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EDITED BY
Vassilis Martiadis,
Asl Napoli 1 Centro, Italy

REVIEWED BY
Pasquale Scognamiglio,
ASL Napoli 3 Sud, Italy
Fabiola Raffone,
Asl Napoli 1 Centro, Italy

*CORRESPONDENCE
Yu-Tao Xiang
ytxiang@um.edu.mo
Wei Zheng
zhengwei0702@163.com

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Rapid treatment center for depression in China: constructive reflections and transnational implications

Zhan-Ming Shi[1], Xing-Bing Huang[2,3], Yan-Ling Zhou[2,3], Yu-Ping Ning[2,3], Gabor S. Ungvari[4,5], Yu-Tao Xiang[6,7]* and Wei Zheng[2,3]*

[1]Department of Psychiatry, Chongqing Jiangbei Second Hospital, Chongqing Jiangbei Mental Health Center, Chongqing, China, [2]Department of Psychiatry, The Affiliated Brain Hospital, Guangzhou Medical University, Guangzhou, China, [3]Key Laboratory of Neurogenetics and Channelopathies of Guangdong Province and the Ministry of Education of China, Guangzhou Medical University, Guangzhou, China, [4]Section of Psychiatry, University of Notre Dame Australia, Fremantle, WA, Australia, [5]Division of Psychiatry, School of Medicine, University of Western Australia, Perth, WA, Australia, [6]Unit of Psychiatry, Department of Public Health and Medicinal Administration, & Institute of Translational Medicine, Faculty of Health Sciences, University of Macau, Macao, Macao SAR, China, [7]Centre for Cognitive and Brain Sciences, University of Macau, Macao, Macao SAR, China

Enhancing the early diagnosis and standardized treatment of major depressive disorder (MDD), as advocated by the National Health Commission of China, is a key priority in the mental health initiatives of the nation. To achieve this, numerous evidence-based rapid treatment centers for MDD have been established or are currently under development across the country. These centers focus on the following primary treatment modalities for depression: electroconvulsive therapy (ECT), intravenous ketamine/esketamine, esketamine nasal spray, magnetic seizure therapy (MST), and Stanford Neuromodulation Therapy (SNT). This policy and practice review explored the application and modification of these techniques in treating depression in China, addressing their strengths and shortcomings. With particular focus on China's rapid antidepressant treatment strategies (e.g., ECT, intravenous ketamine/esketamine, esketamine nasal spray, MST, SNT), the current policy and practice review described their potential to speed up recovery thereby providing valuable insights for other countries and regions.

KEYWORDS

major depressive disorder, electroconvulsive therapy, ketamine, esketamine, esketamine nasal spray, magnetic seizure therapy, Stanford Neuromodulation Therapy, rapid treatment center

1 Introduction

Major depressive disorder (MDD) is one of the most prevalent mental illnesses, characterized by persistent low mood and diminished interest among several other symptoms (1). In severe cases, patients may exhibit serious psychological and behavioral manifestations, such as hallucinations, delusions, self-harm, and suicidal tendencies (2). The prevalence and incidence of MDD have increased recently, particularly in adolescents, probably due to the influence of the COVID-19 pandemic (3, 4).

To address this escalating trend in MDD prevalence, the National Health Commission of China has devised a blueprint of a specialized service aimed at preventing and treating MDD. For instance, the 'Healthy China 2030' initiative called for enhancing the early detection and timely intervention for MDD. The 'Specialized Service Program for Depression Prevention and Treatment' emphasized the necessity of introducing early diagnostic protocols, standardizing treatment modalities, and intensifying intervention strategies particularly for pivotal cohorts such as children, adolescents and expectant and postnatal mothers. To date, numerous general hospitals and mental health facilities across China have established expedited treatment centers for MDD, predominantly focusing on these cutting-edge treatment methods: electroconvulsive therapy (ECT), intravenous ketamine/esketamine, esketamine nasal spray, magnetic seizure therapy (MST), and Stanford Neuromodulation Therapy (SNT). The prompt alleviation of symptoms rapidly reduces patients' suffering, bolsters compliance and enhances overall quality of life (5).

Although the current mainstream rapid antidepressant methods encompass ECT, intravenous ketamine/esketamine, esketamine nasal spray, MST and SNT, ECT remains the predominant and favored approach for swift antidepressant and anti-suicidal interventions in China. In alignment with the objective of rapid antidepressive treatment, each of these major techniques demonstrates distinct advantages: ECT and MST work through immediate neuromodulation, intravenous ketamine/esketamine and esketamine nasal spray act via N-methyl-D-Aspartate (NMDA) receptor antagonism, and SNT operates by regulating biological rhythm. Taken together, these techniques constitute the multimodal intervention framework employed in China's rapid depression treatment centers. ECT is particularly applicable to patients with MDD in special populations, including adolescents, elderly individuals, and patients in perinatal period (6). Currently, research and clinical application of intravenous ketamine/esketamine, esketamine nasal spray, MST, and SNT are predominantly administered to adult MDD patients, with insufficient evidence to support their widespread use in the above-mentioned special populations.

This policy and practice review examined the localization and clinical implementation of these rapid antidepressant techniques in China, with dual emphasis on exploring service delivery shortcomings and prioritizing future research needs. Sharing the experiences of China in rapid antidepressive treatment using these techniques (e.g., ECT, intravenous ketamine/esketamine, esketamine nasal spray, MST, SNT) could offer valuable reference models and strategies for other nations and regions.

2 Methods

As a policy and practice review focusing on experiences in implementation rather than synthesis of evidence, this work did not employ any formal search strategy or inclusion/exclusion criteria for eligibility.

3 Actionable recommendations

3.1 Electroconvulsive therapy

ECT has a history of over 80 years as one of the most efficient interventions for MDD. Its use is more prevalent in China than in most other countries (7), with China probably having the largest cohort of patients receiving ECT globally (8). ECT is used as a pivotal clinical recourse for patients with schizophrenia, bipolar disorder and MDD, especially those resistant to conventional therapies and displaying high suicide risks (9). Because of its relatively moderate efficacy rate of approximately 60.0% (10) and known neurocognitive side effects (11), there are ongoing efforts aiming at refining the clinical application of ECT from various perspectives, including anesthetic selection, stimulation dosage, electrode placement and apnoeic oxygenation.

Concerning anesthetic practices, the combined use of intravenous ketamine/esketamine or their standalone administration emerged as prevalent strategies to enhance ECT's effectiveness. A recent randomized controlled trial (RCT) showed that intravenous esketamine as an anesthetic for ECT yielded superior antidepressant outcome with comparable neurocognitive effects compared to ECT with propofol anesthesia, with higher MATRICS Consensus Cognitive Battery scores in processing speed, working memory, verbal learning, and visual learning (12). Moreover, a meta-analysis suggested that combining intravenous ketamine with other anesthetics may have transient advantages in ameliorating depressive symptoms during the initial phase of ECT (13).

Recent clinical observations have highlighted the significant and immediate antidepressant impact of low-dose ECT (near the seizure threshold) in MDD (14), a finding confirmed by a RCT in China (15). Even in cases of treatment-resistant depression (TRD), nonconvulsive electrotherapy (NET) has demonstrated a comparable therapeutic outcome, yielding response rates as high as 60.0% (16). A systematic review indicated that NET's antidepressant efficacy for MDD is similar to ECT, albeit with notably lesser neurocognitive impairments (17). However, the current Chinese Expert Consensus on ECT does not mention NET for routine clinical application (6). As for the knowledge of, and attitude towards ECT, a recent study found that only 55.4% and 37.0% of caregivers and patients received any pre-treatment education, respectively (18); caregivers were provided with significantly more comprehensive ECT information than patients.

Significantly more caregivers than patients regarded ECT as effective (71.7% versus 53.3%; $p < 0.05$) and approximately half of both groups considered it safe (18).

Furthermore, a novel approach termed hybrid-ECT has been introduced by Rong et al., wherein MDD patients undergo an initial trio of ECT sessions followed by NET instead of continuing standard sessions of ECT (19). Hybrid-ECT may retain ECT's early treatment benefits while capitalizing on NET's advantage of minimizing side effects in the longer term. A RCT assessing hybrid-ECT for MDD showed equivalent antidepressant effects to standard ECT but with fewer adverse events including neurocognitive impairment (20).

Innovations in electrode placements for ECT, ranging from traditional setups like right unilateral, bitemporal, and bifrontal to newer configurations, such as focal, electrically-administered seizure therapy (21), left anterior-right temporal (22), left unilateral (23) and others, have emerged. However, comprehensive research on these novel electrode placements remains relatively scarce, with some (e.g., fronto-frontal, fronto-parietal, temporo-parietal) currently in the computational modeling phase (24).

Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) is a secure, effective new technique now integrated into ECT procedures (25–27). THRIVE facilitates oxygen delivery with features like operational simplicity, temperature stability and humidity control, thereby reducing the risk of gastric reflux and extending safe apnea durations. Patients have reported positive experiences, propelling THRIVE into widespread adoption in general anesthesia practices in recent years (28).

3.2 Intravenous ketamine/esketamine and esketamine nasal spray

Ketamine, a racemic mixture comprising both S- and R-enantiomers, and esketamine, the purified S-enantiomer, share a core mechanism as NMDA receptor antagonists, inducing rapid synaptic plasticity via glutamate surge, alpha-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor activation, and downstream brain-derived neurotrophic factor (BDNF)/mammalian target of rapamycin signaling (29). The key difference lies in esketamine's higher affinity for NMDA receptors due to its S-isomer configuration, potentially enhancing its antidepressant potency at lower doses. While both drugs produce rapid-onset effects (within hours), ketamine's metabolites (e.g., hydroxynorketamine) may contribute to its antidepressant action through non-NMDA pathways, whereas esketamine's effects are more directly tied to NMDA blockade (30, 31). Intravenous ketamine has been approved for use as a sedative, analgesic and general anesthetic since 1970 by the Food and Drug Administration (FDA) (32). Intravenous administration of ketamine/esketamine at sub-anesthetic doses has demonstrated rapid antidepressant and anti-suicidal effects in patients with MDD (33, 34). Both single and repeated doses of ketamine have shown robust antidepressant effect in patients with MDD (35). While the rapid treatment centers for depression in China have adopted this technology and achieved promising results (36–39), intravenous ketamine/esketamine still lack approval for antidepressant indications by the China Food and Drug Administration.

Various methods of administering ketamine/esketamine such as intravenous, intranasal, oral, intramuscular, and subcutaneous have been tried (40). However, there have been no RCTs directly comparing the antidepressant efficacy of different routes of ketamine/esketamine administration. Intravenous and intranasal administration are the most common therapeutic routes. Kheirabadi et al.'s study suggested that oral and intramuscular ketamine may have equivalent antidepressant and greater anti-suicidal effects compared to ECT but with fewer adverse neurocognitive effects (41). A meta-analysis of three RCTs found a significant antidepressant effect of oral ketamine compared to placebo (42). Repeated subcutaneous ketamine injections were found well tolerated and more effective than midazolam, with acute adverse dissociative and other psychopathological symptoms resolved within 2 hours (43). Midazolam is rarely used for anaesthesia for ECT in most Western countries, but not in China (44). Importantly, plasma levels from subcutaneous ketamine administration are comparable to those of intravenous and intramuscular ketamine, but with minimal side effects, suggesting that subcutaneous ketamine is a practical and effective treatment approach (45). In 2019, the FDA approved esketamine nasal spray in combination with oral antidepressants for treating adults with TRD (46) and in 2020, for treating adults with MDD and acute suicidal ideation or behavior (47). In 2023, the China Food and Drug Administration approved it for the same uses in China as in the USA, although its application remains limited. According to the clinical application guidance for esketamine in China (48), intravenous esketamine (0.2-0.4 mg per kilogram of body weight over 40 minutes) can be used for the rapid treatment of MDD. It has been suggested that combining two drugs with different neurochemical pathways can have a synergistic effect, resulting in a faster and stronger antidepressant action (49). By combining ECT with intravenous ketamine/esketamine, a few psychiatric hospitals established an ultra-rapid antidepressant center in 2024. However, the promotion and utilization of intravenous ketamine/esketamine and esketamine nasal spray for MDD in China are still suboptimal (49).

3.3 Magnetic seizure therapy

MST delivers high-intensity magnetic stimulation to induce therapeutic epileptic seizures in specific areas of the brain's vertex in patients with MDD aiming to ameliorate depressive symptoms. Compared to ECT, MST-induced seizures are more localized, potentially resulting in fewer neurocognitive side effects and quicker recovery (50) and as such, MST is viewed as a plausible alternative to ECT (51). Capitalizing on its advantageous profile of reduced neurocognitive side effects and comparable antidepressant efficacy to ECT (52), a team at Beijing Anding Hospital of Capital Medical University, have adopted an accelerated MST protocol termed daily MST, demonstrating rapid antidepressant effects (53). MST has been

emerging as a novel treatment method in clinical practice, showcasing significant antidepressant efficacy in China (54, 55).

The pathomechanism underlying MST is still not well elucidated. Neuroimaging studies utilizing positron emission tomography/computer tomography scans have revealed post-treatment increases in metabolism in the basal ganglia, orbitofrontal cortex, medial frontal cortex, bilateral frontal cortex and dorsolateral prefrontal cortex, alongside a decrease in the left striatum (56, 57). Discrepancies in brain activation within the ventral anterior cingulate have been noted between MDD responders and non-responders (56). Resting-state functional magnetic resonance imaging (fMRI) and structural MRI studies have indicated enhanced functional connectivity between the subgenual anterior cingulate cortex (sgACC) and the parietal cortex following MST treatment, correlating positively with clinical improvement. Changes in grey matter volume have been observed in the bilateral parietal cortex but not associated with treatment outcomes (58). Moreover, MST has been shown to selectively modulate brain network dynamics for therapeutic benefits (59–61) and to enhance aperiodic neural activity linked to increased neural inhibition (62). In terms of neuroplasticity, MST can boost neuroplasticity in excitatory and inhibitory circuits originating from the left dorsolateral prefrontal cortex (DLPFC), and it also diminishes long-interval cortical inhibition over the right frontal cortex and induces neuroplastic changes in the frontal cortex, possibly through long-term potentiation - like mechanisms (63). Furthermore, MST can facilitate the central motor pathway elevating motor cortex excitability (54). These findings suggest a potentially shared neural mechanism of action between ECT and MST, underscoring MST's promise as an effective MDD treatment, particularly for non-responsive or patients intolerant to conventional antidepressants. Nonetheless, the mechanism of action of MST warrants further investigation, with additional clinical trials to validate its efficacy and safety. Given its minimal impact on neurocognitive function, MST holds promise as a rapid antidepressant modality.

3.4 Stanford Neuromodulation Therapy

Traditional transcranial magnetic stimulation (TMS) is imprecise to stimulate localized targets (64), it demonstrates modest efficacy (65), and requires long intervention periods (e.g., 37.5 minutes per session, 5 sessions weekly spanning 4–6 weeks) (66). In recent years, numerous optimization strategies for TMS have emerged, including theta burst stimulation (TBS) (67) and deep TMS (68). Accelerated intermittent TBS (aiTBS), a variant of TBS involving multiple sessions distributed across several days has gained widespread clinical utilization, reducing the treatment duration and total impulse count and demonstrating swift antidepressant and anti-suicidal effects in MDD (69, 70).

Another TBS form, SNT, has also exhibited rapid antidepressant effects (71). Notably, two open-label studies and one RCT have indicated a remission rate of approximately 90.0%, even in treatment-resistant patients, without significant adverse events (72–74). A few hospitals in China offer original Stanford protocol for MDD (75–77). The standard SNT protocol includes: 1) the adoption of an efficient repetitive TMS form, known as iTBS; 2) implementation of multiple iTBS sessions daily at optimally spaced intervals; 3) the application of a higher cumulative pulse dose of stimulation; and 4) personalized targeting for stimulating the left DLPFC to the sgACC circuit (72). However, in the absence of functional connectivity-guided targeting in most hospital settings, clinicians typically resort to standard aiTBS approaches (69, 78). Moreover, the evidence supporting SNT predominantly derives from Caucasian populations, leaving the efficacy and safety of these parameters in Asians still uncertain. Further investigations are warranted to ascertain the occurrence of treatment-emergent (hypo)mania in MDD and bipolar depression patients at intensified and concentrated treatment doses administered with SNT.

4 Discussion

4.1 Clinical/procedural issue

China's experience in implementing rapid treatment for depression may provide valuable insights for other nations seeking to establish such services. Specifically, clinicians in China have developed innovative modifications to ECT, pioneered accelerated MST protocols. A unique aspect involves close collaboration between psychiatrists and anesthesiologists to facilitate efficient treatment delivery. For resource-limited settings where SNT is impractical, aiTBS may serve as a viable alternative, demonstrating comparable antidepressant efficacy. These adaptations highlight how context-specific innovations could enhance accessibility to rapid antidepressant interventions across diverse healthcare conditions. The optimal therapeutic dosage of intravenous ketamine/esketamine and esketamine nasal spray may vary across different countries and regions. For instance, the commonly used dose of intravenous ketamine in China is 0.5 mg per kilogram of body weight administered over 40 minutes (79), with adjustments required based on individual patient factors and local clinical guidelines.

To date, China has established specialized management and treatment programs for patients with severe mental disorders, incorporating regular follow-up visits, treatment assistance, and rehabilitation guidance, with particular emphasis on integrated whole-course disease management services (80). However, such comprehensive programs have not yet been systematically implemented for patients with MDD. This service gap could lead to suboptimal treatment adherence following acute-phase therapy, insufficient rehabilitative support, and ultimately hinders patients' successful social reintegration.

Several factors limit the widespread use of intravenous ketamine/esketamine and esketamine nasal spray in China. First, as a psychotropic anesthetic, intravenous ketamine/esketamine and esketamine nasal spray is strictly regulated in China and must be administered under medical supervision in designated medical facilities. This strict regulation restricts its use. Furthermore, China currently lacks a formal expert consensus or guidelines on

intravenous ketamine/esketamine and esketamine nasal spray therapy for patients with MDD, thereby failing to establish standardized protocols for off-label use, signing of informed consent, scheduling of intravenous ketamine/esketamine and esketamine nasal spray, risk assessment, systematic adverse effect evaluation using validated rating scales (81), and longitudinal monitoring requirements. Considering the side effects of intravenous ketamine/esketamine and esketamine nasal spray and the distinctive characteristics of adolescent brain development and its susceptibility to drug reactions, the utilization of intravenous ketamine/esketamine and esketamine nasal spray in adolescents needs more rigorous evaluation and monitoring. Second, it is still unknown whether intravenous ketamine/esketamine and esketamine nasal spray have addictive properties as an adverse effect of the treatment. While the use of intravenous ketamine/esketamine and esketamine nasal spray in China is restricted to medical institutions under direct supervision of healthcare professionals, a policy designed to minimize abuse potential, significant gaps remain in treatment monitoring. The lack of a centralized tracking system allows patients with MDD to seek treatment from different hospitals during a short period without restrictions, which raises serious concerns about potential abuse. Patients with addictive tendencies in China must undergo treatment in drug rehabilitation centers. Fear of addiction and adverse dissociative and other psychopathological symptoms have led some MDD patients to prefer other antidepressant interventions. The long-term safety of intravenous ketamine/esketamine and esketamine nasal spray requires further verification. Finally, the cost of esketamine nasal spray is significantly higher than most other antidepressants and limited medical insurance coverage limits its widespread use in China.

At present, MST lacks an independent fee code within the Chinese medical insurance system. Several hospitals either adhere to the billing standards of TMS or ECT or offer free treatment to MDD patients, thereby hindering the dissemination and utilization of MST. Without formal insurance coverage, most hospitals lack incentives to invest in MST equipment, and patients usually face prohibitive out-of-pocket costs, limiting accessibility to MST despite its therapeutic potential. Moreover, the considerable size and high cost of MST equipment impedes its widespread adoption and application. Several key challenges must be addressed before MST can be established as a viable ECT alternative. First, further research is needed to optimize stimulus parameters, including location and frequency, for treating major mental disorders. Second, while the restricted stimulation range of MST aids in investigating treatment mechanisms, future studies should comprehensively explore these mechanisms, encompassing neurotransmitter activity of, for instance,5-hydroxytryptamine, norepinephrine, and dopamine, neuroplasticity (e.g., BDNF), neuroendocrine functions (e.g., hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-thyroid axis, and hypothalamic-pituitary-gonadal axis), and neuroimaging (e.g., diffusion tensor imaging, voxel-based morphometry, and magnetic resonance spectroscopy). This approach will yield valuable insights for shaping future treatment strategies.

4.2 Comparisons of rapid antidepressant treatments

A recent meta-analysis of six RCTs comparing the efficacy and safety of ECT with ketamine revealed no significant disparity between the two treatments (82). Conversely, another meta-analysis (83) concluded that ketamine, regardless of its administration route, surpassed ECT in effectiveness for MDD patients. Despite the rapid antidepressant effects of these methods, there is a relative dearth of head-to-head RCTs directly comparing them, for instance, ECT versus SNT. It is essential to take into account that ketamine and esketamine can be delivered by various routes, with differences in drug absorption, distribution, metabolism and excretion among them. Also, it is crucial to discern the variances in rapid antidepressant efficacy between ECT and ketamine/esketamine based on different administration routes (84, 85).

While ECT is sometimes combined with intravenous ketamine/esketamine for prompt antidepressant care, the optimal order, interval and frequency of ECT and intravenous ketamine/esketamine administration remain uncertain necessitating further exploration. Establishing a nationwide monitoring network to document the frequency of intravenous ketamine/esketamine and esketamine nasal spray administration in MDD patients and monitor potential addiction risks is imperative.

Regarding ECT versus MST, a meta-analysis of four RCTs (52) and a recent RCT (86) consistently demonstrated that MST's efficacy was comparable to that of ECT. ECT, the globally recommended gold standard for rapid antidepressant treatment (9), yields a lower efficacy rate than SNT (approximately 60.0% versus 90.0%), underscoring the urgent need for exploring the efficacy and safety of ECT in comparison to SNT.

Furthermore, investigating the optimal treatment parameters (e.g., frequency and dosage) of these rapid antidepressant methods for MDD and utilizing artificial intelligence (AI) to forecast changes in depressive symptoms would enable personalized decision-making in clinical practice. To implement AI-based symptom prediction in clinical settings, data requirements include structured clinical variables (e.g., sociodemographics, psychiatric history, comorbidities, prior treatments), standardized psychometric assessments, treatment response metrics (e.g., symptom reduction, remission), longitudinal follow-up data, and, ideally, biomarkers (e.g., neuroimaging and genetic markers), with assessments conducted by psychiatrists and clinical psychologists to ensure reliability (87).

4.3 General/systemic deficiencies

While a variety of rapid antidepressant therapies have been implemented in most cities of China, significant regional disparities persist in mental healthcare infrastructure. For instance, 12.3% of county-level districts lack mental health institutions at all and 31.1% have no psychiatric beds; these deficiencies are concentrated predominantly in the central and western regions of China. Western China demonstrates particularly obvious resource gaps,

having approximately 4-fold fewer open psychiatric beds, psychiatrists, and psychiatric nurses compared to central regions, and 7-11 fold fewer than eastern regions (88). Furthermore, less than 30.0% of mental health institutions nationwide have established psychiatric rehabilitation services, with 66.4% providing rehabilitation services exclusively for inpatients (88). This severely inadequate rehabilitation infrastructure fails to meet service demands, particularly for community-dwelling patients requiring continued care.

There are also significant disparities in access to MDD treatment between rural and urban areas in China. In rural regions, only 5.1% of patients with MDD received any healthcare treatment, compared to 8.9% in urban areas (89). This gap exists mainly due to fewer mental health facilities and lower incomes for rural patients. Additionally, mental health services are mainly located in urban psychiatric hospitals, making travel and relative treatment costs prohibitive for rural patients.

4.4 Ethical issues

Informed consent to ECT for depression mandates full disclosure to the patients' primary guardian, including details on treatment principles, indications, efficacy, and risks. In cases that severe symptoms necessitate urgent ECT but guardians are unavailable, hospitals need to seek legal alternative consent following local regulations. Due to cultural norms emphasizing familial involvement and current and past sociocultural dynamics, most depression patients in China usually rely on family caregivers. However, the overriding decision-making authority often retained by relatives compromises patient autonomy. This situation is not unique to China, patients' autonomy is also compromised in Western societies. In Western contexts, the guardian (if appointed) and the court typically give permission to proceed with ECT, rather than the family, although the family's viewpoint is taken into account. This highlights that China's informed consent model, influenced by its specific legal and cultural context, may not be directly applicable in other settings.

4.5 Limitations

This policy and practice review has several limitations. First, it did not fully frame the findings as a comprehensive report on the development, implementation, and evaluation of rapid treatment centers for depression in China. Second, while implementation science frameworks have been widely applied in health services research, their use in psychiatry, especially with respect to these rapid antidepressant treatment strategies, remains notably limited in China. Future research should apply implementation science frameworks to bridge the gap between evidence-based interventions and routine clinical practice, thereby establishing an all-inclusive implementation model.

5 Conclusion

This policy and practice review provides a comprehensive examination of rapid treatment centers for depression in China focusing on the constructive reflections and transnational implications of the following rapid antidepressant therapies: ECT, intravenous ketamine/esketamine, esketamine nasal spray, MST, and SNT. Based on the findings of this policy and practice review, we propose the following: (1) for depressed patients with suicidal risk, ECT and esketamine nasal spray are preferentially recommended as first-line rapid antidepressant treatment; (2) to create a national registry to monitor intravenous ketamine/esketamine and esketamine nasal spray utilization while ensuring safety compliance. Although numerous evidence-based rapid treatment centers for MDD have been established or are currently under development across the country, the following concerns should be addressed in the future: (1) to assess the long-term safety, addictive properties, and neurobiological consequences of intravenous ketamine/esketamine and esketamine nasal spray in treating MDD; (2) to evaluate whether MST could serve as a viable alternative to ECT for rapid antidepressant effects in MDD; (3) to evaluate the efficacy, safety, and acceptability of standardized SNT protocols across China's diverse clinical settings to establish locally optimized treatment parameters; (4) to determine which rapid antidepressant interventions have the most effective antidepressive and anti-suicide outcomes; (5) to enhance the clinical applicability of these rapid antidepressant interventions in bipolar depression or special populations (e.g., adolescents and perinatal women).

Author contributions

Z-MS: Writing – original draft. X-BH: Writing – review & editing. Y-LZ: Writing – review & editing. Y-PN: Writing – review & editing. GSU: Writing – review & editing. Y-TX: Writing – review & editing. WZ: 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.

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