review articles

Electronic Health Interventions for Patients With Breast Cancer: Systematic Review and Meta-Analyses

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abstract

PURPOSE Ongoing supportive care using electronic health (eHealth) interventions has the potential to provide remote support and improve health outcomes for patients with breast cancer. This study aimed to evaluate the effectiveness of eHealth interventions on patient-reported outcomes (quality of life [QOL], self-efficacy, and mental or physical health) for patients during and after breast cancer treatment and patient-reported experience measures (acceptability and engagement).

METHODS Systematic review with meta-analyses (random-effects model) of randomized controlled trials was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. Nine databases were searched using a prespecified search strategy. Patient-directed eHealth interventions for adult patients during or after active breast cancer treatment measuring QOL, self-efficacy, and mental (depressive, anxiety, and distress symptoms) or physical (physical activity, nutrition, and fatigue) health outcomes were included. Data from eligible full-text articles were independently extracted by six observers.

RESULTS Thirty-two unique studies (4,790 patients) were included. All were health self-management interventions, and most were multicomponent (videos, forums, and electronic reminder systems) websites. Meta-analyses revealed a significant effect of eHealth interventions on QOL (standardized mean difference [SMD], 0.20 [95% CI, 0.03 to 0.36]), self-efficacy (SMD, 0.45 [95% CI, 0.24 to 0.65]), distress (SMD, –0.41 [95% CI, –0.63 to –0.20]), and fatigue (SMD, –0.37 [95% CI, –0.61 to –0.13]). Twenty-five studies (78.1%) measured patient-reported experience measures. Acceptability (n = 9) was high, with high ratings for satisfaction (range, 71%-100%), usefulness (range, 71%-95%), and ease-of-use (range, 73%-92%). Engagement (n = 25) decreased over time, but disease-focused information and interactive support were most engaging.

CONCLUSION eHealth interventions may provide an acceptable and effective strategy for improving QOL, distress, self-efficacy, and fatigue among patients with breast cancer.

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INTRODUCTION

Breast cancer is the most common cancer diagnosed among women worldwide.[1] During active treatment (surgery, chemotherapy, and/or radiotherapy) and the years after (survivorship), many patients experience adverse side effects, including depression, anxiety, and fatigue, which can negatively affect quality of life (QOL).[2-4] The resulting economic burden is high because of costs of procedures, hospital visits, and loss of productivity.[5,6] Ongoing supportive care and health promotion during and after treatment may reduce this burden and improve QOL among survivors.[4,7,8]

In-person support (eg, exercise programs and psychoeducation) during and after treatment can improve patient-reported health outcomes (PROs) such as anxiety, depression, physical activity, and QOL.[9,10] Most programs promote self-management, which can improve self-efficacy[11] and indirect benefits.[9,10] Moreover, leading a healthy lifestyle can reduce risks of cancer recurrence and mortality.[12,13] However, attending in-person visits can be difficult (location, cost, and work)[5] and was exacerbated by cancer care closures during the global COVID-19 pandemic.[14,15]

Electronic health (eHealth) is an accessible strategy to deliver health information. eHealth platforms (eg, websites and videoconferencing) have proliferated during the COVID-19 pandemic.[14,15] Telehealth replaced many in-person appointments[16] and offers a scalable and flexible way to provide support, track PROs,[16-19] and enable continuity of care between hospital visits.[16] Importantly, eHealth strategies are well liked by patients in terms of acceptability and usefulness[20,21] and can promote patient-centered medicine through codesign.[22] There is growing systematic review evidence for eHealth

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Are electronic health (eHealth) interventions (eg, websites and apps) effective for improving patient-reported outcomes among patients during and after breast cancer treatment? This systematic review with meta-analyses investigated the effectiveness, external validity, and patient-reported experience measures of eHealth interventions within the context of the Reach, Effectiveness, Adoption, Implementation and Maintenance framework.

Knowledge Generated

Our findings suggest that eHealth interventions had a broad reach and high uptake from a diverse (international and multilingual) sample of breast cancer survivors. Overall, eHealth interventions were effective for improving patient-reported outcomes (quality of life, self-efficacy, fatigue, and psychologic distress), and repeated contact with health professionals, interactive disease-specific features, and optional content may be key to effectiveness.

Relevance

eHealth interventions may provide an acceptable and feasible strategy to deliver continuity of health support to patients between medical appointments.

interventions effectiveness for physical activity[23,24] and PROs (QOL, stress, fatigue, and sleep)[19,25,26] for patients with breast cancer. However, these often only include one health outcome and/or do not include meta-analyses or evaluations of barriers and enablers to implementation. A high-quality synthesis of randomized controlled trials (RCTs), evaluating numerous health outcomes during and after treatment and evaluating patient-reported experience measures (PREMs) such as acceptability, usefulness, and engagement of eHealth intervention features, is needed to inform future eHealth intervention development and attrition reduction.[26] Therefore, this study aimed to investigate the effectiveness of eHealth interventions to improve PROs (QOL, self-efficacy, and mental [anxiety, depression, and distress] and physical [physical activity, nutrition, and fatigue] health) during and after breast cancer treatment. Implementation was also evaluated using the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM framework)[27] plus PREMs to inform common features of effective interventions.

METHODS

A systematic review with meta-analyses was registered (The International Prospective Register of Systematic Reviews registration number CRD42019122689) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines[28,29] (Data Supplement 1, online only). Table 1 reports the study Population, Intervention, Comparator, Outcomes, and Settings inclusion criteria.

Information Sources and Searches

Nine electronic databases (inception to present) were searched on October 21, 2019, and updated on June 27, 2021: PreMEDLINE, MEDLINE via OvidSP, Cochrane Central Registry of Controlled Trials, Embase via OvidSP, PsycINFO via OvidSP, Allied and Complementary Medicine, Scopus, Web of Science, and Cumulative Index to Nursing and Allied Health Literature via EBSCO. The search included truncations and synonyms of the following terms: breast neoplasms, breast cancer, breast tumor, mobile phone, smartphone, text-, electronic-, or multimedia-message, electronic mail, phone applications, computer, podcast, videos, internet, website, chatroom, message board, activity tracker, electronic health, mobile health, telemedicine, and electronic learning (Data Supplement 1).

Study Selection

Search results were exported to a citation management software program. Following removal of duplicates, titles and abstracts were independently reviewed by A.C.S. (all articles) and J.T.-K. and S.C.M.S. (each reviewed half) against inclusion criteria. Abstracts with unclear information were included for full-text review. Full-text articles were reviewed by A.C.S. (11 articles), R.R. (11 articles), N.H. (14 articles), J.T.–K. (10 articles), S.C.M.S. (11 articles), and Q.T. (11 articles). A.C.S. reviewed all articles to confirm inclusion or exclusion.

Data Collection Process

A prespecified electronic data extraction table following Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines[28,29] and Cochrane Collaboration's Risk of Bias (RoB) tool[30] was developed to extract (1) study information (author, year, country of origin, study design, and sample size); (2) participant information (demographics and medical history); (3) intervention and follow-up durations; (4) intervention and control group details; (5) primary and secondary outcomes; and (6) Cochrane RoB measures. A.C.S. pilot-tested the data extraction table with two articles (reviewed by R.R.). Data from full text articles were extracted by authors J.T.-K. (6 articles), S.C.M.S. (4 articles), R.R. (2 articles), A.C.S. (6 articles), N.H. (7 articles), and Q.T. (4 articles). A.C.S. reviewed all data for accuracy.

TABLE 1. Study Inclusion[a] Criteria, Defined by the PICOS

PICOS Component	Description
Population	Adults (age > 18 years, female or male) with a breast cancer diagnosis who are undergoing or completed active breast cancer treatment (surgery and/or chemotherapy and/or radiotherapy)
Intervention	Patient-directed eHealth interventions (including but not limited to e-mail, videoconference, videos, activity trackers, website, podcast, chatroom, mobile applications, or text messages/SMS)
Comparator	Standard care or control intervention (ie, internet access)
Outcomes	Health-related QOL, self-efficacy, and mental (anxiety, depression, and distress) or physical (physical activity, nutrition, and fatigue) health outcomes
Setting	RCTs conducted in any setting

Abbreviations: eHealth, electronic health; PICOS, population, intervention, comparator, outcomes, and setting; QOL, quality of life; RCT, randomized controlled trial; SMS, short message service.

[a]Excluded: study protocols without outcomes; studies that do not report outcomes of patients with breast cancer/survivors separately to patients with other cancers; symptom reporting only; appointment reminders or cancer screening.

Risk of Bias

The Cochrane Collaboration RoB tool was used to assess RoB of included studies.[30] Domains for assessment included selection bias, including sequence generation and allocation sequence concealment, performance or detection bias via blinding of participants, personnel and outcome assessors, attrition bias via incomplete outcome data, and reporting bias via selective outcome reporting. Criteria for low, unclear, and high RoB within and across studies followed the Cochrane Handbook for Systematic Reviews of Interventions. RoB was independently assessed by authors J.T.-K. (6 articles), S.C.M.S. (4 articles), R.R. (2 articles), A.C.S. (12 articles), N.H. (7 articles), and Q.T. (4 articles). A.C.S. reviewed all RoB assessments to confirm accuracy.

RE-AIM Framework

The RE-AIM framework[27] was used to evaluate potential broader impacts of eHealth interventions. *Reach and representativeness* was evaluated using the percentage of eligible patients enrolled in the study (n enrolled/n eligible × 100) and participant demographics (ethnicity, language, employment [part-/full-time], and education level). *Efficacy* was evaluated using the primary outcome's effect size (95% CI). *Barriers to adoption* were evaluated by who (personnel) recruited participants and where (setting). *Implementation* was evaluated by (1) adherence to intervention (eg, percentage of opened modules and completed intervention components), (2) percentage of dropouts of the most complex intervention (n postintervention follow-up/n baseline × 100), (3) intervention cost, and (4) author-reported plans to upscale or implement. *Maintenance* was evaluated by (1) time (months) results were maintained and (2) when intervention would become available (author-reported).

Statistical Methods

Primary and secondary outcome means and standard deviations (SDs) at postintervention follow-up for intervention and control groups were converted to standardized mean difference (SMD), using Hedges' G.[31] Acknowledging differences across studies because of the varied population, length of intervention and length of follow-up, meta-analyses were performed fitting random-effects models[32]; restricted maximum-likelihood method was used to estimate and pool outcome SMDs (Hedges' G method) and 95% CI.

Quantitative heterogeneity was assessed by reporting the between study variance τ^2, the 95% prediction intervals (which give an estimate where true effects are to be expected for 95% of similar studies that might be conducted in the future), and I^2 (the proportion of variability attributable to heterogeneity rather than sampling error). We also conducted a formal test of homogeneity on the basis of Cochran's Q test ($P < .1$ considered statistically significant) and a series of univariable meta regressions, considered—as fixed-effect covariates—the following variables: population (patients; survivors; and patients and survivors), length of intervention (months), and follow-up (months). We also performed outlier detection and influence analyses using the leave-one-out method and reported Baujat plots to graphically display studies that overly contribute to the heterogeneity.

If studies included multiple intervention arms, only the most complex intervention was used in the meta-analyses, defined as having the largest number of intervention components. Several studies reported different measures of the same or multiple outcomes. To overcome multiplicity, the reductionist approach was used to select the most common measure used between studies for each outcome and separate meta-analyses, and forest plots were performed for each outcome.[33] Outcome variables included in ≤ 2 studies were summarized in-text. For each outcome, small-study effects were evaluated using funnel plots and, when > 10 studies were included in the meta-analysis, regression-based Egger's test for funnel plot asymmetry was used. Statistical analyses were conducted according to the prespecified statistical analysis plan (The International Prospective Register of Systematic Reviews registration CRD42019122689) using RStudio version 1.3.1093.

RESULTS

Thirty-six full-text articles[34-69] with 32 unique studies were identified after removing duplicates and screening (Fig 1), representing 4,790 unique patients (Data Supplement 2, online only). Three studies[49,50,55] used the same study population but only postintervention follow-up (6-month[50]) outcomes are reported. Moreover, participant recruitment for several studies overlapped.[37,49,50,54,55] Only unique intervention groups are compared with control for each study. Ten[34,38,40,43,44,48,58,59,64,65] studies were assessed to have high RoB (Data Supplement 1), plus one study was an outlier with high heterogeneity contribution to QOL[45,46] (Data Supplement 1) and were therefore excluded from meta-analyses.

Study Characteristics

Characteristics of included studies are summarized in Data Supplement 2. All studies were conducted in high-income countries, as defined by the 2020 World Bank gross national income per capita ≥ $12,696 US dollars.[70] Fourteen (43.8%) studies recruited patients during treatment (patients),[37,38,43,47-51,54,56,60,64,67-69] 12 (37.5%) recruited patients after active treatment (survivors),[34-36,41,42,44-46,52,57,61-63,65] five (15.6%) recruited patients and survivors,[39,40,58,59,66] and one (3.1%) recruited patients with metastatic breast cancer.[53] All participants were female (pooled mean age [pooled SD] 51.7 [8.9] years), with 26 studies (81.2%) having female sex as an inclusion criterion[34-42,47,49-54,56-62,64,66-69] (Data Supplement 1). Most participants (3,644/4,790; 76.1%) were diagnosed with early stage (0-III) breast cancer,[34,35,37-51,54,56-62,64-69] and 18 studies (56.2%)[34-38,41,42,44-46,49,50,52,56,58,63,65-67] reported time since breast cancer diagnosis (pooled mean [pooled SD] 23.0 [17.0] months). Studies varied in their reporting of participants' medical history. The proportion of studies that reported that participants had a history of following medical treatments was: surgery 23/32 (71.9%) studies,[34-36,39,41-46,51-53,56-58,60-62,64-69] chemotherapy (22/32; 68.8%),[34,36,39,41-46,48,51-53,56,58,60-62,64-69] radiotherapy (19/32; 59.4%),[34-36,39,41,42,44-46,51,52,56,58,60,62,64-68] endocrine therapy (15/32; 46.9%),[34-36,41,42,44,51,52,60,62,64-67,69] and targeted therapy (9/32; 28.1%).[34-36,41,42,52,60,65,66]

Overview of eHealth Interventions

All interventions were multicomponent and promoted self-management. Most studies (24/32;

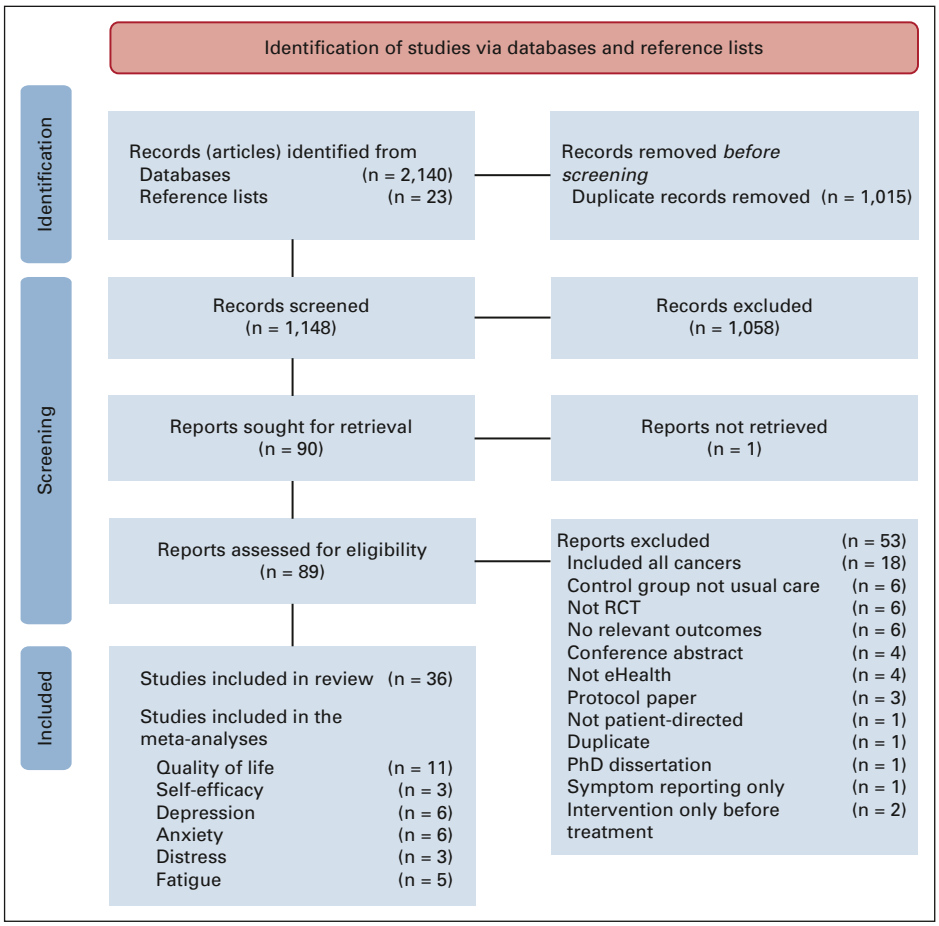

FIG 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 flow diagram of included studies for meta-analyses. eHealth, electronic health; RCT, randomized controlled trial.

75.0%)[34-38,41,42,45-47,49,50,52,54,56,60,62-67] used a website or web-based app. Five studies reported versions of the Comprehensive Health Enhancement Support System (CHESS) website.[37,47,49,50,54,55] Seven interventions (21.9%) were mobile applications[48,53,57,59,61,68,69] and two included a smartwatch.[42,57,61] Interventions included interactive features such as videos (20/32; 62.5%[37,41,42,45-47,49,50,54,56,60,62,64,65,67]), peer-support via chatrooms (9/32, 28.1%[37,38,47,49,50,54]), instant messaging (8/32, 25.0%[37,38,45-47,49,50,54,68,69]), video (4/32, 12.5%[34,44-46,65]), or telephone consultations (13/32; 40.6%[34-37,39,44-47,49,50,54-57,61]) with health professionals. Some also included e-mails (12/32; 37.5%[34,35,38,40-42,52,56,58,59,62,65,67,69]) and text message reminders (3/32; 9.4%)[38,42,59] to engage with websites. Twenty (62.5%) interventions included repeated (> 1) contact with researchers or health professionals[34,36-40,42,44-46,49,50,52-57,59-61,65,68,69] and 7/32 (21.9%)[37,42,44,49,50,54,57,61,65] provided participants with required technology. Six (18.8%) interventions were codesigned with patients.[35,38,60,62,64,66] Intervention duration ranged from 3 weeks[53] to 9 months.[60,64] Most primarily focused on QOL[37,43-47,49,50,55,57-61,68] or mental health (depressive symptoms, anxiety symptoms, and distress),[38,43,48,56,62,65,66] and some on physical health (physical activity, fatigue, and nutrition)[34,57,61] or self-efficacy.[39,64,71] Process evaluations were collected in 25/32 (78.1%) studies (Data Supplement 1).[34-36,38,39,41-50,52,53,56-59,61,62,64-67,69,71,72] Measurement details (questionnaires and domains) and data inclusions and exclusions for the meta-analyses are presented in Data Supplements 1 and 2.

Patient-Reported Outcomes

Quality of life. QOL was measured in 25/32 (78.1%) studies (Data Supplement 2),[34-37,39-42,44-47,49-54,57-62,65,66,68,69] was the primary outcome in 12/25 (48.0%; Data Supplement 1), and 18/25 (72.0%) interventions included repeated health professional or researcher contact.[34,36,37,39-42,44-47,49,50,52-54,57,59,61,65,68,69] Eight studies found a significant effect of their intervention (Data Supplement 1)[34,45-47,53,54,59,68,69]; all included repeated health care professional or researcher contact and 4/8 (50.0%) had QOL as the primary study outcome. Five health-related QOL measures, validated in patients with breast cancer, were used: European Organisation for the Research and Treatment of Cancer QOL Questionnaire C30,[34,35,41-43,45,46,51,62,65,73] WHO QOL-BREF,[53,54,74] Functional Assessment of Cancer Therapy—Breast,[37,39,40,47,49,50,57,58,61,62,65,66,68,69] QOL Adult Cancer Survivors,[42,75] and QOL Breast Cancer Patient Version.[60,76] Higher scores reflected higher QOL. Two outliers were identified[40,45,46] (one with high RoB[40]). The outlier with low RoB had a strong positive effect on QOL. It was the only tailored eHealth exercise program with individual supervision and repeated contact with researchers, and participant adherence rates were high (93.9%). After excluding outliers[40,45,46] and studies with high RoB,[34,40,44,58,59,65] a meta-analysis (n = 11) comparing intervention and control groups at the end of intervention demonstrated a SMD of 0.20 (95% CI, 0.03 to 0.36) increase in QOL favoring the intervention (Fig 2A; Data Supplement 1). Moderate heterogeneity was found between studies with τ^2 of 0.04 and $I^2 = 57\%$ ($P < .01$). Of those with a significant difference,[53,54,68,69] all included personal contact via e-mail, telephone, or chat-room, and were multicomponent apps[53,68,69] or websites.[54] Patient type was a significant moderator for QOL, where studies that only included patients were more likely to result in higher QOL than studies including patients/survivors or only survivors (Data Supplement 1). Age, intervention period, and postintervention follow-up were not significant moderators.

Anxiety and depressive symptoms. Anxiety[36,38,48,52,53,60,64,66,69] and depressive symptoms[36,38,48,52,53,56,64,66,69] were measured in nine studies (Data Supplements 1 and 2). Five (55.6%)[36,38,52,53,69] interventions had repeated health professional or researcher contact; one[38] found a significant effect but had high RoB (Data Supplement 1). Two anxiety and three depressive symptom measures were used: Hospital Anxiety Depression and Stress scale (anxiety or depression subscales),[36,38,41,52,64,66] Beck's Depression Index,[53] Center for Epidemiologic Studies Depression Scale,[56] Spielberger State-Trait Anxiety Scale.[53,60] All scales are reliable and valid measures of transient (state) anxiety or depressive symptoms in patients with breast cancer.[77-80] Higher scores reflect higher anxiety or depressive symptoms. After excluding two studies with high RoB,[38,64] a meta-analysis comparing anxiety (n = 6; Fig 2B) or depressive symptoms (n = 6; Fig 2C) between intervention and control groups at postintervention follow-up demonstrated no significant differences. Low heterogeneity was found between studies (anxiety symptoms: $\tau^2 = 0$, $I^2 = 0.0\%$, $P = .80$; depressive symptoms: $\tau^2 = 0$, $I^2 = 0.0\%$, $P = .46$). Patient type, age, intervention period, and postintervention follow-up were not significant moderators (Data Supplement 1).

Psychologic distress. Nine studies measured psychologic distress (Data Supplement 2).[34,35,38,41,43,44,56,62,65] Five[34,38,43,56,62] found a significant intervention effect, with 4/5 (80%) having distress as the primary study outcome (Data Supplement 1). Four distress measures were used: Memorial Symptom Assessment Scale,[38,41,43] Dutch Distress Thermometer,[35,62] Distress Symptom Checklist,[62,65] and Brief Symptom Inventory.[34,44] All are reliable and valid measures of psychologic distress in patients with breast cancer[81-83]; higher scores reflect higher levels of distress. After excluding studies with high RoB,[34,38,44,65] a meta-analysis (n = 3)[34,35,38,56,62,65] comparing intervention and control groups at postintervention follow-up demonstrated a SMF of –0.41 (95% CI, –0.63 to –0.20) reduction in distress (Fig 2D). Low heterogeneity was found between studies ($\tau^2 = 0$, $I^2 = 0.0\%$, $P = .43$). Interventions with a significant improvement in psychologic distress were self-guided[35,62] or health professional–supported (repeated contact via e-mail or

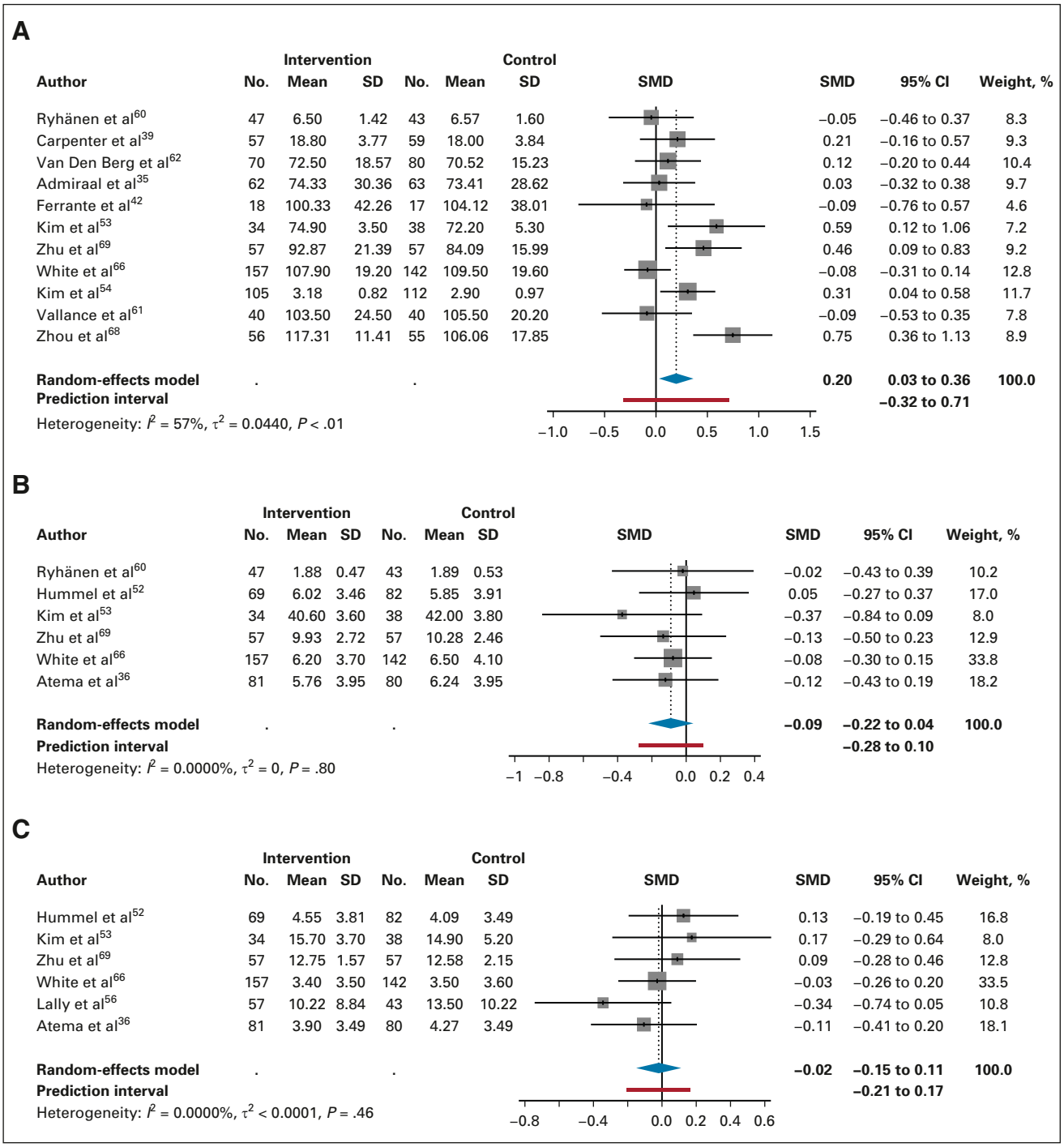

FIG 2. Forest plot of (A) quality of life, (B) anxiety symptoms, (C) depressive symptoms, (D) psychologic distress, (E) self-efficacy, and (F) fatigue outcomes for electronic health randomized controlled trials. SD, standard deviation; SMD, standardized mean difference. (continued on following page)

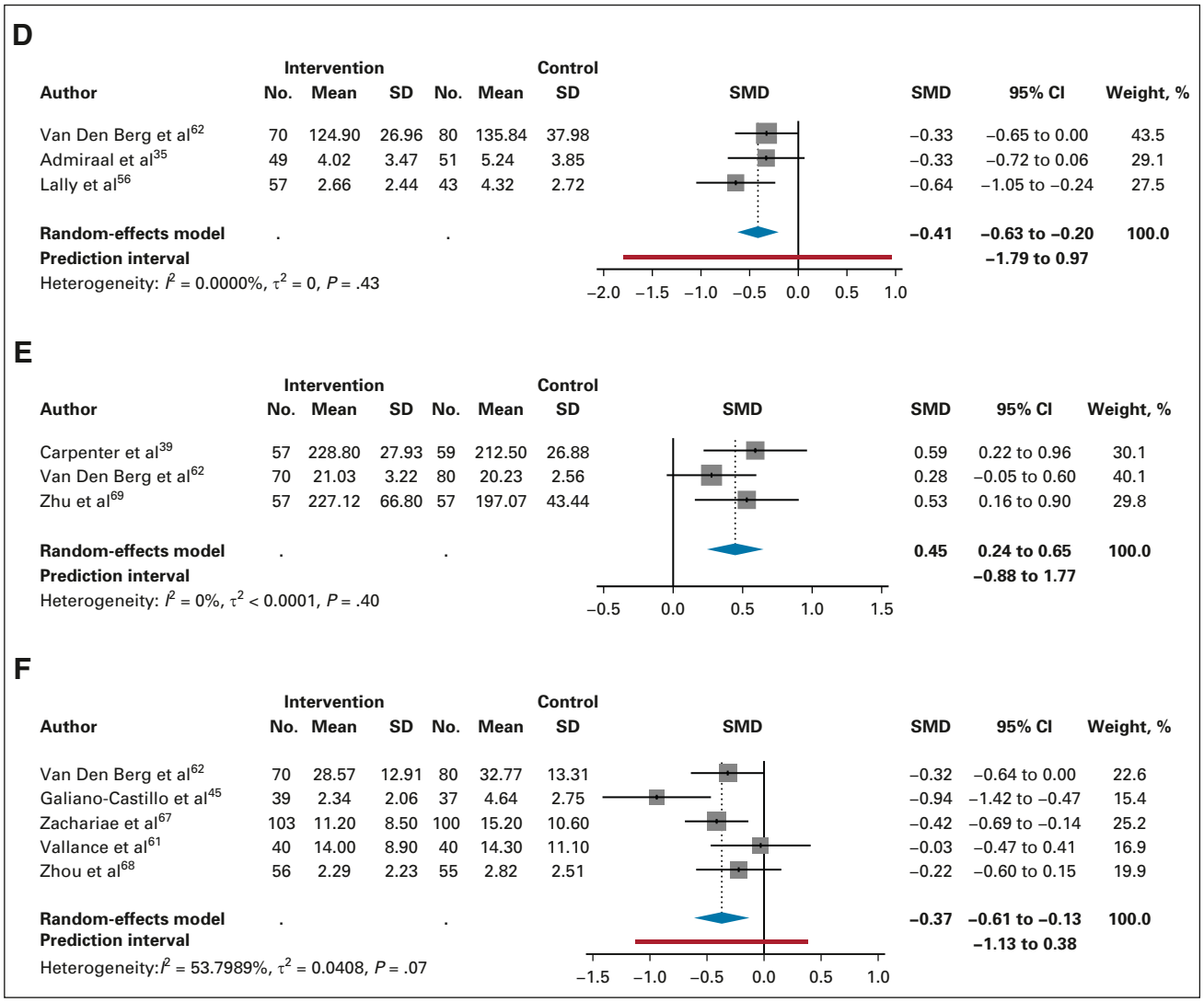

FIG 2. (Continued)

telephone)[56] multicomponent interactive websites with psychoeducation. Patient type, age, intervention period, and postintervention follow-up were not significant moderators (Data Supplement 1).

Self-efficacy. Self-efficacy was measured in seven studies[38-40,42,62,64,69] using validated scales and domains: Cancer Behavior Inventory (self-efficacy for coping with cancer),[38-40,84] Stanford Inventory of Cancer Patient Adjustment,[69,85] Self-Efficacy Scale,[62] CHESS instrument (health self-efficacy),[64] and Health Belief Survey (self-efficacy for physical activity and healthy eating[42]; Data Supplements 1 and 2). After removing two studies with high RoB,[38,40,64] a meta-analysis was conducted for self-efficacy for coping with cancer (N = 3)[39,62,69] comparing intervention to control at postintervention follow-up and found a 0.45 (0.24 to 0.65) increase in self-efficacy (Fig 2E). Low heterogeneity was found between the studies ($\tau^2 < 0.001$, $I^2 = 0\%$, $P = .40$). All three studies found a significant positive effect of the intervention on self-efficacy compared with usual care at follow-up, with 2/3 (66.7%) being the primary outcome. Interventions were multicomponent (videos, discussion groups, and e-mails) web- or app-based self-management programs promoting psychologic adjustment and health tracking during and after treatment. Two[39,69] included repeated researcher or health professional contact and one provided automated weekly e-mails about new website content.[62] Age, intervention period, and postintervention follow-up were not significant moderators (Data Supplement 1). Association between patient types could not be analyzed as there was one study in each patient type.

Fatigue. Fatigue was measured in seven studies[34,44-46,57,61,62,67,68] using validated measures: Checklist Individual Strength (Fatigue Severity Scale),[34,62] Piper Fatigue Scale,[45,46] Functional Assessment of Chronic Illness Therapy-Fatigue,[57,61,67] Numerical Rating Scale (Fatigue subscale[68]; Data Supplements 1 and 2). Functional

Assessment of Chronic Illness Therapy–Fatigue was reverse-scored; therefore, higher scores reflected higher levels of fatigue for all scales. After removing two studies with high RoB,[34,44] a meta-analysis (n = 5) comparing intervention to control at postintervention follow-up found a –0.37 (–0.61 to –0.13) reduction in fatigue (Fig 2F). Moderate heterogeneity was found between studies (τ^2 = 0.04, I^2 = 54%, P = .07). Four studies reported significant improvements in fatigue at follow-up and three[34,45,46,57,61] included repeated health professional or researcher contact. Four studies[57,61,62,67,68] used multicomponent web-based psychoeducation, one included a website, mobile app, and smartwatch,[57,61] and one included a web-based exercise program.[46] Patient type, age, intervention period, and postintervention follow-up were not significant moderators (Data Supplement 1).

Other Outcomes

Three studies measured physical activity[42,45,46,57,61]; all were multicomponent websites and two included a smartwatch and repeated health professional or researcher contact[42,57,61] (Data Supplement 2). The web-based exercise program[45,46] and website plus smartwatch and mobile app[57,61] found significant improvements in physical activity, but the interactive website with smartwatch and text message reminders (n = 37) did not.[42] This study aimed to improve body mass index and nutrition[42] but there was no difference between groups at follow-up.

Patient-Reported Experience Measures

Acceptability. Nine studies (34.6%) evaluated participants' perceived intervention acceptability.[34,35,39,42,45,46,53,56,58,65] Most participants found psychoeducational websites acceptable (satisfaction: 71%-100%[34,35,39,45,46]), useful (71%-95%[35,42,45,46,56,72]), easy to use (73%-92%[42,56,72]), and easy to understand (98%-100%[45,46,56,72]). One study reported that participants found written and video content more useful than psychoeducational activities (76%, 69%, and 49%, respectively),[56,72] and participants of a web-based exercise program found videos valuable (mean rating: 3.8/4; 95%).[45,46]

Engagement. Twenty-five studies (78.1%) evaluated participants' intervention engagement (logins, completed modules, and usage tracking).[34-36,38,39,41-50,52,53,56-59,61,62,64-67,69,72] Participants' engagement was broad, completing 0%-100% modules. Most participants (61%-100%[36,41,42,44,47,48,52,56,58,59,65-67,72]) engaged with the intervention ≥ 1 time (login and opened module). However, nine studies reported engagement dropping over time[41,42,47,48,52,56,58,65,67,72]; 5/9 had repeated contact.[42,47,52,56,65,72] For websites, participants engaged most with content about living with side effects, coping strategies,[41,58] healthy living,[41] advice,[38] blogs,[38] and discussion boards.[58] One study found participant engagement with e-mails was consistently high; 35/37 participants (94.6%) engaged from baseline to 3 months.[65] An avatar-based app game found quests, level-ups, and rewards most engaging.[53]

Risk of Bias

RoB within 29/32 (84.4%) studies was unclear[35-37,39,41,42,47,48,51-54,56,57,60-63,66,67] or high[34,38,40,43,44,49,50,58,59,64,65] because of lack blinding or issues with reporting attrition rates or study protocols (Fig 3; Data Supplement 1). Most studies adequately generated[34-43,45,46,48-51,53,54,56-64,66-69] and concealed allocation.[34-43,45-47,49-51,54,56,57,59-64,66-69] Patient blinding was not possible because of the nature of eHealth interventions and was not considered to increase RoB. However, 22 studies[35-42,44,47-50,52-54,56,57,59-63,66] (68.8%) presented insufficient information to decide (unclear risk) regarding researcher and/or outcome assessor blinding, and four reported not blinding researchers (high risk).[34,43,58,65] Twenty-four (75.0%) studies[34-36,39,41-43,45-48,51-53,56-58,60-63,65-69] reported complete outcome data (low risk) and two had insufficient

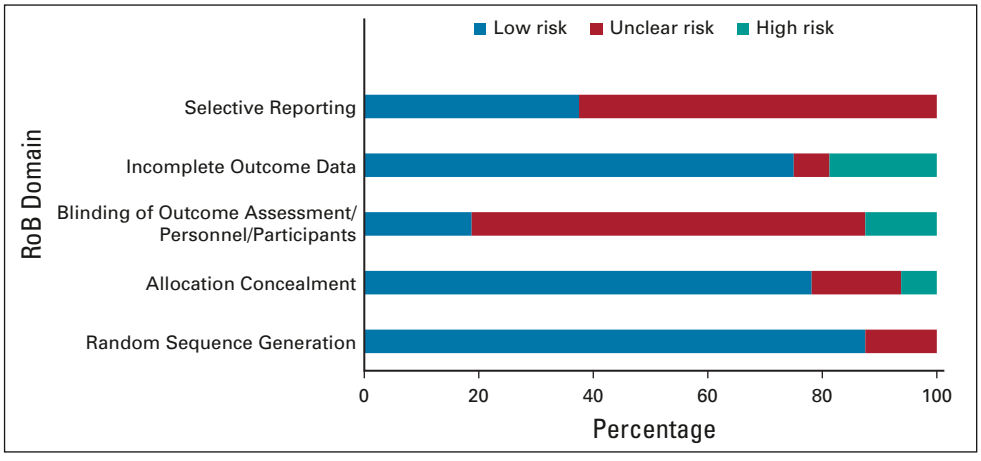

FIG 3. Cochrane risk of bias scores (%low, unclear, and high risk) across bias domains (selective reporting, incomplete outcome data, blinding, allocation concealment, and random sequence generation) for the 18 included breast cancer electronic health studies. RoB, risk of bias.

detail (unclear risk).[37,54] In six studies,[38,40,44,49,50,59,64] attrition was high or varied between groups, but comparisons or reasons for attrition were not provided. Finally, 20/32 (62.5%)[35,37-42,44,47,48,50,51,54,56,58,60,64-69] did not reference a protocol or trial registration (unclear risk). No significant publication bias was found from assessing funnel plots except for distress and fatigue.

RE-AIM Framework

The results are presented in Data Supplement 2. Twenty-eight (87.5%) studies reported reach, with 16/28 (57.1%) reporting 71.9%-92.5% of eligible patients enrolled.[41-43,45-48,51-53,56,57,59,61,62,66,68,69] Ten (69.2%) studies reported 11 ethnicities (Data Supplement 1). Thirty-one studies reported participants' main language, resulting in 10 unique languages (Dutch, English, Norwegian, Mandarin, Swedish, Spanish, Japanese, Korean, Finnish, and Danish). Non-English speakers were excluded in 10/32 (31.2%) studies[37,39,42,44,47,49,50,54,56,57,61,66] (United States and Australia). Twenty-two (68.8%) studies reported employment status; 16.7%-80.3% of participants were employed part- or full-time. Education levels were reported in 29/32 (90.6%) studies, with 20/32 (62.5%) [34,37-40,42,44-46,48-52,54,56,57,59,61,64,66,67] reporting > 50% of participants had *some* university education or higher.

Efficacy (effect size [95% CI] of primary outcome) was reported in 15/32 (46.8%) studies[34-36,39,43,45-47,52,54,56,58,59,62,67,69] (Cohen's d or eta-squared); three studies had a large effect size,[34,45,46,67] five medium,[36,39,52,56,69] and seven small.[35,43,47,54,58,59,62] For adoption barriers, health professionals or researchers conducted recruitment for all studies and 22/32 (68.8%) recruited participants in-person (hospital and cancer center). For implementation, intervention adherence ranged from 29%-100% of participants completing all scheduled components.[34-36,38,39,41-50,52,53,56-59,61,62,64-67,69] Dropouts of the most complex intervention ranged from 1.8% to 37.5%, with 16/32 (46.9%) having ≤ 10% dropouts. Cost was reported in three studies, including a free website and app[42,48] and paid app ($77 US dollars/6 months).[59] Three studies[42,51,59] reported plans to upscale, with the interventions already publicly available. Fourteen (43.8%) studies reported maintenance of results; 6/12 (50.0%) sustaining results for 1.5-12 months.[36,39,41,45-47,59,62,67] Four studies reported if the intervention would become available, with three publicly available[42,51,59] and one unlikely to become available because of capacity required.[45,46]

DISCUSSION

The current systematic review with meta-analyses and RE-AIM framework revealed that eHealth interventions had broad reach, with high uptake among diverse (international and multilingual) patients with breast cancer and a significant positive impact on PROs QOL, health self-efficacy, psychologic distress, and fatigue compared with control postintervention but not anxiety or depressive symptoms. The moderator analysis revealed improved QOL for patients compared with survivors. Intervention dropouts were low and PREMs revealed eHealth interventions were acceptable, useful, and easy to use, but attrition was common. Few studies reported maintenance of the results, intervention cost, or plans to upscale, and the RoB assessment highlighted variation in blinding procedures.

This review revealed that many interventions with a significant improvement in PROs (self-efficacy, QOL, distress, and fatigue) included repeated health professional or researcher contact. Moreover, improvements in QOL occurred during treatment, when patients interact regularly with their health care team.[86,87] All interventions were multicomponent, and studies did not specify which component affected behavior change. However, PREMs revealed participants were most engaged with supportive features such as e-mails, telephone, chat functions, text messages,[46] and health reminders.[53] For example, the CHESS website was associated with improved social support by improving participants' information and emotional-social competence, therefore increasing emotional functioning and QOL.[55] This is consistent with behavior change theories such as Social Cognitive Theory[88] and Control Theory[89] that posit providing encouragement, identifying barriers, and setting and reviewing behavioral goals support behavior change. Moreover, one video-based support group found participants who received peer support rated the intervention significantly higher than those who did not.[65] Similarly, a systematic review of reviews found that eHealth interventions were effective for improving perceived support in patients with various cancers.[90] However, the current systematic review revealed a paucity of studies reporting costs of staff time or plans to scale up, which mirrors RE-AIM findings of a multicomponent adult obesity behavior-change intervention.[91] Other systematic reviews found eHealth interventions cost-effective across specialty areas (pulmonary, ophthalmology, cardiovascular, and public health),[92,93] especially for people in rural areas. This review revealed that incorporating optional low-cost support features such as e-mails, text messages, or chat functions with peers or health professionals may be beneficial, but economic evaluations are needed.

eHealth interventions did not improve anxiety and depressive symptoms. This result may be due to a floor effect, whereby participants' baseline anxiety and depressive symptom scores were within a healthy range. The incidence of anxiety and depression among patients with breast cancer ranges between 18%-33%[94] and 9%-66%,[94,95] respectively. Studies within this review did not recruit anxious or depressed patients. In primary care, some evidence suggests that eHealth interventions can decrease anxiety and depressive symptoms[96] and there is growing evidence of benefits in cancer care.[97] However, more research is needed to evaluate the

effectiveness in patients with breast cancer with anxiety and depression.

Participants within the current systematic review found multicomponent eHealth interventions acceptable, useful, and easy to use, with few dropouts, but engagement reduced over time. This aligns with the Technology Acceptance Model,[98] which posits that user acceptance, usefulness, and ease of use are critical to technology usage. Technology user attrition is common[99] and attributed to a lack of perceived benefit and difficult-to-use interventions. Preprototype user acceptance testing[98] or codesign has potential to improve delivery and engagement,[100] but this review found that few interventions were codesigned. Overall, this review found that participants engaged most with information regarding side effects, healthy living,[41] general advice,[38] and interactive features (blog posts,[38] e-mail contact,[65] and incentives[53]). Other research found that participants were more likely to remain engaged if they enjoyed the intervention, found it useful, easy to use,[99] easy to understand, and trustworthy.[101] There is contradictory evidence that eHealth intervention personalization improves engagement or efficacy.[102-105] However, differentiating between end-user and researcher-chosen personalization may be critical. For example, a recent review[103] found that participants preferred interventions with interactive features that could be turned on/off. Gamification, incentives, and rewards may also improve engagement via extrinsic motivation.[106] Future studies should consider using the TAM to codesign eHealth interventions with end users, and analyzing end-user personalization on engagement and health outcomes.

Although the current review summarized international RCTs targeting various PROs, there are limitations. First, all studies were conducted in high-income countries, with younger, highly educated women, and this may mean those with lower eHealth literacy were not included.[107] Therefore, the results may not be generalizable to low- or middle-income countries or women of older age or less education. Second, RCTs recruiting patients with various cancers and summarized combined results were not included because it was not possible to determine results specific to breast cancer. Non-RCT designs (eg, adaptive trials)[108] were also not included. Third, planned moderator analyses between sexes could not be conducted because all participants were female; most studies excluded men but this is a growing population with minimal support.[109] Finally, the RoB assessment highlighted that most studies did not clearly report blinding procedures or protocols. Importantly, studies with high RoB were excluded from meta-analyses, which improved precision of the treatment effect and the reliability of pooled effects.

In conclusion, this systematic review with meta-analyses revealed that eHealth interventions had a significant positive impact on QOL, self-efficacy, distress, and fatigue at follow-up compared with usual care. Most interventions were multicomponent, web-based, health self-management programs. On the basis of patient preferences, future eHealth interventions should consider including practical disease- and health-management information via videos and written material, social support opportunities, and optional communication features. Importantly, interventions codesigned with end users may improve engagement.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Electronic Health Interventions for Patients With Breast Cancer: Systematic Review and Meta-Analyses

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