levels of aggression upon admission to hospital (56) found that aggressive patients had a greater history of suicide attempts than patients without aggression. These results are consistent with those of previous studies, which found that patients with suicidal behavior in schizophrenia had increased levels of

impulsive-aggressive traits compared to patients with suicidal behavior in other psychiatric disorders (67). However, there are some conflicting studies. For example, a paper (68) like the one we included (55), examined risk factors for suicidal behavior in schizophrenia by measuring the PANSS scale item 'disordered regulation and control of action on inner urges/emotions' (G14). This item was not considered to be a reflection of aggression, and no significant differences were found between schizophrenic patients with suicidal and non-suicidal behavior. In a further noteworthy study (69), a relationship was identified between empathy and neurocognitive functions and the development of suicidal thoughts in schizophrenia among Chinese patients. The authors demonstrated that the general psychopathological symptoms of the PANSS scale were associated with the occurrence of suicidal ideation. However, no separate comparison was provided for the subscale items (69). Furthermore, an increased propensity for aggression has been documented in patients who have attempted suicide in the context of major depressive disorder (70). Additionally, patients with suicidal ideation in depression and bipolar disorder have exhibited higher levels of impulsivity and hostility compared to those without such ideation (71). However, these findings appear to be at odds with the established link between suicidal thoughts and higher harm avoidance (72), suggesting that any act of aggression towards others poses a threat to the aggressor. However, it is important to note that in schizophrenia, there are pronounced cognitive and sensory processing impairments (73, 74), which can result in an underestimation of the stressful situation and a potential lack of understanding of the consequences of one's behavior. Consequently, patients may have an impaired understanding of self-harm.

In other studies incorporated within the scope of this review, the correlation between suicide risk and aggressive behavior is demonstrated through the utilization of mathematical models, namely the construction of predictive models. Aggression was identified as one of several factors that augment the risk of suicide. The utilization of mathematical models facilitates the streamlining and standardization of the identification of patients at risk of suicide. For instance (54, 57), predicted suicide risk by noting that aggression was one of the risk factors, while (61) predicted aggressive behavior in schizophrenia and found that suicidal thoughts and attempts increased it. It is noteworthy that analogous predictive models have been constructed for other disorders, though the factor of aggression was not identified among them. A notable study predicted the overlap between suicide attempt and aggression in young adults, concluding that age and education level were significant risk factors (75). In predicting suicide risk subsequent to a suicide attempt, variables such as psychotic disorders and depression have been identified as significant factors (76). Moreover, data from a meta-analysis demonstrated that experiencing psychosis increased the risk of suicidal ideation (77). Conversely, significant factors in predicting suicide attempt in major depressive disorder were comorbid personality disorder (78) and previous suicidal behavior (79), occurrence of suicidal ideation within a brief period following the initial depressive episode, lower secondary education and comorbid psychiatric disorder (80). Predictors of making a first suicide attempt in depression are high anxiety, elevated cholesterol and thyroid-

stimulating hormone levels (81), and in bipolar disorder, early onset, type I disorder, comorbidity and some neuroimaging parameters (82). Consequently, the integration of predictive methods into contemporary clinical practice holds considerable promise for enhancing diagnostic accuracy (83, 84). However, it is important to note that the widespread implementation of these methods is constrained by a number of limitations (85, 86), primarily due to the multifaceted nature of factors identified as suicide predictors (87).

Concurrently, certain studies have demonstrated an absence of correlation between suicidal risk and aggression. In the studies referenced as (60) and (55), higher psychometric measures of aggression were observed in the group of patients with suicidal behavior and self-harm without intent to die, in comparison to patients with schizophrenia without suicide. However, these results did not reach significant values. A number of studies addressing diverse mental illnesses have not directly considered the aggression factor, yet have demonstrated the significance of violent episodes (88, 89). Conversely, other works have been published that do not consider aggression as a marker of suicide risk in schizophrenia, and therefore it has not been measured with psychometric tools or taken into account in the history (90–92).

In conclusion, it is imperative to acknowledge that patients who have attempted suicide constitute a high-risk group for making subsequent attempts within the initial year following hospital discharge. This risk persists even after the completion of their treatment (93–95). Consequently, patients exhibiting suicidal tendencies and a documented history of aggressive behavior necessitate expeditious and comprehensive psychiatric care, entailing the prescription of ant suicidal medications (21), the implementation of strategies to mitigate aggression (96–98), and the provision of efficacious psychotherapy techniques (99). It is important to note that patients with a history of aggressive behavior are less likely to adhere to therapy, which can complicate the treatment process (100–102). The implementation of preventive measures aimed at averting aggressive behavior in patients diagnosed with schizophrenia is associated with a number of limitations. For instance, risk factors for the development of aggressive behavior in adulthood may include physical and emotional abuse during childhood, which can only be assessed retrospectively (103, 104). This underscores the necessity for preventative interventions by risk groups well in advance of the onset of aggressive symptoms (dysfunctional families). The study of genetic markers (105) and environmental factors (106–109) is a promising avenue for further research.

Another promising direction is treatment aimed at improving cognitive functioning, as a number of cognitive functions are altered in schizophrenia with aggressive behavior: for example, worse working memory but better attention has been reported (110, 111). Some research links cognitive impairment to suicide (112, 113), others say there's no change (17, 114). It is also important to recognize that cognitive decline is one of the axial symptoms of schizophrenia (115–117), therefore a search for more reliable markers is required. As such, cognitive functioning is limited to be used as a major point of application in therapy. Despite this, it is necessary to study cognitive functioning, which is clearly altered in aggression and suicidal behavior in schizophrenia, as there are ways

to correct them. Commonly recognized methods with proven efficacy are the administration of second-generation antipsychotics (118, 119), work with a psychotherapist (110, 120), range of physical activities (121), non-invasive brain stimulation techniques (122). Once again, we note that we cannot speak of the specificity of cognitive impairment, as it is one of the persistent symptoms of schizophrenia that determines mortality in this cohort of patients (19, 20). This area of research is of interest in terms of preventive interventions, as a number of studies have shown that some cognitive abilities are innate (123, 124) or appear earlier than the rest of the symptoms of schizophrenia (125–127). If specific changes in aggression and suicide can be identified in schizophrenia, it will help to identify a group at risk before a suicide attempt or suicidal ideation occurs.

A subsequent analysis of the design and methodology of the included studies identified several limitations. For instance, despite the unifying subject of the single study, there were considerable variations in the methods employed to obtain patient information and psychometric tools, which rendered the analysis of the results challenging. For instance, the article (60) conceptualized physical violence and property damage as manifestations of aggression, the paper (59) documented death threats or assault, the third article exclusively measured physical aggression (61), while the remaining articles employed scales to assess admission to hospital. A similar discrepancy was observed in the case of suicidal behavior assessment in the aforementioned articles. Returning to the methodology of the study, the question arises as to whether it is legitimate to include works and studies on completed suicide and on suicide attempts together in the observation. For instance, the review included a case-control study where the clinical sample comprised cases of completed suicide (59), yet there remains a paucity of understanding regarding whether the disorders identified in suicide autopsies are indicative of individuals who have made suicide attempts (128–130). In one study, the primary sample comprised patients with various psychiatric disorders in addition to schizophrenia, which limits the generalizability of the findings (54). Furthermore, the categorization of study groups is inconsistent, with the majority divided according to the presence or absence of suicidal behavior. However, two studies utilized aggressive (56) or impulsive (57) behavior as the basis for their group divisions. A further noteworthy point pertains to the heterogeneity of the comparison groups. In two studies, the control groups comprised other diagnoses in addition to schizophrenia, thereby introducing further complexity in the analysis of the data (54, 60).

It is important to note that the majority of the studies reviewed did not include substance and nicotine dependence as exclusion criteria. However, it is well-established that substance dependence is a proven risk factor for aggressive behavior (131–133). For instance, the inclusion of patients diagnosed with schizophrenia who also consumed psychoactive substances resulted in distorted outcomes. A mere two studies incorporated substance dependence as an exclusion criterion (54, 56), with the findings of one study being constrained by the fact that the study group comprised patients diagnosed with schizophrenia and additional psychiatric disorders,

as previously discussed. In the second study, the basis for group segmentation was not based on patients' suicidal behavior but rather on their aggressive behavior.

## 5 Conclusion

In summary, the conclusion regarding the impact of aggressive behavior on elevated suicide risk may be deemed as somewhat erroneous. This is due to the significant number of methodological inaccuracies and inconsistencies in the study design that were identified in the included reviews. Consequently, this may not accurately reflect the actual state of the problem.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Author contributions

LB: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. MK: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Resources, Software, Visualization, Writing – original draft, Writing – review & editing. GK: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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## Appendix A

### Search strategy for the PubMed database:

Search: (((aggress\*) AND (suicid\*)) OR (autoaggress\*)) AND (schizophren\*) Filters: from 2009 - 2024

### Search strategy for the Cochrane Library:

(aggress\*):ti,ab,kw AND (suicid\*):ti,ab,kw OR (autoaggress\*):ti,ab,kw AND (schizophren\*):ti,ab,kw with Cochrane Library publication date Between Jan 2009 and Jan 2024 (Word variations have been searched)

### Search strategy for the PsychINFO:

it was carried out by several consecutive queries in accordance with the key search words in previous cases with a limit of one operator: aggress\* AND suicid\* OR autoaggress\* AND schizophren\*

### Search strategy for the Mendeley:

Two searches were performed in succession and the results were included in the study:

aggress suicid schizophren Between 2009 and 2024

aggress autoaggress schizophren Between 2009 and 2024