

Cochrane Corner: Text messaging to improve adherence to drugs for secondary prevention of cardiovascular disease

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Background.

Despite numerous readily available low cost and effective medications for secondary prevention of cardiovascular disease, it has been shown that a substantial proportion of cardiovascular events in people with established atherosclerotic cardiovascular disease are due to poor adherence¹. Worldwide at least 100 million people are thought to have prevalent heart disease, resulting in at least 13 million deaths each year. The majority of these deaths occur in low and middle income countries². Given the complexity of the problem and the variety of settings it occurs in, finding a feasible and scalable intervention to increase adherence poses challenges. Globally there are over 7.5 billion mobile phone subscriptions, and even in low and middle income countries, the penetrance rate is over 90%. Some mobile short messages services (SMS) have been shown to improve medication adherence for chronic conditions such as HIV³. SMS could be a potentially cost-effective and scalable intervention, and do not require that the intended audience need to search for information as it is delivered to them, as opposed to health worker-based interventions that are more expensive and complex to deliver. SMS interventions are seen to be of particular interest in low and middle income countries, where it is difficult to deliver health care into rural and remote communities. SMS also has the advantage of having relatively few side effects⁴. Despite great enthusiasm for using SMS based interventions to improve adherence and improve health outcomes, the evidence is limited⁵. In this summary, we report the results of a recent Cochrane review⁶. While other systematic reviews have addressed the question of using mobile phones for all types of medication adherence, previously no systematic review has only looked at SMS to improve adherence for cardiovascular drugs used in secondary prevention of cardiovascular disease. Furthermore, no previous review has conducted a detailed critical appraisal, including the process (e.g. behavioural science techniques vs simple reminders) of SMS development. To the best of our knowledge this systematic review was the first review to include a questionnaire for authors on how SMS were developed.

Review Methods:

This review followed the methodology of the Cochrane handbook. As per Cochrane guidelines we examined risk of bias and conducted a summary of findings study using GRADEPro. We only included studies where at least 50% of participants had established arterial occlusive events that included coronary artery disease, cerebrovascular artery disease, peripheral artery disease, and atherosclerotic aortic disease, and who were prescribed lipid lowering, blood pressure lowering and antiplatelet medication. In addition, all authors were contacted to further understand bias in the creation of the SMS. We requested the following information. Is the SMS intervention a reminder? Did the authors describe the process to construct the content of the text messages? Did they evaluate causes for non-adherence in the target population? Were psychological theories used to develop the messages to target the identified behavioural determinants of non-adherence? Were behaviour-change techniques employed to develop the messages? Were different text messages developed according to participants' characteristics?

Our primary outcomes included: Adherence to treatment (any definition used in trials), 2. Fatal cardiovascular events, non-fatal cardiovascular events, and Combined CVD event (fatal or non-fatal events). Secondary outcomes included adverse effects, LDL-cholesterol and blood pressure.

Review Findings

This review found seven small (with a total of 1310 participants) and heterogeneous trials, mostly from high income countries. Six of the trials included patients with coronary heart disease, and one on patients with stroke. Only two of the trials had registered protocols. All studies reported on adherence to medications.

Only three out of the seven trials were conducted in a middle income countries, with one study in China (280 participants), one study in Pakistan (200 individuals), and one study in Malaysia (62 participants). Sample sizes of trials ranged from 34 individuals to 521 individuals with a median of 123 individuals. Follow up time of the studies ranged from 30 days (the largest study) to one year (the smallest study) with a median time of eight weeks. The studies used differ substantially in terms of medication reported, adherence scales, which hamper the possibility of meta-analysis.

Six out of seven trials showed some beneficial effect of mobile phone text messaging for medication adherence (Table 1), but the medications studied, the scales that the authors used, and methods of reporting were so diverse that pooling of the results was considered uninformative. Only one study reported on any of our other primary outcomes, all-cause mortality and found two deaths, both in the control arm. No study reported on associated adverse effects. Only one study reported on LDL-cholesterol and found a small reduction. Two studies reported on blood pressure: one found a small reduction, and the other no difference.

Four authors replied to our questionnaire on SMS development. none of the trials used established behavioural techniques to develop the content of SMS to address the modifiable causes of adherence, or that the SMS were tailored to patient characteristics. Two sets of authors reported that the SMS that only reminder SMS were sent out, five study authors reported that an automated system of SMS delivery, and one did not specify, but it is assumed that it did.

Limitations

All trials had either high or unclear risk of bias for at least two domains, and only one had unclear or high risk of bias for at least four domains. This combined with the high level of heterogeneity, small study size and short duration meant that their results were classed as having very low quality. Moreover, all the studies from middle income countries came from cosmopolitan centres with, which limits the ability to transfer their findings to rural populations and low income countries.

Areas in need of further study:

This review shows the need for larger trials with longer follow-up and the use of outcomes of higher clinical relevance. Given the dual problem of high burden of atherosclerotic cardiovascular disease and poor adherence to cardiovascular medications, new trials should have a larger impact if conducted in low and middle-income countries. One such ongoing study is the TXT2Heart randomised trial being conducted in Colombia (<https://clinicaltrials.gov/ct2/show/NCT03098186>) this trial currently has recruited more than 880 participants to date and aims to recruit 1600 individuals and follow them for one year. However even this study is being conducted in urban settings, so to our knowledge no study has been conducted in rural regions. Given the rapid growth of smartphones worldwide, including in low and middle income countries, future studies should also consider the use of personalised health app addressed to tackle adherence

We recommend that future studies should:

1. Use established behavioural techniques to construct SMS that aimed to tackle modifiable causes of non-adherence
2. Use more relevant outcomes, such as surrogate end-points e.g. LDL-C and blood pressure, or ideally CV events
3. Have extended follows up, of at least one year
4. Have a sample size that allows to detect reasonable changes in clinically relevant end-point
5. Use standardised scales to measure adherence

Conclusions

While available evidence suggests that SMS are an effective strategy for promoting adherence to medications for secondary prevention of CVD, the available evidence is of low quality from small, short term trials. More research has to be done, particularly in rural regions and low and middle income countries to increase the evidence.

Table 1. Summary of Findings table

Mobile phone text messaging to improve medication adherence in secondary prevention of cardiovascular disease			
Patient or population: patients with established arterial occlusive events Setting: hospital/ cardiac rehabilitation facility Intervention: mobile phone text messaging Comparison: no intervention or other modes of communication			
Outcomes	Impact	No of participants (studies)	Quality of the evidence (GRADE)
Adherence to treatment	Six out of seven trials showed a beneficial effect of mobile phone text messaging for medication adherence. One trial showed an improved adherence score for the control group compared to the intervention group (smallest and shortest trial)	1310 (7 RCTs)	⊕○○○ VERY LOW ¹²³
GRADE Working Group grades of evidence High quality: We are very confident that the true effect lies close to that of the estimate of the effect Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect			

¹ Downgraded one level of evidence due to unclear or high risk of bias for all studies in at least one domain.

² Downgraded one level of evidence due to inconsistent reporting of outcome.

³ Downgraded one level of evidence due to imprecision of the results in one study and different direction of effect in another study.

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