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From Apps to Agents: Protocol for a Component Network Meta-Analysis of Digital and Artificial Intelligence Interventions for Suicidal Ideation and Behavior

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review stage at the time of initial registration - Preliminary searches.

Conflicts of interest - The authors declare no conflicts of interest.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 November 2026 and was last updated on 28 November 2026.

INTRODUCTION

Review question / Objective Primary question: Which components of digital and artificial intelligence (AI) interventions reduce suicidal ideation and suicidal behavior, and what is the incremental effect of delivery by an AI agent compared with non-agent digital delivery?
Population: participants of any age in any setting. Interventions: digital interventions (apps, web or computer programs, text messages, AI agents, or digital programs blended with face-to-face sessions) targeting suicidality. Comparators: waitlist, no treatment, attention control, usual care, or another active intervention. Study design: randomized controlled trials.
Secondary objectives: (a) to describe how trials of AI agents implement and report safety safeguards and what harms they report; and (b) in trials that deliver the same therapeutic content by an AI agent and by another route, to estimate the effect of AI agent delivery directly and compare it with the component network meta-analysis estimate if both estimates are available.

Rationale Digital interventions for suicide prevention, delivered through smartphone apps, websites, and text messages, have small and heterogeneous effects on suicidal ideation (g = 0.11; Burr et al., 2025), and their effects differ by setting and by whether they are self-guided or blended (Josifovski et al., 2025). These reviews compare whole interventions, so they cannot show which components produce the effect (Abbasi et al., 2025). Newer interventions use conversational agents and large language models that respond to users in real time, yet few randomized trials of AI in suicide prevention exist, and none have been pooled (Fernández-Quijano et al., 2025).
Component network meta-analysis (CNMA) estimates the effect of each component across trials of multicomponent interventions and can connect networks that would otherwise be disconnected (Rücker et al., 2020). It has identified the active components of internet-delivered cognitive behavioral therapy for depression (Furukawa et al., 2021) and of cognitive behavioral therapy for insomnia (Furukawa et al., 2024), but it

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has not been applied to suicidal outcomes. A search of PROSPERO, INPLASY, and OSF Registries on 26 October 2026 found no registered or published CNMA of digital interventions for suicidal ideation or behavior. The wider digital intervention network may provide evidence on the AI agent component when the trial comparisons and component combinations allow its effect to be estimated separately.

Condition being studied Suicidal ideation: thoughts of ending one's life, ranging from passive thoughts of death or wishes to be dead to active thoughts of killing oneself, measured by a validated scale or a suicide item of a broader scale (for example, PHQ-9 item 9).
Suicide plan: thoughts about a specific method, time or place to end one's life, analyzed as the proportion of participants reporting a plan.
Suicide attempt: a non-fatal, self-initiated, potentially injurious act with at least some intent to die. Interrupted and aborted attempts are counted only when the trial reports them as suicide attempts.
Not included: non-suicidal self-injury and self-harm with unassessed or unclear suicidal intent. When suicidal events cannot be distinguished from non-suicidal events, the combined outcome will be excluded. Separately reported suicide attempts remain eligible.
Suicidal ideation is a leading risk factor for suicide attempts and suicide death, and it is common in people with depression and psychological distress.

METHODS

Search strategy The search will combine (1) AND (2) AND (3).
Terms within each block will be joined with OR, including the two lists in block (2). Database-specific subject headings and spelling variants will supplement the text terms, and the strategy will be adapted to each database. Recall will be checked against known eligible trials. No specific component name, age label, or the term CNMA will be required.
(1) Suicide-related: suicid*.
(2) AI agent or digital delivery
AI agent: artificial intelligence, AI, chatbot*, chat bot*, conversational agent*, conversational AI, dialogue system*, virtual agent*, relational agent*, virtual assistant*, large language model*, LLM*, generative AI, generative artificial intelligence, conversational system*, dialog system*, virtual human*, virtual coach*.
Digital delivery: digital intervention*, digital therap*, digital health, smartphone*, mobile app*, mHealth, eHealth, internet-based, web-based, computer-based, online intervention*, text messag*, SMS, e-mental health, computerized intervention*, computerised intervention*, internet-delivered, app-based.
(3) Randomized trial design: randomized, randomised, randomly, controlled trial*, RCT, RCTs. Non-randomized studies will be excluded during screening.
Limits: English-language publications from 1 January 2000 to 30 November 2026. No age or geographical terms will be used; age and setting will be verified during screening.

Participant or population Participants of any age, in any setting (community, school, university, primary care, outpatient, or inpatient), enrolled in randomized controlled trials that measured suicidal ideation, suicide plans, or suicide attempts. Universal, selective, and indicated prevention samples and treatment samples are all eligible.

Intervention Any digital intervention targeting suicidality, delivered through a smartphone app, web or computer program, text messages, or an AI agent, alone or combined with face-to-face sessions. Each arm will be coded for the following components.
Content: psychoeducation; skills training (for example, cognitive restructuring, behavioral activation, problem solving, emotion regulation, mindfulness); safety planning; brief contact; self-monitoring.
Delivery and support: AI agent (software that interprets free-text input and responds, with a large language model or with dialogue selected by natural language processing; chat interfaces that branch only on button choices are not AI agents); closed-loop delivery (sensor or self-report data decide during use when or what content is delivered); therapeutic guidance from a clinician or peer; encouragement (reminders without therapeutic content); face-to-face sessions.
Excluded: digital tools used only for screening or data collection, therapy delivered by a clinician by video or telephone, training of professionals or gatekeepers, and public campaigns.

Comparator Any comparator: waitlist, no treatment, attention control, usual care, or another active intervention. Comparator arms are coded with the same components as intervention arms, plus a waiting component, a non-specific attention component, and usual care. Waitlist and no treatment are the reference. A digital program without any content component is coded as non-specific, so no active arm has the same coding as waitlist or no treatment.

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Study designs to be included Randomized controlled trials, including cluster randomized and pilot trials. Quasi-randomized, non-randomized, and single-arm studies are excluded.

Eligibility criteria Only full reports published in peer-reviewed journals in English between 1 January 2000 and 27 November 2026 are included; conference abstracts, theses, preprints, and trial registry records are excluded. When a suicide item was administered but not reported by arm, authors will be contacted up to three times over six weeks, and trials without these data are excluded from the effectiveness analysis but may contribute to the safety analysis if they include an AI agent arm. Co-interventions such as medication are allowed if available to all arms.

Information sources PubMed (including MEDLINE), Embase, APA PsycINFO, and Web of Science Core Collection will be searched from 1 January 2000 to 27 November 2026. Together these sources cover biomedical, psychological, and interdisciplinary research on digital and AI-agent interventions. In their public health systematic review, Kilian et al. (2024, DOI 10.1016/j.lanepe.2024.100905) searched PubMed and Web of Science alongside MEDLINE, PsycINFO, and Embase via Ovid. Reference lists of included trials and relevant reviews will be checked, and trial authors will be contacted for unreported suicidality data.

Main outcome(s) The primary outcome is suicidal ideation at post-intervention, defined as the assessment closest to the end of the intervention. Suicide plans and attempts will be analyzed separately at post-intervention. Each outcome will also be analyzed separately at the longest follow-up reported after the post-intervention assessment. The synthesis rules in Section 22 apply to each outcome. Suicide plans will be summarized descriptively if the available evidence cannot support meta-analysis. Suicidal ideation will be summarized as a standardized mean difference (Hedges' g), and suicide plans and attempts as risk ratios, counting attempts only if they occurred after randomization. When a trial reports more than one measure of suicidal ideation, a dedicated multi-item suicidal ideation scale is preferred, then a suicidality subscale, then a single suicide item, then a composite measure of suicidal ideation and behavior. The recall period of each measure of suicidal ideation and suicide plans (for example, past week, past two weeks or past month) is extracted. No recall window is prespecified, because instruments differ in the period they ask about; for example, the Beck Scale for Suicide Ideation asks about the past week and PHQ-9 item 9 about the past two weeks. Before any effects are pooled, and without reference to trial results, measures will be grouped by the recall windows reported in the included trials, and this grouping will be documented. Eligible recall windows are pooled in the main analysis, and a sensitivity analysis restricts to measures with comparable recall windows. Measures whose recall period begins before randomization (for example, lifetime) are not used, because they include thoughts that occurred before the intervention. Intention-to-treat data will be used where available.

Additional outcome(s) For trials with an AI agent arm: implementation and reporting of safety safeguards (exclusion of high-risk participants, risk monitoring, crisis detection, escalation to a human, human review of agent output, systematic adverse event collection, reporting of suicide attempts and serious adverse events by arm) and reported harms, including harmful agent responses.

Data management Records will be deduplicated and screened in Covidence. Two reviewers will independently screen titles and abstracts and then full texts, with disagreements resolved by discussion or a third reviewer. Reports of the same trial will be linked so that the trial is the unit of analysis, and selection will be recorded in a PRISMA flow diagram. Reports will be matched on trial registration number, authors, setting, recruitment period, sample size and comparators, and authors will be contacted when it is unclear whether two reports describe the same trial. Two reviewers will independently extract study, intervention, and outcome data and code each arm, including comparator arms, for its components using all available sources, including publications, protocols, supplements, and author correspondence. Before analysis, the citation, registration number, design and interventions recorded for each included trial will be checked against its full text.

Quality assessment / Risk of bias analysis Two reviewers will independently assess the risk of bias for each main outcome with the Cochrane Risk of Bias 2 tool (RoB 2), using the variant for cluster randomized trials where applicable, with disagreements resolved by discussion or a third reviewer. Certainty of evidence for each main outcome will be assessed with CINeMA.

Strategy of data synthesis Analyses will be performed in R with the netmeta package. Suicidal ideation will be summarized as a standardized

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mean difference, and suicide plans and attempts as risk ratios. Trials with no events in any arm will not contribute to the risk ratio for that outcome. Continuous and ordinal measures of suicidal ideation will be analyzed as standardized mean differences, and binary data, such as the proportion of participants endorsing a suicide item, will be converted to standardized mean differences so that all ideation measures can be combined. Cluster randomized trials will be adjusted for clustering, assuming an intracluster correlation coefficient of 0.05 when none is reported.
A random-effects network meta-analysis of whole interventions will first be fitted for each outcome with a connected intervention network. Transitivity will be examined by comparing age group, population risk level, exclusion of high-risk participants, setting, and publication year across comparisons, and consistency will be assessed with local and global tests where the network supports them. The primary analysis is an additive random-effects component network meta-analysis of suicidal ideation at post-intervention. A disconnected intervention network will be considered for component analysis if shared components permit estimation. Components other than AI agent delivery that are present in fewer than three trials will be merged with the most similar component. The AI agent effect will be estimated only when the trial comparisons and component combinations allow it to be estimated separately. If fewer than three trials inform an estimable AI agent effect, it will be reported as exploratory. If the effect cannot be estimated separately, we will report why and describe any direct comparisons and safety findings. The broader digital intervention analysis will proceed where feasible. If the component model cannot be estimated, results will be reported from the network meta-analysis or from pairwise meta-analyses where feasible. If quantitative synthesis is infeasible, results will be described narratively. At each time point, we will summarize suicide plans descriptively if fewer than two independent trials provide usable, comparable data or if no pooled comparison can be estimated. Small-study effects will be examined with contour-enhanced funnel plots if at least 10 trials compare an active intervention with a control.
Trials delivering the same content by an AI agent and by another route will be pooled in a pairwise random-effects meta-analysis if at least three are available, and otherwise described individually. Safety findings will be summarized descriptively.

Subgroup analysis Subgroup analyses will compare (a) trials that did and did not exclude participants at elevated suicide risk, and (b) pilot or feasibility trials with full efficacy trials.

Sensitivity analysis Sensitivity analyses will (a) exclude trials measuring suicidal ideation with a single item, (b) exclude trials at high risk of bias, (c) treat chat interfaces that branch on button choices as AI agents, (d) refit the additive component network meta-analysis in a Bayesian framework, (e) restrict suicidal ideation to measures with comparable recall windows, and (f) exclude composite measures that combine suicidal ideation and behavior, such as the SBQ-R total score.

Language restriction Yes. Only reports published in English will be included.

Country(ies) involved China.

Other relevant information The review will be reported according to PRISMA 2020 and its extension for network meta-analyses. Any changes to the protocol will be dated, recorded with the reason, and reported in the completed review. Planned timeline: searches on 27 November 2026; screening and data extraction December 2026 to February 2027; analysis and reporting March to May 2027.
Current review status: Ongoing.

Keywords suicidal ideation; suicide attempt; digital intervention; conversational agent; large language model; component network meta-analysis; systematic review.

Dissemination plans The review will be submitted to a peer-reviewed journal and presented at conferences, and it will form the first chapter of a doctoral thesis. The coding dataset and analysis code will be shared as supplementary material.

Contributions of each author

Author 1 - Jaden Khuong Tri Huynh. Author 1 conceived the review, designed the protocol and search strategy, will screen studies, extract and code data, conduct the analysis, and drafted the protocol.
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