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Meta-Analysis

Meta Analysis the Effect of Electronic Health-based Self Management in Controlling Blood Pressure in Hipertensive Patients

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ABSTRACT

Background Consistent application of self-management is important in efforts to improve the quality of life and health status of hypertensive patients. Electronic health is here to facilitate self-management of hypertensive patients and provide health information to health workers in real time and promote lifestyle modifications. The purpose of this study was to analyze the influence of electronic health-based self-management on blood pressure control in hypertensive patients.
Subjects and Method: : This study is a meta-analysis using PICO namely Population: Hypertensive patients; Intervention: Self-management based on electronic health; Comparison: No self-management based on electronic health; Outcome: Systolic and diastolic blood pressure. This study uses articles from several databases, i.e Pubmed, Google Scholar, Science Direct and the Cochrane Library using the following keywords "Hypertension" OR "Hypertensive" OR "Blood Pressure" OR "High Blood Pressure" AND "Self Management" OR "Self Care" OR "Self Monitoring" AND "Electronic Health" OR "eHealth" OR "Telemedicine" OR "Telehealth" OR "mHealth" OR "Mobile Health" OR "Mobile Application" OR "Message Text" OR "Phone Calls". Articles included in the research are articles that use English with an RCT study design whose publication is within the period of 2012-2022. The steps in the systematic review are carried out based on the PRISMA flow diagram guidelines. Quantitative analysis was carried out using Review Manager (Revman) 5.3.
Results: There were 9 articles from South Africa, America, South Korea, Spanish, England, Scotland, and Honduras, with a sample size of 3,071 hypertensive patients concluded that electronic health-based self-management could reduce systolic blood pressure by 0.38 units and was statistically significant (SMD= -0.38; 95% CI = -0.55 to -0.20; p<0.001). The meta-analysis synthesized 9 studies with a total sample size = 2.095 hypertensive patients concluded that electronic health-based self-management could reduce diastolic blood pressure by 0.21 units and was statistically significant (SMD= -0.21; 95% CI = -0.29 to -0.12; p< 0.001).
Conclusion: Electronic health-based self-management can reduce systolic and diastolic blood pressure control in hypertensive patients.

Keywords: Self management, electronic health, blood pressure, hypertension

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BACKGROUND

Hypertension is a non-communicable disease, it is said to be hypertension if there is an increase in systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg (WHO, 2013). Hypertension is a

major risk for cardiovascular diseases such as stroke, heart disease, and kidney failure so that it will worsen the patient's quality of life and increase health care costs (Olsen et al., 2016). Hypertension or high blood pressure is a risk factor for morbidity and mortality that globally affects more than 1 billion adults (WHO, 2021).

Based on the results of Basic Health Research (Riskesdas) regarding the prevalence of hypertension sufferers in Indonesia in 2013 it was 25.8% and in 2018 it increased to 34.1% (Ministry of Health, 2018). Controlling blood pressure in hypertensive patients requires ability and compliance in managing behavior in daily life so that blood pressure can be controlled properly (Lee et al., 2021).

Consistent application of self-management is important in efforts to improve the quality of life of people with hypertension and the health status of patients with hypertension, because sufferers are the main actors who will carry out all treatment and also carry out activities that support the success of treating their disease (Boitchi et al., 2021). However, hypertensive patients often fail to control their blood pressure consistently, because hypertensive patients experience difficulties in complying with self-management activities and require long management or even the sufferer's lifetime (Ko et al., 2018).

The application of technology in self-management interventions for hypertensive patients has developed very rapidly. As an example of effective health technology to improve blood pressure control, namely through electronic health (Logan, 2013).

Electronic health is associated with increased communication between patients and health care providers which can improve self-management behavior in chronic diseases, including hypertension (Yardley et al., 2015). The study conducted by Morawski et al. (2018), showed that there were differences in blood pressure in the group that was given intervention using the Medisafe application installed via a smartphone which included reminders, treatment adherence reports, and peer support compared to the control group which only used ordinary care.

Based on this background description, a comprehensive study is needed from various primary studies on the effect of electronic health-based self-management on blood pressure control. The purpose of this study is to analyze how much influence electronic health-based self-management has on blood pressure control in hypertensive patients by synthesizing the results of previous primary studies.

SUBJECTS AND METHOD

1. Study Design

This research is a study that uses systematic review and meta-analysis methods. The articles used were obtained from several electronic databases including Pubmed, Google Scholar, Science Direct and the Cochrane Library with a Randomized Control Trial study design whose publications were from 2012 to 2022. The keywords used in the search were "Hypertension" OR "Hypertensive" OR “Blood Pressure” OR “High Blood Pressure” AND “Self Management” OR “Self Care” OR “Self Monitoring” AND “Electronic Health” OR “eHealth” OR “Telemedicine” OR “Telehealth” OR “mHealth” OR “ Mobile Health” OR “Mobile Application” OR “Message Text” OR “Phone Calls”. Identify articles using the PRISMA flowchart.

2. Steps of Meta-Analysis

The meta-analysis was carried out in five steps as follows:

a. Formulate research questions in the PICO format (population, intervention, comparison, outcome).

b. Search for primary study articles from various electronic databases including Google Scholar, PubMed, and Science Direct and non-electronics.
c. Conduct screening and critical appraisal (Critical Appraisal) of primary research articles.
d. Perform data extraction and synthesize effect estimates into RevMan 5.3.
e. Interpret and conclude the results.

3. Inclusion Criteria

Full paper articles using the Randomized Control Trial (RCT) study design, the relationship size used was the Mean SD, the subjects in the study were hypertensive patients, the intervention provided was in the form of electronic health to assist self-management activities in hypertensive patients, the results reported article is systolic blood pressure or diastolic blood pressure or both.

4. Exclusion Criteria

The exclusion criteria were an articles published in languages other than English, and articles published before 2012.

5. Operational Definition of Variables

Electronic health-based self-management: Utilization of health information technology used to manage health conditions and improve patient-centered care in health systems.

Systolic blood pressure: The pressure of the heart as it pumps blood throughout the body, indicating the pressure in the blood vessels as the heart contracts and pumps blood toward the arteries.

Diastolic blood pressure: The pressure exerted by the blood vessels after the heart pumps, indicating the pressure in the blood vessels when the heart is at rest.

6. Instrument

The systematic study guide used is the PRISMA flowchart guideline and the quality assessment of research articles using the Critical Appraisal Skills Program Randomized Controlled Trial Standard Checklist (CASP for RCT).

7. Data Analysis

The data in this study were analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots are used to determine the effect size and heterogeneity of the data. Data processing is carried out based on variations between studies by determining the use of an analysis model, namely the fixed effect model or the random effect model.

RESULTS

In the meta-analysis process, it begins with determining a research question or what is commonly called a research question. The question in this study is whether self-management based on electronic health affects blood pressure control in hypertensive patients. To further formulate PICO which will be used as a reference as a search for relevant articles. Article searches were conducted through several electronic databases including: Pubmed, Google Scholar, Science Direct and the Cochrane Library. There are 11 articles originating from South Africa, the United States, South Korea, Spain, England, Scotland, Honduras, and England. The article review process can be seen in the PRISMA flowchart as follows.

Figure 2 shows that the research locations for the effect of electronic health-based self-management on blood pressure control were 5 studies from the Americas (5 studies from the United States), 3 studies from the European continent (1 study from Spain, 1 study from England, and 1 study from Scotland), 2 studies from the Asian Continent (2 studies from South Korea), and 1 study from the African continent (1 study from South Africa). Assessment of study quality used the Critical Appraisal Skills Program Randomized Controlled Trial Standard Checklist (CASP for RCT) in research on the effect of

electronic health-based self-management on blood pressure control (see Table 1).

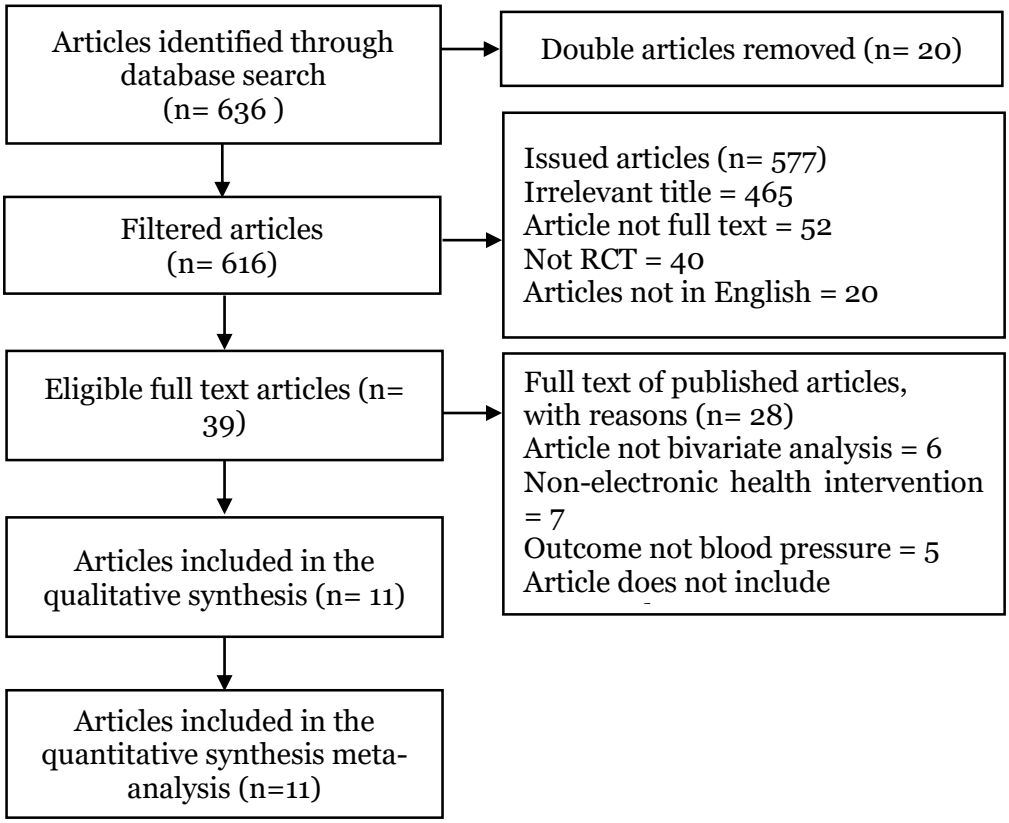

Figure 1. PRISMA flowchart diagram of the Effect of Electronic Health-based Self Management in Controlling Blood Pressure in Hipertensive Patients

Figure 2. Map of the Effect of Electronic Health-based Self Management in Controlling Blood Pressure in Hipertensive Patients

Table 1. Assessment of the quality of randomized controlled trial studies "The effect of electronic health-based self-management on blood pressure control"

Primary Study	Criteria											Total
	1	2	3	4	5	6	7	8	9	10	11	
Bobrow et al., (2016)	1	1	1	1	1	1	1	1	1	1	1	11
Margolis et al., (2013)	1	1	1	1	1	1	1	1	1	1	1	11
Myoungsuk et al., (2019)	1	1	1	1	1	1	1	1	1	1	1	11
Contreras et al., (2018)	1	1	1	0	1	1	1	1	1	1	1	10
McManus et al., (2018)	1	1	1	0	1	1	1	1	1	1	1	10
McKinstry et al., (2013)	1	1	1	1	1	1	1	1	1	1	1	11
Kim et al., (2016)	1	1	1	1	1	1	1	1	1	1	1	11
Piette et al., (2012)	1	1	1	0	1	1	1	1	1	0	1	10
Kim et al., (2015)	1	1	1	0	1	1	1	1	1	1	1	10
Zha et al., (2019)	1	1	1	0	1	1	1	1	1	1	1	10
Bove et al., (2012)	1	1	1	0	1	1	1	1	1	1	1	10

Description of the question criretia:

1 = Does this research answer the research questions clearly?
2 = Was the assignment of participants to the intervention randomized?
3 = Were all participants who entered the study accounted for in the conclusions?
4 = Were the participants, the people who analyzed the results and the researchers blinded?
5 = Were the study groups similar at the start of the randomized controlled trial?
6 = Regardless of the experimental intervention, did each study group receive the same level of care (ie, were they treated the same)?
7 = Were the effects of the intervention reported comprehensively?
8 = Is the accuracy of the reported intervention or treatment effect estimates?
9 = Do the benefits of the experimental intervention outweigh the disadvantages and costs?
10 = Can the results be applied to your local population/in your context?
11 = Will the experimental intervention provide greater value to the people in your care than any existing intervention?

Decription of the answer score

0 = No
1 = Yes

Table 2. Description of the primary studies included in the primary study meta-analysis of the Randomized Controlled Trial (N=3,071)

Author (Year)	Country	P	I	C	O
Bobrow *et al.* (2016)	south Africa	Adult patients (over 21 years) diagnosed with hypertension who are able to use cell phones	Get treatment adherence support via short messages	Usual maintenance	Systolic mean blood pressure
Margolis *et al.* (2013)	United States of America	Hypertensive patients (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mm Hg)	Receive blood pressure telemonitoring at home	Usual maintenance	Systolic mean blood pressure
Myoungsuk (2019)	South Korea	Seniors (age 65 years and over) diagnosed with hypertension who are	Receive long message services and telephone-based health care training	Do not accept long message services and	Systolic mean blood pressure

Author (Year)	Country	P	I	C	O
		able to receive calls or text messages		health care training	
Contreras *et al.* (2018)	Spanish	Hypertensive patients who own and use an iPhone or android cell phone	Monitoring medication adherence through an application installed on a cellphone	Usual maintenance (blood pressure control every 6 months)	Systolic mean blood pressure
McManus *et al.* (2018)	English	Hypertensive patients (age over 35 years) with blood pressure higher than 140/90 mmHg	Blood pressure monitoring via telemonitoring	Usual maintenance	Systolic mean blood pressure
McKinstry *et al.* (2013)	Scotland	Hypertensive patients (age 18 years or older) with blood pressure higher than 145/85 mmHg	Blood pressure measurement via telemonitoring and support via email	Usual maintenance	Systolic mean blood pressure
Kim *et al.* (2016)	United States of America	Hypertensive patients (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mm Hg)	Getting HealthyCircles platform intervention via iPhone	Did not get the HealthyCircles intervention	Systolic mean blood pressure
Piette *et al.* (2012)	Honduras	Patients diagnosed with hypertension (systolic blood pressure ≥140 mmHg)	Electronic-based blood pressure monitoring at home	Usual maintenance	Systolic mean blood pressure
Kim *et al.* (2015)	South Korea	Adult patients (over 20 years) diagnosed with hypertension	Web-based monitoring of blood pressure in hypertensive patients	Not getting web based monitoring	Systolic mean blood pressure

Table 2 is a description of the primary studies included in the meta-analysis, there are 9 articles with a randomized controlled trial design that meet the requirements to be made into a systematic study and meta-analysis related to the effect of electronic health-based self-management on systolic blood pressure control in patients hypertension with various research locations, namely South Africa, the United States, South Korea, Spain, England, Scotland, and Honduras. There are similarities in the primary research, namely the research design using a Randomized Controlled Trial, the research subjects were hypertensive patients, the intervention provided was in the form of electronic health-based self-management with the comparison of not implementing electronic health-based self-management. However, there are differences in the number of samples, namely the smallest number is 31 and the largest sample is 396. The period of publication of the articles is from 2012 to 2022. The size of the relationship used in the meta-analysis study on the effect of electronic health-based self-management on systolic blood pressure control in hypertensive patients is the Mean and Standard Deviation (see table 3).

Table 3. Mean SD of the primary studies included in the primary study meta-analysis of the Randomized Controlled Trial

Author (Year)	Intervention		Control	
	Mean	SD	Mean	SD
Bobrow *et al.* (2016)	132.7	17.5	134.3	17.3
Margolis *et al.* (2013)	125.7	17.72	134.8	17.86
Myoungsuk (2019)	133.61	7.32	143.58	9.49
Contreras *et al.* (2018)	132.2	12	134.4	11
McManus *et al.* (2018)	136.0	16.1	140.4	16.5
McKinstry *et al.* (2013)	140	11.3	144.3	13.4
Kim *et al.* (2016)	133.4	12.9	140.2	18.4
Piette *et al.* (2012)	142.5	22.88	143.6	24.2
Kim *et al.* (2015)	132	15.61	143.2	13

Forest Plot

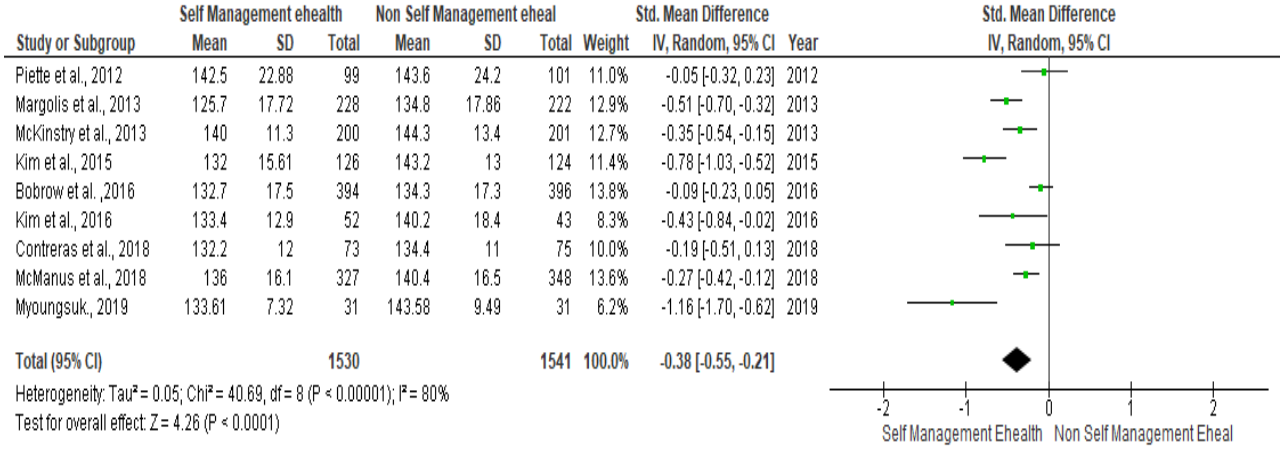

Figure 3. Forest plot of the effect of electronic health-based self-management on systolic blood pressure control in hypertensive patients

The forest plot in Figure 3 shows that there is an effect of electronic health-based self-management on systolic blood pressure control in hypertensive patients and this effect is statistically significant. Hypertensive patients who received electronic health-based self-management had an average systolic blood pressure 0.38 SMD units lower than those who did not receive the intervention (SMD = -0.38; 95% CI = -0.55 to -0.20; p<0.001). The forest plot also shows that the variation in the estimation of the effects of self-management based on electronic health is very heterogeneous between the primary studies that were carried out in this meta-analysis (I^2= 80%; p<0.001) thus calculating the average estimate using the Random Effect Model (REM) approach.).

The funnel plot in Figure 4 from a randomized controlled trial study shows the distribution of effect estimates is the same to the right and left of the vertical mean estimation line, so it does not indicate publication bias.

Funnel Plot

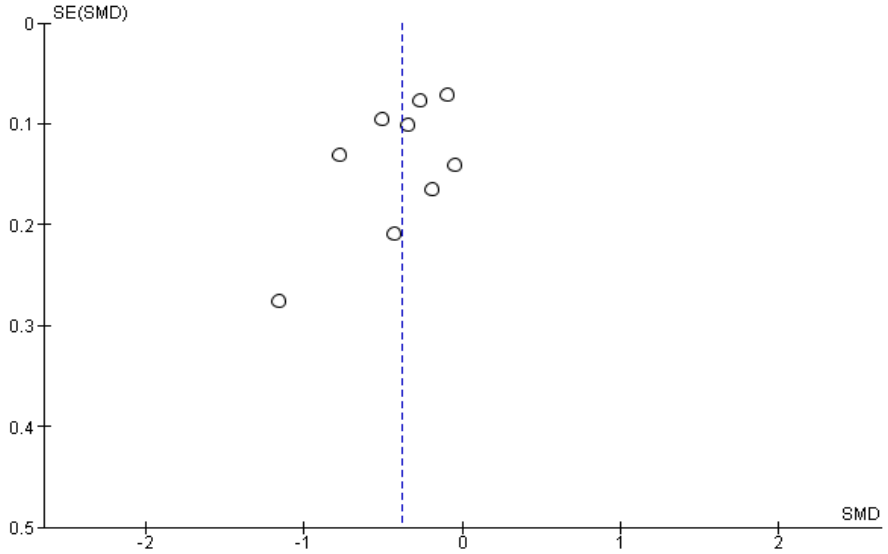

Figure 4. Funnel plot of the effect of electronic health-based self-management on systolic blood pressure control in hypertensive patients

Table 4. Description of the primary studies included in the primary study meta-analysis of the Randomized Controlled Trial (N=2,348)

Author (Year)	Country	P	I	C	O
Zha *et al.* (2016)	United States of America	Hypertensive patients living in underserved urban communities.	Using the iHealth BP7 Wireless Blood Pressure Wrist Monitor app	Not using the iHealth BP7 Wireless Blood Pressure Wrist Monitor	Average diastolic blood pressure
Margolis *et al.* (2013)	United States of America	Hypertensive patients (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mm Hg)	Receive blood pressure telemonitoring at home	Usual maintenance	Average diastolic blood pressure
Myoungsuk (2019)	South Korea	Seniors (age 65 years and over) diagnosed with hypertension who are able to receive calls or text messages	Receive long message services and telephone-based health training	Do not accept long message services and health care training	Average diastolic blood pressure
Contreras *et al.* (2018)	spanish	Hypertensive patients who own and use an iPhone or android cell phone	Monitoring medication adherence through an application installed on a cellphone	Usual maintenance (Control of blood pressure once every 6 months)	Average diastolic blood pressure
McManus *et al.* (2018)	English	Hypertensive patients (age over 35 years) with blood	Blood pressure monitoring via telemonitoring	Usual maintenance	Average diastolic blood pressure

Author (Year)	Country	P	I	C	O
		pressure higher than 140/90 mmHg			
McKinstry *et al.* (2013)	Scotland	Hypertensive patients (age 18 years or older) with blood pressure higher than 145/85 mmHg	Blood pressure measurement via telemonitoring and support via email	Usual maintenance	Average diastolic blood pressure
Kim *et al.* (2016)	United States of America	The patient was diagnosed with hypertension (blood pressure> 140 mmHg/> 90 mmHg	Get the HealthyCircles Platform intervention via iPhone	Did not get the HealthyCircles intervention	Average diastolic blood pressure
Bove *et al.* (2012)	United States of America	Hypertensive patients (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mm Hg)	Internet based blood pressure monitoring	Usual maintenance	Average diastolic blood pressure
Kim *et al.* (2015)	South Korea	Adult patients (over 20 years) diagnosed with hypertension	Web-based remote patient blood pressure monitoring	Not getting web based monitoring	Average diastolic blood pressure

Table 4. is a description of the primary studies included in the meta-analysis, there are 9 articles with the study design Randomized Controlled Trial that meet the requirements to be used as a systematic study and meta-analysis of the effect of electronic health-based self-management on diastolic blood pressure control in patients hypertension with various research locations, namely the United States, South Korea, Spain, England, and Scotland. The size of the relationship used in this meta-analysis study on the effect of self-management based on electronic health in controlling diastolic blood pressure in hypertensive patients is the Mean and Standard Deviation (see table 5).

Table 5. Mean SD of the primary studies included in the primary study meta-analysis of the Randomized Controlled Trial

Author (Year)	Intervention			Control		
	N	Mean	SD	N	Mean	SD
Zha *et al.* (2016)	12	88.08	7.45	13	88.10	9.41
Margolis *et al.* (2013)	228	75.1	17.72	222	80.8	17.86
Myoungsuk *et al.* (2019)	31	82.29	4.79	31	87.88	8.12
Contreras *et al.* (2018)	73	78.76	8	73	82.2	8
McManus *et al.* (2018)	327	78.7	9.7	348	79.9	10.7
McKinstry *et al.* (2013)	200	86.9	11.8	201	88.3	11.2
Kim *et al.* (2016)	52	82.8	11.2	43	85.3	12.1
Bove *et al.* (2012)	120	81.8	12.32	121	82.7	9.31
Kim *et al.* (2015)	126	82.8	9.8	124	83.8	10.6

Forest Plot

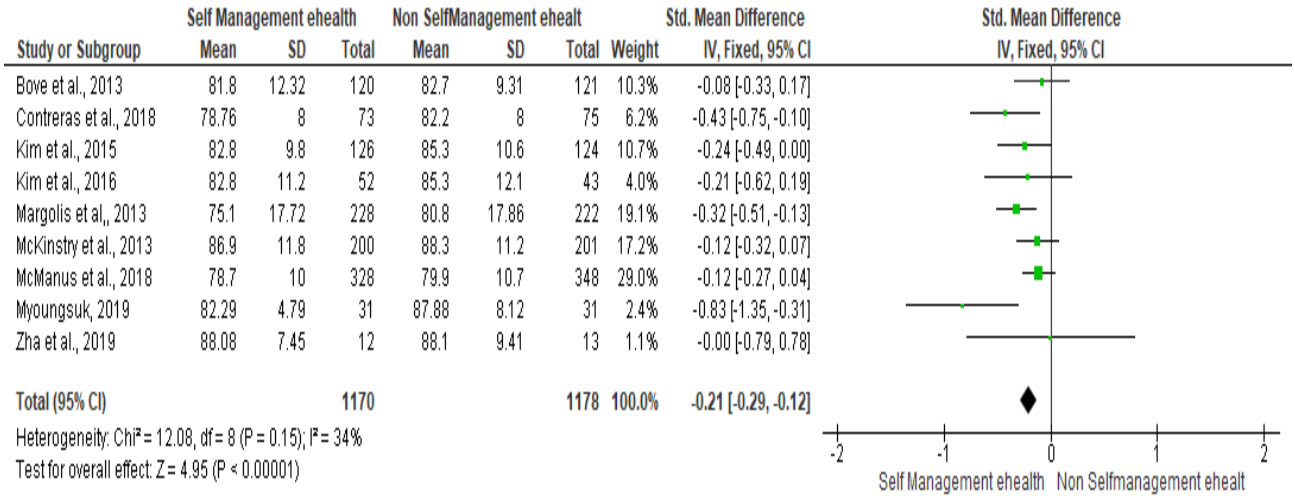

Figure 5. Forest plot of the effect of electronic health-based self-management on diastolic blood pressure control in hypertensive patients

The forest plot in Figure 5 shows that there is an effect of electronic health-based self-management on diastolic blood pressure control in hypertensive patients and this effect is statistically significant. Hypertensive patients who received self-management based on electronic health had an average diastolic blood pressure of 0.21 SMD units lower than those who did not receive the intervention (SMD= -0.21; 95% CI= -0.29 to -0.12; p<0.001) . The forest plots also show variations in the estimation of the effects of self-management based on electronic health with low heterogeneity between primary studies that were carried out in this meta-analysis (I^2= 34%; p= 0.15) thus calculating the average estimate using the Fixed Effect Model approach.

Funnel Plot

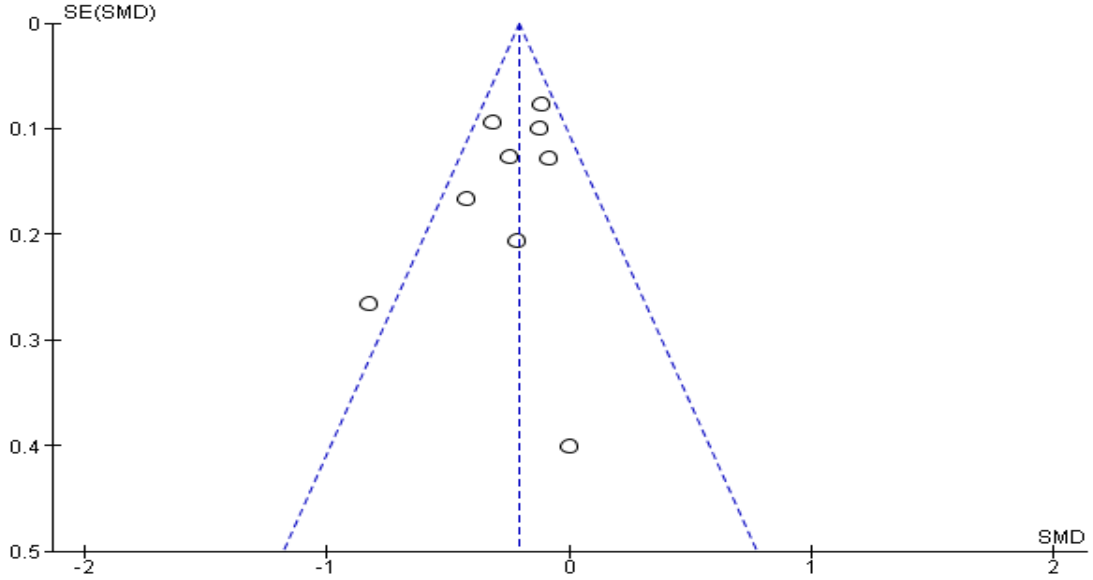

Figure 6. Funnel plot the effect of electronic health-based self management in controlling systolic blood pressure among hypertensive patients

The funnel plot in Figure 6. shows the distribution of effect estimates to the left rather than the right of the average vertical line of effect estimates, indicating a slight publication bias. Because the distribution of these effect estimates is located to the left of the average vertical line which is the same as the location of the average estimated effect (diamond image) in the forest plot which is located to the left of the vertical line of hypothesis 0, the publication bias tends to overestimate the actual effect (overestimate).

DISCUSSION

This systematic study and meta-analysis examines the effect of electronic health-based self-management on blood pressure control in hypertensive patients. This research is considered important because electronic health-based self-management interventions can reduce blood pressure in hypertensive patients by facilitating blood pressure monitoring for hypertensive patients and providing health information to health workers in real time for follow-up and to promote lifestyle modifications.

Effect of electronic health-based self-management on systolic blood pressure control in hypertensive patients

The results of a meta-analysis of 9 articles related to the effect of electronic health-based self-management on systolic blood pressure control in hypertensive patients showed that hypertensive patients who received electronic health-based self-management interventions had an average systolic blood pressure of 0.38 SMD units lower than did not receive the intervention (SMD = -0.38; 95% CI= -0.55 to -0.20; p<0.001).

Pan et al. (2015) stated that telemonitoring carried out at home had the effect of reducing systolic blood pressure which was positively correlated with the use of the application, because many participants in the application of telemonitoring could increase patient awareness and allow for more frequent blood pressure checks, so that hypertensive patients can adhere to regular blood pressure measurements. consistently and hypertensive patients are proven with high percentage results to have adherence in taking medication.

Research conducted by Lee et al. (2018), stated that there was a significant difference in the average change in systolic blood pressure at three months in the monitoring group. It is because the use of mobile applications consisting of independent blood pressure monitoring along with telehealth counseling encourages patients to be able to manage blood pressure, especially in environments that are limited with resources.

Research by Chandler et al. (2019), stated that the average systolic blood pressure was significantly lower during the 9 month trial in the group using the Smartphone Med Adherence Stops Hypertension application compared to patients who only used usual care.

Implementation of electronic health-based self-management in hypertensive patients using the Hello Heart application developed through mHealth technology which was carried out for 22 weeks showed that the group involved in using the Hello Heart application could significantly reduce systolic blood pressure compared to those who did not use the application. (Kaplan et al., 2017).

Effect of electronic health-based self-management on diastolic blood pressure control

The results of a meta-analysis of 9 articles related to the effect of electronic health-based self-management on diastolic blood pressure control in hypertensive patients showed that hypertensive patients who received electronic health-based self-management had an average diastolic blood pressure of 0.21 SMD units lower than those who did not receive

the intervention (SMD = -0.21; 95% CI = -0.29 to -0.12; p<0.001).

Research conducted by Persell et al. (2020), stated that the effect of using a smartphone-based training application in self-management of hypertension and monitoring blood pressure at home was indicated by a decrease in blood pressure with an average of 6.8 mmHg in systolic blood pressure and 3.6 mmHg in diastolic blood pressure.

The effectiveness of sending messages in hypertension prevention programs which include food recording, blood pressure tracking, and educational materials provided by training through a mobile application platform in prehypertensive or hypertensive patients with an average systolic and diastolic blood pressure, significantly decreased in participants who used the application compared to those who do not use the application (Ramos et al., 2017).

In a study by Gong et al. (2020), The results show that the Yan Fu application installed via smartphone in hypertensive patients is effective for hypertension management and supports adherence in medication and blood pressure control which shows a decrease in systolic blood pressure and diastolic blood pressure which is much greater than the control group.

Nolan et al. (2012) in their research shows that e-counseling conducted via the internet makes a significant contribution to community-based programs that aim to reduce cardiovascular disease risk factors among people with hypertension, increase motivation in making behavior changes, and medication adherence. In addition, the e-counseling intervention significantly reduced systolic and diastolic blood pressure in hypertensive individuals and increased adherence to exercise and diet.

The results of the study on the variable systolic blood pressure showed that there was an effect of self-management based on electronic health in reducing systolic blood pressure and it was statistically significant. The diastolic blood pressure variable also shows the effect of electronic health-based self-management in reducing diastolic blood pressure and is statistically significant.

This is because electronic health-based self-management provides positive lifestyle changes, such as medication adherence, regular blood pressure control, implementting a low-fat and salt diet, and physical activity, so that electronic health-based self-management can be used in the hypertension healing process.

This meta-analysis synthesizes 9 randomized controlled trial studies originating from South Africa, the United States, South Korea, Spain, England, Scotland, and Honduras. The overall sample size included in the meta-analysis was 3,071 hypertensive patients. This meta-analysis concluded that electronic health-based self-management could reduce systolic blood pressure by 0.38 units and was statistically significant (SMD= -0.38; 95% CI = -0.55 to -0.20; p<0.001).

This meta-analysis synthesizes 9 randomized controlled trial studies from the United States, South Korea, England, and Scotland. The overall sample size included in the meta-analysis was 2,095 hypertensive patients. This meta-analysis concluded that electronic health-based self-management could reduce diastolic blood pressure by 0.21 units and was statistically significant (SMD= -0.21; 95% CI = -0.29 to -0.12; p<0.001).

AUTHOR CONTRIBUTION

Aulia Siti Nur Rahmah was the principal researcher who collected the data and analyzed the data. Meanwhile Didik Gunawan Tamtomo and Bhisma Murti provided instructions on data analysis and preparation of publication manuscripts.

CONFLICT OF INTEREST

There was no conflict of interest in the study.

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