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Comparative effect of eHealth interventions on hypertension management-related outcomes: A network meta-analysis

Iván Cavero-Redondo[a,b], Alicia Saz-Lara[a,*], Irene Sequí-Dominguez[a], Maria Dolores Gómez-Guijarro[a], Marta Carolina Ruiz-Grao[a], Vicente Martinez-Vizcaino[a,c], Celia Álvarez-Bueno[a]

[a] Health Care and Social Research Centre, Universidad de Castilla-La Mancha, Cuenca, Spain
[b] Rehabilitation in Health Research Center (CIRES), Universidad de las Americas, Santiago, Chile
[c] Universidad Autónoma de Chile, Facultad de Ciencias de la Salud, Talca, Chile

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ABSTRACT

Background: Increasingly, health professionals and patients have begun to be involved in eHealth interventions to assist in the self-management of hypertension. Therefore, this study was aimed at comparing the effect of different types of eHealth interventions (phone calls, blood pressure telemonitoring, emails, web-site, smartphone-app, short message service (SMS) and more than two eHealth interventions) on reducing systolic and diastolic blood pressure, increasing adherence to medication treatment, improving physical activity compliance, controlling blood pressure, and improving quality of life (QoL).
Methods: A systematic search in MEDLINE (via PubMed), EMBASE, Cochrane Central Register of Controlled Trials, and Web of Science databases was conducted to identify experimental studies addressing the effect of eHealth interventions on the self-management of hypertension. Comparative evaluation of the eHealth interventions effect were performed by conducting a standard pairwise meta-analysis and a network meta-analysis for direct and indirect comparisons between eHealth interventions and control/non-intervention.
Results: Fifty-one studies were included in the analysis showing a moderate effect size for more than two types of eHealth interventions (-0.46; 95%CI: -0.64, -0.27, $p < 0.001$ and -0.29; 95%CI: -0.46, -0.13, $p < 0.001$), phone calls (-0.37; 95%CI: -0.57, -0.17, $p < 0.001$ and -0.29; 95%CI: -0.52, -0.07, $p = 0.011$) and smartphone-app (-0.26; 95%CI: -0.50, -0.01, $p = 0.040$ and -0.40; 95%CI: -0.70, -0.10, $p = 0.010$) on reducing both systolic and diastolic blood pressure, respectively. Additionally, i) smartphone-app improved medication adherence by 45%; ii) more than two types of eHealth interventions and emails improved physical activity compliance by 18% and 57% respectively; ii) more than two types of eHealth interventions, phone calls, blood pressure telemonitoring, website and SMS improved blood pressure control between 16% and 30%; and iv) blood pressure telemonitoring showed a week effect on QoL
Conclusions: Our study reported eHealth to be a suitable intervention for the self-management of hypertension. Considering our results and the population's accessibility to eHealth devices, eHealth could be a useful and largely scalable tool for the self-management of hypertension.
Systematic review registration: PROSPERO CRD42020187468.

What is already known

- Although several previous systematic reviews and meta-analyses have shown that of eHealth interventions are effective on controlling and reducing systolic and diastolic blood pressures, none of them have quantitatively compared the effect of different types of eHealth interventions.

What this paper adds

- Using a network meta-analysis approach our study confirms that although almost all types of eHealth interventions appear to be effective for reducing blood pressure in individuals with hypertension, more than two types of eHealth interventions, phone calls and smartphone-apps showed statistically

* Corresponding author.
E-mail address: Alicia.delsaz@uclm.es (A. Saz-Lara).

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significant higher effect on reducing both systolic blood pressure and diastolic blood pressure.

- Considering our results and the population's accessibility to eHealth devices, eHealth could be a useful and largely scalable tool changing the current paradigm of lifestyle prescription, improving patients' self-management of diseases, developing new clinical practice guidelines, and facilitating workflow in everyday clinical consultations.

1. Introduction

Hypertension is estimated to affect 25% men and 20% women worldwide, comprising 1.13 billion people (NCD Risk Factor Collaboration, 2017) in total. Hypertension is one of the leading causes of premature death worldwide, and only 10.9% men and 16.8% women have their blood pressures under control (Mills et al., 2020). Hypertension significantly increases the risks of heart diseases, encephalopathies, kidney diseases, and other diseases (Williams et al., 2018). Furthermore, hypertension is the main risk factor for attributable mortality. Globally, hypertension is estimated to cause 7.8 million deaths, representing 14.0% of all deaths. This amounts to 143 million disability adjusted life years (DALYs), i.e., 5.8% of the total DALYs (Forouzanfar et al., 2017).

Although the management of hypertension depends on the type and severity (Williams et al., 2018), the main target of hypertension management is blood pressure control. Optimal blood pressure control requires self-monitoring of blood pressure levels several times a day, adherence to drug treatment, and modifications in lifestyle habits, including diet, smoking, and physical activity (Unger et al., 2020). In recent years, hypertension self-management has been considered a cornerstone of hypertension care and is believed to play an important role in the prevention of micro and macrovascular complications (Shahaj et al., 2019). Components of self-management include hypertension-related education; healthy eating; physical activity; medication and device usage; prevention, detection, and treatment of acute and chronic complications; coping with psychosocial problems; and problem solving (Villafuerte et al., 2020).

Health professionals and patients are increasingly being involved in digital health or electronic health (eHealth) (U.S. Food and Drug Administration Digital health, 2018), which includes mobile health, mobile and wireless technologies, health information technology, telemedicine, and personalized medicine to improve clinical care, such as public health, health administration, and health-related education (Van Dyk , 2014). However, eHealth is often designed to support the achievement of health goals, such as assisting in the self-management of chronic diseases, including hypertension (Free et al., 2013).

Although several previous systematic reviews (Andre et al., 2019; Xiong et al., 2018; Zullig et al., 2013) and meta-analyses (Choi et al., 2020; Lu et al., 2019; Li et al., 2020, Liu et al., 2013; Ma et al., 2019; Omboni and Guarda, 2011; Omboni et al., 2013; Verberk et al., 2011) have been published on the effect of eHealth interventions mainly on controlling and reducing systolic and diastolic blood pressures, none of them have quantitatively compared the effect of different types of eHealth interventions (phone calls, blood pressure telemonitoring, emails, web-site, smartphone-app, short message service [SMS] and more than two eHealth interventions) on the self-management of hypertension. Therefore, the aim of this network meta-analysis was to compare the effect of different types of eHealth interventions on reducing systolic and diastolic blood pressure, increasing adherence to medication treatment, improving physical activity compliance, controlling blood pressure, and improving quality of life (QoL).

2. Methods

This report follows the Preferred Reporting Items for Systematic Review incorporating Network Meta-analysis (PRISMA-NMA) (Hutton et al., 2016) and the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011), and it has been registered in the PROSPERO database (registration number ID: CRD42020187468).

2.1. Search strategy

We conducted a systematic search in MEDLINE (via PubMed), EMBASE, Cochrane Central Register of Controlled Trials, and Web of Science databases, from their inception to May 2020. Articles reporting the effect of eHealth interventions on the self-management of hypertension based on data from experimental studies were eligible. The full search strategy for the MEDLINE database is presented in Supplementary Table S1. The systematic literature search was complemented by a review of the reference lists of the articles that were considered suitable for the umbrella review.

2.2. Study selection

The inclusion criteria were: (i) participants: people diagnosed with hypertension; (ii) design: randomized controlled trials (RCTs), non-randomized experimental studies (non-RCTs) (including two-arm pre-post studies), and pilot studies with control groups; (iii) types of interventions: studies reporting the effect of eHealth interventions on the self-management of hypertension (phone calls, blood pressure telemonitoring, emails, web-site, smartphone-app and SMS); and (iv) outcomes: changes in systolic and diastolic blood pressure, changes in QoL, blood pressure control, adherence to medication treatment, and physical activity compliance. The exclusion criteria were: (i) non-eligible publication types such as review articles, editorials, comments, guidelines, and case reports; (ii) duplicate reports of the same study and (iii) lack of data to perform the network meta-analysis (prior to exclusion, the authors were contacted via email requesting these data).

The literature search was independently conducted by two reviewers (IC-R and AS-L), and the disagreements were resolved by consensus or by involving a third researcher (CA-B).

2.3. Data extraction and risk of bias assessment

The following data were extracted from the original reports: (1) year of publication; (2) country of study; (3) study design; (4) sample characteristics (disease status [hypertension or uncontrolled hypertension], sample size, and age distribution); (5) type of intervention (phone calls, blood pressure telemonitoring, emails, website, smartphone and SMS); (6) length of intervention; (7) method to measure adherence to medication; and, (8) baseline means of systolic and diastolic blood pressure.

The risk of bias of the included RCTs was assessed using the Cochrane Collaboration's tool for assessing the risk of bias (RoB2) (Higgins et al., 2016). This tool assesses the risk of bias according to six domains: randomization, the assignment of the intervention, adherence to the intervention, missing outcome data, the measurement of the outcome, and the selection of the reported results. Each of the domains was considered to have a low risk of bias, some concerns related to the risk of bias, or a high risk of bias.

Data extraction and quality assessment were independently performed by two reviewers (IC-R and AS-L), and the inconsistencies were resolved by consensus or by the involvement of a third researcher (CA-B). The agreement rate between reviewers was evaluated by calculating the kappa statistics.

2.4. Statistical analysis and data synthesis

2.4.1. Data synthesis and statistical analysis

The included clinical trials were summarized qualitatively in an ad hoc table describing the types of direct and indirect comparisons. As noted above, we conducted our network meta-analysis accordingly with PRISMA-NMA (Hutton et al., 2016) statement distinguishing the following steps:

- A network geometry graph was used to display the evidence in the network for systolic and diastolic blood pressure. In this graph the size of the nodes was proportional to the number of participants in trials who received the intervention specified in the node, the thickness of continuous line connecting nodes proportional to number of participants in trials directly comparing the two treatments (Salanti et al., 2011).
- Consistence assessment, by checking whether the treatment effects estimated from direct comparisons were consistent with those estimated by indirect comparisons procedures. For this aim, we used the Wald test; moreover, we assessed local inconsistency using the side-splitting method.
- Transitivity assessment, to check that the synthesis of direct comparisons of two treatments have been conducted in studies that were similar in the most important clinical and methodological characteristics; thus, it supposed to assume that the populations included in these studies were similar in the baseline distribution of the effect modifier. For this aim we checked that all the participants in the studies included in the network meta-analysis have the same baseline characteristics (age, systolic and diastolic blood pressure) that might modify the treatment effect (Cipriani et al. 2013).
- Comparative evaluation of the interventions effect on systolic and diastolic blood pressure, by conducting a random effects pairwise meta-analysis (DerSimonian and Kacker, 2007) and a network meta-analysis (White, 2015) for comparisons between interventions and control. Additionally, a random effects pairwise meta-analyses were performed for adherence to medication treatment, physical activity compliance, blood pressure control and QoL. The statistical heterogeneity was examined by calculating the I^2 statistic, separately for each statin doses and for each exercise intensity, which ranges from 0% to 100%. According to the values of I^2, the heterogeneity will be considered as not important (0% to 30%), moderate (30% to 50%), substantial (50% to 75%), or considerable (75% to 100%) (Higgins and Green, 2011). The corresponding P values were also be considered. Finally, to determine the size and clinical relevance of heterogeneity the τ^2 statistic was calculated. A τ^2 estimate of 0.04 may be interpreted as a low, 0.14 as a moderate and 0.40 as a substantial degree of clinical relevance of heterogeneity (Stettler et al., 2008). These results were displayed by creating a league table.
- For QoL, systolic ad diastolic blood pressure changes, a standardized mean difference score was calculated using Cohen's d index as the effect size (ES) statistic, in which negative ES values indicated decreases in systolic and diastolic blood pressure in favor of eHealth interventions. Cohen's d values of approximately 0.2 were considered to represent weak effects; approximately 0.5, moderate effects; approximately 0.8, strong effects; and, greater than 1.0, very strong effects (Cohen, 1988). Additionally, relative risk (RR) was used as the risk estimate for adherence to medication treatment, physical activity compliance, and blood pressure control. Adherence to medication treatment was calculated in terms of losing adherence to medication treatment. Blood pressure control, and physical activity compliance were calculated as the risks of not controlling blood pressure, and not performing physical activity at the end of the intervention, respectively.
- Comprehensive scatterplot for clinical comparisons. This graph displays jointly the following estimates: systolic blood pressure (x-axis) and diastolic blood pressure (y-axis) for eHealth type versus placebo comparisons.
- Relative rankings of treatments. Once we had comparatively estimated the effectiveness of the different types of eHealth interventions, the next step was to rank the interventions in order to identify superiority. The probability that each eHealth intervention was the most effective was presented graphically using rankograms (Chaimani et al., 2013). Additionally, the surface under the cumulative ranking (SUCRA) was estimated for each intervention. SUCRA involves the assignment of a numerical value between 0 and 1 to simplify the classification of each intervention in the rankogram. The best intervention would obtain a value for SUCRA close to 1 and the worst intervention would be a value close to 0 (Salanti et al., 2011).
- Subgroup analysis. A subgroup analysis was conducted according to the length of intervention ($\leq$3 months, 4–5 months, 6 months, 7–11 months and $\geq$12months).
- Sensitivity analysis and small study effect. Sensitivity analyses were conducted to assess the robustness of the summary estimates and to detect whether any particular study represented a large proportion of the heterogeneity. For examining the presence of bias due to small study effect, a network funnel plot was used to visually scrutinize the criterion of symmetry (Sterne et al., 2001). All the analyses were conducted in Stata 15.0 (Stata, College Station, Texas, USA).

3. Results

3.1. Systematic review

Fifty-one studies (Supplementary Figure S1) addressing the eHealth interventions for the self-management of hypertension were identified, which were conducted in 18 countries from the continents of North America, Europe, Asia, South America and Africa. These reports were published between 2001 and 2020, and they included studies with the following experimental designs: 39 RCTs, four multicenter RCTs, four cluster RCTs, and four non-RCTs (Table 1).

In the included populations, the participants were aged between 49.0 and 78.3 years, the sample sizes ranged from six to 458 participants in the eHealth intervention groups, and from nine to 457 participants in the control groups. Furthermore, seven studies included two intervention arms, and one study included three intervention arms.

The eHealth interventions were delivered through SMS, emails, blood pressure telemonitoring, phone calls, smartphone-app, website and more than two eHealth interventions approaches (Fig. 1). The lengths of the interventions ranged from 1 to 18 months. Sixteen studies performed analyses for more than one time point.

The baseline systolic and diastolic blood pressure in the studies ranged from 127.5 mmHg to 159.4 mmHg and from 72.8 mmHg to 97.4 mmHg, respectively. Even though the studies used different methods to measure the adherence to drug treatment, most studies used the Morisky Medication Adherence scale (Morisky et al., 1986).

3.2. Transitivity assessment

Participants in different the types of eHealth interventions showed no statistically significant differences in baseline values of age ($p = 0.090$), systolic blood pressure ($p = 0.556$) and diastolic blood pressure ($p = 0.522$).

Table 1
Characteristics of studies included in the systematic review and meta-analysis.

Reference	Country	Study design	Status	Sample size	Mean age, years (mean±SD)	Intervention	Length, months	Medication adherence	Baseline systolic blood pressure, mmHg (mean±SD)	Baseline diastolic blood pressure, mmHg (mean±SD)
Adie and James (2010)	UK	RCT	Hypertension	IG: 29 CG: 27	72.5±NR	Phone calls	6	NR	IG: 144.6 ± 21.6 CG: 147.0 ± 20.8	IG: 85.7 ± 13.7 CG: 80.5 ± 13.1
Ahmed et al. (2016)	United Arab Emitates	Non-RCT	Hypertension	IG: 214 CG: 214	IG: 57.4 ± 11.0 CG: 57.6 ± 11.1	SMS and phone calls	6	Medication refill	IG: 152.4 ± 12.9 CG: 151.3 ± 14.7	IG: 91.6 ± 6.9 CG: 90.4 ± 7.9
Artinian et al. (2001)	USA	RCT	Hypertension	IG: 6 CG: 9	59.0±NR	BP Telemonitoring link	3	NR	IG: 148.8 ± 13.8 CG: 142.4 ± 16.5	IG: 90.2 ± 5.8 CG: 91.2 ± 8.7
Artinian et al., 2007	USA	RCT	Hypertension	IG: 194 CG: 193	IG: 59.1 ± 13.0 CG: 60.2 ± 12.3	Phone calls and BP Telemonitoring link	3, 6 and 12	NR	IG: 156.8 ± 19.6 CG: 155.9 ± 19.2	IG: 89.5 ± 14.0 CG: 88.4 ± 13.0
Bobrow et al. (2016)	South Africa	RCT	Hypertension	IG1: 457 IG2: 458 CG: 457	IG1: 53.9 ± 11.2 IG2: 54.2 ± 11.6 CG: 54.7 ± 11.6	IG1: SMS information IG2: SMS interactive	6 and 12	Days of medication covered	IG1: 135.1 ± 16.9 IG2: 135.6 ± 18.1 CG: 135.4 ± 17.6	IG1: 83.1 ± 11.9 IG2: 83.6 ± 12.0 CG: 83.6 ± 12.4
Bove et al. (2013)	USA	RCT	Hypertension	IG: 120 CG: 121	IG: 61.0 ± 13.6 CG: 58.2 ± 13.5	SMS and phone calls	6	Medication adherence score	IG: 155.9 ± 13.7 CG: 154.4 ± 16.3	IG: 88.9 ± 11.2 CG: 87.6 ± 10.9
Buis et al. (2017)	Austria	RCT	Hypertension	IG: 60 CG: 63	49.0 ± 8.3	SMS	1	Morisky Medication Adherence Scale	IG: 152.7±NR CG: 151.0±NR	IG: 93.5±NR CG: 94.4±NR
Carrasco et al. (2008)	Spain	RCT	Hypertension	IG: 131 CG: 142	IG: 62.1 ± 11.9 CG: 62.8 ± 12.5	SMS	6	NR	IG: 146.2 ± 16.6 CG: 146.8 ± 18.1	IG: 88.5 ± 9.1 CG: 87.4 ± 9.4
Chiu and Wong (2010)	China	RCT	Hypertension	IG: 31 CG: 32	IG: 53.3 ± 7.8 CG: 54.4 ± 7.6	Phone calls	2	Medication adherence score	IG: 147.2 ± 19.0 CG: 148.5 ± 17.9	IG: 90.5 ± 11.4 CG: 88.8 ± 11.9
Cicolini et al. (2014)	Italy	RCT	Hypertension	IG: 100 CG: 98	IG: 59.8 ± 15.0 CG: 58.3 ± 13.9	Emails and phone calls	3 and 6	Morisky Medication Adherence Scale	IG: 150.0 ± 11.0 CG: 153.0 ± 12.0	IG: 87.5 ± 5.7 CG: 88.6 ± 2.3
Earle et al. (2010)	UK	RCT	Hypertension	IG: 72 CG: 65	IG: 59.6 ± 12.0 CG: 57.1 ± 13.0	Smartphone-app	6	NR	IG: 130.5 ± 15.1 CG: 131.8 ± 19.7	IG: 76.9 ± 9.4 CG: 76.6 ± 11.3
Golshahi et al. (2015)	Iran	RCT	Hypertension	IG: 45 CG: 45	IG: 56.8 ± 8.9 CG: 57.5 ± 8.5	SMS	5	Self-reported	IG: 149.6 ± 3.8 CG: 149.6 ± 4.3	IG: 91.2 ± 3.1 CG: 90.8 ± 4.2
Gong et al. (2020)	China	Multicentre RCT	Hypertension	IG: 225 CG: 218	IG: 58.2 ± 7.5 CG: 59.3 ± 7.4	Smartphone-app	6	Morisky Medication Adherence Scale	IG: 140.5 ± 10.4 CG: 141.2 ± 10.1	IG: 83.9 ± 8.6 CG: 82.6 ± 9.6

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Table 1 (*Continued*).

Reference	Country	Study design	Status	Sample size	Mean age, years (mean±SD)	Intervention	Length, months	Medication adherence	Baseline systolic blood pressure, mmHg (mean±SD)	Baseline diastolic blood pressure, mmHg (mean±SD)
Green et al. (2008)	USA	RCT	Hypertension	IG1: 259 IG2: 261 CG: 258	IG1: 59.5 ± 8.3 IG2: 59.3 ± 8.6 CG: 58.6 ± 8.5	IG1: Website IG2: Website + medication management	12	NR	IG1: 152.2 ± 10.0 IG2: 152.2 ± 10.4 CG: 151.3 ± 10.6	IG1: 88.9 ± 8.1 IG2: 89.0 ± 7.9 CG: 89.4 ± 8.0
Hoffmann-Petersen et al. (2017)	Denmark	RCT	Hypertension	IG: 175 CG: 181	IG: 60.5 ± 2.6 CG: 60.4 ± 2.9	BP Telemonitoring link	3	NR	IG: 144.4 ± 11.5 CG: 145.0 ± 12.5	IG: 88.6 ± 7.8 CG: 88.8 ± 6.8
Kerry et al. (2013)	UK	RCT	Hypertension	IG: 187 CG: 194	IG: 71.1 ± 12.6 CG: 72.6 ± 11.4	Phone calls	6 and 12	NR	IG: 140.3 ± 21.3 CG: 135.8 ± 20.7	IG: 75.5 ± 12.4 CG: 72.8 ± 11.1
Kim et al. (2014)	USA	Non-RCT	Hypertension	IG: 184 CG: 185	IG: 70.6 ± 5.0 CG: 71.2 ± 5.6	BP Telemonitoring link	6, 12 and 18	Hill-Bone Medication Adherence scale	IG: 141.0 ± 17.0 CG: 140.0 ± 21.0	IG: 79.0 ± 11.0 CG: 79.0 ± 12.0
Kim et al. (2015)	South Korea	RCT	Uncontrolled hypertension	IG1: 124 IG2: 126 CG: 124	IG1: 56.4 ± 9.9 IG2: 56.1 ± 11.0 CG: 58.8 ± 10.6	IG1: BP Telemonitoring link IG2: BP Telemonitoring link	6	Self-reported	IG1: 142.9 ± 14.5 IG2: 143.1 ± 14.7 CG: 143.2 ± 13.0	IG1: 88.1 ± 8.8 IG2: 87.9 ± 8.8 CG: 88.2 ± 9.5
Kim et al. (2016)	USA	RCT	Hypertension	IG: 52 CG: 43	IG: 57.5 ± 8.6 CG: 57.7 ± 8.7	Smartphone-app and BP Telemonitoring link	6	Morisky Medication Adherence Scale	IG: 136.1 ± 15.2 CG: 145.9 ± 19.5	IG: 81.6 ± 8.0 CG: 81.9 ± 6.8
Lee et al. (2016)	Taiwan	RCT	Hypertension	IG: 170 CG: 212	IG: 57.3 ± 10.9 CG: 58.9 ± 10.7	BP Telemonitoring link	2, 4 and 6	NR	IG: 129.6 ± 14.3 CG: 127.5 ± 21.8	IG: 79.4 ± 10.2 CG: 77.5 ± 16.0
Li et al. (2019)	China	Cluster RCT	Hypertension	IG: 186 CG: 276	IG: 61.7 ± 6.3 CG: 61.3 ± 6.4	Chat	6	Hypertension Self-Efficacy Scale and Hypertension Patients Self-Management Behavior Rating Scale	IG: 135.8 ± 15.9 CG: 135.2 ± 14.8	IG: 83.0 ± 10.1 CG: 81.1 ± 10.8
Liu et al., 2018	Canada	RCT	Hypertension	IG1: 42 IG2: 43 CG: 43	IG1: 57.3 ± 9.1 IG2: 57.6 ± 9.8 CG: 56.1 ± 9.2	IG1: User-driven emails IG2: Expert-driven emails	4	NR	IG1: 140.0 ± 12.3 IG2: 140.3 ± 13.8 CG: 138.6 ± 11.8	IG1: 87.3 ± 9.1 IG2: 89.4 ± 10.5 CG: 87.4 ± 9.2
Liu et al. (2020)	USA	Multicentre RCT	Hypertension	IG: 100 CG: 97	IG: 58.0 ± 10.2 CG: 57.2 ± 7.6	emails	4 and 12	Canadian Hypertension Education Program	IG: 141.5 ± 10.2 CG: 140.6 ± 10.0	IG: 87.3 ± 7.7 CG: 87.3 ± 7.6

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Table 1 (*Continued*).

Reference	Country	Study design	Status	Sample size	Mean age, years (mean±SD)	Intervention	Length, months	Medication adherence	Baseline systolic blood pressure, mmHg (mean±SD)	Baseline diastolic blood pressure, mmHg (mean±SD)
Logan et al. (2012)	Canada	RCT	Uncontrolled hypertension	IG: 55 CG: 55	IG: 62.7 ± 7.8 CG: 63.1 ± 9.0	Smartphone-app and BP Telemonitoring link	12	NR	IG: 139.4 ± 11.6 CG: 139.9 ± 10.6	IG: 73.9 ± 10.6 CG: 75.4 ± 8.7
Madsen et al. (2008)	Denmark	RCT	Hypertension	IG: 113 CG: 123	IG: 55.0 ± 11.7 CG: 56.7 ± 11.6	BP Telemonitoring link	6	NR	IG: 153.1 ± 13.2 CG: 152.2 ± 13.7	IG: 91.2 ± 8.1 CG: 90.5 ± 8.9
Magid et al. (2011)	USA	RCT	Uncontrolled hypertension	IG: 138 CG: 145	IG: 65.1 ± 11.1 CG: 66.7 ± 12.2	BP Telemonitoring link	6	Mediaction possession ratio	IG: 150.5±NR CG: 143.8±NR	IG: 89.4±NR CG: 85.3±NR
Margolis et al. (2013)	USA	Cluster RCT	Hypertension	IG: 228 CG: 222	IG: 62.0 ± 11.7 CG: 60.2 ± 12.2	Phone calls and website	6 and 12	Self-reported	IG: 148.2 ± 12.9 CG: 147.7 ± 13.2	IG: 84.5 ± 11.7 CG: 84.9 ± 11.5
Marquez Contreras et al. (2019)	Spain	Cluster RCT	Hypertension	IG: 73 CG: 75	IG: 57.7 ± 9.0 CG: 57.1 ± 10.0	Smartphone-app	6 and 12	Medication event monitoring system	IG: 134.7 ± 14.0 CG: 134.5 ± 8.0	IG: 86.3 ± 12.8 CG: 93.1 ± 14.1
McKinstry et al. (2013)	UK	Multicentre RCT	Uncontrolled hypertension	IG: 200 CG: 201	IG: 60.5 ± 11.8 CG: 60.8 ± 10.7	SMS, emails and BP Telemonitoring link	6	Morisky Medication Adherence Scale	IG: 153.1 ± 15.2 CG: 152.5 ± 14.5	IG: 92.4 ± 11.6 CG: 90.1 ± 11.4
McMahon et al. (2005)	USA	Multicenter RCT	Hypertension	IG: 37 CG: 35	IG: NR CG: NR	Website	12	NR	NR	NR
McManus et al. (2010)	UK	RCT	Hypertension	IG: 234 CG: 246	IG: 66.6 ± 8.8 CG: 66.2 ± 8.8	BP Telemonitoring link	6 and 12	NR	IG: 152.1 ± 11.9 CG: 151.8 ± 11.9	IG: 85.0 ± 8.5 CG: 84.5 ± 9.6
McManus et al. (2018)	UK	RCT	Uncontrolled hypertension	IG: 389 CG: 393	IG: 67.0 ± 9.3 CG: 66.8 ± 9.4	BP Telemonitoring link	6 and 12	Medication Adherence Rating Scale	IG: 153.2 ± 14.3 CG: 153.1 ± 14.0	IG: 85.5 ± 10.0 CG: 86.0 ± 10.3
Meurer et al. (2019)	USA	RCT	Hypertension	IG: 28 CG: 27	IG: 49.0 ± 13.0 CG: 50.0 ± 12.0	SMS	3	NR	NR	NR
Milani et al. (2017)	USA	Non-RCT	Uncontrolled hypertension	IG: 156 CG: 400	IG: 68.0 ± 10.0 CG: 68.0 ± 10.0	Phone calls	3	Medication refill	IG: 147.0 ± 19.0 CG: 147.0 ± 5.0	IG: 81.0 ± 12.0 CG: 81.0 ± 8.0
Morawski et al. (2018)	USA	RCT	Uncontrolled hypertension	IG: 210 CG: 202	IG: 51.7 ± 10.5 CG: 52.4 ± 10.1	Smartphone-app	3	Morisky Medication Adherence Scale	IG: 151.4 ± 9.0 CG: 151.3 ± 9.4	NR
Myoungsuk et al. (2019)	South Korea	RCT	Hypertension	IG1: 30 IG2: 32 IG3: 31 CG: 31	IG1: 77.5 ± 6.4 IG2: 77.2 ± 6.7 IG3: 78.3 ± 6.6 CG: 77.5 ± 6.9	IG1: Phone calls IG2: emails IG3: phone calls and emails	2	Morisky Medication Adherence Scale	IG1: 141.2 ± 18.3 IG2: 142.9 ± 12.1 IG3: 142.0 ± 13.3 CG: 140.0 ± 11.6	IG1: 87.1 ± 10.5 IG2: 87.3 ± 7.9 IG3: 86.6 ± 5.6 CG: 88.1 ± 6.4

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Table 1 (*Continued*).

Reference	Country	Study design	Status	Sample size	Mean age, years (mean±SD)	Intervention	Length, months	Medication adherence	Baseline systolic blood pressure, mmHg (mean±SD)	Baseline diastolic blood pressure, mmHg (mean±SD)
Neumann et al. (2015)	Germany	RCT	Hypertension	IG: 30 CG: 30	IG: 54.7 ± 17.9 CG: 52.9 ± 19.0	BP Telemonitoring link	3	NR	IG: 142.8 ± 11.1 CG: 141.4 ± 12.6	IG: 82.8 ± 10.4 CG: 82.8 ± 10.4
Nolan et al. (2012)	Canada	RCT	Hypertension	IG1: 63 IG2: 97 CG: 227	IG1: 57.0 ± 7.3 IG2: 55.7 ± 6.8 CG: 56.7 ± 7.7	emails	4	NR	IG1: 134.6 ± 19.1 IG2: 143.3 ± 16.7 CG: 139.6 ± 18.1	IG1: 77.1 ± 9.5 IG2: 80.9 ± 9.8 CG: 80.1 ± 10.5
Nolan et al. (2018)	Canada	RCT	Hypertension	IG: 35 CG: 33	IG: 58.0 ± 11.7 CG: 57.2 ± 8.7	emails	4 and 12	REACH tool	IG: 141.5 ± 11.7 CG: 140.6 ± 11.6	IG: 87.3 ± 8.8 CG: 87.3 ± 8.7
Pan et al. (2018)	China	RCT	Uncontrolled hypertension	IG: 52 CG: 55	IG: 56.6 ± 9.7 CG: 57.8 ± 10.9	BP Telemonitoring link	1, 3 and 15	NR	IG: 148.3 ± 7.1 CG: 147.9 ± 8.7	IG: 88.0 ± 7.5 CG: 87.0 ± 8.4
Park et al. (2009)	South Korea	Non-RCT	Hypertension	IG: 28 CG: 21	IG: 53.2 ± 6.9 CG: 54.6 ± 11.0	SMS	2	NR	IG: 135.7 ± 8.8 CG: 133.9 ± 9.3	IG: 90.4 ± 6.7 CG: 91.0 ± 9.9
Persell et al. (2018)	USA	RCT	Hypertension	IG1: 262 IG2: 278 CG: 254	IG1: 53.6 ± 9.7 IG2: 51.6 ± 9.5 CG: 53.0 ± 9.5	IG1: Website IG2: Website + education	3, 6 and 12	Self-reported	IG1: 148.6 ± 17.5 IG2: 145.5 ± 17.5 CG: 141.5 ± 15.9	IG1: 89.1 ± 12.4 IG2: 89.5 ± 12.1 CG: 86.9 ± 12.0
Pezzin et al. (2011)	USA	Cluster RCT	Uncontrolled hypertension	IG1: 197 IG2: 221 CG: 217	IG1: 65.7 ± 10.1 IG2: 64.2 ± 11.1 CG: 64.3 ± 10.5	IG1: emails IG2: emails + education	3	NR	IG1: 155.9 ± 21.7 IG2: 154.3 ± 20.1 CG: 156.1 ± 20.2	IG1: 86.7 ± 13.9 IG2: 86.8 ± 12.2 CG: 88.1 ± 16.0
Piette et al. (2012)	Honduras and Mexico	RCT	Hypertension	IG: 99 CG: 101	IG: 58.0 ± 1.3 CG: 57.1 ± 1.1	Phone calls	1.5	Morisky Medication Adherence Scale	IG: 153.2 ± 2.1 CG: 150.0 ± 2.1	NR
Rifkin et al. (2013)	USA	RCT	Uncontrolled hypertension	IG: 28 CG: 15	IG: 68.5 ± 7.5 CG: 67.9 ± 8.4	BP Telemonitoring link	6	Morisky Medication Adherence Scale	IG: 147.0 ± 17.5 CG: 146.0 ± 8.8	IG: 77.0 ± 12.3 CG: 81.0 ± 10.9
Rinfret et al. (2009)	Canada	RCT	Uncontrolled hypertension	IG: 111 CG: 112	IG: 55.0 ± 11.0 CG: 57.0 ± 13.0	Phone calls	12	Medication refill	IG: 141.0 ± 11.0 CG: 140.0 ± 9.0	IG: 81.0 ± 9.0 CG: 80.0 ± 10.0
Schroeder et al. (2020)	USA	RCT	Hypertension	IG: 148 CG: 147	IG: 52.5 ± 11.0 CG: 54.2 ± 11.5	SMS and phone calls	6 and 12	Self-reported	IG: 132.2 ± 18.8 CG: 135.1 ± 20.1	IG: 81.1 ± 11.5 CG: 82.0 ± 13.6
Varis and Kantola (2010)	The Netherlands	RCT	Hypertension	IG: 89 CG: 68	IG: NR CG: NR	BP Telemonitoring link	13 and 14	NR	IG: 159.4 ± 18.3 CG: 158.8.1 ± 16.8	IG: 97.4 ± 8.9 CG: 97.2 ± 9.1

(*Continued on next page*)

Table 1 (*Continued*).

Reference	Country	Study design	Status	Sample size	Mean age, years (mean±SD)	Intervention	Length, months	Medication adherence	Baseline systolic blood pressure, mmHg (mean±SD)	Baseline diastolic blood pressure, mmHg (mean±SD)
Wakefield et al. (2014)	USA	RCT	Uncontrolled hypertension	IG: 53 CG: 55	IG: 57.7 ± 10.8 CG: 62.5 ± 10.9	BP Telemonitoring link	3	NR	IG: 142.0 ± 15.0 CG: 144.4 ± 16.4	NR
Yi et al. (2015)	USA	RCT	Uncontrolled hypertension	IG: 409 CG: 419	IG: 61.3 ± 11.9 CG: 61.3 ± 12.2	Website	10	NR	IG: 151.5 ± 16.4 CG: 152.1 ± 15.0	IG: 83.9 ± 11.2 CG: 82.3 ± 10.6
Yoo et al. (2009)	South Korea	RCT	Hypertension	IG: 57 CG: 54	IG: 57.0 ± 9.1 CG: 59.4 ± 8.4	Smartphone-app and SMS	3	NR	IG: 140.2 ± 18.7 CG: 138.7 ± 17.8	IG: 84.4 ± 10.0 CG: 83.3 ± 10.0

RCT: randomized control trial; IG: intervention group; CG: control group; NR: not reported; SMS: short message service; BP: blood pressure.

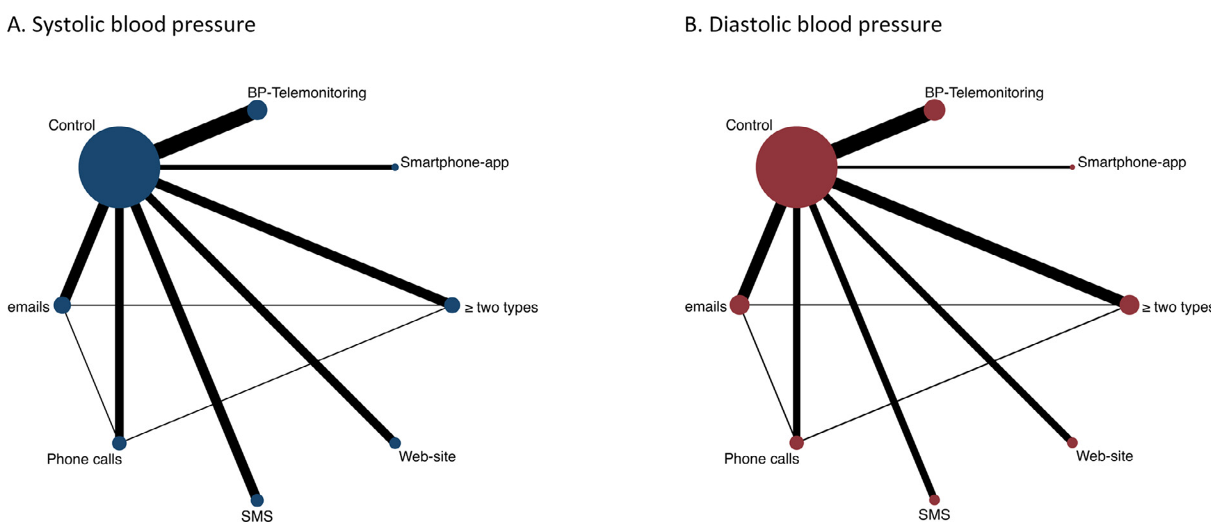

Fig. 1. Network of available comparisons between eHealth interventions in: (A) systolic blood pressure and (B) diastolic blood pressure. Size of node is proportional to number of participants randomized in each eHealth intervention, and thickness of continuous line connecting nodes is proportional to number of trials directly comparing the two e Health interventions. / BP: blood pressure; SMS: short message service.

3.3. *Risk of bias*

As evaluated by the RoB2 tool, 60.8% of the studies showed some concerns in the risk of bias, with 23.5% and 15.7% studies showing high and low risks of bias in the overall bias, respectively. High risks of bias in the studies were mainly due to the randomization process and the deviations from the intended intervention domains (Supplementary Figures S2 and S3).

3.4. *Effect on systolic and diastolic blood pressure*

In Table 2, considering the network meta-analysis estimates (lower diagonal), all types of eHealth interventions were effective in reducing systolic blood pressure, being more than two types of eHealth interventions (ES = −0.46; 95%CI: −0.64, −0.27, $p < 0.001$) the most effective in reducing systolic blood pressure. Furthermore, more than two types of eHealth interventions, phone calls, blood pressure telemonitoring, web-site and smartphone-app were effective in reducing diastolic blood pressure, being the latter the most effective (ES = −0.40; 95%CI: −0.70, −0.10, $p = 0.014$) (Table 2).

When effects on systolic and diastolic blood pressure were included in a comprehensive scatterplot, more than two types of eHealth interventions, phone calls and smartphone-app showed a statistically significant moderate effect on reducing both systolic and diastolic blood pressure (Fig. 2).

3.5. *Effects on adherence to medication treatment, physical activity compliance, blood pressure control, and QoL*

Smartphone-app (RR = 0.55; 95%CI: 0.33, 0.93, $p = 0.004$) showed higher effect on adherence to medication treatment. Additionally, more than two types of eHealth interventions (RR = 0.82; 95%CI: 0.74, 0.90, $p < 0.001$) and emails (RR = 0.43; 95%CI: 0.20, 0.90, $p = 0.026$) showed effect on physical activity compliance. All the types of eHealth interventions, except emails and smartphone-app showed effect blood pressure control. Finally, only blood pressure telemonitoring showed a weak increase of QoL (ES = 0.16; 95%CI: 0.01, 0.31, $p = 0.032$) (Table 3).

Table 2
Pooled mean differences on systolic blood pressure (A) and diastolic blood pressure (B). Upper right triangle gives the pooled standardized mean differences from pairwise comparisons (column intervention relative to row), lower left triangle pooled standardized mean differences from the network meta-analysis (row intervention relative to column).

A. Systolic blood pressure							
Control	**−0.28 (−0.51, −0.05)**	**−0.52 (−0.96, −0.09)**	**−0.21 (−0.32, −0.10)**	**−0.25 (−0.40, −0.10)**	**−0.13 (−0.22, −0.04)**	**−0.34 (−0.55, −0.12)**	**−0.21 (−0.32, −0.09)**
−0.46 (−0.64, −0.27)	≥ two types	−0.01 (−0.52, 0.49)	NA	0.32 (−0.18, 0.82)	NA	NA	NA
−0.37 (−0.57, −0.17)	0.08 (−0.18, 0.35)	Phone calls	NA	0.28 (−0.22, 0.79)	NA	NA	NA
−0.25 (−0.38, −0.13)	0.21 (−0.02, 0.43)	0.06 (−0.20, 0.32)	BP-Telemonitoring	NA	NA	NA	NA
−0.28 (−0.45, −0.10)	0.18 (−0.07, 0.43)	0.10 (−0.16, 0.36)	−0.02 (−0.24, 0.28)	emails	NA	NA	NA
−0.27 (−0.44, −0.11)	0.19 (−0.06, 0.43)	0.10 (−0,16, 0.36)	−0.02 (−0.23, 0.19)	0.00 (−0.24, 0.24)	Web-site	NA	NA
−0.26 (−0.50, −0.01)	0.20 (−0.10, 0.51)	0.12 (−0.20, 0.43)	0.00 (−0.27, 0.28)	0.02 (−0.28, 0.32)	0.02 (−0.28, 0.31)	Smartphone-app	NA
−0.21 (−0.40, −0.02)	0.24 (−0.02, 0.51)	0.16 (−0.11, 0.44)	0.04 (−0.19, 0.27)	0.06 (−0.19, 0.32)	0.06 (−0.19, 0.31)	0.04 (−0.26, 0.35)	SMS
B. Diastolic blood pressure							
Control	**−0.29 (−0.52, −0.07)**	**−0.36 (−0.58, −0.13)**	**−0.17 (−0.28, −0.07)**	−0.10 (−0.21, 0.00)	**−0.29 (−0.52, −0.06)**	**−0.32 (−0.44, −0.19)**	**−0.19 (−0.33, −0.04)**
−0.29 (−0.46, −0.13)	≥ two types	0.05 (−0.45, 0.55)	NA	0.33 (−0.16, 0.83)	NA	NA	NA
−0.29 (−0.52, −0.07)	0.00 (−0.27, 0.27)	Phone calls	NA	0.27 (−0.23, 0.77)	NA	NA	NA
−0.16 (−0.27, −0.05)	0.14 (−0.06, 0.34)	0.14 (−0.39, 0.11)	BP-Telemonitoring	NA	NA	NA	NA
−0.10 (−0.26, 0.05)	0.19 (−0.03, 0.42)	0.19 (−0.07, 0.45)	0.05 (−0.14, 0.24)	emails	NA	NA	NA
−0.18 (−0.34, −0.02)	0.11 (−0.12, 0.35)	0.11 (−0.16, 0.39)	−0.02 (−0.22, 0.17)	−0.08 (−0.30, 0.15)	Web-site	NA	NA
−0.40 (−0.70, −0.10)	−0.10 (−0.44, 0.24)	−0.10 (−0.48, 0.27)	−0.24 (−0.56, 0.08)	−0.29 (−0.63, 0.05)	−0.22 (−0.56, 0.13)	Smartphone-app	NA
−0.19 (−0.42, 0.05)	0.10 (−0.18, 0.39)	0.10 (−0.22, 0.42)	−0.03 (−0.29, 0.22)	−0.09 (−0.37, 0.19)	−0.01 (−0.30, 0.27)	0.21 (−0.17, 0.59)	SMS

NA: not available; BP: blood pressure; SMS: short message service.

Table 3
Meta-analyses for pooled effect of eHealth interventions on adherence to medication, physical activity compliance, blood pressure control and quality of life.

	Adherence to medication treatment			Physical activity compliance			Blood pressure control			Effect on QoL		
Subgroup	n	Relative risk(95%CI)	I2	n	Relative risk(95%CI)	I2	n	Relative risk(95%CI)	I2	n	Effect size(95%CI)	I2
≥ two types	5	0.79(0.48, 1.01)	91.3	**3**	**0.82(0.74, 0.90)**	**0.0**	**3**	**0.75(0.57, 0.99)**	**75.5**	–	–	–
Phone calls	3	0.44(0.09, 2.13)	90.7	2	0.82(0.37, 1.81)	0.0	1	0.34(0.18, 0.65)	–	2	−0.04(−0.24, 0.16)	0.0
BP-Telemonitoring	6	0.99(0.92, 1.05)	44.2	1	0.95(0.80, 1.12)	–	**4**	**0.71(0.52, 0.97)**	**65.5**	**2**	**0.16(0.01, 0.31)**	**0.0**
emails	1	0.26(0.11, 0.61)	–	**3**	**0.43(0.20, 0.90)**	**69.3**	2	0.95(0.74, 1.22)	0.0	**–**	**–**	**–**
Web-site	3	1.01(0.84, 1.22)	0.0	3	0.84(0.71, 1.01)	0.0	**5**	**0.70(0.55, 0.90)**	**79.1**	2	−0.00(−0.13, 0.12)	0.0
Smartphone-app	**3**	**0.55(0.33, 0.93)**	**82.0**	–	–	–	2	0.87(0.60, 1.27)	78.7	**–**	**–**	**–**
SMS	3	0.70(0.48, 1.02)	78.1	1	0.85(0.43, 1.68)	–	**5**	**0.84(0.75, 0.93)**	**0.0**	–	–	–

QoL: quality of life; BP: blood pressure; SMS: short message service.

3.6. Treatment ranking

For systolic blood pressure, more than two types of eHealth interventions showed the higher SUCRA (91.9%), following by phone calls (75.8%) and emails (51.6%). For diastolic blood pressure, smartphone-app showed the higher SUCRA (86.3%), following by more than two types of eHealth interventions (74.9%) and phone calls (72.7%)(Supplementary Fig. S4).

3.7. Subgroup analysis

For systolic blood pressure, phone calls (ES = −0.92; 95%CI: −1.46, −0.38, p = 0.001) and blood pressure telemonitoring (ES = −0.23; 95%CI: −0.47, −0.00, p = 0.047) showed effect when the intervention length was ≤3 months; emails (ES = −0.29; 95%CI: −0.50, −0.08, p = 0.006) showed effect when the intervention length was 4–5 months; smartphone-app (ES = −0.40; 95%CI: −0.55, −0.26, p < 0.001), blood pressure telemonitoring (ES = −0.26; 95%CI: −0.39, −0.13, p < 0.001) and website (ES = −0.17; 95%CI: −0.32, −0.01, p = 0.039) showed effect when the intervention length was 6 months; and emails (ES = −0.33; 95%CI: −0.53, −0.13, p = 0.001), blood pressure telemonitoring (ES = −0.23; 95%CI: −0.39, −0.07, p = 0.004) and website (ES = −0.11; 95%CI: −0.20, −0.31, p = 0.009) showed effect when the intervention length was ≥12 months. For diastolic blood pressure, phone calls (ES = −0.52; 95%CI: −0.99, −0.05, p = 0.031) and more than two types of eHealth interventions (ES = −0.41; 95%CI: −0.61, −0.20, p < 0.001) showed effect when the intervention length was ≤3 months; smartphone-app (ES = −0.37; 95%CI: −0.54, −0.21, p < 0.001) and blood pressure telemonitoring (ES = −0.18; 95%CI: −0.29, −0.07, p = 0.001) showed effect when the intervention length was 6 months; and web-site (ES = −0.40; 95%CI: −0.68, −0.12, p = 0.005) showed effect when the intervention length was ≥12 months (Table 4).

Table 4
Subgroup analysis based on length of intervention by type of eHealth intervention.

Subgroup	≤3 months n	≤3 months Effect size(95%CI)	≤3 months I2	4–5 months n	4–5 months Effect size(95%CI)	4–5 months I2	6 months n	6 months Effect size(95%CI)	6 months I2	7–11 months n	7–11 months Effect size(95%CI)	7–11 months I2	≥12 months n	≥12 months Effect size(95%CI)	≥12 months I2
Systolic blood pressure															
≥ two types	3	−0.31(−0.66, 0.05)	62.5	-	-	-	5	−0.14(−0.49, 0.22)	89.9	-	-	-	2	−0.27(−0.70, 0.16)	71.5
Phone calls	**3**	**−0.92(−1.46, −0.38)**	**77.6**	-	-	-	2	−0.09(−0.28, 0.11)	0.0	-	-	-	2	−0.25(−0.56, 0.06)	70.9
BP-Telemonitoring	**9**	**−0.23(−0.47, −0.00)**	**73.3**	1	0.42(0.21, 0.62)	-	**12**	**−0.26(−0.39, −0.13)**	**68.7**	-	-	-	**6**	**−0.23(−0.39, −0.07)**	**69.7**
emails	3	−0.07(−0.27, 0.12)	45.3	**5**	**−0.29(−0.50, −0.08)**	**69.3**		-	-	-	-	-	**2**	**−0.33(−0.53, −0.13)**	**0.0**
Web-site	2	−0.04(−0.16, 0.09)	0.0	-	-	-	**3**	**−0.17(−0.32, −0.01)**	**57.6**	1	−0.03(−0.16, 0.10)	-	**5**	**−0.11(−0.20, −0.03)**	**0.0**
Smartphone-app	2	−0.31(−0.85, 0.23)	93.3	-	-	-	**3**	**−0.40(−0.55, −0.26)**	**0.0**	-	-	-	1	−0.25(−0.57, 0.07)	-
SMS	3	−0.35(−0.93, 0.23)	69.4	1	−0.37(−0.78, 0.04)	-	4	−0.06(−0.18, 0.06)	45.3	-	-	-	2	−0.17(−0.35, 0.01)	72.8
Diastolic blood pressure															
≥ two types	**3**	**−0.41(−0.61, −0.20)**	**0.0**	3	0.82(0.74, 0.90)	0.0	5	−0.22(−0.58, 0.15)	90.4	-	-	-	2	−0.15(−0.54, 0.24)	65.1
Phone calls	**2**	**−0.52(−0.99, −0.05)**	**41.8**	-	-	-	1	−0.09(−0.62, 0.44)	-	-	-	-	1	−0.33(−0.60, −0.07)	-
BP-Telemonitoring	7	−0.09(−0.24, 0.05)	36.5	1	0.23(0.02, 0.44)	-	**12**	**−0.18(−0.29, −0.07)**	**59.1**	-	-	-	6	−0.19(−0.37, 0.00)	70.8
emails	3	−0.00(−0.14, 0.13)	0.0	5	−0.15(−0.33, 0.04)	41.3	-	-	-	-	-	-	1	−0.19(−0.47, 0.09)	-
Web-site	1	−0.64(−0.92, −0.36)	-	-	-	-	2	−0.60(−1.31, 0.10)	93.9	1	−0.08(−0.21, 0.06)	-	**3**	**−0.40(−0.68, −0.12)**	**74.9**
Smartphone-app	1	−0.23(−0.42, −0.05)	-	-	-	-	**2**	**−0.37(−0.54, −0.21)**	**0.0**	-	-	-	1	−0.33(−0.65, −0.01)	-
SMS	2	−0.32(−0.92, 0.27)	66.9	1	−0.31(−0.73, 0.11)	-	2	−0.15(−0.32, 0.03)	0.0	-	-	-	-	-	-

BP: blood pressure; SMS: short message service.

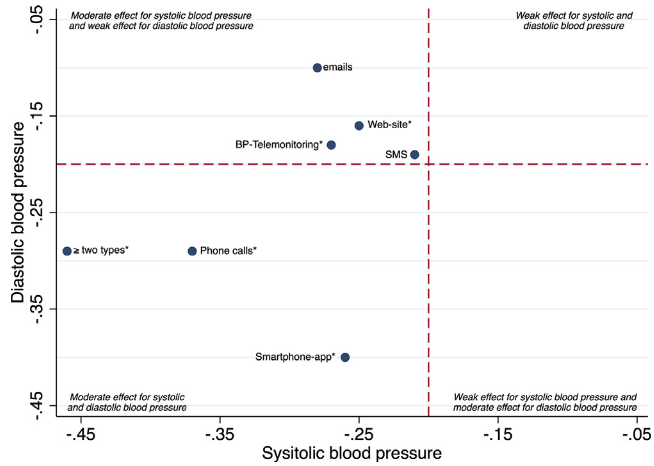

Fig. 2. Scatterplot for the effect of eHealth interventions vs. placebo for systolic blood pressure (x-axis) and diastolic blood pressure (y-axis). Treatments lying on the lower left-hand side quarter showed a moderate effect for both systolic blood pressure and diastolic blood pressure. / * Means statistically significant effect in both systolic blood pressure and diastolic blood pressure. BP: blood pressure; SMS: short message service.

3.8. Sensitivity analysis, heterogeneity and small study effect

The pooled mean difference was not significantly modified when the individual study data were removed, one at a time, from any pairwise comparison analysis. Furthermore, phone calls (I^2= 89.4, τ^2=0.255), more than two eHealth interventions (I^2= 79.7, τ^2=0.084) and smartphone-app (I^2= 76.0, τ^2=0.044) for systolic blood pressure and more than two eHealth interventions (I^2= 77.7, τ^2=0.076) and website (I^2= 85.1, τ^2=0.054) showed considerable heterogeneity. Finally, there was evidence of small study effect in funnel plot asymmetry and Egger test for emails in both, systolic blood pressure (p = 0.007) and diastolic blood pressure (p = 0.015).

4. Discussion

This network meta-analysis provides an overview of the evidence comparing eHealth interventions for the self-management of hypertension. Although almost all types of eHealth interventions appear to be effective for reducing blood pressure (systolic blood pressure, diastolic blood pressure or both) in individuals with hypertension, more than two types of eHealth interventions, phone calls and smartphone-app showed statistically significant higher effect on reducing both systolic and diastolic blood pressure. Additionally, in terms of intervention length, for both systolic and diastolic blood pressure, phone calls were effective when intervention length was less than 3 months, blood pressure telemonitoring when intervention length was 6 months and website when intervention length was more than 12 months. Finally, (i) smartphone-app improved medication adherence by 45%; (ii) more than two types of eHealth interventions and emails improved physical activity compliance by 18% and 57% respectively; (iii) more than two types of eHealth interventions, phone calls, blood pressure telemonitoring, website and SMS improved blood pressure control between 16% and 30%; and (iv) blood pressure telemonitoring showed a week effect on QoL.

In line with our results, previous systematic reviews and meta-analysis have evidenced that eHealth interventions reduce systolic and diastolic blood pressure, could improve medication adherence and blood pressure control among people with hypertension (Andre et al., 2019; Choi et al., 2020; Lu et al., 2019; Li et al., 2020, Liu et al., 2013; Omboni and Guarda, 20112013; Verberk et al., 2011; Ma et al., 2019; Xiong et al., 2018; Zullig et al., 2013). From a more comprehensive clinical point of view, our meta-analysis adds important results to the growing evidence, showing which type of eHealth intervention is better for the management of hypertension, not only in reducing systolic and diastolic blood pressure but also in improving adherence to treatment, physical activity compliance blood pressure control, and increasing QoL among patients with hypertension.

The effectiveness of hypertension treatments has been demonstrated by numerous studies (Tocci et al., 2020). However, in clinical practice, < 40% subjects with hypertension have their blood pressures under control (Beaney et al., 2019). The main reason for treatment failure in the control of hypertension is non-compliance with treatment (Poulter et al., 2020). The effectiveness of a treatment does not exclusively depend on the appropriateness of the therapeutic decision, rather it is ultimately conditioned by the collaboration of the patient (Kretchy et al., 2015). Although much time and money are invested in finding effective drugs, little attention is paid to whether the drugs are being used properly. Additionally, two other therapeutic pillars, smoking and exercise, are more or less neglected by the population. Our findings show clinicians potential approaches based on eHealth interventions for management of hypertension.

Furthermore, our findings show that the most effective methods for blood pressure control are the use of more than two types of eHealth interventions, phone calls or blood pressure telemonitoring. The use of these eHealth interventions is increasing among people in both developed and developing countries, and it is a growing technology in use worldwide (World Health Organization, 2017). The use of mobile phones and blood pressure telemonitoring for eHealth interventions allows for a new healthcare model and makes healthcare more accessible by facilitating communication between the patient and the healthcare professional, allowing remote monitoring and stratification of the patients and performing remote interventions at the time when they can have the greatest impact (Omboni et al., 2016). The importance of eHealth interventions must be highlighted in times like these when face-to-face contact must be limited, particularly in clinical settings, where the transmission of infectious diseases, namely influenza and Sars-CoV-2, may be higher. Additionally, it seems that the current treatment concept will lead to an increased use of eHealth in daily clinical practice (Smith et al., 2020).

This network meta-analysis has some limitations that should be acknowledged. Some of these limitations are common to meta-analyses (e.g., publication bias, selection bias, and limited availability of complete information from study reports). First, the limited number of samples included in the evaluation of some eHealth interventions, and the possibility that unpublished studies in these types of eHealth interventions may have modified the results of the meta-analysis. Second, some interventions (more than two types of eHealth interventions, phone calls, smartphone-app or website) showed a considerable level of heterogeneity, and thus should be interpreted with caution. Third, the results of this network meta-analysis were obtained after some data manipulation (estimating RRs and ESs from the raw data of the included studies), which could generate some bias. Fourth, a wide variety of tools were used to measure adherences to medication treatment and physical activity compliance. Finally, 25.5% of the studies included in the systematic review showed a high risk of bias.

In summary, our study supports that eHealth is a suitable intervention for the self-management of hypertension. Considering our results and the population's accessibility to mobile phones, eHealth could be a useful and largely scalable tool for the self-management of hypertension. Therefore, it is essential that well-designed RCTs with higher statistical power be conducted in the future to strengthen the currently weak evidence, in order to demonstrate that over time, effective eHealth interventions could change the current paradigm of lifestyle prescription, improve patients' self-management of diseases, develop new clinical practice guidelines, and facilitate workflow in everyday clinical consultations.

Disclosures

The lead authors and manuscript's guarantor affirm that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Iván Cavero-Redondo: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Alicia Saz-Lara:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Irene Sequí-Dominguez:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Maria Dolores Gómez-Guijarro:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Marta Carolina Ruiz-Grao:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Vicente Martinez-Vizcaino:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Celia Álvarez-Bueno:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing.

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Supplementary materials

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