Exploring digital health tools for depression management in primary health care: systematic review and meta-analysis

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Abstract

Background: As information and communication technologies are increasingly integrated to enhance care quality, digitalization is transforming health systems. Digital health tools offer promising solutions within mental health, particularly in the treatment of depression, which currently affects 5% of the global population and has been predicted to be the leading disease burden by 2030. Primary care, often a patient's first contact with healthcare, plays a critical role in the treatment of depression, especially with the increased demand for mental health care since COVID-19. Digital tools present significant potential to improve care accessibility and efficacy in primary care settings.

Objective: The aim of this study is to assess the efficacy of digital health tools for the management of depression within primary care.

Methods: A systematic review and meta-analysis of the literature was carried out following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Studies that recruited adult patients with depressive symptoms or a diagnosis of depressive disorder, treated with a digital intervention, and evaluated the effectiveness of a digital health tool were eligible. The primary outcome was identification of the digital health tool used for the intervention and the reduction of depressive symptoms. Only controlled trials were included in the review. The risk of bias in the original randomized controlled trials (RCTs) was assessed with version 2 of the Cochrane risk-of-bias tool for randomized trials, while non-RCTs were evaluated using the Joanna Briggs Institute (JBI) critical appraisal checklist for quasi-experimental studies.

Results: A total of 29 controlled trials met the inclusion criteria. The digital health tools identified were web-based platforms, mobile apps, phone calls, text messages, and decision algorithms. A random effects meta-analysis was used to assess the efficacy of interventions in reducing depressive symptoms. All studies were rated as having some concerns regarding the risk of bias, or even a high risk of bias, especially due to the inability to blind patients, participants, and assessors. The most common digital intervention was cognitive-behavioral therapy. The meta-analysis revealed that digital health tools had a significant effect on depressive symptoms compared with control groups (g = -0.22, 95% CI: -0.37; -0.06, I2 = 79.64%). At 6 to 12-month follow-up, the random effects meta-analysis showed that digital health tools had a significant effect on depressive symptoms compared with

control groups (g = -0.19, 95%CI: -0.29; -0.09, I2 = 53.42%). Post-intervention subgroup analyses based on the severity of depressive symptoms at baseline (p = 0.878) and type of intervention were non-significant (p = 0.110). A significant inverse relationship was observed between gender and effect size (B = -0.02, p = 0.022). Post-intervention meta-regression using mean age as a moderator demonstrated a trend toward significance (B = -0.02, p = 0.064).

Conclusions: Digital health tools, the majority of which are based on cognitive behavioral therapy, are effective in reducing the symptoms of depression, especially in combination. However, symptom severity does not predict suitability for digital treatment, and our findings highlight the need for gender-sensitive studies and strategies that will engage older adults. As digital interventions have yet to be included in clinical practice guidelines and treatment strategies, studies such as this are essential to support their integration into real-world practice.

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Digital health tools, the majority of which are based on cognitive behavioral therapy, are effective in reducing the symptoms of depression, especially in combination. However, symptom severity does not predict suitability for digital treatment, and our findings highlight the need for gender-sensitive studies and strategies that will engage older adults. As digital interventions have yet to be included in clinical practice guidelines and treatment strategies, studies such as this are essential to support their integration into real-world practice.

Keywords

Digital health; eHealth; mHealth; telemedicine; depression; primary health care

Background

Information and communication technologies (ICT) are now part of daily life for most of the global population and have been introduced into many health systems over the past few decades [1]. In this context, digital health is defined as the field of knowledge and practice relating to the integration of technology into health systems with the aim of improving health [2]. To ensure equitable and universal access to quality health services, the World Health Organization (WHO) has developed a global strategy to integrate digital health into the health systems of all member states, including those with limited access to technology [3].

A thorough analysis of care processes for different health conditions is imperative for determining the potential value of incorporating technology, for developing specific implementation strategies, and ensuring adoption [4]. Depression currently affects 5% of the global population and, in 2004, WHO predicted that depression will be the largest global disease burden by 2030. Primary care, the first and easiest point of contact with a healthcare system for many people, provides the opportunity for a holistic approach, an essential factor given the significant co-occurrence of non-communicable diseases and mental disorders [5–7]. The aftermath of the COVID-19 pandemic has increased demand for mental health consultations, especially among younger populations [8,9]. Various initiatives are being developed around the world to improve the management of depression in primary care using eHealth. One strategy is telemedicine, for which the COVID-19 pandemic has been a clear adoption catalyst. This has proved useful among patients suffering from mild mental health problems and those who prefer remote consultations and counseling to in-person visits [10].

Another potential strategy for depression management is mobile apps (mHealth). Although there are many available, a literature review of mobile health applications in mood disorders such as depression, bipolar disorder, and dysthymia has highlighted the need for validation and systematic clinical trials. Among 30 commercially available apps, only 26.7% were supported by strong scientific evidence [11]. A meta-analysis conducted on the efficacy of mobile applications in the management of depression compared with waiting lists, minimal interventions, and standard clinical practice showed moderately positive effects of mobile applications compared to minimal interventions. However, the effect was greater in trials that compared apps with minimal interventions or waiting lists than in trials that compared apps with standard clinical practice. Interventions that combined hybrid formats, such as the use of apps alongside face-to-face consultations, were the most effective [12]. Another possible strategy is telemedicine-based collaborative care. Several studies have shown that this model of care, delivered from primary care by multidisciplinary teams of professionals, improves outcomes for depression [13-16]. A study of various healthcare centers in remote regions of the United States demonstrated greater efficacy when collaborative care was based on telemedicine. Moreover, when telemedicine is used in remote areas telemedicine collaborative care appears to be more effective in both treatment response and remission rate [17].

Considering the above, the aim of this study is to conduct a systematic review to assess the efficacy of digital health tools for depression management in primary care.

Methods

A systematic review and meta-analysis of the literature was performed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [18]. The protocol for this systematic review and meta-analysis was registered on PROSPERO on December 25, 2023 (CRD42023489354).

Search strategy

A scoping search was performed by an information specialist (EHR) to identify relevant search terms resulted in the following: “digital health,” “eHealth,” “depression”, and “primary health care”. These terms were applied individually and combined according to controlled vocabulary to retrieve studies published from 2014 to February 2024 in 5 electronic databases: CENTRAL (Wiley), MEDLINE (Ovid), Embase (Elsevier), APA PsycINFO (EBSCOhost), and CINAHL (EBSCOhost). To retrieve published clinical trials, these terms were applied in all databases except CENTRAL: the search filter designed for this purpose is published in the CATDH search filters database [https://searchfilters.cadth.ca]. The literature search strategies executed in each database are detailed in Supplementary File 1. In addition, the reference lists of all eligible studies were screened to identify additional studies meeting the inclusion criteria.

Inclusion and exclusion criteria

Studies were included if they recruited adult patients with elevated depressive symptoms (i.e., scoring above the cut-off criteria on a validated depression screening instrument) or diagnosed with depressive disorder with or without other affective symptoms in primary care (diagnosed by a clinician or using any recognized diagnostic criteria); and patients or professionals used any type of digital health tool; and assessed its efficacy in primary care depression management. Any comparator other than eHealth interventions was considered, including passive (e.g., no intervention, usual care, or waiting list) or active (e.g., antidepressants or face-to-face psychotherapy) groups. Randomized controlled trials (RCTs) and nonrandomized studies with at least 10 participants were included, as were studies published in any language, conducted in any country, and in any context of primary care setting.

Studies were excluded if they recruited children or adolescents aged ≤18 years, or the aim of the intervention was a different condition but included the measurement of depressive symptoms. Uncontrolled studies, observational studies, conference abstracts, letters, commentaries, essays, book chapters, qualitative studies, study protocols, and reviews were also excluded.

The primary outcome was to identify the digital health tools used in primary care depression management. The secondary outcome was evaluation of the efficacy of digital interventions, as measured by improvement in depressive symptoms and other patient-reported measures.

Risk-of-bias assessment

The risk of bias in the original RCTs was assessed using version 2 of the Cochrane risk-of-bias tool for randomized trials [19]. The risk of bias in non-RCTs was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for quasi-experimental studies [20]. Quality assessment was performed by 2 independent reviewers (AFC, AD), and any disagreements were resolved by a third reviewer (SM, DC).

Study selection and data extraction

All retrieved studies were imported into Covidence ®, a web-based software program for systematic reviews, and duplicates were automatically removed. Four reviewers (AFC, ADD, SM, DC) independently reviewed all titles and abstracts to preselect those studies meeting the inclusion criteria. The full texts of potential studies were screened for eligibility by the same 4 reviewers. Any disagreement was resolved by two more reviewers (JVA, CC). Data extraction was first piloted by four reviewers (AFC, ADD, SM, DC) in four studies to clarify any discrepancies. Data from the remaining studies were extracted by two reviewers and verified by two other reviewers. The consensus variables were: first author, year of publication, country, setting, study design, number of participants, female ratio, baseline depression tool, intervention and control details, outcome measures, comorbid condition, target of the intervention (professionals or patients), intervention

length [14], eHealth intervention, eHealth tool, co-intervention, type of communication, type of professionals, hybrid intervention, narrative description of the tool and the intervention. To gather information about intervention details and elements, we primarily relied on the intervention descriptions provided in the original studies, but also referred to other publications relating to the same study that provided more comprehensive descriptions.

Data synthesis and analysis

A narrative synthesis was conducted for the studies that could not be included in the meta-analysis due to a lack of comparable data. Pairwise meta-analyses were conducted using STATA (v17; StataCorp, College Station, TX, USA) on studies with sufficiently comparable data. To minimize methodological heterogeneity, meta-analyses of RCTs were performed to assess the efficacy of digital tools with a similar target population (i.e., web-based platforms or mobile apps for patients) and compared to similar comparators (i.e., passive controls such as treatment-as-usual or waiting lists).

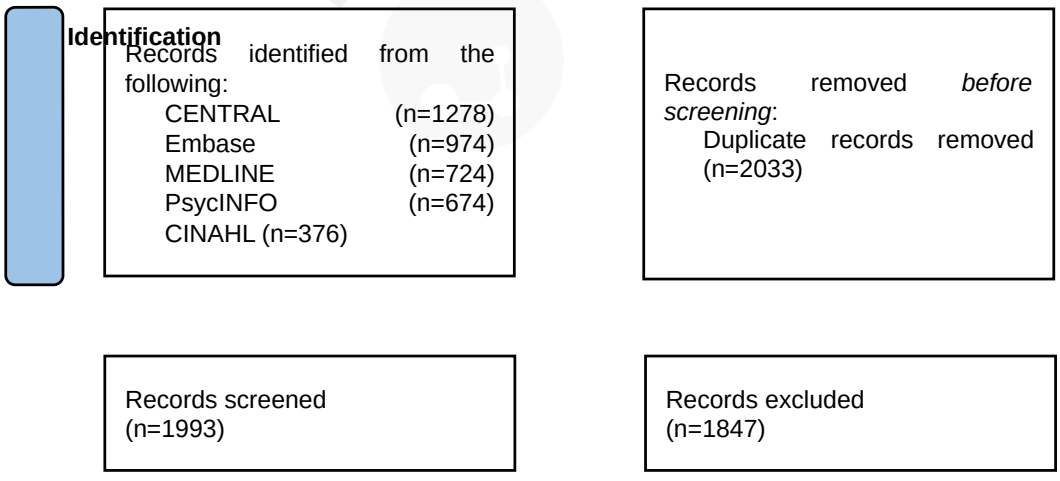
For the meta-analyses, a random-effects model using the Sidik-Jonkman method as the tau estimator was applied. As different depression measurements were used across studies, the effect sizes were represented as standardized mean differences (Hedges' g) with 95% confidence intervals. Statistical heterogeneity among studies included in the meta-analyses was assessed using the Higgins I^2 statistic. Sources of heterogeneity were explored using subgroup analyses for categorical variables and meta-regression for continuous variables. The following post-hoc subgroup analyses were performed: baseline depression level (mild vs moderate vs moderately severe vs severe) and intervention type (web-based vs mobile app). Mean age and ratio of female participants were used as moderators of efficacy in the meta-regression. Publication bias was assessed using the Egger test, and the trim-and-fill method was applied to correct for potential funnel plot asymmetry.

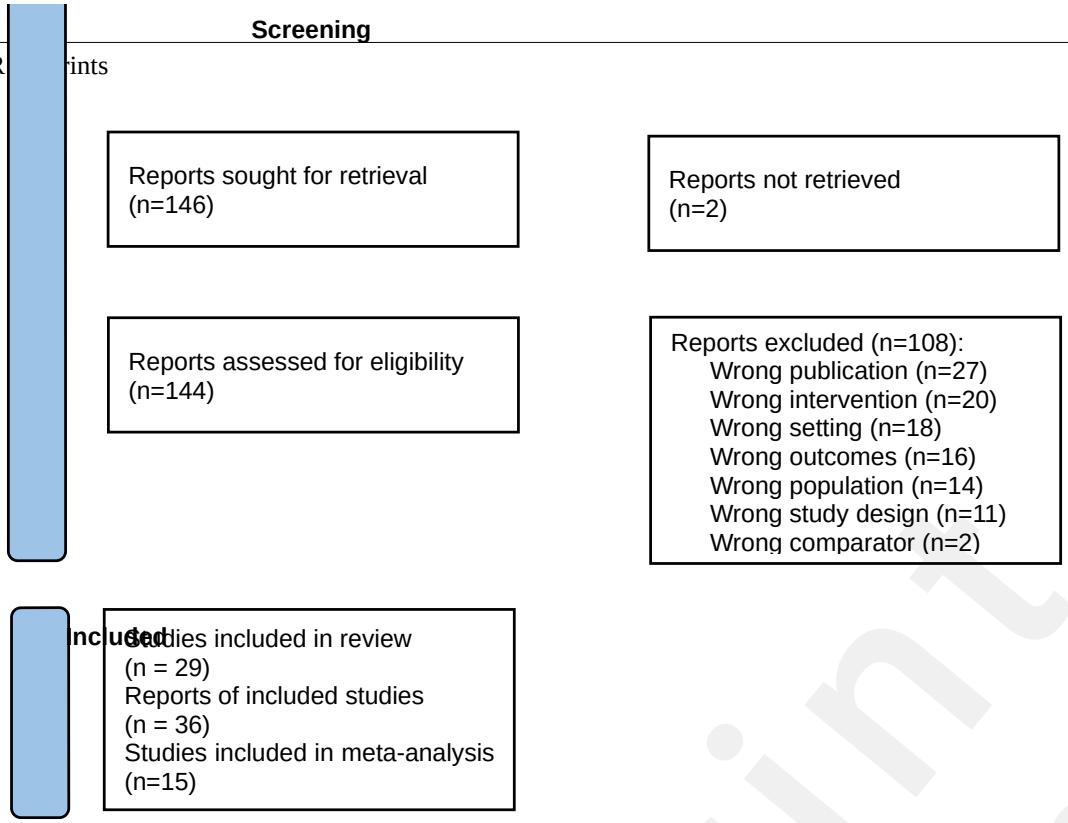
Results

Overview

The initial search of electronic databases yielded 4026 references. After removing duplicates (2033), 1993 studies were screened by title and abstract and 146 full-text studies were assessed for eligibility. Finally, 29 studies were included in the review, and 7 studies were identified as secondary references from these studies (Supplementary File 2). Reasons for excluding studies and a flowchart of the selection process are shown in Figure 1.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the selection process.





Characteristics of the included studies

Table 1 shows the main characteristics of the included studies. The studies comprised a total sample of 10200 participants, with a mean age of 42.10 years. Of the participants, 73.96% identified as female, and in most studies, participants had moderate depressive symptoms at baseline (15/29, 51,72%).

In terms of geographic distribution, 44.83% (13/29) of studies were conducted in Europe [21-33]; 41.38% (12/29) in North America [34-45]; 6.90% (2/29) in South America [46,47]; 3.45% (1/29) in Africa [48]; and 3.45% (1/29) in Australia [49]. Most studies (93.10% 27/29) were RCTs, while two studies were non-randomized controlled trials [26,47].

Digital health tools used in primary care

Table 1 also provides detailed information about the interventions and digital health tools used in primary care for depression management. Most interventions were targeted at patients (24/29, 82.76%), with intervention durations ranging from 4 to 52 weeks.

The digital health tools identified were web-based platforms, mobile apps, phone calls, text messages and decision algorithms. A web-based intervention was conducted in 34.48% (10/29) of studies, with an average duration of 9.17 weeks [23,24,26,28,31,36,42,43,47,49]. A total of 34.48% (10/29) of studies used hybrid tools (i.e., web-based intervention supported by phone calls, app intervention supported by phone calls, web-based intervention supported by messages, or decision algorithm with text messages), with an average intervention period of 12.89 weeks [22,25,27,29,30,33,37,44,46,48]. Mobile app interventions were included in 13.79% (4/29) of the studies, with an average intervention period of 10 weeks [35,38,41,45]. Phone calls were used in 13.79% (4/29) of studies, with an average intervention duration of 42 weeks [21,34,39,40]. In 1 out of 29 studies (3.45%), the intervention was designed specifically for professionals and involved the use of a decision algorithm

for treatment [32].

Internet-based cognitive behavioral therapy was the basis of the intervention in 58.62% (17/29) of the studies. In terms of comparators, 65.52% (19/29) of the studies used Treatment-As-Usual [TAU]; 17.24% (5/29) used improved usual care; 10.34% (3/29) used a waiting list; 3.45% (1/29) used collaborative stepped care; and 3.45% (1/29) used both TAU and active controls.

Most studies in which the control group was based on improved usual care included specific training in depression management for primary care professionals prior to the intervention.

More information about the types of therapy used and the efficacy of these interventions can be found in Supplementary File 3.

Table 1. Characteristics of the included studies.

Study, year	Country	Design	Sample size [intervention/control]	Age [years], mean	Gender [women], %	Depression symptomatology at baseline	Target	Intervention and eHealth tool	Type of professionals	Control	Lenght [weeks]
Adewuya et al [48], 2019	Nigeria	RCT[a]	895 (439/456)	34,98	55,4	Moderate-severe (PHQ-9)	Patients and professionals	Text messages and phone-calls	Community health workers, psychologists	Collaborative stepped care	14
AfWinklerfeltHammarberg et al [21], 2022	Sweden	RCT[a]	376 (192/184)	41,2	71,3	Moderate (MADRS-S)	Patients	Phone calls	Nurses	Usual care	12
Aikens et al 2022 [34]	USA	RCT[a]	204 (108/86)	48,6	80,8	Moderate-severe (PHQ-9)	Patients	Phone calls (automated interactive voice response)	Primary care team	Improved usual care	52
Balestrieria et al [22], 2020	Italy	RCT[a]	98 (66/32)	NR[e]	NR[e]	Moderate-severe (PHQ-9)	Professionals / patients	Decision support system (CompTMAP) / text messages	General practitioners	Usual care	NR[e]
Collins et al [26], 2018	Ireland	CT [b]	79 (60/19)	35,86	67,1	Moderate (PHQ-9)	Patients	Web-based (MindWise 2.0)	Self-help	Waiting list	NR[e]

Dahne et al [35], 2019	USA	RCT[a]	52 (24/19/9)[c]	43,79	84,6	Moderate-severe (BDI-II)	Patients	Mobile app (Moddivate / Moodkit)[f]	Self-help	Usual care	8
Eriksson et al [27], 2017	Sweden	RCT[a]	90 (52/38)	NR[e]	NR[e]	Moderate (BDI-II)	Patients	Web-based (ICBT - Depressionshjälpen®) / email or phone calls	Psychologists	Usual care	12
Fletcher et al [49], 2021	Australia	RCT[a]	1868 (933/935)	35,80	66,33	Mild/ moderate/ severe (PHQ-9)	Patients	Web-based (Target-D)	Self-help and nurses	Usual care	12
Gilbody et al [28], 2015	United Kingdom	RCT[a]	691 (210/242/239)	39,86	67	Moderate-severe (PHQ-9)	Patients	Web-based (Beating the Blues / MoodGYM)[d]	Self-help	Usual care	16
Gili et al [29], 2020	Spain	RCT[a]	221 (54/54/56/57)[d]	NR[e]	NR[e]	Moderate (PHQ-9)	Patients	Web-based / messages	Psychologists	Improved usual care	4-8
Graham et al [38], 2020	USA	RCT[a]	146 (74/72)	42,3	81,5	Moderate (PHQ-9)	Patients	Mobile App (Intellicare)	Clinical psychologists and coaches	Waiting list	8
Hallgren et al [30], 2016	Sweden	RCT[a]	945 (317/312/316)	43	73	Moderate (MADRS)	Patients	Web-based and messages	Psychologists	Usual care / exercise[f]	12
Hange et al [31], 2017	Sweden	RCT[a]	77 (46/31)	36,20	68	Mild/ Moderate[g] (MADRS)	Patients	Web-based (Depressionshjalpen)	Self-help	Usual care	12

Harrison et al [32], 2022	United Kingdom	RCT[a]	20 (10/10)	51,4	78	Moderate (MADRS)	Professionals	Decision algorithm (Antidepressor Advisor [ADeSS])	General practitioners	Usual care	15-18
Ishrat Husain et al [39], 2023	Canada	RCT[a]	502 (256/246)	41,3	66,5	Moderate (PHQ-9)	Patients	Phone calls	General practitioners, Mental health technician, psychiatrists	Improved usual care	52
Kim et al [40], 2023	USA	RCT[a]	144 (76/68)	38,9	60	Moderate-severe (PHQ-9)	Patients	Phone calls	Coaches, general practitioners, psychiatrists	Improved usual care	52
Kivi et al [33], 2014	Sweden	RCT[a]	92 (45/47)	36,6	66	Moderate (BDI-II)	Patients	Web-based (PRIM-NET Depressionshjälpen®) / phone calls or email	Psychologists	Usual care	12
Löbner et al [23], 2018	Germany	RCT[a]	647 (320/327)	43,30	68,40	Moderate (BDI-II)	Patients	Web-based (Moodgym)	Self-help	Usual care	6
McCue et al [41], 2022	USA	RCT[a]	40 (20/20)	36,4	84	Moderate-severe / moderate[f] (PHQ-9)	Patients	Mobile App [Pathway]	General practitioners	Usual care	18
Montero-Marin et al	Spain	RCT[a]	296 (98/96/1	42,95	75,40	Moderate (BDI-II)	Patients	Web-based (Smiling is	General practitioners,	Improved usual care	12

[24], 2016			02)[c]					fun therapy guided or non-guided)	psycotherapist or self-help		
Murillo et al [42], 2020	USA	RCT[a]	29 (15/14)	40	75,86	Moderate (PHQ-9)	Patients	Web-based	NR[e]	Usual care	8
Rojas et al [46], 2018	Chile	RCT[a]	250 (111/139)	41,3	86,4	Severe (BDI)	Professionals / patients	Web-based (video-calls) / phone calls	General practitioners, psychologist, social workers, midwives, nurses with phychiatrists	Usual care	24
Rojas et al [47], 2014	Chile	CT[b]	81 (39/42)	39,6	66,2	Severe (BDI-I)	Professionals	Web-based	Health care practitioners, mental health practitioners	Usual care	12
Rollman et al [43], 2018	USA	RCT[a]	704 (302/301/101)[c]	41,3	86,4	Moderate (PHQ-9)	Patients	Web-based (Beating the Blues / online support)	College graduates with mental health research experience	Usual care	24
Salisbury et al [25], 2016	United Kingdom	RCT[a]	609 (307/302)	49,60	68,50	Moderate-severe / moderate[h] (PHQ-9)	Patients	Web-based / phone calls (Living Life to the Full Interactive	NR[e]	Usual care	12

								programme)			
Segal et al [44], 2020	USA	RCT[a]	460 (230/230)	48,3	75,6	Mild (PHQ-9)	Patients	Web-based (Mindful Mood Balance) / Phone calls	NR[e]	Usual care	12
Stiles-Shields et al [45], 2019	USA	RCT[a]	30 (10/10/10)[c]	NR[e]	NR[e]	Moderate-severe (PHQ-9)	Patients	Mobile App (Boost Me / Thought Challenger)[f]	NR[e]	Waiting list	6
Stuart et al [36], 2022	USA	RCT[a]	302 (148/154)	47,2	81,1	Moderate (PHQ-9)	Patients	Web-based (Thrive iCBT)	NR[e]	Usual care	8
Wright et al [37], 2022	USA	RCT[a]	175 (95/80)	47,00	84,50	Moderate-severe (PHQ-9)	Patients	Web-based (Doog Days Ahead)	NR[e]	Usual care	12

[a] RCT: randomized controlled trial
[b] CT: controlled trial
[c] The first 2 numbers are intervention groups, the third the control group.
[d] The first 3 numbers are intervention groups, the third the control group.
[e] NR: not reported.
[f] More than 1 different intervention or more than 1 different control.
[g] Mild for the intervention group and Moderate for the control group.
[h] Moderate-severe for the intervention group and Moderate for the control group.

Quality assessment of the included studies

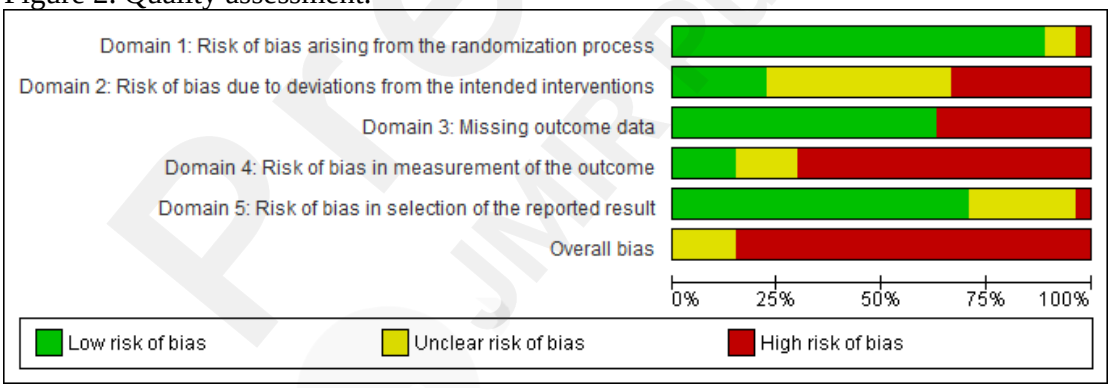
The risk of bias across RCTs was assessed using the 5 key domains of Cochrane's RoB-2 tool (Figure 2).

Most studies were judged to have a low risk of bias related to the randomization process. A large proportion of trials adequately described their randomization methods, with random sequence generation and allocation concealment clearly reported. Risk of bias due to deviations from intended interventions was widely distributed, with just over half the studies rated as having a low risk of bias. A significant number of studies were categorized as having either some concerns or a high risk of bias, mostly due to the inability to blind patients and professionals. The domain of missing outcome data posed a considerable challenge across studies. A significant number of studies were classified as having a high risk of bias, indicating substantial issues with incomplete data or inadequate reporting on how missing data was addressed. These issues included high rates of attrition, incomplete follow-up, and a lack of appropriate imputation methods. The risk of bias in the measurement of outcomes varied across studies, with many demonstrating a low risk, particularly where validated and reliable outcome measures were used. However, a notable number of studies were judged to have a high risk of bias, primarily due to potential measurement bias from lack of blinding and the use of subjective outcome measures prone to bias. Most studies were assessed as having a low risk of bias in the domain of selection of the reported result, with the majority providing pre-specified analysis plans and reporting all expected outcomes.

Overall, all studies were rated as having some concerns regarding the risk of bias, or even a high risk of bias, especially due to the inability to blind patients, participants, and assessors.

More information on the quality assessment for each study is available in the Supplementary file 4.

Figure 2. Quality assessment.



The two non-randomized studies [26,47] were assessed using the JBI checklist for quasi-experimental studies. Overall, the main reasons for risk of bias were the inability to determine whether participants in the comparison groups received similar care aside from the intervention of interest, and the lack of multiple pre-intervention measurements. A complete assessment of the non-randomized studies can be found in Supplementary File 5.

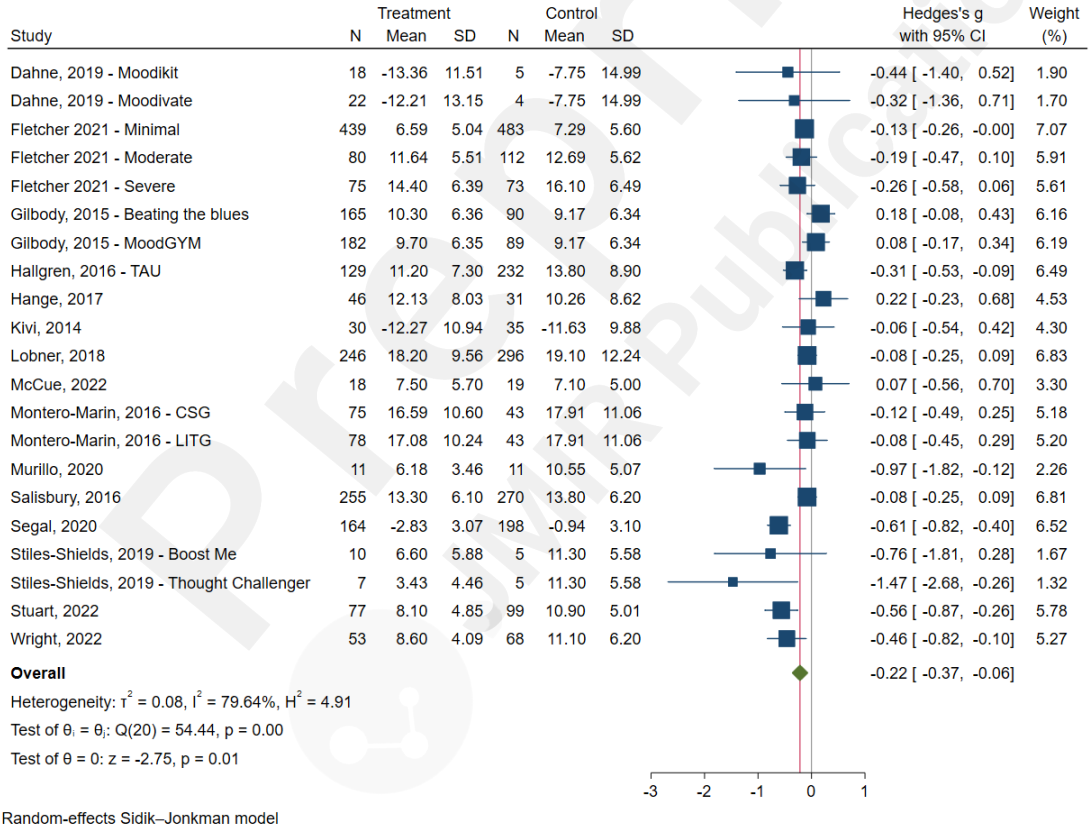
Efficacy of digital health tools

1. *Digital health tools for patients*

Fifteen RCTs (21 comparisons, n = 4391) compared the efficacy of digital health tools and passive control on **post-intervention** depressive symptoms [23-25,28,30,31,33,35-

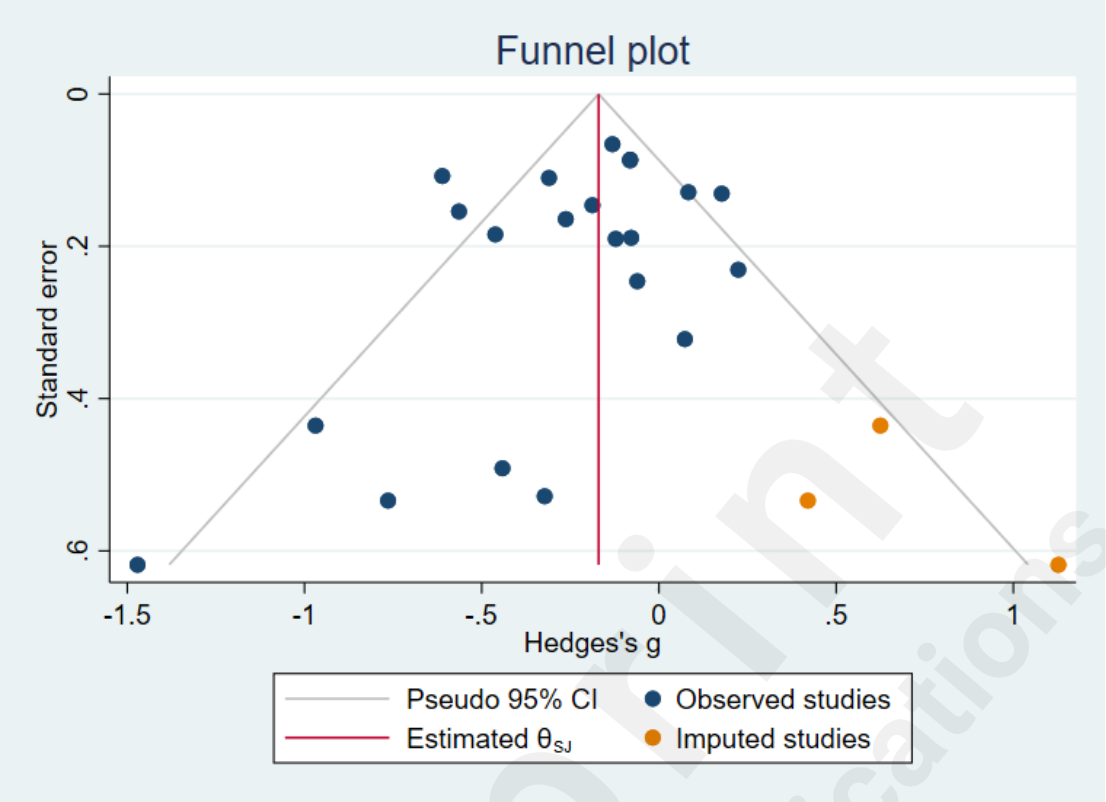
37,41,42,44,45,49] and were pooled using meta-analysis. Most studies compared digital health tools with TAU or improved usual care [21,23-25,27-31,33-37,39-44,49]; 3 studies used a waiting-list as control group [26,38,45]; and one study compared them with other active interventions, such as physical exercise [30]. Depressive symptoms were assessed using the PHQ-9 in 9 studies [25,28,36,37,41,42,44,45,49]; 4 studies used the BDI-II [23,24,33,35]; and the remaining two used the MADRS [30,31]. Baseline levels of depressive symptoms varied widely across studies, with most recruited patients experiencing moderate or moderate-to-severe symptoms. The characteristics of the digital health tools also varied, with 7 studies implementing web-based interventions [23,24,28,31,36,42,49], 5 using several digital health tools interventions [25,30,33,37,44], and 3 assessing the efficacy of a mobile app [35,41,45]. The duration of interventions ranged from 6 to 18 weeks, with most studies applying the intervention for 12 weeks [24,25,31,33,37,44,49]. Overall, the random effects meta-analysis showed a significant effect of digital health tools on depressive symptoms compared with control groups (g = -0.22, 95%CI: -0.37; -0.06), with significant heterogeneity across studies (I^2 = 79.64%) (Figure 3).

Figure 3. Random effects meta-analysis (digital health tools vs passive control for patients).



A subgroup analysis based on the severity of depressive symptoms at baseline (p = 0.878) and type of intervention were non-significant (p = 0.110) (Supplementary File 6). A significant inverse relationship was observed between gender and effect size, with a higher proportion of female participants correlating with reduced efficacy of digital health tools (B = -0.02, p = 0.022). The meta-regression analysis using mean age as a moderator, while not statistically significant, demonstrated a trend toward significance (B = -0.02, p = 0.064), suggesting that older age might be associated with slightly lower efficacy for these tools. The Egger's test was non-significant (p = 0.090); however, the overall effect size was considerably reduced after adjusting through the trim-and-fill

procedure (g = -0.17, 95%CI: -0.35, 0.01) (Figure 4).
Figure 4. Funnel plot with trim-and-fill analysis (post-intervention).



Nine studies, which could not be included in the meta-analyses due to insufficient data, assessed the efficacy of digital health tools for patients. Eight compared with passive controls and one with an active control. Eight were RCTs [27,29,30,34,38-40,43] and one was a CT [26].

Aikens et al. [34] conducted an RCT to determine whether automated telephone support improves self-management in comparison to improved usual care. A significant reduction in depressive symptoms was observed in the intervention group.

Collins et al. [26] conducted a CT to determine whether a web-based program could be useful in the treatment of depression and anxiety compared with the waiting list. No significant reduction in depressive symptoms was observed, but there was a significant reduction in anxiety.

Eriksson et al. [27] conducted an RCT to determine whether an internet-based cognitive behavioral therapy program with telephone support was more effective than standard clinical practice. Although improved work ability was associated with reduced depressive symptoms, there was no significant improvement compared with the control group.

Gili et al. [29] conducted a 4-arm RCT in which 3 groups received low-intensity psychological interventions, compared with one group assigned to improved usual treatment. The intervention group also received enhanced usual treatment as the professionals had undergone a training program. The internet-based interventions were found to be more effective than the control group.

Graham et al. [38] conducted an RCT to determine the efficacy of mobile applications compared with a waiting list. Sustained efficacy was shown in the use of the mobile apps compared to the control group.

Ishrat Husain et al. [39] conducted an RCT to determine the efficacy of a transdiagnostic, call-based collaborative care model for people with depression, anxiety or alcohol risk compared with enhanced usual care. The control group received TAU and full assessments for the same months. No significant improvement was observed in

the intervention group.

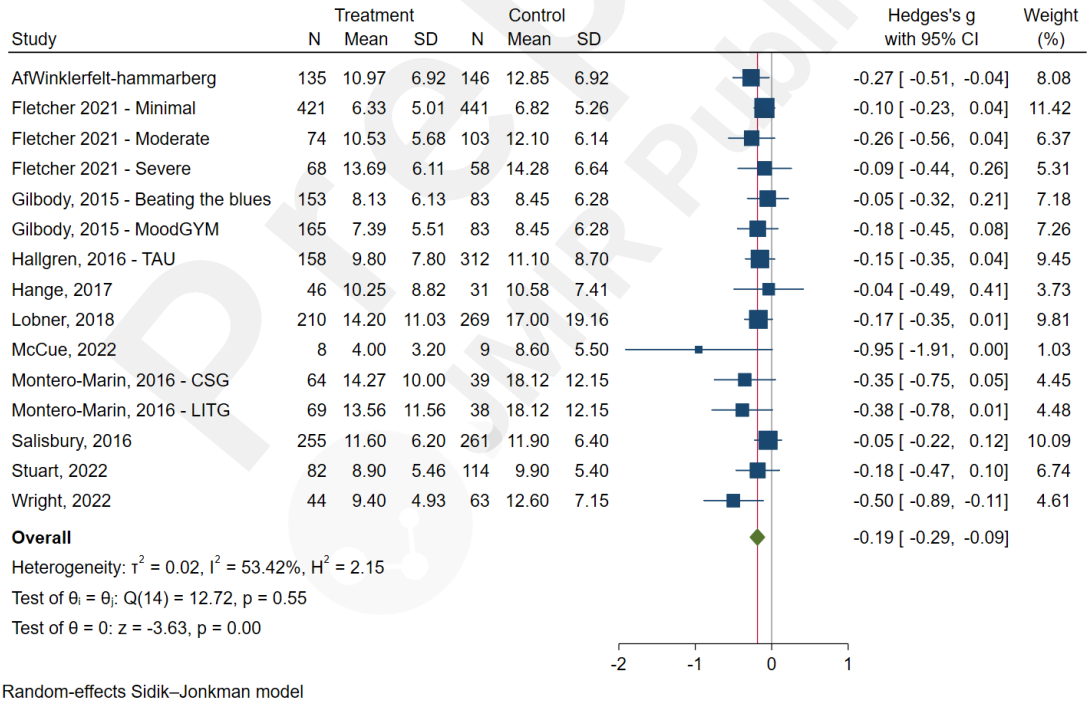
Kim et al. [40] conducted an RCT to evaluate the impact of collaborative telephone care on the care of people with depression and alcohol risk compared with enhanced usual care. While a significant reduction in alcohol consumption was observed in the intervention group, no significant reduction in depressive symptoms was found.

Rollman et al. [43] conducted a 3-arm RCT to determine the efficacy of an online in-patient support group with online cognitive behavioral therapy, and whether the latter was more effective than usual care. Significant improvement was observed in the cognitive behavioral therapy group compared with the other two groups.

Furthermore, results from the exercise arm in the Hallgren et al. study [30] could not be included in the metanalysis as this had an active control. Hallgren et al. [30] conducted a 3-arm RCT to compare the efficacy of exercise, internet-based cognitive behavioral therapy and TAU. In the short term, both intervention groups reported significant improvements compared with the control group. After 12 months depressive symptoms had decreased significantly in all three groups.

Twelve studies (17 comparisons, n = 4002) assessed the efficacy of digital health tools on depressive symptoms at **6- to 12-month follow-up** [21,23-25,28,31,36,37,41,49,50] and were pooled using meta-analysis. Overall, the random effects meta-analysis showed a significant effect of digital health tools on depressive symptoms compared with control groups (*g* = -0.19, 95%CI: -0.29; -0.09), with moderate heterogeneity across studies (I^2 = 53.42%) (Figure 5).

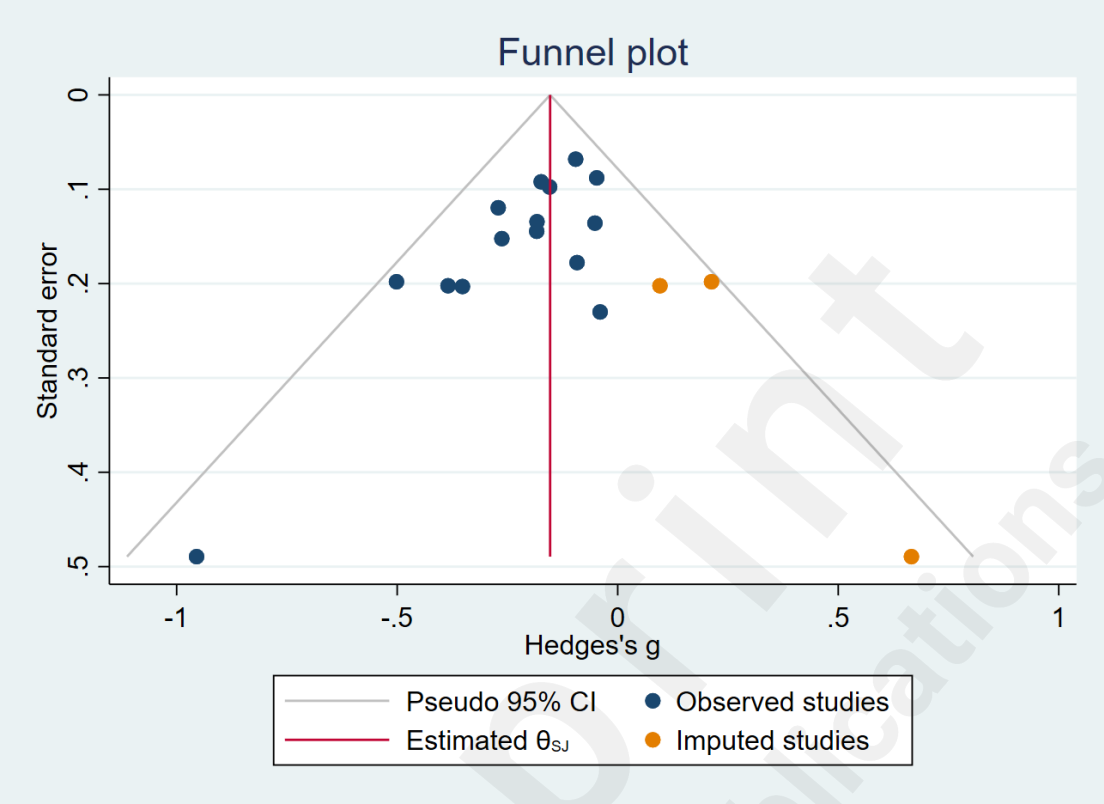
Figure 5. Random effects meta-analysis (digital health tools on depressive symptoms at 6- to 12-month follow-up).



The subgroup analysis based on the severity of depressive symptoms at baseline was non-significant (p = 0.542) (Supplementary File 6). A meta-regression analysis using gender as a moderator, while not statistically significant, demonstrated a trend toward significance (B = -0.02, p = 0.060), suggesting that female gender may be associated with a slightly lower efficacy for these tools. No significant moderator effect of age was found (p = 0.841). The Egger's test suggested publication bias (p = 0.046), and the overall effect size was slightly reduced after adjusting through the trim-and-fill

procedure (g = -0.15, 95%CI: -0.28, -0.03) (Figure 6).

Figure 6. Funnel Plot with trim-and-fill analysis (follow-up).



2. Digital health tools for professionals and/or patients

Of the 5 studies—4 RCTs [22,32,46,48] and 1 non-randomized studies [47]—that assessed the efficacy of digital health tools for healthcare professionals and/or patients, 4 compared with TAU and one compared with an active control.

Harrison et al. [32] and Balestrieria et al. [22] used a support algorithm to guide the choice of depressive treatment. Harrison et al [32] concluded that the algorithm was technically feasible to address some treatment gaps. Balestrieria et al. [22] concluded that a combination of the algorithm and telemedicine can be more effective than TAU.

Rojas et al. have addressed the efficacy of collaborative remote care compared with TAU in 2 studies: a non-randomized controlled trial in which primary care professionals in the intervention group received advice from a psychiatrist in 2014 [47], and an RCT with the same aim in 2018 [46]. In addition to collaborative care, patients were offered follow-up phone calls. Greater satisfaction and adherence were observed, although no improvement in depressive symptomatology was shown.

Adewuya et al. [48] conducted an RCT to determine if text-message support in collaborative stepped care was more effective than collaborative stepped care alone. It was concluded that collaborative stepped care combined with text message support significantly improved adherence and outcomes.

Discussion

This systematic review has analyzed 29 studies involving 10200 patients with depressive symptoms. Although some trials focused on professional support, most

interventions were directed at middle-aged individuals with moderate depressive symptoms. The majority of interventions were web-based or used several digital tools, and the TAU was often the comparator. A meta-analysis of 15 studies that analyzed the efficacy of interventions compared with a passive control group showed a positive effect for digital interventions. However, there were no differences in efficacy according to the type of digital tool used, and lower efficacy in women and older people.

Digital health is becoming increasingly relevant in health systems around the world. Therefore, identifying digital health tools used in primary care can enable health systems to assess the value of technology for depression management in primary care and, if appropriate, design specific implementation strategies for their use. All the factors discussed here are based on the results of this study and the existing literature, with the understanding that there is appreciable intra-individual variability, and that each intervention must be evaluated within the context of each system. Therefore, the results cannot be systematically extrapolated to all individuals or settings.

Firstly, a statistically significant decrease in depressive symptomatology was observed post-intervention. Although the decrease in depressive symptoms was small, the effect of digital intervention was maintained at 6 and 12 months, indicating that it is not only effective during the intervention, but also endures over time. This continuity of effect suggests that digital therapies are a good strategy for the treatment of depression. However, this review has only evaluated purely digital interventions: other studies have shown the benefits and greater effect of hybrid interventions—i.e. the complementarity of face-to-face and digital therapy—compared to face-to-face or digital intervention [51-54]. It is worth noting that although several studies have demonstrated the high potential of digital interventions for the treatment of depression, they are not considered first-line treatment in any major clinical practice guidelines [55,56]. Therefore, it would be beneficial to re-validate these results through community-randomized trials in real environments.

Although no statistical differences in efficacy were found according to the type of digital tool used, it was observed that the use of several tools in the same intervention had a potentiation effect and increased symptom reduction. The majority of digital interventions were based on cognitive behavioral therapy, consistent with the findings of Himle et al. [57]. Although, like all treatments, cognitive behavioral therapy has its limitations and may not be equally effective for all people, it appears to enhance intervention and therefore, if feasible, could be considered a first-line digital treatment plan.

This review has also shown that the severity of initial symptoms in these studies was not related to the efficacy of the digital intervention. These findings are consistent with the literature. Mohr et al. [58] found that patients with mild, moderate, and moderate/severe depression symptoms all showed significant improvement with mobile app use and concluded that intervention was effective regardless of symptom severity. Our results, together with the literature, show that initial symptom severity is not useful for determining whether a person is a candidate for digital mental health treatment. However, the main clinical practice guidelines recommend stepped care for the treatment of depression. In this sense, as initial symptomology does not determine whether the person is a candidate for digital intervention, it would be beneficial to train clinicians to recognize at which stage of treatment digital intervention would be beneficial for the patient.

A significant inverse relationship was observed between gender and effect size at post-intervention and a trend toward significance at follow-up. Most participants in the studies reviewed were women. Pre-established gender roles in society and social

expectations of male and female identity generally lead to differences in the presentation of depressive symptoms. Having analyzed gender differences in depression literacy and stigma following an educational program, Townsend et al [59] reported that women had significantly higher depression literacy and lower stigma than men. It is therefore possible that women are more likely to recognize and report symptoms of depression. In a secondary analysis of a 3-arm RCT aimed at demonstrating the efficacy of three psychotherapies, Aguilar-Latorre et al. [60] found the same trend as this study in non-digital therapies, with women showing less improvement in depressive symptoms. To achieve an antidepressant response comparable to that of men, the authors suggest that the greater psychosocial burden generally associated with women be compensated for by greater psychological support. Therefore, based on the above assumptions, further studies would be needed to determine whether digital interventions are actually less effective in women or whether there is simply a need to develop digital interventions in a gender-sensitive way.

Digital mental health interventions have great potential for treating the long-term health conditions that are common among older people, as well as the isolation and loneliness that can result from reduced mobility. Although age was not statistically significant at post intervention or follow-up in this study, it is worth noting that digital illiteracy and exclusion have tended to increase with age. However, over the last decade and especially during the COVID-19 pandemic, acceptance and uptake of technology has increased among older people [61,62]. The meta-analysis of 21 studies by Qiu Y. et al [63] showed a moderate effect in favor of digital interventions for depression in older adults. Thus, education and training strategies to include older people in the use of digital mental health therapies would be beneficial.

Limitations

This review has a number of limitations. Firstly, as psychological interventions are often professional-dependent and a wide variety of digital interventions (web-based, mobile apps, phone calls, text messages, etc.) were utilized, there was a high degree of heterogeneity between studies. To address this issue, a meta-regression model was performed to make the study subgroups more homogeneous.

It should be noted that, as the vast majority of studies were conducted in western, high-income countries and culturally adapted studies were excluded, the generalizability of our results is limited. However, it was considered of interest to identify digital interventions that were as generic as possible, as the implementation of any digital intervention in a primary care setting should be adapted and piloted according to the country in which it is located.

A high risk of bias was identified across all studies, raising concerns about the reliability of results. Although validated tools were used to assess this risk of bias, these tools are not fully adapted to the analysis of digital and psychological interventions, in which blinding is often challenging. This limitation particularly affects the risk of performance bias (Domain 2: deviations from intended interventions) and detection bias (Domain 4: measurement of outcomes). As a result, the majority of studies exhibited a high risk of bias in these areas, which may have impacted our overall findings.

Finally, the majority of studies measured symptom severity through self-administered questionnaires, most of which do not have control indices (to avoid acquiescence bias, tendency to self-report, etc.) and are therefore clinically questionable. Although these are valid tools and widely used in research, a clinical interview and/or externally administered inventory would be preferable. Furthermore, most studies used TAU as the comparator: more precise results would be obtained by comparing digital intervention with gold standard treatment.

Conclusions

Digital health tools for depression, in the form of web-based tools, mobile apps, treatment algorithms, calls, and text messages, have demonstrated efficacy in the reduction of symptomatology. Many of these interventions are based on cognitive behavioral therapy, and multi-tool interventions have shown greater effects in reducing depressive symptoms. While the severity of depressive symptoms has not been found to be useful in determining whether a person is a candidate for digital treatment, our results highlight a need for gender-sensitive studies in order to tailor interventions according to need and for strategies that can educate and involve older people in digital interventions for depression. As digital interventions have yet to be included in clinical practice guidelines or treatment strategies, studies such as this are essential to support their integration into real-world practice.

Abbreviations

ICT: Information and communication technologies
JBI: Joanna Briggs Institute
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT: Randomized controlled trials
TAU: Treatment As Usual
WHO: World Health Organization

Data availability

The data sets analyzed during this study are available in Supplementary File 7. No new data were generated during this study.

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Conflicts of interest

None declared.

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Supplementary Files

Multimedia Appendixes

Detailed search strategy for each database.
URL: http://asset.jmir.pub/assets/46dbcec1988a64c9df2db3986401227f.docx

Principal and secondary references.
URL: http://asset.jmir.pub/assets/eeeb069ae5038c7ec7bb885428506261.docx

Information about interventions and efficacy.
URL: http://asset.jmir.pub/assets/6ba92b5d093bdbb2cb0934fa909dca14.docx

Quality assessment detailed for each study.
URL: http://asset.jmir.pub/assets/6af1769ef4ff02ab912a5aff9c6c98ba.docx

Quality assessment of non-randomized studies.
URL: http://asset.jmir.pub/assets/2f35527f790b6a9c9b839716718bff4c.docx

Subgroup analysis based on the severity of depressive symptoms at baseline and type of intervention.
URL: http://asset.jmir.pub/assets/3ea52fd8c8e130661545a4aafd783d9a.docx

Data sets analyzed.
URL: http://asset.jmir.pub/assets/09a7e743d63758ab80d182bc9425f628.docx