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Systematic review and meta-analysis of adverse events in clinical trials of mental health apps

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Mental health apps are efficacious, yet they may pose risks in some. This review (CRD42024506486) examined adverse events (AEs) from mental health apps. We searched (May 2024) the Medline, PsycINFO, Web of Science, and ProQuest databases to identify clinical trials of mental health apps. The risk of bias was assessed using the Cochrane Risk of Bias tool. Only 55 of 171 identified clinical trials reported AEs. AEs were more likely to be reported in trials sampling schizophrenia and delivering apps with symptom monitoring technology. The meta-analytic deterioration rate from 13 app conditions was 6.7% (95% CI = 4.3, 10.1, I^2 = 75%). Deterioration rates did not differ between app and control groups (OR = 0.79, 95% CI = 0.62–1.01, I^2 = 0%). Reporting of AEs was heterogeneous, in terms of assessments used, events recorded, and detail provided. Overall, few clinical trials of mental health apps report AEs. Those that do often provide insufficient information to properly judge risks related to app use.

Smartphone app-based interventions and monitoring tools have the potential to revolutionize the delivery of mental health care. Alongside their cost, scalability, and anonymity advantages, app-based solutions can deliver personalized treatment content round the clock using passive, active, and metadata continuously collected from consumers[1]. A considerable number of mental health apps have recently been developed and tested[2]. Growing evidence from randomized controlled trials (RCTs) demonstrates that apps delivered as a stand-alone intervention option can effectively reduce a range of mental health symptoms[3]. Apps may also play a useful role as an adjunct to treatment in the clinical care of severe mental illness[4].

Despite their potential, mental health apps are not suitable for all and may inadvertently induce negative effects in some patients. Research on psychological treatment has traditionally focused on its benefits, and comparatively less is known about the occurrence of negative effects. Experts have begun to formulate a consensus to guide future research on adverse events (AE) from both standard[5] and web-based[6] psychological treatments, including how to define, assess, and report them. AEs can range from mild (frustration, anonymity concerns) to more moderate (emergence of novel symptoms, symptom deterioration), and to severe (events that require higher-level care, such as hospitalization and suicidality), and their severity can depend on the perceived impact it has on the patient. Occurrence of AEs may or may not be directly related to the treatment being used[7]. Validated symptom measures are typically used to estimate deterioration rates, while clinical interviews, checklists, open-ended questions, and self-report questionnaires can identify AEs beyond mere symptom escalation[6].

Innovations in smartphone technology come with new challenges and risks that must be systematically and carefully considered. Concerns have been raised that apps that promote frequent mood monitoring may contribute to the maintenance of depression in some patients due to negative processing bias induced by the daily confrontation of distressing experiences[8]. This poses an even larger risk in self-guided apps, which typically lack in-built mechanisms for checking patient safety in real-time. There have also been cases of chatbots inadvertently offering harmful advice and encouraging destructive behaviors[9], forcing groups of users to demand the removal of the chatbot from the market. Psychological consequences of, or concerns with, a privacy breach of sensitive health data have also been cited, particularly since the amount of data that can be gathered by apps is enormous. This is compounded by the fact that many apps are not sufficiently transparent with information regarding data security or provide written policies that are too technical for the average user to fully understand[10,11]. The thousands of apps available for download in a largely unregulated market have prompted concerns about the quality of content offered. Content reviews show that mental

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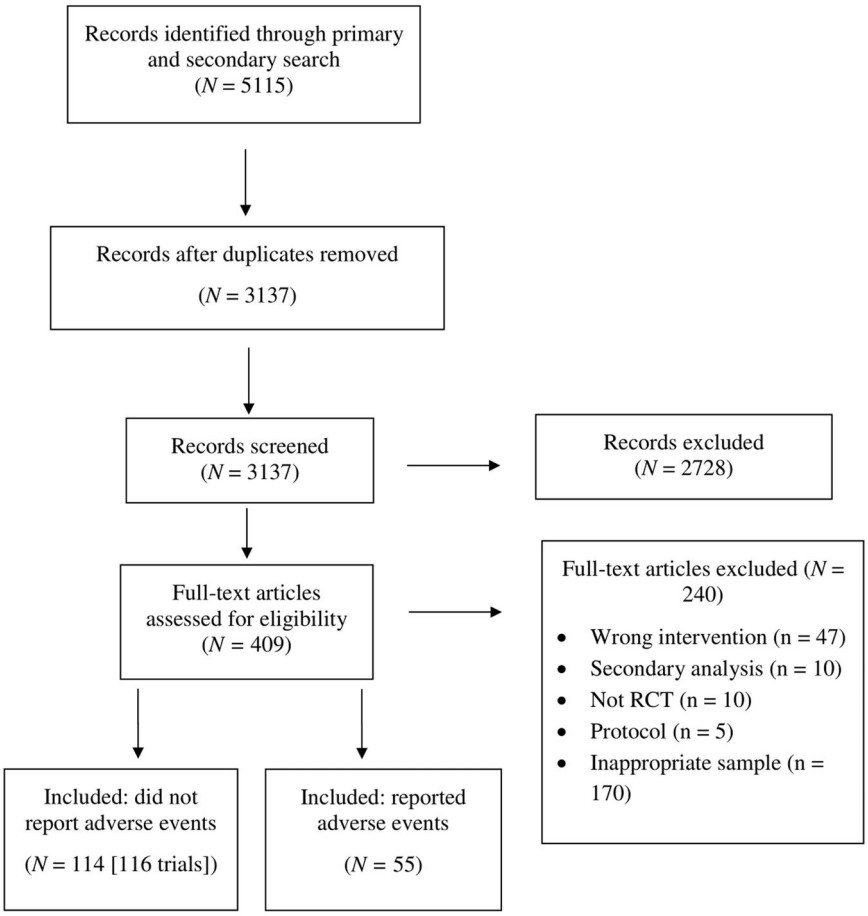

Fig. 1 | Flowchart of literature search. this figure describes the process of selecting and screening studies, from database searching to studies that met full eligibility criteria.

health apps developed by non-researcher and non-clinician groups do not strongly follow evidence-based guidelines and, sometimes, include unsafe information[12–14]. Analysis of user reviews shows that non-evidence-based apps are viewed less favorably and have more potential to cause negative effects[15].

Best practice recommends that intervention safety is evaluated at the clinical trial stage through routine monitoring of AEs[16]. RCTs of mental health apps present a critical opportunity to report on the frequency, nature, and extent of AEs, as such information can be used by patients, professionals, policymakers, and regulators when deciding whether to use, recommend, certify, or prescribe a specific app. This could also help to realize the promise of precision medicine, whereby patients are matched to specific treatments they are most likely to benefit from based on their unique attributes[17]. However, whether the occurrence of AEs is rigorously assessed for and reported in RCTs of mental health apps remains unclear. We investigated the frequency with which AEs were reported in clinical trials of mental health apps.

Specifically, we aimed to:

1. Identify the proportion of clinical trials of mental health apps that report AEs.
2. Examine whether certain trial characteristics are associated with the likelihood of reporting of AEs.
3. Calculate weighted average deterioration rates and determine whether deterioration rates differ from app and control groups.
4. Identify what other AEs (beyond deterioration) have been reported and understand how frequently they occur.

Results

Study characteristics

The search identified 171 trials (169 papers) that tested an app in a sample pre-selected for mental health problems. Of these, 55 (32%) reported AEs (Fig. 1). The target samples in these 55 trials included depression ($k = 18$), general anxiety ($k = 3$), schizophrenia/psychosis ($k = 7$), post-traumatic stress ($k = 5$), specific phobia ($k = 4$), social anxiety ($k = 1$), bipolar ($k = 2$), eating disorders ($k = 1$), suicidal ideation ($k = 2$), general distress ($k = 2$), and mixed or dual diagnoses ($k = 10$). More trials used diagnostic interviews ($k = 30$) over self-report ($k = 25$) instruments to pre-select participants. There were 48 control conditions, the most common being inactive controls ($k = 21$), followed by care as usual ($k = 14$) and placebo controls ($k = 13$). Only 22 trials (42%) were considered to have a lower risk of bias, defined as meeting four or five of the criteria (see Table 1 for characteristics of trials that reported AEs).

App interventions

There were 62 app conditions, 35 of which comprised an app that was publicly available for download. Thirty-nine app conditions were coded as CBT-based, 43 contained symptom monitoring features, one contained chat-bot technology, and 26 offered some degree of professional guidance. Only 11 trials delivered an app that contained functionality alerting clinicians or researchers of possible adverse events, enabling timely intervention or crisis consultation. For example, three trials[18–20] delivered the MONSENO app that contained a feedback loop between the patients and the clinic, where the self-monitored data was sent to the clinic allowing for the study provider to review the data and contact the patients if there were signs of deterioration. Similar feedback loops were also presented in the *FOCUS*[21] (for serious mental illness), *Recovery Record*[22] (an eating disorder aftercare program), *IntelliCare*[23] (transdiagnostic-focused) *EMPOWER*[24] (for psychosis), *ClinTouch*[25] (for schizophrenia), *Kokoro*[26] (for depression), and *Spark*[27] (for depression) app-based platforms. In all cases, the apps monitored symptom fluctuations and

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Table 1 | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Ainsworth (2013)[68]	Schizophrenia	Diagnostic interview	Not named (12)	Self-monitoring	Yes	NR	NR	NR	Text message (12)	Yes	+ ? + ? ?
Araya (2021)[34]	Depression	Self-report (PHQ-9 ≥ 10)	CONEMO (657)	Behavioral activation	NR	NR	Yes	NR	Usual care (655)	Yes	+ + − sr +
Bell (2023)[63]	Depression & anxiety	Self-report (PHQ-8 ≥ 10 and GAD-7 ≥ 10)	Mello[a] (29)	CBT & third-wave	Yes	NR	NR	NR	Waitlist (26)	Yes	+ + − sr +
Bell (2020)[49]	Psychosis	Diagnostic interview	SAVVy (17)	Coping strategy enhancement	Yes	NR	Yes	Yes	Usual care (17)	Yes	+ + − + +
Ben-Zeev (2018)[21]	Serious mental illness	Diagnostic interview	FOCUS (82)	Multidisciplinary	Yes	NR	Yes	NR	Group treatment (81)	Yes	+ ? + sr +
Blanco (2023)[69]	Depression	Self-report (CES-D ≥ 16)	NR (29) NR (28)	CBT CBT	Yes Yes	NR NR	NR Yes	NR	Placebo monitoring app (30)	Yes	+ ? + + +
Bröcker (2022)[44] Study 2	PTSD	Diagnostic interview	Guided PTSD Coach[a] (5) Unguided PTSD Coach[a] (5)	CBT	Yes Yes	NR NR	Yes NR	Yes	None	Yes	+ ? − sr −
Bruhns (2023)[29]	Depression	Diagnostic interview	MCT & More[a] (79)	CBT & third-wave	NR	NR	NR	NR	Waitlist (80)	Yes	+ + − sr +
Bruhns (2021)[70]	Depression	Self-report (PHQ-9 > 0)	MCT & More[a] (208)	CBT & third-wave	NR	NR	NR	NR	Waitlist (215)	NR	+ + − sr −
Carl (2020)[35]	Anxiety	Diagnostic interview	Daylight[a] (128)	CBT	Yes	NR	NR	NR	Waitlist (128)	Yes	+ + − sr +
Chan (2023)[41]	Depression	Diagnostic interview	proACT-S[a] (167)	CBT	NR	NR	NR	NR	Waitlist (163)	Yes	+ ? − sr +
Christoforou (2017)[71]	Agoraphobia	Self-report (self-identified)	Agoraphobia Free (86)	CBT	Yes	NR	NR	NR	Placebo app (84)	NR	+ + + sr −
Dahne (2023)[36]	Depression	Self-report (PHQ-8 ≥ 10)	Goal2Quit[a] (114)	CBT	Yes	NR	NR	NR	Information handouts (50)	NR	? ? − sr +
Depp (2019)[51]	Serious mental illness	Diagnostic interview	CBT2go[a] (85) SM (85)	CBT Self-monitoring	Yes Yes	NR NR	Yes Yes	Yes	Usual care (85)	Yes	+ + − sr −
Depp (2023)[50]	Serious mental illness	Diagnostic interview	mSTART (38)	Self-monitoring	Yes	NR	Yes	Yes	START - face-to-face treatment (40)	Yes	? ? + − +
Donker (2019)[73]	Acrophobia	Self-report (AC ≥ 45.45)	Zerophobia[a] (96)	CBT	Yes	NR	NR	NR	Waitlist (97)	NR	+ + − sr +
Donker (2022)[74]	Aviophobia	Self-report (FAS ≥ 56)	Not named (77)	CBT	Yes	NR	NR	NR	Waitlist (77)	NR	+ + − sr −
Faurholt-Jepsen (2020)[18]	Bipolar	Diagnostic interview	Monsenso[a] (97)	Self-monitoring	Yes	NR	Yes	NR	General smartphone use (49)	Yes	+ + + sr −
Faurholt-Jepsen (2021)[52]	Bipolar	Diagnostic interview	Monsenso[a] (47)	CBT	Yes	NR	Yes	Yes	General smartphone use (51)	Yes	+ + + + +
Forman-Hoffman (2024)[92]	Depression	Self-report (PHQ-9 ≥ 10)	Meru Health Program[a] (54)	CBT & third wave	NR	NR	Yes	NR	Waitlist (46)	Yes	+ ? − sr +
Garety, (2021)[53]	Psychosis	Diagnostic interview	SlowMo (181)	CBT	NR	NR	Yes	Yes	Usual care (181)	Yes	+ ? − sr −

Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Ghaemi (2022)[59]	Schizophrenia	Diagnostic interview	PEAR-004 (56)	CBT	NR	NR	Yes	Yes	Placebo app (56)	Yes	+ ? + + –
Graham (2020)[23]	Depression or anxiety	Self-report (PHQ-8 ≥ 10 or GAD-7 ≥ 8)	IntelliCare[a] (74)	CBT	Yes	NR	Yes	NR	Waitlist (72)	Yes	+ ? – + +
Gumley (2022)[24]	Schizophrenia	Diagnostic interview	EMPOWER (42)	Cognitive interpersonal	Yes	NR	Yes	Yes	Care as usual (31)	Yes	+ + – + +
Hensler (2022)[37]	PTSD	Self-report (PTSD Checklist ≥10)	PTSD Coach[a] (89)	CBT	Yes	NR	NR	NR	Waitlist (90)	Yes	+ + – sr +
Hilt (2023)[62]	Depression (rumination)	Self-report (self-identified)	CARE (72)	Mindfulness	Yes	NR	NR	NR	Symptom monitoring (80)	Yes	? ? + + +
Josifovski (2024)[60]	Suicidal ideation	Self-report (self-identified)	BrighterSide (275)	CBT & third wave	Yes	NR	NR	NR	Waitlist (275)	NR	? ? – sr +
Kerber (2023)[61]	Internalizing disorders	Self-report (GAD-7 > 4 or PHQ-9 > 4 or MSPI > 6)	MindDoc[a] (523)	CBT & third wave	Yes	NR	NR	NR	Waitlist (522)	NR	? ? – sr +
Krzystanek (2019)[54]	Schizophrenia	Diagnostic interview	MONEO (199)	Cognitive training	NR	NR	Yes	Yes	Placebo app (91)	Yes	? ? + ? –
Kulikov (2023)[55]	Depression	Self-report (self-identified)	Spark Direct[a] (35)	CBT	Yes	NR	NR	Yes	Placebo app (25)	Yes	+ ? + sr –
Kusumadewi (2023)[93]	Anxiety	Self-report (GAD-7 ≥ 5)	GAMA-AIMS[a] (43)	CBT	Yes	NR	NR	NR	Face-to-face CBT (43)	Yes	? ? + sr –
Lacey (2023)[64]	Phobia	Self-report (BSSSP ≥ 4)	oVRcome[a] (63)	CBT/VR	NR	NR	NR	NR	Waitlist (63)	Yes	+ ? – sr –
Lewis (2020)[25]	Psychosis	Diagnostic interview	ClinTouch[a] (40)	Self-monitoring	Yes	NR	Yes	Yes	Care as usual (41)	Yes	+ ? – ? –
Mantani (2017)[26]	Depression	Diagnostic interview	Kokoro (81)	CBT	Yes	NR	NR	Yes	Pharmacotherapy (83)	Yes	+ + + + +
McCloud (2020)[72]	Depression & anxiety	Self-report (HADS ≥ 8)	Feel Stress Free[a] (84)	CBT	Yes	NR	NR	NR	Waitlist (84)	NR	+ + – sr +
McCue (2022)[56]	Depression	Diagnostic interview	Pathway[a] (20)	Multidisciplinary	Yes	NR	Yes	Yes	Care as usual (20)	Yes	+ ? – sr –
Miller-Graff (2021)[40]	PTSD	Self-report (PCL-5 ≥ 33)	PTSD Coach[a] (41)	CBT	Yes	NR	NR	NR	Waitlist (46)	Yes	+ ? – sr +
Minami (2018)[45]	Mood disorder	Diagnostic interview	mSMART Mind (unclear N)	Mindfulness	Yes	NR	Yes	Yes	Care us usual (unclear N)	Yes	? ? – sr ?
Neumayr (2019)[22]	Eating disorder	Diagnostic interview	Recovery Record[a] (20)	CBT	Yes	NR	Yes	NR	Care as usual (20)	Yes	+ ? – sr –
Nicol (2022)[58]	Depression & anxiety	Self-report (self-identified)	W-GenZ (10)	Multidisciplinary	Yes	Yes	NR	Yes	Waitlist (8)	Yes	? ? – sr ?
Peake (2024)[27]	Depression	Self-report (self-identified)	Spark[a] (80)	CBT	Yes	NR	NR	NR	Placebo app (80)	Yes	? ? + sr ?
Pratap (2018)[94]	Depression	Self-report (PHQ-9 ≥ 5)	Project EVO (83) iPST (112)	Cognitive training Problem solving	NR NR	NR NR	NR NR	NR	Placebo app (79)	NR	? ? + sr ?

Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Raevuori (2021)[46]	Depression	Diagnostic interview	Meru Health Program[a] (63)	CBT & third wave	NR	NR	Yes	Yes	Care as usual (61)	Yes	+ + − + +
Röhr (2021)[65]	PTSD	Self-report (PDS-5 ≥ 11)	Sanadak (65)	CBT	Yes	NR	NR	NR	Information resources (68)	Yes	+ + − sr +
Roy (2021)[66]	Anxiety	Diagnostic interview	Unwinding Anxiety[a] (32)	Mindfulness	Yes	NR	Yes	Yes	Care as usual (33)	Yes	+ + − sr −
Sakata (2022)[47]	Depression	Self-report (PHQ-9 ≥ 5)	Resilience Training (1654)	CBT	Yes	NR	NR	NR	None (factorial trial)	NR	+ + + sr +
Steare (2020)[95]	Psychosis	Diagnostic interview	My Journey 3 (20)	Multidisciplinary	Yes	NR	Yes	Yes	Care as usual (20)	Yes	? + − − +
Stolz (2018)[39]	Social anxiety	Diagnostic interview	Not named (60)	CBT	NR	NR	Yes	NR	Waitlist (30) Computer CBT (60)	Yes	+ ? − + +
Sun (2022)[67]	Depression and anxiety	Self-report (PHQ-9 or GAD-7 above mild cut-off)	Mindfulness for Growth and Resilience (57)	Mindfulness	NR	NR	Yes	NR	Placebo app (57)	Yes	+ + + + +
Taylor (2023)[42]	Depression	Self-report (PHQ-8 ≥ 5)	Activate your mood[a] (102) Mind your mood[a] (101) Finding happiness[a] (100)	Behavioral activation CBT ACT	Yes NR NR	NR NR NR	NR NR NR	NR	Waitlist (102)	NR	+ + − sr +
Tessier (2020)[57]	Schizophrenia	Diagnostic interview	Not named (12)	Psychoeducation	NR	NR	NR	NR	Nurse-led intervention (11) Care as usual (10)	Yes	+ ? – sr ?
Tønning (2021)[20]	Depression	Diagnostic interview	MONSENSO[a] (59)	CBT	Yes	NR	Yes	Yes	Care as usual (61)	Yes	+ + − + +
Torok (2022)[28]	Suicidal ideation	Self-report (single item)	LifeBuoy[a] (228)	DBT	Yes	NR	NR	NR	Placebo app (227)	NR	+ + + + +
White (2024)[48]	Depression	Diagnostic interview	Radar-base[a] (50)	Self-monitoring	Yes	NR	NR	NR	Placebo app (50)	NR	+ ? + sr –
Zhao (2023)[43]	PTSD	Self-report (PCL-5 ≥ 31)	Not named (78) Not named (76)	ACT Mindfulness	NR	NR	NR	NR	Waitlist (67)	Yes	+ ? – sr +
Trials that did not report adverse events											
Abbott (2018)[96]	Anxiety	Self-report (BAI ≥ 21)	Headspace[a] (97)	Mindfulness	NR	NR	NR	NR	Waitlist (66)	NR	+ ? − sr +
Adam (2020)[97]	Depression & anxiety	Self-report (PHQ > 9 and/or GAD-7 > 5).	Rose[a] (30)	Multidisciplinary	Yes	NR	NR	Yes	Waitlist (15)	NR	+ ? – sr +
Akin-Sari (2022)[98]	OCD	Self-report (OCI-R > 2 SD above mean)	GG OCD, Anxiety and depression[a] (25)	CBT	NR	NR	NR	NR	Waitlist (22)	Yes	? ? − sr +
Anastasiadou (2020)[99]	Eating disorder	Diagnostic interview	TCApp[a] (53)	CBT	Yes	NR	Yes	Yes	Face-to-face CBT (53)	Yes	+ ? + sr +
Arean (2016)[100]	Depression	Self-report (PHQ-9 ≥ 5)	Project EVO (209) iPST (211)	Cognitive training CBT	NR NR	NR NR	NR NR	NR	Placebo app (206)	NR	+ ? + + +
Arias (2020)[101]	Phobia	Diagnostic interview	Not named (18)	CBT	NR	NR	NR	NR	Waitlist (18)	Yes	+ + − sr +

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Trials that reported adverse events											
Bantjes (2024)[102]	Depression or anxiety	Self-report (PHQ-9 or GAD-5 ≥ 10)	Super Better (126)[a]	CBT	NR	NR	NR	NR	Placebo app (124) Remote group CBT (121)	Yes	+ ? + sr +
Bastiaansen (2022)[103]	Depression	Diagnostic interview	Do-module (55) Think-module (55)	Self-monitoring Self-monitoring	Yes Yes	NR NR	Yes Yes	Yes	Care as usual (51)	Yes	? ? – sr +
Bentz (2021)[104]	Phobia	Diagnostic interview	Easy Heights[a] (39)	CBT	NR	NR	NR	NR	Placebo app (38)	Yes	+ + + + +
Ben-Zeev (2021)[105]	Serious mental illness	Self-report (self-identified)	CORE (154)	Multidisciplinary	NR	NR	NR	NR	Waitlist (161)	NR	? ? – sr +
Biagianti (2023)[106]	Social anxiety	Diagnosis	WASABI (15)	CBT	Yes	NR	Yes	Yes	CBT (7)	Yes	? ? + sr +
Birney (2016)[107]	Depression	Self-report(PHQ score 10–19)	Mood Hacker[a] (150)	CBT	Yes	NR	NR	NR	Information resources (150)	Yes	? ? – + +
Bröcker (2024)[108]	PTSD	Diagnosis	PTSD Coach (32)	CBT	Yes	NR	Yes	Yes	Care as usual (30)	Yes	+ ? – + +
Bush (2017)[109]	Suicidal ideation	Self-report	Virtual Hope Box[a] (58)	Multidisciplinary	NR	NR	Yes	Yes	Care as usual (60)	Yes	+ + – sr +
Catuara-Solarz (2022)[110]	Anxiety	Self-report (GAD-7 score 5–18)	Foundations[a] (95)	CBT	NR	NR	NR	NR	Waitlist (95)	NR	+ + – sr –
Cerea (2020)[111]	OCD	Self-report (ROCI > 21)	GG Relationship Doubts[a] (25)	Cognitive training	NR	NR	NR	NR	Waitlist (25)	Yes	? ? – sr +
Chen (2023)[112]	Schizophrenia	Diagnostic interview	MedAdhere (35)	Medication adherence	NR	NR	Yes	Yes	Care as usual (59)	Yes	+ ? – ? ?
Dahne (2019a)[113]	Depression	Self-report (PHQ-9 > 10)	Aptivate! (22) iCouch CBT (9)	CBT CBT	Yes Yes	NR NR	NR NR	NR	Waitlist (11)	Yes	? ? – sr –
Dahne (2019b)[114]	Depression	Self-report (PHQ-9 > 10)	Moodivate[a] (24) MoodKit (19)	CBT CBT	Yes Yes	NR NR	NR NR	NR	Information resources (9)	Yes	? ? – sr –
Daniel (2022)[115]	Social anxiety	Self-report (SIAS ≥ 28)	Not named (59)	Cognitive training	Yes	NR	NR	NR	Mood monitoring control (55)	Yes	? ? + sr –
Danieli (2022)[116]	Anxiety	Self-report (unclear)	TEO (14) TEO+CBT (16)	CBT	NR	Yes	Yes	NAYes	CBT (16) Waitlist (14)	Yes	? ? – + –
Dworkin (2023)[117]	PTSD	Self-report (≥ 3 symptom clusters on PTSD Checklist)	THRIVE (20) THRIVE (21)	CBT Self-monitoring	Yes Yes	NR NR	Yes Yes	NR	-	Yes	+ ? + sr +
Elbogen (2019)[118]	PTSD	Diagnostic interview	CALM (57)	Cognitive training	NR	NR	Yes	NR	Placebo app (55)	Yes	? ? + + +
Fatori (2023)[119]	Depression	Self-report (EPDS > 7)	Motherly 1.0 (37)	CBT	Yes	NR	Yes	Yes	Placebo app (44)	Yes	? ? + sr +
Faurholt-Jepsen (2015)[78]	Bipolar	Diagnostic interview	MONARCA[a] (39)	Self-monitoring	Yes	NR	Yes	Yes	General smartphone use (39)	Yes	+ + + + +
Franklin (2016a)[120]	Self-harm	Self-report (≥2 cutting episodes)	Not named (55)	Evaluative conditioning (cognitive training)	NR	NR	NR	NR	Placebo app (59)	NR	+ ? + sr +

Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Franklin (2016b)[120]	Self-harm	Self-report (≥2 cutting episodes)	Not named (62)	Evaluative conditioning (cognitive training)	NR	NR	NR	NR	Placebo app (69)	NR	+ ? + sr +
Franklin (2016c)[120]	Self-harm	Self-report (≥1 suicidal behavior)	Not named (75)	Evaluative conditioning (cognitive training)	NR	NR	NR	NR	Placebo app (84)	NR	+ ? + sr +
Funk (2024)[121]	Repetitive negative thinking	Self-report (≥34 RRS)	Not named (41)	CBT	NR	NR	NR	NR	Waitlist (38)	Yes	? ? – sr –
Gao (2022)[122]	Anxiety	Self-report (PSWQ > 40)	Unwinding Anxiety[a] (40)	Third-wave	Yes	NR	NR	NR	Care as usual (40)	Yes	? + – sr +
Ghanbari (2021)[123]	Anxiety	Self-report (STAI > 80)	BCSZone (41)	CBT & third-wave	NR	NR	Yes	NR	Waitlist (41)	Yes	+ ? – sr –
Goulding (2023)[124]	Bipolar	Diagnostic interview	LiveWell (124)	CBT	Yes	NR	Yes	NR	Care as usual (81)	Yes	+ + – + +
Greer (2019)[125]	Anxiety	Self-report (HADS > 7)	Not named (72)	CBT	NR	NR	NR	NR	Placebo app (73)	Yes	+ ? + + +
Guo (2020)[126]	Depression	Self-report (CES-D ≥ 16)	Run4Love (150)	CBT	NR	NR	NR	NR	Information resources (40)	Yes	+ ? – sr +
Ham (2019)[127]	Depression & anxiety	Self-report (BDI-II ≥ 16 or STAI ≥ 39)	HARUToday (28)	CBT	Yes	NR	NR	NR	Placebo app (26) Waitlist (26)	Yes	+ ? – sr –
Hantsoo (2018)[128]	Depression	Self-report (PHQ-9 ≥ 5)	Mood Tracking and Alert + Patient Portal (48)	Self-monitoring	Yes	NR	Yes	NR	Usual Care (24)	Yes	+ ? + sr ?
He (2022)[129]	Depression	Self-report average score on the (CSMHSS)	XiaoE (49)	CBT	NR	Yes	NR	NR	Placebo app (50) Information resources (49)	Yes	+ + – sr +
Heim (2021)[130]	Depression	Self-report (PHQ-9 ≥ 10)	Step-by-Step[a] (67)	CBT	NR	NR	Yes	NR	Information resources (71)	NR	? ? – sr +
Hides (2019)[131]	General distress	Self-report (K-10 > 17)	Music eScape (85)	Multidisciplinary	Yes	NR	NR	NR	Waitlist (84)	NR	+ ? – sr +
Hildebrandt (2020)[132]	Eating disorder	Diagnostic interview	Noom (114)	Self-monitoring	Yes	NR	Yes	Yes	Care as usual (111)	Yes	+ ? – sr +
Hildebrandt (2017)[133]	Eating disorder	Diagnostic interview	Noom (33)	Self-monitoring	Yes	NR	Yes	Yes	CBT guided self-help (33)	Yes	? ? + + +
Hur (2018)[134]	Depression	Diagnostic interview	Todac Todac (24)	CBT	NR	NR	NR	NR	Placebo app (24)	Yes	+ ? + sr –
Jannati (2020)[135]	Depression	Self-report (EPDS ≥ 13)	Happy Mom (39)	CBT	NR	NR	NR	NR	Waitlist (39)	Yes	+ ? – sr ?
Jongeneel (2024)[136]	Voice hearing/ psychosis	Diagnostic interview	Temstem (44)[a]	Coping strategies	Yes	NR	NR	NR	Placebo app (45)	Yes	+ ? + + +
Kageyama (2021)[137]	Depression	Diagnostic interview	SPSRS (16)	Cognitive training	NR	NR	NR	NR	Waitlist (16)	Yes	+ + – sr +
Kauer (2012)[138]	General distress	Self-report (K-10 > 16)	Not named (69)	Self-monitoring	Yes	NR	NR	Yes	Placebo app (49)	Yes	+ + + sr +

Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Kennard (2018)[139]	Suicidality	Diagnostic interview	BRITE (34)	DBT	Yes	NR	Yes	Yes	Care as usual (32)	Yes	+ ? – sr +
Keshen (2019)[140]	Eating disorder	Diagnostic interview	Recovery Record[a] (45)	Self-monitoring	Yes	NR	Yes	Yes	Pencil paper monitoring (45)	Yes	+ + + sr –
Kim (2017)[141]	Anxiety	Self-report (BIA score 8–25)	PsyApp (47)	CBT	Yes	NR	NR	NR	Web intervention (44) Waitlist (44)	Yes	? ? – sr +
Kim (2024)[142]	Panic disorder	Diagnostic interview	Not named (25)	CBT	Yes	NR	NR	NR	Information resources (25)	Yes	+ ? – sr –
Kruzan (2022)[143]	Self-harm	Self-report (>6 episodes of NSSI past year)	TalkLife[a] (110)	Peer support	NR	NR	NR	NR	Information resources (110)	NR	+ ? – sr +
Kuhn (2017)[144]	PTSD	Self-report (PCL-C ≥ 35)	PTSD Coach[a] (62)	CBT	Yes	NR	NR	NR	Waitlist (58)	Mixed	+ ? – sr +
LaFreniere (2023)[145]	Anxiety	Diagnostic interview	SkillJoy (41)	Mixed	Yes	NR	NR	NR	Self-monitoring control (45)	Yes	+ ? + sr +
Li (2021)[146]	Psychosis	Diagnostic interview	SMART (40)	Cognitive training	Yes	NR	Yes	NR	Care as usual (40)	Yes	+ ? – sr –
Linardon (2023)[147]	Eating disorder	Self-report (≥1 binge per fortnight over the past 3 months)	Break Binge Eating (199)	CBT	Yes	NR	NR	NR	Waitlist (202)	NR	+ + – sr +
Linardon (2022)[148]	Eating disorder	Self-report (≥1 binge episode over the past month)	Break Binge Eating (197)	CBT	Yes	NR	NR	NR	Waitlist (195)	NR	+ + – sr +
Liu (2022)[149]	Depression	Self-report (PHQ-9 ≥ 9)	XiaoNan (41)	CBT	NR	Yes	NR	NR	Self-help book (42)	NR	+ ? + sr +
Lukas (2021)[150]	Depression	Self-report (PHQ-9 ≥ 10)	MT-Phoenix[a] (15)	Cognitive training	NR	NR	NR	Yes	Waitlist (15)	Yes	+ ? – sr +
Lukas (2021)[151]	Depression	Self-report (PHQ-9 ≥ 5)	MT-Phoenix[a] (40)	Cognitive training	NR	NR	NR	NR	Waitlist (37)	NR	+ + – sr +
Ly (2015)[152]	Depression	Diagnostic interview	Not named (46)	CBT	NR	NR	Yes	Yes	Face-to-face behavioral activation (47)	Yes	+ + + + +
Ly (2014)[153]	Depression	Diagnostic interview	Not named (40) Not named (41)	CBT Mindfulness	NR NR	NR NR	Yes Yes	NR	-	Yes	+ + + + +
MacKinnon (2022)[154]	Depression	Self-report (PHQ-9 ≥ 10)	Beam[a] (33)	CBT	Yes	NR	Yes	NR	Care as usual (32)	Yes	+ + – sr +
Mao (2023)[155]	Social anxiety	Self-report (SAS-A ≥ 40)	Not named (15)	Cognitive training	NR	NR	NR	NR	Waitlist (15)	NR	? ? – sr –
McLean (2022)[156]	PTSD	Self-report (PCL-C ≥ 31)	Renew[a] (self-guided) (31) Renew with support[a] (31)	CBT	Yes Yes	NR NR	NR Yes	NR	Waitlist (31)	Yes	+ ? – sr +
Miklowitz (2023)[157]	Mood disorder	Diagnostic interview	MyCoachConnect (MCC) (33)	Self-monitoring	Yes Yes	NR NR	Yes Yes	Yes	Placebo app (32)	Yes	+ ? + + ?
Min-Hung (2019)[158]	Anxiety	Diagnostic interview	Not named (31)	Cognitive training	NR	NR	NR	NR	Placebo app (31) Waitlist (31)	Yes	+ ? – sr –

Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Miner (2016)[159]	PTSD	Self-report (PCL-C ≥ 25)	PTSD Coach[a] (25)	CBT	Yes	NR	NR	NR	Waitlist (24)	Mixed	+ ? – sr +
Moberg (2019)[160]	Depression or anxiety	Self-report (PHQ-9 or GAD-7 score 5–14)	Pacifica[a] (253)	CBT	Yes	NR	NR	NR	Waitlist (247)	NR	? ? – sr +
Mohr (2019)[161]	Depression or anxiety	Self-report (PHQ-9 ≥ 10 or GAD-7 ≥ 8)	IntelliCare Coached + recommendation[a] (74) IntelliCare Coached + no recommendation[a] (76) IntelliCare self-guided + recommendations[a] (75) IntelliCare self-guided + no recommendations[a] (76)	CBT CBT CBT CBT	NR NR NR NR	NR NR NR NR	Yes Yes NR NR	NR	-	Yes	? ? + sr +
Motter (2019)[162]	Depression	Diagnostic interview	Not named (25) Not named (21)	Cognitive training Cognitive training	NR NR	NR NR	NR NR	NR	-	Yes	+ + + + +
Myin-Germeys (2022)[163]	Psychosis	Diagnostic interview	ACT-DL/PsyMate[a] (71)	ACT	Yes	NR	Yes	Yes	Care as usual (77)	Yes	+ ? – sr +
Najavits (2023)[164]	PTSD	Diagnostic interview	Seeking Safety[a] (64)	Multidisciplinary	NR	NR	Yes	NR	Placebo app (66)	Yes	+ ? + sr –
Newman (2021)[165]	Anxiety	Self-report (GAD-7 diagnostic criteria)	Not named (50)	CBT	Yes	NR	Yes	NR	Waitlist (50)	Yes	+ + – sr +
Niles (2020)[166]	PTSD	Self-report (PCL-5 ≥ 33)	Not named (336) Not named (323)	Cognitive training Cognitive training	NR NR	NR NR	NR NR	NR	Placebo app (342)	NR	+ ? – sr –
Oh (2020)[167]	Panic disorder	Diagnostic interview	Todaki (23)	CBT	Yes	Yes	NR	NR	Information resources (22)	Yes	? ? – sr –
O'Toole (2019)[168]	Suicidal ideation	Diagnostic interview	LifeApp'tite (60)	Multidisciplinary	Yes	NR	Yes	Yes	Care as usual (69)	Yes	? + – sr +
Pacella-LaBarbara (2020)[169]	PTSD	Self-report (Self-identified)	PTSD Coach[a] (33)	CBT	Yes	NR	NR	NR	Care as usual (31)	Yes	+ ? – sr –
Pahwa (2023)[170]	Bipolar	Diagnostic interview	KIOS Bipolar[a] (65) eMoods[a] (57)	CBT Self-monitoring	Yes Yes	NR NR	NR NR	NR NR	-	Yes	+ ? + ? –
Parkes (2023)[171]	General distress	Self-report (GHQ-12 ≥ 2)	MeT4VeT (24)	CBT	Yes	NR	NR	NR	Placebo app (26)	NR	+ ? + sr ?
Pham (2016)[172]	Anxiety	Self-report (GAD ≥ 6)	Flowy[a] (31)	Mindfulness	NR	NR	NR	NR	Waitlist (32)	NR	? ? – sr –
Ponzo (2020)[173]	Anxiety and distress	Self-report (DASS-A ≥ 7 or DASS ≥ 14)	BioBase (130)	CBT	Yes	NR	NR	NR	Waitlist (132)	NR	+ ? – sr –
Possemato (2023)[174]	PTSD	Self-report (PCL-5 ≥ 33)	PTSD Coach[a] (115)	CBT	Yes	NR	Yes	NR	Care as usual (119)	Yes	? ? – + ?
Possemato (2016)[175]	PTSD	Self-report (PCL-5 ≥ 40)	Self-guided PTSD Coach[a] (10) Guided PTSD Coach[a] (10)	CBT CBT	Yes Yes	NR NR	NR Yes	NR	-	Yes	? ? + sr +
Reid (2011)[176]	General distress	Self-report (K-10 ≥ 16)	Mobiletype (69)	Multidisciplinary	Yes	NR	Yes	Yes	Placebo app (49)	Yes	+ + + sr +
Reininghaus (2023)[177]	Severe mental illness	Diagnostic interview	EMICompass (46)	Compassion-focused	Yes	NR	Yes	Yes	Care as usual (46)	Yes	+ + – + +

Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Rodante (2022)[178]	Suicidal tendencies	Diagnostic interview	CALMA[a] (34)	DBT	Yes	NR	Yes	Yes	Face-to-face DBT (22)	Yes	+ ? + − −
Roepke (2015)[179]	Depression	Self-report (CES-D ≥ 16)	General SuperBetter[a] (97) CBT-PPT SuperBetter[a] (93)	CBT CBT	NR NR	NR NR	NR NR	NR	Waitlist (93)	NR	+ ? − sr +
Roy (2017)[180]	PTSD	Self-report (PCL-C 28–49)	LifeArmor and PE Coach[a] (72)	CBT	NR	NR	Yes	NR	Text messages (72)	Yes	? ? + sr −
Saulnier (2023)[181]	Social anxiety	Self-report (ASI ≥ 6)	BOAST (19)	CBT	Yes	NR	Yes	NR	Waitlist (17)	Yes	? ? − sr −
Sawyer (2019)[182]	Depression	Self-report (EPDS ≥ 7)	eMums Plus[a] (72)	Multidisciplinary	NR	NR	Yes	NR	Care as usual (61)	Yes	+ + − sr +
Schlosser (2018)[183]	Schizophrenia	Diagnostic interview	PRIME (22)	Motivation enhancement	NR	NR	Yes	NR	Waitlist (21)	Yes	? ? − sr +
Schwob (2023)[184]	Social anxiety	Diagnostic interview	ImExposure (43)	CBT (exposure-based)	Yes	NR	NR	NR	Self-monitoring control (39)	Yes	+ ? + sr +
Seo (2022)[185]	Depression	Self-report (EPDS ≥ 9)	Happy Mother (50)	CBT	Yes	NR	NR	NR	Information resources (50)	Yes	? ? − sr −
Shin (2021)[186]	Panic disorder	Diagnostic Interview	Not named (33)	CBT/VR	NR	NR	NR	NR	Waitlist (21)	Yes	+ ? − + +
Six (2022)[187]	Depression	Self-report (PHQ-8 ≥ 5)	Customized AirHeart (45) Non-Customized AirHeart (49)	CBT CBT	Yes Yes	NR NR	NR NR	NR	-	Yes	+ ? + sr ?
Soltani (2024)[188]	Depression	Diagnostic interview	Yara (32)	Multidisciplinary	Yes	NR	NR	Yes	Care as usual (32)	Yes	+ + − sr +
Stallman (2019)[189]	General distress	Self-report (K-10 ≥ 16)	My Coping Plan[a] (28)	Multidisciplinary	NR	NR	NR	NR	Waitlist (28)	NR	+ + − sr +
Stiles-Shields (2019)[190]	Depression	Self-report (PHQ-9 ≥ 10 and QIDS ≥ 11)	Boost Me[a] (10) Thought Challenger[a] (10)	CBT CBT	Yes NR	NR NR	Yes Yes	NR	Waitlist (10)	Yes	+ + − sr −
Sun (2019)[191]	Social anxiety	Self-report (LSAS > 38)	Not named (22)	Cognitive training	NR	NR	NR	NR	Placebo app (19)	NR	? ? + sr −
Sun (2021)[192]	Depression	Self-report (PHQ-9 ≥ 4 or EPDS ≥ 9)	Spirits Healing (84)	Mindfulness	NR	NR	NR	NR	Placebo app (84)	Yes	+ + + sr +
Tan (2023)[193]	Depression or anxiety	Self-report (PHQ-9 ≥ 5 or GAD-7 ≥ 5)	MoodMission[a] (24)	CBT	Yes	NR	NR	Yes	Care as usual (24)	NR	+ ? − sr +
Teng (2019)[194]	Anxiety	Diagnostic interview	Not named (31)	Cognitive training	NR	NR	NR	NR	Placebo app (31) Waitlist (31)	Yes	+ ? − sr −
Tighe (2017)[195]	Depression or suicidality	Self-report (PHQ-9 ≥ 10 or K-10 ≥ 25)	Ibobbly (31)	ACT	Yes	NR	Yes	NR	Waitlist (10)	Yes	+ ? − sr +
van Aubel (2020)[196]	Depression & psychosis	Self-report (CAPE ≥ 2 and MADRS ≥ 10)	ACT-DL/PsyMate[a] (27)	ACT	Yes	NR	Yes	Yes	Attention control (28)	Yes	+ − − + +
van der Meer (2020)[197]	PTSD	Self-report (PC-PTSD-5 ≥ 1)	Support Coach[a] (143)	CBT	Yes	NR	NR	NR	Waitlist (144)	Yes	+ ? − sr −
Vitger (2022)[198]	Schizophrenia	Diagnostic interview	Not named (96)	Multidisciplinary	Yes	NR	Yes	Yes	Care as usual (98)	Yes	+ + − sr +

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Table 1 (continued) | Characteristics of randomized clinical trials

Author	Target sample	Pre-selection method	App name (*n*)	Technique	Symp mon	Chat-bot	Prof guide	Adjunct treatment	Control arm (*n*)	Researcher Contact	RoB
Trials that reported adverse events											
Wallace (2022)[199]	PTSD	Diagnostic interview	BreatheWell[a] (15)	Diaphragmatic breathing	NR	NR	NR	Yes	Care as usual (15)	Yes	? ? – sr ?
Wang (2023)[200]	Depression	Self-report (self-identified)	Not named (9)	CBT	Yes	NR	NR	Yes	Waitlist (9)	NR	+ + – sr ?
Watts (2013)[201]	Depression	Diagnostic interview	Get Happy (22)	CBT	NR	NR	Yes	NR	Computerized CBT (30)	Yes	+ + + sr ?
Yang (2017)[202]	Social anxiety	Self-report (LSAS ≥ 30)	CBM-A (20) CBM-I (20) AIM (16)	Cognitive training	NR	NR	NR	NR	Placebo app (20)	NR	? ? + sr –
Yang (2023)[203]	Anxiety	Self-report (STAI ≥ 39)	HARU[a] (15)	CBT	Yes	NR	NR	NR	Waitlist (15)	Yes	+ ? – ? +
Yeon (2023)[204]	Depression	Diagnostic interview	Metri (23)	CBT	NR	NR	NR	NR	Waitlist (21)	Yes	? ? – sr ?
Zainal (2023)[205]	Anxiety	Diagnostic interview	MEMI (68)	Mindfulness	NR	NR	NR	NR	Placebo app (42)	Yes	+ + + + +
Zainal (2024)[206]	Social anxiety	Self-report (≥20 SPIN)	MEMI (96)	Mindfulness	NR	NR	NR	NR	Placebo app (95)	NR	+ + + sr +
Zhang (2023)[207]	Depression or anxiety	Self-report (EPDS ≥ 9 or GAD-7 ≥ 5)	Not named (80)	Mindfulness	NR	NR	NR	NR	Care as usual (80)	Yes	+ ? – sr +
Zimmer (2021)[208]	Phobia	Diagnostic interview	Phobys[a] (33)	CBT	Yes	NR	NR	NR	Waitlist (33)	Yes	? ? – + +

[a]Indicates that the app is publicly available for download on the AppStore or Google Play store.

Symp mon symptom monitoring features, *prof guide* professional guidance offered, *RoB* risk of bias, *CBT* coded as traditional cognitive-behavioral therapies, behavioral activation, exposure, or problem solving techniques, *PHQ* Patient Health Questionnaire, *CSQ* Client Satisfaction Questionnaire, *SM* self-monitoring, *AC* Acrophobia Questionnaire, *FAS* Flight Anxiety Situations Questionnaire, *InterSePT* Scale for Suicidal Thinking–Plus, *CSMHSS* College Students Mental Health Screening Scale, *CRSQ* Children's Response Style Questionnaire, *MSPI* Mini-Social Phobia Inventory, *BSSSP* Brief Standard Self-Rating Scale for Phobic Patients, *DASA* Dynamic Appraisal for Situational Aggression, *K-10* Kessler Psychological Distress Scale, *CES-D* Centre for Epidemiology Scale-Depression, *PTSD* post-traumatic stress disorder, *AC* Acrophobia Questionnaire, *FAS* Flight Anxiety Situations Questionnaire, *HADS* Hospital Anxiety Depression Scale, *PCL-5* PTSD Checklist for DSM-V, *BAI* Beck Anxiety Inventory, *OCI-R* Obsessive Compulsive Inventory-Revised, *ROCI* Relational Obsessive Compulsive Inventory, *SIAS* Social Interaction Anxiety Scale, *NSSI* non-suicidal self-injury, *ASI* anxiety sensitivity index-3, *QIDS* Quick Inventory for Depressive Symptomatology, *LSAS* Liebowitz Social Anxiety Scale, *CAPE* Community Assessment of Psychic Experiences, *SPIN* social phobia inventory, *EPDS* Edinburgh Postnatal Depression Scale, *NR* not reported.

domains assessed in order include sequence generation, allocation concealment, blinding of participants, blinding of outcome assessor or self-report (sr), and intention-to-treat analysis. + = criterion met, ? = unclear, and – criterion not met.

Table 2 | Comparison of trials that did versus did not report adverse events

Variable	Eligible RCTs: Adverse events not reported *N* (%)	Eligible RCTs: Adverse events reported *N* (%)	*p*
Target sample			
Mood disorder (yes)	34 (29.1%)	21 (38.2%)	0.232
Any anxiety disorder (yes)	45 (38.5%)	13 (23.6%)	0.055
Schizophrenia/ psychosis (yes)	6 (5.1%)	9 (16.4%)	**0.015**
Mixed/dual diagnoses (yes)	10 (8.5%)	8 (14.5%)	0.231
Self-harm/ suicidality (yes)	8 (6.8%)	2 (3.6%)	0.403
App features			
Publicly available (yes)	54 (39.4%)	33 (53.2%)	0.069
CBT (yes)	72 (52.6%)	39 (62.9%)	0.173
Cognitive training (yes)	21 (15.3%)	2 (3.2%)	**0.013**
Symptom/mood monitoring (yes)	70 (51.1%)	43 (69.4%)	**0.016**
Chatbot (yes)	5 (3.6%)	1 (1.6%)	0.436
Professional guidance (yes)	50 (36.5%)	26 (41.9%)	0.465
Adjunct to other treatment (yes)	29 (24.8%)	19 (34.5%)	0.183
Eligibility selection			
Self-report	73 (62.4%)	28 (50.9%)	0.154
Diagnostic interview	44 (37.6%)	27 (49.1%)	
Control group			
Inactive	53 (49.1%)	21 (43.8%)	0.485
Care as usual	22 (20.4%)	14 (29.2%)	
Placebo	33 (30.6%)	13 (27.1%)	
Other trial features			
Active therapeutic comparison (yes)	9 (7.8%)	6 (10.9%)	0.496
Researcher-participant contact (yes)	87 (75.7%)	42 (76.4%)	0.919
Risk of bias			
Low	38 (32.5%)	22 (40.0%)	0.334
Higher	79 (67.5%)	33 (60.0%)	

Percentages in parenthesis reflect the number of trials with that characteristic divided by the total number of trials that did or did not report AEs (e.g., 21 trials that sampled patients with mood disorders and reported AEs divided by 55 [total number of trials that reported AEs]). There were 62 and 137 app conditions among trials that did and did not report AEs, respectively, and 48 and 108 control conditions among trials that did and did not report AEs, respectively (these were denominators used to calculate percentages in parentheses).
Bold values identify statistical significance ($p < 0.05$).

cases of deterioration or worsening could be reviewed by a clinical team that offered support. Another suicide-focused app, *LifeBuoy*[28], contained a "help" button that, if pressed, sent an email to the research team that the participant wanted to be contacted by the clinical psychologist. All other apps tested did not mention any recordings of AEs or handling of deterioration within the device.

Comparison of trials that did versus did not report adverse events

Table 2 presents the results comparing trials that did ($k = 55$) versus did not ($k = 116$) report AEs. Three significant group differences emerged. First, trials sampling individuals with schizophrenia/psychosis were significantly more likely than not to report AEs. Second, trials that delivered an app that contained symptom/mood monitoring features were also more likely than not to report AEs. Third, trials that delivered a cognitive training app were significantly less likely to report AEs. Table 1 also presents the characteristics of the 116 trials that did not report AEs.

Methods used to assess adverse events

Seventeen of 55 trials reporting AEs used validated outcome assessments to measure the worsening of primary symptoms. Several trials adapted existing items ($k = 2$), created new items ($k = 6$), or incorporated questions with open-ended responses ($k = 4$) to inquire about possible AEs. Seven trials administered clinical interviews to inquire about AEs. Only three trials[29–31] used a validated instrument designed to AEs events from psychological interventions. These instruments included the Inventory for Assessing Negative Effects of Psychotherapy[32] and the Negative Effects Questionnaire[33]. Some trials reported AEs using objective data (hospitalization rates) while 12 trials did not explicitly state their method of assessment (see Supplementary Table 1 for further detail).

Meta-analysis on deterioration rates

Ten trials reported data on deterioration rates[27,34–43]. Deterioration rates were reported for symptoms of depression ($k = 7$), general anxiety ($k = 2$), PTSD ($k = 3$), and social anxiety ($k = 1$). The footnote in Table 3 presents the operationalization of deterioration among the 10 trials that reported these data.

From 13 app conditions, the weighted average deterioration rate combining all outcomes was 6.7% (95% CI = 4.3, 10.1), with high heterogeneity ($I^2 = 75\%$). There were 1,672 participants that contributed to this analysis (mean per condition = 128.6). Similar weighted average deterioration rates were found for depression- and anxiety-specific outcomes, although the number of conditions was low (Table 3).

From eight control conditions, the weighted average deterioration rate combining all outcomes was 10.1% (95% CI = 5.8, 16.7), with high heterogeneity ($I^2 = 85\%$). There were 1,462 participants that contributed to this analysis (mean per condition = 182.7). Similar weighted average deterioration rates were found for different control conditions and when limiting the analyses to depression- and anxiety-specific outcomes.

Table 3 also presents the nine comparisons between app and control conditions on deterioration rates. Although overall deterioration rates were lower among participants allocated to app conditions, this difference failed to reach significance (OR = 0.79, 95% CI = 0.62, 1.01, $p = .062$). There were 1472 participants total in the app condition (mean = 163.5) and 2310 in the control condition that contributed to this analysis (mean = 256.6). Non-significant differences were also observed when restricting the analyses to different control groups and for different symptom outcomes.

Absence of adverse events

Table 4 presents the frequency of trials overall and by target disorder reporting a particular AE, as well as the frequency of trials that reported the occurrence of an AE for app and control arms. Eight trials explicitly stated that no AEs had occurred[21,23,41,44–48].

Severe adverse events

Twenty trials reported one or more severe AEs. The most frequent severe AE was [re]hospitalization, reported in 14 trials, which were most commonly directed at mood or schizophrenia-spectrum disorders[20,22,24,26,49–58]. Rates of [re]hospitalizations ranged from <1 to 36%. One trial reported that one participant was hospitalized for feeling overwhelmed at the point of app installation[24]. Eleven trials (20%), most frequently directed at patients with mood disorders, reported the presence of self-harm or suicidal ideation/intent, with rates ranging from <1-55%[26–28,34,36,53,58–62]. None of these cases were attributed to the app or study-related procedures. Three trials (5.4%), two targeting schizophrenia-spectrum disorders and one targeting mood disorders, reported deaths (ranged from 1 to 11 cases), none of

Table 3 | Meta-analyses on deterioration rates

App conditions	*N* conditions	Est (95% CI)	I^2	
Overall	13	6.7% (4.3, 10.1)	75%	
Depression only[a]	8	6.0% (3.3, 10.7)	82%	
Anxiety/PTSD only	6	8.4% (4.6, 14.7)	67%	
General anxiety[b]	2	7.5% (1.3, 34.0)	89%	
PTSD[c]	3	10.6% (6.7, 16.4)	0%	
Social anxiety	1	1.7% (0.2, 10.9)	0%	
Control conditions				
Overall	8	10.1% (5.8, 16.7)	84%	
Inactive control	5	7.3% (2.8, 17.4)	85%	
Care as usual	2	18.6% (6.9, 41.5)	91%	
Depression only	5	10.2% (5.5, 18.1)	85%	
Anxiety/PTSD only	4	10.7% (4.7, 22.5)	85%	
Comparisons	***N* comparisons**	**OR (95% CI)**	I^2	***p***
Apps vs. control				
Overall	9	0.79 (0.62, 1.01)	0%	0.062
Inactive control only	6	0.79 (0.53, 1.16)	0%	0.243
Care as usual control only	2	0.79 (0.58, 1.09)	0%	0.164
Depression symptoms only	6	0.82 (0.63, 1.08)	0%	0.151
Anxiety symptoms only	5	0.85 (0.58, 1.24)	2%	0.403

[a]Depression deterioration was defined as either: increase in PHQ-9 scores from low or moderate to severe; BDI score ≥10 from baseline; increase in PHQ-9 scores larger than a minimally clinically important differences; or increase in PHQ-8 score of ≥5 from baseline.
[b]General anxiety deterioration was defined as either: increase in GAD-7 score of ≥5 from baseline, or increase in GAD-7 scores larger than a minimally clinically important differences.
[c]PTSD deterioration was defined as either: ≥10 point increase in PCL-5 scores; or clinically significant change in PCL-5 scores according to Jacobson and Truax (1991) definition.
social anxiety deterioration was defined as pre-post increase in either Social Phobia Scale, Liebowitz Social Anxiety Scale, or the Social Interaction Anxiety scale of at least the reliable change index definition.

which were attributed to the app or trial procedures[24,34,54]. One trial reported the occurrence of violence and referral to crisis care, which were not attributed to app or trial procedures (Supplementary Table 1)[53].

Other adverse events

We identified nine types of other AEs reported across trials. The most common type observed in this category includes self-reported (via unvalidated, open-ended items) worsening of overall mental health or specific mood, anxiety, or psychotic symptoms. This occurred in a minority of participants (<10%) among 14 trials. Ten of these either did not specify the cause of symptom worsening or explicitly stated that it was unrelated to trial procedures[34,35,37,49,53,63–67], while the other four included specific items that directly identified symptom worsening due to the intervention[29,68–70].

Physical complaints were reported as AEs in five trials[34,35,53,63,66], spanning anxiety, mood, and schizophrenia-spectrum disorders. Types of physical complaints included bodily pain and headaches. None of these AEs were attributed to the app or study-related procedures.

One trial in depressed patients[70] reported the presence of other AEs according to 119 responses from app group participants who completed the Inventory of Negative Effects in Psychotherapy Questionnaire, which included increased financial concerns ($n = 2$; 1.7%), relationship problems ($n = 2$; 1.7%), and increased stigmatization fears ($n = 12$; 10%). Another trial in participants with generalized anxiety[35] reported the presence of cognitive impairments across both app and control groups, including concentration (51% endorsed vs. 74%, respectively) and memory problems (40% endorsed vs. 62%, respectively).

App-induced adverse events

Ten trials reported four types of app-induced ad AEs. The most common ($N = 6$) was distress due to certain in-app features, occurring in less than 5% of participants across trials[20,25,62,64,68,71]. App features reported to be distressing were symptom monitoring, distraction games, background music, and push notifications. Two trials reported that one participant each experienced anxiety due to technical difficulties associated with accessing the app[35,72]. Two other trials of virtual reality apps reported that a modest number of participants (25% and 8%) experienced one or more symptoms of transient cyber sickness[73,74]. Another trial[72] noted that one participant reported feeling too reliant on the app, which was rated as mild severity.

Discussion

This review sought to identify and assess the reporting of AEs in clinical trials of mental health apps. We found that only one in three trials (55/171) report AEs, with target samples typically spanning mood, anxiety, or schizophrenia-spectrum disorders. The reporting of AEs was heterogeneous. Trials typically used either validated outcome scales, clinical interviews, self-created items, or open-ended questions to assess AEs, while several were not explicit with their method of assessment. Types of AEs reported ranged from severe AEs to symptom escalation/deterioration, to physical, financial, and social complaints, and to app-induced negative reactions. However, the level of detail provided was typically limited; for example, it was difficult to decipher whether cases of hospitalizations were due to a new or an existing mental health problem, or to a physical health concern. Often it was unclear whether AEs were or were not directly related to app or trial-related protocols. Trials that did report app-induced AEs found that either a small number of participants were affected, or that events were perceived as mild in severity.

We identified factors associated with the likelihood of reporting of AEs. Trials that sampled patients with schizophrenia-spectrum disorders were more likely than not to report AEs. This likely reflects that studies on schizophrenia are conducted with more oversight and assessment of risk[75] given heightened concern for potential AEs[76]. Research on schizophrenia also had advanced measurements of AEs[77] and efforts to standardize reporting. Trials delivering apps with symptom monitoring features were

Table 4 | Frequency of trials reporting different adverse events

		Target problem						Trial condition	
	Total trials (*N* = 55)	Mood	Anxiety	Psychosis/ Schiz	Mixed	Self-harm/ suicide	Other	Reported in app cond	Reported in control cond
Adverse Event Type	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)		*N* (%)	*N* (%)
None reported by authors	8 (15%)	5 (62%)	1 (13%)	0	2 (25%)	0		-	-
Severe Adverse Event									
Hospitalization	14 (26%)	5 (36%)	0	5 (36%)	3 (22%)	0	1 (7%)	11 (20%)	10 (18%)
Self-harm/suicidal ideation or intent	11 (20%)	5 (45%)	0	2 (18%)	2 (18%)	2 (18%)	0	9 (16%)	8 (15%)
Death	3 (5%)	1 (33%)	0	2 (66%)	0	0	0	3 (5%)	1 (2%)
Violent episode	1 (2%)	0	0	1 (100%)	0	0	0	1 (2%)	1 (2%)
Crisis care referral	1 (2%)	0	0	1 (100%)	0	0	0	1 (2%)	1 (2%)
Other Adverse Event									
Poorer overall mental health	7 (13%)	3 (43%)	1(14%)	2 (29%)	1 (14%)	0	0	7 (13%)	2 (4%)
Subjective mood/anxiety symptom increase	5 (9%)	0	4 (80%)	0	1 (20%)	0	0	3 (5%)	2 (4%)
Subjective stress increase	3 (5%)	0	1 (33%)	1 (33%)	1 (33%)	0	0	2 (4%)	2 (4%)
Subjective psychotic symptoms increase	1 (2%)	0	0	1 (100%)	0	0	0	0	1 (2%)
Physical health complaints	5 (9%)	1 (20%)	2 (40%)	1 (20%)	1 (20%)	0	0	5 (9%)	3 (5%)
Financial concerns	1 (2%)	1 (100%)	0	0	0	0	0	1 (2%)	0
Relationship problems	1 (2%)	1 (100%)	0	0	0	0	0	1 (2%)	0
Increased stigmatization fears	1 (2%)	1 (100%)	0	0	0	0	0	1 (2%)	0
Cognitive impairments	1 (2%)	0	1 (100%)	0	0	0	0	1 (2%)	1 (2%)
App-induced Adverse Event									
Distress due to technical difficulties	2 (4%)	0	1 (50%)	0	1 (50%)	0	0	-	-
Distress due to in-app features	6 (11%)	2 (33%)	2 (33%)	2 (33%)	0	0	0	-	-
Feeling too reliant on the app	1 (2%)	0	0	0	1 (100%)	0	0	-	-
Cyber sickness	2 (4%)	0	2 (100%)	0	0	0	0	2 (4%)	0

also more likely to report negative effects. This finding may reflect greater recognition of the potential risks associated with symptom monitoring in some, despite conflicting evidence attesting to its efficacy in certain circumstances[2]. For example, a series of trials evaluating the Monsenso monitoring app in bipolar disorder found a higher risk of depressive episodes among the intervention over control groups[18,52,78]. In some patients, repeated symptom monitoring may require confronting and increased awareness of distressing experiences[78]. Finally, trials that administered cognitive training apps were less likely to report AEs, which could reflect a prevailing scientific view that interventions like these that indirectly target mental health symptoms via cognitive training may not necessarily come with risks, and as such are not typically addressed in this subfield.

The weighted deterioration rate among those allocated to app conditions was 6.7% (95% CI = 4.3–10.1%), which was similar in magnitude when restricting the analyses to depression- and anxiety-specific outcomes. These estimates are comparable to deterioration rates reported in meta-analyses on face-to-face psychotherapy[79] and internet-based interventions[80]. It is important to note that the definition of deterioration differed from study to study, further highlighting the importance for the field to develop a standardized definition or cut-point for patient deterioration. We also found no significant difference in deterioration rates between the app and control groups. However, this finding should not be taken as conclusive evidence that deterioration rates are equivalent across app and control groups, as only nine comparisons contributed to these analyses. Perhaps authors omit reporting deterioration rates because the number of participants who deteriorate is too low to detect any between-group differences. Future trials should aim to report rates of deterioration so that they can be pooled in meta-analyses and be used to generate important insights about AEs.

It is worth mentioning that symptom deterioration is typically assessed during follow-up appointments after prolonged engagement with an app, which can lead to missed opportunities for timely intervention. To address this, it is essential to implement in-built mechanisms that provide real-time feedback to professionals when symptom deterioration is detected. Currently, very few existing apps tested in the included trials incorporate this patient-provider feedback loop, so deterioration likely happens much before professionals are made aware. By developing apps that include such features, we can enhance our understanding of AEs and improve our ability to respond effectively to patients' needs.

This review has several limitations. First, estimated deterioration rates should only be considered preliminary. Only a small number of trials reported data on deterioration, which could mean that these are not representative of all mental health app trials. Furthermore, the

operationalization of deterioration differed across studies, which highlights the importance of developing a consensus about how deterioration should be defined. Second, it is possible that many trials underestimated the degree of AEs given evident rates of early dropout. Trials do not typically report reasons for dropout, and it be that some dropped out due to AEs, which were not captured. Third, we only included RCTs, like what has been done in other reviews of AEs in psychotherapy[81] and pharmacotherapy[82]. We adopted this criteria as it enabled better between-study comparisons and because a prior consensus statement[6] recommended that AEs in digital health interventions be reported in randomized trials to allow for causal inferences and hypotheses on the likely mechanisms that underpin their occurrence. However, we recognize that AEs may have also been reported in uncontrolled pilot/feasibility studies that were not captured in this review. Fourth, we only included the main outcome paper from RCT designs. It is possible that trial investigators report safety data in separate or forthcoming publications that were not captured in this review. The decision to exclude supplementary papers was driven by the challenge of maintaining a reproducible and systematic approach. Many supplementary papers on app safety may not include the key terms used in our search strategy, potentially resulting in incomplete identification of relevant studies. Addressing this would have required hand-searching all available trial documents for supplementary publications, some of which might remain unpublished. This would compromise the structured, replicable methodology central to systematic reviews. Nevertheless, we acknowledge that some primary papers lacking AE data may plan to publish such information in the future. Future updates to this review could explore strategies to incorporate these supplementary papers while adhering to systematic review guidelines.

The overall low rates of reporting AEs expose patients to risky apps today and limit the potential of the next generation of apps to be safer. While other research has begun moving towards guidelines for AE reporting in digital interventions for specific conditions[77,83–85] the need for guidelines across the broader mental health field in relation to apps is clear. Accordingly, we offer our expert opinion on what future research should consider with respect to AEs in this field, supported by our findings:

1. Reporting AEs should be considered standard practice. The overall low rate of studies reporting on AEs (32%) reflects the need for improvement; however, this trend is not unique to app trials but has been observed in standard psychotherapy trials[81] possibly because there is an underlying assumption that psychological treatments can range from helpful to ineffective, but not harmful. Given the heterogeneity of reporting methods utilized today and the lack of standardized scales to assess AEs beyond deterioration, the development of new tools to measure risk is critical. To ensure uptake, both funders and journals can support implementation by requesting the inclusion of new tools in proposals and papers, respectively.
2. Studies should include digital control conditions to assess risks due to specific apps versus the general use of a smartphone itself. Our results of no statistical significance between comparisons of the app and controls on deterioration underscores the need for improved study methodology to better understand direct versus indirect harms related to engaging in digital tools.
3. The need for consistent reporting on harm (recommendation #1) should not abnegate necessary research into the currently unexplored and novel risks that apps may pose. Current reporting scales do not consider emerging risks of digital technology and how use itself may impact mental health, cognition, and social functioning[86]. Foundational research into these potential and emerging risks is critical to ensuring a full understanding of how apps may, or may not, cause harm.
4. Patients and app users should be empowered to report the AEs of apps themselves. In the UK, the MHRA offers the Yellow Card Scheme for collecting and monitoring information on suspected AEs, and in the US the FDA has schemes like MedWatch to enable voluntary reporting by consumers, patients, and health professionals. Clarifying how such systems may apply to apps and the scope of reporting for apps could provide a conduit for immediate and real-world data on the safety of apps today.
5. Researchers should consider the method of inquiry for assessing AEs. At times there may not be a straightforward tool to administer to investigate which AEs a device may induce. However, it is still necessary for users to be asked specifically if they have encountered any AEs from the use of the digital device. Expecting users to report AEs is appropriate, but may inadvertently overlook the emergence of other AEs. This approach is especially necessary for technology devices since the full landscape of possible harms is not fully understood relative to other device types.
6. In light of the strong focus on deterioration data, this review highlights the potential to use deterioration rates in quantifying the risk-benefit equation for regulatory approval processes. By illustrating how these rates can be reported alongside treatment gains, we encourage researchers to routinely include this metric in their evaluations. Viewing deterioration not merely as a negative outcome, but as a valuable data point, can support the development of new apps. This would promote a more comprehensive assessment of therapeutic efficacy and emphasize the role of deterioration data in informing and strengthening regulatory decisions.

In conclusion, reporting of AEs in clinical trials of mental health apps is inconsistent and suboptimal, with only one in three trials reporting AEs. To expedite research in this field, we provide a series of recommendations for reporting AEs in future clinical trials so that the public, professionals, and regulatory bodies can better assess the risks and benefits of mental health apps. Better methods to detect and accurately predict the likelihood of harm are needed to ensure that each patient can be matched to a suitable intervention.

Methods

Identification and selection of trials

This review (PROSPERO pre-registration ID: CRD42024506486) was conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[87]. Supplementary Table 2 presents a PRISMA checklist. We searched (May 2024) the Medline, PsycINFO, Web of Science, and ProQuest Dissertations databases by combining key terms "smartphone*" OR "mobile phone" OR "cell phone" OR "mobile app*" OR "iPhone" OR "android" OR "mhealth" OR "m-health" OR "cellular phone" OR "mobile device*" OR "mobile-based" OR "mobile health" AND "anxiety" OR "agoraphobia" OR "phobia*" OR "panic" OR "post-traumatic stress" OR "mental health" OR "mental illness*" OR "depress*" OR "affective disorder*" OR "bipolar" OR "mood disorder*" OR "psychosis" OR "psychotic" OR "schizophre*" OR self-harm" or "self-injury" OR "severe mental" OR "serious mental" OR "eating disorder" AND random* OR "clinical trial".

We included (i) RCTs (ii) that tested the effects of a mental health smartphone app, (iii) among samples pre-selected for mental health problems. A smartphone app was defined as software application designed for mobile devices, optimized for specific operating systems that uses device hardware features and can function offline once installed. We included samples pre-selected, either via diagnostic interview or self-report, for elevated depression, anxiety, schizophrenia/psychosis, self-harm, bipolar, eating disorders, or general psychiatric distress. Any control condition was permitted, as were trials that compared two or more mental health apps. Trials that delivered an app-based intervention augmented with traditional treatment or usual care were also included, but apps delivered in conjunction with a computer-based intervention were excluded (combining different digital delivery formats would not make it possible to understand AEs in the context of smartphone technology specifically). Published and unpublished trials were eligible. Two independent researchers screened for full texts of

included studies, with disagreements resolved through consensus (94% agreement).

Quality assessment and extraction

We used criteria from the Cochrane Collaboration Risk of Bias tool to assess for risk of bias[88]. These criteria include random sequence generation, allocation concealment, blinding of participants or personnel, blinding of outcome assessment, and completeness of outcome data. Each domain was rated as high risk, low risk, or unclear.

We also extracted the following information: target sample, method of pre-selection (diagnostic or self-report), app name, public availability, app technique, whether professional guidance was offered, the presence or absence of mood/symptom monitoring or chat-bot features if the app was delivered as a stand-alone intervention, the comparison condition, sample size, and whether participant-researcher contact was described. These characteristics were extracted for trials that did and did not report AEs. We also extracted relevant information about AEs in the subset of trials that reported this. Data extraction, including risk of bias ratings, was performed by three independent researchers, and disagreements were resolved by consensus (91% agreement rating across all domains).

Analytical approach

Three analytical approaches were adopted. First, chi-square analyses were performed to compare trials that did versus did not report AEs on various study characteristics.

Second, meta-analyses were conducted on symptom deterioration rates at post-test using Comprehensive Meta-Analysis[89]. To estimate rates of deterioration, we calculated the weighted pooled event rate using random effects models. Weighted deterioration rates were calculated separately for those allocated to app and control groups. If multiple measures of deterioration were used, the mean of the effect sizes for each measure within the study was calculated, before the effect sizes were pooled. Event rates were converted to percentages after pooling for ease of readability.

Odds ratios (OR) were also calculated using random effects models to compare deterioration rates between app and control conditions. ORs were computed separately for each trial, weighted by their inverse variance, and pooled to create a summary effect[89]. ORs < 1 indicate that deterioration rates were lower in the app group than in the control group. Heterogeneity was assessed by reporting the I^2 statistic[90].

One study explicitly reported zero cases of deterioration[41]. Per recommendations[91], we added a continuity correction of 0.5 to both the number of events and the number of non-events across all arms of that study.

Third, findings pertaining to other AEs were summarized qualitatively. We summarize the instruments used to assess negative effects, the types of AEs reported, the number of trials that assessed each AE, and the occurrence of AEs. We also make the distinction between AEs that were specifically induced by the app and AES that occurred during or after the intervention period that were potentially unrelated to the app.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on request.

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