

Effectiveness of mobile text reminder in improving quality of life, medication and physical exercise adherence in patients living with HIV/AIDS: a systematic review

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Abstract

Background: Mobile text reminders(SMS) is considered a viable strategy for targeting/facilitating healthy behavioural change such as improved adherence to prescribed physical exercises(PE) and medication(antiretroviral therapy-ART) and likewise the quality of life(QoL) in people living with HIV/AIDS(PLWHA). Thus, the literature was appraised for evidence of its effectiveness.

Method: A systematic review of eight databases–AMED,CINAHL,Cochrane Library,EMBASE,EMCARE,Ovid MEDLINE,PsycINFO, and PubMed-was conducted using the Cochrane Collaboration Protocol. Only randomized control trials (RCTs) investigating the impact of SMS on either QoL or PE or ART adherence or a combination of these variables in PLWHA were included in the review. Inclusion was not restricted to a particular type, frequency, and duration of intervention or follow-up period after the intervention. Two independent reviewers determined the eligibility of the studies. Data were extracted and the risk of bias was assessed with the PEDro tool.

Result: A pooled estimate of effect could not be calculated due to the heterogeneity of methods and outcome measures. Therefore, a narrative synthesis of nine studies that met the inclusion criteria(n=1621 participants at study completion) comprising males/females aged \geq 18years, was done. There was a significant improvement in medication adherence except in three underpowered studies. However, the effect size of the intervention is not provided in all studies. The only study on the QoL was underpowered and reported no significant change while there were no RCTs on PE.

Conclusion: Personalised SMS reminder:3-5times/week x 6months, 30mins before medication time, OR SMS:weekly x 30days, OR SMS:either short or long x daily or weekly x 48weeks, OR customized dynamic SMS:via a personalized cellular phone reminder system(ARemind) with several daily reminder events matching patients ART dosing x 6weeks OR 4educative SMS/week x 4weeks OR real-time SMS reminder triggered by a-30mins delay in medication, with/without usual care, show promising evidence of significant improvement in adherence to ART in PLWHA. However, it is uncertain if the findings are of clinical significance because the effect size is unknown. Moreover, the observed heterogeneity in the methods/outcome measures warrants a cautious interpretation of findings. There is a lack/paucity of RCTs and therefore no evidence of SMS effectiveness on adherence to PE/improvement of QoL.

Background

In the management of chronic diseases, behavioural adaptation to ensure adherence to prescribed intervention is often the key link to success or failure of treatment. In Human immune deficiency virus/Acquired immune deficiency syndrome (HIV/AIDS), the two mainly prescribed treatment is highly active antiretroviral therapy (HAART) and lifestyle modifications, particularly physical activity [1-3]. HAART slows down disease progression, prevent transmission and boosts immunity [4] while physical activity has been found to improve bone health and immune function [5], mood [6], body composition [7] function [8] and self-rated quality of life [9]. Therefore, adherence to these interventions is an important index for good treatment outcomes and possibly the survival of the patients. However, as with other chronic conditions, adherence to remedial interventions has been the major problem of patients and holds the key to effective clinical management of HIV-infected individuals. The intervention strategies that will ensure such adherence to both treatment prescriptions will require adopting effective behavioural strategies of which the use of mobile text reminder has been recommended. Several authors [4,10] expressed the view that high growth in mobile technology has provided another tool for chronic disease management [10], including enhancing adherence to treatment regimens especially in resource-limited settings [4], and therefore, the literature was appraised to guide practice.

The use of mobile text reminders was considered important because targeting an individual with repetitive information overtime has been found to influence the action of the memory neural circuits which may be required for a change towards the desired adherence habit [11-13]. The major theory associated with the utilization of mobile text reminders to improve adherence to treatment is the health belief model [14]. The key elements of this model include Perceived susceptibility, Perceived severity, Perceived Benefits, Perceived barriers, Cues to action, and Self-efficacy. These elements help identify key decision-making points that influence health-seeking behaviour [14], and some of which are targeted while using mobile text reminders to enhance adherence to treatment. The expectation that a person will take a health-related action to address the individual's perceptions of the threat posed by HIV-related disability, or to realise the benefits of taking preventive action by participating in physical activity or compliance to medication, is calibrated with cultural, socioeconomic, and environmental factors which form and modify the decision to act

There is a lack of synthesized evidence from the literature on the effectiveness of mobile text reminders as an effective adherence strategy for compliance with medication and physical exercise prescription in HIV conditions. Therefore, it is not known whether this strategy is effective as a behavioural change intervention that could be explored to the advantage of PLWHA, hence this study. The current review sought to address the following main review question: Is mobile text reminder effective in improving quality of life (QoL), adherence to HAART medication and physical exercise prescription in People living with HIV/AIDS (PLWHA) based on reports from studies published in the databases from 1990 to August 2019? To answer the review question, specific review objectives included determining the effects of SMS, - compared to usual care, on adherence to HAART medication and physical exercise, and quality of life in PLWHA.

Methods

This systematic review was certified according to the international Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY register) (registration number: INPLASY202040048). INPLASY202060016

Eligibility Criteria

Eligibility criteria considered for selecting studies in the review include:

Inclusion criteria:

1. Type of study:

Original research manuscripts in peer-review journals and conferences proceeding were included if published in the English Language. Original research manuscripts in peer-reviewed journals and conferences proceeding were included if published in the English language. This review included Randomized control trials (RCTs). Studies for the review of the following objectives were evaluated: the effect of mobile text in (i). improving quality of life, (ii) adherence of HAART medication, and (iii) physical exercise prescription in PLWHA.

2. Participants:

The review included studies involving adult human participants aged ≥ 18 years. Studies that investigated PLWHA on HAART were included. No specific limitation was considered concerning the setting of the studies to be incorporated. Thus, studies carried out in clinics, health centres, hospitals, or community settings were also included.

3. Intervention:

RCTs that accessed or evaluated the impact of mobile text reminders in HIV patients were included. Inclusion was not restricted to a type, frequency, and duration of intervention or follow-up period after the intervention.

4. Comparator:

Studies comparing mobile text reminders with other treatment options including usual care or no treatment were included in this systematic review.

5. Duration of intervention:

There was no confinement on the length of the administration of the intervention and the follow-up should be ≤ 6 months post-intervention.

6. Outcome measures:

The primary outcomes of interest included: adherence to drug prescription and physical activity. Studies that also investigated intervention effectiveness or quality of life were included in this review. Studies were included irrespective of the type of outcome measure utilized, provided any of the outcomes of interest were accessed.

Exclusion criteria:

- Studies not published in the English language
- Studies that included in addition to mobile text reminders, other behavioural change components.
- Non-randomized controlled trials, pre-test post-test designs, crossover designs and other quasi-experimental studies will be excluded
- In the case of similar publications from the same study, the most recent or most comprehensive publication was used.

Information sources and search strategy

An extensive search strategy, which was formulated to identify applicable studies to be used for the review was piloted (Appendix I) and implemented. The search strategy formulated to search the bibliographic database and grey literature was conducted utilizing keywords, terms from medical subject heading (MeSH), with a combination of Boolean logic in the title, abstract and text for the population, intervention, study design, and outcomes. This strategy was used differently for the three selected outcomes. PubMed search strategy is shown in Appendix I. This strategy was modified to the syntax and subject heading of other databases. This includes the search of the eight bibliographic databases Allied and Complementary Medicine Database (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, EMBASE, EMCARE, Ovid MEDLINE, PsycINFO, and PubMed), trial registers and directory of open-access repository websites by the reviewers – N.S.C and E.F.E) - using controlled vocabularies and keywords: HIV/AIDS, Seropositive, aerobic exercises, resistance exercises, strengthen exercises, physical exercises, exercise program, exercise intervention, mobile text reminders, SMS, and QoL. Additionally, searches were performed from the reference lists of identified studies. and grey literature; and the selection of studies for inclusion was based on eligibility criteria. This procedure was created following the rules of the Cochrane Handbook for Systematic Reviews [15] and advice for Health Care Review by the Centre for Reviews and Dissemination [16].

Study record, selection process, and data management

Literature search results were exported into RefWorks™ to check for duplication of studies. Considering the inclusion criteria, eligibility questions, and structures for the studies, considerations to the two levels of eligibility assessment were produced, piloted, and if required, refined. Bibliographic records were exported from RefWorks™ into Microsoft Excel (Microsoft 2013), to facilitate the management selection of articles for inclusion. The screening was performed in two phases: the first phase involved the screening of titles and abstracts utilizing the inclusion and exclusion criteria to identify potentially important

articles and was carried out by E.F.E (reviewer 1). The results of the first screening were independently cross-checked by I.F.O (reviewer 2) based on the review eligibility criteria. The second phase of screening involved a screening of the articles selected from phase one screening by reviewer 1. This was cross-checked by reviewer 2. Differences of opinions occurring at any stage regarding inclusion or exclusion were resolved by discussion and reflection, in consultation with S.C.I. The reasons for excluding studies were properly documented in the QUOROM flow chart (Figure 1).

Quality appraisal for included studies

The methodological rigour of the selected studies was assessed using the Physiotherapy Evidence Database (PEDro) quality appraisal tool. The PEDro is an 11-item scale in which the first item relates to external validity and the other ten items assess the internal validity of a clinical trial. One point is given for each satisfying criterion (except for the first item) yielding a maximum score of 10. The higher the score, the better the quality of the study and the following point scale is used: 6-10 (High); 4-5 (fair or moderate); ≤ 3 (poor). A point for a particular criterion was awarded only if the article explicitly reported that the criterion was met. A score of one was given for each yes answer and zero for no, unclear, and not applicable (N/A) answers. The overall score was reported as a tally of all "yes" answers out of 10 based on the applicable answers for each study. Scores of individual items from the critical appraisal tool were added to present the total score. The reviewers thoroughly appraised the selected studies independent of each other. Areas of differences were resolved by discussion and reflection, or in consultation with the third reviewer. Appraisal of the qualities of the included studies was carried out upon completion of study selection and full-text screening during data extraction and synthesis. After this, the quality of the review was reported.

Data Item

Data were collected from variables including authors' references, participants' characteristics, inclusion and exclusion criteria, study sample size, components of the intervention, the intervention setting, who delivered the intervention, the duration of the intervention and follow-up (where available), attrition rate, aspects of outcome assessed, the outcome measurement, methods/techniques, results, conclusions and funding sources.

The variables for which data were collected include:

- i. Authors
- ii. Participants' characteristics (including age range, gender, sample size)
- iii. Study sample size (also groups sample size where available)
- iv. Intervention (setting, blinding, intervention delivery, type of intervention, duration of intervention and components of intervention)
- v. Attrition rate
- vi. Control
- vii. Outcome(s) assessed and outcome measures/techniques
- viii. Summary of Results.
- ix. Conclusions and funding sources

Quality appraisal and risk of bias

Adopting the Cochrane Collaboration Tool for Risk of Bias Assessment (Table 8.5a of the Cochrane Handbook for Systematic Reviews of Interventions), risk of bias for each of the included studies was evaluated by two reviewers in six key domains: (i) selection bias (random sequence generation, allocation concealment); (ii) performance bias (blinding of personnel and participants); (iii) detection bias (blinding of outcome assessments); (iv) bias due to attrition (incomplete outcome data, including dropouts and withdrawals); (v) reporting bias (selective reporting) and (vi) other bias (other sources of bias not elsewhere addressed).¹⁸ To facilitate the assessment of the possible risk of bias for each intervention study, reviewer 1 and reviewer 2 independently collected information using the PEDro tool for risk of bias assessment including sequence generation, allocation concealment, blinding, adequate follow-up, between-group comparison and selective outcome reporting [15]. The procedures undertaken to assess each domain for each study was explicitly described and rated as 'high risk' or 'low risk'. The risk of bias in a study was reported as unclear if there were insufficient details in the original study. In such instances, the study investigators were contacted to provide the required details. The judgments for the risk of bias was made independently by the first reviewer and the same with the second reviewer, based on the criteria for judging the risk of bias [15]. Both reviewers made judgments regarding the risk of bias independent of each other. Areas of differences were resolved by discussion and reflection, or in consultation with S.C.I.

Data synthesis and assessment of heterogeneity

The review question on the effectiveness of mobile text reminders in enhancing the quality of life, adherence to HAART medication and physical exercise prescription in PLWHA was answered. In doing this, all quantitative study outcomes which analyzed the effectiveness of this intervention were presented, examined, and combined in a proof table (Table 4). The proper statistical method was used for different variables: for a continuous variable, weighted mean differences were applied when outcomes are uniform or standard mean difference when different outcomes are used with CI of 95% while for a dichotomous variable, the Risk ratio was applied with CI of 95%. Meta-analysis was not done to find pooled effect sizes across studies, using a random-effect model due to the high level of heterogeneity of intervention effects. Heterogeneity was assessed through the Cochran's χ^2 test (10% significance level) and Higgins I² for which values of 25%, 50% and 75% show low, medium, and high heterogeneity respectively (as stipulated by the guidance in/the Cochrane Handbook for Systemic Reviews of Interventions).

Data and Sensitivity analysis

Heterogeneous studies were interpreted by narrative synthesis following the guideline of the Centre for Reviews and Dissemination to explore the relationship and findings between and included studies [16].

Rating quality of evidence and strength of recommendation.

The quality of evidence of the studies was not evaluated to determine the strength of recommendation in the systematic review, due to the high level of heterogeneity of intervention effects. The individual study was graded as high risk of bias or low risk of bias, and then again individual evidence statement for this review was graded from 'High Quality' to 'Very Low Quality' according to the criteria.

How this review is reported

This systematic review is reported using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines [17], with all items relevant to the review included.

Results

Search result

The initial search yielded 1026 potential papers. Following deduplication, 1020 potential papers were identified and screened for the title and abstract content. Thereafter, 996 papers were excluded and 24 papers were found eligible. Also, three eligible papers were identified from further hand searches, and thus, 33 papers were read and screened for eligibility, with 9 papers meeting the review's eligibility criteria and were included in the review (Figure I - PRISMA flow diagram). Reasons for exclusion of studies following full-text screening include population group which is PLWHA who are substance and alcohol dependent, depressed and psychologically unstable patient, pilot studies, research protocols, and papers that combined the required intervention with another intervention or mode of communication.

Characteristics of included studies

All the included studies were randomized controlled trials and contributed a total of 1621 participants (Table 1). The number of participants in the 6 included studies ranged from 100 [18] to 120 [19] PLWHA. Participants involved in the included studies were ≥ 18 years of age, with most of them on HAART medication for at least one month. The clinical characteristics between the intervention and control groups do not differ significantly at baseline.

Outcome measures

Different studies utilized different outcome measurement tools for evaluating the same outcome. For instance, medication adherence was assessed using: self-report [18, 20-23]; medication event monitoring system [23, 24]; Visual analogue scale [18, 20]; pill count [18, 22]; micro-electronic monitoring [22]; pharmacy refill data [20]; community programs for clinical research on AIDS adherence self-report questionnaire [18]; quality of life [20]; interviewer-administered self-report questionnaire [25]; simplified medication adherence self-report questionnaire [26]; and wise-pill monitor [19].

Quality appraisal and risk of bias assessment

The PEDro tool for the risk of bias assessment was adopted for this review (Table 2). Four studies [18, 24-26] were judged as moderate quality studies while the other five studies [19-23] were judged as high-quality studies.

Eligibility Criteria

Authors of the 9 studies [18-26] reported on the inclusion and exclusion criteria used in recruiting and screening participants for their respective studies. Hence, a low risk of bias was evident for all included studies.

Random allocation

All included studies [18-26] reported using the randomization process to allocate the eligible participants into the different groups (Experimental and control groups). Thus, low risk for selection bias was also evident for the included studies.

Concealment of Allocations

Only three studies [20-22] reported concealment from the participants in the different groups they were randomly allocated to, and thus, may affect the overall selection bias.

Baseline similarity

All participants in the included studies have similar baseline characteristics of the measured outcome variables, and therefore, the groups were relatively equivalent at baseline.

Bias on blinding

Two studies [20, 22] reported on the blinding of therapists during the intervention period, but none reported on blinding the subjects while three studies reported on blinding the assessors [20-22] and thus have a low risk of bias.

Between-group comparison

All included studies [18-26] reported on performing the between-group comparison.

Adequate follow-up

Out of the nine included studies, six studies [20, 21, 23-26] reported having an adequate follow-up.

Intention to treat analysis

Out of the nine included studies, only four studies [19, 22, 25, 26] reported on not using intention to treat analysis.

Point estimate and variability

Three out of the included studies [24-26] reported the desired outcomes without using point estimate and variability.

Outcomes reported in included studies

For adherence (Table 3), all included studies [18-26] reported on medication adherence while none reported on physical activity adherence, while one study reported on the quality of life [20].

Effects of intervention

Except where otherwise stated, the effects of the intervention are reported as a comparison of the intervention group versus the control group (Table 3).

I. Medication adherence

Nine studies [18-26] provided data on medication adherence. One high quality trial [20] reported no statistically significant change using different outcome measures which include: visual analogue scale: $p = 0.542$; self-report: $p = 0.999$; and pharmacy refill data: $p = 0.617$. However, on sensitivity analysis, more participants in the SMS group achieved adherence of $>90\%$ at six months. Another moderate quality study [24] reported a significant change in one intervention group (weekly SMS: $p = 0.03$) out of the four intervention groups, using the medication event monitoring system as the outcome measure. The remaining three intervention groups (Daily SMS: $p = 0.92$, Short SMS: $p = 0.27$, Long SMS: $p = 0.24$) reported no significant change, while another high-quality trial [22] reported no significant change using different outcome measures as follows; self-report: $p = 0.2435$, pill counting: $p = 0.6038$ and micro-electronic monitoring: $p = 0.1946$. Another high-quality trial [23] reported a significant change or improved adherence using some outcome measures which include: medication event monitoring system: $p = 0.002$, and composite adherence score: $p = 0.0094$. It also reported no significant change using the following outcome measure: - self-report: $p = 0.0689$, and pill count $p = 0.1529$. Similarly, two studies (16, 19) reported that mobile text reminder has a significant effect on adherence to medication, provided the participants are adequately followed up. One of them is a moderate-quality trial [18] which used the community programs for clinical research on AIDS adherence self-report questionnaire: $p = 0.027$; and visual analogue scale: $p = 0.006$, as outcome measures. The other study is a high-quality trial [21] which used self-report ($p = 0.006$), as the outcome measure. Another moderate-quality trial [25] reported a significant change in medication adherence using an interviewer-administered self-report questionnaire ($p = 0.05$) as the outcome measure. Another moderate-quality trial [26] reported no significant change in medication adherence using simplified medication adherence self-report questionnaire: $p = 0.198$, as the outcome measure. Another high-quality trial [19] reported a significant change in medication adherence using a wise-pill monitor: (group 1, $p = 0.039$; group 2, $p = 0.028$) as the outcome measure. Some studies reported participants' preference for privacy and requested certain codes to be used for some words.

II. Quality of life

One study [20] reported no significant difference in the quality of life between the intervention group and the control group using SF-12 scale score Quality of life assessment form ($p = 0.629$) as the outcome measure.

Discussion

Nine trials determining the effectiveness of mobile text reminders in improving quality of life, adherence to medication, and physical exercise prescription in PLWHA on the HAART regimen were reviewed. Studies included in the review were mostly of high or moderate methodological quality with a low or moderate risk of bias.

Adherence to medication

The results from six [18, 19, 21, 23- 25] out of the nine studies included in this review show that there exists a potential for a mobile text reminder to improve medication adherence. Mobile text reminders have a significant effect on medication adherence irrespective of the outcome measurement tool used to measure medication adherence. One moderate quality study considered the frequency of the intervention that would bring about an increase in adherence [24]. The study reported a significant effect of only weekly but not daily SMS intervention on medication adherence using a medication event monitoring system as the outcome measure. Habituation or the diminishing of a response to a frequently repeated stimulus may explain these findings and daily messages might also have been considered intrusive by the participants. Also, poor retention habit is likely in this population due to life-long management of the disease and reasons for such is diverse and depends on the individual (e.g depression, stigma), interpersonal (e.g patient-provider relationship) and structural (insurance eligibility) factors. Therefore, the health belief model predicts that barriers to mobile text reminders in this context may lie with the environmental and personal

characteristics of an individual. This may improve with counselling and education on the benefits of physical exercise and provides sufficient cues for a positive response when mobile text reminders are deployed in patient management.

Three studies (two high and one moderate quality studies) reported no significant effect of the mobile text reminder on medication adherence [20, 22, 26], which may be related to the fact that the sample size used was powered to detect a 20% difference in adherence between both groups but the difference found was much less. Moreover, the Kenya trials [21, 24] ran up to one year while the Cameroon trials [20] ended at six months. Thus, the duration of the trials might be insufficient to observe a significant effect, and likewise the length of time the participants have been on HAART. However, none of the studies reported on the effect size of medication adherence in the intervention group versus the control group. Although the review reports the effectiveness of mobile text reminder in improving adherence to medication, this should be interpreted with caution due to the following reasons:

- i. Participant's failure to report the measure of adherence for both intervention and control group,
- ii. The use of a mostly subjective measure of adherence may affect the estimate of effect because under or over-estimation can occur during the process of the interview (self-reporting) due to factors such as difficulty in remembering all the details of the drugs. This is important because participants' self-report is the principal measure used in the studies included in this review, and various types of questionnaires were used which may elicit varied responses. Importantly, the validity of participants' responses is questionable because they have not been compared with objective adherence measure, and patients may attempt to please their caregiver or avoid confrontation, and
- iii. The use of different intervention frequencies (daily, once per week, twice per week, thrice per week) in the various studies made it difficult to compare the results across the various studies in the review. This difficulty became more obvious when it is considered that some studies reported nothing about the frequency of the prescribed intervention used.
- iv. The use of different outcome measures to estimate the effect of the same intervention across the included studies in this review makes it difficult to compare effects across the groups. In recognition of this challenge, one study [21] which showed positive effects of the mobile text reminder on adherence to medication in PLWHA expressed some reservations by stating that its applicability to other countries needs to be evaluated since various outcome measures were used to assess medication adherence in contemporary literature. Therefore, there is a need for researchers to come up with a standardized outcome measure to reduce bias in the result.

Despite the above reasons, mobile text reminder has shown potential benefits in helping patients to remain adherent to treatment.

Physical activity adherence

No study reported the effectiveness of mobile text reminders on physical exercise adherence in an HIV population. Therefore, it is uncertain what the estimate of the effectiveness of mobile text reminders in improving adherence to a physical exercise regimen in PLWHA, will be. The lack of reliable evidence to guide practice in this regard is an important gap in the literature because physical exercise has been found to ameliorate co-morbidities associated with HIV/AIDS as it tends to improve cardiovascular fitness, increase bone mineral density, improve muscle strength and lean body mass, improve instability of fat metabolism, reduce risk of fracture and invariably enhance the quality of life in people living with HIV/AIDS [27, 28]. Also, a previous study [29] examined the automated mHealth intervention for physical activity promotion and reported significant differential in activity levels such that participants receiving mobile texts increased their daily steps over those not receiving texts by 2,534 (95% CI: 1,318–3,750; $P < 0.001$) and over blinded controls by 3,376 (95% CI: 1,951–4,801; $P < 0.001$). The secondary outcome shows that the unblinded-texts group increased its total activity time by 21 min/day (23% increase) and aerobic time by 13 min/day (160% increase), which was statistically significant compared to the other groups. This should have implications for the overall wellbeing of participants because the World Health Organisation (WHO) reports [30] that about 60% of people's quality of life and health depends on their lifestyle and personal behaviour. Therefore, if mobile texts could improve physical activity level in individuals, it would likewise improve their quality of life, and may also be applicable in PLWHA. An earlier narrative review of the literature [31] found that mobile text reminders resulted in improved treatment outcomes in 77% (46/60) of the studies, which may indicate its relevance in health care settings. Another review [32] of the literature found that among 16 RCTs, 10 reported significant improvement with the use of mobile phone text messaging in clinical and healthy behaviour interventions, and six RCTs reported differences suggesting positive trends. Another systematic review [33] on the use of Mobile Apps and SMS Messaging as Physical and Mental Health Interventions show improvement in physical health and significant reductions of anxiety, stress, and depression. Therefore, studies that investigate the effectiveness of mobile text reminders on adherence to physical activity among PLWHA may provide clinicians with relevant information that may impact the treatment outcome in this population.

Quality of life

Only one study [20] which is of a high quality reported the effect of mobile text reminders on quality of life and found no significant improvement in the QoL of the participants following the intervention with mobile text reminders. However, there is insufficient evidence to draw a valid scientific conclusion in this context. Invariably, more RCTs are required to explore the benefits of adhering to medications and physical exercises on QoL following the intervention with mobile text reminders in PLWHA. However, evidence from a recent systematic review [33] of empirical studies in different patient populations shows that patients perceive mobile health or mHealth (including mobile apps, SMS text messaging, app combined with SMS text messaging) to be effective as a treatment method, and show significant, positive improvements on health and well-being. It was reported that peri-menopausal women [34] and elderly cancer patients in upper-middle-income countries, can benefit from the effects of mHealth as a strategy for adopting improved health behaviour and quality of life, self-regulation, self-monitoring and overall health [35]. A systematic review [36] of the literature indicated that mhealth positively impacted on chronic disease outcomes, improving attendance rates, clinical outcomes, and health-related quality of life (HRQoL), and was cost-effective. Therefore, there could be translational benefits in adopting the same strategy in PLWHA which cannot be determined in our study considering the paucity of literature available in this area and highlights the need for future high-quality RCTs. High-quality RCTs in this area is important because the quality of life in PLWHA is an important factor that provides a basis for evaluating the impact of different interventions designed to improve wellbeing [37, 38]. However, it has socio-cultural

dimensions and means different things to different people depending on their specific requirements, culture, goals, and expectations [39, 40]. QoL comprises multiple factors that in combination, add up to an individual sense of living well. For PLWHA, quality of life is often seen as a good health condition (physical and mental well-being), being functionally independent, engaging in social relationships, and economic opportunities. Moreover, quality of life assessment helps in making decisions about areas of need and the planning of interventions in the management of PLWHA [37]. These diverse definitions and perceptions of the quality of life across cultural communities would imply that the metrics for gauging this variable may likely vary across socio-cultural boundaries and cannot be determined by a few studies otherwise it should be addressed in the local context of the study site. Overall, if mobile text reminders can improve adherence to medication as already seen in this study, then it should likewise have a positive effect on the QoL.

Conclusions

Implication for practice

Our study show promising evidence of significant improvement in adherence to ART in PLWHA using the following prescriptions of mobile text reminder: Mobile text – personalized SMS reminder: 3-5 times/week x 6 months, when delivered 30 mins before medication time + usual care (regular health education in the clinic including informational pamphlets, psychological support and personalized health education from nurses and physician), OR SMS; delivered weekly x 30 days, OR SMS; either short or long delivered at daily or weekly frequency x 48 weeks, OR customized dynamic SMS delivered via a personalized cellular phone reminder system (ARemind) with several daily reminder events matching patients ART dosing x 6 weeks OR 4 educative SMS/week x 4 weeks OR real-time SMS reminder triggered by a-30 mins delay in medication + adherence counselling.

The overall findings of this review are very important because the common lifestyle changes required in HIV conditions include adopting habits that improve the physical activity level, especially a lifestyle of physical exercise. Such healthy habits, (such as adherence to medications, and physical activity lifestyle), have a direct impact on an individual's health in chronic conditions [41]. Thus, it is recommended that once a patient has been diagnosed as having a chronic health condition like HIV, the above major lifestyle changes need to be implemented [42, 43] and requires a mobile text reminder system to ensure adherence to the prescribed regime. This is important because just as with other chronic conditions, adherence to prescribed interventions has been the major problem of patients and holds important significance for effective clinical management of HIV-infected individuals. Consequently, the use of mobile text reminders as a behaviour change intervention strategy should be considered in the broader framework of the health belief model. Thus, mobile text reminders may be considered as cues which influence the key decision-making points of action to achieve perceived health benefits of taking preventive actions by participating in physical activity, or compliance to medication to address the individual's perceptions of the threat posed by HIV-related disability, and may be useful in the implementation of clinical management plans for the patients. The findings of our study agree with previous views which hint of the reminder systems as a potential delivery mode in the clinical setting for behaviour change techniques (adherence to medication/physical exercises) [44] likely to improve clinical outcomes including QoL of in PLWHA, apart from educational meetings, educational detailing, and audit and feedback [45, 46]. Overall, researchers included in this review reported numerous benefits from using SMS reminders, including ease of use, low cost of services, and rapid automated message delivery with minimal risks to health. Moreover, most participants found the reminders to be acceptable, and only a few adverse events have been reported with a mobile text reminder. However, it requires further investigation to generate a reliable estimate of effects that will guide practice.

Implication for research

The implications of the findings of this study for research suggest priorities for future research that will address the remaining uncertainties already highlighted in this study around this topic. Thus, while the results of this systematic review are promising, however, the observation of heterogeneity in the methods and outcome measures employed to evaluate the same treatment outcomes made it difficult to compare the effects of the intervention across multiple studies. Besides, the heterogeneity in the methods and outcome measures warrants a cautious interpretation of the findings. Also, it is not certain if these findings are of clinical significance because the effect size of the interventions was not provided in the studies. Similarly, the only study on the effects of mobile text reminders on QoL included in this review reported no significant effects. However, the sample size of the study is underpowered to detect differences between the intervention group and the control group, and thus, its findings are unreliable. Therefore, there is a need for further evidence to conclude the effectiveness of mobile text reminders in improving adherence to medication in PLWHA. Also, there is limited evidence on the effects of mobile text reminders on health outcomes such as QoL as well as lack of RCTs (evidence) on the effectiveness of mobile text reminders on physical exercise adherence in PLWHA. These are important gaps in the literature that need to be addressed in future studies to guide practice. The observation that all the sufficiently powered studies included in this review report that mobile text reminder is effective in ensuring adherence to medication in PLWHA highlight the possibility of the relevance of mobile text reminder in HIV care. Therefore, it is recommended that:

- i. future studies should examine the effects of the frequency and timings of the messages; message content; optimal development processes, and process evaluations to assess the mechanisms by which messages affect the receivers.
- ii. More adequately powered, good quality, randomised controlled trials should be conducted, particularly in resource-limited settings.
- iii. Long-term trials are also needed because in most cases there is a need for life-long adherence to treatments.
- iv. It is of importance that standardised outcome measures and approaches of measuring adherence (development of free and validated scores) are developed and used so that outcomes can be pooled across studies.
- v. Furthermore, no review has examined how text messages are created, and if short message service is more effective if tailored to fit individual patient's characteristics, and if some patients benefit more than others. However, more researchers should include this in their trials.
- vi. It is further recommended that the development of mobile text messages should follow some theoretical framework, and text messages should be developed specifically for the target population and intervention.

Limitation Of Study

The findings of this review might be limited for the following reasons: i) the included studies were small, heterogeneous, and included participants not minding their adherence level, li) Due to heterogeneity in the methods and outcome measure, it was difficult to conduct a meta-analysis of the included study. Therefore, this review cannot benefit from pooled estimates to determine evidence of effects across studies, lii) Inclusion of studies regardless of where the participants were recruited and enrolled, lv) Studies were not excluded based on how the text messages were developed, or if they were one way versus two ways, v) Language restrictions were applied in this review, and thus may not reflect the totality of the evidence in this area since other studies published in other languages other than English were excluded, and finally, vi) Each study has at least one risk of bias domain judged as high risk.

Abbreviations

Human immune deficiency virus	HIV
Acquired immune deficiency syndrome	AIDS
Antiretroviral therapy	ART
Highly antiretroviral therapy	HAART
People living with HIV/AIDS	PLWHA
Short Message Service	SMS
Quality of Life	QoL
Risk of bias	ROB
Review Manager	RevMan
Randomized control trials	RCTS
Medical subject heading	MeSH
Allied and Complementary Medicine Database	AMED
Cumulative Index to Nursing and Allied Health Literature	CINAHL
Excerpta Medica database	EMBASE
Allied and Complementary Medicine Database	AMED
Physiotherapy Evidence Database	PEDro
Not Applicable	N/A
Grading of Recommendations Assessment Development and Evaluation	GRADE
International platform of registered systematic review and meta-analysis protocols	INPLASY
Preferred Reporting Items for Systematic Reviews and Meta-analyses	PRISMA
health-related quality of life	HRQoL

Declarations

Ethics approval and consent to participate

This is not applicable as human subjects are not involved.

Consent to publish

Not applicable

Availability of data and materials

The datasets supporting the conclusions of this article are available in the institutional University of Nigeria repository and will be made easily available on request when required.

Competing interests

The authors declare that there is no conflict of interest

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Authors' Contributions

SCI and UV conceived the study, participated in literature search and review, data extraction, study design and coordination, performed the statistical analysis, and helped draft the manuscript. EAD, participated in data extraction and helped drafted the manuscript. EFE, and IFO participated in literature search and review, data extraction and helped draft the manuscript. HM, AAT, OUP, and GF participated in the design of the study, coordination, and helped draft the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1: Study characteristics

STUDY (year) Country	Location of study	PARTICIPANTS (number; age in years) Disease stage	INTERVENTION	MEDICATION ADHERENCE	PHYSICAL ACTIVITY ADHERENCE	QUALITY OF LIFE	CONCLUSION
Ruan et al,2017 ¹⁸	China	(n=100; age: ≥18yrs) Were on ART for not more than 3 months	G1: mobile text reminder (SMS;6 months) + usual care G0: usual care (regular health education in the clinic including informational pamphlets, psychological support and personalized health education from nurses and physician)	CPCRA adherence self-report questionnaire VAS on a 100-point scale			It shows preliminary significant efficacy in improving adherence to ART medication in people living with HIV
Mgbuagwu et al,2012 ²⁰	Cameroon	(n=200; age: ≥21yrs) Has been on ART for at least one month	G1: mobile text reminder (SMS;1x per week for 6 months) + usual care G0: usual care (regular ART counselling and home visits)	Visual analogue scale Self-report Pharmacy refill data		SF-12 scale score quality of life assessment form	The intervention did not significantly improve adherence to ART after 6 months
Lester et al,2010 ²¹	Kenya	(n=538; age: >18yrs) Initiating ART for the first time	G1: mobile text reminder (SMS; weekly for 30 days) G0: Standard care	Self-report (about missed pill)			Intervention is more likely to significantly improve patient's adherence to ART compared to patients who received the standard care alone
Pop- eleches et al,2011 ²⁴	Kenya	(n=431; age:>18yrs) Initiated ART for less than 3 months prior to enrollment	G1: mobile text reminder (SMS; either short or long at daily or weekly frequency for 48 weeks) G0: no intervention	Medication event monitoring system			Intervention is an important tool in achieving an optimal treatment response
da Costa et al,2012 ²²	Brazil	(n=21; average age:34.62 ± 6.92yrs) Have taken first or second antiretroviral regimen and having viral load of400copies/ml for at least 3 months and CD4+ cell counts>200/mm ³	G1: mobile text reminder (SMS for 4 months) G0: no intervention	Self- reported adherence Pill counting microelectronic monitors (MEMS)			No significant change but the Intervention can stimulate more participants in the intervention group to be adherent to their treatment for at least 4 months
Hardy et al,2011 ²³	Boston, USA	(n=23; age: ≥18yrs) Were on a stable regimen of antiretroviral therapy for at least 3 months	G1: Mobile text reminder of which is a cellular phone (personalized text message for 6 weeks) G0: beeper for 6 weeks	Self-report Pill count Medication event monitoring system			Adherence increased and remained significantly higher in the group that received cellular phone

				Composite adherence score	
Nsagha et al, 2016 ²⁵	Cameroon	(n=90; age: ≥18yrs) Had been on A antiretroviral for at least one month	G1: Mobile text reminder (4 educative SMS/week at equal intervals for 4 weeks) G0: Standard treatment and care	Self-report using interviewer administered questionnaire	SMS significantly improved adherence to antiretroviral, key constraint which affects adherence to antiretroviral medication can be addressed using SMS
Mao et al, 2018 ²⁶	Australia	(n=98; age: ≥18yrs) Has been on antiretroviral therapy	G1: Two-way SMS (3×per week for 6 weeks) G2: Two-way SMS (2×per week for 6 weeks) G0: One-way non-specific greeting message (1×per week for 6 weeks)	Self-report using SMAQ (simplified medication adherence questionnaire)	No significant change was found but SMS messaging could have broader impact on reducing health and social inequity
Sabin et al., 2015 ¹⁹	China	(n=120; age: ≥18 yrs) Receiving or initiating antiretroviral therapy	Suboptimal adherence group (<90%) G1: real-time SMS reminder triggered by a-30 mins delay in medication + adherence counselling G0: Usual care + adherence counselling Optimal adherence group (>90%) G1: real-time SMS reminder triggered by a-30 mins delay in medication + adherence counselling G0: Usual care + adherence counselling	Wise-pill monitor	Use of triggered SMS reminder based on objective adherence data from the wise-pill monitor significantly improved antiretroviral therapy adherence in HIV population

SMS=short message services; CPCRA=community programs for clinical research on Aids; MEMS=medication event monitoring system or micro-electronic monitors; VAS= visual analogue scale; GI=Intervention group; G0=control group

Table 2: Quality Appraisal/Risks of Bias of included studies (PEDro Tool)

Study	Eligibility Criteria	Random allocation	Concealed allocation	Baseline comparability	Blinding of subjects	Blinding of therapist	Blinding of assessors	Adequate follow-up	Intention to treat analysis	Between-group comparison	Pr es ar vā
Ruan et al,2017 ¹⁸	YES	YES	NO	YES	NO	NO	NO	NO	YES	YES	YI
Mgbuagwu et al,2012 ²⁰	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	YI
Lester et al,2010 ²¹	YES	YES	YES	YES	NO	NO	YES	YES	YES	YES	YI
Pop-eleches et al,2011 ²⁴	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	N
da Costa et al,2012 ²²	YES	YES	YES	YES	NO	YES	YES	NO	NO	YES	YI
Hardy et al,2011 ²³	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	YI
Nsagha et al,2016 ²⁵	YES	YES	NO	YES	NO	NO	NO	YES	NO	YES	N
Mao et al,2018 ²⁶	YES	YES	NO	NO	NO	NO	NO	YES	NO	YES	N
Sabin et al.,2015 ¹⁹	YES	YES	NO	YES	NO	NO	NO	NO	YES	YES	YI

The PEDro tool was used to determine and summarize the quality of the included studies

Table 3: Data extraction of findings (except where specified, results are presented as Int. group vs Cont. group)

Study	Timepoint	Medication adherence & Outcome	Physical activity adherence & Outcome	Quality of life & Outcome
Ruan et al,2017 ¹⁸	Immediately post intervention	100%: [Int.42(89.3) vs Cont.34(72.3)]; Z=2.208; p=0.027; 80%-99%: [Int.3(6.4) vs Cont.3(6.4)]; <79%: [Int.2(4.3) vs Cont.10(21.3)]; <i>CPCRA adherence</i> [Int. (98.72±2.35) vs Cont. (93.11±6.51)]; Z=2.735; p=0.006; <i>Visual Analogue Scale</i>		
Mgbuagwu et al,2012 ²⁰	Immediately post intervention	[Int.72(71.3) vs Cont.66(66.7)]; p=NS; <i>Visual Analogue Scale</i> [Int.80(79.2) vs Cont.78(79.0)]; p=NS; <i>self-report</i> [Int. (3.8±1.48) vs Cont. (3.7±1.34)]; p=NS; <i>pharmacy refill data</i>		[Int.(3.79±0.585) vs Cont. (3.75±0.583)];p=NS; <i>SF-12 scale score Quality of life assessment form</i>
Lester et al,2010 ²¹	Immediately post intervention	[Int.168(62%) vs Cont.132(50%)]; p=0.006; <i>self-report questionnaire</i>		
Pop-eleches et al,2011 ²⁴	Immediately post intervention	4 intervention groups with subgroups Int.group1: [Int.0.41 vs Cont.0.40]; p=NS Int.group2: [Int.0.53 vs Cont.0.40]; P=0.03 Int.group3: [Int.0.47 vs Cont.0.40]; P=NS Int.group4: [Int.0.47 vs Cont.0.40]; p=NS; <i>medication event monitoring system</i> Subgroups Subgroup 1: [Int.0.40 vs Cont.0.40]; p=NS Subgroup2: [Int. 0.53 vs Cont.0.40]; p=NS Subgroup3: [Int.0.42 vs Cont.0.40]; p=NS Subgroup4: [Int.0.53 vs Cont.0.40]; p=NS Subgroup5 [Int.0.47 vs Cont.0.40]; p=NS; <i>medication event monitoring system</i>		
da Costa et al,2012 ²²	Immediately post intervention	[Int.8(100.00%) vs Cont.11(84.62%)] Z=1.1663; p=NS; <i>self-report</i> [Int.4(50.00%) vs Cont.5(38.46%)] Z=0.5189; p=NS; <i>pill counting</i>		

		[Int.6(75.00%) vs Cont.6(46.15%)]; Z=1.2972; p=NS; <i>micro-electronic monitoring</i>
Hardy et al,2011 ²³	Immediately post intervention	[Int.92.6(77.5-107.7) vs Cont.72.4(56.5-88.3)]; p=NS; <i>self-report</i> [Int.82.7(68.7-96.8) vs Cont.69.1(54.2-83.9)]; p=NS; <i>pill count</i> [Int.89.7(76.5-102.9) vs Cont.56.3(42.4-70.3)]; p=0.002; <i>medication event monitoring system</i> [Int.83.4(70.0-96.9) vs Cont.56.3(42.2-70.4)]; p=0.0094; <i>composite adherence score</i>
Nsagha et al,2016 ²⁵	Immediately post intervention	[Int.64.4% vs Cont.44.2%];p=0.05; <i>interviewer-administered self-report questionnaire</i>
Mao et al,2018 ²⁶	Immediately post intervention	Two intervention groups Int.group 1: [Int.81.0% vs Cont.72.7%]; P=NS Int.group 2: [Int.94.7% vs Cont.72.7%]; P=NS; <i>simplified medication adherence self-report questionnaire</i>
Sabin et al.,2015 ¹⁹	Immediately post intervention	Suboptimal adherers group [Int.93.3% vs Cont. 84.7%]; p=0.039 Optimal adherers group [Int.97.8% vs Cont. 91.7%]; p=0.028; <i>wise-pill monitor</i>

Int.=Intervention group; Cont.=Control group; p=p value; Int.group1=Daily SMS; Int.group2=Weekly SMS; Int.group3=Short SMS; Int.group4=Long SMS; Subgroup1=Daily, Short SMS; Subgroup2=Weekly, Short SMS; Subgroup3=Daily, Long SMS; Subgroup4=Weekly, Long SMS; Subgroup5=Any treatment; SMS=Short message service; NS=Not significant; CPCRA=community programs for clinical research on AIDS adherence self-report questionnaire

Figures

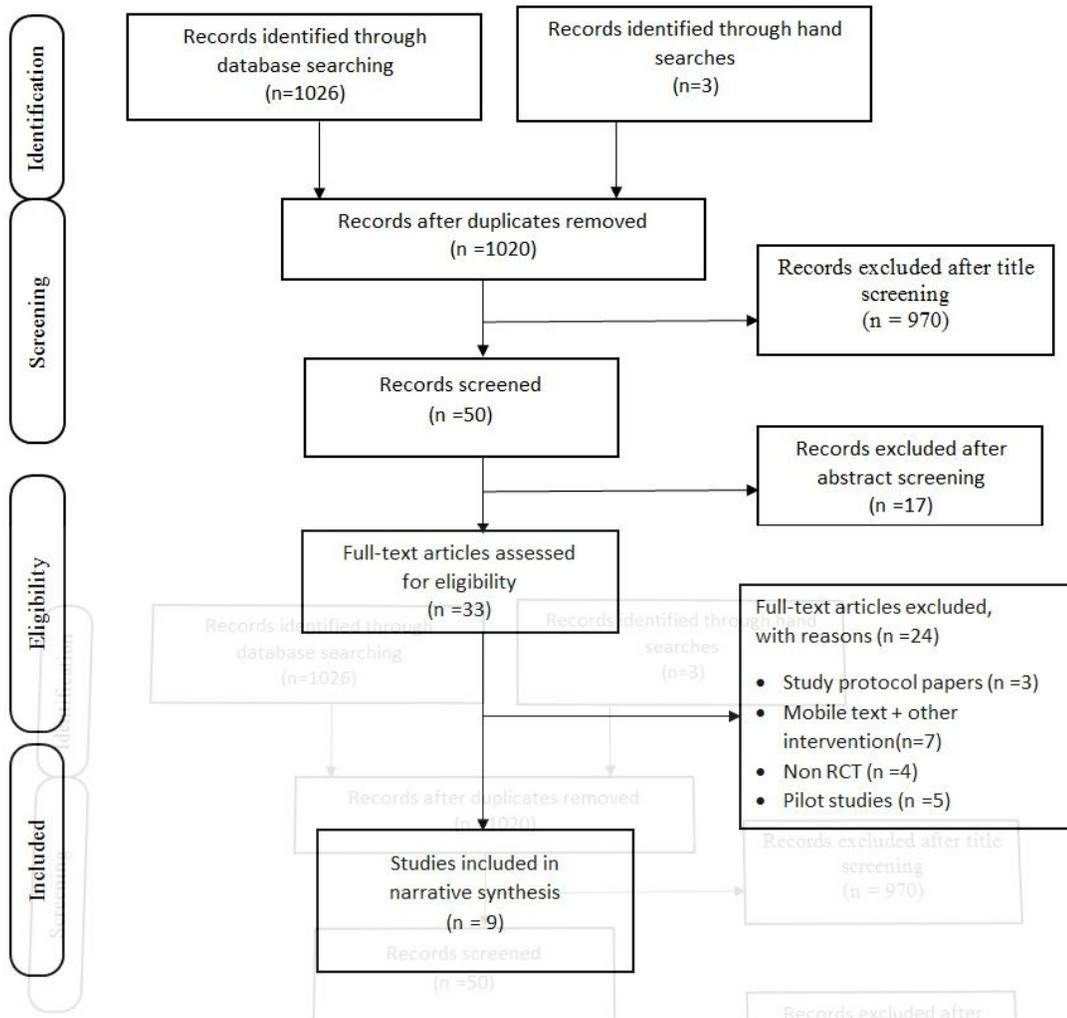


Figure 1

PRISMA checklists for adherence to medication, adherence to physical exercises, Quality of life

Supplementary Files

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- [AppendixI\Searchstrategy.docx](#)