Text-Based Messaging Interventions for Improving Medication Adherence among Community-Dwelling Adults with Hypertension: A Systematic Review and Meta-Analysis

Sharyn Loh*
Department of Cardiology, Portfolio Manager at Wilson Asset Management, Singapore

Abstract

Background: As a leading cause of morbidity and mortality, Hypertension is a pressing global concern. Adherence to antihypertensive is a cornerstone of effective antihypertensives therapy. However, suboptimal medication adherence is widespread. Mobile health technology i.e. text messaging is a promising tool that can promote medication adherence with a wide-reaching effect on population health.

Aims: To critically assess the effectiveness of text-based messaging interventions for improving medication adherence among community-dwelling adults with Hypertension.

Methods: Studies were identified through a detailed search of six databases by two independent reviewers: PubMed, Embase, Cochrane, PsycINFO, CINAHL and Scopus. Studies included were: (1) published in English, since 2000; (2) randomised controlled trials; (3) done on community-dwelling adults diagnosed with Primary/ Essential Hypertension; (4) utilised 1 or 2-way text messaging, tailored text messaging, interactive voice response and text-based mobile applications; and (5) with medication adherence-related outcomes. Data extraction was conducted based on the Cochrane Handbook for Systematic Reviews of Intervention, and relevant studies underwent a study appraisal using the Cochrane Risk of Bias Tool.

Results: Twelve studies were included in the final review. Text-based messaging interventions exhibited a small statistically significant effect on medication adherence scores and systolic blood pressure reduction while the effect on controlled blood pressure and adherence remains uncertain. Subgroup analyses revealed having a multifaceted content on Hypertension management may be more effective than solely medication adherence content or reminders.

Significance of the study: There is limited evidence that text messaging-based interventions resulted in improved medication adherence and blood pressure control as a result of adherence. With the rise of mobile health, future studies exploring the cost effectiveness and feasibility of tailored and interactive text messaging interventions are warranted to influence the use of public health resources into the development of communication tools as a public health strategy for promoting medication adherence.

Keywords: Medication adherence • Text messaging • Hypertension • Compliance

Background

According to the World Health Organization (WHO), more than one billion people live with Hypertension worldwide. While ideal blood pressure (BP) is recommended to be 120/80mmHg or less, Chronic Hypertension is diagnosed after multiple readings of ≥ 140/ ≥ 90mmHg on two separate occasions or more [1]. For every three individuals, one is estimated to suffer from Hypertension by 2025 [2]. Based on WHO reports, the high disease burden can involve up to 10.2 million deaths and 208 million disability-adjusted life years in developed and developing countries [3].

Poorly-controlled BP and arterial remodelling lead to end-organ damage in multiple sites [4]. This warrants adequate Hypertensive control through the use of antihypertensive and non-pharmacological means [5].

Lifestyle modifications like healthy eating habits are advocated alongside medical management to reduce BP [6]. Treatment with multi-agent disease therapy such as-beta-blockers and ACE-inhibitors have proliferated rapidly, with new drugs produced by pharmaceutical companies [7]. A positive correlation was found between greater adherence to Hypertension medications and decrease in cardiovascular complications [8]. However, there is often suboptimal medication adherence (MA) [9]. Hypertension continues to be uncontrolled in populations at risk of poor MA resulting from economic, cultural or social factors [10].

Adherence is defined as the extent to which patients’ actions correspond with the agreed clinical recommendations that were mutually decided upon by patients and healthcare providers; including medication dosing regimen, intake interval and time [11].

Failure of MA is noteworthy as both patients and the healthcare system are adversely affected. When poor adherence is undetected and unaddressed, patients require a greater number of medications and increased dosage for disease control, resulting in polypharmacy. This results in higher treatment expenses incurred, higher risks of adverse effects and a higher risk of mortality [12].

Medication non-adherence in patients is a lost opportunity for therapeutic benefit and results in substantial disease deterioration and rising healthcare costs [13]. The cost of non-adherence is huge, amounting to billions of dollars a year. A bulk of the costs of medication non-adherence is attributed to hospital admissions that were preventable [14]. Moreover, poor MA leads to increase in cost-burden for caregivers and loss of work productivity [15]. Contrariwise, MA results in cost savings for patients and taxpayers dollars [16].

At present, a myriad of interventions to target MA are available. A meta-analysis revealed that mediated delivery of interventions is as effective as face-to-face delivery [17]. As face-to-face interventions targeting long-term care management necessitates the active use of healthcare resources which are labour-intensive and costly, mediated interventions of lower cost-effective measures like text messaging serve as a novel alternative.
Short message service (SMS) or text messaging involves the creation and instantaneous exchange of alphanumeric messages that are 160 characters or less [18]. Among interpersonal mobile communication channels, SMS has been the most frequently utilised form of communication. Research has shown that 99% of received mobile text messages are opened by users, and 90% of all mobile text messages are read upon receiving it in less than three minutes [19].

Presently, there are limited reviews examining text messaging interventions in a hypertensive cohort. SRs conducted on health in improving MA had limitations whereby the inclusion criteria of one review necessitated the usage of a mobile device with a wireless connection which might have missed out on simple text messaging [20], and another review focused on application-based tools with BP targeted as the primary outcome [21].

A literature review conducted to appraise mobile phone-based interventions in Hypertension management had methodological limitations with no eligibility criteria to guide the search and only three databases utilised in the search strategy, with clinical trials and SRs included in the analysis [22]. We were aware of a SR that explored SMS for Hypertension management [23]. However, only BP measurement was considered as an outcome. Moreover, its focus was on cardiovascular disease (CVD) as the population group was broad which included adults with Diabetes, smoking and obesity besides Hypertension.

While there have been similar SRs evaluating text messaging on glycaemic control in Diabetes Mellitus, secondary prevention on CVD [24-26], and others evaluating mHealth for the management of chronic diseases [27-29], a thorough search yielded no distinct SR reviewing the effectiveness of text messaging on MA as a primary outcome in a hypertensive cohort.

Paucity of such reviews propelled the conduction of this SR to critically appraise text message usage in improving MA among community-dwelling adults with Hypertension. Our secondary outcome is BP control due to MA, as a positive correlation is established between them [30]. Findings from this review may contribute to the current literature and inform the use of text-based messaging interventions as a plausible MA strategy.

Methods

This review adopted guidelines from The Cochrane Handbook for Systematic Reviews of Interventions Version 6.1 [31] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [32].

Eligibility criteria

To guide the search, the following inclusion criterion was established. Studies that met the PICOS criteria were selected.

Population

Community-dwelling adults ages 18 and above diagnosed with Primary Hypertension or Essential Hypertension. Studies that included individuals with Resistant Hypertension or Hypertension related to a known secondary cause were excluded as those are of a different aetiology.

Intervention

Text messaging-based interventions; including but not limited to SMS, unidirectional or bidirectional text messaging and tailored text messages. Text messages had to be the main intervention component and their content had to target improving MA.

Comparator

Comparators were no intervention, active control or usual care.

Outcomes

Primary outcome of interest was MA. Secondary outcome was BP, an indirect adherence measurement, as poorly-controlled BP is associated with low adherence to an antihypertensive-drug regimen [33].

Study Design

RCTs of any type were considered.

Information sources and search strategy

The databases employed for searching consisted of PubMed, Web of Science, Scopus, EMBASE, CINAHL, PsyCINFO, Cochrane and ProQuest dissertations and theses. A search strategy was developed using specific database Mesh terms. Keywords and index terms were explored and truncated using syntax rules of the respective databases. Boolean operators (OR & AND) were utilised to combine search terms. The electronic search strategy for the databases can be viewed.

Additionally, ongoing trials at clinicaltrials.gov, grey literature and specific journals of interest were manually searched. Subsequently, hand searching was performed to scrutinize and identify additional studies from the reference lists of similar SRs. EndNote software X9 was employed to manage bibliographies and references. Searching in the electronic databases was last conducted in September 2020. Titles and abstracts of identified studies were screened by two reviewers (R1 and R2) based on the predefined inclusion criteria. Full texts of screened articles were reviewed for final inclusion. When necessary, a third independent reviewer (R3) resolved disagreements.

Kappa statistic was used to assess interrater reliability to ensure consistency and clarity at the screening stage [34]. We recorded excluded studies in the “Characteristics of excluded studies” table and provided the reasons for exclusion. The PRISMA flow diagram depicted the flow of information through the different phases of the SR, where the number of records identified and used for analysis were documented.

Data Extraction

Data was extracted using a piloted standardised extraction form from the Cochrane Handbook for Systematic Reviews of Interventions. Two reviewers independently extracted data, with the accuracy verified through data comparison. For each study, extracted data characteristics included the study setting, study design, participant’s demographics, and details of the intervention, control and outcome of interests.

Methodological Quality

The methodological quality of eligible studies were assessed by R1 and R2 independently using the Cochrane Risk of Bias (ROB) Tool. Each study was rated based on the quality criteria of 6 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective outcome reporting. For each domain, high, low or unclear ROB was selected for appraisal. Rationale was provided to support the judgement for unclear ROB. Any discrepancy was reconciled by a team consensus.

Data Analysis

RevMan software (Review Manager Version 5.4) was used to conduct statistical analysis. The mean difference and risk ratio (RR) was used to determine continuous and dichotomous outcomes respectively [35]. Each study’s mean standard deviation and sample size of the post-SBP outcomes and/or post MA scores were extracted and data was pooled using the DerSimonian and Laird random-effects model.

Statistical heterogeneity was quantified by the I-square ($I^2$) statistic where $I^2$ 0-40%(might not be important), 30-60%(moderate), 50-90%(substantial) and 75-100% (considerable) were utilised as reference. If considerable heterogeneity was present, studies were not pooled and were narratively summarised.
Studies with MA and controlled BP presented as percentages were manually converted to be analysed as dichotomous outcomes where the event is the "number of participants who are adherent to medications" and the "number of participants with controlled BP" respectively. Studies with ambiguous data were consulted with the study authors and were omitted when there was uncertainty.

Study Selection

Initial database search yielded 858 records. After the removal of 294 duplicates, 566 records were screened. 519 records were excluded due to irrelevance based on the eligibility criteria. Subsequently, 47 records were reviewed in full-text. The two reviewers met and two inconsistencies were present but were resolved during a discussion. Therefore, the inter-rater agreement was 100%. A final consensus on 12 records was obtained. Figure 1 details the selection process using the PRISMA flow diagram.

Summary of Studies

In total, twelve RCTs were selected for this SR. The studies were published between 2015 and 2020. Amongst the studies, one was conducted in South Africa, two in Iran one in Bangladesh, one in South Korea, one in Urmia, two in the United States, one in Palestine, one in Lebanon, one in Finland and another in Chile [38-43]. Three studies solely targeted MA, three studies solely targeted Hypertension management with an emphasis in BP control while six studies targeted both behaviours [44-54]. Intervention duration ranged from two to 12 months. The scale most frequently used for assessing MA was the Morisky Adherence Scale and Hill-Bone Medication Adherence Scale. The participants' demographics and studies’ characteristics are elaborated in.

Text message characteristics

The studies’ text message characteristics are detailed in. Two studies integrated SMS as a co-intervention component [55,56]. Bobrow et al. examined the effects of two types of text messaging; Interactive and integrated SMS as a co-intervention component [55,56]. Bobrow et al. The studies’ text message characteristics are detailed in.

Quality ratings

All twelve studies were rated “unclear” ROB overall. Only two studies had published protocols and five registered in clinical trial registries. Most studies described random sequence generation and specified the method of randomisation i.e. block randomization. The unclear risk for performance bias was found in 91.7% (11 out of 12 studies) as blinding of participants were either not stated or only single-blind. Moreover, nine studies had an unclear ROB in allocation concealment. Only one study indicated “high” risk for selective outcome reporting [68]. The attrition rate ranged from 0% to 17%. Four studies had an ITT analysis conducted. Of the four studies, two incorporated missing data management. Collectively, there were numerous unclear judgments due to the lack of clarity on different domains across all studies, resulting in a decrease in the summative methodological evidence quality (Appendix 2). Summary of individual bias assessments are detailed in Table 1. Although some RCTs contain multiple arms, only text-based messaging and usual care arms were compared. We understand that multiple-treatment arms are possible sources of multiplicity in an RCT and an “among-group” statistical assessment poses difficulty in interpretation. As only one comparison is of interest, analysing multiple arms would not add value to the review. Moreover, in employing a Bonferroni or equivalent multiplicity correction factor to prevent type I error in multiple analyses, there is a likelihood of having a type II error instead [67]. Hence, the team predetermined to analyse only the text messaging and standard care arms.

Medication adherence

A total of nine studies assessed MA as an outcome. Six studies used validated adherence scales for measuring adherence [68-69]. They did not specify whether the self-made compliance questionnaire solely assessed medication compliance or other compliance domains including medication. Bobrow reported median and range instead of mean and standard deviation. With insufficient information, the data could not be manually converted using a method reported by literature. Study authors were contacted for clarification respectively but there was no reply. Hence, those data were not included for analysis. Amongst the nine studies, three were analysed using dichotomous data and three were analysed using continuous data. A summary of the outcome measures is presented in Table 2.

The pooled estimates of three studies that reported continuous data for post MA scores examining a total of 336 participants were conducted from two to three months. A meta-analysis employing the random-effects model revealed a statistically significant overall effect of standardised mean difference (SMD) 0.50 [0.10, 0.89] in favour of the text messaging group (Figures 2 and 3). The meta-analysis of eligible RCTs on the dichotomous outcome of MA which was defined as the event to be the "number of participants who are adherent to medications" is depicted in Figure 4 and indicates a 1:10 RR with [0.95, 1.28] confidence interval that neither favoured experimental nor control group using the M-H method and random-effects model (I²=0%). The forest plot also revealed the distribution of the pooled data with overlaps of confidence intervals, indicating statistically insignificant differences amongst studies. A non-significant P-value for the Cochran Q statistic indicated that the eligible trials were homogeneous (Figure 4).

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Bobrow et al. (2018) used the proportion of days of medication covered (PDC) as a MA outcome measurement. Out of 1157 participants, 248(82.8%), 225(59.7%) and 190(49.4%) had at least 80% of PDC for antihypertensive medications for the information-only message group, interactive message group and usual care group respectively, indicating both messaging groups being more effective than usual care.
Mehta et al. (2019) measured MA as the proportion of days the patient opened the pill bottle or responded to the text message. MA rates were 70.8% and 77.0% during the intervention for patients in the electronic pill bottles and bidirectional messaging arms respectively. No significant correlation was found between bidirectional messaging or adherence with pill bottles and SBP change.

Blood pressure

A total of nine studies assessed BP as an outcome. Four studies were analysed as dichotomous outcomes for BP control while eight studies were analysed as continuous outcomes for post SBP values.

Post SBP

The pooled estimates of eight studies that reported continuous data for post SBP values examining a total of 3865 participants were conducted from a span of one to 12 months. A meta-analysis employing the random-effects model yielded a large statistically significant overall effect of SMD -0.14 [-0.20, -0.08] in favour of the text messaging group without heterogeneity ($I^2=0\%$) and overall effect $Z=4.32$($P<0.0001$). Thus, text messaging-based interventions proved effective in decreasing SBP (Figure 5).

**Post SBP subgroup analysis**

A subgroup analysis was conducted to explore if the difference in text message content will have any outcome changes. A more significant SBP decrease was found in the intervention group compared to the controlled group post-intervention $Z=3.87$($P=0.0001$), with SMD -0.16mmHg [-0.24, -0.08] when the text messages content included MA and other Hypertension management-related content in the six RCTs. Similarly, there was SBP reduction in the intervention group compared to the controlled group post-intervention $Z=2.11$($P=0.03$), with SMD -0.10 [-0.20, -0.01] when the message included MA-related content only. This suggests that while MA-related content is sufficient to improve Hypertension management whereby...
the SBP value decreases, having a multifaceted content on Hypertension management may be even more effective.

Controlled BP

The figure below presents the pooled meta-analysis examining controlled BP in the four studies. The meta-analysis on the dichotomous outcome of controlled BP showed a RR of 1.02 [0.98, 1.07] which neither favoured experimental nor control group, suggesting inconclusive findings. There was slight heterogeneity (I²=26%, P=0.25). The forest plot showed overlaps of the confidence intervals, indicating statistically insignificant differences amongst studies.

Discussion

Medication adherence

Medication adherence is crucial for attaining optimal BP control in Hypertension and improved patient health. The meta-analysis of the three studies revealed that text-based messaging interventions had a significant effect on improving adherence scores in individuals with Hypertension compared to usual care. This is consistent with studies that have shown that SMS usage increases MA.

In contrast, the meta-analysis of the RRs of the three studies revealed that text messaging-based interventions had no significant effect on MA. The confidence interval crossed the line of null effect, indicating inadequate evidence. This may be due to the statistically small sample size of the studies that resulted in sampling error and lower precision.

Adherence is a multifaceted phenomenon influenced by numerous factors. The causes of medication non-adherence are multifactorial which can be intentional or unintentional. Intentional non-adherence occurs when patients make the conscious decision in not taking the prescribed medication for reasons that are rational in nature upon analysis. Such reasons include adverse reactions developed from the medication or the perception of side effects. This creates a support and monitoring system which may lead to higher engagement and motivation for lifestyle modifications. Presently, there are limited interactive and bidirectional messaging trials, rendering the effectiveness of text messaging of such nature uncertain. Hence, more trials are needed to determine the true effect of such interventions.

Blood pressure

The meta-analysis of the eight studies revealed that text-based messaging interventions had a significant effect in improving SBP in individuals with Hypertension, with a small SBP reduction of -0.14mmHg. This is consistent with a previous meta-analysis which used SMS for Hypertension management. One possibility for the favourable effect is that four studies developed their educational content based on established guidelines, namely the Eighth Joint National Committee (JNC8), Korean Society of Hypertension, WHO, up-to-date papers and Ministry of Public Health (MOPH). This finding suggests that adults with Hypertension may benefit from educational content on MA in accordance with such guidelines.

As two studies solely focused on medication-taking in their text message whereas the other six studies included other aspects of Hypertension self-management like physical activity, diet and smoking, a subgroup analysis was conducted to determine if there will be a difference in the outcome. Findings revealed that while both types of content led to SBP reduction, text messaging covering a wider range of Hypertension management content other than MA led to a greater decrease in SBP. A possibility for this is due to the different lifestyle changes such as exercise habits and diet that are known to directly influence BP. Suboptimal MA is recognized as a primary cause of failure in achieving BP control. Additionally, lifestyle factors including physical inactivity and high salt intake were found to be associated with inadequate BP control.

The meta-analysis of the four studies revealed that text messaging-based interventions had no significant effect on controlled BP. The development of atherosclerosis is accelerated and enhanced by BP elevation. Poor MA is recognized as a serious risk factor for atherosclerosis and a principal factor why Hypertension and its relative risks are not well-controlled. Moreover, a high adherence to antihypertensive medications is found to be associated with higher odds of BP control. Besides, heterogeneity was low and all studies had similar cut offs for controlled BP, whereby BP<140/90mmHg constituted controlled BP (Table 3). Therefore, the inconclusive results are unexpected.
Despite a decrease in the pooled SBP results, the decrease was insufficient to reach the achievement of BP control. This may be attributed to the statistical small sample size of the studies, resulting in sampling error and lower precision. Regardless of post-BP and adherence outcomes, all studies failed to investigate them after a year follow-up. Hence, long-term effects of text messaging-based interventions remain unknown. RCTs with extended follow-up periods will be beneficial for investigating long-term outcomes and strengthening the potential of such interventions for extensive dissemination and utilization.

This SR demonstrates that despite improvements in MA scores and a slight SBP reduction, there are inconclusive findings on whether text messaging-based interventions resulted in MA improvement and BP control due to adherence. A possible reason can be attributed to patient factors that affect pharmacokinetics of the drug. Comedications, comorbidities and frailty status may alter clinical outcomes of drug treatment. This is especially relevant in this review, where the participants’ age range from 36 to 93 years old. Pharmacokinetics of medications can be affected by age and decrease the capability of treatment compliance. Ageing results in hardening of arteriolar walls, calcification and modification in wall elasticity. This leads to atherosclerosis and disruption in the pacemaker function of the heart, resulting in raised BP. As age is a non-modifiable risk factor, this might be a reason for inability to achieve controlled BP even with the intervention to improve MA.

Nevertheless, as Hypertension is related to a constellation of other risk factors, the global risk reduction is posited to become the gold standard in clinical management. This SR highlights the potential text messaging-based interventions possess to improve MA and BP control in adults with Hypertension. While text messages are similar to other electronic forms of communication, its highly interactive nature distinct itself from others. Technology usage for promoting behavioural strategies may facilitate the adoption and integration of medication consumption in daily life. As compared to conventional behavioural and educational methods which had unsatisfactory results, text messaging serves as an innovative, inexpensive and practical alternative.

Moreover, SMS is attractive due to its potential in overcoming geographic and financial barriers facing remote populations. This is evident in Saleh et al., study where educational health SMS content like lifestyle and importance of medication compliance led to a significant SBP reduction and increased the odds of BP control in a rural community. Being the most frequently used form of technology worldwide, mobile phones possess high potential in influencing large populations. Findings from this SR suggest that providing medication reminders and medication-related education through text messaging can encourage patients in adopting a healthy lifestyle and supporting disease self-management.

Strengths and limitations

An extensive search was conducted to find as many studies as possible by also searching for grey literature and unpublished studies. Only studies in English were included which could have resulted in language and publication bias. For the record, four non-English studies were excluded and those could have increased the accuracy of pooled estimates of the text messaging effects. Some studies had insufficient information regarding the intervention and the data which was excluded in the analysis due to lack of correspondence from study authors. Notably, Maslapak et al., had outcome reporting bias, a major component of selective reporting bias which could be a threat to the validity of the review results. Moreover, a number of studies had small sample sizes, increasing the likelihood of sampling error and contribute to a degree of bias in the meta-analysis. Hence, the meta-analysis results should be interpreted with caution. Larger, more robust trials with greater sample sizes are needed to provide more reliable results with greater power and precision.

Implications

The findings of this review serve as a stepping stone for future research. While an overall SBP reduction and increased MA scores were found, there were inconclusive findings on BP control and adherence to medication. There were slight variations among studies, including intervention duration, frequency and type of medication reminder or Hypertension-related educational content.

While simple text messaging interventions have potential for scaling up and reaching the masses at a comparatively low cost per person, messages with greater complexity may come with a higher cost per capita. As technology continues to advance, text messaging interventions have evolved to incorporate more complex components. Some examples include personalization features, tailoring and interactivity as used in Tahkola and Schroeder.

As the rest of the studies did not encompass this tailored component, more of such trials are warranted to gain more thorough comprehension. Furthermore, cost analysis of interventions, especially those with complex features beyond simple text messaging were not examined in the studies. While Bobrow et al highlighted that interactive messaging results in better response, Mehta et al concluded that bidirectional messaging regarding MA did not produce improvements in BP control. As such advanced functions will require substantial cost and greater use of resources, besides having more high-quality RCTs that utilise text-based messaging interventions with advanced features; future research should also examine the cost-effectiveness and feasibility to inform the use of public health resources into the development of such communication tools in the promotion of MA.

Summary

Hypertension is prevalent in both economically advanced and developing countries, resulting in a significant impact on CVD burden worldwide. Medication non-adherence is a global issue and remains an unmet challenge to healthcare professionals.

According to WHO, “increasing the effectiveness of adherence interventions may have far greater impact on the health of the population than any improvement in specific medical treatments.” In recent times, mobile phones usage has vastly spread among communities and is the fastest adopted technology in high and low-income countries. Due to the ubiquitous nature of mobile phone usage, text messaging may serve as a reminder system to largely target unintentional non-adherence and reduce intentional non-adherence in Hypertension.

Despite numerous promising results from some studies, this review demonstrates an overall limited evidence of text messaging-based interventions in improving MA and BP control as a result of adherence. Nevertheless, text-based messaging interventions have the potential to encompass innovative features to overcome medication no adherence by providing drug intake reminders coupled with healthy lifestyle education.

References


