



One-way Versus Two-way Text Messaging on Improving Medication Adherence: Meta-analysis of Randomized Trials

David S. Wald, MD, FRCP, Shahena Butt, MSc, Jonathan P. Bestwick, MSc

Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, United Kingdom

ABSTRACT

BACKGROUND: Mobile telephone text messaging is a simple potential solution to the failure to take medications as directed. There is uncertainty over the effectiveness of 1-way text messaging (sending text message reminders only) compared with 2-way text messaging (sending reminders and receiving replies confirming whether medication has been taken) as a means of improving medication adherence.

METHODS: A meta-analysis of 8 randomized trials (1994 patients) that tested the effectiveness of text messaging on medication adherence was performed. The trials were divided into 2 groups: trials using 1-way text messaging versus no text messaging and trials using 2-way text messaging versus no text messaging. The summary estimates of the effect of the 2 methods of text messaging (1-way or 2-way) were compared.

RESULTS: The summary relative risk estimate was 1.04 (95% confidence interval, 0.97-1.11) for 1-way text messaging and 1.23 (95% confidence interval, 1.13-1.35) for 2-way text messaging. The difference in effect between the 2 methods was statistically significant ($P = .007$).

CONCLUSIONS: Two-way text messaging is associated with substantially improved medication adherence compared with 1-way text messaging. This has important implications in the provision of mobile-based messaging in the management of patients taking medication for the prevention of chronic disease.

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KEYWORDS: Adherence; Medication; Text message

It has been estimated that approximately half of all patients prescribed medication for the treatment or prevention of chronic disorders do not take it as prescribed.^{1,2} In the United Kingdom, the annual cost of prescription medications in 2012 was approximately £10 billion, and in the United States, it was approximately \$325 billion, so the likely cost of nonadherence, in both wasted medicines and hospitalization through avoidable illness, is substantial.^{3,4}

More than 90% of the UK and US population own a mobile phone,^{5,6} and the use of text messaging is increasing

as a means of communication between patients and their physicians to arrange appointments, increase immunization, and adjust treatment.⁷⁻⁹ It also may improve medication adherence by reminding patients to take their medication and identify who has not taken their medication, so the cause for not doing so can be corrected. Randomized trials testing the use of text messaging on medication adherence have been published and yield conflicting results, some suggesting a benefit and others no benefit. The studies divide into those in which text messages were sent as reminders to take a medicine at a specific time (1-way messaging) and those in which a text message was sent and a reply requested to remind and to determine whether the medication had been taken (2-way messaging). It is not known how the 2 approaches compare and whether one is worthwhile but not the other. Clarifying this is important because there are now more than 160 different mobile telephone applications designed to improve medication adherence, all using 1-way rather than 2-way messaging.¹⁰

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Requests for reprints should be addressed to David S. Wald, MD, FRCP, Wolfson Institute of Preventive Medicine, Charterhouse Square, London EC1M 6BQ.

E-mail address: d.s.wald@qmul.ac.uk

This prompted us to conduct a meta-analysis of randomized trials assessing the value of text messaging on medication adherence to see whether the uncertainty could be resolved.

MATERIALS AND METHODS

We searched medical databases (PubMed, Embase, Ovid, and Cochrane Library) for randomized controlled trials that assessed the extent to which text messaging improved adherence to medication over time. The search terms used were ["adherence," "persistence," "compliance," or "concordance"] and ["text-messaging," "mobile phone," "SMS," or "smartphones"].

Studies were included that reported medication adherence in terms of the number of doses taken as a proportion of the total number of doses prescribed over a specified time period and classified participants in each randomized group as adherent or nonadherent according to whether the percentage of doses taken, exceeded a specified cutoff (eg, adherent to medication if >80% of prescribed doses were taken over the previous 28 days). We also sought information on whether the text messaging was 1-way messaging (text message reminders sent but no reply requested) or 2-way (text message reminders sent and a reply requested as to whether the medication had or had not been taken as prescribed).

The primary search generated 243 citations that reduced to 58 on inspection of the titles and review of the abstracts and to 9 on review of the published reports. An additional 3 articles were identified through hand-searching the citation lists of relevant studies and review articles, and 4 were excluded because relevant data were not reported, yielding 8¹¹⁻¹⁸ studies for inclusion in the analysis. Data were abstracted independently by 2 investigators who assessed for risk of bias using the Cochrane Collaboration tool,¹⁹ and the datasets were cross-checked.

For each study, estimates of adherence in each randomized group were extracted from trial results or determined from the reported data. The relative differences in adherence between the text and no text groups (equivalent to a relative risk) were determined for each trial. A fixed-effects meta-analysis was used to combine the relative differences, separately for trials using 1-way messaging and trials using 2-way messaging, and the summary estimates of effect were compared using meta-regression, taking a difference to be statistically significant at $P < .05$. Meta-regression was also used to examine possible sources of heterogeneity including, percentage cutoff used to define adherence, method of assessing adherence (self-report vs pill counting), duration of assessing adherence, mean age of patients, and proportion of patients who were male. All analyses were performed using Stata version 12. (StataCorp LP, College Station, Tex).

RESULTS

Table gives details of the studies in the meta-analysis, including data on 1994 patients (mean age, 64 years; 49% were male). Five studies were on patients receiving treatment for human immunodeficiency infection, 2 studies were on patients receiving blood pressure or lipid-lowering treatment, and 1 study was on individuals receiving malaria prophylaxis. The overall risk of bias was low for all trials, apart from 2; 1 trial had an unexplained imbalance in the number of participants in each randomized group,⁹ and 1 trial did not use an intention-to-treat analysis¹¹ (**Supplementary Table**, available online).

Figure is a meta-analysis plot

showing the effect of text messaging on medication adherence in each trial, according to whether 1-way or 2-way messaging was used; the summary relative risk estimates were 1.04 (95% confidence interval, 0.97-1.11) for 1-way messaging and 1.23 (95% confidence interval, 1.13-1.35) for 2-way messaging. One-way messaging had little, if any, effect, but 2-way messaging was effective. The difference in effect between 1-way and 2-way messaging was statistically significant ($P = .007$). Meta-regression analysis showed no effect of text messaging on adherence according to the percentage (proportion of all pills taken) cutoff used to define adherence, duration of assessment of adherence, mean age, or proportion of patients who were male.

Adherence was measured using electronic monitoring (Medication Event Monitoring System) in 2 of the 1-way messaging trials,^{12,15} self-reporting in 2 trials,^{13,14} and pill counts in 1 study¹¹; there was no evidence of heterogeneity between trials using these different methods ($P = .321$). Self-reporting was used in all 2-way messaging trials,¹⁶⁻¹⁸ with no evidence of heterogeneity ($P = .597$).

DISCUSSION

The results of this meta-analysis show a clear effect of text messaging on improving medication adherence when 2-way text messaging was used but not when 1-way text messaging was used, a 23% improvement (13% to 35%) compared with a 4% improvement (−3% to 11%), respectively. The contrasting effects were consistent across trials of different medications and medical disorders.

This result has important implications. It indicates that most medication adherence applications available for downloading onto mobile smartphones (160 such applications were available and reviewed in 2012)¹⁰ are of little or no use because they use 1-way message reminders. The findings from this meta-analysis do not exclude a small useful effect of 1-way messaging (a 4% improvement with an 11% upper confidence limit) but show that a 2-way communication is better. The results indicate that patients are approximately 20% more likely to adhere to medication

CLINICAL SIGNIFICANCE

- Two-way text messaging (reminder plus patient reply) improves medication adherence by 23% (95% confidence interval, 13-35), whereas 1-way text messaging (reminder only) has little or no effect.

Table Details of Randomized Trials Included in Meta-analysis

Trial (First Author)	Year of Publication	No. of Subjects	Duration of Trial (mo)	Mean Age (y)	Male (%)	Medication Prescribed	Text Messaging	Medication Use		
								Method of Assessment*	Period of Assessment (d)	Cutoff That Defined Adherence*
Contreras ¹¹	2014	67	6	56	55	BP lowering	1-way	Pill counts	90	>80%
Ollivier ¹²	2009	335	1	26	96	Malaria prophylaxis	1-way	MEMS	28	100%
Mbaugbaw ¹³	2012	200	6	40	27	HIV treatment	1-way	Self-report	7	100%
da Costa ¹⁴	2012	21	4	34	0	HIV treatment	1-way	Self-report	30	>95%
Pop-Eleches ¹⁵	2011	428	12	35	34	HIV treatment	1-way	MEMS	84	>90%
Wald ¹⁶	2014	301	18	60	55	BP and/or lipid lowering	2-way	Self-report	28	>80%
Lester ¹⁷	2010	538	12	36	35	HIV treatment	2-way	Self-report	30	>95%
Maduka ¹⁸	2013	104	4	36	50	HIV treatment	2-way	Self-report	7	>95%

BP = blood pressure; HIV = human immunodeficiency virus; MEMS = Medication Event Monitoring System (electronic date and time record of doses removed from pill bottle).
 *Patients were classified as adherent if (number of medication doses taken/number of medication doses prescribed) × 100 over specified time period before end of trial exceeded the specified percentage cutoff.

if 2-way messaging is used compared with 1-way messaging.

Generally, failure to take medication as prescribed is classified as intentional or unintentional. One-way messaging may be helpful in the latter category, providing a simple reminder, but not the former, which requires a further enquiry into the reason for not taking a medication and action to resolve this. Two-way messaging provides the opportunity for both. In the INTERACT trial, which tested the effect of text messaging on the use of blood pressure or lipid-lowering treatment, patients were contacted by phone

if their text message reply indicated they had not taken their medication as prescribed, and this led to 20 of 23 patients who had discontinued treatment because of concerns over the benefits or harms of their medication, resuming treatment. In the trial by Maduka and Tobin-West,¹⁸ which tested the effect of text messaging on adherence to antiretroviral therapy in Nigeria, patients were asked to acknowledge the text message reminders and indicate their need for further counseling or information that was provided by phone. In the WeTel Kenya trial,¹⁷ which also assessed adherence to antiretroviral treatment, patients were asked

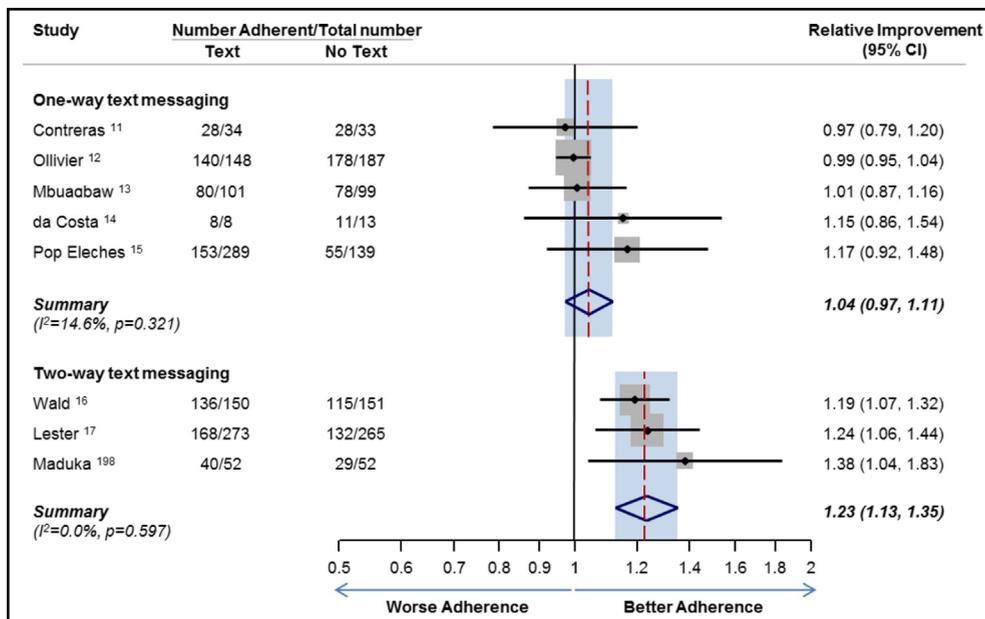


Figure Meta-analysis plot of randomized trials of text messaging on medication adherence according to use of 1-way messaging and 2-way messaging. CI = confidence interval.

to confirm their health status, and those who reported a problem were phoned within 2 days to assist with medical issues, in most reported cases.

In all but 3 trials, adherence was assessed by self-reporting, which relies on an accurate recall of doses missed over a time period and is prone to reporting error. The accuracy of electronic monitoring (Medication Event Monitoring System) or pill counting depends on medication actually being taken when the pack is opened and the monitored package being the patient's only source of drug. Notwithstanding these inherent limitations, there is no reason to expect such error to differ systematically between the 2 randomized groups in a trial, so the relative differences in adherence within trials are likely to be unbiased. There was also no evidence of heterogeneity between assessment methods used, although the power to detect small effects was limited. No trial directly compared 1-way with 2-way messaging in a single study, but this should not detract from the evidence from our prespecified analysis comparing the 2 approaches in different trials.

CONCLUSIONS

Two-way text messaging is a useful method for improving medication adherence and confers benefit across a range of therapies, but 1-way text messaging has little or no effect.

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SUPPLEMENTARY DATA

Supplementary table accompanying this article can be found in the online version at <http://dx.doi.org/10.1016/j.amjmed.2015.05.035>.

Supplementary Table Assessment of Risk of Bias in Trials of Text Messaging on Medication Adherence

Trial (First Author)	Random Sequence Generation	Allocation Concealment	Binding of Participants	Power Analysis	Missing Data	Selective Reporting	Other Sources of Bias:		Overall Risk
							Intention-to-Treat Analysis Used		
Contreras ¹¹	Low	Low	n/a	Low	Low	Low	Low		Low
Ollivier ¹²	Unclear	Low	n/a	Low	Low	Low	Low		Moderate
Mbaugbaw ¹³	Low	Low	n/a	Low	Low	Low	Low		Low
da Costa ¹⁴	Low	Low	n/a	Low	Low	Low	High		Moderate
Pop-Eleches ¹⁵	Low	Low	n/a	Low	Low	Low	Low		Low
Wald ¹⁶	Low	Low	n/a	Low	Low	Low	Low		Low
Lester ¹⁷	Low	Low	n/a	Low	Low	Low	Low		Low
Maduka ¹⁸	Low	Low	n/a	Low	Low	Low	Low		Low

n/a = not available.