

Protocol for Using Mobile Phone Text Messaging to Improve Adherence to Highly Active Antiretroviral Therapy

Hui-Chen Chu^[a]; Nai-Ying Ko^{[a],*}

^[a] Department of Nursing, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

*Corresponding author.

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Abstract

Interventions for improving medication adherence that can become part of patients' daily life are critical as the therapy is lifelong. Medication adherence is the cornerstone of highly active antiretroviral therapy (HAART). With the blooming of cell phone ownership worldwide, research using mobile phone strategies to improve HAART adherence has increased. In addition, there are over 28 million mobile phone subscribers in Taiwan (Institution of Information Industry, 2011). We carried out a literature review selection using the population, intervention, comparison and outcome(s) (PICO) format. We used evidence gathered by evidenced-based methods to construct a clinical guideline. Evidence from two randomized control trials and two systematic reviews that used the mobile phone as the intervention was included in the protocol. A protocol for using mobile phone texting as an intervention to improve adherence was thereby established.

Key words: Mobile phone; Adherence; Intervention; HAART

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INTRODUCTION

According to the Joint United Nations Programme HIV/AIDS (2010) (Joint United Nations Programme on HIV/

AIDS (UNAIDS), a total of 2.5 million AIDS-related deaths have been averted since antiretroviral therapy was introduced in 1995. In addition, research had demonstrated its ability to decrease mortality rate as well as improve quality of life (Wohl *et al.*, 2006). For instance, using highly active antiretroviral therapy (HAART) decreased the national mortality rate from 64% to 4% in Taiwan (Center for Disease Control, Department of Health, Taiwan (2010). The effectiveness of HAART relies on medication adherence (Hyle *et al.*, 2012). Antiretroviral therapy decreases the plasma viral load. By decreasing the viral load, the incidence of opportunistic infection and disease progression is limited. At the same time, an increased CD4 cell count is strongly associated with decreasing opportunistic infections. As a result, the quality of life is indirectly improved (Wohl *et al.*, 2006; Hyle *et al.*, 2012; Reda & Biadgilign, 2012). However, a 95% or greater adherence rate is required to achieve the optimal effect, while the actual adherence rate ranges from 55% to 75% (Mills *et al.*, 2011). In Taiwan, mobile phone subscriptions reached 28.29 million in mid-2011, which is 122 mobile phones per 100 residents (Institution of Information Industry, 2011). The census of citizens living with HIV was 17,823 in June 2011 (Centers for Disease Control, Taiwan, ROC, 2011). It is reasonable to assume that the mobile phone ownership of HIV-infected people is close to the national average. Therefore, this study aimed to formulate an evidence-based protocol for using mobile phone text messaging to improving the adherence rate.

LITERATURE REVIEWS OF EVIDENCE

Forming a foreground question is the first step of the evidence-based research method (Nollan *et al.*, 2005). It usually contains four components, termed PICO (Nollan *et al.*, 2005). The 'P' stands for patient population of interest; in this study the targeted population was HIV-infected people with HAART. 'I' stands for intervention of interest

which in this study was mobile texting. ‘C’ is comparison of interest, which was omitted. ‘O’ is the outcome of interest, in our case improved adherence. Therefore, the evidence that fulfilled all the components of this PICO format was extracted to construct the final protocol. Second, we used keyword searching of the Cochrane Library, PubMed, Web of Science, and CINAHL Plus full-text online databases to find evidence that fulfilled the PICO format. The search keywords were, “adherence” or “improve adherence”, “intervention” or “strategy”, and “mobile phone”. The inclusion criterion was adults >20 years old; mobile phone text messaging was the independent variable; and comparison intervention was standard care or none.

From the evidence, adults who were initiating ART were selected as the population of interest in this protocol. Since patients with experience of HAART or prior treatment failure might be complicated cases that require more clinical treatment or medications, we focused on patients who were on their initial HAART regimen as they were likely to have fewer confounding factors with regard to the optimal outcomes of the treatment (see Table 1 for review chart).

Table 1
Protocol of using mobile phone text message

PICO	Operational definition
Patient	Adult patient who had initiated ART within 3 months Mobile Phone Text Message
Intervention	Short message or a slogan Weekly message Patient have to respond within 48 hours
Comparison	Not specified
Outcome	Self-report adherence >90% for up to 12 month Viral Suppression <50 copies/ml at 12 th month of HAART Evaluation should be performed at time of initiating treatment, first month after treatment then every 3 to 6 months if stable.

A weekly short message or slogan is an effective intervention to improve adherence on HAART (Horvath *et al.*, 2012; Pop-Eleches *et al.*, 2011). The common rule about the content of the mobile texting message is protecting the patient’s confidentiality. The message should provide no clue about the patient’s HIV status or current treatment. From the evidence, long and short message do not differ in terms of the outcomes (Pop-Eleches *et al.*, 2011). Therefore, a short message or slogan was sufficient for the protocol. On the frequency of messaging delivery, a weekly message achieves statistically significant results but a daily message does not. In sum, a short weekly message was selected for the intervention (Horvath *et al.*, 2012; Pop-Eleches *et al.*, 2011; Barnighausen *et al.*, 2011; Lester *et al.*, 2010) (see Table 2).

Table 2
Evidences on Participants

Author/Year of publication	Population selected	Level of Evidence
Horvath, Azman, Kennedy & Rutherford, 2012	PLWH, on HAART	Meta-Analysis/ I
Barnighausen <i>et al.</i> , 2011	Patients initiating ART; IDU and MSM are at risk-population	Systematic Reviews/ I
Lester <i>et al.</i> , 2010	Adult Patients initiating ART	RCT/II
Pop Eleches <i>et al.</i> , 2010	Adult patient who had initiated ART within 3 months	RCT/II

Finally, for the outcome indicator, plasma HIV-1 RNA viral load (pVL) is reliable. This is a biomarker that is commonly used in assessing the effect of HAART. Generally, plasma viral load decreases by log² after 2 weeks of treatment; after 24 weeks, it is undetectable [14] (<50 copies/ml). On the other hand, if a patient has been fully compliant but the progress of viral depression did not meet the expectation, resistance should be considered. Currently, pill counts, medication event monitoring systems (MEMS), pharmacy refill records and self-reporting methods are commonly used to measure medication adherence [7] [16]. In the pill-count method, patients may avoid actual counting, so the pharmacy refill record is more suitable as an indirect measurement. MEMS is based on a cap with an electronic chip which records each opening of the medication bottle. However, it is a costly device, and is programmed for one pill daily with no information on the numbers of pills taken per opening [15]. Therefore, self-reported adherence has become the most common method of choice [7]. Moreover, self-reported results are strongly correlated with plasma viral load [16] [17]. Self-reporting is a cost-effective method in a resource-limited setting. It is a convenient tool in most of health care settings as well. Compared with MEMS, it can be used for prescriptions with a mixed medication regimen, as HAART usually combines at least 3 kinds of medicine. However, social desirability or memory limitation might cause a 5-20% over-estimation of adherence [18]. Nonetheless, self-reporting is highly sensitive for detecting non-adherence, which is relatively valuable in clinical practice. In sum, the evidence suggested that pVL is a reliable biomarker as an outcome measurement for self-reported adherence.

PROTOCOL FORMAT BASED ON LITERATURE REVIEW

From the evidence-based research results (Horvath *et al.*, 2012; Pop-Eleches *et al.*, 2011; Barnighausen *et al.*, 2011; Lester *et al.*, 2010), mobile texting as an intervention proved efficient in patients initiating HAART. Furthermore, the content of the text message could be

a short sentence or a slogan that would not reveal the patient's current HIV/AIDS status. A weekly message is sufficient to reach the maximum effect. The optimal outcome of a self-reported adherence rate of 95% or greater should be expected for up to a year. In addition, viral load suppression should be monitored at baseline, at 4, 12 and 24 weeks of treatment, and every 3 months

thereafter. A protocol of using mobile text messaging as an intervention to improve adherence to HAART has been established using evidence-based method. A flow-chart for clinical practice is shown in Figure 1. The protocol is not only effective but also easy to merge with current clinical practice.

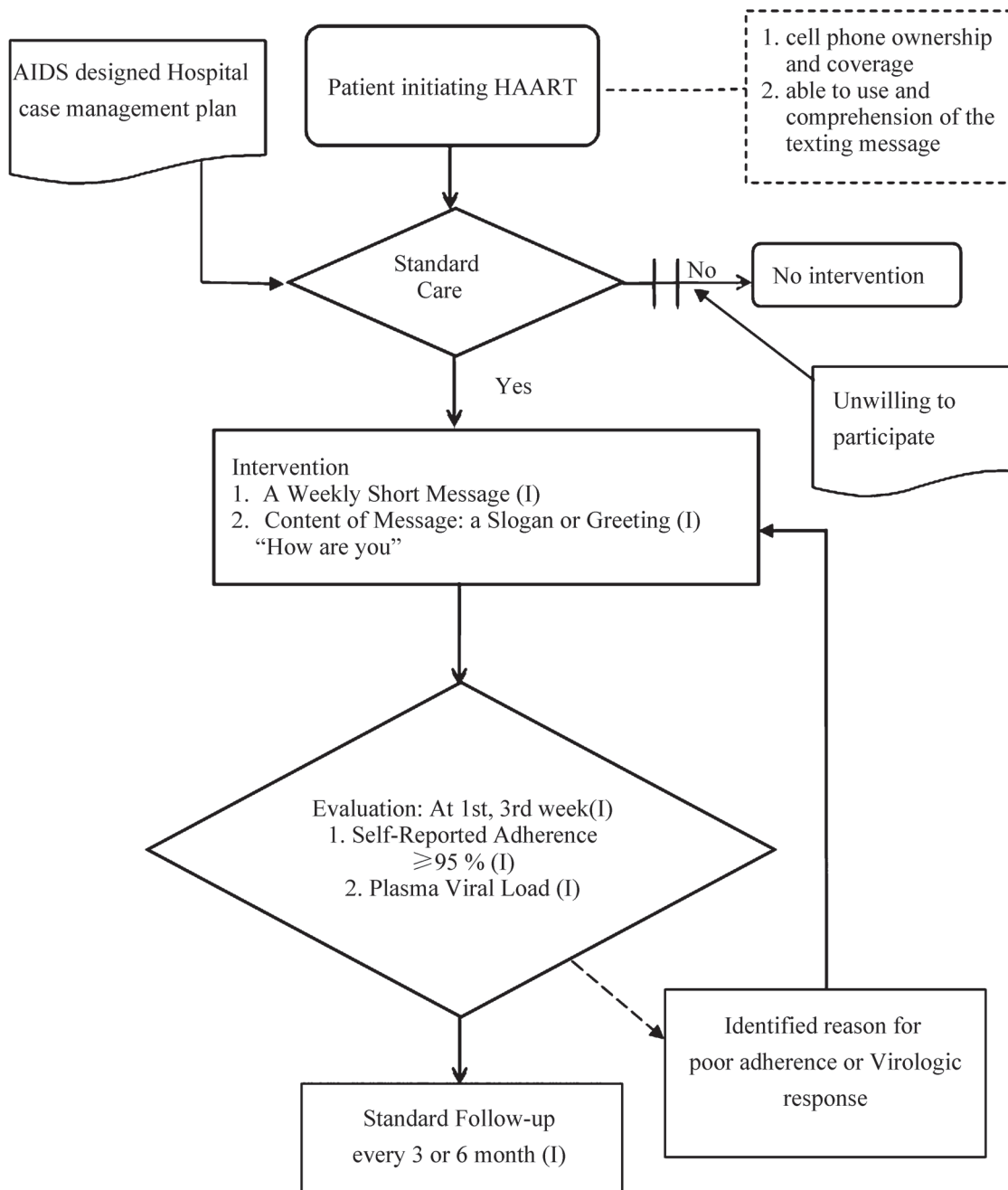


Figure 1
Protocol of Using Mobile Phone Text Message on Improving Adherence to HAART

CONCLUSION

The protocol combines the popularity of mobile phone ownership with the necessity of adherence to HAART. It merges healthcare into the patient's daily life. Therefore, the content of the message is relatively important. It should not reveal the recipient's HIV-infected status. Greetings or slogans have been tested sufficiently in reviewed studies. Moreover, to embed the protocol into the clinical setting, the content of the text message should be agreed between patients and healthcare providers. A weekly short message is more effective than a daily short message. However, two experimental studies that were included in the evidence were conducted for 48 to 52 weeks. As HAART is a lifelong treatment, the effectiveness for long-term use needs to be established. In sum, a weekly short mobile phone message is an effective intervention to increase patient adherence to HAART.

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APPENDIX

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5*)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**"	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or n-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/ follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/ follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or n-of-1 trial	Randomized trial of (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/ follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

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* OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson