

Original Paper

A Home-Based Serious Game for Cognitive Control Training in Major Depressive Disorder: Randomized Controlled Trial

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Abstract

Background: Serious games are increasingly explored as scalable, engaging interventions for major depressive disorder (MDD). However, most trials evaluating game-based interventions rely on weak comparators or inactive controls, making it difficult to disentangle intervention-specific effects from nonspecific benefits.

Objective: This study aimed to evaluate the effectiveness and feasibility of a home-based serious game targeting cognitive control (CC) training in adults with MDD, compared against a closely matched active control game.

Methods: This was a home-based, minimal-contact, parallel-group randomized controlled trial. Adults aged 18 to 65 years with a current *DSM-5* (*Diagnostic and Statistical Manual of Mental Disorders* [Fifth Edition]) diagnosis of MDD were recruited via clinical referrals from a mental health center in Israel between November 2021 and April 2023. Participants completed 30 sessions of 30 minutes each over 6 weeks. The experimental arm received Legends of Hoa'manu (LoH), an adaptive action-based serious game integrating CC training with emotional stimuli, whereas the control arm received a closely matched game (LoH_control) with comparable aesthetics and structure but without adaptive CC training or emotional content. The preregistered primary outcome was change on the Montgomery-Åsberg Depression Rating Scale (MADRS), and the secondary outcome was feasibility. Tertiary outcomes included depression severity, illness severity, global improvement, well-being, functioning, participation, rumination, and response and remission; CC and durability were exploratory. Participants were randomized 1:1 (computer-generated pseudorandom sequence, permuted blocks of 4), with allocation concealed until after baseline. Participants and outcome assessors were blinded to allocation.

Results: Of 57 randomized participants (LoH: n=28, 49%; LoH_control: n=29, 51%), 48 (84%) completed postintervention, and 44 (77%) completed 1-month follow-up; all 57 were analyzed by intention-to-treat using linear mixed models. The mean adherence was 20.7 (SD 9.48) of 30 (69%) sessions, early abandonment was uncommon (<10% of sessions), and all 3 post hoc feasibility benchmarks were met. Both arms showed significant reductions in depressive symptoms over time ($P<.001$; $\eta^2_p=0.49$); MADRS reductions were 6.8 (95% CI 3.4-10.3) points in LoH and 9.8 (95% CI 6.4-13.3) in LoH_control, with no significant group×time interaction ($F_{1,49.4}=1.57$; $P=.22$; $\eta^2_p=0.03$). CC composite scores improved modestly over time ($P=.045$; $\eta^2_p=0.09$). No intervention-related adverse events were reported.

Conclusions: This is among the first randomized trials of a home-based serious game combining action-based gameplay with CC training against a closely matched active control in MDD. Both arms improved comparably, with no added benefit from the targeted training, implicating nonspecific, engagement-related processes. The findings indicate that comparator design matters

in digital mental health. Home-based serious games are feasible and could widen access to care, but no-contact and dismantling trials must identify the active components.

Trial Registration: Israeli Ministry of Health Clinical Trials Registry MOH_2021-07-20_005979; https://clinical-trial.health.gov.il/clinicaltrials/?MOHResearchId=MOH_2021-07-20_005979

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Introduction

Major depressive disorder (MDD) is a recurring and seriously impairing condition and a leading contributor to global disability [1,2]. Despite available pharmacological and psychotherapeutic treatments, more than two-thirds of patients fail to achieve remission after first-line pharmacotherapy, and 15% to 30% remain treatment resistant [3]. Even responders frequently experience residual symptoms and treatment-related side effects [3,4]. There is therefore a pressing need for scalable, accessible add-on or alternative treatment strategies.

One candidate target is cognitive control (CC), that is, the goal-directed mental operations encompassing inhibition, working memory (WM), shifting, and attentional control [5,6]. Cognitive models of depression posit that deficits in CC, particularly impaired inhibition and WM updating, sustain depressive symptoms by allowing mood-congruent negative information to persist in WM and by impairing disengagement from negative thoughts [7-10]. Difficulty disengaging from negative content fosters rumination, a less adaptive form of emotion regulation, which in turn maintains negative affect and increases vulnerability to recurrent depressive episodes [9,11,12]. Consistent with this account, CC deficits have been reported in adults with current or remitted MDD [13-17], although findings are not uniform [18,19]. Neuroimaging studies link these deficits to dysfunction in prefrontal regions, including the anterior cingulate and dorsolateral prefrontal cortices [20]. Functional imaging in depressed adults further shows reduced recruitment of these regions during cognitively demanding tasks, suggesting that CC-related networks may be a tractable target for intervention. Together, these findings provide a plausible mechanistic rationale for interventions that train CC as an indirect means of reducing depressive symptoms.

Computerized CC training paradigms, typically involving repeated practice with adaptive difficulty, may serve as such a therapeutic approach [21]. Importantly, in this framework, CC training is not conceived as a direct treatment for depression analogous to psychotherapy or pharmacotherapy; rather, any reduction in depressive symptoms is expected to arise indirectly, as a downstream consequence of improved inhibition, WM updating, and attentional disengagement from negative material, and, in turn, reduced rumination [22,23].

However, computerized CC training studies in both clinically depressed individuals and preclinical depression have shown mixed effects on depressive symptoms.

Specifically, several trials have reported reductions in rumination or depressive symptoms following CC training [24-26], whereas others found no benefit beyond placebo training [11]; recent meta-analyses and reviews likewise indicate that effects tend to be small and inconsistent [22, 23,27-29]. Augmenting CC training with emotionally salient stimuli has been proposed to better target affective regulation deficits [30-32], and some studies using emotional CC training have reported improvements in depressive symptoms. Among these, there is a small subset of interventions specifically designed for remote digital delivery [30,33]. Even so, findings remain inconsistent: recent meta-analyses conclude that benefits of CC training on mood tend to be small and not always condition specific [22,23,34].

Adherence is a critical determinant of training success but is often poor in conventional CC interventions, which rely on repetitive exercises with minimal interactivity [22, 35,36]. Higher adherence is generally associated with larger training effects [37], yet many participants do not reach effective dosing thresholds [36]. This challenge is amplified in MDD, where reduced motivation and anhedonia are core features that further depress engagement with repetitive, low-reward tasks [37,38]. Serious games, digital games designed for purposes beyond entertainment, offer a way to integrate adaptive challenge, immersive context, and reward-based motivation into cognitive training [39-44]. Action video games in particular have been associated with improvements in attentional control and CC [45,46], and their combination of time pressure, multisensory coordination, and continuous prediction provides mechanics theoretically aligned with CC training [40,47].

Few studies, however, have combined home-based delivery with action game mechanics in clinically depressed adults. Remote tablet-based interventions have shown good adherence and sustained engagement [42], and action games have demonstrated promising cognitive benefits in depressed samples [48,49]; yet, these elements have rarely been integrated in a single trial. Keefe et al [41] delivered a remote, action game-inspired intervention for 6 weeks and observed improvements in sustained attention but no advantage over an active control on depressive symptoms. Earlier work by Anguera et al [39,40,50] in older adults reported gains in CC and modest mood benefits, although these did not consistently extend across mood measures. A home-based, action game-based intervention for adults with current MDD, evaluated against a closely matched active control game, has therefore not yet been reported.

This trial addressed this gap by evaluating Legends of Hoʻaʻmanu (LoH), a home-based, tablet-delivered serious game that integrates action mechanics, adaptive CC training, and emotional stimulus identification, against a closely matched active control game. The active control (LoH_control) was designed to match LoH on patient involvement and time on task, while omitting the action mechanics that are hypothesized to drive cognitive improvements [51] so that any superiority of LoH over LoH_control on clinical outcomes or CC could be attributed to those specific mechanics.

We tested the following hypotheses derived from our study aims:

- (H1) Effectiveness (preregistered primary end point): Experimental group participants would show larger reductions in depressive symptoms on the Montgomery-Åsberg Depression Rating Scale (MADRS) from baseline to postintervention than those randomized to the matched control game; this benefit would persist at 1-month follow-up.
- (H2) Feasibility (preregistered secondary end point): The video game intervention would be feasible, defined per the trial registration as $\geq 50\%$ of randomized participants completing ≥ 20 of the 30 prescribed sessions. Additional feasibility metrics (retention, adherence, and intrinsic motivation [Intrinsic Motivation Inventory] interest/enjoyment) and 3 post hoc benchmarks drawn from comparable digital mental health trials are reported as complementary reference points.
- (H3) Tertiary outcome superiority (preregistered tertiary end point): Participants randomized to LoH would show larger improvements on the preregistered tertiary outcomes than those randomized to the matched control game.
- (H4) We tested an exploratory mechanistic hypothesis (not formally preregistered): gains in CC would be associated with reductions in depressive symptoms, consistent with cognitive models implicating CC deficits in MDD.

Both H1 and H3 were preregistered as directional, confirmatory superiority hypotheses and are reported here as such. However, we note that prior evidence for CC training in depression is mixed, with effects that are often small or not condition specific [22,23,34]; superiority over a closely matched, engaging active control was therefore uncertain a priori and is best understood as a hypothesis the present trial was designed to test rather than a strongly expected outcome.

Methods

Open Science Practice

This trial was prospectively registered with the Israeli Ministry of Health Clinical Trials Registry (registration number MOH_2021-07-20_005979) on July 12, 2021, before enrollment of the first participant. The first participant was enrolled on November 21, 2021. The registration record

is directly accessible at [52]. As the registry record is maintained in Hebrew, an English translation is provided in [Multimedia Appendix 1](#). We note that the registry's brief public summary lists some early administrative details (delivery on a "mobile phone," a "2- to 4-week" training period, and reassessment "after 3 months") that are inconsistent with the registry's own detailed requirements and with the full preregistered protocol; the trial was conducted as specified in the protocol—a tablet-delivered, 6-week intervention with a 1-month follow-up—as reported here.

The study protocol and deidentified data are available on the Open Science Framework (OSF) repository [53]. No amendments were made to the registered protocol after trial initiation. Three deviations from the registered design are noted: (1) the realized sample size was 57 rather than the preregistered 60 (a 5% shortfall), which occurred because enrollment closed at the end of the funded recruitment window and was further constrained by COVID-19-related delays to clinical referrals and onsite assessments during 2021-2022; (2) 1 participant assigned to LoH_control inadvertently received the LoH intervention owing to an intervention distribution error (1/57, 1.8% protocol-execution deviation); and (3) the Global Assessment of Functioning, which was listed in the trial registration, was not administered.

The trial is reported in accordance with the CONSORT (Consolidated Standards of Reporting Trials) 2025 statement [54] and its CONSORT-EHEALTH (Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Telehealth) extension for web- and mobile-delivered interventions [55]; completed checklists are provided in [Checklist 1](#).

Participants

Trial Setting

Data collection for the trial took place between November 21, 2021, and April 2023. Participants with a current depressive episode were recruited from "Merhavim" Medical Center. Eligible participants from all racial, ethnic, and gender categories were aged between 18 and 65 years. A minimum score of 13 on the 17-item Hamilton Rating Scale for Depression (HDRS-17) [56] was required. Additional inclusion criteria were a primary *DSM-5* (*Diagnostic and Statistical Manual of Mental Disorders* [Fifth Edition]), diagnosis of MDD, with a single or recurrent episode, with the additional requirement of a current episode with a duration of ≥ 4 weeks. Participants needed to be without antidepressant medication or on an adequate (ie, at least the lowest effective) and stable (ie, for ≥ 6 weeks) dosage. Concomitant psychotherapy was allowed if ongoing for at least 3 months prior to baseline. Participants were excluded from the study if they met any of the following criteria: problematic gaming, as assessed by the Gaming Disorder Test [57]; a diagnosis of a significant neurological disorder or comorbid psychiatric disorder; any relevant unstable medical condition (eg, acute or unstable cardiac disease); use of an investigational drug within 6 weeks prior to baseline; or

suicidal risk, indicated by a score of 4 to 6 on item 10 of the MADRS or a suicide attempt during the current depressive episode.

Recruitment and Screening

Participants were recruited through clinical referrals from psychiatrists, psychologists, and social workers at Merhavim Medical Center. Interested individuals were contacted via phone by a member of the study team and invited to an in-person screening visit (V_0) at Merhavim, where eligibility was assessed. No flyers, social media, or website-based recruitment were used.

Sample Size

A power analysis was conducted using G*Power (version 3.1.9.7; Heinrich Heine University Düsseldorf) [58]. Sample size estimation was based on the CC outcome. Prior randomized trials of computerized cognitive training in individuals with elevated depressive symptoms have reported medium-to-large effects on clinical outcomes ($d \approx 0.73$ on depressive symptoms [24]). This effect size assumption was further supported by meta-analytic estimates of computerized cognitive training effects on depressive symptoms [30] and

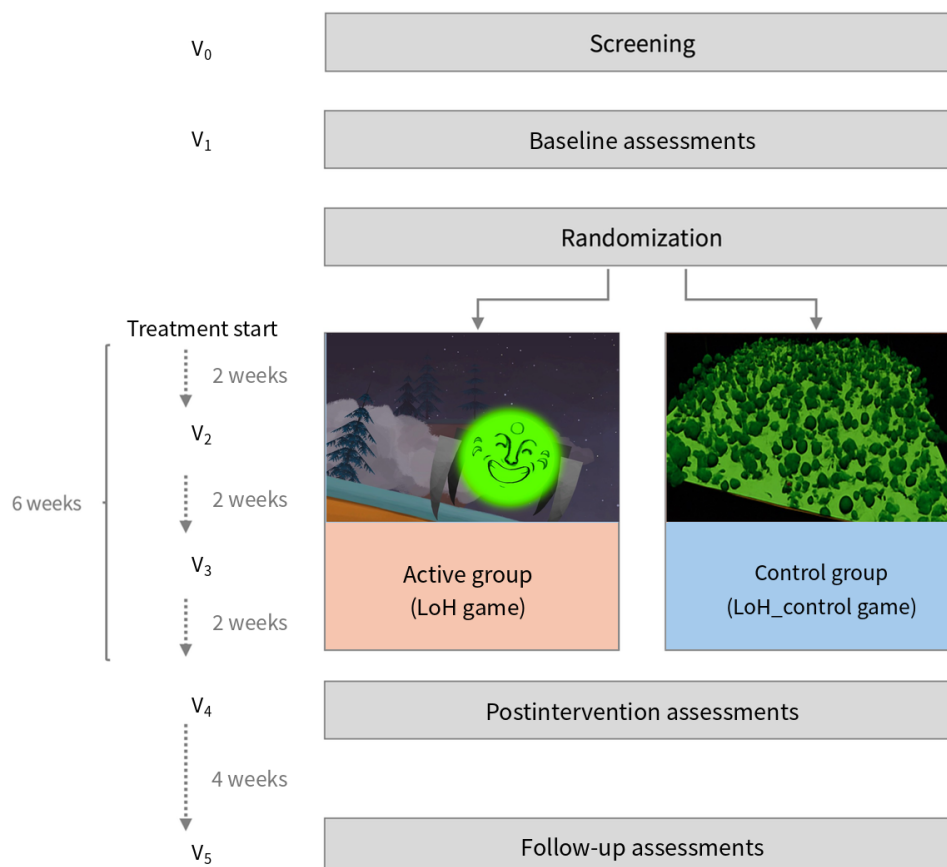
by earlier cognitive-emotional training trials in MDD and in older adults [32,33,39,40]. To allow for a more conservative estimate, we planned for a medium effect size (Cohen $d=0.65$). Under this assumption, a total sample size of 60 participants (30 per group) provides 80% power to detect a between-group difference at an α of .05. These effect size estimates were derived largely from trials using inactive or minimal-treatment comparators. A comparison against a closely matched active control likely corresponds to a smaller true between-arm difference; the assumed effect size of 0.65 should therefore be regarded as optimistic, and the trial was likely underpowered for the effect sizes expected between 2 engaging digital interventions (see “Limitations” section).

Study Design and Procedures

Trial Design

The study was a double-blind randomized controlled trial. Figure 1 depicts the study design. Interested participants were screened for eligibility (V_0). Eligible participants were assessed at baseline (V_1) and were then randomized in a 1:1 ratio to receive either the active LoH game intervention or the matched active control arm (LoH_control).

Figure 1. Study design of the home-based, parallel-group randomized controlled trial of LoH (active) versus a closely matched active control game (LoH_control) in adults with MDD ($n=57$ randomized). Study visits are denoted V_0 (screening) through V_5 (1-month follow-up). The full assessment battery was administered at 3 visits (V_1 : baseline, V_4 : postintervention, and V_5 : follow-up). During mid-intervention assessments (V_2 and V_3), only the following assessments were administered: MADRS, PHQ-9, CGI-S, CGI-I, and RRS-22. CGI-I: Clinical Global Impressions-Improvement; CGI-S: Clinical Global Impressions-Severity; LoH: Legends of Hoa'manu; MADRS: Montgomery-Åsberg Depression Rating Scale; MDD: major depressive disorder; PHQ-9: Patient Health Questionnaire-9; RRS-22: Ruminative Responses Scale (22-item).



Randomization

Randomization used a validated computer-generated pseudorandom sequence with permuted blocks of 4 (1:1 allocation ratio), prepared by the co-principal investigator (PI), who had no contact with participants. Participants were assigned sequentially in order of enrollment. The allocation list was held by the PI; after completion of baseline assessment, the PI released the participant's assignment to the unblinded staff member responsible for intervention distribution. Outcome assessors remained blinded to allocation. No additional allocation concealment procedures (eg, centralized automated assignment) were used. Both the active and the control games were self-administered, and study staff were available to assist remotely whenever needed.

Blinding

Overview

Participants were blinded to their group assignment and did not know whether the game they played was considered active or control; assessors were fully blinded to both group assignment and the game administered. Blinding was assessed by asking participants to guess their group allocation at weeks 1 and 6.

Participants were asked to train for up to 5 days per week for a period of 6 weeks, which equaled a total of 30 treatment sessions. Each session consisted of 30 minutes of training for an expected total of 15 hours of gameplay. As per protocol, in case of missing or canceled treatment sessions, participants were allowed to complete training over the weekends and during week 7 directly after the treatment period but before the postintervention assessment. Participants were asked to maintain a consistent training environment, including minimizing potential distractions, and were encouraged to adhere to a regular training schedule. By promoting these consistent conditions, we sought to ensure the training could be delivered in an optimal and focused setting. A subset of the assessments was repeated 2 and 4 weeks from the beginning of training (V_2 and V_3 , respectively). The full assessment battery was repeated within a week of the end of the treatment period (V_4 ; postintervention; always at least 24 hours after training was completed), and approximately a month later (V_5 ; follow-up assessment).

Session Orientation and Supported Start

During the V_1 baseline visit, after randomization and tablet handover, an unblinded staff member gave a brief in-person walkthrough of how to operate the tablet and the assigned game and then sat alongside the participant while they completed their first 30-minute training session. This ensured the participant could navigate the interface, troubleshoot technical issues, and be at ease with the setup before continuing the remaining intervention independently at home. Subsequent sessions were entirely self-administered. Unblinded study staff remained reachable by phone for technical or logistical questions throughout the 6-week training period. On a per-need basis, unblinded study

staff would provide reminders or encouragement to participants who appeared to have difficulty adhering to training procedures.

Outcomes

Overview

The trial was prospectively registered with depressive symptom change on the MADRS as the primary end point, feasibility as the secondary end point, and tertiary end points spanning symptoms, well-being, rumination, function, and participation. Exploratory end points included CC change, durability across the 1-month follow-up, as well as treatment expectancy and intrinsic motivation. This analysis follows this structure; intrinsic motivation is reported within the secondary feasibility framework—consistent with standard practice in feasibility studies of digital mental health interventions (deviation is disclosed here per CONSORT recommendations). A within-arm exploratory analysis testing whether CC gains are associated with depressive symptom reductions is reported as an additional mechanistic analysis (not formally preregistered as a hypothesis).

The trial was designed as a feasibility and effectiveness study, and its outcome hierarchy follows the preregistration and was not altered post hoc. The MADRS was chosen as the primary (effectiveness) end point following clinical standards for depression trials. Feasibility was the secondary end point because, given the novelty of this home-based, minimal-contact serious game intervention, establishing that the protocol could be delivered and completed per protocol was a central goal of this first trial. CC was exploratory, assessed to probe the proposed training mechanism rather than as a confirmatory clinical outcome, and, because the assessment battery shares task demands with the LoH training mini-games, change on it cannot be cleanly interpreted as generalizable transfer (see “Discussion” section).

Primary Outcome (MADRS)

The preregistered primary outcome was change in depressive symptoms on the MADRS [59], from baseline (V_1) to postintervention (V_4), reflecting the hypothesis that the LoH intervention would reduce depressive symptoms more than the active control game. Statistical inferences for the primary outcome were performed at an α of .05. The MADRS is a clinician-administered scale with 10 items scored on a 7-point scale (0–6). The total score ranges between 0 and 60, with higher scores indicating greater depression severity.

Secondary Outcome (Feasibility)

Feasibility outcomes comprised (1) adherence (completed training sessions and total minutes played); (2) retention at postintervention (V_4) and follow-up (V_5); and (3) intrinsic motivation, assessed at the end of week 1 and at V_4 with the Intrinsic Motivation Inventory (IMI [60]). All 5 IMI subscales (interest/enjoyment, effort/importance, perceived competence, perceived choice, and pressure/tension) are reported separately; pressure/tension serves as a proxy for subjective tolerability (lower scores indicate greater tolerability).

The preregistered feasibility threshold was completion of ≥ 20 of the 30 prescribed sessions by $\geq 50\%$ of randomized participants. We additionally applied 3 post hoc benchmarks drawn from comparable digital mental health trials [40,61,62]: retention at $V_4 \geq 70\%$, mean adherence $\geq 60\%$, and mean IMI interest/enjoyment in the active arm above the scale point (4/7)—framed as reference points rather than prespecified criteria. Expanded session-level in-game involvement metrics from server-side gameplay logs are reported in [Multimedia Appendix 2](#); these correspond to the “training progress” pillar of the 4-pillar cognitive training evaluation framework of Harvey et al [63] (reabeled from “training engagement” in the framework of Harvey et al to avoid confusion with the engagement framework of Plass et al [64]).

Tertiary Outcomes

Tertiary outcomes were chosen because CC deficits in MDD are theorized to operate through perseverative negative thinking that, in turn, impairs everyday functioning and reduces well-being. The preregistered selection also follows current state-of-the-art recommendations for computerized cognitive training trials [63]. It included MADRS-based response ($\geq 50\%$ reduction from baseline) and remission (MADRS ≤ 10) rates. The other tertiary outcomes capture (1) near-transfer—depressive symptoms; (2) far transfer—severity of illness, global improvement, and rumination; and (3) ecological transfer—well-being, functional capacity, plus participation in daily activities. Depression severity, a near-transfer measure, was assessed using the Patient Health Questionnaire-9 (PHQ-9 [65]), a self-reported measure with scores ranging from 0 to 27. Severity of illness, a more distant transfer measure, was assessed using the Clinical Global Impressions-Severity (CGI-S) scale [66]. The CGI-S is a clinician-rated measure used to evaluate the overall severity of a patient’s illness at a given time based on the rater’s clinical experience, ranging from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). Global improvement was assessed using the companion Clinical Global Impressions-Improvement (CGI-I) scale [66], a clinician-rated measure of change relative to the patient’s condition at admission, ranging from 1 (very much improved) through 4 (no change) to 7 (very much worse). Rumination was assessed using the full Ruminative Responses Scale (RRS-22 [67]), a 22-item self-reported scale measuring participants’ tendency toward repetitive negative thinking. Items are rated on a 4-point Likert scale, ranging from 1 (almost never) to 4 (almost always), and a total score is derived, with higher scores indicating greater levels of rumination.

Concerning ecological transfer, well-being was measured using the World Health Organization (WHO)-5 Well-Being Index [68], a 5-item self-reported scale with positively worded statements scored on a 6-point Likert scale, ranging from 0 (none of the time) to 5 (all of the time), assessing subjective well-being over the past 2 weeks. Higher scores reflect better well-being. Functional capacity was assessed using the University of California, San Diego, Performance-based Skills Assessment (UPSA [69]), which evaluates functional capacity in 5 domains: medication management,

financial management, using the telephone and communication, using public transportation, and planning leisure activities, using a simulation of 11 daily life tasks. Final scores range from 0 to 100. The Adult Subjective Assessment of Participation (ASAP [70]), a self-reported questionnaire, documents subjective and objective participation dimensions in daily life occupations of adults. Indices of objective participation include diversity (the percentage of activities in which the person participates) and intensity or frequency (ie, the prevalence of participation in activities). This measure also tracks activities that were stopped. Subjective dimensions include enjoyment (perceived pleasure in activities) and satisfaction (perceived fulfillment from participation), both rated on 7-point scales.

Exploratory Outcomes

Change in CC was preregistered as an exploratory outcome, motivated by the mechanistic hypothesis that the LoH intervention trains CC. It is reported alongside the primary and tertiary end points in the “Results” section. CC was assessed using a computerized cognitive assessment battery, the Adaptive Cognitive Evaluation (ACE; Neuroscience, University of California, San Francisco [71]). We administered 6 ACE tasks, collectively measuring inhibitory control, cognitive flexibility, WM updating, sustained attention, and visuospatial WM. One of the tasks (Fileter, measuring visual WM) was excluded from analyses because many participants did not understand the task demands. On the basis of factor analyses of the remaining 5 tasks, a CC composite score was created from normed scores. ACE task outcomes and factor analysis are given in [Multimedia Appendix 3](#).

Additional exploratory analyses included treatment credibility and outcome expectancy, assessed at the end of week 1 and at V_4 with the Credibility/Expectancy Questionnaire (CEQ [72]; credibility 3–27, expectancy 3–27, higher scores indicate greater credibility/expected benefit). In addition, durability of treatment effects was defined as change in all outcomes between baseline (V_1) and 1-month follow-up (V_5) and is reported for each end point alongside the V_1 to V_4 analysis.

Interventions and Comparators

Design Rationale and Shared Features

The intervention is described using the TIDieR (Template for Intervention Description and Replication) checklist categories; a TIDieR summary table covering both arms is provided in [Multimedia Appendix 4](#). The interventions were developed using Unity (version 2019.4.28f1; Unity Technologies). LoH and LoH_control versions 1.1.10 to 1.1.13 were used, corresponding to early bug corrections in the overall running performance, save system, and data collection, none of which affected the game content per se.

The distinction between the experimental (LoH) and active control (LoH_control) arms is not between a cognitively demanding and a cognitively inert condition, but between involvement matched and mechanism specific. Both arms

load on cognitive engagement in the sense of Plass et al [64], offering structured goals, unambiguous feedback, and clear challenges. Critically, LoH_control was designed to match LoH on the patient's ability to become involved with the game and thus spend time on task (involvement matched) while omitting the action mechanics hypothesized to challenge and train attention and CC (mechanism specific). In addition, LoH leverages both cognitive and affective engagement [64]—the latter via emotionally valenced facial expressions in the N-back and Go/No-Go modules, which target the mood-congruent attentional bias implicated in MDD [30-33]—whereas LoH_control relies exclusively on cognitive engagement. Importantly, LoH_control was designed to have a similar look and feel as the active LoH game and to also induce robust in-game involvement.

Interventions were developed in Unity and distributed directly to participants through tablets with the assigned game installed on them. Gameplay metrics (session duration and in-game involvement metrics) were automatically logged and transmitted to the study server. Each game was played during 30-minute sessions, within which several tasks were iterated. Both game versions place the player in an adventure world with tasks and subtasks while they discover the Village, a hub designed to maintain the players' engagement by allowing them to exchange the points earned during play to personalize their game world via various aesthetic upgrades. Participants in both arms received identical instructions regarding gameplay and schedule.

Experimental Game

The game LoH is designed as a cognitive training platform that integrates emotional and cognitive elements through various interactive challenges. The game architecture combines fast-paced action video game mechanics—centered around a core action game hub where players control a friendly creature navigating flying sequences that demand both divided and focused attention [73]—with targeted cognitive training mini-games. LoH is specifically designed to provide structured variability and adapt to individual player abilities through a multidimensional, probabilistic dynamic difficulty adjustment [74]. By continuously adapting task demands across multiple parameters, this system maintains each player within their zone of proximal development throughout training [74], sustaining the level of controlled processing required for cognitive skill acquisition—beyond merely reducing boredom or frustration [51].

LoH includes 7 such dynamically adjusted mini-games, each targeting a specific CC ability such as WM, inhibitory control, cognitive flexibility, sustained attention, divided attention, and multitasking, as detailed in [Multimedia Appendix 4](#). Additionally, a deductive reasoning task is included as a supplementary, nonadaptive mini-game. LoH incorporates emotional stimuli (eg, emotionally valenced facial expressions in the N-back and Go/No-Go tasks) to specifically target the mood-congruent attentional bias implicated in MDD—that is, the tendency to direct attention toward negatively valenced stimuli [7]. Positive reinforcement elements (collecting coins, personalized rewards)

provide additional motivational scaffolding [75]. An earlier version has been shown to successfully enhance attentional control in children [76].

Active Control Game

The active control game (LoH_control) was designed to match the aesthetic and structural elements of the experimental game, an important feature to maintain experimental blinding. Critically, its mini-games lack the adaptive cognitive training components of LoH and its action-based high attentional demands. It consists of a central hub game and 4 distinct mini-games (a modified, no-action version of the flight hub, visual search, peripheral vision task, and decoration). These activities emphasize the slow and deliberate movement of focused attention through tasks such as guiding a bird character to collect resources, focusing on auditory cues in a peripheral vision task, or spotting concealed targets in a cluttered map. These activities were selected based on prior research that used similar tasks as control conditions for depressed or dysphoric participants [26]. As such, the control game does not challenge attentional control as much as LoH. Moreover, unlike LoH, which incorporates positive emotional reinforcement through collecting happy coins and working with happy facial expressions, the control game lacks emotionally salient features. Players were presented with a fixed sequence of these 4 mini-games, each played twice within the same training session. A description of the control mini-games is given in [Multimedia Appendix 4](#).

Patient and Public Involvement

Adults with lived experience of depression contributed to the design of the LoH intervention prior to trial launch through structured user-feedback sessions. Feedback informed the gameplay tempo, the visual aesthetic of the Village hub, the wording and pacing of in-game instructions, and the difficulty calibration of the adaptive mini-games. Patients and members of the public were not involved in setting the research question, designing the trial protocol, interpreting study results, or preparing this manuscript. Findings will be disseminated to participants on request via the corresponding author and through lay summaries posted to the OSF repository.

Harms

Adverse events (CONSORT 2025 harms item) were assessed via open-ended questioning at each scheduled visit (V₂-V₅); spontaneous reports during between-visit phone contacts with study staff were also recorded. No adverse events related to the intervention were reported during the trial in either arm. Beyond adverse event surveillance, depressive symptom severity, including suicidality (MADRS item 10), was rated by a clinician at every study visit, providing continuous monitoring of clinical status throughout the trial. Per the protocol's prespecified stopping rules, any participant showing documented suicidal ideation (MADRS item 10 above the protocol-defined threshold) or a suicide attempt after commencing active or control training, emergent hypomanic or manic symptoms, or clinically

significant deterioration in the investigator's judgment, would be withdrawn from study treatment and referred to their treating clinician for appropriate care; investigators reviewed clinical status at each visit and could withdraw a participant at any time on clinical grounds. The absence of a validated safety questionnaire is acknowledged in the "Limitations" section.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Helsinki Committee of Merhavim Medical Center (approval 670-21) and the Ethics Committee of the Faculty of Medicine at the Hebrew University of Jerusalem (approval 0388-20-HMO). All participants provided written informed consent at V_0 prior to any study procedure. Participants received NIS 250 (approximately US \$82); compensation was not contingent on adherence or completion, so that it could not pressure continued participation. All data were deidentified using study IDs; a single linking file was stored separately on a password-protected drive accessible only to the PI and unblinded staff. No figures or multimedia appendices contain images of identifiable participants.

Statistical Methods

Analytic Approach

All statistical analyses were conducted using R (R Foundation for Statistical Computing) [77,78]. Analysis was conducted by a person blinded to the group assignment (Mattan S Ben Shachar). Baseline measures were compared between groups, and the association between attrition and baseline measures was assessed, using t tests and chi-square tests. The primary analysis followed the intention-to-treat principle, retaining all randomized participants in their originally assigned groups. All outcomes with a baseline assessment were analyzed using linear mixed models (LMMs). LMMs with maximum likelihood estimation provide unbiased estimates under the missing-at-random assumption and were used as the primary handling strategy. We report here ANOVA-like omnibus F tests with Satterthwaite degrees of freedom. These models include fixed effects for time (baseline, postintervention, and follow-up), group (active vs control), and the time $\times$ group interaction. Random intercepts were specified for participants to account for individual variability at baseline.

As loss to follow-up at postintervention was strongly associated with the number of completed training sessions rather than with baseline symptom severity, the number of completed sessions (mean centered) was included as an additional covariate in all outcome models to reduce potential attrition-related bias and to make the missing-at-random assumption more plausible. This covariate was not part of the preregistered analysis plan and is itself a postrandomization variable; we therefore also report unadjusted models (omitting this covariate) as a sensitivity analysis in [Multimedia Appendix 5](#), which yielded materially identical conclusions.

For significant time $\times$ group interactions, post hoc comparisons with Bonferroni correction were conducted. Effect sizes are reported using partial η^2_p with 2-tailed 90% CIs, and estimated mean differences are reported with 95% CIs. Statistical inference for the primary outcome (H1: MADRS group $\times$ time) was performed at an α of .05. Tertiary outcome (H3) and exploratory analyses (CC, durability, mechanism, and predictors) are reported with unadjusted P values.

The secondary feasibility outcomes include the preregistered feasibility threshold (H2: $\geq 50\%$ of randomized participants completing ≥ 20 of the 30 prescribed sessions) assessed as a descriptive proportion against the registered threshold. Feasibility, in-game involvement, and intrinsic motivation metrics were evaluated using descriptive statistics, independent-sample t tests for continuous measures, and chi-square tests (with Yates continuity correction) for categorical comparisons. Session-level gameplay-log comparisons (early abandonment and per-session active gameplay duration) were analyzed with mixed effects models, including a random intercept for participant to account for the nesting of sessions within participants ([Multimedia Appendix 2](#)). As an exploratory analysis, we examined the association between within-participant changes in CC and change in depressive symptoms. We first computed residual scores by regressing baseline scores out of postintervention and follow-up measurements separately. This approach allowed for the examination of change independent of initial differences, controlling for baseline variability and regression to the mean.

Missing Data

Participant-level missing data (loss to follow-up) were 16% (9/57) at postintervention (V_4) and 23% (13/57) at 1-month follow-up (V_5). Item-level missing data within completed assessments were minimal. The primary analytic strategy of linear mixed models with maximum likelihood estimation under the missing-at-random assumption (described earlier) accommodates this level of missingness. We assessed the missing data mechanism using Little test of missing completely at random; the test was nonsignificant for the primary outcome and for the other clinical measures, with a single borderline exception. As a sensitivity analysis, we repeated the primary group $\times$ time analyses under multiple imputation by chained equations ($m=20$). Both analyses are reported in [Multimedia Appendix 6](#) and yielded conclusions consistent with the primary models.

Results

Participants and Baseline Characteristics

Demographic and baseline characteristics of the study sample are summarized in [Table 1](#). The participant flow is given in [Figure 2](#). Following eligibility assessment ($n=60$), 57 of 60 (95%) participants were randomized to either the active (28/57, 49%) or control (29/57, 51%) intervention. The sample was predominantly women (21/28, 75% and 18/28, 64.3% in the control and active arms, respectively) with an

average age of 38 (SD 12) years. The groups were well matched on demographic characteristics (all $P \geq .10$) and on depression severity at baseline (HDRS-17: mean 24.52, SD 4.98 vs mean 22.50, SD 6.02, in the control and active

arms, respectively). On the basis of the HDRS-17 scores, participants presented with moderate to severe depression at baseline, with mean scores in the severe range for the control arm and upper moderate range for the active arm.

Table 1. Baseline demographic and clinical characteristics of the study sample (N=57).

Characteristics	Active (n=28)	Control (n=29)	Statistic	P value
Demographics				
Female, n (%)	18 (64.3)	21 (75) ^a	0.76 ^b	.38
Age (years), mean (SD)	37.68 (11.96)	38.30 (13.05) ^a	-0.19 ^c	.85
Marital status, n (%)				
Married or living with partner	15 (53.6)	12 (42.9) ^a	0.64 ^b	.42
Single	11 (39.3)	10 (35.7)	0.08 ^b	.78
Divorced or separated	1 (3.6)	6 (21.4)		.10 ^d
Widowed	1 (3.6)	0 (0) ^a		>.99 ^d
Native language, n (%)				
Hebrew	16 (57.1)	15 (53.6)	0.07 ^b	.79
Russian	11 (39.3)	10 (35.7) ^a	0.08 ^b	.78
Other	1 (3.6)	3 (10.7) ^a		.61 ^d
Education (years), mean (SD)	14.21 (3.50)	13.61 (4.61)	-0.55 ^c	.59
Currently employed, n (%)	18 (64.3)	14 (50) ^a	1.17 ^b	.28
Clinical characteristics				
HDRS-17 score, mean (SD)	22.50 (6.02)	24.52 (4.98)	-1.38 ^c	.17
On antidepressants, n (%)	20 (71.4)	19 (65.5)	0.23 ^b	.63
Comorbidities, n (%)				
Cardiac disease	0 (0)	0 (0)	N/A ^e	N/A
Seizures	0 (0)	1 (3.4)	N/A	N/A

^aData missing for 1 control participant; percentages are based on N=28.

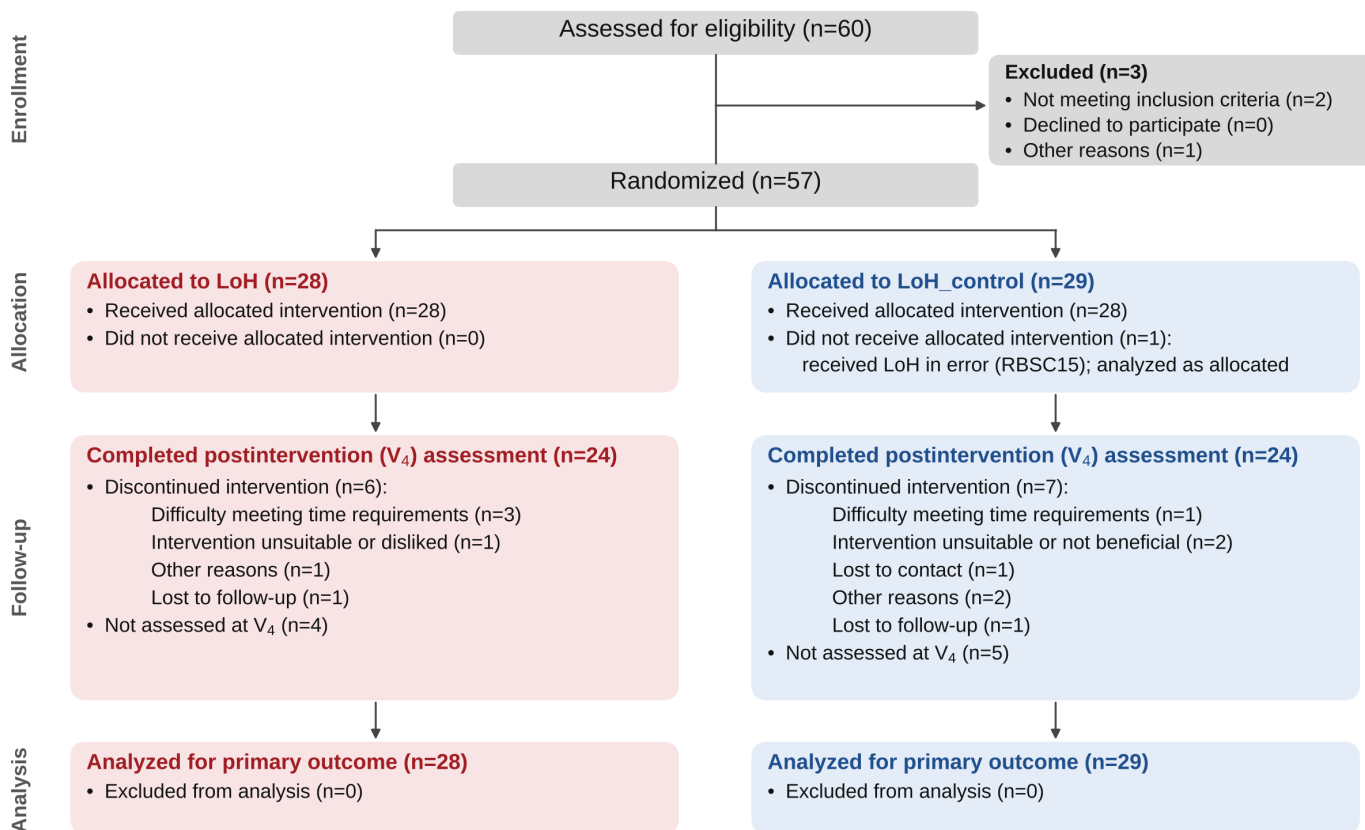
^b χ^2 value.

^c t value.

^dFisher exact test (expected cell counts <5).

^eN/A: not applicable.

Figure 2. CONSORT 2025 flow diagram for the trial of Legends of Hoa'manu (LoH; active) versus a matched active control game (LoH_control) in adults with major depressive disorder. The primary outcome (change in MADRS total score from baseline to postintervention, assessed at visit V₄) was analyzed for all randomized participants under the intention-to-treat principle using linear mixed models on all available data; consequently, the analyzed n equals the allocated n in each arm. One participant randomized to LoH_control received LoH in error (RBSC15) and was analyzed as allocated. Four participants (2 per arm) discontinued training but completed the V₄ primary outcome assessment and were subsequently lost before the 1-month follow-up (V₅), a secondary time point reported in the Results and in [Multimedia Appendix 7](#). "Other reasons" denotes discontinuations for which a specific reason was not recorded (n=1 in LoH; n=2 in LoH_control). LoH: Legends of Hoa'manu; MADRS: Montgomery-Åsberg Depression Rating Scale.



Primary Outcome: Baseline to Postintervention Change in Depression (MADRS)

We report here analyses of changes from baseline (V₁) to postintervention (V₄) for all outcome measures. Analyses of the full dataset, including all midtraining time points (whenever available) and follow-up data, are provided in [Multimedia Appendix 7](#). Note that because the number of sessions completed was found to be a strong predictor of missing patterns postintervention (at V₄), it was controlled for in the analyses. Unadjusted sensitivity analyses omitting this covariate are reported in [Multimedia Appendix 5](#) and yielded the same conclusions. [Table 2](#) includes the data for all outcome measures.

Analysis of the primary outcome (depressive symptoms) revealed a significant reduction in MADRS scores from baseline (V₁) to postintervention (V₄; $F_{1,48.6}=47.52$; $P<.001$; $\eta^2_p=0.49$, 90% CI 0.32-0.61) across both arms. However, the effect of group was not significant ($F_{1,52.6}=0.02$; $P=.90$; $\eta^2_p=0.00$), nor was the group $\times$ time interaction ($F_{1,49.4}=1.57$; $P=.22$; $\eta^2_p=0.03$). Post hoc analyses showed a significant reduction in MADRS scores in both arms (active: -6.83 points, 95% CI -10.26 to -3.41 ; $t_{48.4}=-4.01$; $P<.001$; and control: -9.84 points, 95% CI -13.28 to -6.41 ; $t_{48.0}=-5.76$; $P<.001$).

Table 2. Baseline (V1) and postintervention (V4) scores for primary, tertiary, and exploratory outcome measures by arm.

Domain and measure	LoH ^a /active (randomized n=28)				LoH_control/control (randomized n=29)			
	V ₁ (baseline)		V ₄ (postintervention)		V ₁ (baseline)		V ₄ (postintervention)	
	Mean (SD)	n ^b	Mean (SD)	n ^b	Mean (SD)	n ^b	Mean (SD)	n ^b
Depression								
MADRS ^c	29.39 (7.41)	28	22.92 (9.01)	24	31.35 (7.57)	29	20.38 (10.60)	24
PHQ-9 ^d	18.25 (5.78)	28	14.21 (8.60)	24	19.32 (6.45)	28	14.25 (7.13)	24
Severity of illness								
CGI-S ^e	4.14 (0.97)	28	3.63 (1.53)	24	4.32 (0.95)	28	3.42 (1.59)	24
Rumination								
RRS-22 ^f	58.68 (15.44)	28	50.83 (16.49)	24	59.89 (13.70)	28	56.50 (18.73)	24
Cognitive control								
ACE ^g composite	0.04 (0.84)	28	-0.22 (0.97)	23	0.18 (0.87)	26	0.00 (0.97)	22
Well-being								
WHO-5 ^h	20.43 (19.27)	28	30.83 (23.40)	24	22.71 (19.32)	28	31.83 (27.65)	24
Functional capacity								
UPSA ⁱ	68.12 (13.83)	25	81.11 (9.95)	18	72.85 (14.64)	27	80.95 (14.47)	19
Participation								
Diversity	15.64 (7.29)	28	16.29 (7.23)	24	15.32 (8.39)	28	17.04 (9.62)	26
Stopped activities	17.39 (8.12)	28	18.79 (7.86)	24	19.21 (8.10)	28	18.73 (8.41)	26
Intensity and frequency	4.42 (0.75)	28	4.68 (0.61)	24	4.24 (0.72)	28	4.49 (0.93)	25
Enjoyment	3.65 (1.09)	28	3.84 (1.31)	24	3.99 (1.00)	28	4.16 (1.18)	25
Satisfaction	4.07 (1.05)	28	3.90 (1.27)	24	4.41 (1.06)	28	4.36 (1.13)	25

^aLoH: Legends of Hoa'manu.^bVaries with item-level missingness.^cMADRS: Montgomery-Åsberg Depression Rating Scale. Baseline (V₁) reflects the screening/V₀ assessment.^dPHQ-9: Patient Health Questionnaire-9.^eCGI-S: Clinical Global Impressions–Severity.^fRRS-22: Ruminative Responses Scale-22.^gACE: Adaptive Cognitive Evaluation.^hWHO-5: World Health Organization-Five Well-Being Index.ⁱUPSA: University of California, San Diego Performance-Based Skills Assessment.

Secondary Outcome (Feasibility)

Feasibility Threshold and Benchmarks

Full feasibility metrics are provided in [Multimedia Appendix 2](#). The preregistered feasibility threshold for gameplay completion was met: 30 of 57 (52.6%; 95% CI 39.9%-65%) randomized participants completed ≥ 20 of the 30 prescribed sessions, exceeding the preregistered $\geq 50\%$ threshold; among the 53 participants with recoverable gameplay data, 30 of 53 (56.6%; 95% CI 43.3%-69%) met this threshold.

The 3 additional post hoc benchmarks were also met. First, retention was high at both postintervention (48/57, 84%; $\geq 70\%$ benchmark) and follow-up (V₅: 44/57, 77%). Attrition was comparable across arms (active: 6/28, 21%; and control: 7/29, 24%; [Figure 2](#)). Specifically, 5 participants in the control arm discontinued participation during the first 2 weeks of the intervention, and 2 discontinued training later but completed the postintervention (V₄) assessment before being lost to follow-up. In the active arm, 2 participants discontinued their participation during the first 2 weeks of the intervention and 2 after week 2 (V₂); 2 further participants discontinued training later but completed the V₄ assessment before being lost to follow-up. The reasons for discontinuation are reported by arm in [Figure 2](#); the most common

were difficulty meeting the protocol's time requirements and finding the intervention unsuitable or not beneficial. Second, the mean adherence exceeded the 60% benchmark—participants completed, on average, 20.7 (SD 9.48) sessions of the 30 allotted sessions (mean 69%, SD 31.6%), with no significant between-group difference ($t_{50}=1.25$; $P>.05$). Third, the intrinsic motivation benchmark was met, with mean IMI interest/enjoyment in the active arm of 4.56 (SD 1.49) exceeding the scale midpoint (4/7).

In-Game Involvement

Server-side gameplay logs were recovered for 53 of 57 randomized participants (LoH: 27/28, 96%; and LoH_control: 26/29, 90%) due to hardware failure. The mean active gameplay duration per session was 26.2 (SD 8.7) minutes for LoH and 28.7 (SD 8.3) minutes for LoH_control, closely matching the prescribed 30-minute dose. Early abandonment (active gameplay <15 minutes) was uncommon and did not differ between arms (LoH: 41/503, 8.2% vs LoH_control: 30/564, 5.3%; mixed-effects logistic regression with a random intercept for participant, $z=1.76$; $P=.08$). Sessions were distributed across all day parts, and 25% occurred on weekends (LoH: 126/503, 25%; LoH_control: 137/564, 24.3%), with similar patterns in both arms, indicating

integration into varied daily schedules. Weekly mean session duration was stable across weeks 1 to 6 in both arms, with no evidence of gameplay fatigue. The catch-up provision at weekends and/or in week 7 was used by 27 of 27 LoH and 25 of 26 LoH_control participants and accounted for approximately 28% of all sessions in both arms (LoH: 143/503, 28.4%; LoH_control: 157/564, 27.8%). Per-participant adherence was heterogeneous: 33% (9/27) of LoH and 58% (15/26) of LoH_control participants completed $\geq 80\%$ of prescribed sessions, while 30% (8/27) of LoH and 23% (6/26) of LoH_control completed fewer than half. This range is typical of remote digital mental health interventions and represents a target for personalization in future trials. Among discontinuers, all completed at least two sessions before quitting. Full distributions, statistical tests, and figures are reported in [Multimedia Appendix 2](#).

Intrinsic Motivation

Full results are given in [Multimedia Appendix 8](#). At the end of week 1, IMI ratings were broadly comparable between arms for all subscales, except for perceived competence, which was higher in the control arm ($t_{39.98}=-2.74$; adjusted $P=.03$; mean difference -0.90 , 95% CI -1.56 to -0.24).

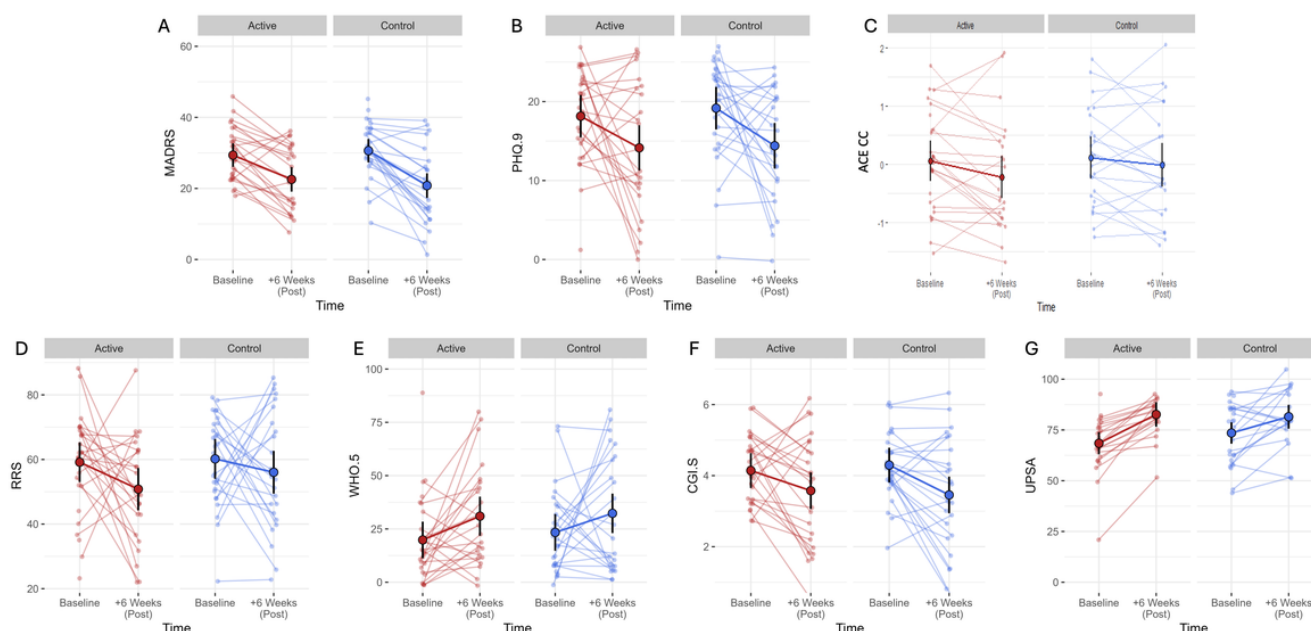
At postintervention (V_4), the active arm reported higher interest/enjoyment ($t_{47.79}=2.71$; adjusted $P=.02$; mean

difference 1.15, 95% CI 0.30-2.00) and higher effort/importance ratings ($t_{48}=2.84$; adjusted $P=.02$; mean difference 0.93, 95% CI 0.27-1.59) than the control arm, indicating that the active intervention was perceived as more enjoyable and more effortful. Pressure/tension scores were in the low-to-moderate range in both arms at both time points (LoH: mean 3.62, SD 1.58 at week 1; mean 3.90, SD 1.37 at V_4 ; LoH_control: mean 3.08, SD 1.21 at week 1; mean 3.13, SD 1.56 at V_4). Between-group comparisons were nonsignificant at week 1 ($t_{45.0}=1.38$; $P=.17$, mean difference 0.54, 95% CI -0.25 to 1.33) and at V_4 ($t_{47.9}=1.85$; $P=.07$; $d=0.52$, mean difference 0.77, 95% CI -0.06 to 1.60). Although the V_4 difference was not statistically significant, the effect size estimate ($d=0.52$) was in the direction of higher pressure/tension in LoH, consistent with the more attentionally demanding action game format.

Changes Between Baseline and Postintervention on Tertiary Outcome Measures

The results for the preregistered tertiary outcomes are summarized next and are depicted in [Figure 3D-G](#).

Figure 3. Change in outcome measures from baseline (V_1) to postintervention (V_4) by arm (LoH in red; LoH_control in blue). Scores are shown for (A) MADRS (clinician-rated depressive symptoms); (B) PHQ-9 (self-rated depression severity); (C) ACE CC composite score; (D) RRS-22 (rumination); (E) WHO-5 (well-being); (F) CGI-S (clinician-rated illness severity); and (G) UPSA (functional capacity). Thin lines: individual participants; thick lines: group means with error bars. ACE: Adaptive Cognitive Evaluation; CGI-S: Clinical Global Impressions–Severity; MADRS: Montgomery–Åsberg Depression Rating Scale; PHQ-9: Patient Health Questionnaire-9; RRS-22: Ruminative Responses Scale-22; UPSA: University of California, San Diego Performance-Based Skills Assessment; WHO-5: World Health Organization-5 Well-Being Index.



MADRS-Based Response and Remission

MADRS response ($\geq 50\%$ reduction from baseline) and remission (MADRS ≤ 10) rates at postintervention and 1-month follow-up were computed, comparing groups using

2-sided Fisher exact tests with nonresponder imputation for missing MADRS scores. The results, indicating no between-group differences, are summarized in [Multimedia Appendix 9](#).

Depressive Symptoms (PHQ-9)

Changes from V_1 to V_4 showed a significant effect of time ($F_{1,49,16}=10.72$; $P=.002$; $\eta^2_p=.018$, 90% CI 0.04-0.33). However, there were no significant effects of group ($F_{1,49,8}=0.18$; $P=.67$; $\eta^2_p=0.004$) nor a significant group×time interaction ($F_{1,49,8}=0.08$; $P=.78$; $\eta^2_p=0.002$; [Figure 3A,B](#)).

Rumination (RRS-22)

The effect of time was not statistically significant ($F_{1,98}=3.75$; $P=.06$; $\eta^2_p=0.04$, 90% CI 0.00-0.11). However, there was no significant effect of group ($F_{1,98}=0.97$; $P=.33$; $\eta^2_p=0.01$), nor a group×time interaction ($F_{1,98}=0.43$; $P=.51$; $\eta^2_p=0.004$).

Well-Being (WHO-5)

World Health Organization-Five Well-Being Index (WHO-5) demonstrated a significant improvement over time ($F_{1,46,5}=5.17$; $P=.03$; $\eta^2_p=0.10$, 90% CI 0.01-0.24). However, there were no significant effects for group ($F_{1,46,6}=0.27$; $P=.60$; $\eta^2_p=0.006$) nor a group×time interaction ($F_{1,47,03}=0.06$; $P=.80$; $\eta^2_p=0.001$).

Severity of Illness

Severity of illness, measured using the CGI-S scale, demonstrated a significant improvement over time ($F_{1,49,2}=13.55$; $P<.001$; $\eta^2_p=0.22$, 90% CI 0.07-0.36). However, there were no significant effects for group ($F_{1,52,8}=0.003$; $P=.96$; $\eta^2_p=0.00$) nor a group×time interaction ($F_{1,50,1}=0.52$; $P=.47$; $\eta^2_p=0.01$). Post hoc within-group comparisons showed a nonsignificant reduction from baseline to postintervention in the active arm (−0.57 points; 95% CI −1.11 to −0.03; $t_{48,8}=-2.10$; Bonferroni-adjusted $P=.08$) and a significant reduction in the control arm (−0.84 points; 95% CI −1.38 to −0.30; $t_{48,3}=-3.11$; Bonferroni-adjusted $P=.006$). As these P values are Bonferroni-adjusted for multiple comparisons and the CIs are unadjusted, the active-arm interval can exclude zero while its adjusted P value exceeds .05.

Global improvement was assessed with the clinician-rated CGI-I scale, which rates change relative to admission (1=very much improved to 7=very much worse; 4=no change). As CGI-I is defined relative to admission and therefore has no baseline value, it was not entered into the baseline-to-follow-up mixed models used for the other measures; instead, improvement was summarized descriptively and between-arm differences were tested at each postbaseline assessment. Participants were rated as improved: pooled CGI-I scores were significantly below the “no change” anchor at both postintervention (mean 2.96, SD 1.40; $t_{47}=-5.16$; $P<.001$; $d=-0.74$) and follow-up (mean 2.50, SD 1.32; $t_{43}=-7.53$; $P<.001$; $d=-1.14$), with 65% (31/48) of participants rated as at least minimally improved at postintervention and 75% (33/44) at follow-up (20/48, 42% and 25/44, 57%, respectively, rated much or very much improved). There was no significant difference between arms at postintervention ($F_{1,46}=0.17$; $P=.68$; $\eta^2_p=0.004$) or follow-up ($F_{1,42}=0.46$; $P=.50$; $\eta^2_p=0.01$).

Functional Capacity

Functional capacity, measured using the UPISA scale, showed a significant improvement over time ($F_{1,38,9}=33.16$; $P<.001$; $\eta^2_p=0.46$, 90% CI 0.26-0.59). However, there were no significant effects for group ($F_{1,49,2}=0.34$; $P=.56$; $\eta^2_p=0.007$), nor a group×time interaction ($F_{1,39,6}=2.56$; $P=.12$; $\eta^2_p=0.06$). Post hoc analyses revealed significant improvement from baseline to postintervention in UPISA for both the active (14.19 points; 95% CI 8.60-19.79; $t_{38,8}=5.13$; $P<.001$) and the control (8.04 points; 95% CI 2.58-13.51; $t_{38,5}=2.98$; $P=.01$) groups.

Participation (ASAP Scale)

Objective (diversity and frequency) and subjective (enjoyment and satisfaction) aspects of participation did not differ by time, group, nor group×time interaction. The full analyses of the ASAP can be found in [Multimedia Appendix 7](#).

Exploratory Analyses

Cognitive Control

Composite scores (normed to the V_1 data), comprising the individual scores of the 5 tasks (TNT, Stroop, Flanker, TaskSwitch, and SAAT), were computed for the ACE battery assessments, which were administered at V_1 and V_4 . Composite scores significantly improved from baseline to postintervention ($F_{1,44,6}=4.36$; $P=.04$; $\eta^2_p=0.09$). However, there were no significant effects of group ($F_{1,51,7}=0.79$; $P=.38$; $\eta^2_p=0.015$), nor a significant group×time interaction ($F_{1,45,5}=0.49$; $P=.49$; $\eta^2_p=0.01$). Post hoc analyses revealed that the changes between V_1 and V_4 were not significant for the active (−0.28 points; 95% CI −0.56 to 0.003; $t_{44,5}=-1.99$; $P=.11$) nor for the control arm (−0.14 points; 95% CI −0.42 to 0.15; $t_{44,5}=-0.97$; $P=.67$; [Figure 3C](#)).

Treatment Credibility and Expectancy (CEQ)

Credibility did not differ between arms at either time point (week 1: LoH: mean 12.96, SD 7.22; LoH_control: mean 15.00, SD 6.38; $t_{47,7}=-1.07$; $P=.29$, 95% CI for the between-arm difference −5.88 to 1.80; V_4 : LoH: mean 13.29, SD 7.47; LoH_control: mean 13.46, SD 5.95; $t_{44,0}=-0.09$; $P=.93$; 95% CI for the between-arm difference −4.04 to 3.70) and was stable within each arm over time, indicating that the matched control design sustained equivalent perceived credibility across arms. Credibility and outcome expectancy are distinct constructs, however, and comparable credibility did not entail comparable expectancy: outcome expectancy was higher in LoH_control than in LoH at week 1 (mean 12.87, SD 6.14 vs mean 9.29, SD 5.63; $t_{48,9}=-2.17$; $P=.04$; $d=-0.61$, 95% CI for the between-arm difference −6.89 to −0.27), indicating that control participants began the trial expecting more benefit; however, it did not differ between arms at V_4 (mean 10.75, SD 6.18 vs mean 9.35, SD 6.66; $t_{46,9}=-0.77$; $P=.45$; 95% CI for the between-arm difference −5.06 to 2.27). Both arms showed small numerical reductions in expectancy from week 1 to V_4 , more pronounced in LoH_control ($\Delta=-1.99$, paired $t_{23}=-1.82$; $P=.08$).

Predictors of Change

We exploratorily examined several factors as predictors of change in MADRS symptoms. First, the relations between changes in CC (using standardized composite scores) and clinical measures were assessed using residualized change scores, calculated by regressing postintervention scores on baseline scores for all measures. Changes in CC were *not* significantly associated with changes in depressive symptoms (MADRS: $r=0.05$, 95% CI -0.25 to 0.34 ; $t_{43}=0.33$; $P=.74$; PHQ-9: $r=0.04$, 95% CI -0.25 to 0.33 ; $t_{43}=0.28$; $P=.78$), quality of life (WHO-5: $r=-0.12$, 95% CI -0.40 to 0.18 ; $t_{43}=-0.79$; $P=.44$), or rumination (RRS-22: $r=0.15$, 95% CI -0.15 to 0.43 ; $t_{43}=1.02$; $P=.31$).

Next, we examined whether perceived choice (subscale of IMI) was associated with change in MADRS scores following treatment (see full results in [Multimedia Appendix 10](#)). In short, higher perceived choice significantly predicted greater MADRS improvement in the active arm only ($B=1.41$; adjusted $P=.006$), with this relationship reversed for the control arm.

Next, we examined whether blinding guesses were related to improvement in MADRS scores across the study population. The results showed that there was no significant difference in MADRS change between the active and control arms, regardless of participant guesses in the blinding check (see full analysis in [Multimedia Appendix 10](#)). Finally, the association between game progression metrics and change in MADRS and CC scores are summarized in [Multimedia Appendix 11](#).

Blinding Checks

Blinding was assessed at the end of week 1 and at the end of the 6-week intervention. There was no significant difference in participant guesses between the active and control treatment groups. At the end of week 1, 12/26 (46%) participants in the active arm and 20/28 (71%) participants in the control arm correctly guessed their group assignment (group comparison: $\chi^2_1=2.60$; $P=.11$). At week 6, 17/25 (68%) participants in the active arm and 12/23 (52%) participants in the control arm correctly guessed their group assignment (group comparison: $\chi^2_1=0.68$; $P=.41$). Full results are given in [Multimedia Appendix 12](#).

Discussion

Interpretation

This randomized controlled trial examined the feasibility and effectiveness of a home-based, action-based serious game (Legends of Hoa'manu; LoH) for individuals with MDD, compared against a closely matched active control game. Four findings can be mapped directly to our hypotheses. First, the superiority hypothesis on the primary end point (MADRS) was not supported. Depressive symptoms improved over time across both arms, with no significant group $\times$ time interaction. Second, the feasibility hypothesis (secondary end point) was supported. A majority of randomized participants met the preregistered session completion threshold, retention

was high at both postintervention and follow-up, and the additional post hoc reference benchmarks for adherence and intrinsic motivation were met. In particular, participants rated the active intervention as more enjoyable and more effortful than the control. Third, the tertiary outcome superiority hypotheses were not supported. Several tertiary outcomes improved over time across both arms, although not all showed clear improvement, with no significant group $\times$ time interactions. Improvements in depression scores were maintained at a 4-week follow-up, with no significant deterioration in any outcome measure. Finally, exploratory analyses examined the proposed CC mechanism and a hypothesis-generating predictor of clinical response. The mechanism analysis was not supported as individual changes in CC scores were not associated with changes in depressive symptoms or rumination. Interestingly, within the active arm only, postintervention perceived choice (subscale from IMI) predicted greater reductions in depression symptoms—a hypothesis-generating finding that warrants replication. This set of results offers insights into the potential benefits and limitations of gamified cognitive interventions for depression while raising questions about mechanisms of therapeutic change.

Participants in both arms showed reductions in depressive symptoms in the range generally considered clinically meaningful for MADRS [79]. In several additional measures—including CGI-S, RRS-22, and MADRS—descriptive improvements were numerically larger in the control arm, although the absence of significant group $\times$ time interactions cautions against direct between-arm contrasts. This pattern is consistent with growing evidence that closely matched active digital controls can produce substantial symptom change [11,41,48,49,80,81]. Several nonspecific processes plausibly contribute to this convergence, such as structured daily activity analogous to behavioral activation [80,82], intermittent on-demand contact with study staff and ad hoc adherence reminders, as well as possible expectancy effects, and natural fluctuation including regression to the mean, which cannot be ruled out in the absence of a no-contact or waitlist arm [83]. This is reinforced by our CEQ data showing higher initial outcome expectancy in the control arm, which itself contributes to nonspecific symptom change in psychotherapy trials [84].

These mechanisms are common to many psychological and digital interventions and are difficult to disentangle without additional control conditions [83]. Beyond nonspecific factors, it is worth noting that LoH_control was not designed to be cognitively inert. The same logic applies broadly in the action video game literature, where games such as Tetris—which engage visuospatial attention, WM, and rapid decision-making—are routinely used as active controls precisely because they match the experimental condition on general cognitive engagement while omitting the specific action mechanics hypothesized to drive transfer effects in healthy individuals [46,73]. LoH_control was designed following this same principle. Its tasks involve attention, structured goals, and reward but lack the adaptive difficulty, action video game mechanics, and emotionally valenced stimuli that constitute the theoretically active ingredients of

LoH [30-33,45,46,73]. The absence of superiority therefore raises the question of which specific components carry therapeutic weight, a question that future dismantling designs would be better positioned to address. Furthermore, the attentional demands embedded in LoH_control (visual search, peripheral vision, and deliberate target spotting) may have provided meaningful attentional stretch for adults with current MDD—a population whose baseline attentional capacity is typically lower [13,14,19] than that of young healthy adults in whom action game effects are most established [46]. Together, these features argue for future trials to include a no-contact or business-as-usual comparator alongside an active control, to better separate intervention-specific effects from the broader benefits of structured digital engagement.

The observed improvement in functional capacity (UPSA) in both arms is consistent with growing recognition that quality of life and functional capacity are key treatment outcomes in mental health beyond symptom reduction [85].

The relatively high retention and adherence observed here are noteworthy given both the intensity of the protocol (a 6-week, 30-session course) and its home-based, minimal-contact delivery. These rates are comparable to earlier digital interventions for MDD that were delivered in clinic or used fewer, less intensive sessions [32,33,40,44], and the present trial extends that work by showing that comparable feasibility can be achieved with a home-based protocol. The additional feasibility dimensions assessed beyond retention and adherence, including intrinsic motivation, daily life integration, subjective tolerability, and the gameplay-log analyses, provide further preliminary evidence of real-world fit.

The intervention used a minimal-contact, home-based design: after an in-person onboarding visit (V_1), the 6-week training phase was entirely self-administered with no scheduled remote clinician sessions, and most mid-study assessments (V_2 and V_3) were conducted by video—in contrast to many interventions labeled “remote” or “at-home” that incorporate substantial scheduled clinician contact. This feasibility may be attributable in part to the carefully designed game environment shared by both arms (structured schedules, aesthetic coherence, and motivating in-game goals [86]). Adherence was nevertheless heterogeneous across participants, suggesting that personalization may be needed to address adherence challenges in future home-based interventions for MDD. More broadly, home-based delivery of this kind may help overcome the stigma- and access-related barriers that often prevent individuals from seeking traditional mental health services [87].

While the preregistered secondary feasibility outcome was supported, the trial’s exploratory mechanistic question—whether LoH would specifically train CC—received a less affirmative answer. Specifically, although CC composite scores improved modestly over time across the full sample, the absence of a group $\times$ time effect and the lack of association between CC change and MADRS change do not support the targeted cognitive control account that motivated this trial. Several alternative explanations merit consideration. First, the ACE battery, which was used to assess CC, was administered

at baseline and postintervention, allowing for test-retest effects. Indeed, practice and familiarity effects on computerized cognitive tasks are well documented [88] and may have contributed to the small improvement observed in both arms. Moreover, the ACE tasks share substantial cognitive overlap with the LoH training mini-games (ie, both target response inhibition, task-switching, and sustained attention), which complicates interpreting any observed change as either generalizable transfer or task-specific learning [89]. Second, even the control game involved attention-demanding visuospatial tasks, structured goals, and reward elements, which could plausibly engage attentional networks despite not being designed as cognitive training. Third, the effect size for CC change was small, and the trial may have been underpowered to detect smaller, mechanistically meaningful contrasts in CC. The observed change on the ACE composite is best interpreted as a modest, time-related shift on a standardized composite score rather than a clinically interpretable index of cognitive recovery, consistent with the recognition that transfer from CC training is typically narrow and stimulus bound [89,90].

Within the active arm, higher postintervention perceived choice (IMI subscale) was associated with greater reduction in depressive symptoms. This finding should be interpreted with caution: it is post hoc, based on a single subscale among several tested, derived from a modest sample, and not corrected for multiple comparisons. It nevertheless converges with self-determination theory and prior work, suggesting that autonomy-supportive experience contributes to engagement and therapeutic response in digital and game-based interventions [51,86]. We therefore frame it as hypothesis generating: future adequately powered trials should test perceived choice as a candidate predictor of clinical response and as a potential target for autonomy-supportive design features (eg, schedule flexibility, optional content paths, and self-paced progression). We do not interpret this association as evidence for a specific cognitive training mechanism, nor for personalization frameworks more broadly.

Limitations

Several limitations should be considered. First, and most importantly, the trial used a closely matched active control without a no-contact or business-as-usual comparator. Although this matched design is a methodological strength, both arms improved comparably on the primary and tertiary outcomes, so we cannot rule out regression to the mean, time-related natural recovery, or contact-related expectancy effects [83], nor can we isolate the specific contribution of the targeted CC and action game components from the broader effects of structured digital activity. This concern is compounded by the unsupported exploratory CC mechanism analysis; yet whether this reflects insensitivity of the ACE composite, practice effects, the multicomponent nature of LoH, or the absence of a true mechanistic effect cannot be determined here. Second, the sample ($n=57$) was powered for a medium-to-large between-group effect ($d=0.65$), and was likely underpowered for the smaller differences expected when 2 engaging digital interventions are compared. Third, the exploratory analyses—including

the perceived-choice finding—were post hoc and uncorrected for multiple comparisons and require replication. Fourth, our feasibility assessment was narrow as it did not include validated usability or acceptability scales (eg, the System Usability Scale [91]) or systematic capture of technical barrier metrics or support contacts, and the 3 additional benchmarks were post hoc rather than preregistered. Fifth, the battery included no neural measures, limiting tests of mechanistic predictions about prefrontal engagement [20]. Finally, follow-up was limited to 1 month, so longer-term durability is unknown.

Conclusions

This trial demonstrates that a 6-week, home-based, 30-session serious game intervention for MDD is feasible to deliver and acceptable to participants. To our knowledge, it is among the first trials to combine home-based, minimal-contact delivery with action game mechanics and a closely matched active digital control in adults with current MDD, differentiating it from prior studies that relied on weak or inactive comparators. Adults with MDD engaged with both an action-based, adaptive CC game and a closely matched active control game, and both arms showed clinically meaningful reductions in depressive symptoms and improvements in well-being and functional capacity. The trial did not demonstrate superiority

of the active intervention, nor did it support the hypothesized CC mechanism, suggesting that, when compared against an engaging active control, nonspecific, engagement-related processes rather than CC training per se may drive symptom change. For the broader digital mental health field, our findings make 2 contributions: comparator design matters, as closely matched active digital controls can produce substantial symptom change; and the state-of-the-art evaluation framework for computerized cognitive training (training progress, near transfer, far transfer, and ecological transfer) [63] can be applied to a home-based, action-based intervention in adults with current MDD.

Practically, these results indicate that scalable, minimal-contact home-based serious games are deliverable outside the clinic and could help widen access to depression care and reduce stigma- and access-related barriers [87], provided future dismantling trials identify which gameplay components carry therapeutic weight. Future work should incorporate no-contact comparators to estimate nonspecific effects, augment behavioral measures with neural ones sensitive to the proposed mechanism, define richer feasibility criteria a priori, and test whether motivational signals such as perceived choice can guide personalization within stepped-care models.

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Generative AI Use

The authors declare the use of generative AI (GenAI) in the research and writing process. According to the GAIDeT (Generative AI Delegation Taxonomy; 2025), the following tasks were delegated to GenAI tools under full human supervision: code generation, data analysis, visualization, reproducibility testing, proofreading and editing, reformatting, and quality assessment. The GenAI tool used was Claude Opus 4.8 (Anthropic). Responsibility for the final manuscript lies entirely with the authors. GenAI tools are not listed as authors and do not bear responsibility for the final outcomes. AI (Claude Opus 4.8) assistance in data analysis was limited to specific supplementary analyses (missing data/missing completely at random, and multiple-imputation sensitivity analyses) and to computing derived descriptive statistics. The primary outcome analyses were conducted by the study statisticians. All AI-assisted code and analyses were verified by the study statistician; no data were collected or generated by AI, and the authors take full responsibility for all results, content, and interpretations.

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The funders had no role in the design of the study; the collection, analysis, or interpretation of data; the writing of the manuscript; or the decision to submit for publication.

Data Availability

Deidentified participant-level data and the study protocol are available in the Open Science Framework repository [53].

Authors' Contributions

MN, DB, and LL conceptualized the study. MN, DB, and LL designed the trial and developed the study methodology. AP, ZM, DB, and MN led the development of the intervention and game software. EB, TS, NL, and LL oversaw clinical implementation of the trial. NO, NL, NA, EB, TS, and LL conducted participant recruitment and data collection. NO, NA, MF, AP, and DB performed the formal analyses and curated the data. NO and MN wrote the initial draft of the manuscript. All

authors contributed to reviewing and editing the manuscript. MN and LL supervised the project. MN and DB acquired funding. All authors approved the final manuscript.

Conflicts of Interest

AP, ZM, MN, and DB are inventors on a patent concerning dynamic difficulty adjustment mechanics in gamified cognitive training interventions. International Publication Number: WO 2023/006189A1. Priority date: July 27, 2021. The patent is co-owned by the University of Geneva and Hebrew University of Jerusalem, which are committed to open access. The game (ie, Legends of Hoa'manu) intervention used in this study is available for noncommercial academic research use upon request through licensing or collaboration agreements. The remaining authors declare no conflicts of interest.

Multimedia Appendix 1

English translation of the trial registration record.

[\[DOCX File \(Microsoft Word File\), 18 KB-Multimedia Appendix 1\]](#)

Multimedia Appendix 2

Expanded feasibility metrics from gameplay logs.

[\[DOCX File \(Microsoft Word File\), 171 KB-Multimedia Appendix 2\]](#)

Multimedia Appendix 3

Cognitive control assessments (Adaptive Cognitive Evaluation): task outcomes and factor analysis.

[\[DOCX File \(Microsoft Word File\), 17 KB-Multimedia Appendix 3\]](#)

Multimedia Appendix 4

LoH: description of game modules.

[\[DOCX File \(Microsoft Word File\), 1150 KB-Multimedia Appendix 4\]](#)

Multimedia Appendix 5

Adjusted versus unadjusted sensitivity analyses.

[\[DOCX File \(Microsoft Word File\), 17 KB-Multimedia Appendix 5\]](#)

Multimedia Appendix 6

Missing data analyses.

[\[DOCX File \(Microsoft Word File\), 15 KB-Multimedia Appendix 6\]](#)

Multimedia Appendix 7

Full analyses.

[\[DOCX File \(Microsoft Word File\), 878 KB-Multimedia Appendix 7\]](#)

Multimedia Appendix 8

Analysis of the Intrinsic Motivation Inventory (IMI) and Credibility/Expectancy Questionnaire (CEQ).

[\[DOCX File \(Microsoft Word File\), 119 KB-Multimedia Appendix 8\]](#)

Multimedia Appendix 9

Response and remission rates.

[\[DOCX File \(Microsoft Word File\), 17 KB-Multimedia Appendix 9\]](#)

Multimedia Appendix 10

Predictors of change in Montgomery-Åsberg Depression Rating Scale scores.

[\[DOCX File \(Microsoft Word File\), 122 KB-Multimedia Appendix 10\]](#)

Multimedia Appendix 11

Game performance analyses.

[\[DOCX File \(Microsoft Word File\), 19 KB-Multimedia Appendix 11\]](#)

Multimedia Appendix 12

Blinding analysis.

[\[DOCX File \(Microsoft Word File\), 148 KB-Multimedia Appendix 12\]](#)

Checklist 1

CONSORT-EHEALTH checklist.

[\[PDF File \(Adobe File\), 97 KB-Checklist 1\]](#)

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. American Psychiatric Publishing; 2013. [doi: [10.1176/appi.books.9780890425596](https://doi.org/10.1176/appi.books.9780890425596)] ISBN: 978-0-89042-554-1
2. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Psychiatry*. Feb 2022;9(2):137-150. [doi: [10.1016/S2215-0366\(21\)00395-3](https://doi.org/10.1016/S2215-0366(21)00395-3)]
3. McIntyre RS, Alsuwaidan M, Baune BT, et al. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. *World Psychiatry*. Oct 2023;22(3):394-412. [doi: [10.1002/wps.21120](https://doi.org/10.1002/wps.21120)]
4. Cuijpers P, Miguel C, Harrer M, et al. Cognitive behavior therapy vs. control conditions, other psychotherapies, pharmacotherapies and combined treatment for depression: a comprehensive meta-analysis including 409 trials with 52,702 patients. *World Psychiatry*. Feb 2023;22(1):105-115. [doi: [10.1002/wps.21069](https://doi.org/10.1002/wps.21069)]
5. Miyake A, Friedman NP. The nature and organization of individual differences in executive functions: four general conclusions. *Curr Dir Psychol Sci*. Feb 2012;21(1):8-14. [doi: [10.1177/0963721411429458](https://doi.org/10.1177/0963721411429458)] [Medline: [22773897](https://pubmed.ncbi.nlm.nih.gov/22773897/)]
6. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex “Frontal Lobe” tasks: a latent variable analysis. *Cogn Psychol*. Aug 2000;41(1):49-100. [doi: [10.1006/cogp.1999.0734](https://doi.org/10.1006/cogp.1999.0734)] [Medline: [10945922](https://pubmed.ncbi.nlm.nih.gov/10945922/)]
7. LeMoult J, Gotlib IH. Depression: a cognitive perspective. *Clin Psychol Rev*. Apr 2019;69:51-66. [doi: [10.1016/j.cpr.2018.06.008](https://doi.org/10.1016/j.cpr.2018.06.008)] [Medline: [29961601](https://pubmed.ncbi.nlm.nih.gov/29961601/)]
8. Joormann J, Tanovic E. Cognitive vulnerability to depression: examining cognitive control and emotion regulation. *Curr Opin Psychol*. Aug 2015;4:86-92. [doi: [10.1016/j.copsyc.2014.12.006](https://doi.org/10.1016/j.copsyc.2014.12.006)]
9. Vander Zwalmen Y, Hoorelbeke K, Liebaert E, Nève de Mévergnies C, Koster EHW. Cognitive remediation for depression vulnerability: current challenges and new directions. *Front Psychol*. 2022;13:903446. [doi: [10.3389/fpsyg.2022.903446](https://doi.org/10.3389/fpsyg.2022.903446)] [Medline: [35936259](https://pubmed.ncbi.nlm.nih.gov/35936259/)]
10. Whitmer AJ, Gotlib IH. An attentional scope model of rumination. *Psychol Bull*. Sep 2013;139(5):1036-1061. [doi: [10.1037/a0030923](https://doi.org/10.1037/a0030923)] [Medline: [23244316](https://pubmed.ncbi.nlm.nih.gov/23244316/)]
11. Zetsche U, Neumann P, Bürkner PC, Renneberg B, Koster EHW, Hoorelbeke K. Computerized cognitive control training to reduce rumination in major depression: a randomized controlled trial. *Behav Res Ther*. Jun 2024;177:104521. [doi: [10.1016/j.brat.2024.104521](https://doi.org/10.1016/j.brat.2024.104521)] [Medline: [38615373](https://pubmed.ncbi.nlm.nih.gov/38615373/)]
12. Joormann J. Is the glass half empty or half full and does it even matter? Cognition, emotion, and psychopathology. *Cogn Emot*. Feb 2019;33(1):133-138. [doi: [10.1080/02699931.2018.1502656](https://doi.org/10.1080/02699931.2018.1502656)] [Medline: [30067167](https://pubmed.ncbi.nlm.nih.gov/30067167/)]
13. Ahern E, White J, Slattery E. Change in cognitive function over the course of major depressive disorder: a systematic review and meta-analysis. *Neuropsychol Rev*. Mar 2025;35(1):1-34. [doi: [10.1007/s11065-023-09629-9](https://doi.org/10.1007/s11065-023-09629-9)] [Medline: [38315296](https://pubmed.ncbi.nlm.nih.gov/38315296/)]
14. Nuño L, Gómez-Benito J, Carmona VR, Pino O. A systematic review of executive function and information processing speed in major depression disorder. *Brain Sci*. Jan 22, 2021;11(2):147. [doi: [10.3390/brainsci11020147](https://doi.org/10.3390/brainsci11020147)] [Medline: [33499360](https://pubmed.ncbi.nlm.nih.gov/33499360/)]
15. Li FF, Chen XL, Zhang YT, Li RT, Li X. The role of prepotent response inhibition and interference control in depression. *Cogn Neuropsychiatry*. Nov 2021;26(6):441-454. [doi: [10.1080/13546805.2021.1987872](https://doi.org/10.1080/13546805.2021.1987872)] [Medline: [34617501](https://pubmed.ncbi.nlm.nih.gov/34617501/)]
16. Yitzhak N, Shimony O, Oved N, Bonne O, Nahum M. Less inhibited and more depressed? The puzzling association between mood, inhibitory control and depressive symptoms. *Compr Psychiatry*. Jul 2023;124:152386. [doi: [10.1016/j.comppsy.2023.152386](https://doi.org/10.1016/j.comppsy.2023.152386)] [Medline: [37075621](https://pubmed.ncbi.nlm.nih.gov/37075621/)]
17. Wright L, Lipszyc J, Dupuis A, Thayapararajah SW, Schachar R. Response inhibition and psychopathology: a meta-analysis of go/no-go task performance. *J Abnorm Psychol*. May 2014;123(2):429-439. [doi: [10.1037/a0036295](https://doi.org/10.1037/a0036295)] [Medline: [24731074](https://pubmed.ncbi.nlm.nih.gov/24731074/)]
18. Kriesche D, Woll CFJ, Tschentscher N, Engel RR, Karch S. Neurocognitive deficits in depression: a systematic review of cognitive impairment in the acute and remitted state. *Eur Arch Psychiatry Clin Neurosci*. Aug 2023;273(5):1105-1128. [doi: [10.1007/s00406-022-01479-5](https://doi.org/10.1007/s00406-022-01479-5)] [Medline: [36048295](https://pubmed.ncbi.nlm.nih.gov/36048295/)]
19. Semkovska M, Quinlivan L, O’Grady T, et al. Cognitive function following a major depressive episode: a systematic review and meta-analysis. *Lancet Psychiatry*. Oct 2019;6(10):851-861. [doi: [10.1016/S2215-0366\(19\)30291-3](https://doi.org/10.1016/S2215-0366(19)30291-3)] [Medline: [31422920](https://pubmed.ncbi.nlm.nih.gov/31422920/)]
20. Pizzagalli DA, Roberts AC. Prefrontal cortex and depression. *Neuropsychopharmacol*. Jan 2022;47(1):225-246. [doi: [10.1038/s41386-021-01101-7](https://doi.org/10.1038/s41386-021-01101-7)]

21. Zang GY, Rao K, Wu J, He Y, Tang Y, Shi L. Digital therapeutics for cognitive impairment: exploring innovations, challenges, and future prospects. *J Med Internet Res*. Jun 12, 2025;27:e73689. [doi: [10.2196/73689](https://doi.org/10.2196/73689)] [Medline: [40504630](https://pubmed.ncbi.nlm.nih.gov/40504630/)]
22. Koster EHW, Hoorelbeke K, Onraedt T, Owens M, Derakshan N. Cognitive control interventions for depression: a systematic review of findings from training studies. *Clin Psychol Rev*. Apr 2017;53:79-92. [doi: [10.1016/j.cpr.2017.02.002](https://doi.org/10.1016/j.cpr.2017.02.002)]
23. Motter JN, Pimontel MA, Rindskopf D, Devanand DP, Doraiswamy PM, Sneed JR. Computerized cognitive training and functional recovery in major depressive disorder: a meta-analysis. *J Affect Disord*. Jan 1, 2016;189:184-191. [doi: [10.1016/j.jad.2015.09.022](https://doi.org/10.1016/j.jad.2015.09.022)] [Medline: [26437233](https://pubmed.ncbi.nlm.nih.gov/26437233/)]
24. Calkins AW, McMorran KE, Siegle GJ, Otto MW. The effects of computerized cognitive control training on community adults with depressed mood. *Behav Cogn Psychother*. Sep 2015;43(5):578-589. [doi: [10.1017/S1352465814000046](https://doi.org/10.1017/S1352465814000046)] [Medline: [24589123](https://pubmed.ncbi.nlm.nih.gov/24589123/)]
25. Hoorelbeke K, Koster EHW. Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: evidence from a double-blind randomized controlled trial study. *J Consult Clin Psychol*. Feb 2017;85(2):135-146. [doi: [10.1037/ccp0000128](https://doi.org/10.1037/ccp0000128)] [Medline: [27362792](https://pubmed.ncbi.nlm.nih.gov/27362792/)]
26. Barlati S, Nibbio G, Bellomo A, et al. Effectiveness of cognitive remediation in subjects with major depressive disorder: a multicenter randomized controlled study in a real-world setting. *Eur Psychiatry*. Aug 4, 2025;68(1):e106. [doi: [10.1192/j.eurpsy.2025.10073](https://doi.org/10.1192/j.eurpsy.2025.10073)] [Medline: [40754805](https://pubmed.ncbi.nlm.nih.gov/40754805/)]
27. Sociali A, Borgi M, Pettorruso M, et al. What role for cognitive remediation in the treatment of depressive symptoms? A superiority and noninferiority meta-analysis for clinicians. *Depress Anxiety*. Jul 2022;39(7):586-606. [doi: [10.1002/da.23263](https://doi.org/10.1002/da.23263)] [Medline: [35536033](https://pubmed.ncbi.nlm.nih.gov/35536033/)]
28. Bai A, Pei C, Li X, Zhu X, Huo L. Effects of working memory training on depressive symptoms: a systematic review and meta-analysis of randomized controlled trials. *Transl Psychiatry*. Mar 2, 2026;16(1):173. [doi: [10.1038/s41398-026-03857-2](https://doi.org/10.1038/s41398-026-03857-2)] [Medline: [41765936](https://pubmed.ncbi.nlm.nih.gov/41765936/)]
29. Goldberg Z, Kuslak B, Kurtz MM. A meta-analytic investigation of cognitive remediation for mood disorders: efficacy and the role of study quality, sample and treatment factors. *J Affect Disord*. Jun 1, 2023;330:74-82. [doi: [10.1016/j.jad.2023.02.137](https://doi.org/10.1016/j.jad.2023.02.137)] [Medline: [36868388](https://pubmed.ncbi.nlm.nih.gov/36868388/)]
30. Schweizer S, Grahn J, Hampshire A, Mobbs D, Dalgleish T. Training the emotional brain: improving affective control through emotional working memory training. *J Neurosci*. Mar 20, 2013;33(12):5301-5311. [doi: [10.1523/JNEUROSCI.2593-12.2013](https://doi.org/10.1523/JNEUROSCI.2593-12.2013)] [Medline: [23516294](https://pubmed.ncbi.nlm.nih.gov/23516294/)]
31. Schweizer S, Auer T, Hitchcock C, Lee-Carbon L, Rodrigues E, Dalgleish T. Affective Control Training (AfeCT) reduces negative affect in depressed individuals. *J Affect Disord*. Sep 15, 2022;313:167-176. [doi: [10.1016/j.jad.2022.06.016](https://doi.org/10.1016/j.jad.2022.06.016)] [Medline: [35792299](https://pubmed.ncbi.nlm.nih.gov/35792299/)]
32. Iacoviello BM, Wu G, Alvarez E, et al. Cognitive-emotional training as an intervention for major depressive disorder. *Depress Anxiety*. Aug 2014;31(8):699-706. [doi: [10.1002/da.22266](https://doi.org/10.1002/da.22266)] [Medline: [24753225](https://pubmed.ncbi.nlm.nih.gov/24753225/)]
33. Iacoviello BM, Murrough JW, Hoch MM, et al. A randomized, controlled pilot trial of the Emotional Faces Memory Task: a digital therapeutic for depression. *NPJ Digit Med*. 2018;1:21. [doi: [10.1038/s41746-018-0025-5](https://doi.org/10.1038/s41746-018-0025-5)] [Medline: [30854473](https://pubmed.ncbi.nlm.nih.gov/30854473/)]
34. Théron A, Pezzoli P, Abbas M, Howard A, Bowie CR, Guimond S. The efficacy of cognitive remediation in depression: a systematic literature review and meta-analysis. *J Affect Disord*. Apr 1, 2021;284:238-246. [doi: [10.1016/j.jad.2021.02.009](https://doi.org/10.1016/j.jad.2021.02.009)] [Medline: [33631438](https://pubmed.ncbi.nlm.nih.gov/33631438/)]
35. Sirey JA, Banerjee S, Marino P, et al. Adherence to depression treatment in primary care: a randomized clinical trial. *JAMA Psychiatry*. Nov 1, 2017;74(11):1129-1135. [doi: [10.1001/jamapsychiatry.2017.3047](https://doi.org/10.1001/jamapsychiatry.2017.3047)] [Medline: [28973066](https://pubmed.ncbi.nlm.nih.gov/28973066/)]
36. Turunen M, Hokkanen L, Bäckman L, et al. Computer-based cognitive training for older adults: determinants of adherence. *PLoS One*. 2019;14(7):e0219541. [doi: [10.1371/journal.pone.0219541](https://doi.org/10.1371/journal.pone.0219541)] [Medline: [31291337](https://pubmed.ncbi.nlm.nih.gov/31291337/)]
37. Li Z, He H, Chen Y, Guan Q. Effects of engagement, persistence and adherence on cognitive training outcomes in older adults with and without cognitive impairment: a systematic review and meta-analysis of randomised controlled trials. *Age Ageing*. Jan 2, 2024;53(1):afad247. [doi: [10.1093/ageing/afad247](https://doi.org/10.1093/ageing/afad247)] [Medline: [38266127](https://pubmed.ncbi.nlm.nih.gov/38266127/)]
38. Horne SJ, Topp TE, Quigley L. Depression and the willingness to expend cognitive and physical effort for rewards: a systematic review. *Clin Psychol Rev*. Aug 2021;88:102065. [doi: [10.1016/j.cpr.2021.102065](https://doi.org/10.1016/j.cpr.2021.102065)] [Medline: [34274800](https://pubmed.ncbi.nlm.nih.gov/34274800/)]
39. Gunning FM, Anguera JA, Victoria LW, Areán PA. A digital intervention targeting cognitive control network dysfunction in middle age and older adults with major depression. *Transl Psychiatry*. May 4, 2021;11(1):269. [doi: [10.1038/s41398-021-01386-8](https://doi.org/10.1038/s41398-021-01386-8)] [Medline: [33947831](https://pubmed.ncbi.nlm.nih.gov/33947831/)]
40. Anguera JA, Gunning FM, Areán PA. Improving late life depression and cognitive control through the use of therapeutic video game technology: a proof-of-concept randomized trial. *Depress Anxiety*. Jun 2017;34(6):508-517. [doi: [10.1002/da.22588](https://doi.org/10.1002/da.22588)] [Medline: [28052513](https://pubmed.ncbi.nlm.nih.gov/28052513/)]

41. Keefe RSE, Cañadas E, Farlow D, Etkin A. Digital intervention for cognitive deficits in major depression: a randomized controlled trial to assess efficacy and safety in adults. *Am J Psychiatry*. Jul 2022;179(7):482-489. [doi: [10.1176/appi.ajp.21020125](https://doi.org/10.1176/appi.ajp.21020125)] [Medline: [35410496](https://pubmed.ncbi.nlm.nih.gov/35410496/)]
42. Weller S, Schroeder PA, Plewnia C. Gamification improves antidepressant effects of cognitive control training-A pilot trial. *Front Digit Health*. 2022;4:994484. [doi: [10.3389/fdgth.2022.994484](https://doi.org/10.3389/fdgth.2022.994484)] [Medline: [36339520](https://pubmed.ncbi.nlm.nih.gov/36339520/)]
43. Ruiz M, Moreno M, Girela-Serrano B, et al. Winning the game against depression: a systematic review of video games for the treatment of depressive disorders. *Curr Psychiatry Rep*. Jan 2022;24(1):23-35. [doi: [10.1007/s11920-022-01314-7](https://doi.org/10.1007/s11920-022-01314-7)] [Medline: [35113313](https://pubmed.ncbi.nlm.nih.gov/35113313/)]
44. Bergmann M, Wollbrandt I, Gittel L, et al. Effects of a video game intervention on symptoms, training motivation, and visuo-spatial memory in depression. *Front Psychiatry*. 2023;14:1173652. [doi: [10.3389/fpsy.2023.1173652](https://doi.org/10.3389/fpsy.2023.1173652)] [Medline: [37692312](https://pubmed.ncbi.nlm.nih.gov/37692312/)]
45. Wang P, Liu HH, Zhu XT, Meng T, Li HJ, Zuo XN. Action video game training for healthy adults: a meta-analytic study. *Front Psychol*. 2016;7:907. [doi: [10.3389/fpsyg.2016.00907](https://doi.org/10.3389/fpsyg.2016.00907)] [Medline: [27378996](https://pubmed.ncbi.nlm.nih.gov/27378996/)]
46. Bediou B, Adams DM, Mayer RE, Tipton E, Green CS, Bavelier D. Meta-analysis of action video game impact on perceptual, attentional, and cognitive skills. *Psychol Bull*. Jan 2018;144(1):77-110. [doi: [10.1037/bul0000130](https://doi.org/10.1037/bul0000130)] [Medline: [29172564](https://pubmed.ncbi.nlm.nih.gov/29172564/)]
47. Kühn S, Berna F, Lüdtke T, Gallinat J, Moritz S. Fighting depression: action video game play may reduce rumination and increase subjective and objective cognition in depressed patients. *Front Psychol*. 2018;9:129. [doi: [10.3389/fpsyg.2018.00129](https://doi.org/10.3389/fpsyg.2018.00129)] [Medline: [29483888](https://pubmed.ncbi.nlm.nih.gov/29483888/)]
48. Kowal M, Conroy E, Ramsbottom N, Smithies T, Toth A, Campbell M. Gaming your mental health: a narrative review on mitigating symptoms of depression and anxiety using commercial video games. *JMIR Serious Games*. Jun 16, 2021;9(2):e26575. [doi: [10.2196/26575](https://doi.org/10.2196/26575)] [Medline: [34132648](https://pubmed.ncbi.nlm.nih.gov/34132648/)]
49. Gliosci R, Barros Pontes e Silva T. Therapeutic interventions with videogames in treatments for depression: a systematic review. *Games Health J*. Aug 1, 2023;12(4):269-279. [doi: [10.1089/g4h.2022.0094](https://doi.org/10.1089/g4h.2022.0094)]
50. Anguera JA, Jordan JT, Castaneda D, Gazzaley A, Areán PA. Conducting a fully mobile and randomised clinical trial for depression: access, engagement and expense. *BMJ Innov*. Jan 2016;2(1):14-21. [doi: [10.1136/bmjinnov-2015-000098](https://doi.org/10.1136/bmjinnov-2015-000098)] [Medline: [27019745](https://pubmed.ncbi.nlm.nih.gov/27019745/)]
51. Pasqualotto A, Parong J, Green CS, Bavelier D. Video game design for learning to learn. *Int J Human-Computer Interact*. Jul 3, 2023;39(11):2211-2228. [doi: [10.1080/10447318.2022.2110684](https://doi.org/10.1080/10447318.2022.2110684)]
52. Nahum M. The feasibility and efficacy of remote cognitive control training in adults suffering from major depression: a randomized controlled pilot study [in Hebrew]. Israeli Ministry of Health; 2021. MOH_2021-07-20_005979. URL: https://clinicaltrials.health.gov.il/clinicaltrials/?MOHResearchId=MOH_2021-07-20_005979 [Accessed 2026-10-15]
53. Lerner N, Assa N, Pasqualotto A, Bavelier D, Nahum M. Examining the effectiveness and feasibility of a cognitive control videogame on alleviating depression: a randomized controlled trial. *Open Science Framework*. 2026. URL: <https://osf.io/zuf9c/> [Accessed 2026-10-07]
54. Hopewell S, Chan AW, Collins GS, et al. CONSORT 2025 statement: updated guideline for reporting randomised trials. *BMJ*. Apr 14, 2025;389:e081123. [doi: [10.1136/bmj-2024-081123](https://doi.org/10.1136/bmj-2024-081123)] [Medline: [40228833](https://pubmed.ncbi.nlm.nih.gov/40228833/)]
55. Eysenbach G, CONSORT-EHEALTH Group. 10.2196/jmir.1923. *J Med Internet Res*. Dec 31, 2011;13(4):e126. [Medline: [Medline: 22209829](https://pubmed.ncbi.nlm.nih.gov/22209829/)]
56. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. Feb 1, 1960;23(1):56-62. [doi: [10.1136/jnnp.23.1.56](https://doi.org/10.1136/jnnp.23.1.56)]
57. Pontes HM, Schivinski B, Sindermann C, et al. Measurement and conceptualization of gaming disorder according to the World Health Organization framework: the development of the gaming disorder test. *Int J Ment Health Addiction*. Apr 2021;19(2):508-528. [doi: [10.1007/s11469-019-00088-z](https://doi.org/10.1007/s11469-019-00088-z)] [Medline: [34899099](https://pubmed.ncbi.nlm.nih.gov/34899099/)]
58. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. May 2007;39(2):175-191. [doi: [10.3758/bf03193146](https://doi.org/10.3758/bf03193146)] [Medline: [17695343](https://pubmed.ncbi.nlm.nih.gov/17695343/)]
59. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. Apr 1979;134(4):382-389. [doi: [10.1192/bjp.134.4.382](https://doi.org/10.1192/bjp.134.4.382)]
60. McAuley E, Duncan T, Tammen VV. Psychometric properties of the Intrinsic Motivation Inventory in a competitive sport setting: a confirmatory factor analysis. *Res Q Exerc Sport*. Mar 1989;60(1):48-58. [doi: [10.1080/02701367.1989.10607413](https://doi.org/10.1080/02701367.1989.10607413)] [Medline: [2489825](https://pubmed.ncbi.nlm.nih.gov/2489825/)]
61. Eldridge SM, Lancaster GA, Campbell MJ, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS One*. 2016;11(3):e0150205. [doi: [10.1371/journal.pone.0150205](https://doi.org/10.1371/journal.pone.0150205)]

62. Bell ML, Whitehead AL, Julious SA. Guidance for using pilot studies to inform the design of intervention trials with continuous outcomes. *Clin Epidemiol*. 2018;10:153-157. [doi: [10.2147/CLEP.S146397](https://doi.org/10.2147/CLEP.S146397)] [Medline: [29403314](https://pubmed.ncbi.nlm.nih.gov/29403314/)]
63. Harvey PD, McGurk SR, Mahncke H, Wykes T. Controversies in computerized cognitive training. *Biol Psychiatry Cogn Neurosci Neuroimaging*. Nov 2018;3(11):907-915. [doi: [10.1016/j.bpsc.2018.06.008](https://doi.org/10.1016/j.bpsc.2018.06.008)] [Medline: [30197048](https://pubmed.ncbi.nlm.nih.gov/30197048/)]
64. Plass JL, Homer BD, Kinzer CK. Foundations of game-based learning. *Educ Psychol*. Oct 2, 2015;50(4):258-283. [doi: [10.1080/00461520.2015.1122533](https://doi.org/10.1080/00461520.2015.1122533)]
65. Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatr Ann*. Sep 2002;32(9):509-515. [doi: [10.3928/0048-5713-20020901-06](https://doi.org/10.3928/0048-5713-20020901-06)]
66. Guy W. Clinical Global Impressions, ECDEU Assessment Manual for Psychopharmacology, Revised (DHEW Publ NoADM 76-338). National Institute of Mental Health; 1976:218-222. URL: <https://archive.org/details/ecdeuassessmentm1933guyw> [Accessed 2026-10-07]
67. Nolen-Hoeksema S, Morrow J. A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta Earthquake. *J Pers Soc Psychol*. Jul 1991;61(1):115-121. [doi: [10.1037//0022-3514.61.1.115](https://doi.org/10.1037//0022-3514.61.1.115)] [Medline: [1890582](https://pubmed.ncbi.nlm.nih.gov/1890582/)]
68. Topp CW, Østergaard SD, Søndergaard S, Bech P. The WHO-5 Well-Being Index: a systematic review of the literature. *Psychother Psychosom*. 2015;84(3):167-176. [doi: [10.1159/000376585](https://doi.org/10.1159/000376585)] [Medline: [25831962](https://pubmed.ncbi.nlm.nih.gov/25831962/)]
69. Patterson TL, Goldman S, McKibbin CL, Hughs T, Jeste DV. UCSD performance-based skills assessment: development of a new measure of everyday functioning for severely mentally ill adults. *Schizophr Bull*. 2001;27(2):235-245. [doi: [10.1093/oxfordjournals.schbul.a006870](https://doi.org/10.1093/oxfordjournals.schbul.a006870)] [Medline: [11354591](https://pubmed.ncbi.nlm.nih.gov/11354591/)]
70. Jarus T. The Israeli assessment of participation for adults [in Hebrew]. *Isr J Occup Ther*. 2006;15:H93-H111. URL: <http://www.jstor.org/stable/23468905> [Accessed 2026-10-07]
71. Younger JW, O'Laughlin KD, Anguera JA, et al. Better together: novel methods for measuring and modeling development of executive function diversity while accounting for unity. *Front Hum Neurosci*. 2023;17:1195013. [doi: [10.3389/fnhum.2023.1195013](https://doi.org/10.3389/fnhum.2023.1195013)] [Medline: [37554411](https://pubmed.ncbi.nlm.nih.gov/37554411/)]
72. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry*. Jun 2000;31(2):73-86. [doi: [10.1016/s0005-7916\(00\)00012-4](https://doi.org/10.1016/s0005-7916(00)00012-4)] [Medline: [11132119](https://pubmed.ncbi.nlm.nih.gov/11132119/)]
73. Bavelier D, Green CS. Enhancing attentional control: lessons from action video games. *Neuron*. Oct 9, 2019;104(1):147-163. [doi: [10.1016/j.neuron.2019.09.031](https://doi.org/10.1016/j.neuron.2019.09.031)] [Medline: [31600511](https://pubmed.ncbi.nlm.nih.gov/31600511/)]
74. Pasqualotto A, Fanourakis M, Menestrina Z, et al. A novel multidimensional dynamic difficulty adjustment algorithm: use case in a cognitive training video game. *Psychol Methods*. Apr 23, 2026. [doi: [10.1037/met0000805](https://doi.org/10.1037/met0000805)] [Medline: [42024305](https://pubmed.ncbi.nlm.nih.gov/42024305/)]
75. Russoniello CV, Fish MT, O'Brien K. The efficacy of playing videogames compared with antidepressants in reducing treatment-resistant symptoms of depression. *Games Health J*. Oct 2019;8(5):332-338. [doi: [10.1089/g4h.2019.0032](https://doi.org/10.1089/g4h.2019.0032)]
76. Pasqualotto A, Altarelli I, De Angeli A, Menestrina Z, Bavelier D, Venuti P. Enhancing reading skills through a video game mixing action mechanics and cognitive training. *Nat Hum Behav*. 2022;6(4):545-554. [doi: [10.1038/s41562-021-01254-x](https://doi.org/10.1038/s41562-021-01254-x)]
77. R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing. 2021. URL: <https://www.R-project.org/> [Accessed 2026-10-07]
78. Kuznetsova A, Brockhoff PB, Christensen RHB. **lmerTest** package: tests in linear mixed effects models. *J Stat Soft*. 2017;82(13):1-26. [doi: [10.18637/jss.v082.i13](https://doi.org/10.18637/jss.v082.i13)]
79. Turkoz I, Alphs L, Singh J, et al. Clinically meaningful changes on depressive symptom measures and patient-reported outcomes in patients with treatment-resistant depression. *Acta Psychiatr Scand*. Mar 2021;143(3):253-263. [doi: [10.1111/acps.13260](https://doi.org/10.1111/acps.13260)]
80. Jia E, Macon J, Doering M, Abraham J. Effectiveness of digital behavioral activation interventions for depression and anxiety: systematic review and meta-analysis. *J Med Internet Res*. 2025;27:e68054. [doi: [10.2196/68054](https://doi.org/10.2196/68054)]
81. Tindall L, Kerrigan P, Li J, Hayward E, Gega L. Is behavioural activation an effective treatment for depression in children and adolescents? An updated systematic review and meta-analysis. *Eur Child Adolesc Psychiatry*. Dec 2024;33(12):4133-4156. [doi: [10.1007/s00787-024-02429-3](https://doi.org/10.1007/s00787-024-02429-3)]
82. Pass L, Lejuez CW, Reynolds S. Brief Behavioural Activation (Brief BA) for adolescent depression: a pilot study. *Behav Cogn Psychother*. Mar 2018;46(2):182-194. [doi: [10.1017/S1352465817000443](https://doi.org/10.1017/S1352465817000443)] [Medline: [28756787](https://pubmed.ncbi.nlm.nih.gov/28756787/)]
83. Shawn Green C, Bavelier D, Kramer AF, et al. Improving methodological standards in behavioral interventions for cognitive enhancement. *J Cogn Enhanc*. Mar 2019;3(1):2-29. [doi: [10.1007/s41465-018-0115-y](https://doi.org/10.1007/s41465-018-0115-y)]
84. Pontén M, Jonsjö M, Vadenmark V, et al. Association between expectations and clinical outcomes in online v. face-to-face therapy - an individual participant data meta-analysis. *Psychol Med*. Apr 2024;54(6):1207-1214. [doi: [10.1017/S0033291723003033](https://doi.org/10.1017/S0033291723003033)] [Medline: [37905404](https://pubmed.ncbi.nlm.nih.gov/37905404/)]

85. Jacobson W, Zhong W, Nomikos GG, Christensen MC, Kurre Olsen C, Harvey PD. Effects of vortioxetine on functional capacity across different levels of functional impairment in patients with major depressive disorder: a University of California, San Diego Performance-based Skills Assessment (UPSA) analysis. *Curr Med Res Opin.* Jan 2020;36(1):117-124. [doi: [10.1080/03007995.2019.1657692](https://doi.org/10.1080/03007995.2019.1657692)] [Medline: [31422713](https://pubmed.ncbi.nlm.nih.gov/31422713/)]
86. Dechantsreiter E, Padberg F, Morash A, et al. Examining the synergistic effects of a cognitive control video game and a home-based, self-administered non-invasive brain stimulation on alleviating depression: the DiSCoVeR trial protocol. *Eur Arch Psychiatry Clin Neurosci.* Feb 2023;273(1):85-98. [doi: [10.1007/s00406-022-01464-y](https://doi.org/10.1007/s00406-022-01464-y)] [Medline: [36271928](https://pubmed.ncbi.nlm.nih.gov/36271928/)]
87. Coombs NC, Meriwether WE, Caringi J, Newcomer SR. Barriers to healthcare access among U.S. adults with mental health challenges: a population-based study. *SSM Popul Health.* Sep 2021;15:100847. [doi: [10.1016/j.ssmph.2021.100847](https://doi.org/10.1016/j.ssmph.2021.100847)] [Medline: [34179332](https://pubmed.ncbi.nlm.nih.gov/34179332/)]
88. Calamia M, Markon K, Tranel D. Scoring higher the second time around: meta-analyses of practice effects in neuropsychological assessment. *Clin Neuropsychol.* May 2012;26(4):543-570. [doi: [10.1080/13854046.2012.680913](https://doi.org/10.1080/13854046.2012.680913)]
89. Smid CR, Karbach J, Steinbeis N. Toward a science of effective cognitive training. *Curr Dir Psychol Sci.* Dec 2020;29(6):531-537. [doi: [10.1177/0963721420951599](https://doi.org/10.1177/0963721420951599)]
90. Sala G, Aksayli ND, Tatlidil KS, Tatsumi T, Gondo Y, Gobet F. Near and far transfer in cognitive training: a second-order meta-analysis. *Collabra.* Jan 1, 2019;5(1):18. [doi: [10.1525/collabra.203](https://doi.org/10.1525/collabra.203)]
91. Brooke J. SUS: a 'quick and dirty' usability scale. In: Jordan PW, Thomas B, Weerdmeester BA, McClelland IL, editors. *Usability Evaluation in Industry.* Taylor & Francis; 1996:189-194. ISBN: 9780748404605

Abbreviations

ACE: Adaptive Cognitive Evaluation
ASAP: Adult Subjective Assessment of Participation
CC: cognitive control
CEQ: Credibility/Expectancy Questionnaire
CGI-I: Clinical Global Impressions-Improvement
CGI-S: Clinical Global Impressions-Severity
CONSORT: Consolidated Standards of Reporting Trials
CONSORT-EHEALTH: Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Telehealth
DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
HDRS-17: 17-item Hamilton Rating Scale for Depression
IMI: Intrinsic Motivation Inventory
LMM: linear mixed model
LoH: Legends of Hoa'manu
MADRS: Montgomery-Åsberg Depression Rating Scale
MDD: major depressive disorder
OSF: Open Science Framework
PHQ-9: Patient Health Questionnaire-9
PI: principal investigator
RRS-22: Ruminative Responses Scale (22-item)
TIDieR: Template for Intervention Description and Replication
UPSA: University of California, San Diego Performance-Based Skills Assessment
WHO-5: World Health Organization-Five Well-Being Index
WM: working memory

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