Intervention Strategies for Improving Patient Adherence to Follow-Up in the Era of Mobile Information Technology: A Systematic Review and Meta-Analysis



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Abstract

Background: Patient adherence to follow-up plays a key role in the medical surveillance of chronic diseases and affects the implementation of clinical research by influencing cost and validity. We previously reported a randomized controlled trial (RCT) on short message service (SMS) reminders, which significantly improved follow-up adherence in pediatric cataract treatment.

Methods: RCTs published in English that reported the impact of SMS or telephone reminders on increasing or decreasing the follow-up rate (FUR) were selected from Medline, EMBASE, PubMed, and the Cochrane Library through February 2014. The impacts of SMS and telephone reminders on the FUR of patients were systematically evaluated by meta-analysis and bias was assessed.

Results: We identified 13 RCTs reporting on 3276 patients with and 3402 patients without SMS reminders and 8 RCTs reporting on 2666 patients with and 3439 patients without telephone reminders. For the SMS reminders, the majority of the studies (>50%) were at low risk of bias, considering adequate sequence generation, allocation concealment, blinding, evaluation of incomplete outcome data, and lack of selective reporting. For the studies on the telephone reminders, only the evaluation of incomplete outcome data accounted for more than 50% of studies being at low risk of bias. The pooled odds ratio (OR) for the improvement of follow-up adherence in the SMS group compared with the control group was 1.76 (95% CI [1.37, 2.26]; P<0.01), and the pooled OR for the improvement of follow-up adherence in the telephone group compared with the control group was 2.09 (95% CI [1.85, 2.36]; P<0.01); both sets showed no evidence of publication bias.

Conclusions: SMS and telephone reminders could both significantly improve the FUR. Telephone reminders were more effective but had a higher risk of bias than SMS reminders.

Citation: Lin H, Wu X (2014) Intervention Strategies for Improving Patient Adherence to Follow-Up in the Era of Mobile Information Technology: A Systematic Review and Meta-Analysis. PLoS ONE 9(8): e104266. doi:10.1371/journal.pone.0104266

Editor: Thomas A. Smith, Swiss Tropical & Public Health Institute, Switzerland

Received April 23, 2014; Accepted July 7, 2014; Published August 6, 2014

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Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and its Supporting Information files.

Funding: This study was funded by the Pearl River Science and Technology New Star (Haotian Lin, 2014J2200060) Project of Guangzhou City and the Cultivation Projects for Young Teaching Staff of Sun Yat-sen University (12ykpy61) of the Fundamental Research Funds for the Central Universities. The sponsors of the study had no role in the design of the study protocol, the data collection, the data analysis, the data interpretation, the writing of the report, or the decision to submit the manuscript for publication.

Competing Interests: The authors have declared that no competing interests exist. Co-author Haotian Lin is a PLOS ONE Editorial Board member. This does not alter the authors adherence to PLOS ONE Editorial policies and criteria.

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Introduction

Follow-up refers to the timely surveillance of health status and guidance in a medication regimen by various methods among patients who visited or were visited by medical staff. [1] Adherence to follow-up (AFU) is most commonly measured as the follow-up rate (FUR), which is also called the attendance rate, [2] retesting rate, [3] or screen rate, [4] with different definitions and calculations according to the specific research background. As a medical process characterized by long-term observation, AFU plays an irreplaceable role in chronic disease management. [5–8] In addition to the treatment effect, AFU seriously affects clinical research implementation: participants who are enrolled but do not complete a trial (study attrition) can undermine the internal and external validities of the findings and cause bias when participants are not lost randomly but rather have certain characteristics. Loss to follow-up usually necessitates that more participants be enrolled to attain adequate power for the trial results to be valid, which may increase the trial's cost or duration or delay important results [9].

Given the significance of AFU, studies were performed to investigate the measurements of and related factors influencing FUR [10] and, in particular, to explore effective, novel interventions to improve FUR in the era of mobile information technology. [11] This technology has greatly affected the way people live and work and has also been convenient for medical practice. [12] However, most published studies have focused more on adherence to medication and less on AFU, and few have simultaneously assessed the nature and relative effectiveness of compliance interventions across the broad spectrum of patient conditions and compliance measures. [13] In our previous randomized controlled trial (RCT; ClinicalTrials.gov, NCT01417819), we demonstrated a successful and practical intervention with short message service (SMS) reminders to significantly improve the AFU of families with clinically meaningful pediatric eye care in a setting with limited resources. [2] In the present study, we aimed to systematically evaluate the published RCTs reporting on the impact of AFU in patients with SMS and/or telephone reminders, both of which are the most used features, although varying in cost and convenience, in the era of mobile information technology.

Methods

Literature Sources

A comprehensive search of databases, including Medline, EMBASE, PubMed, and the Cochrane Library, was conducted using the search terms "telephone", "text message", "SMS", "adherence", "compliance", "follow up", and "attendance". We also searched conference abstracts and the reference lists of the studies identified by the search. The latest search date was February 4, 2014. Two authors independently screened titles and abstracts to determine potential eligibility for this meta-analysis. When screening discrepancies occurred, consensus was achieved after further discussion.

Inclusion and Exclusion Criteria

We carefully reviewed all potentially relevant articles, and inclusion was restricted to RCTs. The included studies described the impact of SMS or telephone reminders on increasing or decreasing the FUR, and the control group did not receive a reminder of any type. To avoid including duplicate data, the newest and most informative article was selected when multiple studies were conducted by the same authors.

Date Extraction and Outcome Measure

Two authors independently extracted the data from the selected articles. The primary outcome was the FUR (also known as the attendance rate, retesting rate, nonattendance rate, or screen rate), defined as the proportion of patients attending their appointment at the originally scheduled time. [14] If the FUR was calculated more than once, according to different follow-up periods, the initial data were used. We abstracted or calculated the odds ratio (OR) in the intervention group compared with the OR in the controls as the primary effect measure for the study.

Quality Assessment and Statistical Analysis

To determine whether the selected studies were appropriate for inclusion in the meta-analysis, two authors assessed each trial independently and resolved disagreements via consensus. The risk of bias in each trial was assessed according to Cochrane methodology, [15] considering random sequence generation, allocation concealment, the blinding of patients and personnel, incomplete outcome data, selective reporting, and other biases. The heterogeneity of each trial was determined through a visual inspection of forest plots and with a standard Chi² test and an inconsistency (I²) statistic. [16] P values<0.05 indicated significant heterogeneity. Additionally, for I²<25%, we used fixed-effects meta-analysis to estimate the common OR (95% CI); for I² = 25 to 75%, we used random-effects meta-analysis; and for I²>75%,

because the heterogeneity was too great for a summary estimate to be calculated, subgroup analysis was needed. The statistical analysis was performed using the Rev Man Computer program (Version 5.0. The Cochrane Collaboration, 2008, The Nordic Cochrane Centre, Copenhagen, Denmark) using two-sided hypothesis testing with alpha = 0.5. For the dichotomous data, ORs were used.

Results

Of the 441 titles and abstracts screened, only 18 RCTs were identified in our systematic review, including 10 studies only focused on SMS reminders, 5 only focused on telephone reminders, and 3 focused on both SMS and telephone reminders (Figure 1). All 18 RCTs were published in English between 1995 and 2014 and were from 9 countries. The 13 RCTs [2,3,17–27] on SMS reminders included 3276 patients with and 3402 patients without SMS reminders, and the 8 RCTs [25–32] on telephone reminders reported on 2666 patients with and 3439 patients without telephone reminders. The most used (7/18) measurement index of adherence to follow-up was the attendance rate in the included studies, and the nonattendance rate and the attendance rate at the first appointment/visit were the second and third most used (Table 1).

According to the Cochrane methodology, the risk of bias of the included studies was assessed by considering adequate sequence generation, allocation concealment, blinding, the evaluation of incomplete outcome data, lack of selective reporting, and lack of other biases (Figure 2). For SMS reminders for the respective Cochrane factors, the studies at low risk of bias had values (a quantitative index of the risk of bias, range 0–100%) of 76.9%, 61.5%, 69.2%, 100%, 53.8%, and 23.1%; the studies with unreported features and a moderate risk of bias had values of 7.7%, 15.4%, 7.7%, 0%, 30.8%, and 61.5%; and the studies at high risk of bias had values of 15.4%, 23.1%, 23.1%, 0%, 15.4%, and 15.4%. For telephone reminders for the respective Cochrane factors, the studies at low risk of bias had values of 37.5%, 12.5%, 62.5%, 25.0%, and 25.0%; the studies with unreported features and a moderate risk of bias had values of 50.0%, 37.5%,



Figure 1. Flowchart of the included and excluded studies. doi:10.1371/journal.pone.0104266.g001

First author	Year	Country	Recruitment period	Study design	Inclusion- exclusion criteria	Consecutive patients	Electronic reminder type	Measurement of adherence to follow-up
Clough [23]	2014	Australia	N/A	RCT	Yes	Yes	SMS	Attendance rate at first appointment
Downing [3]	2014	Australia	N/A	RCT	Yes	Yes	SMS	Retesting rate
Wang [24]	2014	China	Dec.2011–Mar.2012	RCT	Yes	N/A	SMS	Attendance rate
Narring [22]	2013	Switzerland	Nov.2010–Apr.2011	RCT	Yes	N/A	SMS	Proportion of unexplained missed appointments without prior notification
Lin [2]	2012	China	Dec.2010–Aug.2011	RCT	Yes	Yes	SMS	Attendance rate at first visit
Odeny [19]	2012	America	Sep.2010-Apr.2011	RCT	Yes	N/A	SMS	Return rate at day 7
Prasad [20]	2012	India	Sep.2010-Dec.2010	RCT	Yes	N/A	SMS	Attendance rate
Taylor [21]	2012	Australia	N/A	RCT	Yes	N/A	SMS	Nonattendance rate
Liew [18]	2009	Malaysia	N/A	RCT	Yes	N/A	SMS	Nonattendance rate
Fairhurst [17]	2008	UK	Aug.2004–Feb.2005	RCT	Yes	N/A	SMS	Nonattendance rate
Goelen [32]	2010	Belgium	N/A	RCT	Yes	N/A	Telephone	Mammography rate
Roberts [31]	2007	UK	N/A	RCT	N/A	N/A	Telephone	Attendance rate
Sawyer [30]	2002	Australia	Aug.1998–Jan.1999	RCT	N/A	N/A	Telephone	Attendance rate
Vivier [29]	2000	America	Jul.1998–Sep.1998	RCT	Yes	N/A	Telephone	Proportion of children immunized
Ferson [28]	1995	Australia	N/A	RCT	N/A	N/A	Telephone	Immunization rate
Chen [27]	2007	China	Apr.2007–May.2007	RCT	Yes	Yes	SMS+Telephone	Attendance rate
Leong [26]	2006	Malaysia	Apr.2005-Oct.2005	RCT	Yes	N/A	SMS+Telephone	Attendance rate
Bos [25]	2005	Netherlands	N/A	RCT	N/A	N/A	SMS+Telephone	Attendance rate
doi:10.1371/journa	al.pone.0104	266.t001						

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Figure 2. Risk-of-bias graphs. Panel A, evaluation of the study quality of RCTs on SMS reminders; Panel B, evaluation of the study quality of RCTs on telephone reminders. The green bar means reported and a low risk of bias, the yellow bar means unreported and a moderate risk of bias, and the red bar means unreported and a high risk of bias. doi:10.1371/journal.pone.0104266.g002

37.5%, 25.0%, 50.0%, and 50.0%; and the studies at high risk of bias had values of 12.5%, 50.0%, 50.0%, 0%, 25.0%, and 25.0%.

The ORs of the included studies regarding the improvement of follow-up adherence in the SMS group compared with the control

group (Figure 3) ranged from 0.74 to 6.92, and the pooled OR was 1.76 (95% CI [1.37, 2.26]; P<0.01). The ORs of the included studies regarding the improvement of follow-up adherence in the telephone group compared with the control group (Figure 4)

	Experim	ental	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Clough2014	62	70	63	69	3.8%	0.74 [0.24, 2.25]	
Bos2005	42	51	77	92	5.0%	0.91 [0.37, 2.25]	
Odeny2012	387	592	356	596	12.4%	1.27 [1.01, 1.61]	-
Narring2013	386	462	423	529	11.3%	1.27 [0.92, 1.76]	
Taylor2012	304	342	283	337	9.7%	1.53 [0.98, 2.38]	
Fairhurst2008	167	189	188	226	8.2%	1.53 [0.87, 2.70]	
Leong2006	194	329	161	335	11.6%	1.55 [1.14, 2.11]	
Liew2009	260	308	238	309	10.2%	1.62 [1.08, 2.43]	
Chen2007	538	615	498	619	11.5%	1.70 [1.24, 2.32]	
Wang2014	18	25	10	25	3.4%	3.86 [1.18, 12.61]	
Downing2014	17	62	2	32	2.3%	5.67 [1.22, 26.33]	
Lin2012	132	135	108	123	3.1%	6.11 [1.72, 21.66]	
Prasad2012	76	96	39	110	7.5%	6.92 [3.69, 12.97]	
Total (95% CI)		3276		3402	100.0%	1.76 [1.37, 2.26]	•
Total events	2583		2446				
Heterogeneity: Tau ² =	0.12; Chi ²	= 38.84	4, df = 12	(P = 0.0)	0001); I ² =	= 69%	
Test for overall effect:	Z = 4.38 (F	P < 0.00	01)				Favors control Favors experimental

Figure 3. Comparison of the FUR between the SMS and the control groups. doi:10.1371/journal.pone.0104266.g003

	Experim	ental	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Leong2006	196	329	156	335	17.5%	1.69 [1.24, 2.30]	-
Chen2007	542	614	498	619	16.3%	1.83 [1.33, 2.51]	
Bos2005	66	73	77	92	1.8%	1.84 [0.71, 4.78]	+
Goelen2010	435	1336	358	1940	55.3%	2.13 [1.81, 2.51]	
Roberts2007	89	104	183	258	4.3%	2.43 [1.32, 4.47]	
Sawyer2002	93	101	56	70	1.5%	2.91 [1.15, 7.36]	
Viviwe2000	26	60	12	71	1.7%	3.76 [1.68, 8.40]	
Ferson1995	35	49	20	54	1.5%	4.25 [1.85, 9.75]	
Total (95% CI)		2666		3439	100.0%	2.09 [1.85, 2.36]	•
Total events	1482		1360				
Heterogeneity: Chi ² =	8.22, df = 1						
Test for overall effect:	Z=11.78	Favors control Favors experimental					

Figure 4. Comparison of the FUR between the telephone and the control groups. doi:10.1371/journal.pone.0104266.g004

ranged from 1.69 to 4.25, and the pooled OR was 2.09 (95% CI [1.85, 2.36]; P<0.01).

To further assess the pooled results of the relationship between reminder effects and the FUR, Funnel plots (Figure 5) were applied for publication bias testing. We found that both SMS and telephone reminders were significantly related to improvement of the FUR, with no evidence of publications bias (Begg's test, P=0.161 (continuity corrected), Figure 5A; Begg's test, P=0.266(continuity corrected), Figure 5B) and with high heterogeneity between studies ($I^2=69\%$, P=0.001, Figure 3; $I^2=15\%$, P=0.31, Figure 4). After omitting each study one by one and recalculating the combined estimates for the remaining studies, the main results were not notably altered (all P>0.05).

Discussion

In the present study, we have provided a comprehensive review of the literature and quantitative estimates of associations between SMS/telephone reminders and the FUR from RCTs around the world. Our results indicated that SMS and telephone reminders both could significantly improve the FUR, and telephone reminders had a greater probability but also a higher risk of bias than did SMS reminders. At the time of our literature search, only 18 RCTs were identified in our systematic review. A total of 3276 patients with and 3402 patients without SMS reminders and 2666 patients with and 3439 patients without telephone reminders were described in these studies. There is RCT evidence of reasonable quality showing that SMS and telephone interventions aimed at improving FUR can be effective.

AFU is considered to play an essential role in chronic disease management characterized by long-term observation and is important to choose the optimal timing of surgery, deliver cascade of care, detect complications associated with the surgery, collect outcome data, and diagnose recurrent disease. [33] For example, a postoperative follow-up program is recommended for nearly all cancers in the National Comprehensive Cancer Network. [1] Patients with glaucoma also require life-long treatment and followup care to preserve vision. [5] Prolonged surveillance and medication can prevent deterioration from hepatitis B to cirrhosis or hepatocellular carcinoma. Loss to follow-up is the major reason for hepatitis recurrence. [6] The importance of follow-up is also emphasized for the management of coronary artery diseases, [8] cerebral infarction, [34] diabetes, [35] asthma, [36] chronic kidney disease, [7] obesity, [37] chronic sinusitis, [38] cataract, [39] and amblyopia, [40] among others. Practically, even a carefully designed treatment plan does not yield the expected results with a lack of adherence (patients' behaviors in terms of taking medication, following diets, or executing lifestyle changes coinciding with healthcare providers' health and medical advice). [41] In addition to the treatment effect, lack of AFU seriously affects clinical research implementation by undermining the internal and external validities of the findings [42], attrition bias [43], increasing the trial's cost and duration and delaying the acquisition of important results [9].

An important aspect of health interventions in areas with limited resources is that they must be inexpensive and ideally take advantage of existing resources. [44] In the era of mobile information technology, mobile telephone communication has been suggested as a method to improve the delivery of health services around the world, and randomized trials of mobile health technology interventions have created a substantial evidence base for the management and prevention of a broad range of disorders. [12] In the present systematic review, we found that the pooled OR for the improvement of the FUR in the SMS group compared with the control group was 1.76 (95% CI [1.37, 2.26]; P<0.01) and the pooled OR for the improvement of the FUR in the telephone group compared with the control group was 2.09 (95% CI [1.85, 2.36]; P<0.01). Although telephone reminders had a greater probability than SMS reminders in improving the FUR, cell phone SMS interventions are believed to be more practical and well suited to different settings. After telephone numbers are collected, automated SMS reminders are presumably more efficient and less expensive than live telephone calls. [45] Furthermore, electronic mail reminders are mainly a focused mobile mode in addition to SMS and telephone reminders. Certain studies have demonstrated significant reductions in clinical non-attendance. [46] Considering the variability of usage, qualitative analysis was not performed in the present study [47].

Several limitations of this meta-analysis should be considered. First, a risk of bias existed in and varied between different studies. Considering adequate sequence generation, allocation concealment, blinding, the evaluation of incomplete outcome data, and lack of selective reporting, the majority of the studies on SMS reminders were at low risk of bias (evaluations >50%). However, for the studies



Figure 5. Funnel plots for publication bias testing. Panel A, SMS reminder effect; Panel B, telephone reminder effect. Each point represents a separate study on the indicated association. The vertical line represents the mean effect size. Generally, the points are distributed symmetrically as an inverted funnel, indicating minor publication bias. doi:10.1371/journal.pone.0104266.g005

on telephone reminders that were at low risk of bias, only the evaluation of incomplete outcome data accounted for more than 50%. The quality of allocation concealment and blinding was poorest for telephone reminders as more than 80% of the studies were at moderate or high risk of bias. Second, AFU in the included studies varied in its definition and calculation methods, although the measurements of AFU were interchangeable. Third, the specific nature of the interventions and their settings were not considered and discussed, including the ages and habits of the patients with mobile telephone usage, which might influence the effect of SMS

and/or telephone reminders, [11,48]. Fourth, studies that have used other terms, have included FUR as secondary endpoints, or utilized a different definition of FUR or different calculation methods may have been missed. One RCT that tested the efficacy of SMS reminders on adherence to antiretroviral therapy among patients attending a rural clinic in Kenya was not included, [49] because the primary outcome of this study was whether adherence exceeded 90% during each 12-week period of analysis and the 48-week study period but was not the actual proportion of patients attending their appointment (as defined in our current study). Therefore, selection bias may exist and the results of this study may not be actually applicable to all settings worldwide. Despite the above limitations, our meta-analysis found convincing evidence that SMS and telephone reminders both could significantly improve the FUR. Telephone reminders had a greater probability but a higher risk of bias than SMS reminders. Research on intervention strategies for improving patient adherence to follow-up is still limited, and more studies are required.

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Supporting Information

Checklist S1 PRISMA checklist. (DOC)

Author Contributions

Conceived and designed the experiments: HL. Performed the experiments: HL XW. Analyzed the data: HL XW. Contributed reagents/materials/ analysis tools: XW. Contributed to the writing of the manuscript: HL XW.

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