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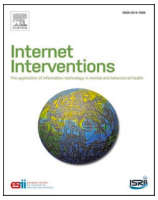

Additive effects of adjunctive app-based interventions for mental disorders - A systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Background: It is uncertain whether app-based interventions add value to existing mental health care.
Objective: To examine the incremental effects of app-based interventions when used as adjunct to mental health interventions.
Methods: We searched PubMed, PsycINFO, Scopus, Web of Science, and Cochrane Library databases on September 15th, 2023, for randomised controlled trials (RCTs) on mental health interventions with an adjunct app-based intervention compared to the same intervention-only arm for adults with mental disorders or respective clinically relevant symptomatology. We conducted meta-analyses on symptoms of different mental disorders at postintervention. PROSPERO, CRD42018098545.
Results: We identified 46 RCTs (4869 participants). Thirty-two adjunctive app-based interventions passively or actively monitored symptoms and behaviour, and in 13 interventions, the monitored data were sent to a therapist. We found additive effects on symptoms of depression ($g = 0.17$; 95 % CI 0.02 to 0.33; $k = 7$ comparisons), anxiety ($g = 0.80$; 95 % CI 0.06 to 1.54; $k = 3$), mania ($g = 0.2$; 95 % CI 0.02 to 0.38; $k = 4$), smoking cessation ($g = 0.43$; 95 % CI 0.29 to 0.58; $k = 10$), and alcohol use ($g = 0.23$; 95 % CI 0.08 to 0.39; $k = 7$). No significant effects were found on symptoms of depression within a bipolar disorder ($g = -0.07$; 95 % CI -0.37 to 0.23, $k = 4$) and eating disorders ($g = -0.02$; 95 % CI -0.44 to 0.4, $k = 3$). Studies on depression, mania, smoking, and alcohol use had a low heterogeneity between the trials. For other mental disorders, only single studies were identified. Only ten studies had a low risk of bias, and 25 studies reported insufficient statistical power.
Discussion: App-based interventions may be used to enhance mental health interventions to further reduce symptoms of depression, anxiety, mania, smoking, and alcohol use. However, the effects were small, except for anxiety, and limited due to study quality. Further high-quality research with larger sample sizes is warranted to better understand how app-based interventions can be most effectively combined with established interventions to improve outcomes.

1. Introduction

Although there is a wide range of empirically supported treatments for mental disorders (Andrews et al., 2018; Cuijpers et al., 2023), there is still room for improvement (Huhn et al., 2014; Leichsenring et al., 2022). Current limitations of available treatments include high patient dropout rates, non-response, and high risk of relapse (Fernandez et al., 2015; Gloster et al., 2020; Hennemann et al., 2018). To further improve

Abbreviations: ACT, acceptance and commitment therapy; CBT, cognitive-behavioural therapy; CG, control group; CPP, child parent psychotherapy; DBT, dialectic behavioural therapy; F2F, face-to-face; IG, intervention group; MBSR, mindfulness-based stress reduction; MBCT, mindfulness based cognitive therapy; MI, motivational interviewing; PI, prediction interval; PM, psychiatric medication; PTSD, posttraumatic stress disorder; SMI, serious mental illness; RCT, randomised controlled trial.

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efficacy of these treatments, integrating smartphone applications (apps) for patients in therapy is heralded as having potential (Barnett, 2018). The personal and trusting relationship that users often have with their devices may make app-based interventions a promising avenue for supporting mental health. Opportunities for integrating app-based interventions in the context of psychological and psychiatric treatments are versatile. An app could assist the patient in transferring helpful behaviour learned in therapy into everyday life through repetitious or additional, personalised psychoeducation, motivation, skill training (e.g., relaxation) (Lui et al., 2017), and symptom monitoring (self-report and sensory-based) (Luxton et al., 2011). It can also provide support in severe distress and facilitate communication and support with the healthcare provider (Van Daele et al., 2021). Moreover, the use of an app can improve homework adherence through features within the app, such as reminder functions and brief interactive interventions (Tang and Kreindler, 2017).

Despite the potential benefits of using app-based interventions as adjuncts, previous research has primarily focused on the effects of standalone app-based interventions compared to waitlist or active control conditions (Goldberg et al., 2022). And although previous reviews, comments, perspectives, and statements have described the potential benefits of adjunctive app-based interventions (Anastasiadou et al., 2018; Bond et al., 2023; Ramadas et al., 2023; Torous et al., 2021), only two studies have systematically examined the additional benefits using adjunctive designs (app-based interventions + intervention versus intervention alone). A meta-analysis by Lindhiem and colleagues, conducted in 2014, indicated that using additional mobile technology-based interventions compared to strictly onsite interventions may increase the effectiveness of psychological interventions (SMD = 0.27; 95 % CI 0.04 to 0.50; $p < 0.05$) (Lindhiem et al., 2015). However, this meta-analysis calculated an overall effect across different mental disorders, including topics outside of mental health, such as weight loss and outdated digital application formats such as personal digital assistants or text messages. Out of the ten studies included in this meta-analysis, only one investigated the additional effects of an app-based intervention (Gustafson et al., 2014). A more recent meta-analysis by Linardon and colleagues, conducted in 2018, examined a broader range of app-supported smartphone interventions and identified five randomised clinical trials (RCTs) with adjunctive designs. For depressive symptoms, there was no significant reduction ($g = 0.26$; 95 % CI -0.09 to 0.61) in four RCTs, and for generalised anxiety symptoms, one RCT revealed no significant difference ($g = 0.05$; 95 % CI -0.27 to 0.38) (Linardon et al., 2019). However, both these meta-analyses provided limited information about the characteristics of the interventions, and neither conducted subgroup analyses to examine the robustness of outcomes based on the quality of the included studies.

As a result, this meta-analysis differs from prior meta-analyses described above in several key ways. Firstly, this meta-analysis focused exclusively on app-based interventions, excluding other forms of mobile technologies. Secondly, our study specifically aimed to assess the incremental effects of app-based interventions when used adjunct to mental health interventions, compared to a control group that receives the same intervention without the adjunctive app-based component. Consequently, we aimed to identify a broader range of studies addressing various mental disorders and provide a more comprehensive description of the intervention characteristics. Finally, we intended to systematically evaluate the quality of the included studies by assessing the risk of bias and conducting subgroup analyses to examine its impact.

2. Methods

The meta-analysis was preregistered at PROSPERO, CRD42018098545, and reporting followed the PRISMA 2020 guidelines (see Appendix A for checklist) (Page et al., 2021). There were small deviations from the original protocol. Instead of the previous version of the risk of bias tool, we used the updated Rob 2.0 tool (Sterne et al., 2019). We revised the initial plan of limiting the review to English or German publications, and there were no restrictions on the publication language.

2.1. Search strategy and selection criteria

We searched PubMed, PsycINFO, Scopus, Web of Science, and the Cochrane Library. The literature search was completed by September 15th, 2023. The search combined four sets of key themes: mobile application, mental disorder, RCT, and adjunctive intervention (see Appendix B for search strings). Further, reference lists of reviews, meta-analyses, and eligible studies were screened.

To be included in the meta-analysis, studies needed to fulfil the following criteria: 1) RCTs that 2) investigated the additional effect of an app-based intervention as an adjunct to an intervention compared to an intervention-only arm, where the primary intervention for the comparable groups was the same. The app-based intervention could be added before, during, or as aftercare as an intervention for mental health (i.e., cognitive-behavioural therapy (CBT), pharmacotherapy) in a nonspecific setting (i.e., face-to-face, online) with 3) the intent to reduce symptoms of or improve mental health. The trials must have included 4) adult participants (≥18 years) with 5) diagnosed mental disorders (defined as in the DSM or ICD) or respective clinically relevant symptomatology operationalised and assessed by a rating scale (except for smoking cessation trials where research often accepts self-report smoking addiction or behaviour), and must be 6) published peer-reviewed articles in any language. We defined a mobile application as software designed to run on a smartphone.

2.2. Data extraction and quality assessment

After duplicate removal, two reviewers (L.M.F. and K.K.W.) independently screened all titles and abstracts for potentially eligible full-text articles. Full-text articles were then reviewed independently. Inter-rater reliability is reported by using kappa, where values are rated as fair ($\kappa = 0.4$ to 0.59), good ($\kappa = 0.6$ to 0.74), or excellent ($\kappa > 0.75$) (Orwin, 1994). Disagreement was resolved by discussion. Two master's psychology students extracted data on study design (sample size, statistical power as reported in the study, study inclusion criteria, country, target outcome), sample characteristics (age, sex, ethnicity/race), intervention details (setting, theory basis framework, intervention components), and outcomes (length of post and follow-up, adherence, outcome measures of interest on a level of summary estimates).

2.3. Quality assessment

The study quality, based on the outcome, was independently assessed by the same group of Master's students and upon completion of their degree and leaving the university, by L.M.F. and J.K.K., both Master's degree psychologists, using the Cochrane risk-of-bias tool (RoB2) (Higgins et al., 2019; Sterne et al., 2019). This tool evaluates five domains of bias, each addressing specific issues that may affect the results of RCTs:

(1) Bias arising from the randomisation process: Determine whether the allocation sequence was random and adequately concealed and whether baseline differences between groups suggest a problem with the randomisation process;
(2) Bias due to deviations from intended intervention: Determine whether participants, carers, or people delivering the intervention were blinded, if deviations from the intended intervention occurred due to the experimental context, and whether they were unevenly distributed between groups, potentially affecting the outcome. Assess whether an appropriate analysis was used to estimate the impact of the intervention assignment, and if not, consider the potential significant influence on the result.

(3) Bias due to missing outcome data: Determine if data were accessible for all, or the majority (at least 95 %), of the randomised participants. Assess whether the results were biased by missing outcome data and consider whether the missing outcome data depended on the true values.
(4) Bias in measurement of the outcome: Determine whether the method used to measure the outcome was appropriate and assess the potential differences in how the outcome was measured or ascertained between the groups. Also, consider whether outcome assessors were blinded and whether their knowledge of the interventions received could have biased the outcome assessment.
(5) Bias in the selection of the reported result: Determine whether the trial analysis followed a pre-specified plan. Also, assess whether the numerical result under evaluation could have been selected from multiple outcome measurements within the same outcome domain or from various data analyses based on the results.

Each domain produces a distinct rating (either 'low', 'some concerns', or 'high'). When combined, these ratings form the basis for the overall bias assessment, which is also categorised as 'low', 'some concerns', or 'high'. Disagreements were discussed with L.M.F. and K.K.W., and inter-rater reliability was reported.

2.4. Statistical analyses

Our data extraction process prioritised intention-to-treat data and focused on postintervention outcomes for each target variable. We compared mental health interventions with and without an adjunctive app-based intervention, which served as the control condition. We calculated Hedges' *g* for continuous outcome data using means, standard deviations, or mean differences with 95 % CI. We also calculated odds ratios based on event rates before transforming them into Hedges' *g*. If more than one measurement per outcome in a trial was reported as the primary outcome, all outcomes were reported when the study results were not pooled due to the limited number of comparison studies available. If there were enough comparisons available, but multiple primary outcomes were reported, L.M.F. and K.K.W. selected the outcome with the best-validated instrument based on the level of validity found in the literature (Cuijpers, 2016). We pooled trials targeting the same mental disorder to generate the mean effect size expressed as Hedges' *g*, the 95 % CI, and *P*-value (*p*) for each investigated outcome. A positive effect size indicates a beneficial effect of the adjunct app-based intervention compared with the control condition. An effect size of 0.2 indicates a small effect, meaning a small added value to the primary intervention, 0.5 a moderate effect, and 0.8 a large effect (Higgins et al., 2019). We present single calculated mean effect sizes for target outcomes in which too few comparisons ($k < 3$) were available to pool data. Since we expected the trials to be heterogeneous, we applied a random effects model in all analyses. If trials reported two comparisons to one control comparison, we combined the groups to create a single pairwise comparison, or if this was not applicable (for instance, when the intervention or the setting of the intervention group differed significantly), we divided the sample size of the shared group to avoid inflating statistical power (Higgins et al., 2019). We also pooled effects on depression and anxiety, regardless of whether the outcome was primary or secondary. We performed subgroup analyses on setting and risk of bias with a minimum of three studies. These analyses were conducted using a mixed-effects analysis, with the random-effects model summarising the studies within each subgroup and the fixed-effects model testing for significant differences between the subgroups.

We assessed heterogeneity between the trials using I^2 and its 95 % CI to express the percentage of the total variance, which can be explained. Heterogeneity was considered low when I^2 was 25 %, moderate (50 %), and high (75 %) (Higgins et al., 2003). We included the prediction interval (PI) to estimate the effect size range in future studies (Borenstein et al., 2017). A wide PI suggests potential variation and unpredictability in outcomes across different contexts, while a narrow PI reflects more confidence in consistent effects.

To examine small-study effects (as potential indicators of publication bias), we examined the funnel plot visually and conducted an Egger's test (Sterne et al., 2005). When funnel plot asymmetry was found, the Duval and Tweedy trim-and-fill procedure was performed (Duval and Tweedie, 2000). Outcome robustness was tested by conducting separate analyses: 1) excluding studies with a high risk of bias and 2) analysing only studies with a low risk of bias.

We completed all statistical analyses with Comprehensive Meta-Analysis Software, version 4.0 (Borenstein et al., 2022), and the R software programme (version 4.2.2) using the meta package (version 6.1.0) (Balduzzi et al., 2019).

3. Results

3.1. Study selection

After the removal of duplicates and exclusion based on the title and abstract, 158 records remained for full-text screening. Of these, 46 studies fulfilling the inclusion criteria remained (see Appendix C for a list of excluded studies with a brief reason). We contacted the authors of 20 studies with insufficient effect size data and retrieved datasets for 19 studies. Two studies (Ghaemi et al., 2022; Price et al., 2022) using a sham-app as an active control condition were excluded from quantitative analyses because of incomparability with studies using inactive control conditions. Consequently, 46 studies were included in the systematic review, and 43 studies for 46 comparisons were included in the meta-analysis (Fig. 1). Inter-rater reliability of the full-text eligibility check was fair ($\kappa = 0.51$).

3.2. Study and participants characteristics

The included studies were primarily conducted in high-income countries, with 21 studies (46 %) in North America and 16 studies (35 %) in Europe.

Primary target outcomes of the 46 included studies were symptoms of depression ($k = 6$), anxiety disorders ($k = 3$), smoking ($k = 11$), alcohol ($k = 6$), drug use ($k = 1$), co-occurrence of drug and alcohol use ($k = 1$), eating disorders ($k = 3$), psychotic disorders ($k = 3$), bipolar disorder ($k = 4$), schizophrenia/schizoaffective or bipolar disorder within one sample grouped as serious mental illness (SMI) ($k = 1$), posttraumatic stress disorder (PTSD) ($k = 2$), suicidal and non-suicidal self-injury behaviour ($k = 2$), suicide risk ($k = 2$), and somatic symptom disorder ($k = 1$). Several studies also assessed symptoms of depression ($k = 22$) and anxiety ($k = 10$) as primary or secondary outcomes.

In total, 4869 participants with sample sizes ranging from $n = 21$ (Rodante et al., 2022) to $n = 349$ (Gustafson et al., 2014) were included in this meta-analysis. Eighteen studies were conducted as pilot studies, and an additional seven reported insufficient statistical power. Consequently, 25 studies (54 %) fell below the acceptable threshold of 80 % power (1-β) to detect a statistically significant effect if it exists. In detail, the studies that reported insufficient statistical power targeted the following primary outcomes: smoking cessation (6/11), alcohol use (4/6), eating disorders (3/3), depression (2/6), suicidal and non-suicidal self-injury behaviour (2/2), PTSD (2/2), suicide risk (2/2), psychotic disorders (2/3), bipolar disorder (1/4), and drug and alcohol use (1/1).

2406 (49 %) participants were female, and the mean age was 38.68 years (SD range 1.6 to 13.46). Among 23 studies, 15 reported a majority of White or Non-Hispanic participants, and five reported a majority of Black or African American participants. Primary interventions lasted between brief advice (exact duration not reported) (Krishnan et al., 2019) and 12 months (Gustafson et al., 2014). The additional app-based interventions lasted between 12 days (Krishnan et al., 2019) and 12 months (Carrasco-Hernandez et al., 2020; McKay et al., 2022).

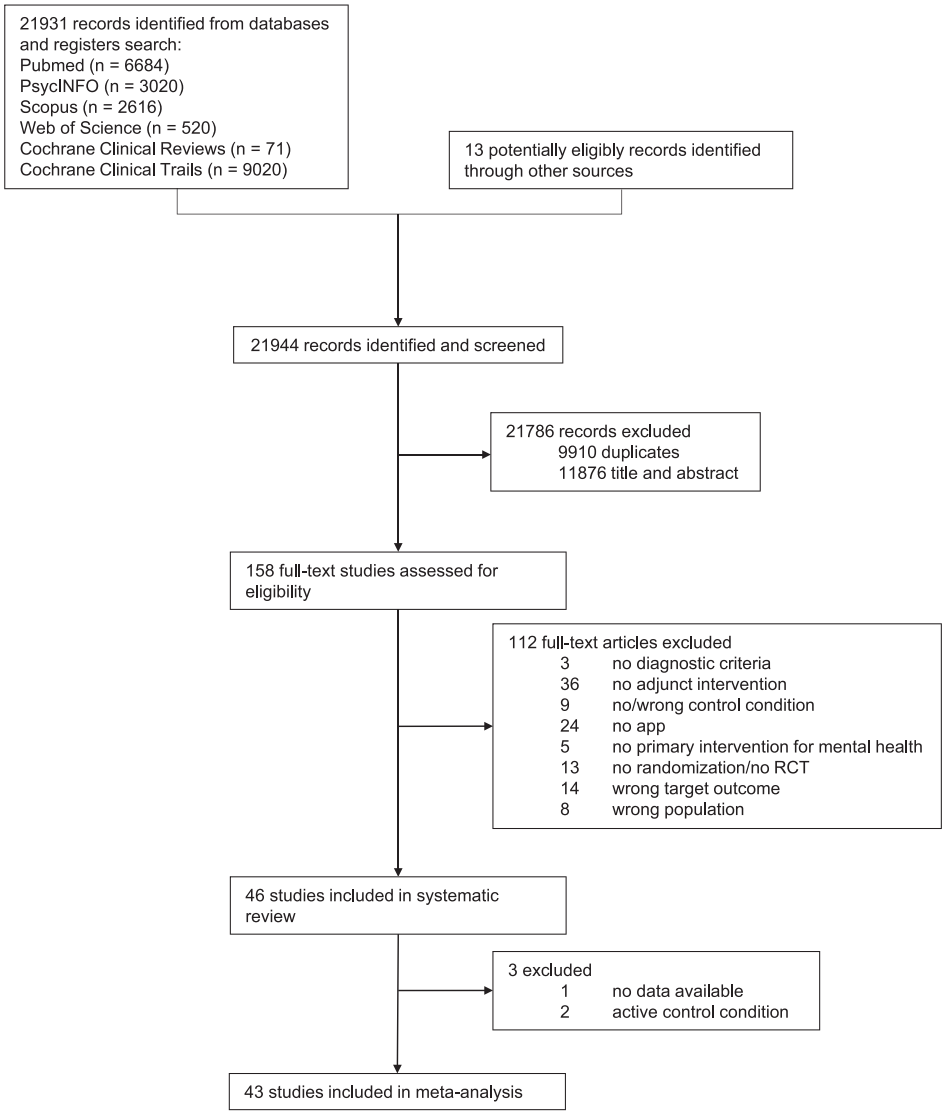

Fig. 1. PRISMA flowchart.

Of the 47 different primary interventions, face-to-face (group or individual) was the most common delivery setting (85 %; $k = 40$), typically as ongoing interventions (81 %; $k = 38$). Six primary interventions (13 %) were provided as aftercare, three (7 %) had already been conducted, and the app-based intervention was the sole aftercare. The majority of the primary interventions were based on CBT (45 %; $k = 21$) or behavioural approaches (15 %; $k = 7$), and included psychiatric medication (55 %; $k = 26$).

The majority of the 44 different adjunctive app-based interventions were based on behavioural approaches, including activity or mood monitoring (48 %; $k = 21$) or CBT (39 %; $k = 17$). The category system from Weisel and colleagues (Weisel et al., 2019) was used to categorise the components of the adjunctive app-based interventions. Most app-based interventions included static content such as psychoeducational texts or audio-guided relaxation (73 %; $k = 32$), and symptom or behaviour monitoring, whether through patient-reported entries or automatically collected smartphone data, was part of 32 app-based interventions (73 %). In 13 interventions, the monitored data were sent to a therapist (30 %). In 25 app-based interventions (57 %), reminders or prompts were sent to improve adherence.

Adherence data such as access rate, days spent in the intervention, response rate, and completion rate were reported for primary interventions in 15 studies (33 %) and for adjunctive app-based interventions in 34 studies (74 %). The reported completion rate of the primary intervention programme in the intervention and control group ranged between 33.39 % (Asayut et al., 2022) and 98.33 % (Aharonovich et al., 2017), and no significant differences between the intervention and the control group were reported in 11 comparisons ($g = 0.01$; 95 % CI -0.13 to 0.15, $p = 0.852$; $I^2 = 0.0$ %; 95 % CI 0.0 to 60.2; PI -0.13 to 0.19). The reported completion rate of the adjunctive app-based intervention programme ranged between 22 % (Goulding et al., 2023) to 93 % (Faurholt-Jepsen et al., 2015), from which five completed less and 13 completed more than half of the intervention programme.

An overview of the selected study and intervention characteristics, including the components and a brief description of each app-based intervention can be found in Table 1 and Appendix E.

3.3. Quality assessment

The risk of bias assessments for the included studies are presented in Fig. 2. Overall, ten studies had a low risk of bias, 19 had some concerns, and 17 had a high risk of bias. The high risk of bias was mainly due to the domains deviations from intended intervention ($k = 9$), missing outcome data ($k = 6$), and measurement of the outcome ($k = 6$). In

Table 1
Intervention characteristics.

Source	Total n	Primary target Outcome	Setting primary intervention	Framework intervention	
				Primary intervention	Adjunctive app intervention
Aharonovich et al. (2017)	47	Drug use and alcohol use	F2F (individual)	MI	Behavioural (monitoring)
Asayut et al. (2022)	156	Smoking cessation	F2F (individual), PM	MI	MI
Bastiaansen et al. (2020)	161	Depression	IG 1, IG 2: F2F (individual or group), PM	IG 1, IG 2: CBT, PM	IG 1:CBT, behavioural (monitoring) IG 2: CBT, behavioural (monitoring)
Bell et al. (2020)	34	Hearing voices within a psychotic disorder	F2F (individual), PM	Behavioural, PM	CBT, behavioural (monitoring)
Boettcher et al. (2018)	140	Social anxiety	Internet	CBT	CBT
Carrasco-Hernandez et al. (2020)	240	Smoking cessation	PM	PM	Behavioural
Cheung et al., (2015)[a]	136	Smoking cessation	IG 1, IG 2: Self-help manual after outpatient intervention (aftercare)	IG 1, IG 2: Behavioural, PM	IG 1, IG 2: CBT
Chulasai et al. (2022)	273	Smoking cessation	F2F (individual, group), telephone, PM	MI	MI
Depp et al. (2019)	229	Schizophrenia/Schizoaffective or bipolar disorder	IG 1, IG 2: F2F (individual), PM	IG 1, IG 2: CBT, PM	IG 1: CBT IG 2: Behavioural (monitoring)
Depp et al. (2023)	77	Suicide risk	F2F (group)	CBT	CBT, behavioural (monitoring)
Durmaz et al. (2019)	132	Smoking cessation	F2F (individual)	MI, counselling	Behavioural
Farren et al. (2022)	111	Alcohol use	F2F (group) after inpatient intervention (aftercare)	CBT	CBT
Faurholt-Jepsen et al. (2015)	67	Bipolar disorder	F2F (individual), PM	Supportive, PM	Behavioural (monitoring)
Faurholt-Jepsen et al. (2020)	129	Bipolar disorder	F2F (individual), PM	Supportive, PM	CBT, behavioural (monitoring)
Faurholt-Jepsen et al. (2021)	98	Bipolar disorder	F2F (individual), PM after inpatient intervention (aftercare)	CBT, PM	CBT, behavioural (monitoring)
Gao et al. (2022)	71	Anxiety regarding sleep	PM	PM	Mindfulness
Ghaemi et al. (2022)[b]	110	Schizophrenia	PM	PM	IG: CBT; CG: sham control app
Goulding et al. (2023)	205	Bipolar disorder	F2F (individual), PM	Behavioural, PM	Behavioural (monitoring)
Gustafson et al. (2014)	349	Alcohol use	F2F (individual), PM after inpatient intervention (aftercare)	CBT, PM	Self-determination theory
Hammond et al. (2021)	61	Alcohol use	F2F (group)	CBT	Behavioural (monitoring)
Hantsoo et al. (2018)[c]	72	Depression	Smartphone app	Psycho-education	Behavioural (monitoring)
Hildebrandt et al. (2017)	66	Binge eating	F2F (individual), self-help manual	CBT	Behavioural (monitoring)
Juarascio et al., (2023)	56	Bulimia nervosa	F2F (individual), smartphone app	CBT, behavioural (monitoring)	Just-in-time adaptive interventions (CBT)
Keeler et al., (2022)	80	Binge eating	F2F (individual), PM	CBT, PM	Neurocognitive training
Krebs et al. (2019)	38	Smoking cessation	F2F (individual) or telephone, self-help manual, PM	Behavioural, PM	Social cognitive theory
Krishnan et al. (2019)	89	Smoking cessation	F2F (individual) concluded	Psycho-education	Behavioural (monitoring)
Kristjansdottir et al. (2013)	135	Somatic symptom disorder	Inpatient intervention concluded, internet (aftercare)	CBT, PM	ACT, self-determination theory
Law et al. (2023)	29	Non-suicidal self-injury behaviours (self-harm)	F2F (individual), PM	Psychosocial, PM	CBT
Lewis et al. (2020)	81	Psychotic disorder with a history of experiencing psychotic episodes	F2F (individual), PM	Psychosocial, PM	Behavioural (monitoring)
Liu et al. (2023)	51	Alcohol use	F2F (individual), PM after inpatient intervention (aftercare)	MI, PM	CBT, behavioural (monitoring), 12-step principles
Mackintosh et al. (2017)	58	Anger in PTSD	F2F (group)	CBT	CBT
Mantani et al., 2017)	164	Depression	Smartphone, PM	CBT, PM	CBT
McKay et al. (2022)	133	Alcohol use	F2F (group)	12-step principles	Self-determination theory
Mellentin et al. (2019)	110	Alcohol use	Outpatient intervention concluded	CBT, PM	Neurocognitive training
O'Connor et al. (2020)	100	Smoking cessation	F2F (group)	ACT	ACT
O'Toole et al. (2019))	129	Suicide risk	F2F (individual)	Supportive, problem-solving	CBT
Paquette et al. (2023)	145	Drug use	F2F (group)	Behavioural	Behavioural
Price et al. (2022)[b]	57	Smoking cessation	F2F (individual, group)	Seeking Safety, MI, CPP	IG: Resonance breathing; CG: Sham breathing
Raevuori et al. (2021)	124	Depression	IG 1: F2F (individual), PM IG 2: F2F (individual)	IG 1: CBT, PM IG 2: CBT	IG 1, IG 2: Behavioural, CBT MBCT, MBSR
Rodante et al. (2022)	21	Suicidal and non-suicidal self-injury behaviours	F2F (group), telephone, PM	DBT, PM	DBT
Roy et al. (2021)	63	Generalised anxiety disorder	F2F (individual), PM	CBT, PM	Mindfulness
Schlam and Baker (2020)	30	Smoking cessation	F2F (individual), telephone, PM	Behavioural, PM	Behavioural
Schmädeke and Bischoff (2015)	92	Depression	Inpatient intervention concluded	CBT, PM	CBT
Schnall et al. (2022)	40	Smoking cessation	F2F (individual), telephone, PM	3-step programme	Behavioural (monitoring)
Tønning et al. (2021)	120	Depression	F2F (individual), PM	CBT, PM	CBT, behavioural (monitoring)

(*continued on next page*)

Table 1 (*continued*)

Source	Total n	Primary target Outcome	Setting primary intervention	Framework intervention	
				Primary intervention	Adjunctive app intervention
Wallace et al. (2022)	30	Emotion regulation in PTSD	F2F (individual, group)	Diaphragmatic breathing, CBT	Diaphragmatic breathing

ACT: acceptance and commitment therapy; CBT: cognitive-behavioural therapy; CG: control group; CPP: child parent psychotherapy; DBT: dialectic behavioural therapy; F2F: face-to-face; MBSR: mindfulness-based stress reduction; IG: intervention group; MBCT: mindfulness based cognitive therapy; MI: motivational interviewing; PM: psychiatric medication; PTSD: posttraumatic stress disorder.

[a] For further descriptive and quantitative analyses IG1 and IG2 were combined.

[b] Study excluded from quantitative analyses due to unique active control condition.

[c] Study was excluded from quantitative analyses because no outcome data was available.

detail, the following studies had a high risk of bias: smoking cessation (4/11), alcohol use (2/6), depression (2/6), suicidal and non-suicidal self-injury behaviour (2/2), PTSD (2/2), alcohol and drug use (1/1), anxiety (1/3), psychotic disorders (1/3), SMI (1/1), and somatic symptom disorder (1/1). Inter-rater reliability of risk of bias domains was good ($\kappa = 0.66$).

3.4. Additive effects of adjunctive app-based interventions on mental disorders

Pooled between-group effect sizes at postintervention of app-based interventions used as an adjunct to an intervention, compared to an intervention-only arm, are shown in Table 2.

3.4.1. Depression

Adjunctive app-based interventions targeting symptoms of depression had a mean effect size of $g = 0.17$ (95 % CI, 0.02 to 0.33, $p = 0.03$; $I^2 = 0.0$ %; 95 % CI 0.0 to 70.8; PI -0.03 to 0.38; $k = 7$ (Bastiaansen et al., 2020; Mantani et al., 2017; Raevuori et al., 2021; Schmädeke and Bischoff, 2015; Tønning et al., 2021); see Fig. 3a for forest plot). When studies with a low risk of bias were pooled, the effect became larger ($g =$ 0.32; 95 % CI, 0.09 to 0.56; $k = 3$ (Bastiaansen et al., 2020; Mantani et al., 2017)). Subgroup analysis with the primary intervention in a face-to-face setting, including psychiatric medication, detected no difference ($g = 0.16$; 95 % CI -0.06 to 0.38; $k = 4$ (Bastiaansen et al., 2020; Raevuori et al., 2021; Tønning et al., 2021)).

No difference was found for symptoms of depression regarding primary and secondary outcomes ($g = 0.03$; 95 % CI -0.07 to 0.13, $p =$ 0.578; $I^2 = 13.9$ %; 95 % CI 0.0 to 48; PI -0.19 to 0.25; $k = 22$ (Bastiaansen et al., 2020; Bell et al., 2020; Boettcher et al., 2018; Farren et al., 2022; Faurholt-Jepsen et al., 2015; Faurholt-Jepsen et al., 2020; Faurholt-Jepsen et al., 2021; Goulding et al., 2023; Keeler et al., 2022; Law et al., 2023; Lewis et al., 2020; Liu et al., 2023; Mackintosh et al., 2017; Mantani et al., 2017; O'Toole et al., 2019; Raevuori et al., 2021; Schmädeke and Bischoff, 2015; Schnall et al., 2022; Tønning et al., 2021; Wallace et al., 2022); see Appendix F for forest plot Fig. F.1).

3.4.2. Anxiety

Anxiety symptoms as primary outcome were targeted in three comparisons (Boettcher et al., 2018; Gao et al., 2022; Roy et al., 2021) and revealed a significant pooled effect size of $g = 0.80$ (95 %; CI 0.06 to 1.54, $p = 0.033$; see Appendix F for forest plot Fig. F.2) with high heterogeneity ($I^2 = 87.4$ %; 95 % CI 64.3 to 95.5; PI -8.31 to 9.92).

When anxiety symptoms were both primary and secondary outcomes ($k = 10$ (Bell et al., 2020; Boettcher et al., 2018; Farren et al., 2022; Gao et al., 2022; Keeler et al., 2022; Liu et al., 2023; Raevuori et al., 2021; Roy et al., 2021; Wallace et al., 2022)), there was no difference between the comparison groups ($g = 0.15$; 95 % CI -0.2 to 0.5, $p = 0.412$; see Appendix F for forest plot Fig. F.3) with high heterogeneity ($I^2 = 77.9$ %; 95 % CI 59.6 to 87.9; PI -1.06 to 1.35).

3.4.3. Bipolar disorder

For bipolar disorder, a significant reduction of manic symptoms was observed across four comparisons (Faurholt-Jepsen et al., 2015; Faurholt-Jepsen et al., 2020; Faurholt-Jepsen et al., 2021; Goulding et al., 2023) in favour of the intervention group ($g = 0.20$; 95 % CI 0.02 to 0.38, $p = 0.031$; see Appendix F for forest plot Fig. F.4) with low heterogeneity ($I^2 = 0.0$ %; 95 % CI 0.0 to 84.7; PI -0.20 to 0.59). When studies with a low risk of bias were pooled, the difference was no longer significant ($g = 0.18$; 95 % CI, -0.06 to 0.42; $k = 3$ (Faurholt-Jepsen et al., 2015; Faurholt-Jepsen et al., 2020; Goulding et al., 2023)).

For depressive symptoms within bipolar disorder, no difference was found across the identical comparisons ($g =$ -0.07; 95 % CI -0.37 to 0.23, $p = 0.630$; $I^2 = 61.8$ %; 95 % CI 0.0 to 87.2; PI -1.29 to 1.15; see Appendix F for forest plot Fig. F.5).

3.4.4. Smoking and alcohol use

Smoking had ten comparisons (Asayut et al., 2022; Carrasco-Hernandez et al., 2020; Cheung et al., 2015; Chulasai et al., 2022; Durmaz et al., 2019; Krebs et al., 2019; Krishnan et al., 2019; O'Connor et al., 2020; Schlam and Baker, 2020; Schnall et al., 2022) with a mean effect size of 0.43 (95 % CI 0.29 to 0.58; $p < 0.001$; see Fig. 3b for forest plot). For alcohol use, there were seven comparisons (Aharonovich et al., 2017; Farren et al., 2022; Gustafson et al., 2014; Hammond et al., 2021; Liu et al., 2023; McKay et al., 2022; Mellentin et al., 2019) included with a mean effect size of 0.23 (95 % CI 0.08 to 0.39; $p = 0.002$; see Fig. 3c for forest plot). Both analyses showed a low heterogeneity ($I^2 = 0.0$ %). The effects remained when studies with a high risk of bias were excluded for smoking ($g = 0.52$; 95 % CI, 0.34 to 0.7; $k = 6$ (Cheung et al., 2015; Chulasai et al., 2022; Durmaz et al., 2019; Krishnan et al., 2019; O'Connor et al., 2020; Schnall et al., 2022)) and for alcohol use ($g =$ 0.21; 95 % CI 0.05-0.37; $k = 5$ (Farren et al., 2022; Gustafson et al., 2014; Liu et al., 2023; McKay et al., 2022; Mellentin et al., 2019)). Subgroup analyses revealed no differences ($p = 0.686$) in smoking cessation studies that featured face-to-face interactions as their primary intervention setting ($g = 0.43$; 95 % CI, 0.13 to 0.74; $k = 3$ (Durmaz et al., 2019; Krishnan et al., 2019; O'Connor et al., 2020)) when compared to studies that combined face-to-face interactions with telephone support and nicotine patches ($g = 0.45$; 95 % CI, 0.07 to 0.82; $k =$ 3 (Chulasai et al., 2022; Schlam and Baker, 2020; Schnall et al., 2022)). For alcohol use, studies with face-to-face settings as primary intervention showed a slightly larger effect ($g = 0.36$; 95 % CI 0.06 to 0.66; $k = 3$ (Aharonovich et al., 2017; Hammond et al., 2021; McKay et al., 2022)).

3.4.5. Eating disorders

For eating disorders, no difference was found ($g = -0.02$; 95 % CI -0.44 to 0.4, $p = 0.934$; $I^2 = 54.8$ %; 95 % CI 0.0 to 87.1; PI -4.46 to 4.42; $k = 3$ (Hildebrandt et al., 2017; Juarascio et al., 2023; Keeler et al., 2022); see Appendix F for forest plot Fig. F.6).

3.4.6. Single comparisons of somatic symptom disorder, serious mental illness (schizophrenia/schizoaffective or bipolar disorder within one sample), psychotic disorders, drug use, posttraumatic stress disorder, suicidal and non-suicidal self-injury behaviours, and suicide risk

For somatic symptom disorder (Kristjansdottir et al., 2013), a single comparison suggests an effect of adjunctive app-based on symptom

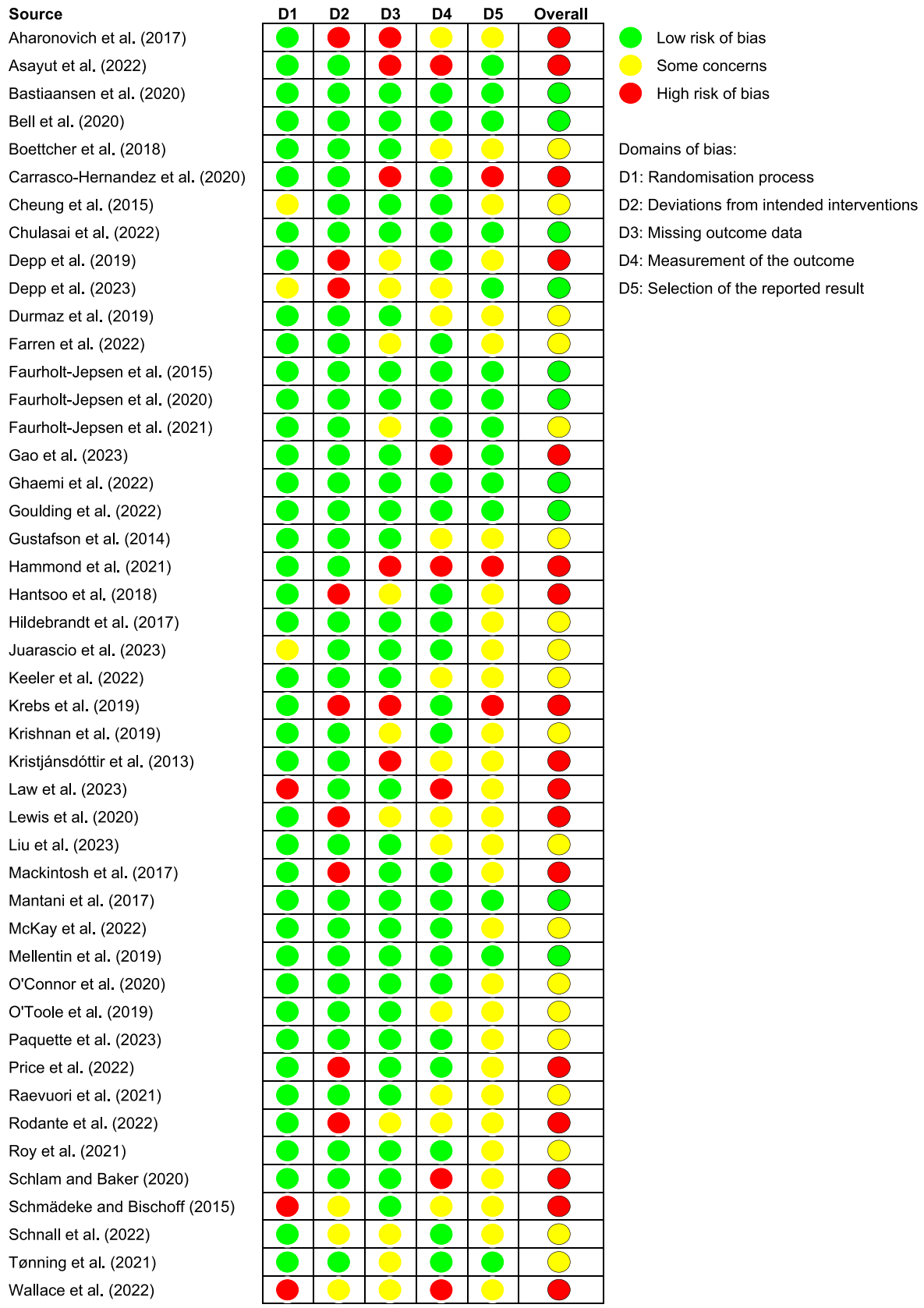

Fig. 2. Risk of bias assessment.

Table 2
Postintervention between-group effect sizes.

Outcomes		Number of comparisons, *k*	n		Meta-analysis		Heterogeneity	
			IG	CG	Hedges' *g* (95 % CI)	*p*-value	I^2 (95 % CI)	Prediction interval
Depression								
	All comparisons	7	345	289	0.17 (0.02 to 0.33)	0.030	0.0 % (0.0 to 70.8)	-0.03 to 0.38
	Only some concerns and low risk of bias	6	295	205	0.19 (0.02 to 0.36)	0.032	2.6 % (0.0 to 76.3)	-0.08 to 0.46
	Only low risk of bias	3	173	83	0.32 (0.09 to 0.56)	0.008	0.0 % (0.0 to 89.6)	-1.20 to 1.85
	Only F2F and PM as setting	4	187	136	0.16 (-0.06 to 0.38)	0.161	0.0 % (0.0 to 84.7)	-0.33 to 0.65
	As primary and secondary outcome	22	961	832	0.03 (-0.07 to 0.13)	0.578	13.9 % (0.0 to 48)	−0.19 to 0.25
Anxiety								
	All comparisons	3	130	132	0.80 (0.06 to 1.54)	0.033	87.4 % (64.3 to 95.5)	-8.31 to 9.92
	As primary and secondary outcome	10	306	301	0.15 (-0.2 to 0.5)	0.412	77.9 % (59.6 to 87.9)	-1.06 to 1.35
Bipolar disorder: manic symptoms								
	All comparisons	4	289	210	0.2 (0.02 to 0.38)	0.031	0.0 % (0.0 to 84.7)	-0.2 to 0.59
	Only low risk of bias	3	242	159	0.18 (-0.06 to 0.42)	0.144	26.1 % (0.0 to 92.3)	-1.92 to 2.28
Bipolar disorder: depressive symptoms								
	All comparisons	4	289	210	−0.07 (-0.37 to 0.23)	0.630	61.8 % (0.0 to 87.2)	-1.29 to 1.15
	Only low risk of bias	3	242	159	-0.13 (-0.54 to 0.29)	0.542	73.8 % (12.5 to 92.2)	-4.93 to 4.67
Smoking cessation								
	All comparisons	10	599	618	0.43 (0.29 to 0.58)	< 0.001	0.0 % (0.0 to 62.4)	0.26 to 0.61
	Only some concerns and low risk of bias	6	372	395	0.52 (0.34 to 0.7)	< 0.001	0.0 % (0.0 to 74.6)	0.27 to 0.78
	Only F2F as setting	3	133	188	0.43 (0.13 to 0.74)	0.006	0.0 % (0.0 to 89.6)	-1.56 to 2.43
	Only F2F, telephone, PM as setting	3	173	167	0.45 (0.07 to 0.82)	0.019	26 % (0.0 to 92.3 %)	-2.97 to 3.86
Alcohol use								
	All comparisons	7	350	356	0.23 (0.08 to 0.39)	0.002	0.0 % (0.0 to 70.8)	0.04 to 0.43
	Only some concerns and low risk of bias	5	300	303	0.21 (0.05 to 0.37)	0.016	0.0 % (0.0 to 79.2)	-0.05 to 0.47
	Only F2F as setting	3	98	100	0.36 (0.06 to 0.66)	0.018	0.0 % (0.0 to 89.6)	-1.59 to 2.31
Eating disorders								
	All comparisons	3	97	93	-0.02 (-0.44 to 0.4)	0.994	54.8 % (0.0 to 87.1)	-4.46 to 4.42

IG: intervention group; CG: control group; F2F: face-to-face; PM: psychiatric medication.

reduction ($g = 0.4$; 95 % CI 0.06 to 0.74, $p = 0.022$). For SMI (schizophrenia/schizoaffective or bipolar disorder within one sample) (Depp et al., 2019), no differences were found for two comparisons ($g = 0.11$; 95 % CI -0.28 to 0.5, $p = 0.570$ and $g = 0.24$; 95 % CI -0.16 to 0.64, $p = 0.240$). For symptoms of psychotic disorders two studies (Bell et al., 2020; Lewis et al., 2020) found no differences between the conditions ($g = 0.55$; 95 % CI -0.12 to 1.21, $p = 0.11$ and $g = 0.12$; 95 % CI -0.33 to 0.57, $p = 0.599$). For drug use, one study (Aharonovich et al., 2017) found a positive effect ($g = 0.63$; 95 % CI 0.02 to 1.24, $p = 0.042$), while another study (Paquette et al., 2023) found a negative effect ($g = -1.5$; 95 % CI -1.92 to -1.08, $p < 0.001$). Out of two studies targeting emotion regulation in PTSD, one found no effects (Mackintosh et al., 2017) across multiple primary outcomes ($g = 0.03$ to 0.2; 95 % CI -0.48 to 0.71, $p = 0.446$ to 0.904), whereas the other study (Wallace et al., 2022) found a significant effect ($g = 1.45$; 95 % CI 0.66 to 2.24, $p < 0.001$). For suicidal and non-suicidal self-injury behaviours both studies (Law et al., 2023; Rodante et al., 2022), each with multiple primary outcomes, found no differences ($g = -0.38$ to 0.80; 95 % CI -1.27 to 1.72; $p = 0.087$ to 0.756) and ($g = -0.82$ to -0.19 (95 % CI -2.02 to 0.95; $p = 0.61$ to 0.749) (results for multiple outcomes Supplementary Appendix F Table F.1). For suicide risk one study (Depp et al., 2023) found no difference ($g = 0$; 95 % CI -0.51 to 0.51, $p = 1$), while another study (O'Toole et al., 2019) found a negative effect ($g = -0.41$; 95 % CI -0.75 to -0.06, $p = 0.022$).

3.5. Publication bias

Visual inspection of the funnel plots and non-significant Egger's tests indicated no publication bias (funnel plots and Egger's test results Supplementary Appendix G).

4. Discussion

In this meta-analysis, we identified 46 RCTs with 48 comparisons that evaluated the potential incremental effect of an app-based intervention adjunct to a primary intervention compared to the primary intervention-only arm for a range of mental disorders. The large majority of RCTs were published in the past five years (76 %: 2019 to 2023), reflecting the growing research interest and the emerging

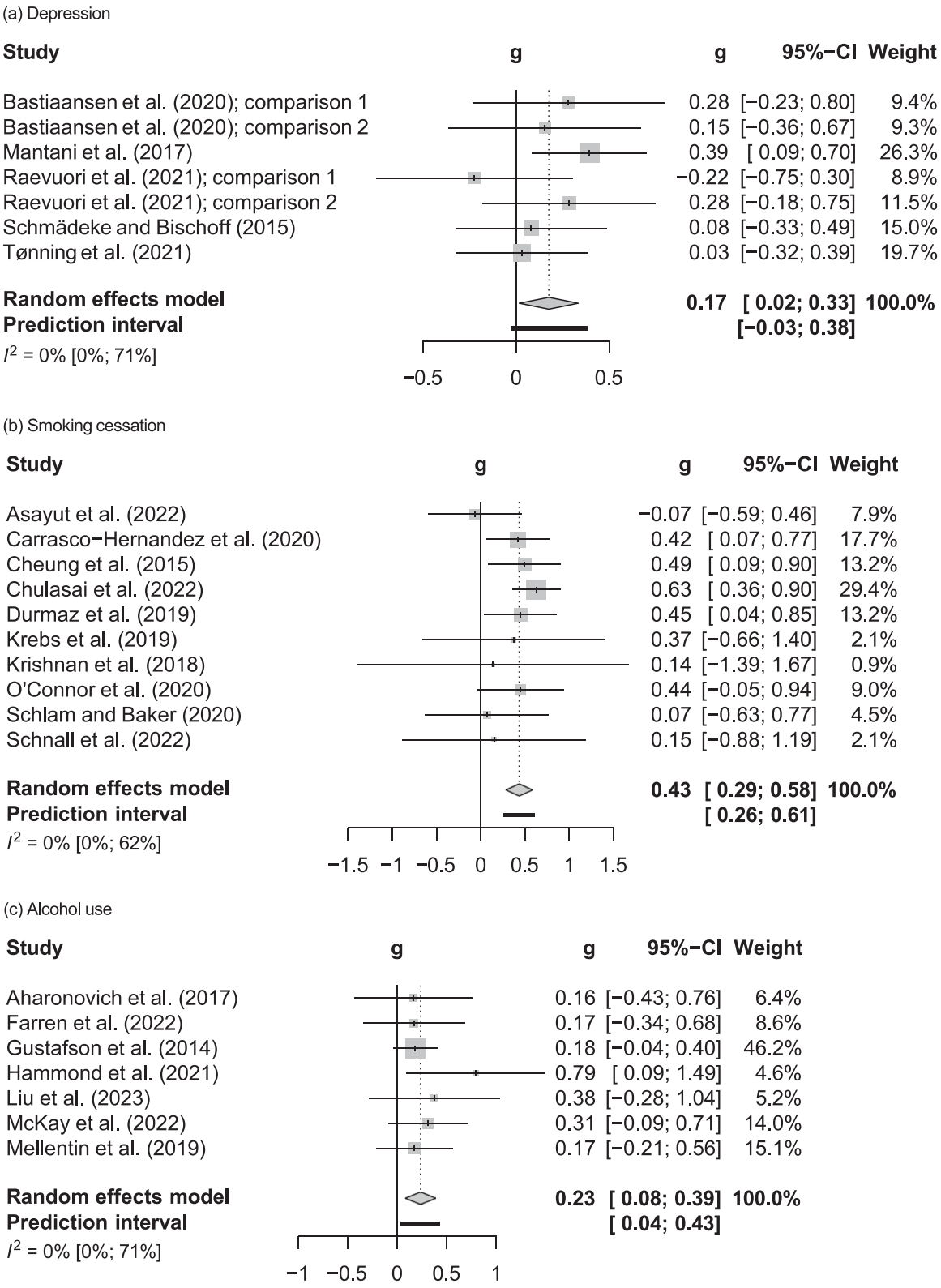

Fig. 3. Forest plots depicting additional effects of adjunctive app-based interventions for symptoms of (a) depression, (b) smoking cessation, and (c) alcohol use.

importance of this specific field. We found significant positive pooled incremental effects of adjunctive app-based interventions directly targeting symptoms of depression ($g = 0.17$), anxiety ($g = 0.8$), mania ($g = 0.2$), smoking cessation ($g = 0.35$), and alcohol use ($g = 0.23$) and no significant effects on depressive symptoms within bipolar disorder ($g = -0.07$) and eating disorders ($g = -0.02$). For depression ($g = 0.32$), the results remained for studies with low risk of bias. Single studies targeting somatic symptom disorder, SMI (schizophrenia/schizoaffective or bipolar disorder within one sample), psychotic disorders, drug use, PTSD, suicidal and non-suicidal self-injury behaviours, and suicide risk have found mixed results.

The effect size for depression as a primary outcome is consistent with

previous research (Linardon et al., 2019). Still, this meta-analysis identified more comparisons ($k = 7$ compared to $k = 4$), and the pooled effect size reached significance. The observed effects on manic symptoms stand in contrast to a meta-analysis encompassing app-based interventions for bipolar disorder in general, not limited to adjunct designs, where no significant effect was found (Anmella et al., 2022). However, this contrast is not solely due to the broader scope of the other meta-analysis; three out of four studies were identical. The distinctions arise from our inclusion of a more recent study by Goulding and colleagues (Goulding et al., 2023), which contributed to a substantial single effect size that significantly impacted the overall effect. It is noteworthy that the other meta-analysis pooled pre-post change scores. Conversely, the results for depressive symptoms within bipolar disorders are consistently non-significant in both meta-analyses. Additionally, limitations in interpreting the results are acknowledged, considering the inherent nature of this chronic disease, which is characterised by fluctuations between depressive and manic episodes. Consequently, a point assessment at postintervention might be overly short-sighted. This emphasises the need for greater standardisation in the research of efficacy and effectiveness of app-based interventions for bipolar disorder to mitigate heterogeneity, as advocated by Anmella and colleagues in their meta-analysis (Anmella et al., 2022).

The pooled effect sizes for anxiety, smoking cessation, alcohol use, and eating disorders are, to our knowledge, the first systematic evaluation in a meta-analysis. The small effects found for depression, smoking cessation, and alcohol use indicate that an additional benefit is possible. However, it is worth noting that the found additive effect may be small due to ceiling effects. For depression, further research could focus on identifying subgroups of patients who may benefit more from adjunct app-based interventions, for example, patients with mild to moderate depression. The treatment of substance use disorders benefits from more intense treatment, which can be challenging to deliver due to limited resources and patient engagement (Bachrach and Chung, 2021). Therefore, app-based interventions could be a valuable and resource-saving tool to extend the impact of standard care. Despite the high prevalence of anxiety disorders in the population (Stein et al., 2017), only three studies were identified, mirroring the low number previously observed for standalone smartphone interventions (Weisel et al., 2019). This finding is surprising, considering that an adjunctive app-based intervention could serve as a valuable tool for facilitating exposure exercises or behavioural experiments. Although the observed effect was substantial, its interpretation should be approached with caution due to the small number of comparisons, the overall limited quality of the studies and the high heterogeneity. The results for eating disorders mirror the complexity of treatment as found previously for standalone app-based interventions (Linardon et al., 2020).

A substantial majority of the identified app-based interventions, 32 (73 %), employed either passive or active monitoring of symptoms or behaviours, underscoring the potential of digital phenotyping and mobile sensing (Montag and Baumeister, 2023). However, in less than half of these interventions, 13 (30 %), the tracked data was transmitted to a therapist. Yet, this discrepancy highlights a pivotal aspect of adjunctive app-based interventions as a potential crucial bridge between patient and therapist. In an optimal scenario, this feature supports both parties. For the patient, heightened motivation to track progress may arise, especially with the awareness that the therapist is informed. Simultaneously, the therapist, equipped with comprehensive and timely information, can seamlessly adjust the course of treatment, perceiving their role as indispensable without harbouring concerns about being supplanted by digital technologies.

To enhance mental health care, future research should dedicate attention to unravelling and optimising this key element. Understanding the dynamics of data transmission between patients and therapists within app-based interventions can be essential for enhancing the overall effectiveness and acceptance of these interventions within the landscape of mental health treatment.

5. Limitations

Our study has several important limitations. First, 36 (78 %) of the identified studies had a moderate or high risk of bias, reflecting the need for future, more standardised research on this topic. Second, sample sizes varied between the studies, and most studies were underpowered, emphasising the need for larger studies based on a priori power calculations (Harrer et al., 2023). Third, the inter-rater reliability of agreement regarding inclusion during the full-text screening stage was relatively low, primarily due to the inclusion criteria for the intervention and the control group having the same primary intervention. Many studies did not initially provide sufficient information, necessitating discussion between the raters. Fourth, as is often the case in mental health research, heterogeneity is high. We identified different settings, theoretical frameworks, and contents of the primary and app-based interventions. However, the number of identical settings and content was too small to test for differences between subgroups, such as face-to-face with or without psychiatric medication. Future research should, therefore, focus on potential moderators of intervention effects. Fifth, in this meta-analysis, we focused on postintervention comparisons. Yet, it would be beneficial to investigate whether the observed effects persist or change in follow-up assessments. Therefore, future research should explore long-term effects.

6. Conclusion

In summary, while the concepts and potential targets of adjunctive app-based interventions have been thoroughly discussed in previous reviews, comments, perspectives, and statements, the research field is still in its early stages. Consequently, the results should be interpreted with caution due to the small number of comparisons and studies with a low risk of bias. Cautiously, we can conclude that adjunctive app-based interventions for mental disorders can have a significant additional effect in reducing symptoms of depression, anxiety, and mania, as well as aiding smoking cessation and addressing alcohol use disorder. Given these effects and more robust results for smoking and alcohol use, we recommend that practitioners explore available adjunct app-based interventions in their region and discuss potential interventions with their patients. Nevertheless, future research should involve larger, standardised studies, with a specific focus on optimising data transmission between patients and therapists through active or passive monitoring of symptoms or behaviours. This research should also explore determining optimal timing, dosage, and content, aiming to integrate these interventions effectively with established approaches for maximum benefit.

Declaration of competing interest

M.H. is an employee of the Institute for Health Trainings Online (GET.ON/HelloBetter), which aims to implement scientific findings related to digital health interventions into routine care. H.B. reports having received consultancy fees, fees for lectures or workshops from chambers of psychotherapists and training institutes for psychotherapists, and license fees for an Internet intervention. D.D.E. has served as a consultant to/on the scientific advisory boards of Sanofi, Novartis, Minddistrict, Lantern, Schoen Kliniken, Ideamed, German health insurance companies (BARMER, Techniker Krankenkasse), and a number of federal chambers for psychotherapy. D.D.E. is stakeholder of the GET.ON Institute/HelloBetter, which aims to implement scientific findings related to digital health interventions into routine care. M.B. is stakeholder of the mentalis GmbH, which aims to implement scientific findings related to digital health interventions into routine care. L.M.F., K.K.W., J.K.K., and P.C. declare no competing interests.

Data availability

The datasets collected and used in this meta-analysis are available from the corresponding author upon reasonable request.

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CRediT authorship contribution statement

"D.D.E., L.M.F., and K.K.W. conceived and designed the study, including the literature search strategy. K.K.W., L.M.F., and research assistants independently searched, screened, selected the articles, and extracted the data. J.K.K. and L.M.F. independently conducted the risk of bias assessment." L.M.F. and K.K.W. had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. L.M.F. wrote the first draft of the manuscript under the supervision of M.B. All authors contributed to interpreting the findings and revising the manuscript. All authors reviewed and approved the final manuscript.

Appendices. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.invent.2023.100703.

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