

Research Article

**Mobile SMS Reminders for Increasing Medication Adherence****Siddharth Sarkar*, Priya Sivashankar, Hirmalini Seshadri**

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ABSTRACT

Short Messaging Service (SMS) text reminders provide a promising approach for increasing medication adherence. This review evaluates the literature from randomized controlled studies, observational studies as well as qualitative studies pertaining to efficacy of SMS reminders for improving the medication adherence. SMS interventions have been studied for a variety of disorders from medical and surgical specialties. Studies have emerged from across the globe and have evaluated different schedules of text reminders ranging from multiple times a day, once daily to less frequent once weekly SMS. The results of trials and observational studies of SMS reminders have been largely positive. This intervention is particularly appealing to developing countries which have witnessed increasing mobile access in the community setting. The review also highlights the issues to be considered while conducting research with this intervention modality.

Keywords: Medication Adherence, Text Messaging, Chronic Disease, Research Design, Randomized Controlled Trial**INTRODUCTION**

Medication non-adherence is a common clinical problem which is associated with sub-optimal clinical outcomes and increased health-care costs.¹⁻³ Several chronic disorders including diabetes mellitus, hypertension, schizophrenia, and bipolar disorder are associated with medication non-adherence, which leads to poorer clinical outcomes and exacerbated complications of the disorder.^{1,4,5} The causes of non-adherence to medications can be manifold including those which are patient related and health-care system related.^{3,6,7}

Access to mobile technology has grown rapidly in the last two decades and is increasingly being used in the health-care sector for a variety of purposes.^{8,9} Mobile technology has seen many applications in the clinical setting including promoting medication adherence. Medication adherence can be increased using SMS (Short Messaging Service) or "text" reminders, voice reminders and special applications ("apps") to remind patient to take medications. Out of these, SMS or text reminders are probably the least intrusive to the patient privacy and can be delivered through simpler mobile phones, enabling potential access to a larger number of clients. Hence, SMS reminders offer a promising method of promoting medication adherence among patients, especially those who suffer from chronic conditions and are required to take medications for a long period of time.

Several studies have evaluated the efficacy of SMS text reminders in enhancing the adherence to medications. These have included randomized controlled trials, observational studies as well as qualitative studies. The expansion of research in this area calls for a synthesis of

the evidence. Previous reviews on the topic have either focussed on a single disorder,^{10,11} or have assessed various aspects of SMS reminders but not specifically medication adherence,¹² or have used varied mobile technologies but not specifically text SMS reminders.¹³ Since, SMS reminders offer a concrete simple and less resource intensive method for promoting adherence with much potential for developing countries, this review takes a look at the literature pertaining to SMS or text reminders in improving the medication adherence in the clinical context.

MATERIALS AND METHODS

The present review aimed to synthesize findings from studies which had evaluated SMS text based reminders for promoting medication adherence. Peer-reviewed studies which had utilized text SMS services as an intervention with the aim of increasing the medication adherence in the clinical setting were included in the study. The review was not constrained to a particular disorder or organ system. The review attempted to include both quantitative and qualitative studies. Those studies which included SMS reminders as a part of a comprehensive package of mobile based interventions were not included in this review. Those studies which evaluated only other aspects of service delivery (like disease detection or reporting of events) were not included in the present review if they did not explicitly evaluate efficacy of SMS reminders on medication adherence.

The present review was conducted using Pubmed and Google Scholar electronic databases. The MESH term of "Medication Adherence" was combined with "SMS" OR "text messages" to identify suitable abstracts and



records. Additional studies were identified using cross references. Unpublished materials were not sought as a part of this review. Hand searches were not carried out as a part of the review, and the review was restricted to electronic searches only.

The abstracts of the identified studies were then scrutinized by two of the investigators (SS and PS) for inclusion in the study. Data was extracted from the included studies about the type of the study (randomized controlled trial, observational study or qualitative study), place of the study, the disorder assessed, number of subjects enrolled, method of assessment of adherence and outcome findings. Risk of bias assessment was not conducted for the studies in this review. This was because even the high quality studies assessing the efficacy of SMS reminders have the limitations of not being able to conduct intervention blinding effectively. Since this review aimed to cover a range of disorders and a variety of study methodologies, pooled summary assessment were not used. However, basic themes of inferences were drawn from the included studies. The differences in the outcomes in terms of the difference in efficacy rates or adherence rates were represented, along with the study described *p* value for determining the differences in outcome.

RESULTS

The search strategy for the present review is depicted in Figure 1. A total of 44 studies were included in this review which included 24 randomized controlled trials, 11 observational studies and 9 primarily descriptive studies. These are discussed further.

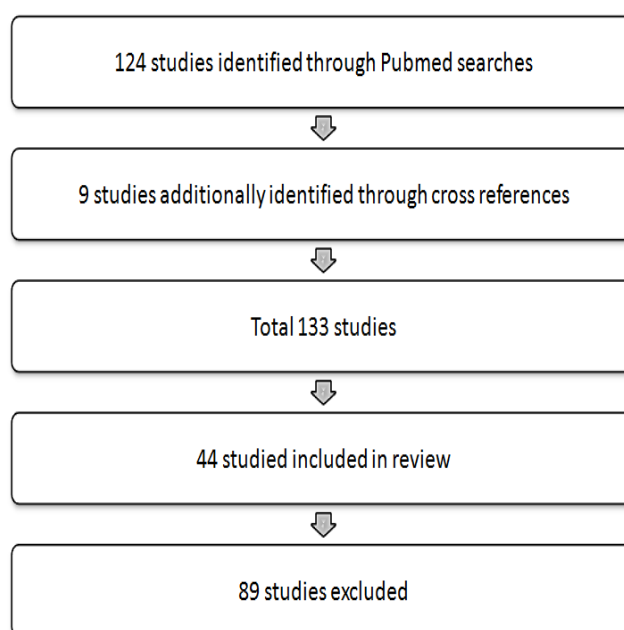


Figure 1: Identification of studies pertaining to SMS reminders for improving medication adherence

Results from the randomized controlled studies of SMS reminders are summarized in Table 1.

Studies have evaluated the efficacy of SMS reminders for medication adherence for a variety of disorders including from asthma, diabetes, HIV, acne, tuberculosis, psychotic disorders, epilepsy and others.

Randomized controlled trials have also evaluated medication adherence in apparently healthy population receiving health promotion interventions.^{34,35}

Table 1: Randomized controlled trials evaluating SMS reminders

Author, Year	Place	Health Condition	Sample size	Intervention and Control	Results
Arora ¹⁴	USA	Diabetes -mellitus	128	Twice daily text messages for 6 months versus no intervention	Self reported medication adherence significantly increased in the text messages group as compared to controls
Boland ¹⁵	USA	Glaucoma	70	Daily messages (text or voice) versus treatment as usual	Improvement in adherence intervention group while no significant difference in control (53% to 64%; <i>p</i> <0.05),
Huang ¹⁶	Taiwan	Various medical disorders	1198	SMS reminding medications versus no messages	Intervention group had 2.2 times decreased rates of missed doses and 3.2 times decreased rates of delayed doses than controls
Louch ¹⁷	UK	Diabetes mellitus Type 1	18	Daily text reminders underpinned by theory of planned behaviour constructs versus weekly messages	No significant differences between the groups with respect to self-reported insulin injection
Lua and Neni ¹⁸	Malaysia	Epilepsy	136	SMS messages with printed educational material versus educational material only	Better medication adherence and clinic attendance among the intervention group (<i>p</i> <0.05)
Quilici ¹⁹	France	Acute coronary syndrome	546	SMS Daily reminders over one month versus standard care	Non-adherence rates lower in SMS group than standard care (2.8% versus 7.2%, <i>p</i> = 0.02)
Vervloet ²⁰	Netherlands	Diabetes mellitus Type 2	104	SMS reminders when patients forget to take medications versus no reminders over 6 months	Reminded patients tended to miss doses less frequently than non-reminded patients thought difference was not significant (15% versus 19%, <i>p</i> = 0.065)



Boker ²¹	USA	Acne	40	Twice daily text messages for application of medication for 12 weeks versus controls	Mean adherence rates did not differ significantly between the intervention and control groups (33% versus 36%, p = 0.75)
Castano ²²	USA	Oral contraceptive continuation	962	Educational daily text messages for 180 days versus routine care	Continuation of OCP was better in the group received educational text messages than controls (64% versus 54%, p = 0.005)
da Costa ²³	Brazil	HIV	21	SMS reminders versus no reminders	Non significant differences between intervention and control groups as per self reported adherence (100% versus 84%, p = 0.243)
Iribarren ²⁴	Argentina	Tuberculosis	37	SMS reminder, text-in and educational messages versus standard care	SMS intervention did not statistically improve adherence to TB treatment (RR 1.49, CI 0.90-2.42).
Mbuagbaw ²⁵	Cameroon	HIV	200	Weekly standardized motivational text message versus routine care	No difference in reported missed doses between intervention and control (RR 1.01, 95% CI 0.87, 1.16; p>0.999)
Montes ²⁶	Spain	Antipsychotics for schizophrenia	254	Daily SMS reminders for 3 months to take medications versus routine care	Mean change in Medication Adherence Questionnaire was -1.0 in SMS group and -0.7 in control group, with significant differences between the groups (p = 0.02)
Petrie ²⁷	New Zealand	Asthma	216	Individually tailored text messages for 18 weeks versus no messages	Text messages group had better rates of prescribed inhaler doses (37.7% versus 23.9%, p < 0.05).
Suffoletto ²⁸	USA	Antibiotics in patients discharged from emergency department	200	Daily SMS query about prescription pickup, dose taken and educational feedback versus usual printed discharge instructions	No differences in adherence between participants in intervention group and controls (57% vs. 45%; p = 0.10)
Hardy ²⁹	USA	HIV	23	Daily bidirectional personalized SMS versus beepers	Composite adherence better for text messages group as compared to control (83.4% versus 56.3%, p = 0.009)
Pop-Eleches ³⁰	Kenya	HIV	431	Daily or Weekly short or long SMS versus controls	Weekly SMS reminders associated with better adherence (p = 0.03), but not daily SMS reminders
Shett	India	Diabetes mellitus	215	Customized SMS once in 3 days versus standard care	HBA1c as a marker of adherence showed greater improvement in the intervention group
Hou ³¹	USA	Contraception	82	SMS reminders for taking oral contraceptive versus no intervention	Non significant differences in number of missed pills per cycle between intervention and control (4.9 versus 4.6, p = 0.60)
Lester ³²	Kenya	HIV	538	Weekly SMS versus treatment as usual	Patients in SMS reminder group had more chances of retention (RR 1.23, CI of 1.06 to 1.45, p = 0.006)
Strandbygaard ³³	Denmark	Asthma	26	Daily SMS reminders for adherence to treatment till 12 weeks versus treatment as usual	SMS reminders associated with better adherence at 12 weeks when compared to controls (Absolute difference in mean adherence 17.8%, p = 0.019).
Armstrong ³⁴	USA	Sunscreen Application	70	Daily SMS reminders over 6 weeks versus no reminders	Adherence rate better among those receiving reminders versus controls (56.1% versus 30.0%, p < 0.001)
Cocosi ³⁵	Brazil	Health promotion	102	Text messages reminders with request for confirming taking the medication intake, versus no text messages	Non-significant difference between intervention and control groups with regards to medication adherence
Ollivier ³⁶	France	Malaria prophylaxis	424	Daily reminder SMS for 28 days versus no reminders	No statistically significant differences between the SMS reminder and control group (p = 0.84)
Márquez Contreras ³⁷	Spain	Hypertension	104	Twice weekly reminders and messages versus control	Adherence rate of 91.9% in intervention group versus 88.1% in control group, difference non-significant

HIV Human Immunodeficiency virus, OCP Oral Contraceptive Pill, SMS Short Messaging Service



Though many of the studies have originated from USA, studies have also emerged from other countries like Argentina, Brazil, Cameroon, Denmark, France, India, Kenya, Malaysia, Netherlands, New Zealand, UK, Spain and Taiwan. Sample sizes for these studies have ranged from less than 20¹⁷ to over 1000.¹⁶ Most studies have evaluated the efficacy of daily SMS. Treatment as usual or standard care was the most common control group. Efficacy of the SMS intervention had been evaluated in a variety of ways, though self-reported adherence was the most common method of representing the outcomes. The efficacy of SMS reminders was largely positive, though some of the studies did not find SMS reminders more effective than the control group.^{17,20,21,23,24,28,31,35–37}

The data from the observational studies are depicted in Table 2. Several observational studies have documented the efficacy of SMS reminders in promoting adherence. These observational studies have originated mainly in the

USA, but also have come from India and Italy. Text messages have been demonstrated to improve adherence in disorders including asthma, diabetes, HIV, paediatric liver transplant cases, psoriasis and psychotic disorders. The SMS reminder methodology have included proprietary automated message systems (e.g. SIMON³⁸ and mHealth⁴²), daily schedule, flexible reminder schedules, educational messages, and even two way text messaging system.

In two-way messaging system, not only the study investigators send reminder or educational messages, but the patients are expected to send messages back reporting their intake of medications or any other problems. Adherence has been evaluated over the course of the week and one study reported adherence to be better on weekdays than weekends.⁴⁰ In a comparison of voice and text based reminders, a study found that voice reminders were preferred by the clients.⁴⁶

Table 2: Observational and qualitative studies evaluating SMS reminders

Author, Year	Place	Health Condition	Sample size	Intervention	Results
Estep ³⁸	USA	Sickle Cell Disease	55	SIMON [®] automated text message reminder	Improved hematologic parameters with SMS intervention reflecting better adherence. Hospitalization and medication possession ratio did not significantly increase.
Balato ³⁹	Italy	Psoriasis	40	Daily SMS for 12 weeks providing reminders and education in intervention versus usual care in matched controls	Patients receiving text messages reported improved quality of life, greater improvement in disease severity and medication adherence as compared to matched controls.
Dowshen ⁴⁰	USA	HIV	25	Daily SMS reminders for medication for 24 weeks with a response requested for ascertaining medication intake	Overall mean adherence was 57.4% with adherence being more on weekdays than weekends
Lewis ⁴¹	USA	HIV	52	Two way text messaging	Improved adherence among those initially non-adherent, liked by participants, improved CD4 counts
Arora ⁴²	USA	Diabetes	23	mHealth – Three times a day messages	Improvements seen in adherence, as well as exercise, food and foot care
Foreman ⁴³	USA	Varied disorders	580	Text messaging reminder system and a matched cohort	Proportion of days covered by medication better in SMS group than control cohort (0.85 versus 0.77, p < 0.001)
Granholm ⁴⁴	USA	Psychotic disorders	55	Flexible SMS schedule over 12 weeks, up to many times a day	Medication adherence improved significantly only for individuals who were living independently.
MacDonell ⁴⁵	USA	Asthma	6	Daily SMS messages for 14 days (time based), expected to make event based SMS for symptom exacerbation	All participants expressed positive feedback about the service. About 40.0% reported confusion with event-based messages and most preferred time-based messages.
Sidney ⁴⁶	India	HIV	139	Weekly reminders (SMS as well as interactive voice)	Voice reminders more preferred than SMS reminders for adherence
Miloh ⁴⁷	USA	Paediatric liver transplant	41	Text reminders over 1 year to promote adherence to immunosuppressants	Reduction in cellular rejection rates though drop in Tacrolimus levels at the end of intervention, suggesting risk of rejection
Dunbar ⁴⁸	USA	HIV	25	Two-way text message system	Reported to be helpful in promoting adherence

HIV Human Immunodeficiency Virus, SMS Short Messaging Service



Many studies have put forth qualitative data for the role of SMS reminders for enhancing medication adherence. Albino⁴⁹ conducted interviews with patients suffering from tuberculosis and reported that SMS technology may be an efficient method to transmit reminders, motivational texts on treatment, and health education information. Similarly, Lei⁵⁰ reported that four-fifths of patients with tuberculosis had favourable opinion towards SMS reminders. Person⁵¹ reported that one third tuberculosis patients endorsed text message reminders to take medications. Younger population was more likely to accept text message reminders, while African American and Hispanic subjects were more likely than White subjects to endorse text message reminders. Baranowski⁵² evaluated 14 patients with HIV and 13 care providers, and suggested several benefits of mobile technology in promoting adherence including ease of use, access, convenience, and confidentiality. Curioso⁵³ reported that HIV infected individuals had positive perception about receiving SMS reminders for improving adherence, but expressed the need for the SMS to be simple and concise. Keränen and Liikkanen⁵⁴ reported that SMS reminders worked well for patients with

Parkinson's disease on treatment. Britto⁵⁵ demonstrated that an SMS reminder system customized by teens themselves for treatment of asthma may have positive effects on improving medication adherence.

Sahm⁵⁶ reported that patients on antidepressants with unintentional non-adherence were largely willing to receive SMS reminders to remind them for taking the medication. Mall⁵⁷ have suggested that mental health service users supported SMS text messaging for reminding for both medication adherence and appointment adherence. However, Ting⁵⁸ reported that SMS reminders in cases of childhood SLE improved adherence for clinic visits, but not medication adherence.

The studies not included in the review and the reasons thereof are mentioned in Table 3. The most frequent reason of non-inclusion was the lack of explicit measurement of medication adherence. Other reasons included utilization of interactive voice response system, using smartphones or other devices but not mobile delivered text messages, or using other outcome measures. Studies on appointment adherence were not considered for the review.

Table 3: Studies excluded from the Review

Author, Year	Place	Reason of Non-inclusion
Hughes ⁵⁹	UK	Feasibility study of internet and communication technology for rheumatology patients
Ahlers-Schmidt ⁶⁰	USA	Focuses on immunization but not medication
Belzer ⁶¹	USA	Not limited to SMS services
Creary ⁶²	USA	Used smartphone or computer
Curran ⁶³	Kenya	SMS used to assess risk behaviour, but not medication adherence
Haberer ⁶⁴	Uganda	Text messages used to collect data about adherence, but not as an adherence promotion measure
Haberer ⁶⁵	Uganda	SMS based queries used to assess adherence
Hanauer ⁶⁶	USA	Assessed blood glucose monitoring and not medication adherence
Harbig ⁶⁷	Denmark	Special device but not mobile SMS used
Horvath ⁶⁸	USA	Did not assess medication adherence
Ingersoll ⁶⁹	USA	Did not evaluate adherence specifically
Johnson ⁷⁰	USA	Used pager system
Mao ⁷¹	China	Does not report about medication adherence
McCall ⁷²	USA	RFID-based Medication Adherence Intelligence System being used
Mira ⁷³	Spain	Specialized app used
Moyer ⁷⁴	Kenya	Did not assess use of mobile technology on medication adherence
Osborn and Mulvaney ⁷⁵	USA	IVR system used
Piette ⁷⁶	USA	IVR system used
Safren ⁷⁷	USA	Pager and not mobile text messages used
Seid ⁷⁸	USA	SMS part of a comprehensive intervention program
Simoni ⁷⁹	USA	Pager and not mobile text messages used

Reviews and protocol of studies not mentioned in the list

DISCUSSION

The present review suggests that SMS text reminders can be utilized to promote medication adherence for a range of health conditions. SMS text reminders have been

largely efficacious studied across various parameters of medication adherence including self-reported adherence, pill counts and biochemical measures. Studies have emerged from across the globe and have evaluated the efficacy of text reminders across a variety of disorders.



This suggests the broad potential applicability of this mode of intervention for medication adherence promotion. Increased availability of mobile phones in developing countries have made SMS reminders as a lucrative option for improving compliance to medications.^{80,81} The wider access to mobile phones in the developing countries driven by low instrument and subscription rates is being tapped for health promotion.^{82,83} This suggests the potential role of SMS reminders in the emerging developing economies.

The review suggests that a variety of SMS text delivery options are available for improving adherence. Most of the studies have used daily text SMS reminders, probably because medications need to be taken on a daily basis especially for chronic disorders. Some studies have attempted to link the timing of medication reminder to be just prior to the medication timing. Some studies have required that the patient send a message back to the investigators after the intake of medications²⁹ attempting to ensure that the patient is bound to report his compliance. However, concern has been raised about the response rates achieved by this method. Majority of the randomized trials have utilized at least once daily messaging schedule. A few studies have utilized weekly or twice-weekly messages to promote adherence,^{32,37} a less frequent messaging schedule being probably less intrusive. Though there have a lack of head-to-head studies comparing the message frequency schedules, one study did find that improved adherence with weekly rather than daily messaging schedule.³⁰

The content of the message is likely to have an impact on the overall efficacy rates of the intervention. However, a study which compared customized theory driven messages were to regular health promotion messages did not find statistically significant differences between the groups.¹⁷ While one study did find advantage of SMS reminders as an add-on to usual printed educational material,¹⁸ another study failed to find difference between SMS reminders and printed medication instructions at discharge.²⁸ The SMS message may comprise simple reminder, a reminder eliciting a feedback, a reminder customized to patient's choice, an educational note, or a motivational quote. Each of these SMS templates/formats are likely to influence the motivation and practicalities of medication intake to a different extent.⁸⁴ Health-care planners need to take into consideration patient preferences while choosing a format of SMS delivery for improving adherence.

SMS text messages have found application among a variety of medical and surgical specialties for promoting medication adherence. This has ranged from internal medicine, psychiatry, dermatology, paediatrics, obstetrics and gynaecology, ophthalmology, cardiology, neurology, allergy and immunology and others. The diseases catered to have been typically chronic disorders, which require adherence to long term medications. However, SMS text reminders have also been utilized for short term

treatment like a course of antibiotics in the post-operative period²⁸ or for routine care like applying sunscreen or contraception. The utilization of SMS reminders for improving adherence is not constrained by disorders, and can be customized to the medication regimen.

Several challenges have been encountered while attempting to objectively study the efficacy of SMS reminders in promoting adherence. First, is the issue of recruiting a suitable control group for demonstrating superior efficacy. Most of the studies have relied on treatment as usual/standard care as the control group. But participants of SMS 'intervention' are anyway likely to report a more favourable outcome due to 'expectancy' effect, especially when informed consent is obtained at the time of recruitment explaining the rationale and objectives of the study. Alternative suitable controls could be non-reminder SMS text messages (like motivational or educational texts), or an alternative theory backed method of adherence improvement (like emails or telephone calls). The second issue pertains to blinding of the participants. The intervention and control group in a randomized controlled trial evaluating SMS reminders can hardly be blinded. This is again likely to produce favourable outcomes towards SMS reminders when it is the sole active intervention. The third issue pertains to access and usability of a mobile phone. Several studies have reported that a proportion of patients and/or caregivers either did not possess a mobile phone or had difficulty in using it,^{23,47} leading to difficulty in using SMS reminder as an intervention in this subset of population. This issue is also experienced when the target population is not able to comprehend English language well and the SMS is provided in English. Vernacular text messages have been tried as an alternative in such situations, but may not be supported by routine mobile phones resulting in difficulty of access. Fourth, is the issue of the optimum frequency of the SMS text messages. Medication regimen can be fairly complicated with patients needing to take pills several times a day. In that situation, whether the text messages should be sent multiple times a day, or once a day, or at a lesser frequency can be deliberated upon. Excess number of messages can be exhausting for the patient, and can lead to the SMS reminder being ignored as a reflex. On the other hand, less frequent messages can translate to patient 'forgetting' about the medications on the days SMS are not sent. Fifth issue pertains to assessment of outcomes. Self-reported outcomes are more likely to be influenced and inflated by subject expectancy effects, as compared to biochemical parameters like HbA1c. Hence, wherever possible, objective measures of adherence may be better than subjective reports. The sixth issue relates to the recipient of the SMS reminder. Typically the patient himself or herself receives the messages, but the caregiver may be the recipients of such reminders in the cases of paediatric patients and mental health service users. Lastly, the issue of confidentiality needs caution,



especially for patients suffering from potentially stigmatizing conditions like HIV and psychiatric disorders. Inadvertent disclosure of the disease status to someone else who has access to the patient's mobile may have distressing consequences for the patient. Researchers need to be cognizant of these issues when planning interventions to evaluate efficacy of SMS text reminders.

Given the largely positive efficacy of SMS reminders for improving medication adherence, the question that remains is whether such an intervention can be scaled up to provide routine service to a larger number of individuals. Such an option would be appealing given the demonstrated efficacy, but at the same time would pose additional resource burden to the health care system and/or the patient. From a service perspective, receiving reminder SMS should be voluntary, subjected to explicit written consent of the patient. This would keep the perspectives of health care providers and patients clear relating to confidentiality issues. Funding for this additional intervention is another challenge. Cost analysis and cost effectiveness studies for SMS reminder intervention is likely to inform about the financial input required for such an intervention.⁸⁵ Public private partnerships and help of Non-Governmental Organizations (NGOs) and benefactors may be sought in developing countries to extend the benefits of this intervention to the underserved areas. Other relevant factors that determine medication adherence need also need to be given a thorough consideration,^{6,7} and attempts should be made to ameliorate them. Synergistic effects of different adherence promotion measures with SMS reminders need to be considered for improving patient outcomes further.

The findings of the review need to be considered in the light of strengths and limitations. The strengths of the study include consideration of varied disorders for evaluation of efficacy as well as inclusion of observational and qualitative studies. The limitations of the present review includes restricting searches to selected databases, focusing on SMS text messages only, excluding studies where SMS reminders not the main intervention, and having limited scope for qualitative evaluation of acceptability and patient preferences. Moreover, the present review did not attempt a quantitative pooled analysis of the results from various studies, or assess risk of bias of individual studies.

To conclude, SMS reminders offer a promising intervention for improving medication adherence, especially for chronic disorders. This has a special appeal for developing countries which has seen rapid development of telecommunication facilities, and growing access to mobile phones. Future studies need to assess SMS reminders with appropriate active control interventions. Cost-effectiveness analysis may be conducted to assess the financial input required for sustaining such interventions on the longer run. Ecological studies with scaled up mobile SMS reminders

may be conducted in the future, which would enable to demonstrate the efficacy of SMS reminders in the naturalistic setting.

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