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Effectiveness of Internet-based Support Interventions on Breast Cancer Patients : A Systematic Review and narrative synthesis

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Title page

Title of the article Effectiveness of Internet-based Support Interventions on Breast Cancer Patients:A Systematic Review and narrative synthesis

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ABSTRACT

Objective To identify the elements and assess effectiveness of Internet-based support intervention on psychological distress, symptoms of anxiety and/or depression, physical variables (distress, severity, and/or prevalence), social support, self-efficacy, and quality of life in patients with breast cancer patients and guide future research in this field.

Design Systematic review and narrative synthesis

Methods Web of Science, Cochrane Library, PubMed, MEDLINE, PSycINFO, CINAHL, China National Knowledge Infrastructure and other databases were searched by computer and assisted by manual search. The search time frame is since the establishment of the database to June 2021. Included were randomized controlled trials (RCTs) or quasi-experimental (QE) studies focusing on Internet-based support interventions in breast cancer patients. The quality of the evidence was assessed with the Cochrane risk of bias tool and the quality evaluation criteria of the Australian JBI evidence-based Health Care Center.

Results Out of 2842 articles, 136 qualified articles were preliminarily identified. After further reading the full text, 35 references were included, including 30 randomized controlled trials and 5 quasi-experimental studies. Internet-based support interventions have demonstrated positive effects on women's quality of life and physical variables(distress, severity, and/or prevalence), but inconsistent effectiveness has been found on psychological distress, symptoms of anxiety and/or depression, social support, and self-efficacy.

Conclusions Internet-based support interventions are increasingly being used as clinically promising interventions to promote the health outcomes of breast cancer patients. Future research needs to implement more rigorous experimental design and include sufficient sample size to clarify the effectiveness of this Internet-based intervention.

PROSPERO registration number CRD42021271380.

Keywords: breast cancer Internet; support; effectiveness; systematic review

Strengths and limitations of this study

- ► Comprehensive search using a sensitive search strategy identified a lot of potential correlation research.
- ► Tailored Internet-based support intervention that included comprising multicomponent is needed for breast cancer.
- ► Multifaceted interventions that included information support , symptom management , behavior management , psychological support, communication with health professionals or peer support appear to be useful in improving the quality of life among breast cancer.
- ► Due to the differences in research subjects, intervention contents, intervention programs, outcome indicators, and measurement instruments, no data synthesis was conducted for meta-analysis, and only narrative analysis was conducted.
- ► There is insufficient evidence to determine whether any component combination is superior to other component combinations in improving the quality of life.

INTRODUCTION

Breast cancer is currently the most common malignant tumor in women worldwide[1]. Breast cancer (BC) ranks first in the incidence of female malignant tumors. World Health Organization(WHO) data show that the number of new cases of breast cancer in 2020 is as high as 2.26 million, exceeding lung cancer for the first time, becoming the world's largest high incidence of cancer[2]. The treatment of breast cancer patients is based on the comprehensive treatment of surgery, supplemented by chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and other treatment methods. As the health system's effectiveness in early diagnosis and treatment has improved, the number of breast cancer survivors has also increased significantly[3]. However, the diagnosis and treatment of breast cancer bring patients varing degrees of symptomatic distress in the short term, such as pain, limited limb function, hair loss, nausea and vomiting, bone marrow suppression, and long-term physical and psychological distress symptoms such as impaired body image, fatigue, sleep disturbance, anxiety and depression, which seriously affect the quality of life, especially during chemotherapy. [4-6] The importance of supporting patients adequately regarding symptoms resulting from diagnosis and treatment has been widely recognized[7] . However, there are still many female breast cancer patients

who report unmet supportive care needs, and these needs are mostly in the health system/information and psychology fields[8, 9]. Besides, the patient's symptom distress, self-efficacy, and social support are three interrelated factors that affect a person's ability to cope with chronic diseases[10].All the above may lead to poor quality of life for patients with breast cancer.

The survival rate of breast cancer is expected to continue to increase, leading to an increase in the number of patients requiring long-term care: this poses a challenge for the patients themselves, their families, and oncology services. However, geographical distance restrictions and scheduling issues challenge the feasibility of clinical face-to-face supportive care interventions[11].

To identify and meet the needs of this large patient population, the healthcare system is urged to develop and adopt (cost-effective) plans to educate and support patients. Conventional healthcare, however, can hardly achieve these goals because of time constraints, distance restrictions, high cost, and so on[11]. Thus, Internet technology is now common in both developed and developing countries (WHO 2011), and as the reform of medical rationalization reduces or restricts face-to-face services, the use of technologies to evaluate, educate, support, and interact with patients has become increasingly common. The use of smartphones and tablet applications, social media, and other mobile devices-provided support programs will become more and more common in the future. These tools can facilitate the provision of cancer care services to survivors in rural areas[12]. In addition, they are also used in treatment management to monitor symptoms, physical activity, psycho-oncology, and nutrition[13]. They support cancer survivors to develop a healthier lifestyle[14]. Moreover, to provide better support to cancer survivors, they may help promote coordination between interdisciplinary cancer treatment teams[15].

At present, medical personnel can provide customized supportive care for patients with the Internet as the carrier and information technology as the means (including mobile communication technology, cloud computing, Internet of Things, big data, etc.), which is also increasingly favored by cancer patients [16, 17]. Internet-based support interventions are defined as smartphones and tablets (including apps), websites, social media and other mobile devices-delivered support programs to provide information and facilitate communication regarding self-care management and adverse effects related to toxicities owing to breast cancer therapy[7, 18, 19]. Previous original studies have measured the effectiveness of Internet-based support interventions in cancer patients on psychological distress[20, 21], social support[22], physical symptoms (severity and/or distress)[23], and QUALITY OF LIFE[24, 25]. Besides,

more evidence is needed. In this fast-developing research field, it is important to regularly recapitulate its status. In addition, China is the world's most populous country, breast cancer is one of the most common malignant tumors in Chinese women[26]. This article integrates articles published in Chinese or English to help understand the impact of Internet-based support interventions on breast cancer patients at the global level[22] .

This systematic review aims to synthesize and descriptively analyze the effectiveness of Internet support intervention studies on psychological distress, symptoms of anxiety and/or depression, physical variables (distress, severity, and/or prevalence), social support, self-efficacy, and quality of life in breast cancer patients in English and Chinese.

METHODS

We performed a systematic review based on PRISMA guidelines, and it was registered in PROSPERO (CRD 42021271380) from https://www.crd.york.ac.uk/PROSPERO/display_ record. php?RecordID=271380.

Search strategy

Seven electronic databases were searched: Web of Science, Cochrane Library, PubMed, MEDLINE, PSycINFO, CINAHL, China National Knowledge Infrastructure. We searched the articles from the inception of each database to June 2021. The search keywords included “breast neoplasm OR breast cancer” AND “Telemedicine OR online OR Internet OR connected health OR telehealth OR e-health OR m-health OR e-intervention OR e-technology OR computer OR mobile application OR mobile device OR social media OR WeChat” AND “patient education OR intervention OR support OR teaching OR instruction* OR program* OR psychoeducat* OR self-management OR Social Support OR support system* OR support group*”

Inclusion and Exclusion Criteria

In this systematic review, we included the following: (1) The population is adult women with breast cancer patients, (2)Studies about Internet-based support interventions, defined as smartphones and tablets (including apps), website, social media and other mobile devices-delivered support programs to provide information and facilitate communication regarding self-care management and adverse effects

related to toxicities owing to breast cancer therapy, (3)All interventional study types including non-randomized controlled trials or quasi-experimental intervention studies were considered,(4) Outcome variables in the study included one of the following, such as psychological distress, symptoms of anxiety and/or depression, physical variables (distress, severity and/or prevalence), social support, self-efficacy and QUALITY OF LIFE, and (5) Articles were written in English or Chinese.

Studies were excluded for the following reasons: (1) if they focused on Internet-based support interventions related to other types of cancer, (2) Study types include review, non-clinical study, meta-analysis, etc, (3) The full text cannot be obtained; (4) Repeated publications.

Study selection and data extraction

All stages of study selection, data extraction was conducted by two researchers independently, and disagreements were resolved by consultation with a third researcher. For included studies, the following data were extracted with a pre-specified data extraction form, including population characteristics (groups, sample), study characteristics (author(s), country and year of publication), intervention characteristics (theoretical framework and description), and outcome characteristics (primary outcomes and main conclusions).Missing data would be obtained from authors by email, if possible.

Data synthesis

The data synthesis was undertaken following CRD's guidance[27]. This study follows the narrative synthesis method of Popay *et al*, and conducts narrative synthesis in a systematic and transparent way, focusing on the effect and content elements of intervention measures[28]. The heterogeneity of the data in terms of interventions, instruments, and outcome measures did not allow for comparison between studies or clinically meaningful interpretations. A meta-analysis was therefore not considered to be appropriate for analyzing the data.

Assessment of risk of bias

The quality of RCTs and pre-post design studies was assessed using the Cochrane Collaboration' risk of bias tool[29]. This tool rates 7 domains as having a low, unclear, or high risk of bias. These domains consist of sequence generation, allocation concealment, participants' and study personnel's blinding; outcome assessment blinding; outcome data completeness; selective outcomes' reporting; and other

threats to validity, including intervention contamination, baseline imbalance, and carry-over effect in cross-over trials).In addition, we used the quality evaluation criteria of the Australian JBI evidence-based Health Care Center to evaluate the documentation quality of quasi-experimental studies. The overall quality of the quasi-experimental research is evaluated from 9 items including causality, baseline, intervention, control, outcome index measurement, follow-up and analysis.

Patient and Public Involvement

No patient involved.

RESULTS

Selection of studies

A total of 2842 references were obtained through database retrieval and reference traceback. After reading the titles and abstracts to exclude duplicates, 136 references were obtained through preliminary screening. After further reading the full text, 35 references were finally included per all inclusion and exclusion criteria established for the systematic review.

Study characteristics and risk of bias

Characteristics of the included studies are summarized in Table 1. A total of 35 articles were included in this literature review. Sixteen studies were undertaken in mainland China, six in the United States, two in the Netherlands, two in Australia, two in Sweden, One study each in Taiwan, Turkey, Switzerland, Italy, Japan, Korea and Ireland. Twenty-eight study designs were RCTs, the other seven study designs were quasi-experimental studies.

The transmission carriers of Internet support intervention include website platform (n=9), mobile application program (n=13), WeChat platform (n=11), comprehensive health enhancemen t system (n=1), survival nursing system (n=1), and follow-up system based on clinical decision support algorithm (n=1). There are 10 articles on personalized customization intervention.

In this review, of the 30 randomized controlled trials included, 6 were rated as grade C in methodological quality, 23 were rated as grade B, and 1 was of high quality, as shown in Table 1. Among the 5 experimental studies included in this review, the quality grade is B, as shown in Table 2.

Description of participants

The 35 studies consisted of 5368 patients. The participant sample sizes ranged from 29 to 638 participants. The mean ages ranged from 41.1~59.9 years. Seven studies analyzed patients with locally or locally advanced cancer (stages I-III), whereas three sthdies only included cancer patients with stages I-II[30-32]. Five studies included solely patients who had completed cancer treatment during their follow-up[33-37], twenty-seven studies only included patients during treatment and four studies patients in all treatment phases [34, 35, 38, 39].

Content elements of Internet-based support Intervention Internet-based support

Internet-based support intervention involves six topics: (1) Information support (n=33): including breast cancer disease, treatment and rehabilitation-related knowledge, available aid resources or organizational service information, expert consultation or outpatient consultation arrangements, and expert lectures. (2) Symptom management (n=9): including patients' self-assessment and monitoring of their physiological symptoms, medical staff' s self-management guidance for patients, automatic feedback of symptom management APP or system, and symptom early warning processing combined with clinical risk algorithm. (3) Behavior management (n=3): including medication compliance management, limb functional exercise compliance management, infusion port maintenance, healthy lifestyle management. (4) Psychological support (n=7): divided into self-guidance and professional guidance. Self-guided psychological support is realized by the corresponding modules of intervention independently completed by breast cancer patients. Professionally guided psychological support is conducted through e-mail interaction with the therapists or online interaction with groups of other breast cancer patients. It includes negative emotional self-assessment or monitoring, cognitive behavioral therapy, mindfulness training, expressive writing to alleviate physical image distress, psychological education, cognitive behavioral therapy, reflective diary, meditation training, etc. (5) Communication with health professionals via mail/web (n=28): The main form is that breast cancer patients directly contact with health professionals and ask questions, health professionals give advice or emotional support to breast cancer patients. (6) Peer support (n=20): Support information and rehabilitation experience sharing are mainly provided by other breast cancer patients.

Intervention providers were mainly nurses or physicians, a few multidisciplinary teams brought together by physicians, nurses, dietitians, rehabilitators, psychotherapists, and information engineers. In terms of intervention sample size, due to the study conditions, most of the interventions were conducted in small

samples, with single-group sample sizes mostly concentrated in 30-60 individuals, and only six studies with sample sizes of 61-100, and only seven studies with sample sizes of more than 100, while only three studies with sample sizes of less than 30.

On the basis of intervention duration, the majority of the 26 intervention studies focusing on the chemotherapy phase of breast cancer conducted four to six chemotherapy cycles, and the intervention duration was mostly three to six months; only two studies lasted nine months, while the intervention duration in the other five studies ranged from two weeks to six weeks, and four studies did not explicitly report the duration of the intervention (Foley).

With reference to intervention content, Internet-based support interventions included evidence-based health education messages, symptom self-monitoring/tracking and management, self-management skills training (healthy lifestyle management), journal writing or sharing, question-and-answer counseling by professionals, establishing channels of communication with peers, sharing videos of role models' journeys, relaxation training, psychoeducation, and cognitive-behavioral therapy.

Interventions and associated outcomes

In this systematic review, the Internet-based support interventions were evaluated for their effectiveness on Quality of life, anxiety and/or depression, psychological distress, physical variables, social support, and self-efficacy.

Quality of life

Eighteen studies reported on Quality of life with significant positive intervention effects reported by seventeen. In seven RCTs and four quasi-experimental studies conducted in China, the Quality of life score of the intervention group was higher than that of the control group[36, 37, 40-48]. A web-based tailored psychoeducational intervention for breast cancer patients who completed curative-intent primary treatment reported that improvements in distress, distress-related problems and Quality of life were observed in both study groups but no significant differences[49].

Symptoms of anxiety and/or depression

Eleven studies found inconsistent results regarding the impact of the Internet-based Support Interventions on symptoms of anxiety and/or depression. The results of three RCTs and one quasi-experimental study in

China included in this review showed that Internet-based support interventions significantly improved quality of life, anxiety and depression in breast cancer patients[37 43, 47, 48]. In the other three RCTs, the patients reported the lower scores of anxiety or depression than control group($P < 0.05$)[50-52]. The limitations of other studies may explain the insignificant effects of the intervention, such as short follow-up time[53, 54], underrepresentation of the research subjects[55], that is, the lack of human-computer interaction in the system[30], the relatively normal degree of anxiety, depression, and psychological distress.

Psychological distress

Five studies reported inconsistent results concerning the effectiveness of Internet-based support interventions on psychological distress. In an RCT study of online expressive writing focused on self-compassion, participants in the intervention group reported significantly less body image-related distress and greater body appreciation than only expressive writing participants in the control group[50]. In one pretest-posttest design, which findings supported the positive effects of the Internet Cancer Support Group on psychological symptoms[38]. In the other three RCT concerning psychological education and group medical consultation, patients in the intervention group reported lower scores of psychological distress than the control group, but this difference was not significant[31 49 34].

Physical variables/symptoms

Fifteen studies reported on physical symptoms, including physical symptom distress, physical symptom severity, and prevalence or number of symptoms. All except one[40] which was conducted in China showed positive significant intervention effects. In four non-randomized studies and three RCT studies conducted in China, patients in the intervention group reported significantly improved symptoms of lymphedema[56], body image distress[46], fatigue symptoms [47 57], nausea and vomiting and other gastrointestinal discomfort symptoms[32, 44 57], and postoperative complications[42]. In the other six studies, three of them are RCTs[36 58 59], one is pilot RCT[60], and the other two are randomized pretest-posttest designs[38, 39], symptom distress was significantly lower in the intervention group, and there was a trend toward lower symptom severity and symptom prevalence. In an RCT study in Sweden, an interactive application-based symptom management intervention significantly reduced the prevalence of nausea, vomiting, feeling sad, loss of appetite, and constipation during neoadjuvant chemotherapy[61].

Social support

Two studies showed that the online interventions did not significantly improve patients' social support. In one RCT, Internet-based support intervention did not significantly change social support relative to the effect of usual care alone at 3 months[36]. However, the longer women used the Internet-based support program, the higher women perceived social support. One study focused on online support groups did not significantly improve patient perceived social support, which effectiveness appeared influenced by other factors, such as background and disease[38].

Self-efficacy

Self-efficacy was reported in six studies, of which three studies had significant positive intervention effects on it. In three RCTs conducted in China, concerning a breast cancer e-support program[36], a full-process information management system for breast cancer patients based on clinical decision support[62] and follow-up of innovative approaches based on WeChat platform[63], the intervention groups reported improved self-efficacy than control groups. In the other three RCTs, regarding a web-based expert support self-management program[33], a computer-based educational program[30], and the Internet Cancer Support Group[38], participants in the two groups showed no significant differences in self-efficacy.

DISCUSSION

This review examines the effectiveness of Internet-based support interventions for various health outcomes in patients with breast cancer. Due to the rapid growth of online interventions in this group in recent years, this review focuses on studies published over the past five years. A total of 35 studies were identified.

In the research field of supporting and caring for breast cancer, the content elements of Internet intervention include information support, symptom management, behavior management, psychological support, contact with medical staff and peer support. In some studies, information support or psychological support is provided to breast cancer patients only through Internet intervention[50, 52, 53]. However, in addition to providing information support or psychological support, most studies also provide comprehensive interventions such as symptom management, peer support and interaction with

medical staff. Breast cancer patients believe peer support is more useful in interacting with professionals than simply providing care information or psychological support[31, 47]. In addition, some studies based on evidence-based self-help intelligent information technology system can provide personalized customized information for patients, reduce the information burden unrelated to specific diagnosis or cancer stage, and to some extent solve the information limitation caused by the imbalance of health resources in various regions[31, 44, 47, 49, 54, 55, 61, 62.] In the future, it is necessary to organize multidisciplinary teams to develop elements and programs for personalized assessment and comprehensive intervention of Internet support interventions, and to involve breast cancer patients from end users in the process of intervention research and development. Based on the current situation of uneven resources of experts in various regions, the research and development of intelligent decision-making system can be explored to realize the customization and recommendation of personalized schemes.

The optimal duration of Internet-based support interventions remains to be explored. The limited duration of follow-up for Internet-based interventions hinders the long-term effects of such Internet-based support interventions. Most of the studies included in this review were followed up for no more than 6 months, and only 5 studies were followed up for 9, 12 or 18 months[30, 46, 57, 59, 63]. In current and future studies, there is a need to extend the periodicity and follow-up of the Internet support intervention to explore whether this intervention has long-term benefits for breast cancer. In addition, the charging and sustainability of the Internet support platform should be considered in the integration into the daily care of patients and needs to be further explored.

Quality of life is a major prognostic indicator for breast cancer patients, as diagnosis and treatment often result in significantly impaired quality of life[4]. Modern oncology disciplines unanimously believe that the quality of life of cancer patients is more representative of the cure effect and recovery status of the patient than the survival period and mortality rate[64]. Overall, Internet-based support interventions can improve the quality of life of breast cancer patients. Only one study does not support this view. On the one hand, the reason may be that the intervention content of this study is unitary, and only psychological and information intervention is carried out. The measurement standard of quality of life includes many aspects such as physiology, psychology and society, and is affected by many factors. On the other hand, affected by the differences in ethnic culture, people in different regions will have differences even if they use the same measurement scale.

The National Comprehensive Cancer Network (NCCN)[65] currently defines" psychological distress" as an unpleasant emotional experience of psychological, social, and/or spiritual nature caused by multiple factors, which can further aggravate physical symptoms, impact treatment compliance and quality of life. The negative emotions of cancer patients are affected by many factors, such as disease cognition, social support and physiological status. The results of this review show that the effect of Internet-based support intervention on reducing negative emotions of breast cancer patients is still controversial. It is suggested that future research needs to further analyze the promotion and obstacle factors of Internet psychological support intervention, and explore improvement strategies to better implement and promote network intervention[30, 34, 53].

This review included 15 studies that reported indicators related to physiical symptoms. Eight studies focused on the alleviation of physical symptoms in breast cancer patients, and the other seven studies focused on the severity of physical symptoms in patients. Few studies focused on the changes of other measurement indicators, such as the prevalence or number of physical symptoms. Indeed, the goal of symptom management is not necessarily to prevent symptoms, but to reduce their severity and impact on psychological distress and quality of life. Kearney et al[66] reported that monitoring and reporting of symptoms may also manifest as an increase in symptom severity depending on the time of assessment or patient self-report, better reflecting actual symptom burden and providing a clearer target for intervention.

Lack of social support for patients with chronic diseases including breast cancer is associated with poor emotional health, increased depressive symptoms and poor quality of life[67]. Besides, studies also have shown that improving self-efficacy can promote behavior change, improve self-management ability, quality of life, and confidence in coping with illness[68]. Although social support and self-efficacy are important factors influencing the quality of life of breast cancer patients, this review found that there are limited studies evaluating the impact of Internet-based support interventions on these two outcomes. Although social support and self-efficacy are important factors affecting the quality of life of breast cancer patients, this review found that the effect of Internet-based support intervention on these two measurement indicators is still controversial, which needs further discussion in future research.

Limitations

First, due to language restrictions, only published literature in Chinese and English from this review. Second, this review focused on only six health outcomes to test the effectiveness of Internet-based interventions; therefore, the amount of literature selected may have been reduced. To obtain a more comprehensive picture, future reviews could include other health outcomes such as supportive care needs, satisfaction with cancer treatment, and decisional conflict/pain. Again, the heterogeneity of the included studies in terms of sample and methodology, the different age and tumor stages of the study population, the differences in the content, modality, frequency, and duration of the interventions adopted by the studies, and the different measurement tools for the same outcome indicators did not lend themselves to a combined study; therefore, this review is only a descriptive study of the findings. Finally, some of the studies included in this review had small sample sizes[51, 53, 60]. The insignificant impact may be due to a lack of statistical power rather than a true intervention nullification.

Conclusion

The results of this review suggest that Internet-based support intervention can have a positive effect on patients with breast cancer, and can effectively improve the quality of life of patients. However, the effect of Internet-based support intervention on patients ' physical symptoms, social support, self-efficacy, anxiety, depression and other negative emotions is still controversial, which is worthy of further discussion in future intervention studies. In the future, it is necessary to standardize Internet-based support interventions (content, form, frequency, duration), formulate a unified evaluation index system, design larger sample, multi-center randomized controlled trials, and further explore the long-term intervention effect of Internet-based support nursing on breast cancer patients. Medical professionals can combine the existing or new Internet-based interventions with the clinical nursing path of breast cancer patients and their daily life self-management to improve the quality of life among breast cancer patients. With the participation of multidisciplinary teams and breast cancer patients, the research and development of intelligent decision-making system is explored to realize the customization and recommendation of personalized intervention programs.

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Contributors Yw H& Qq L: study design, data collection and analysis, drafting and revising the manuscript. FZ: supervision of study design, data collection and analysis, revising the manuscript. Jy S: supervision of study design, data collection and analysis, revising the manuscript.

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Ethics approval statement Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data Availability Statements Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

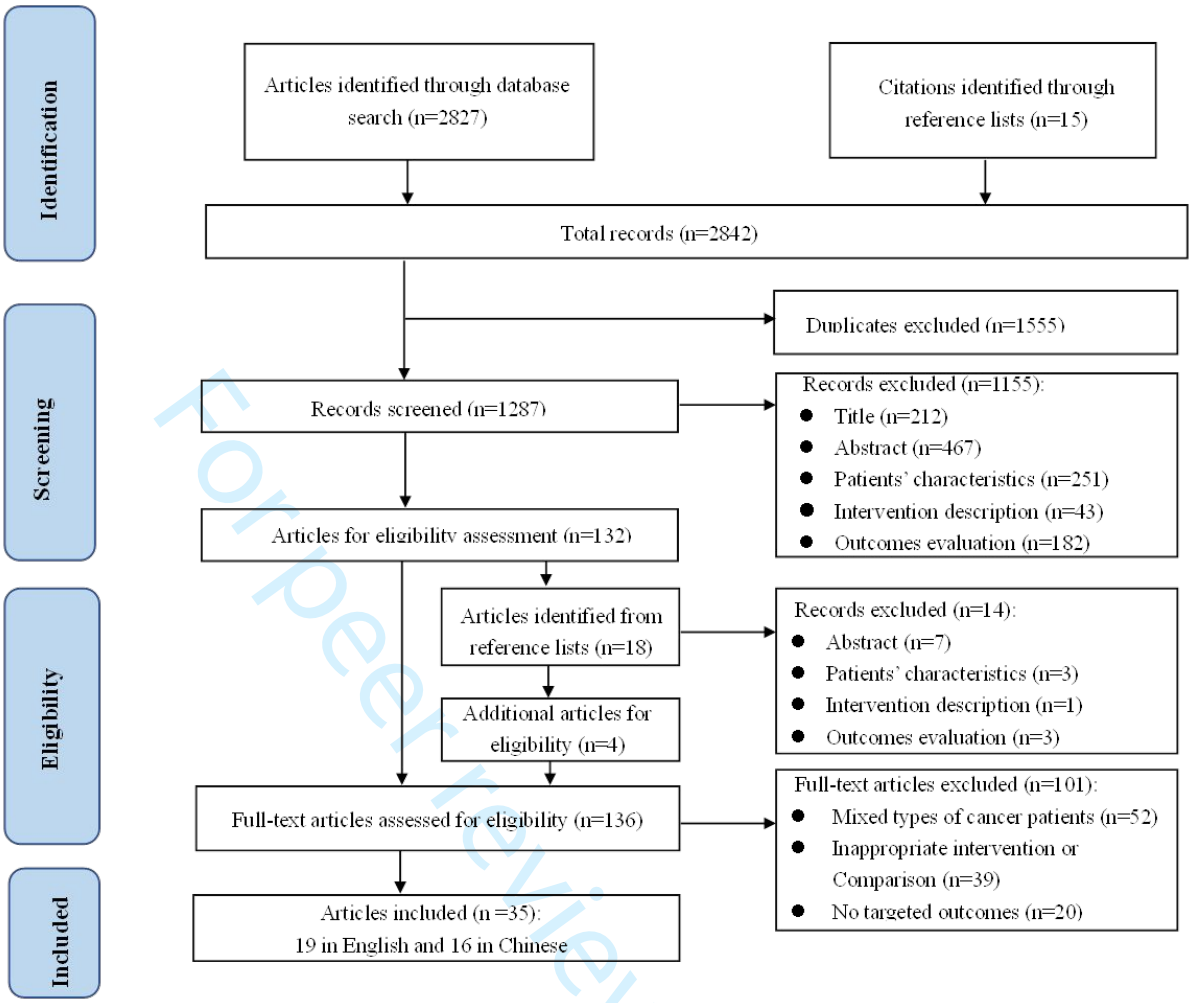

Fig. 1 Flowchart of Search and Selection Process

Table 1 Risk of Bias Assessment Tool for RCTs

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Quality rade
Im,2020[39]	+	?	?	+	+	+	+	B
Zhou,2019[37]	+	?	+	+	+	+	+	B
Visser,2018[34]	?	?	-	-	+	+	+	C
Zhou,2020[40]	+	+	+	?	+	+	+	B
Rosen,2018[35]	+	-	-	-	+	+	+	B
Foley,2016[53]	+	?	?	?	+	+	+	B
Sherman,2018[50]	+	?	?	?	+	+	+	B
Lally,2020[31]	+	?	?	?	+	+	+	B
Ventura,2017[30]	+	+	?	?	+	+	+	B
Admiraal,2017[49]	+	+	-	-	+	+	+	B
Korkmaz,2020[52]	+	?	?	?	+	+	+	B
Hou,2020[69]	+	+	+	+	+	+	+	A
Fjell,2020[61]	+	+	?	?	+	+	+	B
Villani,2018[51]	?	?	?	?	+	+	+	C
White,2018[55]	+	?	?	?	+	+	+	B
Zhu,2018[36]	+	+	?	+	+	+	+	B
Wheelock,2015[59]	+	?	?	?	+	+	+	B
Graetz,2018[60]	+	+	?	?	+	+	+	B
Egbring,2016[58]	+	+	?	?	+	+	+	B
Chee,2016[38]	+	?	?	+	+	+	+	B
Handa,2020[54]	+	?	?	?	+	+	+	B
Wang,2017[43]	+	?	?	?	+	+	+	B
Wang,2019[57]	?	?	?	?	+	+	+	C
Kim,2020[33]	+	?	?	?	+	+	+	B

Table 1 Risk of Bias Assessment Tool for RCTs

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Quality grade
Chen,2015[48]	+	?	?	?	+	+	+	B
Peng,2020[46]	?	?	?	?	+	+	+	C
Wang,2019[45]	+	?	?	?	+	+	+	B
Li,2018[44]	?	?	?	?	+	+	+	C
Liu,2019[63]	?	?	?	?	+	+	+	C
Du,2021[62]	+	?	?	?	+	+	+	B

Key: "+" =low risk of bias; "-" –high risk of bias; "?" – unclear risk of bias. Item 1: Random sequence generation; Item 2: Allocation concealment; Item3: Blinding of participants and personnel; Item 4: Blinding of outcome assessment; Item 5: Incomplete outcome data; Item 6: Selective outcome; Item 7: Other sources of bias

Table 2 Risk of Bias Assessment Tool for quasi-experimental studies

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Quality grade
Yue,2020[56]	Y	Y	N	Y	Y	N	Y	CT	Y	B
Zhou,2019[41]	Y	CT	Y	Y	Y	N	CT	CT	Y	B
Xu,2017[42]	Y	Y	Y	Y	Y	Y	CT	CT	Y	B
Dai,2017[32]	Y	CT	CT	Y	Y	Y	CT	CT	Y	B
Li,2017[47]	Y	CT	CT	Y	Y	Y	CT	CT	Y	B

Key: Y=yes, N=no, CT=cannot tell. Item 1: Was the causal relationship in the study clearly stated? Item 2: Was the baseline comparable between the groups? Item 3: Were the other measures received by the groups the same, except for the intervention to be validated? Item 4: Was a control group established? Item 5: Were multidimensional measures of outcome indicators performed before and after the intervention? Item 6: Was follow-up complete, and if not, were missing visits reported and measures taken to address them? Item 7: Were the outcome indicators measured in the same way for all study groups? Item 8: Were the measures of outcome indicators reliable? Item 9: Were the data analysis methods appropriate?

Table 3 Data abstraction of the included studies

Author/year	Country	Study Design	Size(I/C)	Intervention group			Control	Duration	Outcome indicators of interest
				Delivery	Content elements	personalized customization			
Im, et al[39] 2020	USA	RCT	49/66	Web	①⑤⑥	No	CAU	3 months	C
Zhou, et al[37] 2019	CHN	RCT	66/66	WeChat	①⑤⑥	No	CAU	12 weeks	B
Visser, et al[34] 2018	NL	RCT	50/59	APP	①⑤⑥	No	CAU	3 months	C
Zhou, et al[40] 2020	CHN	RCT	55/56	WeChat	①⑤⑥	No	CAU	6 months	AD
Rosen, et al[35] 2018	USA	RCT	55/57	APP	①④	No	Waiting list	8 weeks	A
Foley, et al [53]2016	IRL	RCT	26/13	APP	①	Yes	CAU	1 weeks	B
Sherman, et al[50] 2018	AUS	RCT	155/149	Web	④	No	Expressive writing＋CAU	NA	BC
Ventura, et al [30] 2017	SE	RCT	121/105	Support system	①⑤	No	CAU	9 months	BE
Lally, et al[31] 2020	USA	RCT	43/57	Web	①④⑥	Yes	CAU	12 weeks	C

Table 3 Data abstraction of the included studies

Author/year	Country	Study Design	Size(I/C)	Intervention group			Control	Duration	Outcome indicators of interest
				Delivery	Content elements	personalized customization			
Admiraal, et al[49] 2017	NL	RCT	69/69	Web	①④	Yes	CAU	12 weeks	AC
Korkmaz, et al [52] 2020	TR	3-arm RCT	24/24/24	Web	①	No	brochure education /CAU	1 month	AB
Hou, et al[69] 2020	TW	RCT	59/53	APP	①②③④⑤⑥	No	CAU	3 months	A
Fjell, et al[61] 2020	SE	RCT	75/74	APP	①②⑤	Yes	CAU	2 weeks	AD
Villani, et al[51] 2018	Ita	RCT	14/15	Web	④⑤⑥	No	CAU	3 months	B
White, et al[55] 2018	AUS	RCT	177/202	Web	①④	Yes	CAU	6 months	AB
Zhu, et al[36] 2018	CHN	RCT	57/57	APP	①⑤⑥	No	CAU	3 months	ADEF
Wheelock, et al[59] 2015	USA	RCT	41/59	Support system	①②⑤	No	CAU	18 months	D
Graetz, et al[60] 2018	USA	RCT	25/23	APP	②⑤	Yes	App (no reminders)	8 weeks	D
Egbring,et al[58] 2016	Swit	RCT	44/46/49	APP	①②⑤	No	CAU/ App（No reviewed data with a physician.）	42 days	D

Table 3 Data abstraction of the included studies

Author/year	Country	Study Design	Size(I/C)	Intervention group			Control	Duration	Outcome indicators of interest
				Delivery	Content elements	personalized customization			
Chee, et al[38] 2016	USA	RCT	30/35	Web	①⑤⑥	No	CAU	1 month	ACDEF
Kim, et al[33] 2020	KP	RCT	30/30	APP	①③⑤	No	CAU	6 months	F
Handa, et al[54] 2020	JPN	RCT	52/50	APP	①②⑤	Yes	brochure education	12 weeks	B
Wang, et al[43] 2017	CHN	RCT	318/320	APP	①⑤⑥	No	CAU	2 weeks	AB
Wang, et al[57] 2019	CHN	RCT	74/75	WeChat	①⑤⑥	No	CAU	9 months	D
Chen, et al[48] 2015	CHN	RCT	45/45	Web	①⑤⑥	No	CAU	3 months	AB
Peng, et al[46] 2020	CHN	RCT	58/59	WeChat	①⑤⑥	No	CAU	12 months	AC
Wang, et al[45] 2019	CHN	RCT	44/44	WeChat	①⑤⑥	No	CAU	6 months	AD
Li, et al[44] 2018	CHN	RCT	60/60	APP	①②⑤	Yes	CAU	2 weeks	AD
Liu, et al[63] 2019	CHN	RCT	50/50	WeChat	①⑤⑥	No	CAU	12 months	F
Du, et al[62] 2021	CHN	RCT	40/40	Support system	①②⑤	Yes	tel	6 months	F
Yue, et al[56] 2020	CHN	Quasi-experiment study	146/148	WeChat	①⑤⑥	No	CAU	12 months	D

Table 3 Data abstraction of the included studies

Author/year	Country	Study Design	Size(I/C)	Intervention group			Control	Duration	Outcome indicators of interest
				Delivery	Content elements	personalized customization			
Zhou, et al[41] 2019	CHN	Quasi-experiment study	145/153	WeChat	①⑤⑥	No	CAU	6 months	A
Xu, et al[42] 2017	CHN	Quasi-experiment study	75/75	APP +WeChat	①②⑤	No	CAU	2 months	AD
Dai, et al[32] 2017	CHN	Quasi-experiment study	42/47	WeChat	①⑤⑥	No	Extended care (telephone + home follow-up)	6 months	AD
Li, et al[47] 2017	CHN	Quasi-experiment study	58/48	WeChat	①③⑤⑥	Yes	CAU	4 weeks	ABD

Abbreviations: ①Information support; ②Symptom management; ③Behavior management; ④Psychological support; ⑤Communication with health professionals via mail/web; ⑥Peer support; CHN, china; USA, the United States of America; NL, Netherlands; IRL, Ireland; AUS, Australia; SE, *Sweden*; TR, Turkey; TW, Taiwan; Ita, *Italy*; Swit, Switzerland; KP, North Korea ; JPN：japan; Web：website; APP: Application on the smart phone; CAU, Care As Usual; C, Control group; I, Intervention group; NA：Not Available；RCT, randomized control trial **Outcome indicator:** A, quality of life; B, Anxiety and depression; C, Psychological distress; D, Physical variables; E, Social support; F ,Self-efficacy

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Table 2: Search strategy in MEDLINE (PubMed)

1. Breast Neoplasms[MeSH Terms])
2. (breast cancer*[Title/Abstract])) OR (breast neoplasm*[Title/Abstract])) OR (breast carcinoma*[Title/Abstract]))
3. #1 OR #2
4. Internet[MeSH Terms]
5. ((((((((((Tele-medicine[MeSH Terms]) OR (online*[Title/Abstract])) OR (telehealth[Title/Abstract])) OR (e-health[Title/Abstract])) OR (m-health[Title/Abstract])) OR(e-intervention[Title/Abstract])) OR (e-technology[Title/Abstract])) OR (computer[Title/Abstract])) OR (mobile application[Title/Abstract])) OR (mobile device[Title/Abstract])) OR (social media[Title/Abstract])) OR (WeChat[Title/Abstract])))
6. #4 OR #5
7. intervention[Title/Abstract]
8. ((((((((((Patient Education as Topic[MeSH Terms])) OR (support[Title/Abstract])) OR (teaching[Title/Abstract])) OR (instruction*[Title/Abstract])) OR (program*[Title/Abstract])) OR (psychoeducat*[Title/Abstract])) OR (self-management[Title/Abstract])) OR (Social Support[Title/Abstract])) OR (support system*[Title/Abstract])) OR (support group*[Title/Abstract]))
9. #7 OR #8
10. #3 AND #6 AND #9
11. limit 12 to english language

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 3-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Page 5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Page 6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Page 6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 16
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Page 7-9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Page 17-18
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Page 19-22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n/a
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page 11-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page 13-14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Page 13

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Effectiveness of Internet-based Support Interventions on Breast Cancer Patients : A Systematic Review and Narrative Synthesis

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Title page

Title of the article Effectiveness of Internet-based Support Interventions on Breast Cancer Patients:A Systematic Review and Narrative Synthesis

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ABSTRACT

Objective To identify the elements of Internet-based support interventions and assess their effectiveness at reducing psychological distress, anxiety and/or depression, physical variables (prevalence, severity and distress from physical symptoms), and improving quality of life, social support, and self-efficacy among breast cancer patients.

Design Systematic review and narrative synthesis

Data sources Web of Science, Cochrane Library, PubMed, Medline, PSycINFO, CINAHL, CNKI, Wanfang and VIP from over the past five years of each database to June 2021.

Eligibility criteria for study selection Included were randomized controlled trials (RCTs) or quasi-experimental (QE) studies focusing on Internet-based support interventions in breast cancer patients.

Data extraction and synthesis Reviewers independently screened, extracted data and assessed risk of bias (Cochrane Collaboration' risk of bias tool, Joanna Briggs Institute reviewer's manual). Narrative synthesis included the effect and elements of Internet-based support interventions for women with breast cancer.

Results Out of 2842 articles, 136 qualified articles were preliminarily identified. After further reading the full text, 35 references were included, including 30 randomized controlled trials and 5 quasi-experimental studies. Internet-based support interventions have demonstrated positive effects on women's quality of life and physical variables, but inconsistent effectiveness has been found on psychological distress, symptoms of anxiety and/or depression, social support, and self-efficacy.

Conclusions Internet-based support interventions are increasingly being used as clinically promising interventions to promote the health outcomes of breast cancer patients. Future research needs to implement more rigorous experimental design and include sufficient sample size to clarify the effectiveness of this Internet-based intervention.

PROSPERO registration number CRD42021271380.

Keywords: breast cancer;Internet; support; effectiveness; systematic review

Strengths and limitations of this study

- ► It is important to identify the elements of Internet-based support interventions and to understand whether these interventions positively improve breast cancer patients' health outcomes. Comprehensive search using a sensitive search strategy identified a lot of potential correlation research.
- ► Due to the differences in research subjects, intervention contents, intervention programs, outcome indicators, and measurement instruments, no data synthesis was conducted for meta-analysis, and only narrative analysis was conducted.
- ► There is insufficient evidence to determine whether any component combination is superior to other component combinations in improving the quality of life.

INTRODUCTION

Breast cancer is currently the most common malignant tumor in women worldwide [1]. World Health Organization(WHO) data show that the number of new cases of breast cancer in 2020 is as high as 2.26 million, exceeding lung cancer for the first time, becoming the world's highest incidence of cancer[2]. The treatment of breast cancer patients is based on the comprehensive treatment of surgery, supplemented by chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and other treatment methods. As the health system's effectiveness in early diagnosis and treatment has improved, the number of breast cancer survivors has also increased significantly[3].

However, the diagnosis and treatment of breast cancer bring patients varying degrees of treatment toxicities in the short term, such as pain, limited limb function, hair loss, nausea and vomiting, bone marrow suppression, and long-term physical and psychological distress symptoms such as impaired body image, fatigue, sleep disturbance, anxiety and depression, which seriously affect the quality of life[4-6]. The importance of supporting patients adequately regarding symptoms resulting from diagnosis and treatment has been widely recognized [7] . However, there are still many female breast cancer patients who report unmet supportive care needs, and these needs are mostly in the health system/information and psychology fields [8 9]. Besides, the patient's symptom distress, self-efficacy, and social support are three interrelated factors that affect a person's ability to cope with chronic diseases[10]. All the above may lead to poor quality of life for patients with breast cancer.

The survival rate of breast cancer is expected to continue to increase, leading to an increase in the

number of patients requiring long-term care: this poses a challenge for the patients themselves, their families, and oncology services. However, geographical distance restrictions and scheduling issues challenge the feasibility of clinical face-to-face supportive care interventions [11].

At present, medical personnel can provide customized supportive care for patients with the Internet as the carrier and information technology as the means (including mobile communication technology, cloud computing, Internet of Things, big data, etc.), which is also increasingly favored by cancer patients [12 13]. Internet-based support interventions are defined as smartphones and tablets (including apps), websites, social media and other mobile devices-delivered support programs to provide information and facilitate communication regarding self-care management and adverse effects related to toxicities owing to breast cancer therapy[7 14 15].

Internet-based support interventions often take the form of multi-modal interventions, including information support, symptom management, behavior management, psychological support, Communication/Interaction with health professionals and peer support. In order to meet the information and support needs, in the past few years, health care providers have cooperated with information technology professionals to develop self-guided psycho-educational or educational websites or APP[16-20], e-health support systems[21-23] in the field of cancer. In the area of symptom management research, Internet-based support interventions include evidence or knowledge on self-management strategies[23 24], symptom self-reporting[22 25], symptom warning combined with risk rating assessment tools and tailored recommendations[23 25-27]. Internet-based psychological support interventions include self-directed and expert-supported psychological diagnosis, treatment and counseling, are important to help breast cancer patients transition from treatment to recovery [16 19 20 24 28-34]. In the area of symptom management research, Internet-based support interventions include self-report aromatase inhibitor compliance[25 35], keeping a health diary, self-diagnose lifestyle and receiving information about exercise and rehabilitation diet and nutrition from APP modules[24] or health care professionals[36 37]. Internet-based forms of peer support interventions include the provision of breast cancer survivor videos [16 17 34], support group forums or discussion boards [16 17 24 30 38 39], group medical counseling[40], and online and offline recovery volunteer support activities[41 42].

Previous original studies have measured the effectiveness of Internet-based support interventions in cancer patients on anxiety and/or depression[18 29], psychological distress[43 44], social support[45], physical variables[46], and quality of life[47 48]. Among these outcomes of interest, physical variables refer to the

prevalence, severity and distress from physical symptoms[49]. Besides, more evidence is needed. In this fast-developing research field, it is important to regularly recapitulate its status. In addition, China is the world's most populous country, breast cancer is one of the most common malignant tumors in Chinese women[50]. This article integrates articles published in Chinese or English to help understand the impact of Internet-based support interventions on breast cancer patients at the global level[45].

This systematic review aims to identify the elements of Internet-based support interventions and assess their effectiveness at reducing psychological distress, anxiety and depression, physical variables, and improving quality of life, social support, and self-efficacy among breast cancer patients.

METHODS

We performed a systematic review based on PRISMA guidelines, and it was registered in PROSPERO (CRD 42021271380) from https://www.crd.york.ac.uk/PROSPERO/display_ record. php?RecordID= 271380.

Search strategy

Seven electronic databases were searched: Web of Science, Cochrane Library, PubMed, Medline, PSycINFO, CINAHL, CNKI, Wanfang and VIP. We searched the articles from over the past five years of each database to June 2021. (see supplemental file)The search keywords included “breast neoplasm OR breast cancer” AND “Telemedicine OR online OR Internet OR connected health OR telehealth OR e-health OR m-health OR e-intervention OR e-technology OR computer OR mobile application OR mobile device OR social media OR WeChat” AND “patient education OR intervention OR support OR teaching OR instruction* OR program* OR psychoeducat* OR self-management OR Social Support OR support system* OR support group*”. (Full details of the search strategy employed with each database are detailed in online supplemental file).

Inclusion and Exclusion Criteria

In this systematic review, we included the following: (1)The population is adult women with breast cancer patients, (2)Studies about Internet-based support interventions, defined as smartphones and tablets (including apps), website, social media and other mobile devices-delivered support programs to provide information and facilitate communication regarding self-management and adverse effects

related to toxicities owing to breast cancer therapy, (3)All intervention study types including randomized controlled trials or quasi-experimental intervention studies were considered,(4) Outcome variables in the study included one of the following, such as psychological distress, anxiety and/or depression, physical variables, social support, self-efficacy and quality of life, and (5) Articles were written in English or Chinese.

Studies were excluded for the following reasons: (1) if they focused on Internet-based support interventions related to other types of cancer, (2) Study types include review, non-clinical study, meta-analysis, etc, (3) The full text cannot be obtained; (4) Repeated publications.

Study selection and data extraction

All stages of study selection, data extraction was conducted by two researchers independently, and disagreements were resolved by consultation with a third researcher. For included studies, the following data were extracted with a predetermined data extraction form, including study characteristics (author(s), country and year of publication), sample size, intervention characteristics and outcome characteristics. Missing data would be obtained from authors by email, if possible.

Data synthesis

The data synthesis was undertaken following CRD's guidance[51]. This study follows the narrative synthesis method of Popay *et al*, and conducts narrative synthesis in a systematic and transparent way, focusing on the effect and content elements of intervention measures[52].

Assessment of risk of bias

The quality of RCTs studies was assessed using the Cochrane Collaboration' risk of bias tool [53]. This tool rates 7 domains as having a low, unclear, or high risk of bias. These domains consist of sequence generation, allocation concealment, participants' and study personnel's blinding; outcome assessment blinding; outcome data completeness; selective outcomes' reporting; and other threats to validity, including intervention contamination, baseline imbalance, and carry-over effect in cross-over trials). In addition, we used the Joanna Briggs Institute reviewer's manual to evaluate the risk of bias of quasi-experimental studies[54]. The overall quality of the quasi-experimental research is evaluated from 9 items including causality, baseline, intervention, control, outcome index measurement, follow-up and

analysis.

Patient and Public Involvement

No patient involved.

RESULTS

Selection of studies

A total of 2842 references were obtained through database retrieval and reference tracing. After reading the titles and abstracts to exclude duplicates, 136 references were obtained through preliminary screening. After further reading the full text, 35 references were finally included per all inclusion and exclusion criteria established for the systematic review (see figure 1).

Study characteristics and risk of bias

The quality appraisal of the 35 articles is shown in Table 1 and Table 2, and the Characteristics of the included studies are summarized in Table 3 and Table 4. A total of 35 articles were included in this literature review. Sixteen studies were undertaken in mainland China, six in the United States, two in the Netherlands, two in Australia, two in Sweden, One study each in Taiwan, Turkey, Switzerland, Italy, Japan, Korea and Ireland. Thirty study designs were RCTs, the other five study designs were quasi-experimental studies.

The delivery modes of Internet-based support intervention include website platform (n=9), mobile application program (n=13), WeChat platform (n=11), a full-process information manage -ment system (n=1), a web-based computer system (n=1), a computer-based programme (n=1). There are 12 articles on tailored interventions.

Description of participants

The 35 studies consisted of 5368 patients. The participant sample sizes ranged from 29 to 638 participants. The mean ages ranged from 41.1~59.9 years. Seven studies analyzed patients with locally or locally advanced cancer (stages I-III), whereas three studies only included cancer patients with stages I-II [16 21 55]. Five studies included solely patients who had completed cancer treatment during their follow-up[17 28 29 36 40], twenty-seven studies only included patients during treatment and four studies

patients in all treatment phases[28 38 40 56].

Content elements of Internet-based support Intervention Internet-based support

Internet-based support intervention contained six elements : (1) Information support (n=33) [16-21 24 26-32 36-42 55-63]: including breast cancer disease and treatment knowledge, self-management strategies for physical symptoms and recovery, available aid resources or organizational service information, expert consultation or outpatient consultation arrangements, and expert lectures. (2) Symptom management (n=10) [22-27 58-60 62]: including patients' self-assessment and monitoring of their physiological symptoms, medical staff' s self-management guidance for patients, automatic feedback of symptom management APP or system, and symptom early warning processing combined with clinical risk algorithm. (3) Behavior management (n=5) [24 25 35-37]: including medication compliance management, limb functional exercise compliance management, infusion port maintenance, healthy lifestyle management. (4) Psychological support (n=11) [16 19 20 24 28-34]: divided into self-guided and professional guidance/support. Self-guided psychological support is realized by the corresponding modules of intervention independently completed by breast cancer patients. Professionally guided psychological support is conducted through e-mail interaction with the therapists or online interaction with groups of other breast cancer patients. It includes negative emotional self-assessment or monitoring, cognitive behavioral therapy, mindfulness training, expressive writing to alleviate physical image distress, psychological education, cognitive behavioral therapy, etc. (5) Interaction with health care professionals (n=25) [17 22-24 26 29 30 32 34-42 55-62]: The main form is that breast cancer patients directly contact with health professionals and ask questions, health professionals give advice or emotional support to breast cancer patients. (6) Peer support (n=20) [16-18 24 29-32 34 35 37-42 55-57 59 61]: Support information, emotional support and rehabilitation experience sharing are mainly provided by other breast cancer patients.

Intervention providers were mainly nurses or physicians, a few multidisciplinary teams [24 57 58] brought together by physicians, nurses, dietitians, physiatrists, psychotherapists, and information engineers. In terms of intervention sample size, due to the study conditions, most of the interventions were conducted in small samples, with single-group sample sizes mostly concentrated in 30-60 individuals, and only six studies[20 26 29 38 39 58] with sample sizes of 61-100, and only seven studies[19 21 33 39 42 57 59] with sample sizes of more than 100, while only three studies[25 31 34] with sample sizes of less than 30.

Based on the duration of intervention, 22 intervention studies focused on the period from breast cancer diagnosis to radiotherapy and chemotherapy, and the duration of intervention was mostly 3-6 months [16 17 19]

[23 24 27 29 30 32 34 55 57 61]. Only two studies [21 39] lasted nine months, while the intervention duration of the other seven studies[18 31 37 58-60 62] ranged from two weeks to eight weeks.

Interventions and associated outcomes

In this systematic review, the Internet-based support interventions were evaluated for their effectiveness on Quality of life, anxiety and/or depression, psychological distress, physical variables, social support, and self-efficacy. The measurement scales are shown in Table 3 and 4.

Quality of life

Eighteen studies reported on quality of life with significant positive intervention effects reported by seventeen [17-19 24 26 28 30 32 34 37 41 55-61]. In seven RCTs and four quasi-experimental studies conducted in China, the quality of life score of the intervention group was higher than that of the control group [17 29 30 32 37 41 57-61]. A web-based tailored psycho-educational intervention for breast cancer patients who completed curative-intent primary treatment reported that improvements in distress, distress-related problems (practical, family/social, emotional, religious/spiritual, and physical problems) and quality of life were observed in both study groups but no significant differences [20].

Anxiety and/or depression

Eleven studies found inconsistent results regarding the impact of the Internet-based Support Interventions on symptoms of anxiety and/or depression. The results of six RCTs and one quasi-experimental study included in this review showed that Internet-based support interventions significantly improved anxiety and depression in breast cancer patients [18 29 33 34 37 59 61]. The limitations of other studies may explain the insignificant effects of the intervention, such as short follow-up time [27 31], underrepresentation of the research subjects [19], the lack of human-computer interaction in the system[21], the average level of anxiety and depression among participants at baseline was within the normal range for non-clinical samples.

Psychological distress

Five studies reported inconsistent results concerning the effectiveness of Internet-based support interventions on psychological distress. In an RCT study of online expressive writing focused on self-compassion, participants in the intervention group reported significantly less body image-related

distress and greater body appreciation than only expressive writing participants in the control group [33]. In one pretest-posttest design, which findings supported the positive effects of the Internet Cancer Support Group on psychological symptoms [56]. In the other three RCTs concerning psychological education and group medical consultation, patients in the intervention group reported lower scores of psychological distress than the control group, but this difference was not significant[16 20 40].

Physical variables

Seventeen studies reported on physical variables, including the prevalence, severity and distress from physical symptoms**.** All except two studies [30 58] which was conducted in China showed positive significant intervention effects. In five non-randomized studies and four RCT studies conducted in China, patients in the intervention group reported significantly improved symptoms of lymphedema[42 57], body image distress[41], fatigue symptoms[37 39], nausea and vomiting and other gastrointestinal discomfort symptoms[39 55 60], postoperative complications[58] and the prevalence of adverse drug reaction[59]. In the other six studies, three of them are RCTs [17 22 62], and the other two are randomized pretest-posttest designs [38 56], symptom distress was significantly lower in the intervention group, and there was a trend toward lower symptom severity and symptom prevalence. In an pilot RCT in USA [25], Symptom burden increase was higher for the App group compared to the App+Reminder group but did not reach statistical significance. In an RCT study in Sweden, an interactive application-based symptom management intervention significantly reduced the prevalence of nausea, vomiting, loss of appetite, and constipation during neoadjuvant chemotherapy [26].

Social support

Two studies showed that the online interventions did not significantly improve patients' social support. In one RCT, Internet-based support intervention did not significantly change social support relative to the effect of usual care alone at 3 months [17]. However, the longer women used the Internet-based support program, the higher women perceived social support. One study focused on online support groups did not significantly improve patient perceived social support, which effectiveness appeared influenced by other factors, such as socio-demographic background and disease [56].

Self-efficacy

Self-efficacy was reported in six studies, of which three studies had significant positive intervention effects on it. In three RCTs conducted in China, concerning a breast cancer e-support program[17], a full-process information management system for breast cancer patients based on clinical decision support[23] and follow-up of innovative approaches based on WeChat platform[35], the intervention groups reported improved self-efficacy than control groups. In the other three RCTs, regarding a web-based expert support self-management program [36], a computer-based educational program [21], and the Internet Cancer Support Group [56], participants in the two groups showed no significant differences in self-efficacy.

DISCUSSION

This review examines the effectiveness of Internet-based support interventions for various health outcomes in patients with breast cancer. Due to the rapid growth of online interventions in this group in recent years, this review focuses on studies published over the past five years. A total of 35 studies were identified.

In the research field of supporting and caring for breast cancer, the content elements of Internet intervention include information support, symptom management, behavior management, psychological support, contact with medical staff and peer support. In some studies, information support or psychological support is provided to breast cancer patients only through Internet intervention [18 31 33]. However, in addition to providing information support or psychological support, most studies also provide comprehensive interventions such as symptom management, peer support and interaction with medical staff. Breast cancer patients believe peer support [40 64] or interacting with professionals [17 20 21 36 62] is more useful than simply providing care information or psychological support. This suggests that multi-element Internet-based support interventions are favored by breast cancer patients.

In addition, some studies based on evidence-based self-help intelligent information technology system can provide personalized customized information for patients, reduce the information burden unrelated to specific diagnosis or cancer stage, and to some extent solve the information limitation caused by the imbalance of health resources in various regions [16 19 20 23 26 27 37 60]. In the future, it is necessary to organize multidisciplinary teams to develop elements and programs for personalized assessment and comprehensive intervention of Internet support interventions, and to involve breast cancer patients from end users in the process of intervention research and development. Based on the

current situation of uneven resources of experts in various regions, the research and development of intelligent decision-making system can be explored to realize the customization and recommendation of personalized schemes.

For patients who prioritize the use of the Internet to meet the information and support needs, adding face-to-face contact interventions may be insignificant and have little impact on outcomes. For patients who prioritize face-to-face contact as a source of information and support, adding face-to-face contact into Internet intervention research may be important, but this may reduce the explanatory power of the intervention effect of Internet intervention research itself [21].

The optimal duration of Internet-based support interventions remains to be explored. The limited duration of follow-up for Internet-based interventions hinders the long-term effects of such Internet-based support interventions. Most of the studies included in this review were followed up for no more than 6 months, and only 5 studies were followed up for 9, 12 or 18 months[21 22 35 39 41]. In current and future studies, there is a need to extend the periodicity and follow-up of the Internet support intervention to explore whether this intervention has long-term benefits for breast cancer. In addition, the charging and sustainability of the Internet support platform should be considered in the integration into the daily care of patients and needs to be further explored.

Quality of life is a major prognostic indicator for breast cancer patients, as diagnosis and treatment often result in significantly impaired quality of life [4]. Modern oncology disciplines unanimously believe that the quality of life of cancer patients is more representative of the cure effect and recovery status of the patient than the survival period and mortality rate[65]. Overall, Internet-based support interventions can improve the quality of life of breast cancer patients. Only one study does not support this view [20], and the study was a web-based tailored psycho-educational program. Patients were not guided throughout all the problem solving therapy phases and may have been exposed too little to the content of the program to solicit any observable effect, which were their explanation for why their intervention may not have significantly impacted quality of life [20]. On the one hand, the reason may be that the intervention content of this study is unitary, and only psychological and information intervention is carried out. The measurement standard of quality of life includes many aspects such as physiology, psychology and society, and is affected by many factors. On the other hand, affected by the differences in ethnic culture, people in different regions will have differences even if they use the same measurement scale.

The National Comprehensive Cancer Network (NCCN) [66] currently defines" psychological distress" as an unpleasant emotional experience of psychological, social, and/or spiritual nature caused by multiple factors, which can further aggravate physical symptoms, impact treatment compliance and quality of life. The negative emotions of cancer patients are affected by many factors, such as disease cognition, social support and physiological status. The results of this review show that the effect of Internet-based support intervention on reducing negative emotions of breast cancer patients is still controversial. It is suggested that future research needs to further analyze the promotion and obstacle factors of Internet psychological support intervention, and explore improvement strategies to better implement and promote network intervention [21 31 40].

This review included 17 studies that reported indicators related to physical symptoms. Eight studies focused on the alleviation of physical symptoms distress in breast cancer patients, and the other eight studies focused on the severity of physical symptoms in patients. Few studies focused on the changes of other measurement indicators, such as the prevalence or number of physical symptoms. Indeed, the goal of symptom management is not necessarily to prevent symptoms, but to reduce their severity and impact on psychological distress and quality of life. Kearney et al[67] reported that monitoring and reporting of symptoms may also manifest as an increase in symptom severity depending on the time of assessment or patient self-report, better reflecting actual symptom burden and providing a clearer target for intervention.

Lack of social support for patients with chronic diseases including breast cancer is associated with poor emotional health, increased depressive symptoms and poor quality of life[68]. Besides, studies also have shown that improving self-efficacy can promote behavior change, improve self-management ability, quality of life, and confidence in coping with illness[69].–Although social support and self-efficacy are important factors affecting the quality of life of breast cancer patients, this review found that the effect of Internet-based support intervention on these two measurement indicators is still controversial, which needs further discussion in future research.

Limitations

First, due to language restrictions, only published literature in Chinese and English from this review. Second, this review focused on only six health outcomes to test the effectiveness of Internet-based interventions; therefore, the amount of literature selected may have been reduced. To obtain a more

comprehensive picture, future reviews could include other health outcomes such as supportive care needs, satisfaction with cancer treatment, and decision conflict/distress. Again, the heterogeneity of the included studies in terms of sample and methodology, the different age and tumor stages of the study population, the differences in the content, modality, frequency, and duration of the interventions adopted by the studies, and the different measurement tools for the same outcome indicators did not lend themselves to a combined study; therefore, this review is only a descriptive study of the findings. Finally, some of the studies included in this review had small sample sizes [25 31 34]. The insignificant impact may be due to a lack of statistical power rather than a true intervention nullification.

Conclusion

The results of this review suggest that Internet-based support intervention can have a positive effect on patients with breast cancer, and can effectively improve the quality of life of patients. However, the effect of Internet-based support intervention on patients' physical symptoms, social support, self-efficacy, anxiety, depression and other negative emotions is still controversial, which is worthy of further discussion in future intervention studies. In the future, it is necessary to standardize Internet-based support interventions (content, form, frequency, duration), formulate a unified evaluation index system, design larger sample, multi-center randomized controlled trials, and further explore the long-term intervention effect of Internet-based support nursing on breast cancer patients. Medical professionals can combine the existing or new Internet-based interventions with the clinical nursing path of breast cancer patients and their daily life self-management to improve the quality of life among breast cancer patients. With the participation of multidisciplinary teams and breast cancer patients, the research and development of intelligent decision-making system is explored to realize the customization and recommendation of personalized intervention programs.

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Contributors Yw H& Qq L: study design, data collection and analysis, drafting and revising the manuscript. FZ: supervision of study design, data collection and analysis, revising the manuscript. Jy S: supervision of study design, data collection and analysis, revising the manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval statement Not required.

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Data Availability Statements Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Table 1 Risk of Bias Assessment Tool for RCTs

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7
Lally,2020[16]	+	?	?	?	+	+	+
Zhu,2018[17]	+	+	?	+	+	+	+
Korkmaz,2020[18]	+	?	?	?	+	+	+
White,2018[19]	+	?	?	?	+	+	+
Admiraal,2017[20]	+	+	-	-	+	+	+
Ventura,2017[21]	+	+	?	?	+	+	+
Wheelock,2015[22]	+	?	?	?	+	+	+
Du,2021[23]	+	?	?	?	+	+	+
Hou,2020[24]	+	+	+	+	+	+	+
Graetz,2018[25]	+	+	?	?	+	+	+
Fjell,2020[26]	+	+	?	?	+	+	+
Handa,2020[27]	+	?	?	?	+	+	+
Rosen,2018[28]	+	-	-	-	+	+	+
Zhou,2019[29]	+	?	+	+	+	+	+
Zhou,2020[30]	+	+	+	?	+	+	+
Foley,2016[31]	+	?	?	?	+	+	+
Wang,2019[32]	+	?	?	?	+	+	+
Sherman,2018[33]	+	?	?	?	+	+	+
Villani,2018[34]	?	?	?	?	+	+	+
Liu, 2019[35]	?	?	?	?	+	+	+
Kim,2020[36]	+	?	?	?	+	+	+
Im,2020[38]	+	?	?	+	+	+	+
Wang,2019[39]	?	?	?	?	+	+	+
Visser,2018[40]	?	?	-	-	+	+	+
Peng,2020[41]	?	?	?	?	+	+	+

Table 1 Risk of Bias Assessment Tool for RCTs

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7
Chee,2016[56]	+	?	?	+	+	+	+
Wang,2017[59]	+	?	?	?	+	+	+
Li,2018[60]	?	?	?	?	+	+	+
Chen,2015[61]	+	?	?	?	+	+	+
Egbring,2016[62]	+	+	?	?	+	+	+

Key: "+" =low risk of bias; "-" –high risk of bias; "?" – unclear risk of bias. Item 1: Random sequence generation; Item 2: Allocation concealment; Item3: Blinding of participants and personnel; Item 4: Blinding of outcome assessment; Item 5: Incomplete outcome data; Item 6: Selective outcome; Item 7: Other sources of bias

Table 2 Risk of Bias Assessment Tool for quasi-experimental studies

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9
Li,2017[37]	Y	CT	CT	Y	Y	Y	CT	CT	Y
Yue,2020[42]	Y	Y	N	Y	Y	N	Y	CT	Y
Dai,2017[55]	Y	CT	CT	Y	Y	Y	CT	CT	Y
Zhou,2019[57]	Y	CT	Y	Y	Y	N	CT	CT	Y
Xu,2017[58]	Y	Y	Y	Y	Y	Y	CT	CT	Y

Key: Y=yes, N=no, CT=cannot tell. Item 1: Was the causal relationship in the study clearly stated? Item 2: Was the baseline comparable between the groups? Item 3: Were the other measures received by the groups the same, except for the intervention to be validated? Item 4: Was a control group established? Item 5: Were multidimensional measures of outcome indicators performed before and after the intervention? Item 6: Was follow-up complete, and if not, were missing visits reported and measures taken to address them? Item 7: Were the outcome indicators measured in the same way for all study groups? Item 8: Were the measures of outcome indicators reliable? Item 9: Were the data analysis methods appropriate?

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Lally, 2020[16] USA	43/57	Name:Tailored self-mannagement psychoeducational program Structure: Five module of supportive oncology-based psychoeducation and cognitive-behavioral techniques, coping skills, problem solving, communication strategies, and validation.	Delivery: Web Self-guided:√ Automated reminders:× Face-to-face contact: × Tailored: √	Information support; Psychological support; Peer Support.	12 weeks	1.Psychological distress （ DT ， CES-D，IES）	No significant outcomes.
Zhu, 2018[17] China	57/57	Name:Mobile Breast Cancer e-Support Program Structure: Learning Forum (information related to breast cancer disease and symptom management), Discussion Forum (anonymous support group), Consult an Expert (online consultation), and Personal Stories (interview stories of breast cancer survivors).	Delivery: APP Self-guided:× Automated reminders:× Face-to-face contact: × Tailored:×	Information support; Interaction with health care professionals; Peer Support;	3 months	1.QOL (FACT-B) 2.Symptom distress(MDASI) 3.Self-efficacy(SICPA) 4. Social support(MSPSS) 5.Anxiety and depression(HADS)	1. 6.64; 95% CI 0.77-12.50; P=0.03, d=0.46 2. −0.73; 95% CI −1.35 to −0.11; P=.002;d=−0.51 3. 21.05; 95% CI 1.87-40.22; P=0.03; d=0.53 4. No significant outcomes. 5. No significant outcomes.
Korkmaz, 2020[18] Turkey	24/24/ 24	Name: A web-based education program Structure: provides education or coach to breast cancer patients in the pre-operative and post-operative process.	Delivery: Web Self-guided:√ Automated reminders:× Face-to-face contact: × Tailored: ×	Information support	1 month	1.Anxiety (STAI) 2.QOL(SF 36)	1.P＜0.05 2.P＜0.05

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
White, 2018[19] Australia	177 /202	Name:An information- based, breast cancer specific website Structure: information module,emotional responses, support services, family responses and life after cancer, a diary.	Delivery:Web Self-guided:√ Automated reminders:√ Face-to-face contact: × Tailored:×	Information support; Psychological support	6 months	1.Anxiety and Depression (HADS) 2.QOL(FACT-B	1. No significant outcomes. 2.T1-T2 ($\chi 2_{df=1}$ = 6.46, p = 0.01)
Admiraal, 2017[20] Netherlands	69/69	Name: Tailored self-mannagement psychoeducational program Structure: 1) problem orientation; and 2) fully automated and customized psychoeducation for reported problems; and 3) resources and services for reported problems.	Delivery: Web Self-guided:√ Automated reminders:× Face-to-face contact:× Tailored: √	Information support; Psychological support.	12 weeks	1.QOL(EORTC QLQ-C30 and the QLQ-BR23) 2. Psychological distress(DT/PL)	No significant outcomes.
Ventura, 2017[21] Sweden	121/105	Name:Swedish Interactive Rehabilitation Information program Structure: Includes links to web pages and lectures last for 4 hour about two modules: medical issues arising and psycho-social aspects.	Delivery: A computer -based programme Self-guided:× Automated reminders:× Face-to-face contact: × Tailored: ×	Information support	9 months	1.Anxiety and depression (HADS) 2.Self-efficacy (CHESS)	No significant outcomes.
Wheelock, 2015[22] USA	41/59	Name: A Web-Based System for Symptom Management Structure: 3 routine clinic follow-up appointments, self-reported symptoms, with	Delivery:Web+ computer system Self-guided： × Automated reminders:×	Information support; Symptom management; Interaction with health care professionals	18 months	Symptom prevalence (Patients self-reported)	7.36 vs 3.2; P=0.0045

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Wheelock, 2015[22] USA		review by nurse practitioners, targeted education and triage.	Face-to-face contact: × Tailored:√				
Du,2021[23] China	40/40	Name:Follow-up management intervention based on clinical decision support system Structure: fills in the corresponding health status evaluation sheet, the system automatically interprets the results of the evaluation sheet and triggers an abnormal state alarm, the normal state gives a follow-up/treatment reminder, and the abnormal state pushes related health education courses or intervention from medical staff.	Delivery: A full-process information management system Self-guided: × Automated reminders: √ Face-to-face contact: × Tailored: √	Information support; Symptom management; Interaction with health care professionals.	6 months	1.Symptom severity (myelosuppression) 2.Self-efficacy(SUPPH)	1. P＜0.05 2. P＜0.05
Hou, 2020[24] Taiwan	59/53	Name:A Self-Management Support mHealth App Intervention Structure: eight main features(1) evidence or knowledge about breast cancer, (2) exercise and rehabilitation after surgery, (3) diet and nutrition for breast cancer patients, (4) emotional support to prevent anxiety and depression, (5) personal health records to track treatment and side effects, (6)information on social resources, (7) experience sharing, and (8) expert consulting.	Delivery: APP Self-guided:√ Automated reminders:√ Face-to-face contact: × Tailored: ×	Information support; Symptom management; Behavior management Psychological support; Interaction with health care professionals; Peer support	3 months	1.QOL(QLQ-C30 and QLQ-BR23)	83.45 vs 82.23, P=0.03(QLQ-C30) ; 265.53 vs63.13, P=0.04 (QLQ-BR23)
Graetz, 2018[25] USA	25/23	Name: A mobile app for managing adverse symptoms. Structure: test the use of the app designed with and without weekly reminders for patients to report real-time	Delivery: APP Self-guided:√ Automated reminders:√	Information support Symptom management; Behavior management	8 weeks	Symptom distress(FACT-ES)	No significant outcomes.

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
		symptoms and AI use outside of clinic visits with built-in alerts to patients' oncology providers.	Face-to-face contact: × Tailored:√				
Fjell, 2020[26] Sweden	75/74	Name:An interactive app intervention Structure: symptom self- reporting, an alert system for contacting health care professionals, access to self-care advice and a visual chart of symptom history.	Delivery: APP Self-guided:√ Automated reminders:√ Face-to-face contact: × Tailored: √	Information support; Symptom management; Interaction with health care professionals.	2 weeks	1.QOL(EORTC QLQ-C30) 2.Symptom Distress(MSAS)	1. Emotional functioning (P =0.008); nausea and vomiting (P =0.007), appetite loss (P=0.027), constipation (P =0 .007), 2.P =0.033, Effect size(0.26 to 0.34)
Handa, 2020[27] Japan	52/50	Name: A breast cancer patient support system application. Structure:record the patient's subjective and objective symptoms by time and number, provides tips for self-care, including advice on when the patient should go for checkups, and ways to manage side effects	Delivery: APP Self-guided: √ Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Symptom management;	12 weeks	Anxiety and depression(HADS)	No significant outcomes.
Rosen, 2018[28] USA	55/57	Name:App-delivered mindfulness training (AMT) intervention Structure: Includes techniques for calming meditation (eg, focus on the breath) and.	Delivery: APP Self-guided:√ Automated reminders: ×	Information support; Psychological support.	8 weeks	1.QOL (FACT-B)	t(258.40) =3.09, P < 0.01, 95% CI[2.71, 11.90]

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
		insight meditation (eg, cultivating awareness, insight, and compassion)	Face-to-face contact: × Tailored: ×				
Zhou, 2019[29] China	66/66	Name:Cyclic adjustment training intervention Structure: relaxed deep breath training; music listening; anti-cancer stories reading/ listening/watching; adjust experiences and feelings sharing with peers;be instructed to self-ask the following questions.	Delivery:Wechat Self-guided: × Automated reminders: × Face-to-face contactl: √ Tailored: ×	Information support; Psychological support; Interaction with health care professionals; Peer Support	12 weeks	1.Depression (SDS) 2.Anxiety(SAS)	1.F = 26.32, P < 0.001 2.F = 31.85, P < 0.001
Zhou, 2020[30] China	55/56	Name:WeChat-based multi-modal nursing program Structure: provision of information, training, support, and counseling centered and oriented to the needs of breast cancer patients, involving physical, psychological, and social adjustment distress.	Delivery: WeChat Self-guided: × Automated reminders: × Face-to-face contact: √ Tailored: ×	Information support; Psychological support; Interaction with health care professionals; Peer Support.	6 months	1.QOL (FACT-B) 2.Pain/fatigue/ sleep symptom (NRS)	1.F = 16.28, P < 0.001 2. No significant outcomes
Foley, 2016[31] Ireland	26/13	Name:Patient accessed tailored information Intervention Structure: tailored surgical information pertaining to individual patients and the scripts were reviewed by the National Adult Literacy Agency (NALA) and contain basic breast cancer biology, the different treatments used and surgical techniques.	Delivery: APP Self-guided:√ Automated reminders: × Face-to-face contact: × Tailored: √	Information support	2 weeks	1.Anxiety and depression (HADS)	1.P=0.022 (anxiety) P=0.029 (depression)

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Wang, 2019[32] China	44/44	Name: Continuous rehabilitation nursing support intervention Structure: knowledge sharing, health consultations, sharing of feelings and experiences between patients, relax training; cope with negative emotions	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Psychological support; Interaction with health care professionals; Peer support.	6 months	1.QOL(FACT-B) 2.Pain, fatigue, and sleep severity(NRS)	1.P＜0.001 2. No significant outcomes
Sherman, 2018[33] Australia	155/149	Name:Structured Online Writing Exercise Intervention Structure: Individuals could describe their deepest thoughts and emotions with specific prompts focused on self-compassion according to a modified Expressive Writing prompt.	Delivery: web Self-guided：√ Automated reminders：× Face-to-face contact: × Tailored: ×	Psychological support	NA	1.Anxiety and depression (DASS) 2. Body image distress(BIS)	1.P=0 .001 (depression); P=0.007 (Anxiety) 2. P=0.035
Villani, 2018[34] Italy	14/15	Name:E-health Stress Inoculation Training (SIT) intervention Structure: face-to-face counseling with a psychologist, live videos simulating the chemotherapy process, watching live video interviews with women who have experienced breast cancer, relaxation videos with guided meditation audio.	Delivery:Web Self-guided: × Automated reminders:× Face-to-face contact:√ Tailored: ×	Psychological support; Interaction with health care professionals; Peer Support	3 months	1.QOL (FACT-B) 2. Emotional Depression (ERQ)	1. P＜0.05 (3 months after the end of the intervention) 2. P＜0.05 (3 months after the end of the intervention)
Liu, 2019[35] China	50/50	Name: Innovative Follow-Up Intervention Structure: Provide preoperative rehabilitation	Delivery: Wechat Self-guided: ×	Information support; Behavior management;	12 months	Self-efficacy(GSES)	P＜0.05

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
		guidance, discharge follow-up form and endocrine medication survey form, health consultation.	Automated reminders: × Face-to-face contact: × Tailored: ×	Interaction with health care professionals; Peer suport.			
Kim, 2020[36] North-Korea		Name: A web-based expert support self-management program (WEST) Structure: keep a health diary, self-diagnose lifestyle, learn health information and receive individualized feedback from a nurse, phone counseling with experts.	Delivery: APP Self-guided: √ Automated reminders: × Face-to-face contact: × Tailored: √	Information support; Behavior management; Interaction with health care professionals.	6 months	Self-efficacy (Health-specific self-efficacy scales)	No significant outcomes.
Im, 2020[38] USA	66/49	Name:Technology-Based Information and Coaching/ Support Program on Pain and Symptoms Structure: online knowledge or education with cultural characteristics, online assistance resources, group and one-on-one guidance in the form of online forums on the website	Delivery:Web Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: √	Information support; Interaction with health care professionals； Peer Support	3 months	1.Symptom distress(MSAS-SF)	P=0.0229
Wang, 2019[39] China	75/74/\	Name: Specialized case management intervention Structure: Establish case management files, push the answers to patient questions, share knowledge, remind and supervise the implementation of the patient's personal plan daily, including medication, symptoms, and weight.	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Interaction with health care professionals; Peer support.	9 months	Symptom severity(CTCAE)	P＜0.05

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Visser, 2018[40] Netherlands	50/59	Name:Group medical consultations (GMCs) and tablet-based online support group sessions Structure: a face-to-face GMC and an online app, consisting of three tablet-based video GMCs, email, videos and additional information.	Delivery:APP Self-guided: × Automated reminders:√ Face-to-face contact: × Tailored: √	Information support; Interaction with health care professionals; Peer Support.	3 months	1.Psychological distress (SCL-90)	No significant outcomes
Peng,2020[41] China	59/58	Name: Online and offline rehabilitation intervention Structure: online and offline rehabilitation volunteer support activities, Case management file establishment and offline rehabilitation guidance, online rehabilitation knowledge guidance and rehabilitation consultation and Q&A.	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: √ Tailored: ×	Information support; Psychological support; Interaction with health care professionals; Peer support.	12 months	1.QOL (QLQ-BR53) 2.Body image distress(BIS)	1. P＜0.05 2. P＜0.05
Chee, 2016[56] USA	30/35	Name: A culturally tailored Internet cancer support group Structure: (a) interactive online message board by moderated a Registered Nurse; (b) interactive online evidence-based educational sessions; and (c) online resources.	Delivery: Web Self-guided:× Automated reminders:× Face-to-face contact: × Tailored: ×	Information support; Interaction with health care professionals; Peer support	1 month	1.QoL(FACT-B) 2.Symptom distress(MSAS-SF) 3.Social support(PRQ) 4.self-efficacy (CBI)	1.P＜0.10 2.P＜0.10 3.No significant outcomes. 4.No significant outcomes.
Wang,2017[59]	320/	Name:Continuous nursing intervention	Delivery: APP	Information support;	2 weeks	1.QOL(QLSBC)	1.P＜0.01

China	318/	Structure: regularly provides the service like	Self-guided: ×	Symptom management;		2. Anxiety and	2.P＜0.01

Table3 Internet-based Support Interventions RCTs: study characteristics and results

Author/ year/ Country	Sample Size(I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Wang, 2017[59] China		medical information, care reminders, health monitoring and health education	Automated reminders: × Face-to-face contact: × Tailored: ×	Interaction with health care professionals; Peer support.		depression(EESS) 3.Prevalence of adverse reactions	3.P＜0.05
Li,2018[60] China	60/60	Name: Management of chemotherapy adverse events Structure: information support, Alert for chemotherapy adverse events, personalized management from a case manager or multidisciplinary expert, SMS alert feedback.	Self-guided: √ Automated reminders: √ Face-to-face contact: × Tailored: √	Information support; Symptom management; Interaction with health care professionals	2 weeks	1.QOL(FACT-B) 2.Symptom prevalence(CTCAE,v4.0)	1. P＜0.05 2. P＜0.05
Chen, 2015[61] China	45/45	Name:Tracking intervention based on network information platform Structure: Through the system, follow-up nurses participate in the diagnosis and treatment process of the patient during the hospitalization process,provide post-discharge patient greetings, rehabilitation guidance, reminders for follow-up and other nursing services.	Delivery: Web Self-guided: × Automated reminders: √ Face-to-face contact: √ Tailored: ×	Information support; Interaction with health care professionals Peer support	3 months	1.QOL(FACT-B) 2. Depression(CES-D)	1.P＜0.05 2. P＜0.01
Egbring, 2016[62] Switzerland	46/49/ 44	Name: a mobile and Web-based app to record daily functional activity and adverse events. Structure: record functional activity and adverse events , and collaborate with physicians in the monitoring and review of patient-reported	Delivery: APP Self-guided: √ Automated reminders:× Face-to-face contact: × Tailored: ×	Information support; Symptom management; Interaction with health care professionals	42 days	Symptom prevalence (Patients self-reported)	n=1033(supervised APP group) vs n=656（Questionnaire group）;

symptoms.

Table4 Internet-based Support Interventions Quasi-experiment studies: study characteristics and results

Author/year / Country	Sample Size (I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Li,2017[37] China	48/58	Name: Continuous nursing intervention Structure: Includes 3 sections: Rehabilitation Encyclopedia, Personal Center, and Q&A. Rehabilitation Encyclopedia, including diet, exercise, sleep, drugs, psychology and other rehabilitation knowledge. Personal center records patient health files.	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: √	Information support; Behavior management; Interaction with health care professionals Peer support	4 weeks	1.QOL(EORTC QLQ-C30) 2. Anxiety(HAMA) 3.Depression(HAMD) 4.Cancer-related fatigue(BFI)	1. P＜0.05 2. P＜0.05 3. P＜0.05 4. P＜0.05
Yue,2020[42] China	148/146	Name:"Internet +" nursing mode intervention Structure: "Music Oxygen Bar" group activities, case managers tailor-made family rehabilitation plan for patients, wechat provides postoperative rehabilitation knowledge and video, medical consultation, Healing Music and social support.	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Interaction with health care professionals; Peer support	12 months	Lymphedem symptom distress and severity(BCLE-SEI)	P<0.05
Dai,2017[55] China	47/42	Name: Intervention based on nurse-patient communication platform Structure: knowledge sharing, health counseling and one-on-one chat (responsible nurse communicates with 3 to 5 patients via personal WeChat ID)	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Interaction with health care professionals; Peer support	6 months	1.QOL(QLQ-C30) 2. Cancer-related fatigue(BFI)	1. p＜0.01 2. p＜0.05
Zhou,2019[57] China	153/145	Name:Hospital-family collaborative transitional care intervention Structure: provides breast cancer postoperative function exercise method video, rehabilitation knowledge, health lecture activities and expert consultation activities notice, outpatient doctor sitting arrangements daily, shift	Delivery: Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Interaction with health care professionals; Peer support	6 months	1.QOL(FACT-B) 2. lymphedema symptom severity (Circumferential method)	1. P＜0.01 2. P＜0.001

Table4 Internet-based Support Interventions Quasi-experiment studies: study characteristics and results

Author/year/ Country	Sample Size (I/C)	Intervention Description	Intervention characteristics	Intervention Content elements	Duration	Outcomes/ Measurements	Results
Zhou,2019[57] China		nurses conduct WeChat group visits					
Xu,2017[58] China	75/75	Name:An Internet and mobile phone-based case management program Structure: Mobile Internet technology is applied to postoperative case management in breast cancer patients in education, follow-up and remote consultation.	Delivery: App+Wechat Self-guided: × Automated reminders: × Face-to-face contact: × Tailored: ×	Information support; Symptom management; Interaction with health care professionals.	2 months	1. QOL(FACT-B) 2.Postoperative complications prevalence	1.P<0.05 2. No significant outcomes

Abbreviations: I/C:C, Control group; I, Intervention group; NA：Not Available;BIS, Body Image Scale; BCLE-SEI, Breast Cancer and Lymphedema Symptom Experience Index; BIS, 10-item Body Image Scale; BFI, Brief Fatigue Inventory ;CTCAE,Common Terminology Criteria for Adverse Events; CBI,Cancer Behavior Inventory; CES-D, Center for Epidemiological Survey-Depression Scale; DASS-21,The Depression Anxiety Stress Scale-21item; EORTC QLQ-C30, The European Organization for Research and Treatment of Cancer quality of life questionnaire-core 30 ;QLQ-BR23, The European Organization for Research and Treatment of Cancer quality of life questionnaire-breast cancer module 23;ERQ, The Emotion Regulation Questionnaire; EESS, Eysenck Emotional Stability Scale; FACT-B, Functional Assessment of Cancer Treatment-B; FACT-ES ,Functional Assessment of Cancer Therapy-Endocrine Symptoms; GSES, General Self-Efficacy Scale; HADS,The Hospital Anxiety and Depression Scale; HAMA, Hamilton Anxiety Scale； HAMD, Hamilton Depression Scale; MSAS-SF, The Memorial Symptom Assessment Scale–Short Form; MDASI, MD Anderson Symptom Inventory, PRQ, Personal Resource Questionnaire； QLSBCquality of life scale of beast cancer； SICPA， Stanford Inventory of Cancer Patient Adjustment； SCL-90，the Symptom Checklist-90；SAS，Self-Rating Anxiety Scale; SDS，Self-Rating Depression Scale；STAI，The State-Trait Anxiety Inventory；SUPPH，Strategies Used by People to Promote Health； NRS，Numerical rating scale

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Figure Legends

Figure 1 Flowchart of Search and Selection Process

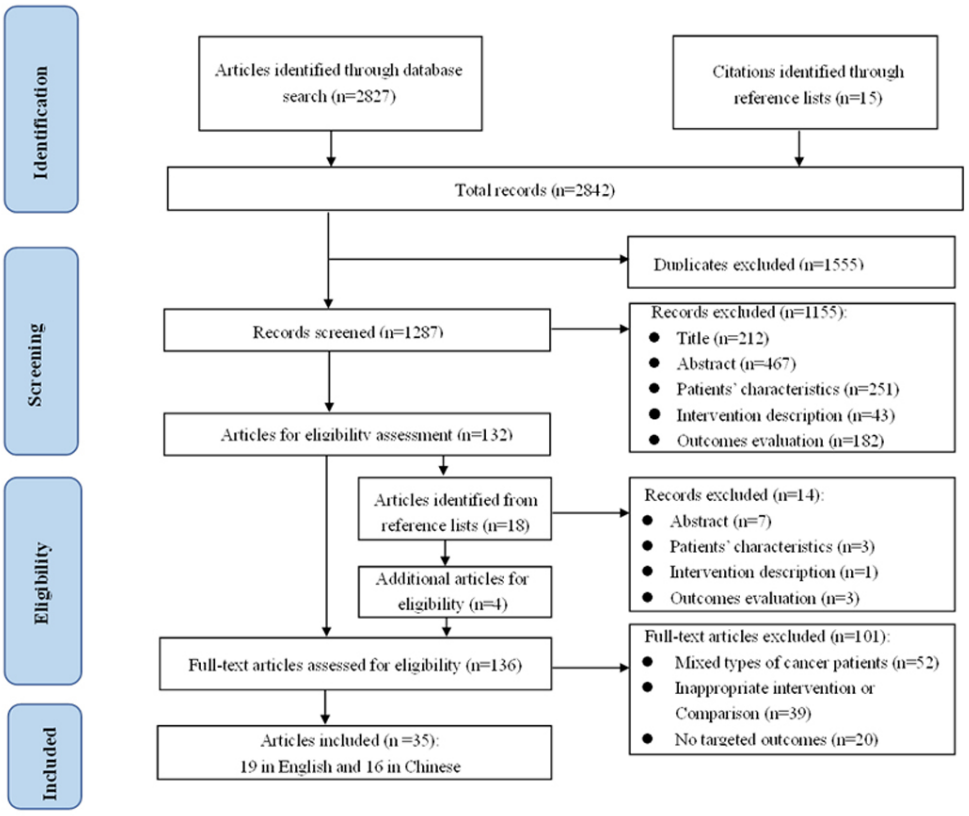

Figure 1. Flowchart of Search and Selection Process

90x90mm (300 x 300 DPI)

Web of Science

1.TS=(“Breast Neoplasm*”) OR TS=(“Breast Cancer*”) OR TS=(“Breast Carcinoma*”) OR TS=(“Breast Tumour*”) OR TS=(“Breast Tumor*”)

2.TS=(Telemedicine) OR TS=(online) OR TS=(Internet) OR TS=(web) OR TS=(“connected health”) OR TS=(telehealth) OR TS=(e-health) OR TS=(m-health) OR TS=(e-intervention) OR TS=(e-technology) OR TS=(computer) OR TS=(“mobile application”) OR TS=(“mobile device”) OR TS=(“social media”) OR TS=(WeChat).

3. TS=(“patient education”) OR TS=(interven*) OR TS=(support*) OR TS=(teach*) OR TS=(instruction*) OR TS=(therap*) OR TS=(program*) OR TS=(psychoeducat*) OR TS=(educat*) OR TS=(rehabilit*) OR TS=(effect*) OR TS=(“self-manag*”) OR TS=(“self manag*”) OR TS=(“self care”) OR TS=(“self-care”) OR TS=(“self help”) OR TS=(“self-help”) OR TS=(“social support”) OR TS=(“support system*”) OR TS=(“support group*”)

4. 1 AND 2 AND 3

Cochrane Library

1. MeSH descriptor: [Breast Neoplasms] explode all trees

2. (Telemedicine):ti,ab,kw OR (online):ti,ab,kw OR (Internet):ti,ab,kw OR (web):ti,ab,kw OR (“connected health”):ti,ab,kw OR (telehealth):ti,ab,kw OR (e-health):ti,ab,kw OR (m-health):ti,ab,kw OR (e-intervention):ti,ab,kw OR (e-technology):ti,ab,kw OR (computer):ti,ab,kw OR (“mobile application”):ti,ab,kw OR (“mobile device”):ti,ab,kw OR (“social media”):ti,ab,kw OR (WeChat):ti,ab,kw

3. (“patient education”):ti,ab,kw OR (interven*):ti,ab,kw OR (support*):ti,ab,kw OR (teach*):ti,ab,kw OR (instruction*):ti,ab,kw OR (therap*):ti,ab,kw OR (program*):ti,ab,kw OR (psychoeducat*):ti,ab,kw OR (educat*):ti,ab,kw OR (rehabilit*):ti,ab,kw OR (effect*):ti,ab,kw OR (“self-manag*”):ti,ab,kw OR (“self manag*”):ti,ab,kw OR (“self care”):ti,ab,kw OR (“self-care”):ti,ab,kw OR (“self help”):ti,ab,kw OR (“self-help”):ti,ab,kw OR (“social support”):ti,ab,kw OR (“support system*”):ti,ab,kw OR (“support group*”):ti,ab,kw

4. #1 AND #2 AND #3

PubMed/Medline

1.(((Breast neoplasms[mh] OR ((breast[mh] OR breast diseases[mh]) AND neoplasms[mh])) AND humans[mh]) OR DCIS[tiab] OR LCIS[tiab] OR ductal carcinoma in situ[tiab] OR lobular carcinoma in situ[tiab] OR (breast[tiab] AND (ductal carcinoma*[ti] OR lobular carcinoma*[ti])) OR ((Breast[ti] OR mammary[ti]) AND (cancer*[ti] OR neoplas*[ti] OR tumor*[ti] OR tumour*[ti] OR carcinoma*[ti] OR malignan*[ti] OR sarcoma[ti] OR lymphoma[ti])))

2. ("Telemedicine OR online OR Internet OR web OR "connected health" OR telehealth OR e-health OR m-health OR e-intervention OR e-technology OR computer OR "mobile application" OR "mobile device" OR "social media" OR WeChat)

3. ("patient education" OR interven* OR support* OR teach* OR instruction* OR therap* OR program* OR psychoeducat* OR educat* OR rehabilit* OR effect* OR "self-manag*" OR "self manag*" OR "self care" OR "self-care" OR "self help" OR "self-help" OR "social support" OR "support system*" OR "support group*")

4. #1 AND #2 AND #3

PSycINFO

1.exp Breast Neoplasms/

2. (breast adj6 cancer$).mp.

3. (breast adj6 neoplasm$).mp.

4. (breast adj6 carcinoma$).mp.

5. (breast adj6 tumour$).mp.

6. (breast adj6 tumor$).mp.

7. 1 OR 2 OR 3 OR 4 OR 5 OR 6

8. ("Telemedicine OR online OR Internet OR web OR "connected health" OR telehealth OR e-health OR m-health OR e-intervention OR e-technology OR computer OR "mobile application" OR "mobile device" OR "social media" OR

WeChat).af.

9. (“patient education” OR interven* OR support* OR teach* OR instruction* OR therap* OR program* OR psychoeducat* OR educat* OR rehabilit* OR effect* OR “self-manag*” OR “self manag*” OR “self care” OR “self-care” OR “self help” OR “self-help” OR “social support” OR “support system*” OR “support group*”).af.

10. 7 AND 8 AND 9

CINAHL

S1. (MH “Breast Neoplasms+”)

S2. TX breast cancer*

S3. TX breast neoplasm*

S4. TX breast carcinoma*

S5. TX breast tumour*

S6. S1 OR S2 OR S3 OR S4 OR S5

S7. TX “Telemedicine OR TX online OR TX Internet OR TX web OR TX “connected health” OR TX telehealth OR TX e-health OR TX m-health OR TX e-intervention OR TX e-technology OR TX computer OR TX “mobile application” OR TX “mobile device” OR TX “social media” OR TX WeChat

S8. TX “patient education” OR TX interven* OR TX support* OR TX teach* OR TX instruction* OR TX therap* OR TX program* OR TX psychoeducat* OR TX educat* OR TX rehabilit* OR TX effect* OR TX “self-manag*” OR TX “self manag*” OR TX “self care” OR TX “self-care” OR TX “self help” OR TX “self-help” OR TX “social support” OR TX “support system*” OR TX “support group*”

S9.S6 AND S7 AND S8

CNKI

AB = ('乳腺癌'+ '乳腺肿瘤') AND AB = ('远程医疗'+ '在线'+'互联网'+ '网络'+'互联网+医疗'+'互联网+医疗健康'+'互联网医疗'+'电子医疗'+'移动医疗'+'移动健康'+'互联网干预'+'移动技术'+'计算机'+'移动 APP'+'移动设备'+'社交媒体'+'微信') AND

AB = ('患者教育'+'干预'+'支持'+'指导' + '治疗' + '方案' + '心理教育' + '教育' + '康复' + '效果' + '自我管理' + '自我照护' + '自我帮助' + '社会支持' + '支持系统' + '支持团体')

Wanfang

(乳腺癌+乳腺肿瘤) * (远程医疗+在线+互联网+网络+ “互联网+医疗”+ “互联网+医疗健康”+互联网医疗+电子医疗+移动医疗+移动健康+互联网干预+移动技术+计算机+移动 APP+移动设备+社交媒体+微信) * (患者教育+干预+支持+指导+治疗+方案+心理教育+教育+康复+效果+自我管理+自我照护+自我帮助+社会支持+支持系统+支持团体)

VIP

(U=乳腺癌 OR U=乳腺肿瘤) AND (U=远程医疗 OR U=在线 OR U=互联网 OR U=网络 OR U=互联网+医疗 OR U=互联网+医疗健康 OR U=互联网医疗 OR U=电子医疗 OR U=移动医疗 OR U=移动健康 OR U=互联网干预 OR U=移动技术 OR U=计算机 OR U=移动 APP OR U=移动设备 OR U=社交媒体 OR U=微信) AND (U=患者教育 OR U=干预 OR U=支持 OR U=指导 OR U=治疗 OR U=方案 OR U=心理教育 OR U=教育 OR U=康复 OR U=效果 OR U=自我管理 OR U=自我照护 OR U=自我帮助 OR U=社会支持 OR U=支持系统 OR U=支持团体)

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page3-Page5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page5/Page 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix A
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Table 3/Table 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Table 3/Table 4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6/Page 7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page5/Page 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7
Study characteristics	17	Cite each included study and present its characteristics.	Page 7-Page 29
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page17-Page 18
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	N/A
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 11-13
	23b	Discuss any limitations of the evidence included in the review.	Page 14
	23c	Discuss any limitations of the review processes used.	Page 14
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 15
Competing interests	26	Declare any competing interests of review authors.	Page 15
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 15

PRISMA 2020 Checklist

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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PRIMSA Abstract Checklist

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. MetaArXiv. 2020, September 14. DOI: 10.31222/osf.io/v7gm2. For more information, visit: www.prisma-statement.org