

ABSTRACT

Background: eHealth potentially enhances quality of care and may reduce health care costs. However, a review of systematic reviews published in 2010 concluded that high-quality evidence on the benefits of eHealth interventions was still lacking.

Objective: We conducted a systematic review of systematic reviews and meta-analyses on the effectiveness/cost-effectiveness of eHealth interventions in patients with somatic diseases to analyze whether, and to what possible extent, the outcome of recent research supports or differs from previous conclusions.

Methods: Literature searches were performed in PubMed, EMBASE, The Cochrane Library, and Scopus for systematic reviews and meta-analyses on eHealth interventions published between August 2009 and December 2012. Articles were screened for relevance based on preset inclusion and exclusion criteria. Citations of residual articles were screened for additional literature. Included papers were critically appraised using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement before data were extracted. Based on conclusions drawn by the authors of the included articles, reviews and meta-analyses were divided into 1 of 3 groups: suitable, promising, or limited evidence on effectiveness/cost-effectiveness. Cases of uncertainty were resolved by consensus discussion. Effect sizes were extracted from papers that included a meta-analysis. To compare our results with previous findings, a trend analysis was performed.

Results: Our literature searches yielded 31 eligible reviews, of which 20 (65%) reported on costs. Seven papers (23%) concluded that eHealth is effective/cost-effective, 13 (42%) underlined that evidence is promising, and others found limited or inconsistent proof. Methodological quality of the included reviews and meta-analyses was generally considered high. Trend analysis showed a considerable accumulation of literature on eHealth. However, a similar percentage of papers concluded that eHealth is effective/cost-effective or evidence is at least promising (65% vs 62%). Reviews focusing primarily on children or family caregivers still remained scarce. Although a pooled (subgroup) analysis of aggregate data from randomized studies was performed in a higher percentage of more recently published reviews (45% vs 27%), data on economic outcome

measures were less frequently reported (65% vs 85%).

Conclusions: The number of reviews and meta-analyses on eHealth interventions in patients with somatic diseases has increased considerably in recent years. Most articles show eHealth is effective/cost-effective or at least suggest evidence is promising, which is consistent with previous findings. Although many researchers advocate larger, well-designed, controlled studies, we believe attention should be given to the development and evaluation of strategies to implement effective/cost-effective eHealth initiatives in daily practice, rather than to further strengthen current evidence.

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KEYWORDS

eHealth; telehealth; telemedicine; review; program effectiveness; cost effectiveness

We also recommend

Effectiveness of Web-based Interventions on Patient Empowerment: A Systematic Review and Metaanalysis

David Samoocha et al., J Med Internet Res, 2010

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Monika Alise Johansen et al., J Med Internet Res, 2012

Clinical Effects of Home Telemonitoring in the Context of Diabetes, Asthma, Heart Failure and Hypertension: A Systematic Review

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Michael Stellefson et al., J Med Internet Res, 2013

Online Prevention Aimed at Lifestyle Behaviors: A Systematic Review of Reviews Leonie F M Kohl et al., J Med Internet Res, 2013

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Lis Ribu et al., JMIR Res Protoc, 2013

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Effectiveness of E-Self-help Interventions for Curbing Adult Problem Drinking: A Meta-analysis Heleen Riper et al., J Med Internet Res, 2011

Increasing Physical Activity With Mobile

The Contribution of Teleconsultation and Videoconferencing to Diabetes Care: A Systematic Literature Review

Devices: A Meta-Analysis Jason Fanning et al., J Med Internet Res, 2012

Fenne Verhoeven et al., J Med Internet Res, 2007

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Introduction

Willem Einthoven started experiments in 1906 with remote consultations via the telephone network and this is when eHealth is likely to have seen first light [1]. It was not until the 1990s when the number of publications in this field of medicine increased dramatically [2]. This was because of the many studies that were carried out involving remote consultations through video-teleconferencing and digital images to give specialists comparable visual inspection of patients as referring doctors [3].

In modern medical practice, eHealth interventions are increasingly present. With nomenclature evolving rapidly, a significant overlap between terms such as eHealth, telemedicine, and telehealth has occurred. The American Telemedicine Association defines telemedicine as "the use of medical information exchanged from one site to another through electronic communications with the purpose of improving the health status of patients," and considers eHealth and telehealth as interchangeable nouns. Both words encompass a broader definition of remote health care and also comprise related services, including nonclinical programs such as education, administration, and research [4]. However, telemedicine is a term that is generally reserved for clinical patient care applications [5]. McLean et al [6] conceptualized the definition of eHealth in a Cochrane review on telehealthcare for asthmatic patients as "the provision of personalized health care at a distance." eHealth contains the following 3 key elements: (1) data obtained from the patient; (2) electronic transfer of data over a distance; and (3) patient-tailored feedback from a health care professional [5,6]. Therefore, communication in eHealth interventions is personalized and interactive in contrast to patient information websites on health and disease.

eHealth potentially enhances the quality of care and reduces health care costs. It may do so by providing patient education and counseling for primary prevention and early detection of disease, replacing face-to-face visits with health care professionals, collecting patient data on medical parameters remotely, among several other mechanisms [6,7]. Because eHealth interventions are considered complex interventions by the Medical Research Council, difficulty may arise in the assessment of the many interacting components of the intervention [8].

In 2010, Ekeland et al [9] published a systematic review of systematic reviews to evaluate the impact of eHealth interventions on health and health care costs. The authors concluded that high-quality evidence on health and economic benefits was still lacking despite the large number of publications. The primary objective of our review is to analyze whether, and to what possible extent, the outcome of recent research supports or differs from these previous conclusions on the effectiveness/cost-effectiveness of eHealth interventions in patients with somatic diseases.

Methods

Overview

Literature searches for systematic reviews and meta-analyses on the effectiveness/cost-effectiveness of eHealth interventions were performed in the following online databases: PubMed, EMBASE, The Cochrane Library, and Scopus. Two of the authors (NE, HO) independently screened all papers' titles and abstracts for relevance. Citations were screened through Web of Science for additional literature.

Search Queries

Similar to Ekeland et al [9], we used the following (simplified) search query to retrieve systematic reviews and meta-analyses on the effectiveness of eHealth interventions: "[eHealth] AND [effectiveness] AND [systematic review OR meta-analysis]." To search for papers on cost-effectiveness, "AND [costs]" was added to the aforementioned syntax. Because Ekeland et al [9] took into consideration published works from 2005 to July 2009, we limited our search results to articles published between August 2009 and December 2012. Extensive search queries are

presented in Tables 1 and 2.

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□ Table 1. PubMed, EMBASE, The Cochrane Library, and Scopus search queries for systematic reviews and meta-analyses on the effectiveness of eHealth interventions (search conducted on September 12, 2013). View this table

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□ Table 2. PubMed, EMBASE, The Cochrane Library, and Scopus search queries for systematic reviews and meta-analyses on the cost-effectiveness of eHealth interventions (search conducted on September 12, 2013).

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Inclusion Criteria

Systematic reviews and meta-analyses on eHealth interventions in adults and/or children with somatic diseases (ie, illnesses with a physical cause, not mental), and those focusing on family caregivers were included. Interventions had to meet the following 3 criteria: (1) data were obtained from the patient or family caregiver, (2) data were electronically transferred over a distance, and (3) personalized feedback was given from a health care professional. Reviews and meta-analyses of individual studies comparing eHealth interventions to usual or no care, and those comparing different eHealth initiatives were assessed. We only accounted for papers reporting health-related outcomes, costs, patient satisfaction, and/or self-management.

Exclusion Criteria

Those eHealth interventions that were not home-based (eg, tele-ICU) or not patient or family caregiver—oriented (eg, education of medical or nursing students and health care professionals) were excluded. We excluded meta-analyses that included nonrandomized studies (eg, cohort studies) unless a subgroup analysis of randomized studies (eg, randomized controlled trials, randomized crossover trials) was performed. In addition, we did not assess papers written in languages other than English or Dutch, and those for which the full-text was not available online. In contrast to Ekeland et al [9], we narrowed the focus of our work by excluding reviews and meta-analyses on nonsomatic disorders (eg, mental disorders such as anxiety, depression, schizophrenia, and posttraumatic stress disorder) and lifestyle changes (eg, smoking cessation and drug intervention programs) to increase the comparability of the included papers and to limit the search results.

Outcome Measures

Health-related effects (eg, morbidity, mortality, quality of life, hospitalization) and health care costs (eg, health care utilization) were defined as primary outcome measures. We considered patient satisfaction and self-management as secondary outcome measures.

Critical Appraisal

Before data were extracted, the included papers were critically appraised using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, formerly QUOROM) Statement [10]. The PRISMA Statement provides an evidencebased 27-item checklist (eg, on objectives, methodology, and limitations) for reporting in systematic reviews and metaanalyses.

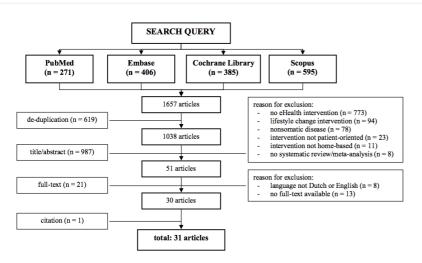
Data Extraction

Based on conclusions drawn by the authors of the included papers, all reviews and meta-analyses were divided into 1 of 3 groups: (1) suitable, (2) promising, or (3) limited evidence that eHealth is effective/cost-effective. Cases of uncertainty were resolved by consensus discussion between 2 authors of the current review (NE, HO). Effect sizes, such as standardized or weighted mean differences, relative risks, odds ratios, and *z* scores, were extracted from papers that included a pooled (subgroup) analysis of aggregate data from randomized studies. No attempt was made to contact authors for missing data. To analyze whether the results of the included papers supported or differed from previous findings by Ekeland et al [9], we performed a trend analysis using basic statistics.

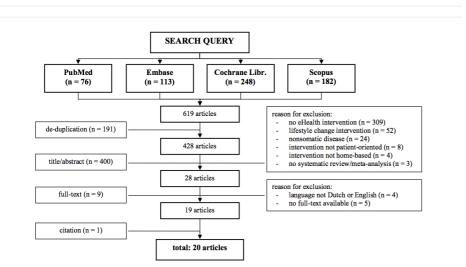
Results

Search Results

The initial search yielded a total of 1657 articles, including 619 articles that reported on cost-related outcome measures (Figures 1 and 2). Following removal of duplicates and screening of the residual papers on preset inclusion and exclusion criteria, 30 eligible reviews remained [6,11-39], of which 19 reported on costs [6,13,14,16,18,19,21-24,26,28,29,31,33,34,37-39]. Subsequent citation screening through Web of Science resulted in 1 additional paper [40]. Thus, a total of 31 reviews were retrieved (Figure 1), of which 20 (65%) reported on costs (Figure 2). Three of 31 reviews (10%) reported primarily on children [28,37,38], and 1 of 31 (3%) focused on the effects of eHealth interventions on family caregivers [26].



□ Figure 1. Flow diagram of the literature search on the effectiveness of eHealth interventions. View this figure



□ Figure 2. Flow diagram of the literature search on the costeffectiveness of eHealth interventions. View this figure

Effects of eHealth Interventions

Results per article are summarized in 3 separate tables, 1 for systematic reviews and meta-analyses reporting eHealth interventions are effective/cost-effective (**Table 3**), a second table for papers showing evidence is promising (**Table 4**), and a third table with papers underlining evidence is lacking, limited, or inconsistent (**Table 5**). **Table 6** demonstrates the effect sizesamong other characteristics-reported in 14 reviews in which a pooled (subgroup) analysis of aggregate data from randomized studies was performed. All tables are presented subsequently.

Effectiveness/Cost-Effectiveness of eHealth Interventions

A total of 7 reviews (23%) showed eHealth interventions are effective on either health or cost-related outcome measures (**Table 3**) [**11-17**]. Study populations consisted of patients with congestive heart failure (CHF) [**13-15,17**], diabetes mellitus [**12,16**], and hypertension [**11**]. Types of interventions that were effective/cost-effective comprised home telemonitoring [**11,13-17**], Web or mobile phone-based education [**12,16**], structured telephone support [**14-16**], and mobile phone-assisted self-management programs [**16**]. Patient acceptance and satisfaction were generally considered high.

Pooled analyses were performed in each of the 7 reviews and demonstrated significant reduction of all-cause mortality, allcause hospitalization, and CHF-related hospital admissions through home telemonitoring and structured telephone support in patients with CHF [13-15,17]. Home telemonitoring also resulted in significant improvement of systolic blood pressure and nonsignificant reduction of diastolic blood pressure, antihypertensive drug use, and therapeutic inertia (ie, unchanged medication despite elevated blood pressure) in hypertensive patients [11]. Web-based education and various mobile phone interventions led to significant improvement of laboratory parameters, such as glycosylated hemoglobin (HbA1c) and lowdensity lipoprotein (LDL) cholesterol, in diabetic patients [12,16]. Qualitative analysis of individual studies revealed several other positive effects of eHealth interventions, including economic benefits [14,16], reduction of the number of visits to outpatient clinics [12], increase of disease-related knowledge and selfmanagement [12,14,16], and improvement of quality of life [13,14,17].

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□ Table 3. Systematic reviews and meta-analyses in which eHealth interventions were shown to be effective/cost-effective. View this table

Evidence on eHealth Interventions is Promising Thirteen reviews (42%) were less confident about the effectiveness/cost-effectiveness of eHealth interventions [18-29,40], but suggested that these initiatives are promising or bear potential (Table 4). Many of the authors claim additional research is needed to clarify efficacy and cost-related issues. Pooled analyses were performed in 4 reviews and presented subsequently [22-24,27]. One review on chronic obstructive pulmonary disease (COPD) demonstrated the capacity of eHealth interventions to significantly reduce the number of patients with 1 or more emergency department visits or hospital admissions-due to exacerbation of pulmonary symptoms-over a 12-month period [23]. eHealth interventions did not significantly improve quality of life and all-cause mortality. Because the interventions were often part of complex interventions, the authors concluded that further investigation is required to determine the precise role of eHealth. Promising effects were also identified for Internet-based peer and clinical visit support programs—among several other eHealth interventions—in acute and chronic pain management [18,22]. Although the Internet was supportive in the treatment of pain, it remained unclear what benefits could be gained and which patients would profit most.

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□ Table 4. Systematic reviews and meta-analyses in which promising evidence on the effectiveness/cost-effectiveness of eHealth interventions was reported. View this table

Qualitative analysis of individual studies revealed many other promising effects of eHealth interventions, for example, Internetbased device-assisted remote monitoring systems in patients with cardiovascular implantable electronic devices [40], in-home telerehabilitation in routine care of patients with stroke and other somatic diseases [20,21], technology-assisted training and support programs for family members of patients with traumatic brain injury [26], and Web-based education to increase patient empowerment [27]. Paré et al [25] assessed the clinical effects of home telemonitoring in patients with a variety of chronic diseases. The authors highlight the fact that home telemonitoring allows for closer follow-up of individual patients' conditions and for early detection of warning signs in case of health deterioration. However, they claim larger trials are needed to confirm the clinical effects of home telemonitoring.

Evidence on eHealth Interventions Is Lacking, Limited or Inconsistent Eleven reviews (35%) underlined that evidence on the effectiveness/cost-effectiveness of eHealth interventions is still lacking, limited, or inconsistent (**Table 5**) [6,30-39]. In many articles, the poor methodological quality of individual studies is criticized, and ambiguous or conflicting findings are emphasized.

McLean et al [6] conducted a Cochrane review of 21 RCTs on a range of eHealth interventions in patients with asthma. Metaanalysis did not show a clinically important improvement of disease-specific quality of life, and no significant reduction of allcause emergency department visits over a 12-month period was found (Table 6). The authors concluded that eHealth is unlikely to result in clinically relevant improvements of health-related outcome measures in patients with relatively mild disease, but does appear to have the potential to reduce all-cause hospital admissions in those with more severe disease.

Shulman et al [37] studied the impact of eHealth interventions involving transmission of blood glucose data in youth with type 1 diabetes mellitus. Pooled analyses showed no apparent effect of the interventions on HbA1c or acute complications, such as severe hypoglycemia and diabetic ketoacidosis (Table 6). The limited data available on patient satisfaction and costs also suggested no differences between the intervention and the comparison group.

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□ Table 5. Systematic reviews and meta-analyses in which no, limited, or inconsistent evidence on the effectiveness/cost-effectiveness of eHealth interventions was reported.

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 Table 6. Characteristics of 14 systematic reviews in which a meta-analysis was performed.
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Methodological Quality of Reviews and Meta-Analyses

Among the systematic reviews and meta-analyses described in the current review are 4 high-quality Cochrane reviews [6,14,23,38]. Following the PRISMA Statement [10], the methodological quality of the other included papers was generally considered high. Nearly all authors provided search queries and selection criteria, described the process of data extraction, presented the results and limitations of individual studies, and demonstrated the implications of their outcome for daily practice and future research. If the authors received external funding, this was reported.

Some discrepancy between reviews was observed in terms of defining eHealth. For example, McLean et al [6] excluded Webbased tools and interventions for self-management in their Cochrane review on asthma patients because health care professionals were not actively involved with the ongoing delivery of the intervention. McGeary et al [22] chose a broader definition in their work on telehealth trials in pain management, including all studies that assessed a technology-based intervention extending care beyond the health care professional's office.

Many authors did not conduct a meta-analysis because of important differences perceived in study populations, interventions and outcome measures [18,19,25,26,31-33, 35,36,39]. Instead, they performed a qualitative analysis of their findings. Several papers presented the results of a pooled analysis or subanalysis, despite substantial heterogeneity (ie, l^2 value >50) [6,12-14,23,24]. Three studies did not report heterogeneity [11,16,38].

Trend Analysis

Since the publication by Ekeland et al in 2010 [9], the number of systematic reviews and meta-analyses on eHealth interventions

in patients with somatic diseases has grown considerably (**Table 7**). In addition, 4 Cochrane reviews have recently been published [**6**,14,23,38]. However, a similar percentage of papers concluded that eHealth is effective/cost-effective or evidence is at least promising (65% vs 62%). Reviews focusing primarily on children or family caregivers still remain scarce. Between 2009 and 2012, home telemonitoring and video-teleconferencing were less frequently subject to a systematic review and/or meta-analysis on eHealth interventions, whereas educational tools and selfmanagement programs were encountered more often. Data on economic outcome measures were less frequently reported in recent papers. Other study characteristics (eg, geographic area) barely differed between our review and the review by Ekeland et al [**9**].

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□ Table 7. Irrend analysis of differences in study characteristics of the current review compared with the review by Ekeland et al [9] published in 2010. View this table

Discussion

The term eHealth can be defined briefly as the delivery of personalized health care at a distance through the use of technology. It is hypothesized that this field of medicine potentially enhances the quality of health care, with simultaneous reduction of health care costs. To support this hypothesis, we undertook a systematic review of systematic reviews and meta-analyses on the effectiveness/ cost-effectiveness of eHealth interventions in patients with somatic diseases. In addition, we performed a trend analysis to compare current findings with results from a systematic review by Ekeland et al published in 2010 [9].

In recent years, literature on eHealth has accumulated considerably. We found a total of 31 reviews, of which 20 (65%) concluded that eHealth interventions are effective/cost-effective or evidence is at least promising. Only 11 reviews (35%) showed no, limited, or inconsistent proof. These findings are consistent with the results from the review by Ekeland et al [9] (Table 7).

Furthermore, trend analysis shows reviews focusing primarily on children or family caregivers still remain scarce. Although a pooled (subgroup) analysis of aggregate data from randomized studies was performed in a higher percentage of more recently published reviews (45% vs 27%), data on economic outcome measures were less frequently reported (65% vs 85%).

Because our review is a systematic review of systematic reviews and meta-analyses, it holds 2 important limitations. Firstly, we relied on the adequate inclusion and critical appraisal of individual studies, as well as on a correct interpretation of study results by the authors of the reviews and meta-analyses included in the current review. We did not investigate whether reviews on similar topics comprised identical studies; neither did we examine possible discrepancies in the analyses of these individual studies when included in more than one review or meta-analysis. Noteworthy, systematic reviews of systematic reviews have been conducted before in other fields of medicine, including reconstructive surgery and neuroradiology [43,44]. Secondly, reviews differed substantially in terms of study populations, intervention components, comparison groups, and outcome measures, for example. Therefore, it is difficult to identify which patients are likely to benefit from which specific intervention. Home telemonitoring and structured telephone support seemed to be effective/cost-effective in patients with

CHF (Table 3), whereas evidence on both interventions seemed limited or inconsistent in patients with chronic pulmonary diseases (Table 5). Meta-analysis was often impeded because of heterogeneity among individual studies. This may have demanded careful conclusions from the authors of that particular review. In several reviews, a pooled (subgroup) analyses was presented despite substantial heterogeneity among individual studies (ie, l^2 value >50) [17,42]. Publication bias may have been the result of the exclusion of small individual studies with negative results, which could have ultimately lead to overestimation of benefits [45,46]. Noteworthy, Ciere et al [32] proposed methodological weaknesses may be partially because of artifacts of poor reporting, rather than being a reflection of poor study design or implementation.

Regarding the aforementioned methodological shortcomings, Ekeland et al [47] performed a systematic review in which they summarize methodologies used in research on eHealth interventions, discuss knowledge gaps, and postulate recommendations for methodological approaches for future research. Furthermore, we agree with recommendations made in previous reports to overcome the problem of between-study differences: researchers should adhere to and make transparent use of reporting guidelines appropriate for specific study designs. These guidelines may include Consolidated Standards of Reporting Trials (CONSORT)-EHEALTH for RCTs on eHealth interventions, Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for observational studies in general, and Workgroup for Intervention Development and Evaluation Research (WIDER) recommendations for the reporting of behavioral interventions [32,48-51].

Because pilot schemes are often limited to fewer than 100 patients, many researchers in the past decade have advocated larger RCTs with standardized study designs to provide definite proof on the effectiveness/cost-effectiveness of eHealth interventions. Results of the recent Whole System Demonstrator trial-involving 3230 patients with diabetes mellitus, COPD, and CHF—showed that eHealth interventions are associated with lower mortality and emergency admission rates [52]. In our opinion, these results should provide an important stimulus to invest in the incorporation of eHealth in daily practice. However, implementation difficulties, such as resistant or refractory behaviors of health care professionals, are an international phenomenon [53]. The Normalization Process Theory (NPT), a sociological theory that provides a framework for understanding the relationship between technology and the social environment, has been used to develop implementation tools such as the eHealth Implementation Toolkit (E-HIT) [54,55].

Although large, well-designed RCTs are likely to further support the evidence on the effectiveness/cost-effectiveness of eHealth initiatives, we believe it is more desirable to focus on overcoming the problematic gap between pilot schemes and daily practice. As proposed in both reviews by Ekeland et al [9,47], formative process assessments and complexity studies can be further explored to achieve this goal.

In conclusion, the number of reviews and meta-analyses on the effectiveness/cost-effectiveness of eHealth interventions in somatic diseases has increased considerably in recent years. The majority of these papers show eHealth is effective/cost-

effective, or at least suggests evidence is promising, which is consistent with previous findings. Data on economic outcome measures were less frequently reported in articles that were published more recently. This is an interesting finding, given the importance of formal cost analyses when considering implementation of eHealth interventions in daily practice. Although many researchers advocate larger, well-designed, controlled studies, we believe attention should be given to the development and evaluation of strategies to implement effective/cost-effective eHealth initiatives, rather than to further strengthen the evidence that has already been made available.

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Conflicts of Interest

None declared.

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Abbreviations

CHF: congestive heart failure

CONSORT: Consolidated Standards of Reporting Trials

COPD: chronic obstructive pulmonary disease

E-HIT: eHealth Implementation Toolkit

HbA1c: glycosylated hemoglobin

ICU: intensive care unit

LDL: low-density lipoprotein

NPT: Normalization Process Theory

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

QUOROM: Quality of Reporting of Meta-analyses

RCT: randomized controlled trial

STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

TREND: Transparent Reporting of Evaluations with Nonrandomized Designs

WIDER: Workgroup for Intervention Development and Evaluation Research

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