SYSTEMATIC REVIEW OPEN

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Interventions for suicidal and self-injurious related behaviors in adolescents with psychiatric disorders: a systematic review and meta-analysis

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As a leading cause of adolescent death, suicidal and self-injurious related behaviors (SSIRBs) is a devastating global health problem, particularly among patients with psychiatric disorders (PDs). Previous studies have shown that multiple interventions can alleviate symptoms and reduce risks. This review aimed to provide a systematic summary of interventions (i.e., medication, physical therapy, psychosocial therapy) for the treatment of SSIRBs among Chinese adolescents with PDs. From inception to September 17, 2023, twelve databases (PubMed, CINAHL, ScienceDirect, PsycINFO, EMBASE, Cochrane Library, Clinical Trial, Web of Science, CEPS, SinoMed, Wanfang and CNKI) were searched. We qualitatively and quantitatively synthesized the included studies. Standardized mean differences (SMDs), risk ratios and their 95% confidence intervals (CIs) used the Der Simonian and Laird random-effects model. Fifty-two studies covering 3709 eligible participants were included. Overall, the commonly used interventions targeting SSIRBs and negative feelings in PDs adolescents with SSIRBs included psychosocial therapy (e.g., cognitive behavioral therapy), medication (e.g., antidepressants), and physiotherapy (e.g., repetitive transcranial magnetic stimulation). Importantly, quetiapine fumarate in combination with sodium valproate (SV) had positive effects on reducing self-injury behaviors score [SMD: −2.466 (95% CI: −3.305, −1.628), $I^2 = 88.36\%$], depression [SMD: −1.587 (95% CI: −2.505, −0.670), $I^2 = 90.45\%$], anxiety [SMD: −1.925 (95% CI: −2.700, −1.150), $I^2 = 85.23\%$], impulsivity [SMD: −2.439 (95% CI: −2.748, −2.094), $I^2 = 0\%$], as well as its safety in comparison with SV alone. No significant difference of adverse reactions was found by low-dose QF ($P > 0.05$). This review systematically outlined the primary characteristics, safety and effectiveness of interventions for Chinese PDs adolescents with SSIRBs, which could serve as valuable evidence for guidelines aiming to formulate recommendations.

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INTRODUCTION

Suicidal and self-injurious related behaviors (SSIRBs) is a devastating global health problem, particularly among patients with psychiatric disorders (PDs) [1, 2]. One or more than one in three patients diagnosed with mood disorders have attempted to suicide [3]. As a leading cause of adolescent death [4], approximately 11 to 43 percent of adolescents with PDs have been diagnosed with SSIRBs, such as non-suicidal self-injury (NSSI), suicidal ideation (SI), self-injurious behavior (SIB), suicidality and suicide attempts (SA), etc [5–8]. SSIRBs invariably lead to negative outcomes in adolescents with PDs [9], including alcohol and drug abuse [10], cognitive impairments, poor interpersonal relationships [11], and violent crimes [12], which even increase the medical burden [13]. The 2019 Global Burden of Disease Study found that self-harm contributes to 319.6 years of life lost, per one hundred thousand population [14]. PDs may contribute to the occurrence of SSIRBs [10, 15]. A systematic review reported that 58% of Chinese adolescents with major depressive disorder (MDD) had NSSI [16]. The suicide rate among patients with mood disorders was approximately 6–10%, 10 times higher than that of non-psychiatric patients [17, 18]. As the most extreme manifestation of PDs, SSIRBs not only increases the risk of PDs, but also aggravates the severity of PDs [19, 20]. The rapid socialization process, the distinct traditional Chinese culture and the highly unbalanced distribution of treatment resources have a certain influence on the occurrence of SSIRBs in Chinese adolescents with PDs [21–24]. Considering the above conditions, it is urgent to explore effective interventions for Chinese adolescents who experienced SSIRBs and PDs [3].

Early studies have shown that interventions for adolescents with PDs affected by SSIRBs can alleviate symptoms and reduce risk. For example, dialectical behavior therapy (DBT) showed positive improvements in emotional dysregulation, depression, and symptoms related to suicidal and self-injurious behaviors among adolescents with borderline personality disorders (BPD) and SSIRBs [25]. In addition, intermittent theta burst stimulation has been shown to reduce SI in adolescents with MDD [26]. On the other hand, anti-suicidal effects of medications (e.g. ketamine)

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have also been observed in adolescents with MDD and SSIRBs [27–29]. Overall, a variety of effective interventions were available for adolescents with PDs and SSIRBs. Numerous reviews and meta-analyses on individual interventions have been published [30–33]. However, there have been few reviews of drug therapy for PDs adolescents with SSIRBs. For example, a meta-analysis among adolescents reported that family therapy could significantly improve the outcome of SI rather than depression [30]. Another review showed that DBT was effective in simultaneously improving NSSI and depression in adolescents [31]. Also, two articles indicated the effectiveness of repetitive transcranial magnetic stimulation (rTMS) in treating MDD with SI [32, 34].

To date, two comprehensive systematic reviews have summarized the effectiveness of psychosocial interventions for NSSI or SSIRBs. Lu JJ et al. found cognitive behavioral therapy (CBT) to be the most common among psychosocial therapy, which is effective for SSIRBs in Chinese adolescents [35]. Qu DY et al. summarized the prevalence, risk factors, and interventions of NSSI among Chinese adolescents in a scoping review [1]. However, several considerations need to be made. First, more comprehensive databases and more precise search strategies should be used; Second, the existing systematic reviews targeting Chinese adolescents focused only on NSSI or SSIRBs but ignored comorbid PDs; Third, drug and physical therapies were not included.

Notably, this is the first study to examine a comprehensive systematic review and meta-analysis of interventions for SSIRBs in Chinese adolescents with PDs. Our study aims to systematically summarize the interventions (i.e., medication, physical therapy, psychosocial therapy) for SSIRBs in Chinese adolescents with PDs. This endeavor has the potential to develop more meaningful strategies for the treatment of SSIRBs associated with PDs. It is proving particularly valuable in promoting the integration of intervention methods into clinical practice and guiding the improvement of clinical guidelines.

METHODS

This meta-analysis was pre-registered in the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY; registration number: 202350069) and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Eligibility criteria and measurement

In accordance with the PICOS tool, the inclusion criteria were defined as follows: Participants (P): Chinese with PDs (e.g., MDD) and SSIRBs (e.g., NSSI, SI, SA); adolescents aged 18 years old and below or the sum of average age and SD ≤ 18 years old [36]. Intervention (I): psychosocial therapy (e.g., CBT); pharmacological therapy (e.g., antidepressants); physical therapy (e.g., rTMS). Comparison (C): no-treatment control or active control. Outcomes (O): effectiveness; and Study design (S): qualitative studies (QSs), randomized controlled trials (RCTs), clinical controlled trials (CCTs), pre-post studies, case reports (CRs). No language limitation was conducted. The primary outcomes included the average score and standard deviation (SD) derived from assessments using the SSIRBs scale, such as the Ottawa self-injury inventory (OSI). Secondary outcomes were the rate of adverse reactions (ADRs), effective rate, as well as mean and SD of scores on other symptom scales, such as self-rating depression scale (SDS); self-rating anxiety scale (SAS), etc.

Search strategy and selection criteria

Literature searching in twelve databases (PubMed, CINAHL, ScienceDirect, PsycINFO, EMBASE, Cochrane Library, Clinical Trial, Web of Science, CEPS, SinoMed, Wanfang and CNKI) was independently carried out by two groups of reviewers (group 1: J.J.L., J.H. and W.T.G.; group 2: Z.X.W., N.Y., Y.B.L. and J.X.G.). The literature searching was conducted from inception to January 31, 2023 and an updating was from January 31 to September 17, 2023. Followed by a review [37], subject and free terms were used: ("auto mutilat*"OR "cutt*" OR "headbang*" OR "overdos*" OR "selfdestruct*" OR "selfharm*" OR "selfimmolat*" OR "selfinflict*" OR "selfinjur*" OR "selfpoison*" OR "suicid*" OR "suicide, attempted" OR "suicidal ideation") AND ("adolescent" OR "teen" OR "youth" OR "teenager") AND ("China" OR "Chinese"). The search terms used for databases were recorded in the Supplementary Figs. 21–29. The titles and abstracts were independently reviewed and the full texts of relevant publications were scrutinized by the same two groups of reviewers. Any inconsistencies were resolved through consultation with a senior reviewer (WIP.P.). Additional studies were identified through manual search among citations in the included articles, previous systematic reviews, and meta-analyses [31, 38–41]. Moreover, we also searched conference papers from the 21st National Conference on Psychiatry and the 17th National Conference on Child and Adolescent Psychiatry of the Chinese Medical Association [42, 43].

Data extraction

Relevant data was independently extracted by two groups of reviewers based on a predesigned Excel data collection sheet. Data included: first author, year of survey and publication, survey province, study type, sampling method, sample size, types of interventions in the control and experimental groups, parameters of drug therapy and physical therapy, setting, intervention duration, types of SSIRBs, types of PDs, age range, mean and SD of participants age, number and proportion of males, definitions of SSIRBs and PDs, and measurements. According to a classification of psychological interventions [44], a new set of psychological interventions were defined as ten categories, including CBT, relationship-based interventions, systemic interventions, psychoeducation, group work with children, psychotherapy, counselling, peer mentoring, intensive service models, and activity-based therapies. Two reviewers (KIG.L. and W.W.R.) independently confirmed the accuracy of the data through a double-check process. Discrepancies were resolved through consultation with an additional reviewer (WIP.P.).

Quality assessment

RCTs were evaluated by the Jadad scale [45]. The overall score varied between 0 and 5 points. The Jadad score of 2 or lower was categorized as low quality, while those with 3 or higher were classified as high quality. CCT studies (0–16 points) and pre-post studies (0–12 points) were assessed using two different version of the National Heart, Lung, and Blood Institute (NHLBI) tailored quality assessment tool [46], which was widely used in previous systematic reviews [47–49]. The Critical Appraisal Skills Programme (CASP) of qualitative studies checklist was used (0–10 points) [50], which was commonly found in some early studies [51–53], while the JBI Critical Appraisal Checklist was utilized for CRs (0–8 points) [54]. Higher scores denoted superior reporting. The evidence level for primary and secondary outcomes was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. According to the evaluation rules, all outcomes can be classified into four categories: very low, low, moderate, or high [55, 56]. Also, the quality of our review was assessed using A MeaSurement Tool to Assess systematic Reviews, version 2 (AMSTAR 2) checklist [57], which included 16 items; each item is given one point if the criterion is met, or a zero point if the criterion is not met, is unclear, or is not applicable. Finally, a total score was categorized into four levels: critical low (0–4 points), low (5–8 points), moderate (9–11 points), and high (12–16 points) [58, 59]. Study quality was independently assessed by two reviewers (W.W.R. and J.J.L.). Discrepancies were resolved through consultation with an additional reviewer (KIG.L.).

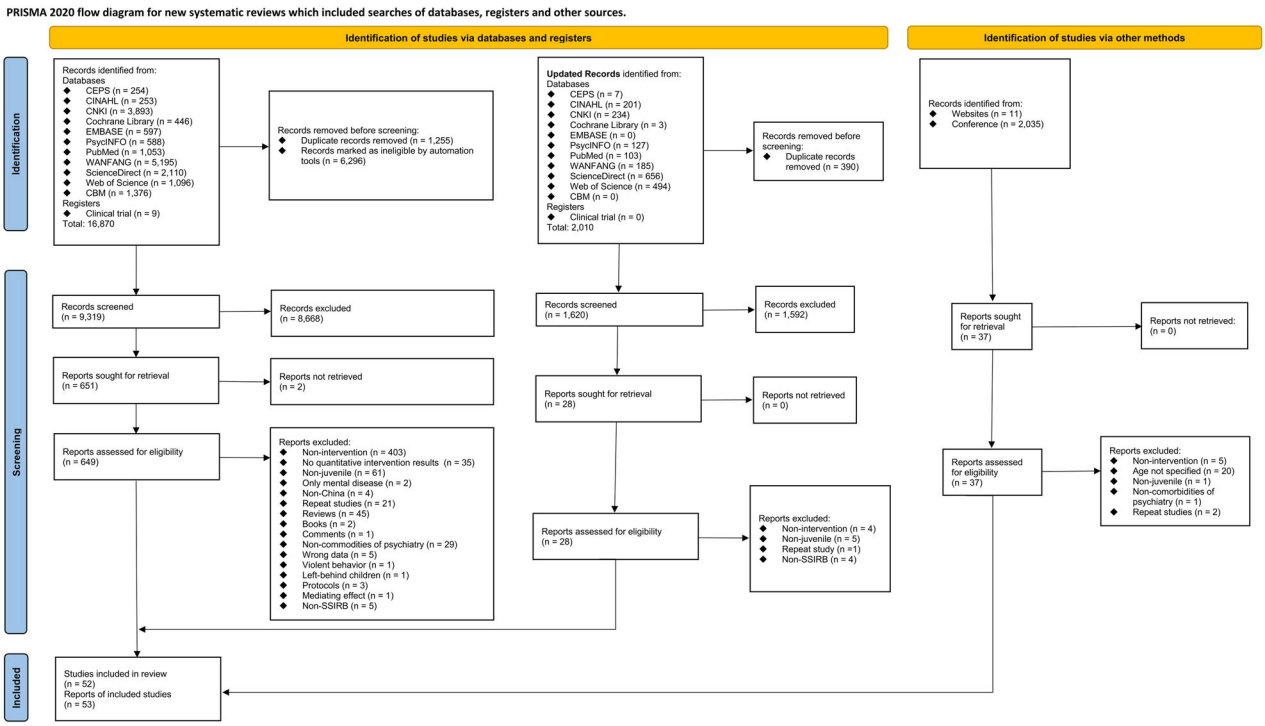

Fig. 1 PRISMA flow diagram. Note: A database search was combined with an independent search, yielding a total of 52 studies included in the review.

Statistical analysis

Qualitative synthesis. The study and intervention characteristics, and outcomes of the effectiveness for multiple interventions were synthesized. Combination therapies are defined as the utilization of two or more different types of interventions, whereas physical therapy, psychosocial therapy and drug therapy were considered as a single intervention.

Meta-analysis. Due to the limited number of included studies, two or more RCT articles with the same characteristics were considered for the meta-analysis: 1. patients with SSIRBs; 2. patients with PDs; 3. relevant assessments. Without involving any comparative intervention, a no-treatment control is served as a neutral comparison for study groups receiving the treatment under investigation. In contrast, the active control involves the integration of a proven intervention into the control group, which is compared with an experimental treatment. Considering the differences in sampling methods, demographic profiles, and assessment tools across studies, the symptom estimates (e.g., self-injurious behavior score, depression score) were presented as standardized mean differences (SMDs) and rate [e.g., effective rate and incidence rate of ADRs] with risk ratio (RRs) and their 95% confidence intervals (CIs) by using the Der Simonian and Laird random-effects model [60]. Between-study heterogeneity was estimated using Cochran's Q test and the I^2 statistic, with an $I^2 \geq 50\%$ or Cochran's Q of $p < 0.05$ indicating significant heterogeneity [61]. The Egger's test, Begg's test and the trim-and-fill method were used to assess publication bias when the number of literature was more than two [62]. The significance level was set at 0.05 (two-tailed). Sensitivity analyses were performed to examine the outlier studies. Meta-analyses were performed using Comprehensive Meta-Analysis software, Version 2.

RESULTS

Study characteristics

A total of 20,926 articles were retrieved from the databases and other sources. Following the removal of duplicate records and the use of automation tools for preliminary exclusion, 10,976 records would be used for screening at the first stage. Through initially reviewing the titles and abstracts, 716 records were identified and selected for full-text retrieval for the second stage of screening. With full-text screening, fifty-two articles contained fifty-three studies with 3709 participants (experimental group = 2034 adolescents vs control group = 1675 adolescents) (Fig. 1) [43, 63–112]. Out of ten articles from international databases, forty-two literatures were from Chinese databases. Twenty-eight (28/53, 53.8%) referred to NSSI. There was no eligible literature from Hong Kong and Macao, with the exception of one study from Taiwan. The majority of studies were distributed in Mainland China (Fig. 2a), mainly in coastal areas and publications showed a decreasing trend from coastal to inland areas. Generally, approximately 55% of therapies (29 in 53) were combination therapies. Physical therapy (e.g., rTMS and ECT) was included in 14 studies, while drug therapy (e.g., antidepressants and antipsychotics) was included in 37 of 53 studies. Additionally, 31 studies included seven psychosocial interventions [e.g., intensive service provision (ISP) and CBT] (Fig. 2b). Forty-eight studies were conducted for MDD adolescents, while 2 were conducted for autism spectrum disorders (ASD), 1 for first episode (FE)-BD, and 2 for multi-PDs. Only 11 studies reported medical records with a diagnosis of FE-MDD, with six of those studies utilized combination therapy. The most common therapy both in non-FE-MDD (32.4%) and in FE-MDD (36.4%) was pharmacological combined psychosocial therapy with no significant difference between two groups ($X^2 < 0.001$, $P = 1.000$). Besides, physical therapy was exclusively employed as a monotherapy in non-FE-MDD, but not observed in patients with FE-MDD.

Assessment quality and outcome evidence

Thirty-four RCTs used the Jadad scale, with 29 studies rated as high quality. The main reason for the low quality of the other 5 studies was the inappropriate method of randomization sequence. The quality of 11 CCTs ranged from 5–9 points, and the mean score was 7.2 points. One QS, 4 CRs and 2 pre-post

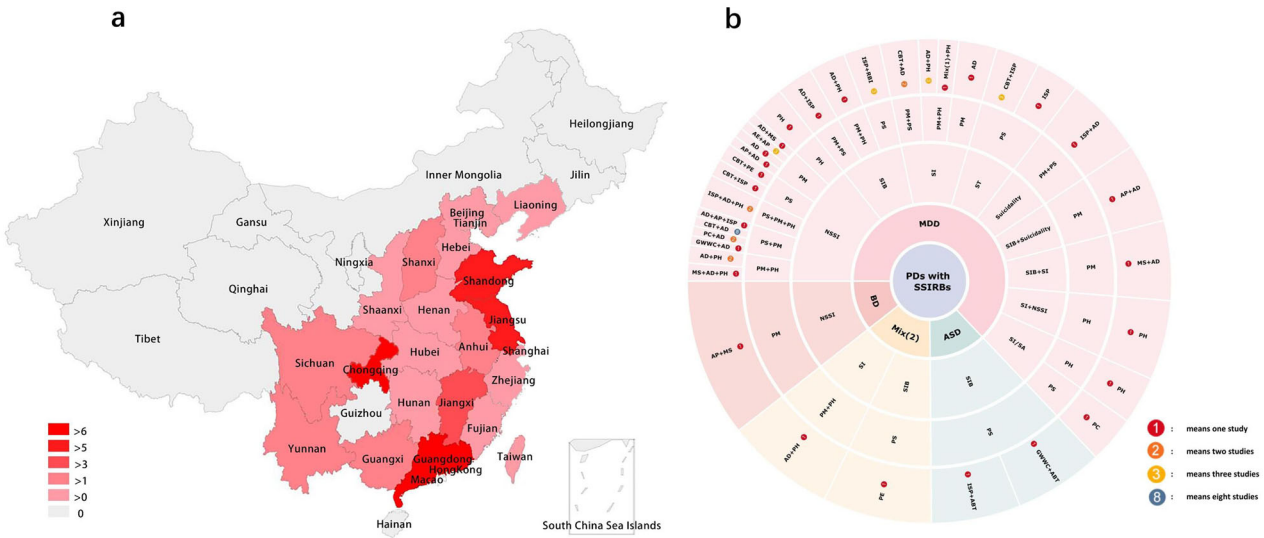

Fig. 2 Visualization of intervention types and locations. a Provincial distribution of 51 included studies (52 included reports). Note: There is a study without reporting experimental address [112], and the distribution map is based on 52 reports from the remaining 51 studies. **b** Interventions for PDs with SSIRBs. Note: Mix(1) means multiple drugs; Mix(2) means PDs; This figure is presented based on the intervention strategies of the experimental group. ABT Activity-based therapy, AD Antidepressants, AE Antiepileptic, AP Antipsychotic, ASD Autism spectrum disorder, BD Bipolar disorder, CBT Cognitive-behavioral therapy, GWWC Group work with children, ISP Intensive service provision, MDD Major depressive disorder, MS Mood stabilizer, NSSI Nonsuicidal self-injury, PC Psychotherapy, PDs Psychiatric Q6 disorders, PM Pharmacological intervention, PH Physical intervention, PS Psychosocial intervention, PE Psychoeducational intervention, RBI Relationship-based intervention, SIB Self-injurious behavior, SI Suicide ideation, SA Suicide attempts, ST Suicidal tendencies, SSIRBs Suicidal and self-injurious related behaviors.

studies were assessed, respectively. Nine studies accounted for more than half of the total score (Table 1). A high quality (12 points) of systematic review was identified by the AMSTAR-2 (Supplementary Table 1). Since all studies we included in the meta-analysis were RCTs, we initially rated four stars. There were some limitations in these RCTs, such as high heterogeneity, risk of bias, and small sample sizes. Given the large effect size, most of the evidence quality were at a medium to low level (Supplementary Table 2).

Major depressive disorder with single behavior

Non-suicidal self-injury

Single therapy: Nine studies were conducted during the COVID-19 epidemic. As of 2021, the number of publications in the next year was about twice as high as in the previous year. Patients were either from inpatient (IP) or outpatient (OP) settings, while 4 studies enrolled subjects without further explanation of the source. The duration of the intervention was between 4 and 12 weeks in eight studies. In four studies, three criteria were used to assess NSSI, namely the ANSAQ, adolescent self-harm scale (ASHS), and the diagnostic and statistical manual of mental disorders -V (DSM-V). In addition, 3 out of 9 studies diagnosed MDD in hospitals, 4 studies used 3 types of indicators, with 1 study using the international classification of diseases-10 (ICD-10), 1 study using the Chinese classification of mental disorders-3 (CCMD-3), and 2 studies using the DSM-V. Others used the mini international neuropsychiatric interview for children and adolescents (MINI-kid) and a guideline [113], respectively. Seven RCTs were high quality (mean score = 3), while one CCT study was rated as 7 and one pre-post study was rated as 8.

In eight studies, the scores of the Hamilton depression scale (HAMD) or a reduced rate were used to assess the effectiveness of the interventions. The remaining studies used the self-rating questionnaire for adolescent (SQAPMPU) and the screen for child anxiety related-emotional disorders (SCARED) to assess depressive and anxious symptoms, respectively. Only one study used transcranial direct current stimulation (tDCS) to the dorsolateral prefrontal cortex (DLPFC), with pseudo-stimulation as control. Compared to pre-intervention, the HAMD-17 score and ASHS decreased significantly ($P < 0.05$). And the effectiveness was greater in the tDCS group, and no ADR was reported.

Six of the nine studies focused on pharmacotherapy, which was a common approach. Apart from one no-treatment control, 2 studies with sertraline and 3 studies with sodium valproate (SV) were routinely considered as control groups. Two studies used magnesium valproate (MV) and sertraline, respectively, and no ADR was reported. However, four studies reported the occurrence of nausea and weakness after taking quetiapine fumarate (QF). In four studies, the risk of self-injury decreased significantly after the intervention ($P < 0.05$). Six studies reported a significant alleviation of depression, anxiety, and impulsivity after the intervention using HAMD-17, symptom checklist-90 (SCL-90), etc. ($P < 0.05$).

Two of nine studies were psychosocial interventions that could be assigned to more than one psychosocial category. CBT was flexibly combined with ISP, a psychoeducational intervention, and no ADR was reported. Zhu P et al. indicated a significant difference in the reduction rate of NSSI (experimental group: 14.29% vs control group: 46.51%, $P < 0.01$). The significant improvement was also seen in the adolescents' depressive symptoms, self-efficacy, and life satisfaction (all $P < 0.05$). Lu HL et al. also reported a similar improvement effect in the teenagers' mobile phone dependence, anxiety symptoms, and depressive symptoms (all $P < 0.05$).

Combined therapies: Seventeen studies were published between 2021 and 2023, of which Li HZ et al. conducted a comparison among 3 groups. Twelve high-quality RCTs with ratings between 3 and 5 were included. In addition, three CCTs received an average rating of 7, with one CR scoring 7. The study durations in hospital was between 2 and 12 weeks. Except for five studies that did not report diagnostic criteria, seven studies assessed MDD using DSM-V, while 5 studies used ICD-10. In addition, the functional assessment of self-mutilation (FASM), the self-injury behavior screening scale (SBSS), the OSI, and the

Table 1. Assessment of study quality characteristics.

Randomized Controlled Trials [45]

Author	1. Described as an RCT	2. Appropriate randomization sequence method	3. Described as double blind study	4. Appropriate double blinding method	5. Description of withdrawals and dropouts	6. Inappropriate description of the method to generate the sequence of randomization	7. Inappropriate description of double blind	Total score
Zou [112]	1	1	0	0	1	0	\	3
Zhu et al. [99]	1	1	1	1	1	0	0	5
Zhang et al. [93]	1	1	0	0	1	0	\	3
Yuan et al. [88]	1	1	1	0	1	0	\	4
Yu et al. [92]	1	1	0	0	1	0	\	3
Xue et al. [109]	1	1	0	0	1	0	\	3
Wang et al. [87]	1	1	0	0	1	0	\	3
Wang et al. [97]	1	0	0	0	1	\	\	2
Quan et al. [105]	1	1	0	0	1	0	\	3
Peng [85]	1	1	1	0	1	0	0	4
Lu et al. [89]	1	1	0	0	1	0	\	3
Lin [84]	1	1	0	0	1	0	\	3
Lin [111]	1	0	0	0	1	\	\	2
Liang et al. [98]	1	1	0	0	1	0	\	3
Li et al. [83]	1	1	0	0	1	0	\	3
Li [106]	1	1	0	0	1	0	\	3
Hu [96]	1	1	0	0	1	0	\	3
Feng [90]	1	1	0	0	1	0	\	3
Ding et al. [91]	1	1	0	0	1	0	\	3
Qiu [101]	1	1	0	0	1	0	\	3
Cai et al. [104]	1	0	0	0	1	\	\	2
Wu et al. [107]	1	1	0	0	1	0	\	3
Tang et al. [95]	1	0	0	0	1	\	\	2
Luo [42]	1	1	0	0	1	0	\	3
Zhu and Zhang [43]	1	1	0	0	1	0	\	3
Zhou et al. [73]	1	1	1	1	1	0	0	5
Chen et al. [78]	1	1	0	0	1	0	\	3
Li et al. [75]	1	1	0	0	1	0	\	3
Li and Peng [67]	1	1	0	0	1	0	\	3
Ma [70]	1	1	0	0	1	0	\	3
Wan et al. [71]	1	1	0	0	1	\	\	3
Wang et al. [65]	1	1	0	0	1	0	\	3
Ye et al. [81]	1	1	0	0	1	0	\	3
Zhang [72]	1	0	0	0	1	\	\	2

1. Was the study described as randomized (this includes words such as randomly, random, and randomization)? (yes/no); 2. Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc.)? (yes/no); 3. Was the study described as double blind? (yes/no); 4. Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc.)? (yes/no); 5. Was there a description of withdrawals and dropouts? (yes/no); 6. Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (e.g. patients were allocated alternately, or according to date of birth, hospital number, etc.).(Described but inappropriate = −1, Described and appropriate = 0); 7. Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g. comparison of tablet vs. injection with no double dummy).(Described but inappropriate = −1, Described and appropriate = 0).

Qualitative Studies [50]

Author	1. Was there a clear statement of the aims of the research?	2. Is a qualitative methodology appropriate?	3. Was the research design appropriate to address the aims of the research?	4. Was the recruitment strategy appropriate to the aims of the research?	5. Was the data collected in a way that addressed the research issue?	6. Has the relationship between researcher and participants been adequately considered?	7. Have ethical issues been taken into consideration?	8. Was the data analysis sufficiently rigorous?	9. Is there a clear statement of findings?	10. How valuable is the research?	Total score
Duan SQ [94]	1	1	1	1	1	0	1	1	1	1	9

1. Was there a clear statement of the aims of the research? 2. Is a qualitative methodology appropriate? 3. Was the research design appropriate to address the aims of the research? 4. Was the recruitment strategy appropriate to the aims of the research? 5. Was the data collected in a way that addressed the research issue? 6. Has the relationship between researcher and participants been adequately considered? 7. Have ethical issues been taken into consideration? 8. Was the data analysis sufficiently rigorous? 9. Is there a clear statement of findings? 10. How valuable is the research?

Table 1. continued

Clinical Controlled Trials [46]

Author	1. Described as an RCT	2. Randomization method	3. Concealed treatment allocation	4. Blinded participants	5. Blinded assessors	6. Similar groups at baseline	7. Low drop-out rate	8. Low differential drop-out rate between groups	9. High adherence to the intervention protocols	10. Avoided other or similar interventions	11. Valid and reliable measures	12. Sufficient sample size	13. Prespecified outcomes or subgroup analyses	14. Consistent randomized group	Total score
Su [100]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Li [102]	0	0	0	0	0	1	0	0	1	1	1	0	0	1	5
Zeng [103]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Zhu et al. [110]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Shao [86]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Xi et al. [63]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Tang et al. [69]	0	0	0	1	1	1	1	1	1	1	1	0	0	1	9
Duan et al. [74]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Cai et al. [80]	0	0	0	0	0	1	1	1	1	1	1	1	0	1	8
Li et al. [64]	0	0	0	0	0	1	1	1	1	1	1	0	0	1	7
Zhang et al. [77]	0	0	0	0	0	1	1	1	1	1	1	0	1	1	8

1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT? 2. Was the method of randomization adequate (i.e., use of randomly generated assignment)? 3. Was the treatment allocation concealed (so that assignments could not be predicted)? 4. Were study participants and providers blinded to treatment group assignment? 5. Were the people assessing the outcomes blinded to the participants' group assignments? 6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)? 7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment? 8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower? 9. Was there high adherence to the intervention protocols for each treatment group? 10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)? 11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants? 12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power? 13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)? 14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?

Pre-post studies [46]

Author	1. Clear study question	2. Prespecified selection criteria	3. Representative sample	4. Eligible samples all enrolled	5. Sufficient sample size	6. Clear description & consistent delivery	7. Valid & reliable outcome measures	8. Blinded assessor	9. Low loss to follow-up	10. Appropriate statistical methods	11. Outcome measured multiple times	12. Individual level data considered in analyses	Total score
Dai et al. [82]	1	1	1	1	NR	1	1	0	1	1	0	NR	8
Chen et al. [68]	1	1	1	1	NR	1	1	0	1	1	0	NR	8

1. Was the study question or objective clearly stated? 2. Were eligibility/selection criteria for the study population prespecified and clearly described? 3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest? 4. Were all eligible participants that met the prespecified entry criteria enrolled? 5. Was the sample size sufficiently large to provide confidence in the findings? 6. Was the test/service/intervention clearly described and delivered consistently across the study population? 7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants? 8. Were the people assessing the outcomes blinded to the participants' exposures/interventions? 9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis? 10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes? 11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)? 12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?

Case report [54]

Author	1. Clear characteristics	2. Clear history	3. Clear clinical condition	4. Clear diagnostic tests, methods, results	5. Clear intervention/ treatment procedure	6. Clear post-intervention clinical condition	7. Describe adverse events (harms) or unanticipated events	8. Describe takeaway lessons	Total score
He et al. [108]	1	1	0	1	1	0	0	1	5
Xu et al. [76]	1	1	1	1	1	1	0	1	7
Pan et al. [79]	1	1	1	1	1	1	1	1	8
Wang et al. [141]	1	1	1	0	1	1	1	1	7

1. Were patient's demographic characteristics clearly described? 2. Was the patient's history clearly described and presented as a timeline? 3. Was the current clinical condition of the patient on presentation clearly described? 4. Were diagnostic tests or methods and the results clearly described? 5. Was the intervention(s) or treatment procedure(s) clearly described? 6. Was the post-intervention clinical condition clearly described? 7. Were adverse events (harms) or unanticipated events identified and described? 8. Does the case report provide takeaway lessons?
NR no report.

ANSAQ were used to assess the risk of self-injury. Furthermore, 6 studies reported ADRs.

Twelve of the seventeen studies were psychosocial therapy in combination with pharmacotherapy, 3 studies used physical and pharmacological combination therapies. And 2 studies includes three types of therapies. Seventeen studies indicated a significant reduction in self-injury or suicide risk, and depression after the intervention. In addition, negative emotions (e.g., impulsivity and anxiety) as well as cognitive functioning and social support also were improved.

Meta-analysis: Compared with no-treatment control group, CBT in combination with antidepressants showed significant benefits for depression (SMD = −1.467; 95%CI = −2.492–−0.442, $I^2 = 88.39\%$, $P < 0.001$) and anxiety (SMD = −2.101; 95%CI = −3.869–−0.333, $I^2 = 95.18\%$, $P < 0.001$). Neither the Egger's nor the Begg's-tests (all P-values > 0.05) revealed any publication bias. In particular, the pooled SMD value remained consistent regardless of the exclusion of any individual study (Supplementary Figs. 12–18). Considering that there are two similar CCT studies, we conducted an additional sensitivity analysis to combine CCT and RCT studies and the findings indicated consistent conclusions. Sensitivity analysis found that CBT in combination with antidepressants indicated significant benefits for depression (SMD = −1.436; 95%CI = −2.158–−0.713, $I^2 = 85.33\%$, $P < 0.001$; Supplementary Figs. 19–20). However, Xi Y et al. used two depression scales. When the HAMD was replaced to Montgomery-Asberg depression rating scale (MADRS), the score was still significant (SMD = −1.254; 95%CI = −1.959–−0.550, $I^2 = 85.32\%$, $P < 0.001$). Neither the Egger's nor the Begg's-tests (all P-values > 0.05) revealed any publication bias.

However, CBT and antidepressants showed a significant effect compared to the active control on depression (SMD = −0.943; 95%CI = −1.414–−0.472, $I^2 = 33.38\%$, $P = 0.212$) and anxiety (SMD = −0.942; 95%CI = −1.323–−0.560, $I^2 = 0\%$, $P = 0.592$). When the HAMD-24 was replaced by the PHQ-9, there was still a significant difference, namely for depression (SMD = −0.905; 95%CI = −1.361–−0.450, $I^2 = 29.44\%$, $P = 0.236$). In addition, Peng HZ et al. replaced the HAMA-14 with generalized anxiety disorder scale-7, and found a similar result for anxiety (SMD = −0.971; 95% CI = −1.354–−0.589, $P < 0.05$, $I^2 = 0\%$, $P = 0.592$). Furthermore, no publication bias was detected by the Egger's and the Begg's-tests (all P-values > 0.05, Table 2). Moreover, significant advantages were found in emotion regulation (SMD = −0.832; 95%CI = −1.342–−0.322, $I^2 = 0\%$, $P = 0.820$).

In comparison with no-treatment control group, the aggregated SMD value of depressive symptom scores was found [−1.587 (95% CI: −2.505, −0.670), $P < 0.05$]. Considerable heterogeneity was reported ($I^2 = 90.45\%$, $P < 0.05$), as well as no publication bias (Begg's test: Z = 1.567, $P = 0.117$; Egger's test: Z = 4.746, $P = 0.132$). The combined SMD of anxiety symptom scores was found [−1.925 (95% CI: −2.700, −1.150), $P < 0.05$]. The results suggested high heterogeneity ($I^2 = 85.23\%$, $P = 0.001$). Nevertheless, no publication bias was detected (Begg test: Z = 1.567, $P = 0.117$; Egger test: Z = 1.053, $P = 0.484$). In addition, the combined RR value for clinical effectiveness was found [−1.204 (95% CI: 1.084, 1.338), $P < 0.05$]. No heterogeneity was found ($I^2 = 0\%$, $P = 0.810$). However, we found publication bias (Begg's test: Z = 1.567, $P = 0.117$; Egger's test: Z = 17.263, $P = 0.037$), with an adjusted RR value [1.167 (95% CI: 1.069, 1.273), $P < 0.05$]. Significant relief of impulsivity was found [−2.439 (95% CI: −2.748, −2.094), $P < 0.05$], while no heterogeneity was detected ($I^2 = 0\%$, $P = 0.989$). In addition, statistically significant positive effects were observed for SIB [−2.466 (95% CI: −3.305, −1.628), $P < 0.05$], with heterogeneity ($I^2 = 88.36\%$, $P = 0.017$).

Contrary to our expectations, no significant difference was observed in the incidence rate of ADRs after QF and SV, with nausea/vomiting [1.194 (95% CI: 0.357, 3.992), $I^2 = 0\%$, $P = 0.668$], dizziness/vertigo [0.864 (95% CI: 0.292, 2.556), $I^2 = 0\%$, $P = 0.704$], xerostomia [1.043 (95% CI: 0.352, 3.092), $I^2 = 0\%$, $P = 0.729$]. A publication bias was found in nausea/vomiting (Begg's test: Z = 1.567, $P = 0.117$; Egger's test: Z = 34.540, $P = 0.018$). In addition, increased BMI [1.217 (95% CI: 0.382, 3.870), $P > 0.05$] and drowsiness/drowsiness/fatigue [1.150 (95% CI: 0.281, 4.713), $P > 0.05$] were not detected with significance, nor was heterogeneity ($P > 0.05$, Table 2). The overall SMD value remained consistent regardless of the exclusion of any individual study (Supplementary Figs. 2–11).

Suicidal ideation. As shown in Table 3, six of the seven studies were conducted between 2017 and 2022, with four published in 2023 and two in 2022. For one study in 2018, the date of the study was not specified. Four studies were IPs and one study was OPs. The mean trial duration was approximately 3.3 weeks and ranged from 1 to 6 weeks. For the assessment of MDD, 7 studies used ICD-10, MINI-kid, DSM-V or DSM-IV, respectively. To define SI, 4 studies used the Beck scale for suicide ideation (BSSI); 1 study used the self-rating idea of suicide scale (SIOSS-26); 1 study used both the Columbia suicide severity rating scale (C-SSRS) and the BSSI; and 1 study used the SI item of HAMD. With an average rating of over 3, 3 RCTs were high quality, while another RCT was rated as 2. In addition, 1 CR was rated as 8, while the other 2 CCTs were rated as 7 and 8, respectively.

With the exception of one study that only used esketamine, the others were combination therapies. The HAMD was widely used to assess the severity of depressive symptoms, while suicide risk was assessed using the BSSI, HAMD-SI and C-SSRS, etc. ECT was applied in 2 studies and resulted in significant improvement in SI and depressive symptoms. In one study, it was observed that high-frequency rTMS showed greater efficacy in the early improvement of MDD than low-frequency rTMS ($\chi^2 = 8.167$, $P < 0.01$). The difference in SI between the two groups was statistically significant (low-frequency group: 36.7% vs. high-frequency group: 63.3%, $P < 0.05$). No ADR was reported. Similarly, Pan F et al. reported positive effect of high-frequency rTMS for depression and suicide risk, with 2 participants experiencing hypomania. Three adolescents experienced drowsiness after each rTMS but without other subjective side effects.

In comparison with sertraline, DBT was combined with sertraline in two studies, which showed a significant therapeutic effect, and no ADR was reported. The total BSSI score, SI intensity and suicide risk decreased after the intervention ($P < 0.01$). In addition, two studies showed very similar efficacy on depressive symptoms, with 1 study (experiment vs. control = 89.47% vs. 63.16%, $P < 0.05$), and the other (experiment vs control = 92.86% vs. 70.00%, $P < 0.05$).

The use of midazolam was associated with fewer adverse effects, particularly nausea, dissociation, etc., by Zhou YL et al. However, significant differences were observed in the mean changes of C-SSRS scores for ideation and intensity from baseline to day 6 between the esketamine group and the midazolam group.[ideation, 2.6 (SD = 2.0) vs. 1.7 (SD = 2.2), $P < 0.01$; intensity, 10.6 (SD = 8.4) vs. 5.0 (SD = 7.4), $P < 0.01$]. The response rates of antidepressants at 4 weeks post-treatment between esketamine and midazolam were 61.5% versus 52.5%. No significant difference in mania symptoms between the two groups was detected ($\chi^2 = 0.384$, $P > 0.05$).

Self-injurious behavior. Five studies have been published in the last three years. Two of the four RCTs were rated as high quality, the other 2 RCTs received 2 each, while the only CCT was rated 9. Three studies used psychosocial therapy alone, while the other two studies used antidepressants with ISP or high frequency rTMS. All studies were conducted in hospital. HAMD was used in 4 studies, while only 1 study used SDS. SIB lasting longer than 5 days or 6 weeks was categorized as SIB in two of five studies, while the others were identified as medical records. In addition,

Table 2. Effectiveness of interventions targeting MDD with NSSI/SIB.

Variables	Number of reports	Case (n)	Control (n)	RRs/SMD (95% CI)	I^2 (%)	Q	*P*	Classic fail-safe N	Begg (*P*)	Egger (*P*)	Trim and fill	
											Adjusted value	RRs/SMD (95% CI)
Antidepressant + CBT for NSSI												
No-treatment control												
Depressive symptom score	4	104	88	−1.467 (−2.492, −0.442)	88.39	25.83	<0.001	75	0.174	0.414	0	−1.467 (−2.492, −0.442)
Anxiety symptom score	4	104	88	−2.101 (−3.869, −0.333)	95.18	62.18	<0.001	101	1.000	0.692	0	−2.101 (−3.869, −0.333)
Active control												
Depressive symptom score[a]	4	62	57	−0.943 (−1.414, −0.472)	33.38	4.50	0.212	21	0.497	0.769	0	−0.939 (−1.322, −0.555)
Depressive symptom score[b]	4	62	57	−0.905 (−1.361, −0.450)	29.44	4.25	0.236	19	0.497	0.784	0	−0.905 (−1.361, −0.450)
Anxiety symptom score[a]	4	62	57	−0.942 (−1.323, −0.560)	0	1.90	0.592	21	0.174	0.354	1	−1.068 (−1.402, −0.735)
Anxiety symptom score[b]	4	62	57	−0.971 (−1.354, −0.589)	0	1.91	0.592	23	0.497	0.363	0	−0.971 (−1.354, −0.589)
Emotion regulation score	2	35	30	−0.832 (−1.342, −0.322)	0	0.05	0.820	-	-	-	-	-
Antiepileptic + Antipsychotic for NSSI												
No-treatment control												
Depressive symptom score	3	137	138	−1.587 (−2.505, −0.670)	90.45	20.94	<0.001	77	0.117	0.132	0	−1.587 (−2.505, −0.670)
Anxiety symptom score	3	137	138	−1.925 (−2.700, −1.150)	85.23	13.54	0.001	120	0.117	0.484	0	−1.925 (−2.700, −1.150)
Effective rate	3	137	138	1.204 (1.084, 1.338)	0	0.42	0.810	7	0.117	0.037	2	1.167 (1.069, 1.273)
Impulsivity score	2	112	113	−2.439 (−2.784, −2.094)	0	<0.001	0.989	-	-	-	-	-
Self-injury behavior score	2	112	113	−2.466 (−3.305, −1.628)	88.36	5.67	0.017	-	-	-	-	-
Adverse drug reaction												
Nausea/vomiting	3	137	138	1.194 (0.357, 3.992)	0	0.81	0.668	0	0.117	0.018	0	1.194 (0.357, 3.992)
Dizziness/faintness	3	137	138	0.864 (0.292, 2.556)	0	0.70	0.704	0	0.602	0.636	0	0.864 (0.292, 2.556)
Xerostomia	3	137	138	1.043 (0.352, 3.092)	0	0.63	0.729	0	0.117	0.059	2	1.359 (0.549, 3.364)
Drowsiness/fatigue	2	77	78	1.150 (0.281, 4.713)	46.68	1.88	0.171	-	-	-	-	-
Increased BMI	2	112	113	1.217 (0.382, 3.870)	0	0.06	0.803	-	-	-	-	-
ISP + RBI for SIB												
No-treatment control												
Depressive symptom score	2	99	99	−1.647 (−2.474, −0.820)	81.10	5.29	0.021	-	-	-	-	-

Effective rate: defined as the clinical effectiveness of interventions for adolescents with MDD and co-occurring NSSI;
CBT cognitive behavioral therapy, *GAD-7* generalized anxiety disorder scale-7, *HAMA* hamilton anxiety scale, *HAMD* hamilton depression scale, *ISP* intensive service provision, *MADRS* montgomery-asberg depression rating scale, *NSSI* non-suicidal self-injury, *PHQ-9* patient health questionnaire-9, *RBI* relationship-based intervention, *SIB* self-injury behavior;
Anxiety symptom score[a]: Peng HZ assessed anxiety symptoms by HAMA-14 [85]; Anxiety symptom score[b]: Peng HZ assessed anxiety symptoms by GAD-7 [85];
Depressive symptom score[a]: Peng HZ assessed depressive symptoms by HAMD-24 [85]; Depressive symptoms score[b]: Peng HZ assessed depressive symptoms by PHQ-9 [85].

Table 3. Characteristics of included studies.

a[a]

No	First author	Study year	Publication year	Study type	Grouping	Sample size A	Sample size B	Assessment	Sample source	Trial duration	Age range	Age (Mean ± SD)	Male Number	Funding
MDD with NSSI (single therapy)														
1	Zhu P	2019	2021	CCT	AS	NA	85	HAMD-17, CE(A), GSES, ASLSS, Incidence of NSSI behavior	IP	4 W	11–18	15.88 ± 3.86	43	Y
2	Zhang JY	2020–2022	2022	RCT	BR	108	105	HAMD-17, HAMA, CE(B), BIS-11, TESS, SBSS	NR	8 W	9–18	16.14 ± 1.52	47	Y
3	Lu HL	2020	2022	RCT	RNT	94	90	ANSAQ, SQAPMPU, SCARED, DSRS	OP	12 W	14–18	15.55 ± 1.19	46	Y
4	Wu J	2020–2021	2022	RCT	RNT	86	86	HAMD-17, BIS-11, PSQI, SF-36, CE(A), ADR, SIBS	NR	8 W	9–18	13.54 ± 2.39	47	N
5	Luo DL	2022–2023	2023	RCT	RNT	60	60	HAMD-17, ASHS, ADR	IP	NR	13–18	NR	NR	N
6	Dai LQ	2021–2022	2023	Pre-post	NA	NA	15	HAMD, OSI	OP	8 W	12–17	14.6 ± 1.35	2	Y
7	Li ZJ	2021–2022	2023	RCT	RNT	120	120	HAMD-17, CE(A), HAMA, SBSS, BIS-11, ADR	NR	2 M	8–18	14.31 ± 2.08	69	N
8	Ma JH	2021	2023	RCT	RNT	156	156	OSI, HAMD-17, MVASHS, RRMVASHS	IP	6 W	12–18	14.00 ± 3.00	40	N
9	Ye CL	2020	2023	RCT	CAN	50	50	CE(B), SCL-90, ADR	NR	8 W	9–18	15.37 ± 1.47	28	N
MDD with NSSI (combined therapies)														
10	Zhu YZ	2019–2021	2022	RCT	RNT	65	59	HAMD-17, FASM, BIS, ADR	NR	4 W	13–18	15.38 ± 1.98	20	N
11	Yuan GC	2020–2021	2022	RCT	RNT	62	62	HAMD, HAMA, CE(B)	IP	8 W	14–18	16.41 ± 0.68	33	N
12	Yu H	2019–2020	2021	RCT	RNT	36	36	HAMD-24, CE(A), TESS, BIS-11, SBSS	IP + OP	2 W	13–18	NR	NR	N
13	Xue ZF	2020–2021	2022	RCT	RNT	75	75	HAMD-17, HAMA, PSSS, ANSAQ	NR	16 W	12–18	15.59 ± 2.3	26	N
14	Wang YP	2020	2022	RCT	RNT	80	74	HAMD-24, OSI, MSQA	NR	5 W	12–18	16.24 ± 2.69	11	N
15	Peng HZ	NR	2021	RCT	RNT	35	30	HAMA-14, HAMD-24, GAD-7, PHQ-9, ASHS, DERS	IP + OP	6 W	12–18	15.43 ± 1.59	7	N
16	Lin XZ	2019–2021	2021	RCT	RNT	30	30	SAS, SDS, AAQ-II, OSI	IP + OP	6 W	12–18	14.67 ± 1.75	1	N
17	Liang QL	2020	2022	RCT	RNT	76	76	HAMD, TAS, ASHS	NR	3 M	12–18	16.07 ± 2.4	10	N
18	Li HZ(a)	2020–2021	2022	RCT	RNT	59	40	OSI, SDS, SAS, BIS-11, ERQ	IP + OP	8 W	13–17	14.9 ± 1.26	6	N
19	Li HZ(b)					59	35					14.72 ± 1.23	3	
20	Hu ZZ	2021	2022	RCT	DL	24	24	ANSAQ, CFQ, AAQ-II, HAMA, HAMD, MCCB	OP	8 W	12–18	15.42 ± 1.72	9	N
21	Ding HQ	2019–2020	2021	RCT	RNT	96	90	CERQ, SIFSD(last 3 months)	IP	4 W	12–18	15.12 ± 1.98	21	Y
22	Zeng QL	2020–2022	2022	CCT	MECT or not	NA	75	HAMD-17, HAMA, OSI, BSSI, DERS, ASLEC, CE(A), ADR	IP + OP	2 W	11–19	15 ± 2.22	7	N
23	Chen L	2021–2022	2023	RCT	RNT	93	90	HAMD-24, SDS, BIS-II, CSCS, ASHS	NR	2 W	12–18	NR	NR	Y

Table 3. continued

a[a]														
No	**First author**	**Study year**	**Publication year**	**Study type**	**Grouping**	**Sample size A**	**Sample size B**	**Assessment**	**Sample source**	**Trial duration**	**Age range**	**Age (Mean ± SD)**	**Male Number**	**Funding**
24	Duan DA	2020–2021	2023	CCT	AS	NA	57	HAMD, ANSAQ, SCSQ,	IP	6 W	12–18	16.84 ± 3.05	20	N
25	Xi Y	2021–2022	2023	CCT	BS	NA	36	HAMD, MADRS, CE(C), SCSQ, QL-Index	NR	3 M	12–18	15.11 ± 2.08	12	N
26	Xu YC	2022	2023	CR	NA	NA	1	SRAS, NOSIE, SAS, SDS	IP	4 W	14	14	0	Y
MDD with SI														
27	Feng YX	2020–2021	2022	RCT	RNT	60	58	HAMD, BSSI	OP	6 W	13–18	15.1 ± 1.42	15	N
28	Zhou YL	2020–2022	2023	RCT	CAN	54	49	C-SSRS, MADRS, BSSI-5, BPRS-5, YMRS, CADSS, SDS, VAS, ADR	IP	5D	13–18	14.7 ± 1.37	6[#]	Y
29	Wan DY	2021–2022	2023	RCT	RNT	38	38	HAMD-24, CE(A), BSSI	IP	6 W	12–18	15.11 ± 1.87	11	N
30	Zhang Y	2022	2023	RCT	RA	96	96	HAMD-24, HAMA, SCSQ, HAMD-SI	NR	2 W	6–18	15 ± 2.54	49	N
31	Pan F	NR	2018	CR	NA	NA	3	MADRS, BSSI, ADR	IP	1 W	15–17	16 ± 0.82	1	Y
32	Cai HP	2017–2021	2023	CCT	NR	NA	174	SIOSS, HAMD-17, RBANS, ADR	IP	2 W	13–18	15.05 ± 0.26	23	Y
33	Li X	2020–2021	2022	CCT	NR	NA	55	HAMD, BSSI	NR	2 W	12–17	15.00 ± 1.70	14	Y
MDD with SIB														
34	Lin G	2020–2021	2022	RCT	RA	62	62	HAMD, HAMA, NSQ, SF-36, ER, MC	NR	4 W	12–18	14.47 ± 1.48	33	N
35	Qiu HJ	2018–2019	2022	RCT	RNT	106	106	SAS, SDS, SCL-90, ISI, OSI, CGI-SI, ADR	NR	12 W	12–18	15.1 ± 0.87	37	N
36	Cai XF	2018–2019	2021	RCT	RA	136	136	HAMD-17	NR	4 W	12–18	14.5 ± 1.67	74	Y
37	Tang YT	2021–2022	2023	CCT	NR	NA	50	HAMA, HAMD, SCSQ, NSQ	NR	NR	10–16	14.24 ± 3.21	18	N
38	Wang XR	2018–2021	2023	RCT	RNT	152	152	HAMD-24, ANSAQ, TESS	NR	4 W	12–18	15 ± 1.48	70	Y
MDD with ST														
39	Wang CL	2010–2012	2013	RCT	RA	165	165	HAMD, CE(B), HAMA, SBQ-R-RC	IP	NR	NR	15.65 ± 1.56	79	N
40	Su M	2020–2022	2022	CCT	BNP	NA	42	NOSIE-30, SF-36, PSQI, Incidence of suicidal behavior, NSQ	NR	NR	13–19	15.3 ± 1.2	0	N
41	Shao HH	2019–2021	2021	CCT	CAN	NA	58	HAMD, SF-36, BSSI, NSQ	IP	1 M	12–17	14.07 ± 1.08	31	N
42	Zhu L	2020–2023	2023	RCT	DL	126	126	SCL-90, SAS, SDS, MoCA, TMT	OP	NR	13–18	16.37 ± 1.05	65	N
MDD with Suicidality														
43	Quan LJ	2018	2020	RCT	RNT	80	80	HAMD-17, SCL-90, SAS, ISI, C-SSRS, CGI-SI, RISI, ADR	NR	12 W	11–18	14.35 ± 3.84	28	Y
MDD with SSIRBs														
44	Li YS	2021	2022	CCT	NR	NA	38	HAMD-17, HAMA, PSQI, BSSI, HCL-32, BPRS, Y-BOCS, PDQ-4+, TESS	IP	4 W	12–19	14.48 ± 1.61	14[#]	N
45	Li SM	2017–2020	2021	RCT	RNT	100	100	HAMD-17, CE(A), SIOSS, ADR	NR	2 M	13–17	15.01 ± 1.25	54	Y

Table 3. continued

a[a]

No	First author	Study year	Publication year	Study type	Grouping	Sample size A	Sample size B	Assessment	Sample source	Trial duration	Age range	Age (Mean ± SD)	Male Number	Funding
46	Tang TC	2005	2009	RCT	RA	73	73	BDI, BSSI, BAI, BHS	School	6 W	12–18	15.25 ± 1.66	25	N
47	Chen XL	2015–2021	2022	Pre-post	NA	NA	278	HAMD-17, CGI-S	NR	NR	12–17	15.41 ± 1.5	41	Y
48	Wang Q	NR	2023	CR	NA	NA	1	SVAS, HAMD-17, HAMA, NSSI frequency (times/W)	OP	10D	17	17	1	Y
ASD with SIB														
49	Zou YR	2012–2014	2016	RCT	RNT	17	17	CARS, ABC, PEP	NR	3 M	NR	NA	NA	N
50	He AN	NR	2018	CR	NA	NA	1	MAS, FAI, FAO	OP	NR	6	6	1	Y
BD with NSSI														
51	Duan SQ	NR	2020	QS	NA	NA	23	NA	IP + OP	NR	12–17	15 ± 1.32	4	Y
PDs with SI														
52	Zhang TH	2015–2018	2021	CCT	NA	NA	29	HAMD-17, HAMD-SI, ADR	IP	2 W	NR	NR	NR	Y
PDs with NSSI														
53	Li XD	2022–2023	2023	RCT	RNT	76	76	YMRS, HAMD-24, BIS-11, Incidence of NSSI behavior, ADR	IP	8 W	12–18	15.12 ± 1.45	41	N

[a]Sample size A: refer to the total number of participants for randomization; Sample size B: refer to the number after intervention;
CE(A), Clinical efficacy assessed by reduction rate of HAMD; CE(B), Clinical efficacy assessed by reduction rate of HAMD and HAMA; CE(C), Clinical efficacy assessed by reduction rate of HAMD and MADRS;
D day(s), *W* week(s), M month(s), # without the number of males after drop-out, *N* No, *Y* Yes, *AAQ-II* Acceptance and action questionnaire-second edition, *ABC* autism behavior checklist, *ADR* adverse reaction, *ANSAQ* adolescent non-suicidal self-injury assessment questionnaire, *AS* admission sequence (odd and even numbers), *ASHS* adolescents self-harm scale, *ASLEC* adolescent self-rating life events check list, *ASLSS* adolescent student's life satisfaction scale, *ASD* autism spectrum disorder, *BD* bipolar disorder, *BAI* beck anxiety inventory, *BDI-II* beck depression inventory-II, *BSSI* beck sale for suicidal ideation, *BHS* beck hopelessness scale, *BIS* barratt impulsiveness scale, *BNP* based on nursing program, *BPRS* brief psychiatric rating scale, *BR* block randomization, *BS* based on strategy, *CADSS* clinician administered-dissociative scale, *CAN* computer arbitrary numbering, *CARS* childhood autism rating scale, *CCT* clinical controlled trial, *CERQ* cognitive emotion regulation questionnaire, *CFQ* cognitive fusion questionnaire, *CGI-S* clinical global impression scale severity, *CGI-SI* clinical global impression-severity of illness, *CR* case report, *CSCS* children's self-concept scale, *C-SSRS* columbia-suicide severity rating scale, *DERS* difficulties in emotion regulation scale, *DL* draw lots, *DSRS* depression self-rating scale, *ER* emotion regulation, *ERQ* emotion regulation questionnaire, *FAI* functional assessment interview, *FAO* functional assessment observation, *FASM* functional assessment of self-mutilation, *GAD-7* generalized anxiety disorder scale-7, *GSES* general self-efficacy scale, *HAMD* hamilton depression rating scale, *HAMA* hamilton anxiety scale, *HCL-32* hypomania check list-32, *IP* inpatient, *ISI* insomnia severity index, *MADRS* montgomery-asberg depression rating scale, *MAS* motivation assessment scale, *MC* medication compliance, *MCCB* MATRICS consensus cognitive battery, *MECT* modified electric convulsive therapy, *MoCA* montreal cognitive assessment, *MSQA* multidimensional sub-health questionnaire assessment, *MDD* major depressive disorder, *MVASHS* the modified version of adolescents self-harm scale, *NSSI* non-suicidal self-injury, *NA* not applicable, *NOSIE* nurses' observation scale for inpatient evaluation, *NR* no report, *NSQ* nursing satisfaction questionnaire, *OP* outpatient, *OSI* ottawa self-injury inventory, *PDQ-4+* personality disorders questionnaire-4+, *PDs* psychiatric disorders, *PDQ-D-20* perceived deficit questionnaire for depression-20, *PEP* psycho-educational profile, *PHQ-9* patient health questionnaire-9, *Pre-post* prepost studies, *PSQI* pittsburgh sleep quality index, *PSSS* perceived social support scale, *QL-Index* quality of life index, *QS* qualitative study, *RA* random allocation, *RBANS* repeatable battery for the assessment of neuropsychological status, *RCT* randomized controlled trial, *RISI* richter self-injury scale, *RNT* random number table, *SIB* self-injurious behavior, *SI* suicide ideation, *SA* suicide attempts, *ST* suicidal tendencies, *SSIRBs* suicidal and self-injurious related behaviors, *S* school, *SAS* self-rating anxiety scale, *SBQ-R-RQ* suicide behaviors questionnaires, *SBSS* self-injury behavior screening scale, *SCARED* screen for child anxiety related-emotional disorders, *SCL-90* symptom checklist-90, *SCSQ* simplified coping style questionnaire, *SDS* self-rating depression scale, *SF-36* short form-36, *SIBS* self-injurious behavior score, *SIFSD* self-injury frequency and severest degree, *SIOSS* self-rating idea of suicide scale, *SQAPMPU* self-rating questionnaire for adolescent, *SRAS* suicide risk assessment scale, *SVAS* suicide-visual analog scale, *TAS* toronto alexithymia scale, *TESS* treatment emergent symptom scale, *TMT* trail making test, *VAS* visual analogue scale, *Y-BOCS* yale-Brown obsessive compulsive scale, *YMRS* young manic rating scale.

b[b]

No	First author	SSIRBs		PDs		Control group			Experimental group		
		Type	Definition	Type	Definition	Sample size	Intervention type	Parameter	Sample size	Intervention type	Parameter
MDD with NSSI (single therapy)											
1	Zhu P	NSSI	NSSI(ANSAQ)	MDD	MDD(ICD-10)	43	RC	NA	42	RC + WLST	NA
2	Zhang JY	NSSI	SIB(frequently, medical record)	MDD	1.MDD(CCMD-3); 2.HAMD-17 ≥ 17	53	SV	SV: 1.0.5 g/D(initial); 2.Increased to 1–1.5 g/D	52	SV + QF	SV:SCG; QF: 1.25 mg/D; 2.Maximum dose≤300 mg/D(adjusted based on conditions and tolerance)
3	Lu HL	NSSI	NSSI (medical record)	FE-MDD	MDD(DSM-V)	45	RHM	NA	45	KTAFBHM	NA
4	Wu J	NSSI	NSSI(medical record)	MDD	1.MDD(medical record); 2.HAMD-17 ≥ 17	43	Sertraline	Sertraline: 1.25–50 mg/D; 2.50–150 mg/D(maintenance, adjusted based on conditions)	43	Sertraline+QF	Sertraline:SCG; QF: 1.50 mg(D1), 100 mg(D2), 200 mg(D3 + D4); 2.100–450 mg/D(divided into 2 doses, adjusted based on conditions)
5	Luo DL	NSSI	ASHS	MDD	1.MDD(medical record); 2.HAMD-17 ≥ 17	30	PST	NR	30	tDCS	tDCS:DLPFC:(cathode with right, anode with left, 20 min, 1–2 mA)

Table 3. continued

No	First author	SSIRBs		PDs		Control group			Experimental group		
		Type	Definition	Type	Definition	Sample size	Intervention type	Parameter	Sample size	Intervention type	Parameter
6	Dai LQ	NSSI	1.OSI:NSSI events≥5(last year) and NSSI events≥1(last 1 M); 2.DSM-V	FE-MDD	1.MDD(MINI-kid); 2.HAMD-17 ≥ 17	NA	NA	NA	15	Sertraline	Sertraline:50 mg/D(initial), maximum dose:100–200 mg/D(adjusted based on conditions)
7	Li ZJ	NSSI	SIB (frequently, medical record)	MDD	MDD criteria [113]	60	SV	SV: 1.0.5 g/D(evening); 2.Maximum dose≤1.5 g/D for twice(adjusted based on conditions)	60	SV + QF	SV:SCG; QF: 1.25 mg/D(initial); 2.Maximum dose≤300 mg/D(before sleep, adjusted based on conditions)
8	Ma JH	NSSI	DSM-V	FE-MDD	MDD(DSM-V)	81	Sertraline	Sertraline: 1.50 mg/D(initial); 2.Increasing to 100–200 mg/D(in 2 W)	75	Sertraline+MV	Sertraline:SCG; MV: 1.0.25 mg/D; 2.Increasing to 1 g/D(in 2 W) 3.Lorazepam(if severe insomnia disorder)
9	Ye CL	NSSI	SIB (frequently, medical record)	MDD	1.MDD(medical record); 2.HAMD-17 ≥ 17	25	SV	SV:0.5 g/D(initial, adjusted based on conditions)	25	SV + QF	SV:SCG; QF: 1.25 mg/D(initial); 2.Maximum dose≤300 mg/D(adjusted based on conditions)
MDD with NSSI(combined therapies)											
10	Zhu YZ	NSSI	NSSI related behaviors frequency≥5(last 4 W)	MDD	1.MDD(ICD-10); 2.HAMD-17 > 17 [167]	29	BH + LC	BH: 1.150 mg/D(initial, morning); 2.Continuous administration without significant adverse effects(4D); 3.150 mg/D(after, morning and evening); LC: 1.0.3 g/D(initial); 2.After 1–2 W, 0.3 g(morning)+ 0.6 g(evening)	30	BH + LC+ Sequential bilateral rTMS	BH:SCG; LC:SCG; rTMS:5 times/W; 1.DLPFC:(start with right, 100% resting motion threshold, 1 Hz, 600 stimulus pulse); 2.DLPFC:(after with left, 120% resting motion threshold, 10 Hz, 1500 stimulus pulse)
11	Yuan GC	NSSI	NSSI (medical record)	MDD	1.MDD(medical record); 2.HAMD-17 ≥ 18; 3.HAMA ≥ 15	31	Escitalopram	Escitalopram: 1.10 mg/D(initial); 2.maximum dose≤20 mg/D(adjusted based on conditions)	31	Escitalopram+CBT	Escitalopram:SCG
12	Yu H	NSSI	NSSI (medical record)	MDD	1.MDD(ICD-10); 2.HAMD-24:21–34	18	Sertraline	Sertraline: 1.25 mg/D(initial); 2.Gradually increasing to 50–150 mg/D	18	Sertraline+rTMS(low frequency)	Sertraline:SCG; rTMS:5 times/W VMPFC:(right, 5 cm anterior to motor cortex, 100% resting motion threshold, 1 Hz, 1200 stimulus pulse)
13	Xue ZF	NSSI	NSSI(last 1 year)	MDD	MDD(ICD-10)	37	Sertraline	Sertraline:50–100 mg/D	38	Sertraline+DBT	Sertraline:SCG
14	Wang YP	NSSI	NSSI(DSM-V)	MDD	MDD(ICD-10)	36	Fluoxetine+HE	Fluoxetine:20 mg/D (morning)	38	Fluoxetine+GPI	Fluoxetine:SCG
15	Peng HZ	NSSI	1.NSSI(DSM-V); 2.SIB > 5(last 1 year)	MDD	1.MDD(DSM-V); 2.HAMD-24 ≥ 20	15	SP + SSRIS	NR	15	SCBT + SSRIS	NR
16	Lin XZ	NSSI	Item one: positive(OSI)	FE-MDD	1.MDD(DSM-V); 2.SDS > 53/SAS > 50	15	Sertraline+HE	Sertraline:100 mg–150 mg/D	15	Sertraline+DBT	Sertraline:SCG
17	Liang QL	NSSI	NSSI criteria [168]	MDD	MDD(medical record)	38	RC+paroxetine	Paroxetine:20 mg/D	38	RC+paroxetine+PPI	Paroxetine:SCG
18	Li HZ(a)	NSSI	NSSI(DSM-V)	MDD	MDD(DSM-V)	20	Sertraline	Sertraline:100 mg–150 mg/D	20	Sertraline+DBT	Sertraline:SCG
19	Li HZ(b)	NSSI		MDD					15	Sertraline+SP	Sertraline:SCG
20	Hu ZZ	NSSI	1.SIB(≥ 5 d last year); 2.SIB(last 1 M); 3.NSSI(DSM-V)	FE-MDD	FE-MDD(medical record)	12	FH + DBT	FH: 1.20 mg/D(initial); 2.maximum dose≤80 mg/D (adjusted based on conditions, after 1 W)	12	FH + ACT	FH:SCG

Table 3. continued

No	First author	SSIRBs		PDs		Control group			Experimental group		
		Type	Definition	Type	Definition	Sample size	Intervention type	Parameter	Sample size	Intervention type	Parameter
21	Ding HQ	NSSI	1.NSSI(resulting in mild/moderate body injury); 2.SIB number≥1(last year)	MDD	MDD(DSM-V)	45	Drug therapy+ physical therapy +RC	NR	45	Drug therapy+ physical therapy+ER	NR
22	Zeng QL	NSSI	NSSI(DSM-V)	MDD	MDD(ICD-10)	34	SSRIS	Sertraline: 1.25–50 mg/D(initial); 2.100–150 mg/D(target); Escitalopram: 1.5–10 mg/D; 2.10–20 mg/D(target); Fluoxetine: 1.10–20 mg/D(initial); 2.20–60 mg/D(target); Duration of sleep medication≤2 W(Zopiclone / Alprazolam, if sleep disorders)	41	SSRIS + MECT	Sertraline:SCG; Escitalopram:SCG; Fluoxetine:SCG; MECT: bitemporal (90–130 mA, 2–4 s, 3–4 times/W, total = 6–12 times); EEG monitoring: confirm effective; Duration of sleep medication≤2 W(Zopiclone / Alprazolam, if sleep disorders)
23	Chen L	NSSI	DSM-V	FE-MDD	MDD(DSM-V)	46	Regular pharmacological therapy+physical therapy +continuous care	NR	44	Regular pharmacological therapy+physical therapy+TTM	NR
24	Duan DA	NSSI	NSSI(medical record)	MDD	1.MDD(DSM-V); 2.HAMD-24 ≥ 20	28	Sertraline	Sertraline:100–200 mg/ D(average dose)	29	Sertraline+DBT	Sertraline:SCG
25	Xi Y	NSSI	NSSI(medical record)	MDD	MDD(medical record)	18	Sertraline+ Fluoxetine	Sertraline:50 mg/D; Fluoxetine:20 mg/D	18	Sertraline +Fluoxetine+CBT	Sertraline:SCG; Fluoxetine:SCG
26	Xu YC	NSSI	NSSI(medical record)	MDD	MDD(medical record)	NA	NA	NA	1	Fluoxetine+QF+ narrative nursing	NA
MDD with SI											
27	Feng YX	SI	BSSI: either item 4 or 5 were "weak" or above	FE-MDD	1.MDD(ICD-10); 2.HAMD-24:8–35	30	Sertraline	Sertraline: 1.50 mg/D(initial); 2.100–200 mg/D(maintenance) 3.decrease to 50 mg/ D(adjusted based on conditions)	28	GDBT+Sertraline	Sertraline:SCG
28	Zhou YL	SI	1.SI(lasting 3 M); 2.C-SSRS:ideation score = 1; 3.BSSI:item 4/5 score = 2	MDD	1.MDD(DSM-V); 2.HAMD-17(moderate–severe depression)	23	Midazolam	Fasted overnight (>8 h, before drug administration, until 2 h after the infusion start); Midazolam(0.02 mg/kg) in 50 ml of 0.9% saline was infused 40 min (D1,3,5)	26	Esketamine	Fasted overnight (>8 h, before drug administration, until 2 h after the infusion start); Esketamine(0.25 mg/kg) in 50 mL of 0.9% saline was infused 40 min (D1,3,5)
29	Wan DY	SI	BSSI: either item 4 or 5 were "weak" or above(1 W)	MDD	1.MDD(DSM-V); 2.HAMD-24 ≥ 20	19	Sertraline	Sertraline: 1.50 mg/D(D1); 2.Increasing to 100 mg/D(in 1 W); 3.Increasing to 100–200 mg/ d(in 2 W)	19	Sertraline+DBT	Sertraline:SCG
30	Zhang Y	SI	HAMD-SI ≥ 1	FE-MDD	1.MDD(ICD-10); 2.HAMD-24 ≥ 20	48	SSRIS+rTMS(low frequency)	SSRIS:NR dosage; rTMS:DLPFC:(right, 1 Hz, 10 stimulus pulse/group, interval time = 5 s, 600 stimulus pulse/ 20 min, 1time/D, 5time/W, total = 2 W, 10times)	48	SSRIS+rTMS(high frequency)	SSRIS:SCG; rTMS:DLPFC:(left, 10 Hz, 100 stimulus pulse/group, interval time = 56 s, 1500 stimulus pulse/20 min, 1time/D, 5time/W, total = 2 W, 10times)
31	Pan F	SI	BSSI ≥ 12	MDD	1.MDD(DSM-IV); 2.MADRS ≥ 20	NA	NA	NA	3	Escitalopram +rTMS(high frequency)	Escitalopram:10 mg/D; rTMS:DLPFC:(left, 10 Hz, 120 trains/5 s, interval time = 15 s, 6000 stimulus pulse/session, total = 1 W, 7times)
32	Cai HP	SI	SIOSS-26 ≥ 12	MDD	1. MDD(DSM-V); 2. HAMD-17 ≥ 17	79	SSRIS	SSRIS:fluoxetine equivalent dosage(10–30 mg)	81	SSRIS + ECT	SSRIS:SCG; ECT:Bilateral temporal lobes(maximum charge

Table 3. continued

No	First author	SSIRBs		PDs		Control group			Experimental group		
		Type	Definition	Type	Definition	Sample size	Intervention type	Parameter	Sample size	Intervention type	Parameter
											delivered:504 mC; output current:0.9 A; frequency:10–70 Hz; pulse width:1 ms; maximum stimulus duration:8 s; 1st W: 1time/D, 5times; 2nd W: 3 times every other day; Propofol:1 mg/kg; Succinylcholine:0.5 mg/kg
33	Li X	SI	1.BSSI > 11(last 1 W); 2.SI(last 1 W)	MDD	1.FE-MDD(DSM-IV; MINI-kid); 2.HAMD-17 ≥ 17	25	NA	NA	30	ECT+multiple pharmacotherapies	ECT:Bilateral temporal lobes (low 0.25 mode, 0.9 A, initial dose: energy percent = age × 0.5, 4 times/W, total: 8 times); Diprivan:1.5 − 2 mg/kg; Succinylcholine:0.5 − 1 mg/kg; Multiple medication: NR dosage
MDD with SIB											
34	Lin G	SIB	SIB (medical record)	MDD	MDD(unipolar, medical record)	31	RC	NA	31	RC + PGPC	NA
35	Qiu HJ	SIB	SIB(≥ 6 W) +insomnia	MDD	1.MDD(CCMD-2-R); 2.Depressive symptoms(moderate/ severe, ≥6 W)	53	Sertraline	Sertraline: 1.10 mg/D(initial,4 W; 2.20 mg/D and maximum dose≤60 mg/D(adjusted based on conditions)	53	Sertraline+SIT	Sertraline:SCG
36	Cai XF	SIB	SIB(medical record)	MDD	1.MDD(ICD-10); 2.HAMD-17 ≥ 20; 3.YMRS ≤ 5	68	RC	NA	68	PGPC	NA
37	Tang YT	SIB	SIB(medical record)	MDD	MDD(medical record)	25	RC	NA	25	PGPC	NA
38	Wang XR	SIB	SIB ≥ 5D	MDD	MDD(ICD-10)	76	Sertraline +Spurious stimulus	Sertraline: 1.25 mg/D(after meal); 2.Maximum dose≤150 mg/ D(adjusted based on conditions)	76	Sertraline +rTMS(high frequency)	Sertraline:SCG; rTMS:DLPFC:(left, 90% resting motion threshold, single stimulation time = 5 s, interval time = 10 s, 10 Hz, 10 min/D, 1time/D, 5 consecutive days of treatment per week, rest for 2D, total = 4 W, 20times)
MDD with ST											
39	Wang CL	ST	ST(SBQ-R)	MDD	MDD(DSM-IV)	81	RC	NA	84	RC + CABSM	NA
40	Su M	ST	ST(medical record)	MDD	MDD(medical record)	21	RPC	NA	21	CCANS	NA
41	Shao HH	ST	Suicidality(last 10 M)	MDD	MDD(medical record)	29	RC	NA	29	RC + CABSM	NA
42	Zhu L	ST	ST(medical record)	MDD	MDD(medical record)	63	RC	NA	63	RC + CABSM	NA
MDD with Suicidality											
43	Quan LJ	Suicidality	Suicidality+ insomnia(≥ 6 W)	FE-MDD	1. MDD(CCMD); 2.Depressive symptoms(nonpsychotic, moderate to severe, ≥6 W)	40	Sertraline	Sertraline: 1.10 mg/D(initial); 2.maximum dose≤20 mg/ D(adjusted based on conditions, 4 W) or maximum dose≤60 mg/D(if poor effect)	40	Sertraline+SIT	Sertraline:SCG
MDD with SSIRBs											
44	Li YS	SIB + SI	BSSI ≥ 6/ SIB(medical record)	FE-MDD	1.MDD(ICD-10); 2.HAMD-17 ≥ 17	27	SGA+ antidepressants	NR	11	Mood Stabilizer (Lithium salt or valproate) +antidepressants	NR
45	Li SM	Suicidality +SIB	Suicidality and SIB(medical record)	FE-MDD	MDD(CCMD-3)	50	Fluoxetine	Fluoxetine:20 mg/D(take with warm water, bedtime)	50	Fluoxetine +olanzapine	Fluoxetine:SCG; Olanzapine:10 mg/D

Table 3. continued

No	First author	SSIRBs		PDs		Control group			Experimental group		
		Type	Definition	Type	Definition	Sample size	Intervention type	Parameter	Sample size	Intervention type	Parameter
46	Tang TC	SI/SA	BSSI > 0	MDD	1.MDD(DSM-IV-TR); 2.Moderate–severe depression(BDI > 19); 3.Moderate–severe anxiety(BAI > 16); 4. Significant hopelessness(BHS ≥ 9)	38	TAU	NA	35	IPT-A-IN	NA
47	Chen XL	SI/SA	1.SI only/SA only(medical record); 2.HAMD(third item) ≥3 [Scores of 3 and 4 indicated expressed suicide intent]	MDD	1. MDD(DSM-IV); 2.HAMD-17(medical record)	NA	NA	NA	278	ECT	Modified bitemporal ECT (brief-pulse, 1st W: 3 times, total: 6–12 times, initial dose: energy percent = age × 0.7, stimulation energy: increased by 5% if the seizure time was <25 s); Diprivan:1.5 − 2 mg/kg; Succinylcholine:0.5 − 1 mg/kg
48	Wang Q	NSSI + SI	SIB frequency = 6 times/W SVAS = 6	MDD	1.MDD(medical record); 2.HAMD-17 = 26	NA	NA	NA	1	rTMS	rTMS: 1.DLPFC:(left, 15 Hz, 110% resting motion threshold, 60 trains of 50 pulsations, single stimulation time = 3.33 s, interval time = 26 s; 2.4times/D, 3000 pulse/time)
ASD with SIB											
49	Zou YR	SIB	SIB (medical record)	ASD	ASD criteria [169]	9	MCME	NA	8	MCME+ musicotherapy	NA
50	He AN	SIB	SIB(medical record)	ASD	ASD(medical record)	NA	NA	NA	1	FBA + TCM	NA
BD with NSSI											
51	Duan SQ	SIB	SIB number ≥2(last 6 M)	Mix	Mix(medical record)	NA	NA	NA	23	TMI	NA
PDs with SI											
52	Zhang TH	SI	HAMD-SI(3-item) ≥1	Mix	1.Mix(DSM-IV); 2.HAMD-17 ≥ 14	12	rTMS(low)+SSRIS	rTMS: Low frequency right DLPFC:1 Hz, 2 trains, 700 pulses per train, 1 s intertrain-interval, 1400pulses per session; 120% motion threshold, 5 sessions/W for 2 W; SSRIS:NR dosage	17	rTMS(high)+SSRIS	rTMS: High frequency left DLPFC:10 Hz, 80 trains, 30pulses per train, 12 s intertrain-interval, 2400pulses per session; 120% motion threshold, 5 sessions/W for 2 W; SSRIS:NR dosage
PDs with NSSI											
53	Li XD	NSSI	DSM-V	FE-BD	BD(DSM-V)	38	LC	LC: 1.20 mg/kg(initial, after meal, 3times/D); 2.500–1000 mg/D(maintenance dose, adjusted based on conditions)	38	Aripiprazole+LC	LC:SCG; Aripiprazole: 1.2 mg/D(initial); 2.5 mg/D(after 2D); 3.Maximum dose≤20 mg/D(adjusted based on conditions)

[b]Sample size is the number of people either in the experimental group or in the control group during the final assessment.

W week(s), *D* day(s), *M* month(s), *s* second, *mg* milligram, *g* gram, *kg* kilogram, *Hz* hertz, *mA* milliampere, *mC* millicoulomb, *ACT* acceptance and commitment therapy, *ANSAQ* adolescent non-suicidal self-injury assessment questionnaire, *ASD* autism spectrum disorder, *ASHS* adolescent self-harm scale, *BAI* beck anxiety inventory, *BDI* beck depression inventory, *BSSI* beck scale for suicidal ideation, *BD* bipolar disorder, *BH* bupropion hydrochloride, *BHS* beck hopelessness scale, *CABSM* cognitive adjustment and behavioral shaping model, *CBT* cognitive behavioral therapy, *CCANS* clinical characteristics analysis and nursing strategies, *CCMD* chinese classification of mental disorders, *C-SSRS* columbia suicide severity rating scale, *DBT* dialectical behavior therapy, *DLPFC* dorsolateral prefrontal cortex, *DSM* diagnostic and statistical manual of mental disorders, *ECT* electroconvulsive therapy, *EEG* electroencephalogram, *ER* emotional regulation, *FBA* functional behavioral assessments, *FE-MDD* first episode-major depressive disorder, *FH* fluoxetine hydrochloride, *GDBT* group dialectical behavior therapy, *GPI* group psychological intervention, *HAMA* hamilton anxiety scale, *HAMD* hamilton depression scale, *HE* health education, *ICD* international classification of diseases, *IPT-A-IN* intensive interpersonal psychotherapy, *KTAFBHM* knowledge-to-action framework-based health management, *LC* lithium carbonate, *MCME* mode combining medicine and education, *MDD* major depressive disorder, *MECT* modified electric convulsive therapy, *MV* magnesium valproate, *MINI-kid* mini international neuropsychiatric interview for children and adolescents, *NA* not applicable, *NR* no report, *NSSI* non-suicidal self-injury, *OSI* ottawa self-injury inventory, *PGPC* parent-child group combined psychological counseling, *PDs* psychiatric disorders, *PPI* positive psychological intervention, *PST* pseudo-stimulation therapy, *QF* quetiapine fumarate, *RC* routine care, *RHM* routine health management, *RPC* routine psychological care, *rTMS* repetitive transcranial magnetic stimulation, *SSIRBs* suicidal and self-injurious related behaviors, *SA* suicidal attempt, *SAS* self-rating anxiety scale, *SBQ-R* suicidal behaviors questionnaire-revised, *SCBT* simplified cognitive behavior therapy, *SCG* same as control group, *SDS* self-rating depression scale, *SGA* second generation antipsychotic drugs, *SI* suicidal ideation, *SIB* self-injurious behavior, *SIT* sensory integration therapy, *SP* supportive psychotherapy, *SIOSS* self-rating idea of suicide scale, *SSRIS* selective serotonin reuptake inhibitors, *SSIRB* suicidal and self-injurious related behaviors, *ST* suicidal tendencies, *SV* sodium valproate, *SVAS* suicide-visual analog scale, *TAU* treatment-as-usual, *TCM* traditional chinese medicine, *tDCS* transcranial direct current stimulation, *TMI* text messaging intervention, *TTM* therml texture maps, *VMPFC* ventromedial prefrontal cortex, *WLST* williams life skills training, *YMRS* young manic rating scale.

three studies used CCMD-2-R and ICD-10. Overall, both depression and self-injury were alleviated after the intervention. In addition, the combination of ISP and relationship-based intervention resulted in higher adherence compared to the control group.

Meta-analysis: Only the depressive symptoms were summarized in two studies with no-treatment control were aggregated, which included a total of 93 samples. The combined SMD value of depressive symptom score was [−1.647 (95% CI: −2.474, −0.820)]. Significant heterogeneity was observed ($I^2 = 81.10\%$, $P = 0.021$, Table 2). The exclusion of a single study did not change the stability of the aggregated SMD value (Supplementary Fig. 1).

Suicidal tendencies. Four studies were included, three of which had a duration of 2 years and one of which had a duration of 3 years. One study was published in 2013, the others were published in the last 3 years. One study used the DSM-V, while three studies were based on medical records. In the absence of a suitable randomization method, the quality of two RCTs was 2 and 3, respectively. Nevertheless, two CCT studies both scored 7.

Psychosocial therapy was used alone. Wang CL et al. showed significant difference in HAMD and HAMA scores between two groups at both 2 and 4 weeks after the intervention ($P < 0.01$). Zhu L et al. used cognitive correction and behavioral shaping nursing to intervene with MDD patients with suicidal tendencies. Symptoms, psychological status, and cognitive functioning improved after the interventions($P < 0.05$). Shao HH et al. demonstrated the combination of CBT and ISP could significantly reduce depressive symptoms and suicide-related score ($P < 0.001$). In addition, the combination of CBT and ISP showed significant improvement in quality of life [psychological ($\chi^2 = 14.83$, $P < 0.001$), physical ($\chi^2 = 10.35$, $P < 0.005$), physiological ($\chi^2 = 10.92$, $P < 0.001$) and social functions ($\chi^2 = 15.61$, $P < 0.001$)]. Su M et al. reported that quality of life, sleep quality and depression improved significantly after implementation of the clinical characteristics analysis and nursing strategies (CCANS) ($P < 0.05$). Specifically, compared with control group, CCANS significantly reduced rates of cutting wrist (9.52% vs. 0%, $P < 0.05$), jumping (14.29% vs. 4.76%, $P < 0.05$), poison ingestion (14.29% vs. 4.76%, $P < 0.05$) and overall suicidal rate (38.09% vs. 9.52%, $P < 0.05$). Importantly, no ADR was reported in these 4 studies.

Suicidality. Quan LJ et al. conducted a high quality RCT of FE-MDD, with sensory integration therapy and sertraline in 2020. The study lasted a total of 12 weeks and several evaluations were conducted. A significant difference in ISI score was found between 2 groups after the intervention (experimental:4.52 ± 1.02 vs. control: 5.27 ± 1.06, $P < 0.01$). The positive number of SI decreased after sensory integration therapy (baseline vs. week 4 vs. week 8 vs. week 12 = 40 vs. 24 vs. 15 vs 5), with a significant difference found in total ADRs, nausea (experimental: 2/40 vs. control: 4/40), drowsiness (experimental: 1/40 vs. control: 3/40), and dizzy (experimental: 3/40 vs. control: 5/40).

Major depressive disorder with multi-behaviors

Five studies applied a single therapy for MDD with multiple behaviors, including 3 of 5 simultaneously studied SSIRBs. Five different scales were used to assess the severity of SSIRBs, including BSSI, SIOSS, clinical global impression scale severity (CGI-S), suicide-visual analog scale (SVAS). Due to the high dropout rate, one CCT was rated as 5 [102]. In addition, the lack of rigorous double-blind studies and randomization methods were the main reasons for the low quality (2 vs. 3) in two RCTs. One pre-post study was rated as 8, while one CR was rated as 7 and one CCT was rated as 5. Four out of five studies were conducted in hospital. The mean trial duration ranged from 10 days to 2 months.

Non-major depressive disorder with SSIRBs

Five studies were conducted: two for ASD with SIB, one for FE-BD with NSSI, one for PDs with SI and one for PDs with SIB. Two of five studies used DSM-V and DSM-IV. On average, one article has been published every two years since the study was established in 2016. The quality of two studies was 9 for QS and 5 for CR, respectively. The other 2 studies were rated as high quality according to the Jadad scale (mean score = 3). One CCT was rated as 8. One study did not specify the source of the sample, the other 4 studies were from IPs or OPs. The average intervention duration was 7.3 weeks, while 2 studies did not specify the duration.

Four out of five studies were single therapy, with only one study using rTMS and SSRIS. Only one study adopted a novel online psychoeducational intervention for MDD adolescents. Duan SQ et al. found that transcripts of semi-structured interviews reduced instances of deliberate self-harm by providing acceptable support to adolescents. One CR reported that traditional Chinese medicine (TCM) and the five elements of music therapy significantly improved the child's sleep and emotions, and SIB was also alleviated. Li XD et al. found that aripiprazole had a significant effect on alleviating the occurrence of NSSI in FE-BD compared to lithium (week 8: experimental: 1/38 vs. control: 8/38, $P < 0.05$) with similar incidence rates of ADRs. Only one study used rTMS with different intensities to affect the left or right DLPFC. Good relief effects were observed for SI, with 22 of 29 adolescents recovering. In contrast, a negative correlation was observed between improvements in HAMD total score and HAMD-SI score ($r = -0.094$, $P = 0.629$).

DISCUSSION

To the best of our knowledge, this was the inaugural systematic review and meta-analysis to summarize the characteristics of interventions for Chinese PDs adolescents with SSIRBs. Geographically distributed along the coast, all studies were located far from underdeveloped areas, highlighting the uneven distribution of mental health resources in China [23]. Nevertheless, almost all of the literature was published in the past four years, with 2 studies in 2020, 9 studies in 2021, and 19 studies in 2022. Notably, the growth trend of publications indicates a tremendous research enthusiasm during the COVID-19 pandemic [114]. ISP and CBT were the most common psychosocial strategies, while the most commonly used medication was antidepressants. In addition, rTMS was the most common physical therapy.

Given the prevailing global circumstances, each of the three major intervention strategies has its own merits and drawbacks. The Times and the Guardian noted that "antidepressants do more harm than good" and "psychiatric drugs are doing us more harm than good" [115]. And antidepressants have been given a black box warning by the Food and Drug Administration, suggesting that they may have an increased risk of suicide in adolescents with PDs [116]. All phenomena have also had unseen negative effects on drug treatment. As a substitute for drug therapy, psychosocial therapy not only circumvents the potential hazards arising from insufficient evidence of efficacy but also mitigates the occurrence of many ADRs which would be a risk factor for COVID-19 complications [117]. From another perspective, the delayed therapeutic response of psychological therapy was also a recognized disadvantage [92]. As a newly explored intervention, physical therapy has been gradually promoted in recent years, whose advantages are fewer ADRs and rapid response [80, 118]. Therefore, three types of existing interventions were comprehensively integrated in our study, which could facilitate the optimization of resource allocation and the improvement of effectiveness.

Psychosocial intervention

Psychosocial therapy was used in 31 studies, representing 7 of 10 major categories of psychological interventions [44]. Our study

suggests that psychosocial therapy was effective, which is consistent with international studies for adolescents with PDs and SSIRBs [11, 30]. However, as the majority of studies involved combination therapies and considered psychosocial therapy as a complementary approach [119–121], it is a challenging to precisely determine the source of therapeutic effectiveness [122].

To date, the effectiveness of CBT and antidepressants in PDs or SSIRBs has been widely recognized [123–125]. Our study suggests that CBT in combination with antidepressants can alleviate symptoms of depression, anxiety, and difficulty in emotion regulation, which is superior to active control. In addition, our result indicated that the experimental group with a no-treatment control seemed to have a stronger effect. Although it has been suggested in the past that patients with and without antidepressant medication derived similar benefits from CBT in terms of anxiety [126, 127], the combination of CBT and sertraline was more effective in relieving anxiety and depression than either treatment alone [128, 129], which is consistent with our findings. The decrease in NSSI and alleviation of depression in adolescents were reported after DBT, which was considered as comprehensive CBT [31]. Another RCT confirmed the positive efficacy of DBT in combination with medication in reducing SA in adolescents with BD [130]. Similar to their findings, our study also found that CBT with antidepressants could decrease self-injury behaviors score in Chinese adolescents with PDs. Lu JJ and colleagues have reported that CBT is the most commonly used intervention for the treatment of SSIRBs in Chinese adolescents [35]. However, our results suggest that ISP has an almost equivalent status with CBT in adolescents with PDs and comorbid SSIRBs. CBT focuses on an individual's psychological and behavioral patterns to achieve a transformation personal control [35]. ISP achieves therapeutic goals by providing comprehensive and highly focused support with attachment and object relations [131]. Additionally, the cultivation of skills not reflected in CBT is integrated into this process and includes the development of self-esteem and the navigation of interpersonal relationships [44]. On the other hand, more conflictual relationships were observed in the families of adolescents with PDs and SSIRBs [132]. Ebrahimi et al. applied parent–child interactions and observed a reduction in depressive symptoms [133], which was also found in our study that demonstrated the positive effectiveness against depression in PGPC. In summary, psychosocial intervention is a promising therapeutic approach.

Online interventions are very popular, especially during the COVID-19 pandemic. Buronfosse et al. demonstrated the effects of hotlines in reducing self-aggressive behavior in patients diagnosed with BPD [134]. Effectiveness in suicide prevention and symptoms improvement has also been reported [135–137]. Although SMS text messaging interventions were first introduced as a productive novel approach in the treatment of Chinese PDs adolescents with SSIRBs [94], the effectiveness was similar to previous studies, with SMS text messaging interventions showing promising potential due to their cost-effectiveness, low-intensity, and widespread acceptability [94, 135]. The importance of psychosocial therapy is essential that it goes beyond symptom management and addresses the complex interplay of psychological, social, and environmental factors. It is an integral part of the holistic treatment of adolescents struggling with mental health problems associated with SSIRBs.

Physical intervention

In our studies, three types (i.e., ECT, tDCS, and rTMS) of non-invasive brain stimulation (NBS) were applied [138], which were feasible and demonstrated to be effective in Chinese adolescents. Although Bloch and colleagues reported that rTMS treatment did not significantly alleviate the severity of SI in MDD adolescents [139], most of studies have confirmed the role of rTMS in alleviating SI in MDD adults [140, 141], our results supported this effectiveness on Chinese adolescents [72, 77, 79]. The factors leading to the differences could be the effects of comorbidities and previous history of ECT were not excluded by Bloch et al. whose study included only 9 participants. However, there is a recognized mechanism that may explain the efficacy of ECT. Cortical inhibition may be enhanced by rTMS, possibly by modulating GABAB receptor-mediated activity, leading to a reduction in SI among depression patients [77, 142]. A weak positive effect on stress-related emotions was found after tDCS treatment [143]. While tDCS was able to significantly alleviate depressive symptoms in our study, which was also shown by Charvet et al. [144]. Furthermore, the alleviation of suicidal symptoms and depression after ECT was demonstrated in our study, which was also found in previous results [145, 146]. The pathogenesis of PDs with SSIRBs has been linked to neurochemical metabolic processes [147], HPA axis dysfunction, and psychosocial factors [148]. By applying external magnetic fields or electric currents to the brain, NBS induces changes in neuronal excitability, thereby affecting cerebral metabolism and neuronal electrical activity [149], with the aim of alleviating symptoms [64, 68].

Contact dermatitis was observed after tDCS with a parameter control above or below 2 mA [150], while no ADR was observed at a current of 1–2 mA. Appropriate parameters may be an associated factor for ADRs. In addition, physical therapy combined with drug treatment had a lower proportion of ADRs than the group receiving drug treatment alone [92, 103]. Therefore, NBS was one of the options for the treatment of Chinese PDs adolescents with SSIRBs. Furthermore, ECT was traumatizing, while both tDCS and ECT had difficulties in accurately determining the location of the stimulus effect. However, today's technology can analyze data in real time and automatically adapt the stimuli to the behavioral state of the brain [151]. This can not only improve controllability and safety, but also increase confidence in the treatment. In the future, the combination of artificial intelligence and targeted electrical brain stimulation offers endless possibilities [152, 153].

Pharmacotherapy

This is the inaugural meta-analysis investigating the effectiveness of pharmacotherapy (antipsychotics and antiepileptics, antidepressants and CBT) in adolescents with MDD and NSSI. Our study showed that QF and sodium valproate (SV) had positive effects on the relief of depressive symptoms, anxiety, impulse symptoms, and self-injury symptoms, as well as safety, compared to SV alone.

There is ample evidence in the literature that defects in gamma-aminobutyric acid (GABA) transmission are associated with MDD [154], while the main neurophysiological basis of MDD is related to dopamine [155]. SV not only prevents the degradation of GABA by inhibiting GABA aminotransferase [156], but also increases the activity of glutamic acid decarboxylase [157], which is the rate-limiting enzyme for the synthesis of GABA [158]. Thus, SV increases brain GABA concentrations and modulates the neuronal. QF is an antagonist with moderate affinity for adrenergic a1 and a2 receptors, serotonergic 5-hydroxytryptamine 2 receptors (5-HT_2 receptors) and dopaminergic D2 receptors; the affinity for serotonergic 5-HT_{1A} receptors is low [159]. By antagonizing 5-HT_{2A} receptors, acting as a partial agonist of 5-HT_{1A} receptors, and antagonizing α2 adrenoceptors, QF increases the release of dopamine from the prefrontal cortex [160]. Based on the potential mechanisms, SV and QF may have an effect on improving anxiety and depressive symptoms [161]. Furthermore, in practice, SV has been shown to be the first choice for the drug treatment of BD, while QF served as a complementary strategy for PDs due to its safety [161]. Previous studies have reported the role of QF in reducing impulsivity and depression [162, 163], which was also reflected in our results. Our study also found a reduction in self-injury scores after taking QF and SV, whereas other studies have reported a similar role for these drugs [164, 165]. In addition, our

study showed that the incidence of ADRs was slightly higher than when taking SV alone, but no significant difference, suggesting that the ADRs caused by low-dose QF were still within an acceptable range. The efficacy, optimal dosage, and compliance of other medications (e.g., ketamine) should be further investigated.

STRENGTHS AND LIMITATIONS

This systematic review and meta-analysis included databases from international and Chinese sources to conduct a comprehensive literature search and use of sophisticated analyses. We described the characteristics of interventions in Chinese PDs adolescents with SSIRBs, and presented meta-analyses for both NSSI and SIB. Our study also included psychosocial, pharmacologic, and physical treatments. In addition, our review also included gray papers from top conferences in Chinese psychiatry.

However, it is important to note some limitations. First, the results should be interpreted with caution due to the small number of studies. Second, except for MDD adolescents with NSSI or SIB, our study did not conduct a meta-analysis of interventions for other SSIRBs in adolescents with PDs due to insufficient data. Third, our study was limited to focusing primarily on interventions and overlooking preventive strategies while using a promising risk calculator for early detection of SA in BD [166]. Fourth, optimal doses and medication compliance were not analyzed due to insufficient data. Finally, comparisons in our study were not possible due to the different components and efficacy of pharmacotherapy in the included studies. Since the articles studied were primarily from Mainland China, the generalizability of these results to other ethnicities may be limited.

CONCLUSIONS

This systematic review described the main characteristics, safety and effectiveness of interventions in Chinese PDs adolescents with SSIRBs. Single therapy and combination therapies have shown varying degrees of safety and effectiveness in relieving symptoms. These findings expanded the means and theoretical basis of mental health treatment to provide benefits for future health care utilization and the economy as a whole. Larger extensive, multicenter RCTs with large sample sizes are needed to evaluate efficacy and safety.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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