SM Journal of Public Health & Epidemiology ISSN: 2473-0661

Research Article

SMS-Based Interventions on Medication Adherence and Blood Pressure Control among Hypertensive Individuals in Low-Resource Settings: A Systematic Review and Meta-Analysis

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Abstract

This study examines the effect of SMS-based interventions on medication adherence and blood pressure. The inclusion criteria were randomized controlled trials and quasi-experimental designs for SMS-based interventions excluding online messaging applications between 2010 and 2022, in English, with participants clinically diagnosed with hypertension on anti-hypertensive medication, aged 18 and above, regardless of comorbidities. PubMed, Google Scholar, and EBSCOHost were used for the search. A risk of Bias assessment was done. Out of the 5,503 articles identified, 11 studies were quality-assessed using the Cochrane risk of bias tool and systematically reviewed. Seven studies were included for the quantitative assessment and analyzed using the continuous random effects model. SMS-based interventions are estimated to increase medication adherence scores by SMD 0.28 (95% CI, 0.12 to 0.44, p = 0.0005) and decrease systolic blood pressure by SMD -0.11 (95% CI, -0.20 to -0.02, p = 0.02). However, it has no benefit in diastolic blood pressure reduction SMD 0.00 (95% CI, -0.25 to 0.24, p = 0.98). Thus, SMS-based interventions can be considered to improve adherence and BP outcomes among patients with hypertension, especially in low-resource settings.

Keywords: SMS-based interventions; Medication adherence; Blood pressure control; Low-resource setting

Background

Hypertension is a medical condition known to affect 650 million to 1.28 billion adults worldwide in the last 30 years. It also increases the risk for life-threatening conditions such as cardiovascular and cerebrovascular diseases. However, despite the widely available evidence that supports the efficacy of antihypertensive medications in controlling blood pressure and preventing hypertensive complications, patient adherence is still reported to be as low as 20- 50% [1]. In low- and middle-income countries, the adherence rate is reported to be about 66% for those receiving treatment, while the hypertension control rate is only 20% [2]. Nonadherence to antihypertensive maintenance medications may be associated with many factors, such as medication cost, poor health literacy and awareness, and individual attitudes. Still, the most cited reason for nonadherence is a patient forgetting to take their medications [3].

The World Health Organization recommends utilizing mobile phones to provide remote health services as a practical solution for maintaining patient health in low-income countries or rural areas. This approach, called mHealth, involves using mobile phones to send text messages or access smartphone applications to improve health outcomes. As mobile phones are widely used globally, particularly in areas with limited resources, they are an excellent option for delivering healthcare services. Studies have shown that SMS-based interventions can enhance medication adherence and health outcomes [4-6]. Hypertension is a chronic health condition that can benefit from these interventions.

Therefore, with the established crucial role of medication adherence in the prevention of the complications of hypertension and with the low statistics on antihypertensive medication adherence, there is a necessity to explore, assess, and thus commit to the development and application of interventions that focus on improving antihypertensive medications adherence and blood pressure control in low-resource settings. This study aims to explore existing literature assessing the effect of SMS-based intervention on medication adherence and blood pressure.

Submitted: 30 May 2024 | **Accepted:** 21 June 2024 | **Published:** 24 June 2024

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Citation: Narca MK, Wee JJ, Tan Punzalan JK (2024) SMS-Based Interventions on Medication Adherence and Blood Pressure Control among Hypertensive Individuals in Low-Resource Settings: A Systematic Review and Meta-Analysis. SM J Public Health Epidemiol 7: 7.

Methodology

Research Design:

This paper reviewed studies on SMS-based interventions' impact on medication adherence and blood pressure among hypertensive individuals. Moreover, despite this paper's intent to find and assess all studies that meet the inclusion criteria, some studies may have been missed, which are attributable to limitations such as the (a) lack of access to other databases (i.e., EMBASE, etc.) which requires payment to access and (b) the limitation of only including studies written in the English language which may introduced language bias. The study also did not determine the best intervention or analyze the intervention duration and frequency's impact.

Criteria

Studies included in this systematic review and meta-analysis were those with randomized controlled trials and quasi-experimental designs that utilized isolated or in-combination SMS-based interventions to improve anti-hypertensive drug compliance and blood pressure between 2010 and 2022. The types of participants that are included in these studies are those (a) clinically diagnosed with hypertension who are on anti-hypertensive medications, (b) 18 years of age and above, and (c) with or without known comorbidities, (d) studies that include participants with other forms of chronic diseases, but the majority are those with hypertension. The outcome variables of the studies included

are (a) *Morisky Medications Adherence Scale* **(MMAS-8**), (b) *Medication Adherence Questionnaire (MAQ), (c) Systolic blood pressure* (**SBP**) and *Diastolic blood pressure* (**DBP**) quantified in mmHG scale and measured using calibrated anabolic sphygmomanometers and stethoscopes, and (4) Pill count. The control variable of the included studies is the absence of SMS-based intervention in the standard of care or those control that does not have a conclusive and direct consequence on assessing the effect of SMS-based interventions on medication adherence and blood pressure outcomes.

Exclusion Criteria

Studies on SMS-based interventions for medication adherence were included only if they provided analysis for specific populations or supplementary materials. Lastly, to focus on interventions appropriate for low-resource settings, studies that utilized SMS-based format interventions integrated into platforms requiring internet access (i.e., WeChat or Viber) were also excluded.

Search Methods for Identification of Studies

The studies were searched and identified through 3 databases, PubMed, Google Scholar, and EBSCOHost. The preliminary index search term used was "hypertension" OR "hypertensive" AND "medication adherence" OR "medication compliance" AND "SMS" OR "text messages" OR "SMS-based interventions." The complete index search terms used for each database are presented in Supplementary Table 1.

Data Collection and Analysis

Selection of Studies: An independent review of each paper's title, abstract, and full text was conducted. Data that were reviewed and extracted were coded into the RevMan 5.4.1 software. The supplementary materials for each study were also utilized whenever available.

Risk of Bias Assessment: Critical appraisal includes (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete data outcome; (6) selective reporting; and (7) other biases. The review did not assess publication bias due to insufficient included trials for proper assessment through funnel plots or regression-based assessments.

Data Analysis: The RevMan 5.4.1 software was used to synthesize the data. The mean difference, standard deviation, 95% confidence interval, and sample size were extracted from the studies included in the quantitative review. A continuous random effects model was used to calculate the standard mean difference between groups.

Measurement of Treatment Effect: The outcome results were calculated for each study using inverse variance and a total confidence interval of 95%. Continuous outcomes such as scores from adherence scales, SBP, and DBP were expressed as mean difference (MD) and were then converted to be evaluated as standardized mean differences (SMD). The interpretation of the standard mean difference is per the recommendations that an SMD value of 0.2 represents minor effects, 0.5 represents moderate effects, and 0.8 represents significant effects [7]. Furthermore, the evaluation of SMD is based on the presentation relative to the outcome being examined.

Assessment of Heterogeneity: The Chi-squared and I2 assessed statistical heterogeneity. Chi-squared results with a p-value of p = >0.05 were interpreted to have a low probability of sampling error. Analysis with I^2 results of 0%-40%; 30%-60%; 50%-90%; 75%-100% were interpreted as having insignificant, moderate, substantial, and considerable heterogeneity, respectively.

Results

Study Selection

The Preferred Reporting of Items for Systematic Review and Meta-Analysis (PRISMA) guides the data collection and analysis process and is depicted in Figure 1. A total of 5,053 studies were identified from the following databases: PubMed (n = 650), EBSCOHost (n = 113), and Google Scholar (n = 4,290). 11 RCTs were included in this review after a systematic search of 5,053 studies from various databases. Three thousand nine hundred forty-six studies were excluded during the title and abstract screening for being irrelevant, and 77 more were excluded for various reasons.

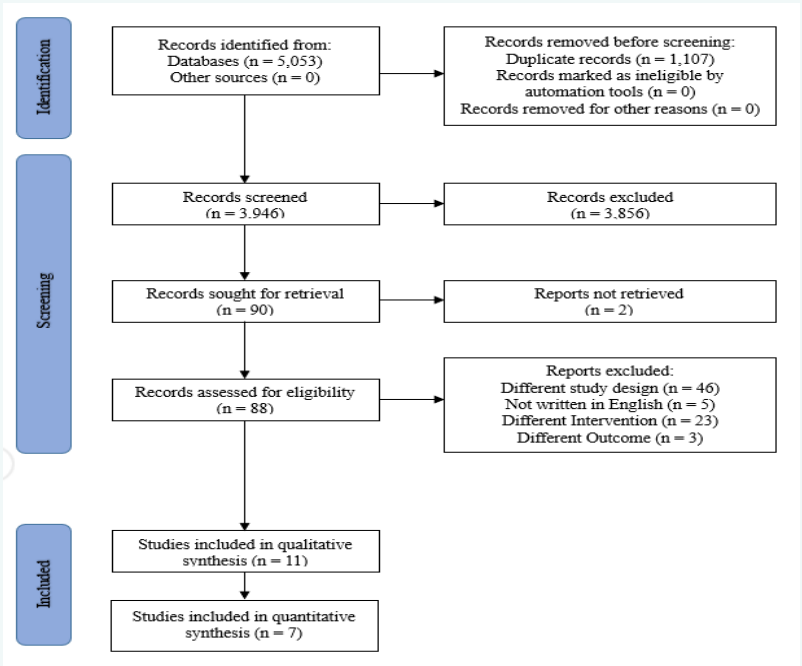

Figure 1: Prisma flow diagram of study identification and selection for inclusion

Description of Studies Included

Out of the 2,854 participants from eleven randomized controlled trials that met the inclusion criteria, the majority (72%) of the studies showed promising results in this area [8-15]. Two (18%) studies utilized other interventions, such as nurse-led programs. The results of the review indicate that reminder text messaging, coupled with educational content on medication, lifestyle habits (such as diet, exercise, smoking cessation, abstinence from alcohol, and weight management), and the consequences of nonadherence, can positively impact medication adherence and reduce blood pressure among hypertensive individuals.

Quality Assessment of Included Studies

Quality assessment of the studies includes (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete data outcome; (6) selective reporting; and (7) other biases. The classification schemes are reported based on the evaluation of the various components and are as follows:

Selection Bias: In two studies [12,14], the method for randomization and allocation concealment needed to be specified, resulting in an unclear selection bias. As a result, it is difficult to make a judgment due to a lack of information. One study was determined to have a high risk for selection bias because the principal investigator administering the intervention conducted the randomization and allocation process [16]. This could lead to bias as the knowledge could impact the delivery of the intervention and the allocation of participants. The remaining eight studies (72%) reported a low risk for selection bias, as proper measures were taken to eliminate or minimize selection bias and were duly reported.

Performance Bias: In 10 (91%) of the studies, performance bias was reported as "low risk" because either the participants, key study personnel, and outcome assessors were blinded or the included studies underwent no blinding. Still, outcome assessments were deemed unlikely to introduce bias. 1 (9%) was assessed with unclear risk for performance bias because the article presented insufficient information to permit judgment of either low or high risk of bias [12].

Attrition Bias: In 10 (91%) studies, the judgment is "low risk" for attrition bias because there are (a) no missing outcomes, (b) the reason for missing outcome data is unlikely to be related to the actual outcome, (c) missing outcome data is balanced in number across intervention groups, or (d) plausible effect size among missing outcomes is not enough to have a clinically relevant impact on observed effect size. Finally, 2 (18%) of the studies had insufficient reporting of attrition and are therefore judged as having "unclear risk [17,18].

Detection Bias: In 10 (91%) studies, detection bias was assessed to have a low risk of bias because either an independent person who was not part of the study or involved in the intervention was tasked with outcome assessment, or no blinding was done. Still, outcome assessments were deemed unlikely to introduce bias. Moreover, 1 (9%) had no blinding of outcome assessment, and it was not indicated whether it affected the result overall. Therefore, insufficient information permits judgment [12]. Thus, it was judged as having an "unclear risk for detection bias."

Reporting Bias: Of 10 studies, 91% reported all the expected primary and secondary outcomes thoroughly. The results of all studies included relevant information like confidence intervals. However, one study (9%) is at high risk for reporting bias because they used the Hill-Bone Compliance to High Blood Pressure Therapy Scale within their study [11].

Overall Risk of Bias: Two of the 11 studies included were deemed high risk for selection and reporting bias. In comparison, four studies considered an unclear risk for selection, performance, detection, and attrition bias. Several studies had unclear or high risks of bias in allocation, random sequence generation, selection, blinding, attrition, and reporting. However, five studies had a low risk of bias for all domains, indicating a range of high to low-quality studies. Supplementary Figures 1 and 2 depict the bias graph and summary risk, respectively.

Restriction of primary analysis

This review established a threshold for the restriction of primary analysis to exclude studies with high or unclear risk of bias for three domains: selection, performance, and detection. The results of the primary analysis can be found in Figure 2. Therefore, 3 of the studies judged as having high/unclear risk for selection bias, performance bias, and detection bias have been excluded from the primary analysis [12,14,16]. The study of Varleta et al., also needed to provide supplementary information that allowed the computation of medication adherence-mean difference between study groups. Additionally, one study that was judged a high risk for reporting bias due to inconsistent data presentation, which may affect the overall effect of interventions, has also been excluded. Hence, four studies were excluded from the primary analysis [11].

Meta-Analysis Results on Medication Adherence Scores

Five studies in the review measured medication adherence using validated standardized scales, four used the Morisky Medication Adherence Scale (MMAS-8), and one used the Hill-Bone Compliance to High Blood Pressure Therapy Scale (HB-HCT). The five studies included and their corresponding study weight is as follows: (1) Akhu-Zaheya et al., 14.6%, (2) Bhandari et al., 24.0%, (3) Buis et al., 15.1%, (4) Pour et al., 8.4%, and Zhai et al., 37.9%. The meta-analysis through a continuous random-effects model found a small but statistically significant estimate of the improvement in adherence scale score 0.28 (95% CI, 0.12 to 0.44, p = <0.05), which favors the experimental (intervention). Furthermore, the test for overall effect is Z = 3.48 (p = 0.0005), indicating a significant pooled effects difference between the two groups, favoring the intervention. Lastly, the test for heterogeneity revealed that Chi-squared = 5.04, df = 4 (p = 0.28), which indicates that there is no significant heterogeneity between studies that are attributable to sampling error, and an I^2 = 21% indicates that there is negligible heterogeneity and the studies included in the review are homogenous.

Meta-Analysis Results on Systolic Blood Pressure

Six studies in the review measure the participants' pre-intervention and post-intervention systolic blood pressures. The six studies included, and their corresponding weight are as follows: (1) Bhandari et al., 8.3%, (2) Bobrow et al., 57.7%, (3) Buis et al., 6.0%, (4) Mehta et al., 4.2%, (5) Pour et al., 3.0%, and (6) Zhai et al., 20.9%. The meta-analysis through a continuous random-effects model found a small, statistically significant estimate of the improvement in systolic blood pressure -0.11 (95% CI, -0.20 to -0.02, p = <0.05), favoring the intervention for reducing systolic blood pressure. Furthermore, the test for overall effect is Z = 2.38 (p = 0.02), indicating a significant pooled effects difference between the two groups, favoring the intervention. Lastly, the test for heterogeneity revealed that Chi-squared = 3.44, df = 5 (p = 0.63), which indicates that there is no significant heterogeneity between studies that are attributable to sampling error and an I^2 = 0% suggests that there is no heterogeneity and that the studies included in the review are homogenous.

Meta-Analysis Results on Diastolic Blood Pressure

Five studies in the review measure the participants' pre-intervention and post-intervention diastolic blood pressure. The five studies included and their corresponding weight are as follows: (1) Bhandari et al., 22.2%, (2) Buis et al., 19.4%, (3) Mehta et al., 16.1%, (4) Pour et al., 13.4%, and (5) Zhai, et al., 28.9%. The meta-analysis through the continuous random-effects model found no significant estimate of the improvement in diastolic blood pressure SMD 0.00 (95% CI, -0.25 to 0.24, p = 0.98). This indicates that the intervention has no significant effect in lowering

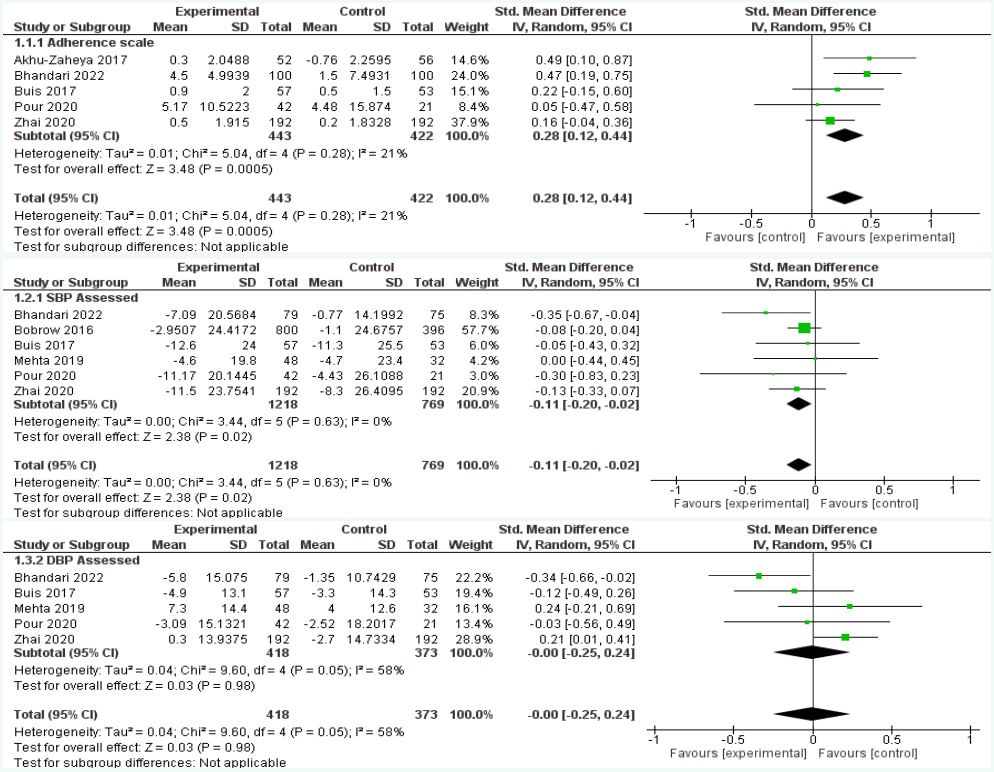

Figure 2: Forest plot using continuous random effects model on the effect of SMS interventions on medication adherence, systolic, and diastolic blood pressure.

diastolic blood pressure compared to control. Moreover, the test for overall effect is Z = 0.03 (p = 0.98), indicating a statistically insignificant pooled effects difference between groups. Lastly, the test for heterogeneity revealed that Chi-squared = 9.60, df = 4 (p = 0.05), which indicates a statistically significant risk for sampling error, and I^2 = 58%, which translates to moderate heterogeneity.

Sensitivity Analysis

Figure 3 depicts the sensitivity analysis conducted with the inclusion of studies at high or unclear risk for the domains of selection bias, performance bias, and detection bias. The seven studies included and their corresponding weight are as follows: (1) Akhu-Zaheya, et al., 14.3%, 2017, (2) Bhandari et al., 15,1%, 2022, (3) Buis et al., 2017, 14.4%, (4) Kes, et al., 2022, 12.2%, (5) Movahedi, et al., 14.8%, 2019, (6) Pour, et al., 2020, 13.2%, and (7) Zhai et al., 2020, 15.5%. The meta-analysis through the continuous random-effects model found a moderate effect in improving medication adherence scores among individuals with hypertension SMD, 0.68 (95% CI, 0.23 to 1.14; p = 0.003). The test for overall effect is Z = 2.94 (p = 0.003), indicating a statistically significant improvement in medication adherence scores. However, the test for heterogeneity revealed that Chi-squared = 75.37, df = 6 (p = <0.00001), which indicates a statistically significant risk for sampling error and an I^2 = 92%, which translates to considerable heterogeneity.

Eight studies in the sensitivity analysis measure the participants' pre-intervention and post-intervention systolic blood pressure. The eight studies included and their corresponding weight are as follows: (1) Bhandari et al., 2022, 13.1%, (2) Bobrow et al., 2016, 16.0%, (3) Buis et al., 2017, 12.1% (4) Kes, et al., 2022, 9.9%, (5) Mehta, et al., 2019, 10.9%, (6) Movahedi, et al., 2019, 13.5% (7) Pour, et al., 2020, 9.6%, and (8) Zhai et al., 2020, 15.0%. The continuous random effects model meta-analysis found a small effect in reducing systolic blood pressure among individuals with hypertension SMD - 0.35 (95% CI, -0.60 to -0.10; p = 0.006). The test for overall effect is Z = 2.74 (p = 0.006), indicating a statistically significant reduction in systolic blood pressure. The test for heterogeneity Chi-squared = 42.36, df = 7 (p = <0.00001) indicates a statistically significant risk for sampling error, and an I^2 = 83% indicates considerable heterogeneity.

The sensitivity analysis measured the pre-intervention and post-intervention of diastolic blood pressure included seven studies. The seven studies included and their corresponding weight are as follows: (1) Bhandari et al., 2022, 15.4%, (2) Buis et al., 2017,14.3%, (3) Kes et al., 2022, 12.4%, (4) Mehta, et al., 2019, 12.9%, (5) Movahedi, et al., 2019, 16.0%, (6) Pour et al., 2020, 11.5%, and (7) Zhai et al., 2020, 17.5%. The meta-analysis through the continuous random effects model found a small but statistically insignificant effect in the reduction of diastolic blood pressure among hypertensive individuals with SMD of -0.13 (95% CI, -0.41 to 0.15; p = 0.36). The test for overall effect is Z = 0.92 (p = 0.36), which indicates a statistically insignificant reduction in diastolic blood pressure. The test for heterogeneity reveals a Chi-squared = 27.84, df = 6 (p = 0.00001), indicating a statistically significant risk for sampling error and an I2 = 78% representing considerable heterogeneity between studies.

Discussion

Studies have shown that SMS-based interventions can improve medication adherence for hypertensive individuals. The interventions often include educational content about hypertension, covering information on medication, lifestyle changes (such as diet, exercise, smoking cessation, and weight loss), and the consequences of not adhering to treatment. Reminder text messages are also commonly

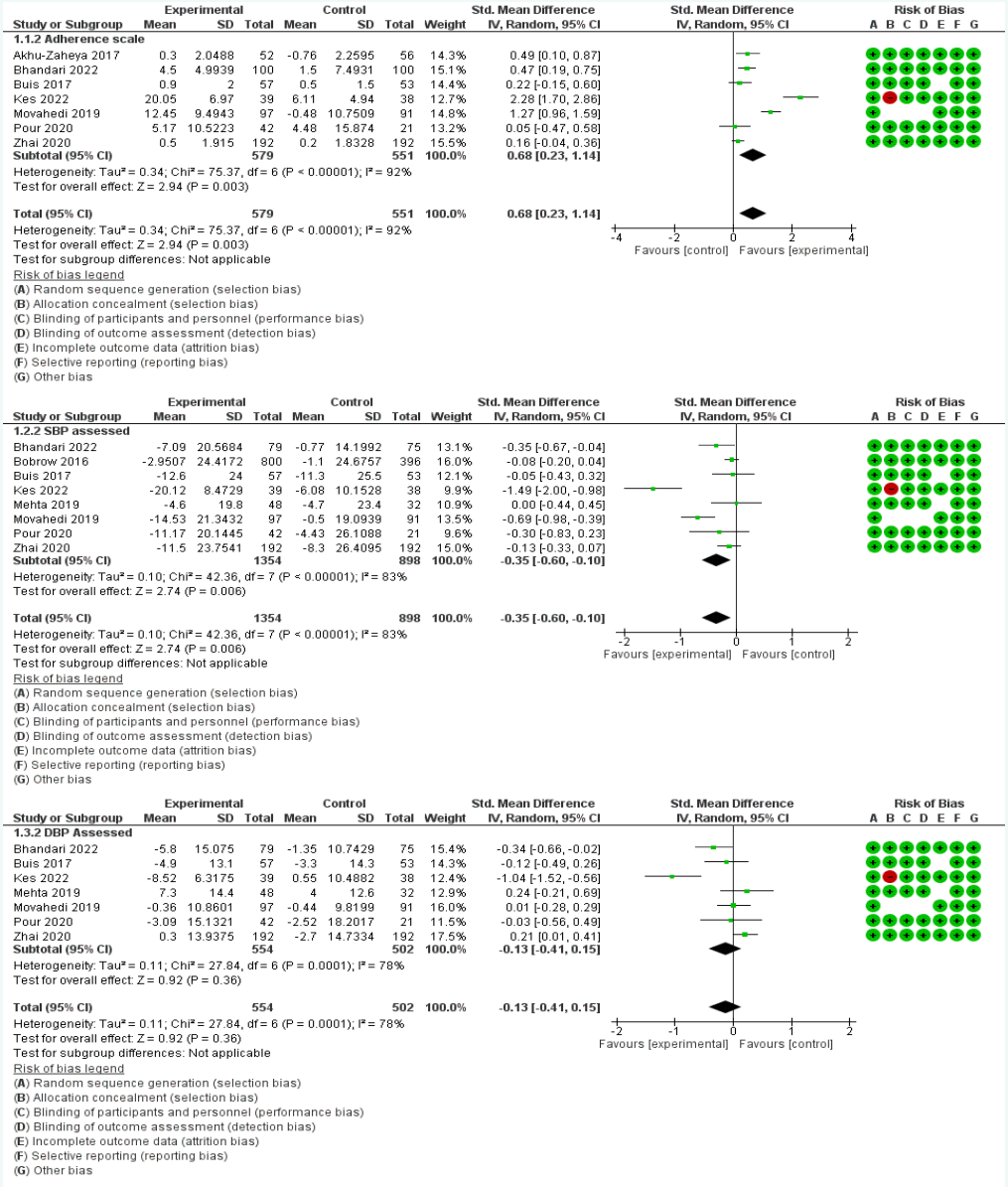

Figure 3: Sensitivity analysis on the effect of SMS interventions on medication adherence, systolic, and diastolic blood pressure.

used. Multiple studies have found that adding educational content can improve medication adherence among hypertensive individuals [15,16,19,20]. Therefore, educational content in SMS-based interventions is recommended to improve medication adherence for hypertensive individuals.

After assessing the quality of studies, it was found that 54% (n=6) had a high or unclear risk for selection bias, performance bias, detection bias, attrition bias, and reporting bias. Evidence-based medicine aims to find the best treatment for patients, so clinical trials need to minimize the risk of treatment effects being altered by confounding variables. The Cochrane Collaboration has defined six critical appraisal domains to ensure trial validity. Blinding and randomization help maintain adherence to these domains, preventing unconscious and intentional manipulation and the perception of treatment effect [21].

This study also tested if the intervention influenced blood pressure. Results of the meta-analysis on systolic and diastolic blood pressure suggest that there is also a statistically significant reduction in the systolic blood pressure SMD -0.11 ($Z = 2.38$, $p = 0.02$), but not in diastolic blood pressure SMD 0.00 ($Z = 0.49$, $p = 0.62$). The results provide validation for the observed effect on blood pressure outcome. These findings are consistent with a recent review in which there had been a reduction in systolic blood pressure of SMD = -0.13 (95% CI, -0.23 to -0.03, p = 0.01). In comparison, the reduction in diastolic blood pressure is SMD -0.06 (95% CI, -0.25 to 0.13, p = 0.56), indicating that text messaging interventions can reduce systolic blood pressure but not diastolic blood pressure [22].

The results of the sensitivity analysis demonstrated that the inclusion of studies that were judged with high or unclear risk of bias for selection bias, performance bias, and detection bias caused an increase in the estimated effect size in terms of the outcomes such as on medication adherence

and systolic blood pressure, however, retained the inconclusive effect of SMS intervention on diastolic blood pressure. The results yielded also showed a drastic increase in between-study heterogeneity for medication adherence, systolic blood pressure, and diastolic blood pressure, reaching 70-100%, which is translated to considerable heterogeneity, thereby demonstrating the effect of including studies judged with high/unclear risk on certain domains to overall heterogeneity.

With this study's findings, using SMS-based interventions is a viable option for improving medication adherence and blood pressure outcomes among hypertensive individuals. Physicians may utilize this form of health care delivery when handling patients that are nonadherent to their maintenance medications. Furthermore, government health agencies may incorporate SMS-based intervention, an affordable and accessible mode of healthcare delivery, into existing health programs and campaigns. Health agencies can assign healthcare professionals to create a standard text message with education material. The message can be saved in databases and automatically sent to registered numbers who agreed to receive the texts, ensuring consistent intervention.

Limitations were found due to varying outcome measures and a high risk of bias in many studies. A random effects model was used to generate pooled effect estimates, considering the random variability of outcome effects across the population. However, most of the included studies were judged to have a high risk of bias in multiple domains, and only studies in English were included. Despite this limitation, the studies were conducted in different countries, accounting for population variability. Lastly, the demographic profile of the study participants needed to be more well-defined in this review.

Conclusion

This review provides information on the effect of SMS-based interventions on medication adherence and blood pressure. The researcher concludes that SMS-based interventions effectively improve antihypertensive drug compliance and reduce systolic blood pressure but not diastolic blood pressure. The findings of this study could provide a practical basis for developing health programs and modes of healthcare delivery that are effective and cost-efficient and addresses nonadherence to maintenance medications and blood pressure control among hypertensive individuals.

The review has laid out a framework and background for future studies related to the present one. The researcher has also identified the current study's limitations and provided recommendations for improving the methodology. These recommendations are: 1) future researchers should conduct a quantitative assessment of the effects of different frequencies, duration, conditions, and content of SMS-based interventions on medication adherence and blood pressure, preferably through a subgroup analysis of studies to address incomplete or limited assessment, and 2) future researchers should perform a meta-regression analysis following the quantitative analysis to address the potential effect of demographic variance on the overall estimates of effects. These improvements will provide important information for future studies.

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