PROTOCOL COVER PAGE

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Artificial Intelligence–Assisted Internet-Based Mindfulness Intervention for Emotional Distress: Protocol for a Randomized Controlled Trial on Long-Term Outcomes and Cost-Effectiveness

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Short title: AI-Assisted Mindfulness Intervention in Emotional Distress

Abstract

Background: Common emotional disorders, such as anxiety and depression, have become major contributors to the global burden of disease. However, current mental health service systems still tend to emphasize treatment over prevention, and there remains a lack of long-term, scalable, and economically evaluated digital interventions for individuals with subclinical emotional distress. Internet-based Mindfulness Intervention for Emotional Distress (iMIED) offers an accessible, scalable, and low-cost approach for early intervention, but its long-term outcomes and cost-effectiveness have yet to be systematically established. **Objective:** This study aims to evaluate the long-term outcomes, cost-effectiveness, and cost-utility of an artificial intelligence-assisted internet-based mindfulness intervention (iMIED) among individuals with subclinical emotional distress through a two-year randomized controlled trial. It also seeks to explore its potential psychological mechanisms, differential preventive effects, and feasibility and acceptability in real-world settings. **Methods:** This study is an assessor-blinded, parallel-group, two-arm randomized controlled trial using a superiority framework. Eligible participants aged 18-65 years will be randomly assigned in a 1:1 ratio to either the iMIED intervention group or the control group. The intervention group will receive a 49-day AI-assisted online mindfulness self-help intervention, while the control group will have access to usual mental health resources. The primary outcomes are anxiety and depressive symptoms, assessed using the Generalized Anxiety Disorder-7 (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9), respectively. Secondary outcomes include asymptomatic remission, reliable deterioration, healthcare resource utilization, quality of life, cost-effectiveness, cost-utility, resilience, mindfulness, perceived stress, life satisfaction, sleep status, and overall anxiety and depression severity and impairment. Exploratory outcomes include engaging in life, distress tolerance, excessive emotional behavior, cognitive flexibility, AI interaction behavioral indicators, and adverse events. Assessments will be conducted at baseline, Weeks 3, 5, and 8, and at 3, 6, 12, 18, and 24 months post-intervention. **Conclusion:** This study will provide evidence on the long-term efficacy and health economic value of digital early intervention for individuals with subclinical emotional distress, and will offer both theoretical and practical support for the

implementation of AI-assisted psychological interventions in public health systems.

Keywords: artificial intelligence-assisted intervention; internet-based mindfulness intervention; emotional distress; subclinical anxiety and depression; randomized controlled trial; long-term effectiveness; cost-effectiveness; digital mental health; prevention; mindfulness intervention

1. Background

The prevalence of common mental disorders, including anxiety and depression, has continued to rise and has become one of the leading contributors to the global burden of disease . However, current intervention research and clinical practice in the field of emotional disorders remain markedly skewed toward treatment rather than prevention, with substantial resources concentrated on individuals who have already developed moderate-to-severe clinical conditions. This tendency has been documented in multiple authoritative studies and policy reports. The World Health Organization (WHO), in its 2022 World Mental Health Report, explicitly noted that nearly 50% of individuals with mental disorders worldwide do not receive timely intervention at the early stages of illness, resulting in worsening symptoms and greater treatment complexity . Such delayed intervention not only leads to poorer prognosis for affected individuals but also imposes a substantial economic burden on society.

In its 2023 strategic plan, the U.S. National Institute of Mental Health (NIMH) explicitly shifted its research focus upstream, emphasizing the need to strengthen research on quantifiable risk states and prodromal phases in order to advance truly preventive psychiatry . This strategic reorientation reflects a growing recognition of the limitations of current clinical models. Against this backdrop, early intervention strategies targeting subclinical or high-risk populations have become especially important. For example, a large network meta-analysis published in The Lancet in 2019 demonstrated that preventive psychological interventions delivered in schools and other community settings significantly reduced the risk of future anxiety and depression among children and adolescents . This study provides strong evidence supporting the advancement of the intervention window to earlier stages.

Emerging evidence further suggests that early intervention is not only clinically effective but also highly cost-effective. An investment case analysis of adolescent mental health in England showed that preventive and early intervention measures for individuals aged 10–19 years yielded substantially

higher health and economic returns on investment than treatment strategies targeting already affected populations . Evidence from specific high-risk populations further reinforces this conclusion. For instance, a 22-year prospective cohort study, the Dutch Bipolar Offspring Study, found that offspring of individuals with bipolar disorder already exhibited significant psychopathological risk during adolescence, underscoring the importance of early identification and intervention within a critical window of opportunity . Similarly, the large RADAR cohort study published in The Lancet Psychiatry demonstrated that cognitive behavioral intervention among community individuals with only mild depressive symptoms (PHQ-9 scores of 5–9) reduced the subsequent risk of developing major depression by 38% (hazard ratio (HR) = 0.62, 95% confidence interval (CI) 0.49–0.78) . Collectively, these findings point to a central conclusion: while the existing intervention model centered on moderate-to-severe clinical populations remains necessary, it is insufficient to address the growing global burden of emotional disorders. A strategic shift of research and clinical resources toward prevention and early intervention, particularly for individuals with subclinical symptoms and other high-risk groups, is a key pathway to improving population mental health and reducing long-term socioeconomic costs. This paradigm shift from disease treatment to health promotion and risk prevention has increasingly been regarded as a core direction for the future development of mental health services .

Subclinical populations generally refer to individuals with scores of ≥5 on the Patient Health Questionnaire-9 (PHQ-9) or the Generalized Anxiety Disorder-7 (GAD-7), but who do not yet meet formal diagnostic criteria. This group represents a critical window for intervention and has several advantages. First, treatment responsiveness appears to be better: subclinical cases receiving preventive cognitive behavioral therapy (CBT) show significantly faster initial reductions in overall symptoms and anxiety scale scores than clinical cases . Second, intervention effects can be substantial: a web-based self-help intervention for subthreshold depression, such as GET.ON Mood Enhancer, demonstrated a large between-group effect size after treatment (d = 0.69), with significant effects maintained at 6-month follow-up . Third, early improvement predicts better prognosis: among individuals with mild major depression, minor depression, or subsyndromal depression, early symptom improvement predicts final treatment outcomes . Fourth, low-intensity intervention is feasible: an eHealth platform that stratified management based on prognostic severity significantly improved PHQ-9 scores at 3 months,

demonstrating the short-term feasibility and benefits of low-intensity interventions for people with mild symptoms .

More importantly, early intervention may effectively prevent the progression of subclinical symptoms into full clinical disorders. Longitudinal evidence suggests that late-adolescent subthreshold depression predicts an elevated risk of major depression and suicidal behavior by age 25, indicating that early intervention may avert illness progression . Randomized controlled trials provide additional support. The internet-based prevention program CATCH-IT for adolescents with subthreshold depression or a history of depression showed that adolescents with subthreshold depression might experience fewer depressive episodes . Likewise, a multicenter randomized trial of a proactive eHealth intervention for individuals with subthreshold depression reported beneficial outcomes at 2-year follow-up , offering direct evidence for the long-term benefits of early intervention.

Against this backdrop, digital mental health interventions, particularly internet-based Mindfulness Intervention for Emotional Distress (iMIED), provide an accessible, scalable, and low-cost solution for early intervention among subclinical populations. Digital interventions can overcome geographical, financial, and stigma-related barriers associated with traditional face-to-face treatment, thereby making large-scale prevention feasible . Existing evidence suggests that iMIED yields significant improvements in anxiety, depression, stress, and sleep outcomes .

Nevertheless, several key gaps remain in the current literature. First, long-term follow-up data are severely lacking. Although short-term findings are promising, evidence regarding the long-term stability of digital interventions in subclinical populations remains scarce, and many trials report follow-up outcomes only up to 6 or 12 months . For example, the ICare Prevent study found small-to-moderate short-term reductions in subclinical anxiety and depression symptoms, but no average long-term effect at 12 months . Randomized controlled trials with follow-up periods of 2 years or longer are exceedingly rare, limiting evaluation of the durability of digital interventions.

Second, cost-effectiveness evidence is extremely limited. To date, only a small number of studies have conducted economic evaluations in specific areas such as post-traumatic stress disorder , whereas cost-effectiveness evidence for individuals with subclinical emotional distress remains largely absent. Given the finite nature of public health resources, clarifying the economic value of digital interventions

is essential for policy decision-making and large-scale implementation.

In light of these issues, the present study proposes a 2-year randomized controlled trial to systematically evaluate the long-term effectiveness and cost-effectiveness of iMIED in individuals with subclinical emotional distress, defined as PHQ-9 or GAD-7 scores ≥5. Specifically, the study aims to: (1) fill the gap in long-term follow-up evidence for digital mental health interventions; (2) provide the first cost-effectiveness analysis for individuals with subclinical emotional distress; and (3) generate high-quality evidence for preventive strategies centered on early identification and early treatment, thereby advancing the intervention window for emotional disorders, reducing disease burden, and improving public health outcomes.

2. Objectives

2.1 Primary Objective

The primary objective of this study is to evaluate, in a 2-year randomized controlled trial (RCT), the preventive effects of an AI-supported mindfulness self-help intervention (iMIED) in individuals with subclinical emotional distress, with particular focus on its effectiveness in reducing anxiety and depressive symptoms. Specifically, the study will compare the trajectories of anxiety and depressive symptoms over follow-up between participants receiving iMIED and those in the control group, and will further assess the potential preventive value of this intervention in subclinical populations. In this way, the study seeks to clarify the public health value of digital mindfulness intervention in reducing the risk of emotional disorders. The primary outcomes to be compared between the iMIED group and the control group are:

Anxiety symptom severity, measured by the Generalized Anxiety Disorder-7 (GAD-7)

Depressive symptom severity, measured by the Patient Health Questionnaire-9 (PHQ-9)

2.2 Secondary Objectives

Building upon the evaluation of iMIED in reducing the occurrence and progression of anxiety and depressive symptoms, the study further aims to assess its cost-effectiveness and cost-utility. Specifically, from a health economics perspective, this study will compare the iMIED group and the control group with respect to mental health service utilization, healthcare resource consumption, and

improvements in quality of life, and will calculate the Incremental Cost-Effectiveness Ratio (ICER) to evaluate the economic feasibility of the intervention within public health systems.

In addition, this study will explore the potential effects of iMIED on other important dimensions of mental health, including sleep quality, perceived stress, resilience, and life satisfaction, as secondary outcome indicators, in order to provide a more comprehensive assessment of its potential benefits for overall psychological well-being.

2.3 Exploratory Objectives

In addition to the primary and secondary objectives, the present study includes several exploratory aims to further deepen understanding of the mechanisms and target populations for iMIED.

First, the study will explore the psychological mechanisms underlying iMIED. Specifically, it will test whether engaging in life, distress tolerance, cognitive flexibility, and excessive emotional behavior mediate intervention effects, thereby examining the theoretical mechanisms proposed by the Psychopathology Diamond Model of emotional distress.

Second, to examine whether the preventive effects of iMIED differ across risk levels, the study will compare intervention effects between a higher-risk group and a lower-risk group, defined as PHQ-9 $\geq$10 or GAD-7 $\geq$10 versus PHQ-9 <10 and GAD-7 <10, respectively, in order to evaluate its potential role within the prevention framework.

Third, the study will explore the contribution of AI-assisted support in digital psychological intervention, including the relationships between chatbot interaction frequency, intensity of personalized feedback, and intervention effects, in order to evaluate the potential added value of AI in enhancing digital mental health intervention outcomes.

Fourth, the study will assess the feasibility and acceptability of iMIED in real-world settings, including adherence, completion rate, usage frequency, and participant satisfaction, to determine its scalability for large-population dissemination.

Fifth, subgroup analyses will be conducted to examine whether intervention effects differ across participants with different sociodemographic characteristics.

3. Methods

3.1 Study Design

This study is an assessor-blinded, parallel-group, two-arm randomized controlled trial (RCT) using a superiority framework to evaluate the long-term outcomes and cost-effectiveness of an AI-assisted mindfulness self-help intervention (iMIED) for the prevention of emotional distress. Specifically, the study will compare iMIED plus access to usual mental health resources with usual mental health resources alone in reducing the onset and progression of anxiety and depressive symptoms. Participants will be randomly allocated in a 1:1 ratio to either the iMIED intervention group or the control group.

A parallel-group design will be adopted. The intervention period will last 8 weeks, with assessments conducted at baseline, Week 3, Week 5, and Week 8, followed by post-intervention follow-up assessments at 3, 6, 12, 18, and 24 months, in order to evaluate both short-term and long-term effects. The trial will employ assessor blinding, meaning that the researchers responsible for outcome evaluation and data analysis will remain unaware of group allocation, thereby reducing assessment bias.

This study also has the characteristics of a pragmatic randomized controlled trial, as the intervention will be implemented in real-world settings to enhance the external validity of the findings in public health practice. The study will not only assess the effects of the intervention on anxiety and depressive symptoms, but will also examine, from a preventive perspective, rates of reliable deterioration and clinically asymptomatic remission.

Furthermore, the study will incorporate health economic methods to evaluate the cost-effectiveness and cost-utility of iMIED within mental health service systems, thereby exploring the potential for large-scale dissemination of digital psychological intervention.

The design, conduct, and reporting of this protocol will follow the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines , and will comply with reporting standards for randomized controlled trials.

3.2 Participants

The inclusion and exclusion criteria are as follows.

Inclusion criteria

Aged 18 to 65 years

PHQ-9 or GAD-7 score ≥5

Able to use a smartphone or other internet-enabled electronic device and possessing sufficient digital literacy to participate in the online intervention and complete follow-up assessments

Willing to participate and able to provide informed consent

Exclusion criteria

Current psychotic disorder or bipolar disorder

Current organic mental disorder, pervasive developmental disorder, severe cognitive impairment, or substance use disorder

Current suicide risk, defined as a score of ≥2 on Item 9 of the PHQ-9

Previous participation in a structured 8-week mindfulness course or the 49-day self-guided course developed by the Peking University Mindfulness Laboratory

3.3 Study Procedures

Participants will be publicly recruited through internet platforms. Recruitment information will be posted on social media, mental health-related websites, and online communities (e.g., Xiaohongshu and WeChat public accounts), together with a study registration link. All study procedures, including screening, informed consent, randomization, intervention delivery, and follow-up assessments, will be completed via an online research platform.

As shown in Figure 1, potential participants will first enter the study registration page through the recruitment link and read an introduction to the study, the eligibility criteria, and the study procedures. After understanding the study objectives, procedures, and potential risks and benefits, participants will be required to sign an electronic informed consent form online before proceeding to the screening process.

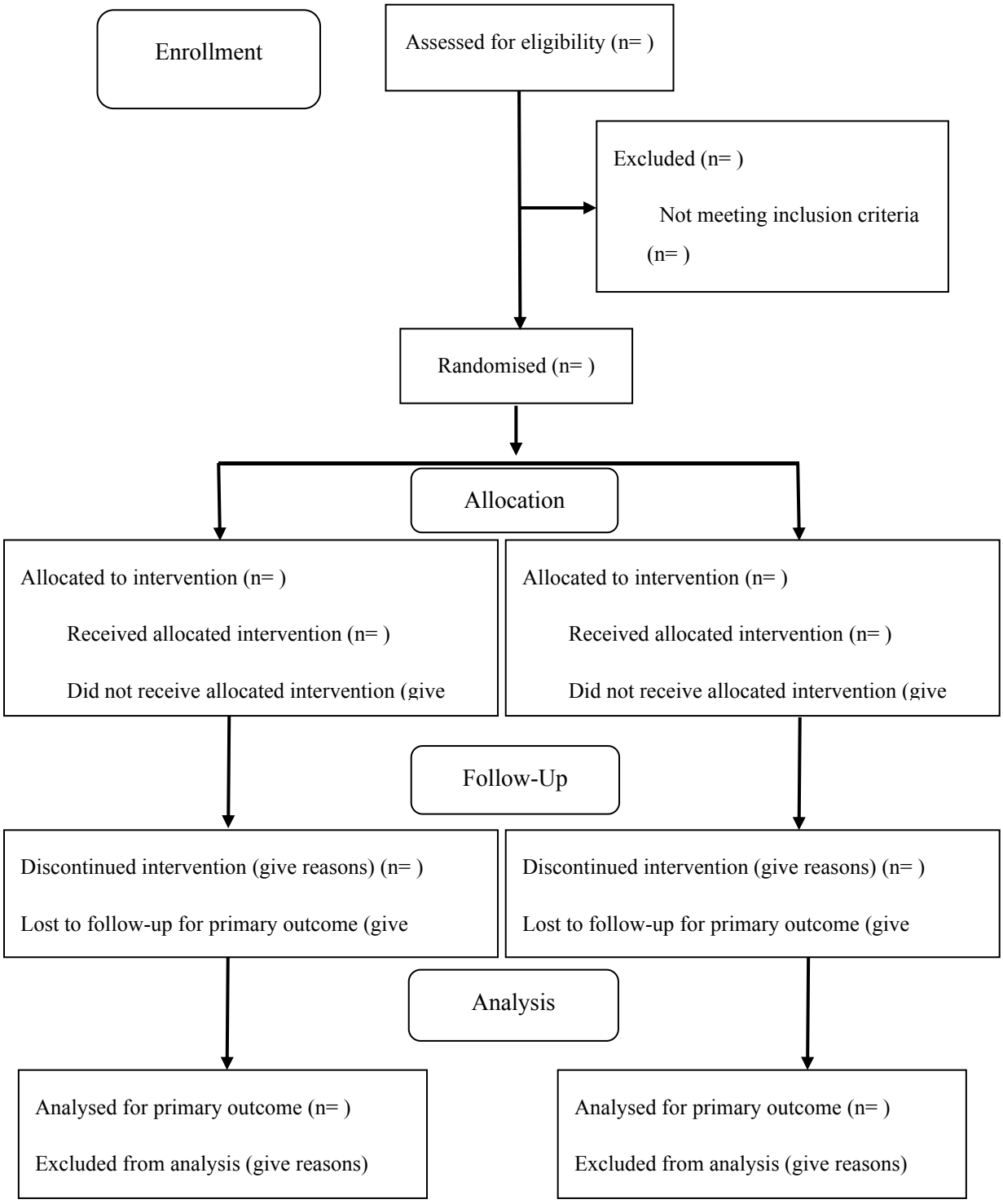
Participants will then complete a structured online screening questionnaire, which includes demographic information, mental health screening measures (e.g., GAD-7 and PHQ-9), and self-report items relevant to the inclusion and exclusion criteria. The system will automatically determine eligibility based on pre-specified rules. Individuals who meet the inclusion criteria and none of the exclusion criteria will be formally enrolled; those who do not meet eligibility criteria will automatically exit the study process.

After initial screening, eligible participants will enter the baseline assessment stage. Baseline measures will include anxiety symptoms (GAD-7), depressive symptoms (PHQ-9), and other relevant psychological indicators via self-report questionnaires. All questionnaires will be completed online and automatically recorded. Upon completion of the baseline assessment, the study platform will use a computer-generated random sequence to allocate participants in a 1:1 ratio to either the iMIED intervention group or the waitlist control group. Following randomization, participants will enter the intervention phase. The intervention group will receive the AI-assisted internet-based Mindfulness Intervention for Emotional Distress (iMIED) according to the study protocol; the control group will not receive this intervention during the trial period, but their autonomous use of usual mental health resources, including but not limited to medication and psychotherapy, will not be restricted during the waiting period.

Throughout the study, participants in both groups will complete online questionnaire assessments according to the study schedule. Self-report measures will be administered at baseline, Week 3, Week 5, Week 8, and at 3, 6, 12, 18, and 24 months after the intervention, in order to evaluate short-term and long-term outcomes. Participants will receive reminders via system notifications or email at each assessment point. All data will be collected and stored on the secure online platform Wenjuanxing. After the intervention group completes the 24-month follow-up, the waitlist group will have the opportunity to receive the same intervention.

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) 2025 Flow Diagram

Flow diagram of the progress through the phases of a randomized trial of two groups (i.e., enrollment, intervention allocation, follow-up, and data analysis)



3.4 Randomization and Blinding

3.4.1 Randomization

This study will use simple randomization to allocate participants in a 1:1 ratio to the iMIED

intervention group or the control group. The random sequence will be generated in advance by an independent researcher who will not be involved in participant recruitment, screening, intervention delivery, or outcome assessment, thereby ensuring the independence and objectivity of the randomization process.

Once participants complete the baseline assessment, the study platform will automatically assign them according to the pre-generated randomization sequence. Members of the research team will not have access to the sequence prior to allocation and will not be able to predict future assignments, thereby ensuring allocation concealment. Group assignment will only be released by the system when participants enter the intervention phase and will then be communicated to the relevant research personnel.

3.4.2 Blinding

Because this is a digital psychological intervention study, full blinding of participants and intervention providers is not feasible. Therefore, blinding procedures will be implemented primarily at the stages of data collection and statistical analysis to minimize potential bias.

(1) Assessor blinding

All assessments will be conducted by independent assessors who are not involved in screening, intervention delivery, or randomization, and who remain unaware of participants' group assignments. Prior to each assessment, participants will be instructed not to disclose their group allocation to the assessors, and assessors will be instructed not to ask participants about their group assignment. To systematically evaluate the quality of blinding, after each assessment the assessor will complete a blinding integrity check form, indicating whether they believe the participant belongs to the intervention group, the control group, or whether they are uncertain. This form will be collected after each assessment to quantify the integrity of blinding.

(2) Blinded data analysis

Primary outcome analyses will be conducted using coded group labels. Statistical analysts will remain unaware of the actual group assignments until the primary analyses have been completed.

(3) Documentation of unblinding events

Routine unblinding will not be performed. If a serious adverse event (SAE) occurs during the trial and the principal investigator determines that knowledge of a participant's group assignment is clinically necessary for safety management, single-case unblinding may be undertaken. All such unblinding events will be documented with respect to time, reason, and involved personnel, and will not affect blinding procedures for other participants.

3.5 Intervention

The Internet-based Mindfulness Intervention for Emotional Distress (iMIED) was developed on the basis of the Mindfulness Intervention for Emotional Distress (MIED) created by Xinghua Liu's research group. It is an evidence-based intervention designed for individuals experiencing emotional distress, and previous short-term studies have demonstrated its beneficial effects in alleviating emotional distress and accelerating symptom improvement in emotional disorders .

Delivered via the internet, the intervention is grounded in the Psychopathology Diamond Model proposed by Xinghua Liu's team . Based on advanced large language models, including Tencent Hunyuan and DeepSeek R1, and supported by an official MIED knowledge base comprising the "Mindfulness Practice" WeChat public account, supervision question-and-answer (Q&A) records, and other official materials produced by Xinghua Liu and colleagues, the team developed an AI assistant called the "MIED Mindfulness Assistant," along with a WeChat self-help mini-program. Together, these tools support participants' learning and practice over a 49-day continuous training period .

iMIED is theoretically grounded in an integrated biopsychosocial framework, with the Psychopathology Diamond Model serving as the core intervention framework. According to this model, the onset and maintenance of emotional distress are closely associated with four key psychological processes: insufficient engaging in life, low distress tolerance, excessive emotional behavior, and poor cognitive flexibility. In response to these mechanisms, MIED proposes four corresponding intervention strategies: increasing engaging in life, regulating distress tolerance, modifying emotional behavior, and enhancing cognitive flexibility, thereby facilitating improvement in emotional distress . See Figure 2.

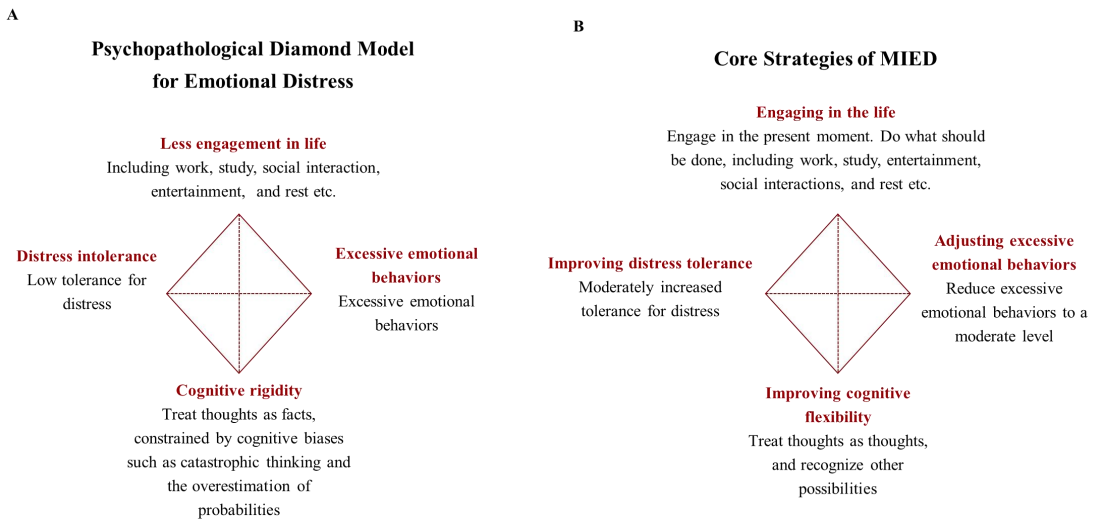


Figure 2. Psychopathological Model and Intervention Strategies of MIED

In practical implementation, the iMIED intervention lasts 49 days, with approximately 30 minutes of learning and practice each day. This includes around 15 minutes of psychoeducational video content and accompanying written learning materials, as well as approximately 15 minutes of audio-guided mindfulness practice. After each session, participants are required to record their daily practice experiences and reflections in the mini-program using a standardized check-in template. In addition, the accompanying AI support system, the "MIED Assistant," can respond to participants' questions in real time during practice, providing necessary clarification and guidance to help them better understand and complete the exercises. The detailed content of the 49-day check-in program is provided in **Appendix 1.**

iMIED has strong potential for clinical application. Its intervention duration is relatively brief (typically 49 days), onset of benefit is relatively rapid, and its four-dimensional pathological mechanisms derived from the biopsychosocial model correspond directly to four intervention strategies. This one-to-one correspondence makes the intervention target clear and closely links etiological understanding with operational techniques, thereby holding promise for more precise intervention and reduced relapse risk.

4. Outcomes

4.1 Primary Outcomes

The primary outcomes are changes in anxiety and depressive symptom severity, assessed using the Generalized Anxiety Disorder-7 (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9), respectively. Both scales are widely used self-report instruments with good reliability and validity for assessing the severity of anxiety and depressive symptoms over the past two weeks. The primary analysis will compare between-group differences in changes in PHQ-9 and GAD-7 scores across the intervention and follow-up periods .

4.2 Secondary Outcomes

(1) Categorical clinical outcomes

In addition to continuous outcomes, a series of categorical clinical outcome indicators will be constructed to assess the effects of the intervention in terms of clinical improvement, symptom recovery, and potential adverse outcomes. These indicators will be derived in accordance with conventional outcome reporting standards and will be based on changes in PHQ-9 and GAD-7 scores.

I. Asymptomatic remission

A more stringent outcome, asymptomatic remission, will be defined as PHQ-9 <5 and GAD-7 <5. These thresholds correspond to the minimal symptom range on the two scales and indicate the virtual absence of clinically meaningful emotional distress .

II. Reliable deterioration

To evaluate potential adverse effects of the intervention, symptom deterioration indicators will also be calculated. Reliable deterioration will be defined as an increase exceeding the reliable change threshold, namely PHQ-9 increase ≥6 points or GAD-7 increase ≥4 points. These indicators will be calculated separately for PHQ-9 and GAD-7 .

Secondary outcomes will also include the economic value of iMIED in public health systems, including both cost-effectiveness and cost-utility. Specifically, the study will comprehensively evaluate the economic value of iMIED relative to the control group by integrating intervention costs, healthcare resource utilization, and changes in quality of life.

(2) Healthcare resource utilization

Healthcare resource utilization will be assessed using the Treatment Inventory of Costs in Patients with Psychiatric Disorders (TIC-P). TIC-P is a widely used health economic instrument in mental health research for assessing psychiatric healthcare use and societal costs, including service utilization, medication use, and productivity losses . In this study, TIC-P will be used to record healthcare resource consumption during the trial, including outpatient visits, medication costs, and other healthcare-related expenditures. To capture healthcare utilization more comprehensively, a self-developed healthcare utilization questionnaire will also be administered.

(3) Health-related quality of life

Quality of life will be assessed using the EuroQol 5-Dimension 5-Level (EQ-5D-5L). This is one of the most widely used instruments in health economic evaluation for measuring health-related quality of life and includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with five response levels . The health utility values derived from EQ-5D-5L will be used to calculate Quality-Adjusted Life Years (QALYs) for cost-utility analysis .

(4) Incremental cost-effectiveness ratio

Based on intervention costs, healthcare resource utilization, and changes in quality of life, the incremental cost-effectiveness ratio (ICER) of iMIED relative to the control condition will be calculated. ICER will be derived by comparing cost differences and effect differences between groups and will be used to evaluate both cost-effectiveness and cost-utility within the public health system . Sensitivity analyses will also be conducted to assess the robustness of the economic results .

(5) Other psychological health indicators

To further explore the potential impact of iMIED on broader dimensions of mental health, the study will assess a number of additional indicators, including resilience, perceived stress, life satisfaction, and sleep status. These variables will be analyzed as continuous outcomes.

A. Resilience

Resilience will be measured using the Connor-Davidson Resilience Scale (CD-RISC), one of the most widely used instruments for assessing the ability to cope with stress and adversity, with good reliability

and validity .

B. Perceived stress

Perceived stress will be measured using the Perceived Stress Scale (PSS), a widely used instrument that assesses individuals' subjective appraisal of stress over a recent period .

C. Life satisfaction

Life satisfaction will be measured using the Satisfaction With Life Scale (SWLS), which assesses individuals' cognitive evaluation of their overall life circumstances and has sound psychometric properties .

D. Sleep status

Sleep status will be assessed using the Insomnia Severity Index (ISI), a brief 7-item self-report scale widely used in clinical and digital health research to assess the severity of insomnia symptoms and their impact on daily functioning .

(6) Related symptoms and functional impairment

In addition, to more comprehensively evaluate the effects of iMIED on emotional distress-related symptoms and functional impairment, this study will include the Overall Anxiety Severity and Impairment Scale (OASIS) and the Overall Depression Severity and Impairment Scale (ODSIS) as secondary outcome measures. The OASIS is a 5-item self-report scale that assesses the frequency and severity of anxiety symptoms, avoidance behavior, and related functional impairment over the past week. Total scores range from 0 to 20, with higher scores indicating greater overall anxiety severity and associated functional impairment. The scale has demonstrated good reliability and validity . The ODSIS is likewise a 5-item self-report scale that assesses the frequency and severity of depressive symptoms, avoidance behavior, and their impact on social and daily functioning over the past week. Total scores range from 0 to 20, with higher scores indicating greater overall depression severity and functional impairment. It has shown good psychometric properties in both clinical and non-clinical samples . In this study, both the OASIS and ODSIS will be analyzed as continuous variables to further assess the effects of the intervention on anxiety- and depression-related functional impairment and overall symptom burden.

(7) Mindfulness

Mindfulness will be assessed using the Five Facet Mindfulness Questionnaire (FFMQ). The FFMQ measures trait mindfulness across five dimensions: observing, describing, acting with awareness, nonjudging of inner experience, and nonreactivity to inner experience. It is one of the most widely used instruments in mindfulness research and has demonstrated good reliability and validity . In this study, the total FFMQ score and its subscale scores will be analyzed as exploratory continuous variables.

4.3 Exploratory Outcomes

Exploratory outcomes are intended to further clarify the mechanisms of action of iMIED, its suitable target populations, and the role of AI support in the intervention.

(1) Psychological mechanism variables

To test the theoretical mechanisms proposed by the Psychopathology Diamond Model of emotional distress, the following psychological variables will be measured:

A. Engaging in life

The Engaging in Life Scale (ELS) will be used to assess the degree to which individuals engage in key life domains such as work, study, social interaction, and sleep, and is an important tool for evaluating levels of engaging in life .

B. Distress tolerance

Distress tolerance will be assessed using the Distress Tolerance Scale (DTS), which measures individuals' capacity to tolerate negative emotional experiences and their regulatory responses to emotional distress . In addition, the Discomfort Intolerance Scale (DIS) will be used to assess tolerance of unpleasant bodily sensations, which has been widely applied in anxiety disorder and emotion regulation research .

C. Excessive emotional behavior

The Excessive Emotional Behavior Scale (EEBS) will be used to assess excessive emotion-driven and avoidant behaviors under negative affective states, thereby providing a more comprehensive assessment of this psychological process . In addition, the Brief Experiential Avoidance Questionnaire

(BEAQ) will be used to further assess experiential avoidance as a core process .

D. Cognitive flexibility

Cognitive flexibility will be measured using the Cognitive Flexibility Inventory (CFI), which assesses individuals' ability to shift cognitive frameworks, generate alternative explanations, and adopt adaptive thinking strategies under stress .

These psychological variables will be incorporated into statistical models as potential mediators, and mediation analyses will be used to examine their role in the pathway linking iMIED to improvements in anxiety and depressive symptoms.

(2) AI interaction indicators

To evaluate the role of AI support in the intervention, the following behavioral data will be recorded: number of interactions with the AI assistant, number of personalized feedback responses, and daily duration of use. Associations between these variables and intervention outcomes will then be analyzed.

(3) Feasibility and acceptability indicators

To assess the scalability of iMIED in real-world settings, the following indicators will be measured: intervention completion rate, average usage frequency, participant adherence (proportion of exercises completed), and user satisfaction. Satisfaction will be measured using the Client Satisfaction Questionnaire (CSQ-8), an 8-item instrument assessing participants' overall satisfaction with the intervention service .

(4) Adverse Events

To evaluate the safety of the intervention, this study will record adverse events (AEs) and serious adverse events (SAEs) occurring during the study period. These events will be defined, documented, and reported in accordance with international clinical trial guidelines, and will be descriptively analyzed with respect to the time of occurrence, severity, relationship to the intervention, and outcomes, in order to comprehensively assess the safety and acceptability of iMIED .

4.4 Sample Size Calculation

Sample size estimation for this study is based primarily on the primary outcomes, namely between-group differences in changes in anxiety symptoms (GAD-7) and depressive symptoms (PHQ-9) over repeated follow-up assessments. Because the study uses a longitudinal repeated-measures design and plans to analyze group, time, and group × time interaction effects using linear mixed-effects models (LMMs), sample size estimation was conducted with reference to repeated-measures designs .

Based on prior internet-based psychological and mindfulness intervention studies, digital mindfulness interventions typically produce small-to-moderate effects on anxiety and depressive symptoms . To ensure a conservative estimate, the group × time interaction effect size was assumed to be Cohen's f = 0.12. A two-sided significance level of $\alpha = 0.05$ and statistical power of 0.80 were specified. The study includes 9 measurement time points: baseline, Week 3, Week 5, Week 8, 3 months, 6 months, 12 months, 18 months, and 24 months. Correlations between repeated measurements were assumed to be approximately 0.50. Based on these parameters, G*Power 3.1 estimated that a minimum sample size of approximately 306 participants would be required for the primary outcome analysis.

Given that the follow-up period extends to 24 months and internet-based intervention studies commonly experience attrition and declining adherence, an attrition rate of 40% was further incorporated into the sample size estimation . After adjustment, the required total sample size was approximately 510 participants. Taking both feasibility and statistical requirements into account, the study plans to enroll a final total of 550 participants, who will be randomized 1:1 to the iMIED intervention group and the control group, with approximately 275 participants per group.

4.5 Data Management

All questionnaire data will be collected online via the Wenjuanxing platform, which participants can access using mobile devices, and stored on its encrypted servers. Informed consent will be signed online through the same platform before the baseline assessment begins, and the relevant documents will be stored in the platform backend and accessible only to authorized research personnel.

The following additional data management procedures will be implemented:

(1) Data coding and de-identification

All personally identifiable information, such as names, telephone numbers, WeChat accounts, and other contact information, will be used solely for screening, study communication, and follow-up arrangements and will not be included in statistical analyses. During data analysis, only a randomly generated unique study ID will be retained. All study variables will be standardized according to a pre-defined data dictionary (e.g., PHQ9_total, GAD7_item3).

(2) Data quality control

Exported raw data will be checked by an independent research assistant for completeness and logical consistency, including screening for anomalies such as completion times shorter than 120 seconds or duplicate IP addresses. Any records flagged as suspicious will undergo secondary review.

(3) Data security and access management

A hierarchical data access management system will be used. A data manager designated by the principal investigator (PI) will be responsible for overall access control and authorization. Each batch-specific research assistant will have access only to the data for their assigned batch. All study data will be stored on encrypted servers and protected by password authentication; unauthorized personnel will not be able to access any raw or processed study data.

(4) Data version control

After data cleaning is completed, the dataset will be frozen and assigned a version number to ensure that all subsequent statistical analyses are performed on a fixed and traceable dataset version.

(5) Data retention and backup

All study data will be retained after trial completion in accordance with the minimum retention period required by national regulations. Automatic server backup mechanisms will be used to prevent data loss. Once the retention period has expired, all data will be destroyed centrally by the data manager.

4.6 Strategies to Improve Adherence to Study Assessments

Several measures will be adopted to improve adherence to study assessments.

First, before each assessment time point begins, research assistants will send multiple reminder messages to participants via the project WeChat group, for example, at the start of the assessment period, 3 days before the deadline, and 1 day before the deadline. If participants fail to complete the assessment on time, research assistants will contact them privately to understand the situation and provide necessary support.

Second, participants will receive compensation ranging from RMB 5 to RMB 40 for each completed assessment, to compensate them for their time and effort. If all assessments are completed as scheduled, participants may receive up to RMB 180 in total compensation.

4.7 Study Oversight and Management

This study compares an AI-assisted online mindfulness intervention for emotional distress (MIED) with a control condition in which participants have access to usual care resources. Participants in the control group may freely receive any form of treatment as usual (TAU), including pharmacotherapy, psychotherapy, or other interventions. The research team will impose no restrictions on whether treatment is received or on the type of treatment chosen, and will not participate in treatment decisions.

As this is a low-risk, non-invasive psychological intervention study, no independent Data Monitoring Committee (DMC) will be established. Consequently, no DMC-related issues regarding membership composition, independence, or conflicts of interest arise.

No interim analysis will be conducted, and no formal stopping rules are specified. No unblinded interim results will be generated or disclosed during the trial. If a serious adverse event potentially related to the psychological intervention occurs, the principal investigator will promptly report it to the ethics committee and consult with the committee regarding whether the trial should be paused or terminated. Medical problems unrelated to the study, such as adverse reactions to routine pharmacological treatment, will be managed according to usual clinical practice.

After trial completion, participants in the intervention group will no longer have continued access to the digital intervention program, but may continue to use usual care services. Participants in the usual

care group may voluntarily choose to receive the same mindfulness intervention after the trial ends.

5. Statistical Analysis

5.1 Overall Analytical Strategy

All statistical analyses will follow the intention-to-treat (ITT) principle, meaning that all randomized participants will be included in the final analyses regardless of whether they fully completed the intervention. This approach preserves the initial between-group balance achieved by randomization and reduces selection bias due to attrition or non-adherence . Continuous variables will be summarized as means and standard deviations or medians and interquartile ranges, while categorical variables will be presented as frequencies and percentages. Baseline characteristics will be compared descriptively between groups to assess post-randomization comparability, in accordance with reporting standards for randomized controlled trials .

Missing data will be handled under the Missing At Random (MAR) assumption (Little & Rubin, 2019). For the primary analyses, linear mixed-effects models (LMMs) will be used. These models rely on maximum likelihood estimation, can yield unbiased estimates in the presence of partially missing data, and make full use of all available observations . In addition, multiple imputation will be applied as a sensitivity analysis, and results before and after imputation will be compared to assess robustness . All statistical tests will be two-sided, with statistical significance set at $p < 0.05$.

5.2 Primary Outcome Analysis

The primary outcomes are longitudinal changes in anxiety symptoms (GAD-7) and depressive symptoms (PHQ-9). Continuous outcomes such as changes in GAD-7 and PHQ-9 scores will be analyzed using linear mixed-effects models. The models will include group (iMIED intervention vs. control), time (baseline, Week 3, Week 5, Week 8, 3 months, 6 months, 12 months, 18 months, and 24 months), and the group × time interaction as fixed effects, with participant included as a random effect (random intercept) to account for the correlation structure of repeated measurements.

The primary parameter of interest will be the group × time interaction, which will indicate whether symptom trajectories differ significantly between the intervention and control groups over follow-up. Model estimates, 95% confidence intervals, and p values will be reported. Where necessary, models will be adjusted for potential confounders such as age, sex, and baseline symptom severity.

5.3 Secondary Outcome Analysis

In addition to continuous outcomes, a series of categorical clinical outcomes will be constructed to assess symptom recovery and potential adverse outcomes. These indicators will be derived according to conventional outcome reporting standards and based on changes in PHQ-9 and GAD-7 scores.

(1) Asymptomatic remission

Asymptomatic remission will be defined as PHQ-9 <5 and GAD-7 <5, corresponding to the minimal symptom range on both scales and indicating the virtual absence of clinically meaningful emotional distress .

(2) Reliable deterioration

To assess potential adverse effects of the intervention, reliable deterioration will be calculated and defined as symptom increase beyond the reliable change threshold: PHQ-9 increase ≥6 points or GAD-7 increase ≥4 points .

All categorical outcomes will be reported as n/N (%), where the denominator is defined as all randomized participants who entered the study (the ITT population). This approach follows the demonstrated recovery principle, under which participants are considered not recovered unless there is explicit follow-up evidence showing recovery; this includes participants lost to follow-up.

Between-group differences in categorical outcomes will be analyzed using logistic regression models, with odds ratios (ORs) and 95% confidence intervals reported. Models will be adjusted a priori for baseline depression severity, baseline antidepressant use, and other relevant covariates. Sensitivity analyses will be conducted to examine the robustness of findings under different missing-data handling approaches and outcome definitions.

(3) Cost-effectiveness analysis

Cost-effectiveness analysis will be conducted from a societal perspective and will comprehensively evaluate both direct and indirect costs. Direct costs will include psychotherapy, psychiatric outpatient visits, pharmacological treatment, and other healthcare resource utilization; indirect costs will primarily include productivity loss associated with emotional distress. These data will be collected using the TIC-P and a self-developed healthcare utilization questionnaire . Total costs will be estimated using a bottom-up approach based on individual-level resource consumption data.

The health economic evaluation will include both cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). In the CEA, the main effectiveness outcome will be asymptomatic remission at 24-month follow-up, defined as PHQ-9 <5 and GAD-7 <5. By comparing the differences in costs and asymptomatic remission between the intervention group and the control group, the incremental cost-effectiveness ratio (ICER) will be calculated as ICER = ΔCost / ΔAsymptomatic Remission Rate, representing the additional cost required for each additional participant achieving asymptomatic remission.

In the CUA, health utility values will be obtained using the EQ-5D-5L with the Chinese value set. Linear interpolation will be used to estimate changes in health utility over the follow-up period, and QALYs will be calculated for each participant. The incremental cost-utility ratio (ICER = ΔCost / ΔQALY) will then be calculated to evaluate the cost-utility of the intervention in terms of health gains.

To assess uncertainty and robustness, 5,000 non-parametric bootstrap replications will be used to construct cost-effectiveness planes and cost-effectiveness acceptability curves (CEACs). If necessary, Seemingly Unrelated Regression (SUR) models will be used to jointly model costs and QALYs while adjusting for covariates such as age, sex, and baseline symptom severity. All costs and utilities will be discounted in accordance with health economic evaluation standards (e.g., annual discount rate of 3%), and final results will be reported from the societal perspective.

5.4 Additional Analyses

(1) Subgroup analyses

To explore potential heterogeneity in intervention effects across different populations, pre-specified exploratory subgroup analyses will be conducted. Subgroup variables will include baseline symptom severity (e.g., PHQ-9 and GAD-7 scores), demographic characteristics (e.g., sex and age strata), and adherence-related digital intervention factors (e.g., number of days using the mini-program). All subgroup analyses will be conducted by including a group × subgroup interaction term in the main model. Because these analyses are exploratory, the results will be used for hypothesis generation only and not as the basis for primary inference.

(2) Mechanism analyses

To explore potential mechanisms of AI-assisted online mindfulness intervention, exploratory analyses will be conducted on several mechanism-related variables.

First, the longitudinal trajectories of mechanism variables such as ELS, DTS, DIS, EEBS, BEAQ, CFI, and FFMQ will be analyzed to examine the effects of the intervention on key psychological processes.

Second, mediation analyses will be conducted using structural equation modeling (SEM) and related methods to evaluate potential mediating pathways linking intervention group to clinical outcomes such as PHQ-9 and GAD-7 through mechanism variables.

Third, moderation analyses will be conducted to test whether baseline variables, such as baseline FFMQ scores, influence the magnitude of intervention effects.

In addition, the study will explore the associative structure between mechanism variables and symptom indicators. To this end, longitudinal network analysis methods, including but not limited to cross-lagged panel networks, network intervention analysis, and time-varying longitudinal network models, will be used to analyze the temporal dynamic interactions between mechanism variables and clinical symptoms from a systems science perspective. By estimating temporal networks and contemporaneous networks, the study aims to identify core bridge nodes within the network. Network Comparison Tests (NCTs) based on permutation procedures will also be used to compare differences between the intervention and control groups in network structure, connectivity strength, and patterns of evolution, so as to explore the dynamic restructuring effects of the intervention on the

symptom-mechanism system.

All mechanism-related analyses are exploratory in nature and are intended primarily to generate hypotheses for future research rather than serve as the basis for primary inference.

5.5 Harms

All adverse events (AEs) and serious adverse events (SAEs) will be summarized descriptively by event type and frequency. If event counts permit, generalized estimating equations (GEE) or logistic regression models will be used to compare group differences in the incidence of SAEs.

5.6 Missing Data Handling

Primary outcome analyses using linear mixed-effects models (LMMs) or Cox proportional hazards models, as well as secondary outcome analyses using linear mixed-effects models (LMMs) and generalized linear mixed models (GLMMs), will be conducted using likelihood-based estimation methods. Under the MAR assumption, these models can directly use all available observed data to yield unbiased estimates. Therefore, the primary analyses will not involve explicit imputation of the raw data.

For analyses involving multivariable joint modeling, such as health economic outcomes or mediation analyses, multiple imputation will be used to handle cross-sectional missingness. The imputation model will include group, time, baseline scores, and demographic variables, and 20 imputed datasets will be generated. Results will be pooled according to Rubin's rules.

In addition to per-protocol (PP) analyses as sensitivity analyses, if the missingness rate for the primary outcomes exceeds 10%, missing-data sensitivity analyses will also be conducted. Specifically, assumption-driven multiple imputation will be performed by applying different offsets to missing values in the intervention group to simulate unfavorable scenarios in which dropouts derive less benefit than predicted by the model. The offset will then be gradually increased until the study conclusions reverse, that is, a tipping-point analysis will be performed. The plausibility of such offsets in clinical reality will then be assessed in order to examine the robustness of the study conclusions under Missing

Not at Random (MNAR) assumptions.

6. Ethics

6.1 Research Ethics Approval

The study will not commence until ethical approval has been obtained from the relevant ethics committee. All study activities will comply with the Declaration of Helsinki and the principles of the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guideline.

If substantial amendments to the study protocol are made, they will be resubmitted for ethics approval. Information in the trial registry will also be updated in a timely manner. If relevant modifications affect participants' rights or interests, participants will be informed appropriately.

6.2 Additional Consent Provisions for Ancillary Studies

This study will not collect biological samples. If ancillary studies related to the trial are conducted in the future, only de-identified study data will be used, and such studies will require additional ethics approval.

Participants may choose whether they consent to the use of their anonymized data for future related research. This decision will not affect their right to participate in the present trial or the treatment they receive.

7. Patient and Public Involvement

Although no formal Patient and Public Involvement (PPI) committee was established for this study, several small-scale feasibility and preliminary effectiveness tests were conducted during the preparatory phase in order to gather feedback from the target population regarding the digital recruitment process, online course experience, and questionnaire burden.

Based on this feedback, adjustments were made to the presentation format of the WeChat

mini-program content, the pacing of check-in reminders, follow-up frequency, and questionnaire length, with the aim of improving acceptability and adherence.

During the trial, the research team will continue collecting participant feedback on intervention experience, technical usability, and potential adverse events in order to further evaluate feasibility and safety. Study findings will be made publicly available after publication, but patients and members of the public will not be directly involved in protocol design, data interpretation, or manuscript preparation.

8. Trial Registration

This trial will be prospectively registered on ClinicalTrials.gov, and the registration number will be added to the protocol and related documents once obtained. Registration will be completed before enrollment of the first participant.

9. Protocol and Statistical Analysis Plan

The trial protocol, including the statistical analysis plan (SAP), will be made publicly available in open-access form on the journal website following publication of the protocol paper. Any substantial updates to the protocol or SAP thereafter will also be archived on ClinicalTrials.gov.

10. Data Sharing

Because the study involves sensitive mental health data from participants and is subject to ethical restrictions, there are currently no plans to publicly share individual-level data.

For reasonable academic requests, researchers may contact the corresponding author. Such requests will be jointly reviewed by the study team and the ethics committee, and, where appropriate, data summaries or statistical support may be provided.

11. Funding and Support

This study has not received funding from any commercial organization, healthcare company, or business entity related to digital mindfulness products.

12. Conflicts of Interest

All investigators declare that they have no financial conflicts of interest. The intervention content (MIED) and digital platform used in this study were independently developed by the research team and are not associated with any commercial interests.

13. Dissemination Policy

The research team plans to disseminate study findings to participants, healthcare professionals, and the public through the following channels:

(1) Updating trial results on ClinicalTrials.gov

(2) Publishing the main study findings and long-term follow-up results in peer-reviewed journals

(3) Providing participants with a plain-language summary of the main findings

(4) Reporting study findings at academic conferences, clinical training events, and professional meetings related to mental health

14. Discussion

The present study proposes a 24-month assessor-blinded, parallel-group, two-arm randomized controlled trial to systematically evaluate the long-term effectiveness, cost-effectiveness, and feasibility of an AI-assisted internet-based Mindfulness Intervention for Emotional Distress (iMIED) in individuals with subclinical emotional distress. This study has clear practical relevance. Anxiety and depression have become major contributors to the global burden of disease, while existing mental health service systems remain largely characterized by a pattern of emphasizing treatment over prevention. The WHO World Mental Health Report (2022) and subsequent commentaries have

emphasized that service priorities should be shifted further upstream toward health promotion, early identification, and preventive intervention, particularly through the development of simple, low-cost, and scalable community-based and digital intervention models .

By focusing on individuals with PHQ-9 or GAD-7 scores ≥5, the present study addresses a population of substantial preventive importance. Recent individual participant data meta-analysis has shown that psychological interventions for subthreshold depression can significantly reduce the subsequent risk of major depressive disorder, supporting the view that the subclinical stage constitutes a critical and modifiable intervention window . Against this background, the study is not limited to mean symptom changes, but also incorporates more clinically interpretable categorical outcomes, including asymptomatic remission and reliable deterioration. This approach helps evaluate the value of the intervention from the perspective of whether it produces meaningful clinical change and is thus more closely aligned with the needs of public health and service decision-making.

Another important contribution of this study lies in its attempt to address two longstanding evidence gaps in digital mental health intervention research: insufficient evidence on long-term efficacy and insufficient evidence from health economic evaluation. In recent years, multiple high-quality reviews and meta-analyses have shown that digital mental health interventions are generally capable of improving depression and anxiety symptoms, but effect sizes are typically small to moderate and vary according to study population, intervention format, guidance intensity, and control condition. At the same time, important limitations remain regarding long-term follow-up, real-world implementation, and overall evidence quality . For mindfulness-based apps specifically, the latest meta-analysis likewise indicates some short-term effects on anxiety and depression, yet high-quality trials with extended follow-up remain relatively scarce . Accordingly, the present study includes a 24-month follow-up period and incorporates both cost-effectiveness and cost-utility analyses into the a priori design, thereby offering a more complete evidence base for evaluating whether digital mindfulness intervention is not only effective but also worthy of wider dissemination.

From a design perspective, the study has several notable strengths. First, it adopts a strongly pragmatic design, with the control group permitted to access usual mental health resources freely. This feature brings the results closer to real-world service conditions and facilitates evaluation of the incremental value of iMIED within existing public health systems. Second, the study simultaneously includes

continuous outcomes, categorical clinical outcomes, economic indicators, implementation indicators, and mechanism variables, thereby allowing a comprehensive evaluation of the intervention from the perspectives of overall symptom change, clinically meaningful improvement, resource allocation efficiency, real-world scalability, and potential mechanisms of action. Third, the study embeds AI-assisted support into a self-guided mindfulness intervention. In theory, such support may improve engagement and adherence by providing timely feedback, personalized explanations, and a greater sense of accompaniment during practice. Existing studies suggest that certain interactive design features in digital mental health interventions, especially those involving chatbot technologies, may be associated with greater symptom improvement; however, evidence remains insufficient regarding which forms of personalized support are genuinely effective. Therefore, the present study's tracking of AI interaction frequency, intensity of personalized feedback, and usage duration may also provide useful evidence for future optimization of digital interventions .

Nonetheless, several limitations should be acknowledged. First, as with most digital mental health intervention trials, full blinding of participants and the intervention process is not possible, and expectancy effects and reporting bias may therefore remain. Second, the study relies primarily on self-report measures to assess anxiety, depression, and related psychological mechanisms. Although PHQ-9 and GAD-7 have strong psychometric properties, they cannot fully substitute for structured clinical interviews. Third, the control group is permitted unrestricted access to usual care resources. While this enhances external validity, it may also increase heterogeneity in treatment exposure and thereby attenuate between-group differences. Fourth, digital mental health interventions commonly face challenges related to fluctuating engagement, declining adherence, and long-term attrition, and recent reviews have identified engagement and retention as critical bottlenecks in the real-world dissemination of digital interventions . Although the present study seeks to mitigate these issues through systematic reminders, financial compensation, behavioral usage tracking, and sensitivity analyses, findings should still be interpreted with caution.

At the health economic level, this study also has potential value. Existing reviews suggest that internet- and mobile-based interventions for depression and anxiety generally show promising cost-effectiveness, but conclusions remain influenced by differences in evaluation frameworks, cost definitions, control

conditions, and target populations. In particular, evidence remains limited for digital mental health promotion and prevention programs targeting non-clinical or subclinical populations . By conducting both cost-effectiveness and cost-utility analyses from a societal perspective and using standard methods such as QALYs, ICERs, bootstrap resampling, and cost-effectiveness acceptability curves, the present study is expected to generate relatively high-quality local evidence regarding the resource allocation value of digital mindfulness intervention in the Chinese context. If iMIED is shown to produce stable clinical benefits and improved quality of life at a relatively low incremental cost, its dissemination across universities, communities, internet platforms, and stepped-care mental health service systems may carry considerable practical significance.

Overall, the present study will evaluate the long-term efficacy, mechanism pathways, implementation feasibility, and economic value of an AI-assisted digital mindfulness intervention in individuals with subclinical emotional distress through an extended follow-up period, a strongly pragmatic design, and a comprehensive outcome framework. Regardless of whether the results support the superiority of iMIED over the control condition, the study will provide important evidence for early intervention strategies targeting subclinical emotional distress, the optimization of digital mental health services, and the standardized development of AI-assisted psychological intervention. In the context of the current transformation in mental health care from disease treatment toward risk prevention and health promotion, the study has clear methodological and public health significance.

Appendix 1. 49-Day iMIED Check-in Schedule

Day	Theme	Mindfulness Practice	Homework
	Week 1		
1	Course Introduction and Goal Setting	Awareness of Breathing (Short)	1. Identify situations involving distress avoidance 2. Choose an appropriate goal
2	Motivation and Commitment	Awareness of Breathing (Short)	1. Complete the decision worksheet 2. Complete the coping plan for difficulties 3. Prepare 3 raisins for tomorrow
3	Mindful Eating of Raisins	Mindful Eating of Raisins	1. Set a fixed practice time for this week 2. Engaging in life: mindful toothbrushing
4	Formal Practice 1: Body	Body Scan	1. First body scan practice 2. Engaging in

Day	Theme	Mindfulness Practice	Homework
	Scan		life: mindful face washing
5	Core Elements of Mindfulness: Awareness and Acceptance	Body Scan	Engaging in life: mindful dressing
6	Nine Attitudes of Mindfulness Practice	Body Scan	1. Mindfulness attitudes2 . Engaging in life: mindful copying/writing
7	Mindful Communication	Body Scan	Engaging in life: mindful communication
	Week 2		
8	Formal Practice 2: Awareness of Breathing	Awareness of Breathing	1. First awareness of breathing practice 2. Set a practice time 3. Engaging in life: others
9	Understanding the Function of Emotions	Body Scan	1. Reflection question
10	Deconstructing the Three Components of Emotion	Awareness of Breathing	1. Nine-dot diagram
11	Thoughts: Judgments and Interpretations of Events	Body Scan	1. Reflection question: understanding thoughts
12	Feelings: Physical and Psychological Experiences at the Time	Awareness of Breathing	1. Reflection question: understanding feelings
13	Behavior: Reactions at the Time	Body Scan	1. Reflection question: understanding behavior
14	Emotion Log	Awareness of Breathing	1. Complete one emotion log
	Week 3		
15	Mindfulness Practice 3: Mindful Stretching	Mindful Stretching	1. Practice experience, insights, or questions 2. Emotion log
16	Sources of Emotional Distress: The Biopsychosocial Systems Model	Mindful Awareness of Breathing	1. Practice experience, insights, or questions 2. Emotion log3. Reflect on the sources of your own emotional distress
17	The MIED Diamond Model	Mindful Stretching	1. Practice experience, insights, or questions 2. Emotion log3. Assess your current condition from four dimensions
18	Engaging in Life	Mindful Awareness of Breathing	1. Practice experience, insights, or questions 2. Emotion log
19	Regulating Distress Tolerance	Mindful Stretching	1. Practice experience, insights, or questions 2. Emotion log
20	Regulating Emotional	Mindful Awareness of	1. Practice experience, insights, or

Day	Theme	Mindfulness Practice	Homework
	Behaviors	Breathing	questions 2. Emotion log
21	Enhancing Cognitive Flexibility	Mindful Stretching	1. Practice experience, insights, or questions 2. Emotion log 3. Weekly summary
	Week 4		
22	Setting Challenging Tasks	Choose one of breathing, body scan, or stretching + Three-Step Breathing Space	1. Set a fixed practice time for this week 2. Set a challenging task
23	Increasing Tolerance for Uncomfortable Sensations	Choose one of breathing, body scan, or stretching	1. Reflect on what bodily sensations you find difficult to tolerate
24	Interoceptive Exposure: Rapid Breathing Exercise	Choose one of breathing, body scan, or stretching	1. Rapid breathing exercise
25	Midterm Summary	Choose one of breathing, body scan, or stretching	1. Midterm summary 2. Evaluate your progress across these four dimensions and reflect on the areas in which you have improved since the start of the course 3. Rapid breathing exercise
26	Choosing an Interoceptive Exposure Exercise That Suits You	Choose one of breathing, body scan, or stretching	1. Find an exercise that can evoke sensations you find difficult to tolerate 2. Review completion of the challenging task
27	Increasing Tolerance for Negative Emotional Experiences	Choose one of breathing, body scan, or stretching	1. Interoceptive exposure practice 2. Review completion of the challenging task
28	Loving-Kindness Meditation	Choose one of breathing, body scan, or stretching + Loving-Kindness Meditation	1. After today's mindfulness practice, complete the loving-kindness meditation practice 2. Review completion of the challenging task 3. Weekly summary
	Week 5		
29	Challenging Task 2	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Set this week's challenging task
30	Mindful Walking	Mindful Walking + Loving-Kindness Meditation	1. Do your first mindful walking practice in this course 2. Interoceptive exposure practice
31	Identifying Excessive Emotional Behaviors	Choose one of standing (or seated) stretching or walking +	1. Reflect on whether you have excessive emotional behaviors

Day	Theme	Mindfulness Practice	Homework
		Loving-Kindness Meditation	
32	A Closer Look at the Three-Step Breathing Space	Choose one of awareness of breathing or walking + Three-Step Breathing Space	1. Make good use of the Three-Step Breathing Space 2. Interoceptive exposure practice
33	Revisiting the Regulation of Emotional Behaviors	Choose one of body scan or walking + Three-Step Breathing Space	1. Review completion of the challenging task 2. Reflect on what excessive emotional behaviors you may have and how action, especially actions that engage you in life, can gradually reduce them
34	Example of Regulating Emotional Behaviors: Coping with Procrastination	Choose one of breathing, walking, or stretching + Three-Step Breathing Space	1. Identify any excessive procrastination behaviors you may have and think of ways to address them 2. Review completion of the challenging task 3. Interoceptive exposure practice
35	Facing More Distress-Avoidant Situations	Choose one of breathing, walking, or stretching + Three-Step Breathing Space	1. Review completion of the challenging task 2. Weekly summary
	Week 6		
36	Challenging Task 3	Mindful Walking + Three-Step Breathing Space	1. Set this week's challenging task 2. Make good use of the Three-Step Breathing Space
37	Learning to Identify Thoughts	Mindful Walking + Three-Step Breathing Space	1. Learn to distinguish between our thoughts and objective facts 2. Make good use of the Three-Step Breathing Space
38	Treating Thoughts as Thoughts	Choose one of breathing, stretching, or body scan + Three-Step Breathing Space	1. Practice mindful awareness of breathing or mindful walking to improve the ability to see thoughts as thoughts 2. Make good use of the Three-Step Breathing Space 3. Integrate mindfulness more into daily life and work
39	The Scope of Acceptance	Choose one of breathing, stretching, or body scan + Three-Step Breathing Space	1. Understand the scope of acceptance in the MIED course 2. Integrate mindfulness more into daily life and work 3. Make good use of the Three-Step Breathing Space
40	Identifying Thinking Traps	Choose one of breathing, stretching, or body scan + Three-Step Breathing Space	1. Review completion of the challenging task 2. Identify thinking traps

Day	Theme	Mindfulness Practice	Homework
41	Cognitive Reappraisal	Choose one of breathing, stretching, or body scan + Three-Step Breathing Space	1. Review completion of the challenging task 2. Reevaluate your thoughts
42	Enhancing Cognitive Flexibility and Engaging in Life	Choose one of breathing, stretching, or body scan + Three-Step Breathing Space	1. Review completion of the challenging task 2. Weekly summary
	Week 7		
43	Challenging Task 4	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Set this week's challenging task
44	Facing Difficult Situations Directly	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Review completion of the challenging task
45	Reviewing What Has Been Learned	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Reflect on your understanding and application of the course content/practices
46	Summarizing Gains and Their Sources	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Look back on the journey so far 2. Understand the sources of your gains
47	Setting New Goals	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Task: future goals
48	Tips for Sustaining Mindfulness Practice	Choose one of breathing, stretching, or body scan + Loving-Kindness Meditation	1. Write down your personal mindfulness toolkit for persistence
49	The End Is Also the Beginning	Choose one of breathing, stretching, or body scan + Three-Step Breathing Space	1. Task: mindfulness integrated into daily life