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MOBILE HEALTH INTERVENTIONS FOR MEDICATION ADHERENCE: A SYSTEMATIC REVIEW

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1. INTRODUCTION

Taking a medicine as prescribed sounds simple, yet in long-term conditions roughly half of patients do not manage it. A review of fifty years of research found that adherence varies widely between patients and is often poor in chronic illness, and the observation has held up well [1, 2]. Missed doses blunt the benefit of antihypertensives, statins, antiretrovirals and antidiabetic drugs, and the downstream costs appear as avoidable admissions, disease progression and wasted prescribing [3]. Adherence is also not a single behaviour. It covers starting a treatment, carrying it out day after day, and persisting with it for months or years, and each phase

Abstract

Poor adherence to prescribed medicines remains a stubborn cause of treatment failure, and mobile technology has been offered as an inexpensive way to address it. This review draws together published trials, systematic reviews and methodological papers on mobile health interventions for medication adherence, reporting no new data. Text message reminders show the most consistent benefit, particularly in HIV treatment and chronic cardiometabolic disease, while smartphone applications and electronic reminder devices have a thinner and more variable evidence base. Effects tend to be modest, short-lived and dependent on engagement. Heterogeneous adherence measures, short follow-up, small trials and weak reporting of intervention content limit confident pooling, and robust long-term, clinically anchored studies are still needed.

has different causes [4]. The regimen matters too: the number of daily doses, the complexity of the schedule and whether the drug produces symptoms all influence persistence. Silent conditions such as

hypertension and dyslipidaemia are especially prone to drift, because nothing the patient feels rewards continued tablet taking [2, 3].

Interventions to improve adherence have been tested for decades. Systematic reviews of the area keep reaching a sober conclusion: the strategies that work tend to be complex, labour-intensive and only modestly effective, and few produce clear gains in clinical outcomes [5, 6]. That backdrop explains the appeal of the mobile phone. Handsets are carried everywhere, they can deliver a prompt at the moment a dose is due, and the marginal cost of an extra message is close to zero. Mobile health, usually shortened to mHealth, was defined by the WHO as medical and public health practice supported by mobile devices [7]. Simplifying the regimen, using fixed-dose combinations and moving to once-daily formulations are usually tried before anything digital, and they remain sensible first steps [5, 6]. Mobile tools are best understood as an addition to these measures rather than a substitute for them, and that framing runs through the rest of this review.

The field has moved quickly from simple one-way reminders to multifunction smartphone applications, connected pill bottles, two-way messaging with clinicians and tools that tie into electronic health records. Early optimism was strong. Reviews of text messaging suggested that it could change health behaviour across a range of conditions, and the first randomised trials in HIV care in Kenya and elsewhere were widely cited [8, 9, 10]. Since then the evidence has grown larger, more critical and more nuanced, and several authors have cautioned that enthusiasm has run ahead of reproducible clinical benefit [11, 12]. Critical appraisal sharpened at the same time. The early systematic reviews of text-message and phone-based interventions found real but uneven effects and judged the quality of many trials to be low, and later syntheses kept returning to the same problems of short follow-up, small samples and unclear description of what the intervention actually contained [11, 12].

This review brings together published systematic reviews, randomised trials and

methodological papers on mHealth interventions for medication adherence, and it reports no new data. It asks which types of intervention have been tested, how adherence has been measured, where the evidence is firmest, what determines whether people keep using the tools, and what limits interpretation. The synthesis is narrative. Pooling is attempted by the cited meta-analyses rather than here, because the underlying trials differ so much in population, comparator and outcome that a single summary figure would mislead more than it informs. The scope is deliberately wide. Interventions are grouped by modality (text messaging, smartphone applications and electronic reminder devices), and the discussion then turns to engagement, equity and privacy, topics that effectiveness trials tend to neglect but that decide whether a tool can survive outside a research setting [7, 13].

2. ADHERENCE AND ITS MEASUREMENT

A common vocabulary helps. The taxonomy proposed by Vrijens and colleagues separates implementation, meaning the extent to which doses are taken as prescribed, from persistence, meaning how long therapy continues, and it asks authors to say which phase an intervention is trying to influence [4]. A reminder system, for instance, acts mainly on implementation, the day-to-day match between the prescribed regimen and what the patient actually takes. It will do little for someone who never collected the first prescription. Much of the older literature blurred these distinctions and used the single word compliance, which makes comparison across studies awkward and obscures why some interventions seem to work only in selected groups. This is more than a matter of tidiness. When a review pools trials that targeted different phases, a null result may simply mean that the intervention was aimed at the wrong problem for part of the sample, and a positive result may hide that the benefit was confined to patients who had already started therapy and were struggling with routine.

Measurement is the weak point of the whole field. Self-report is cheap and widely used, but patients overstate adherence, recall is poor

and social desirability pulls answers upwards, although carefully designed questionnaires retain a place when used with caution [14, 15]. Pill counts and pharmacy refill records are objective in a limited sense, since they show supply rather than ingestion. Electronic monitoring caps such as the medication event monitoring system record each opening of the container and are often treated as a reference method, yet they too cannot confirm that a tablet was swallowed [16]. Drug levels in blood or urine offer the strongest proof, though only for some agents and at some cost. Each method also behaves differently across drug classes and settings, which is why many authors recommend combining two measures, for example a refill record with a brief questionnaire, rather than trusting any single one. The combination costs little and exposes disagreements that would otherwise pass unnoticed [14, 15].

Because of these differences, a trial reporting a rise in adherence from self-report cannot be set beside one using electronic caps without a good deal of care. Studies of antiretroviral therapy often use viral suppression as a biological end point, which is clinically meaningful but also depends on drug resistance, absorption and interactions [9, 13]. In hypertension, blood pressure is a downstream marker influenced by many factors beyond tablet taking. An mHealth review therefore has to read each outcome in context. A modest improvement in a refill-based measure over three months is a different kind of finding from a sustained change in a clinical biomarker over a year. Reading the older literature with this in mind is instructive. Several early positive trials rest on self-reported adherence alone, and some of the most striking effect sizes shrink when electronic monitoring or a laboratory marker is used instead [13, 16].

A related issue concerns the comparator. Many trials compare a mobile intervention with usual care, which in practice means nothing in particular, and so a reminder wins easily against silence. Fewer compare it with a well-designed non-digital alternative, such as a pharmacist telephone call, a blister pack or a pill organiser [17]. Where such head-to-head comparisons exist, the margin

of benefit often narrows. For readers deciding what to adopt, the relevant question is rarely whether a phone prompt beats nothing, but whether it is cheaper or easier to deliver than what a clinic already does. Active comparators also make trials more expensive and recruitment slower, which partly explains why so few exist. Their scarcity should be kept in mind whenever a headline effect size is quoted, because it will almost always be measured against the weakest available alternative.

Technology can also change the act of measurement itself. A smart pill bottle that logs openings, or an app that asks the patient to confirm each dose, generates a continuous record that was never available in earlier trials. This is useful for research, because it allows adherence to be described as a pattern over days and weeks rather than a single percentage. It also means that monitoring and intervention are bundled together, so any improvement may reflect the awareness of being observed as much as the prompt itself. Few studies attempt to separate the two effects. Awareness of observation is a well-known source of bias in adherence research, and it deserves explicit discussion in the design of any trial using monitoring technology [15, 16].

3. TEXT MESSAGING

Short message service (SMS) reminders are the best studied form of mHealth for adherence, partly because they work on any phone and need no data connection. A meta-analysis of randomised trials in chronic disease found that the odds of adherence were roughly doubled with text messaging, with the benefit seen across conditions and across messaging frequencies [18]. The authors translated this into a sizeable absolute gain in the proportion of adherent patients, a result that is clinically useful if it holds, though the trials were heterogeneous and many were small [18, 19]. Pooled estimates should still be read with some caution. Several of the contributing trials were short, relied on self-report and came from specific populations, and the meta-analysts themselves noted that between-trial variability was large and that publication bias could not be excluded [18, 19].

HIV treatment supplied some of the most cited trials. In Kenya, weekly two-way messages asking patients how they were doing improved self-reported adherence and viral suppression compared with standard care [9]. A Cochrane review of the area judged the evidence supportive but of limited certainty, citing the small number of trials and risk of bias [20]. Interestingly, the interactive design in the first trial gave patients a reason to reply, turning a one-way prompt into a short conversation with a nurse. A separate Kenyan trial found that weekly reminders lifted the proportion reaching 90 per cent adherence on electronic monitoring, whereas daily reminders did not, a result that argues against assuming that more frequent contact is always better [10]. Both trials were carried out in clinics with active nursing support, which may not be reproduced elsewhere.

Outside HIV the picture is more mixed. In a single-blind trial in adults with high blood pressure in South Africa, supportive messages gave modest changes in some measures but no clear, lasting improvement in blood pressure control [21]. Reviews of text messaging across chronic conditions report small improvements in process measures, with less consistent effects on clinical control [22]. One reading is that reminders solve forgetfulness but cannot overcome cost, side effects, mistrust of medicines or disbelief that a symptomless condition needs treatment. Those reasons for non-adherence lie outside what a timed buzz can reach. Trials in other long-term conditions have been similarly cautious in their wording. Authors tend to describe improvements in process measures such as clinic attendance or refill timing and to avoid strong claims about disease control, which is a fair reflection of how far a message can reasonably be expected to travel [8, 22].

Message design matters, and the literature offers guidance of uneven quality. Messages that are personalised, that allow a reply, and that carry some motivational content rather than a bare time-of-day alert appear more promising [8, 22]. Frequency is a trade-off. Daily messages risk habituation and irritation, whereas sparse ones may miss the dose they were meant to prompt. Some programmes taper the schedule over time or vary the

wording to keep it fresh. Direct comparisons of these design choices are rare, so most recommendations come from process evaluations and qualitative work rather than from controlled trials. There is a further subtlety. Messages sent at fixed clock times assume that a patient's routine is stable, whereas shift workers, travellers and people with irregular meals may find that the prompt arrives when the dose is already taken or impossible. Flexible timing set by the patient is a simple response that few trials have formally tested [8, 22].

The low-income setting deserves a separate comment. In many African and South Asian programmes, text messaging is the only digital channel that reaches patients reliably, and per-message cost has been the main practical barrier [8, 20]. Cost-effectiveness analyses remain sparse, which is a pity, because a cheap, modestly effective intervention can still be good value at scale. Shared phones, changing numbers and concerns about disclosure of a stigmatised diagnosis also complicate delivery. Programmes that worked had to deal with these practicalities, for example by using neutral wording that does not name the condition. Telecommunication costs, number portability and the practicalities of reaching patients without personal handsets can decide the fate of an otherwise sound message programme [7, 10].

4. APPS, DEVICES AND COMBINED EVIDENCE

Smartphone applications are the natural successor to text messages. They can issue reminders, log doses, show a streak or a chart, store a medication list, and link to a caregiver. Early reviews found many apps on the market but few formally evaluated, and the ones that were tested usually had short follow-up [23, 24]. Content analyses showed that most apps used only a few behaviour change techniques, mainly reminders and self-monitoring, with feedback, goal setting and social support appearing far less often [23, 25]. The evidence on apps is therefore a story of potential rather than demonstrated benefit. Some apps go further and add a camera function to record the tablet being swallowed, or a game element that rewards consistent

use. These features are intriguing and occasionally effective in small studies, but they raise questions about burden and surveillance that are taken up later in this review [23, 24].

Controlled trials of apps exist, though they are fewer and more varied than for text messaging. A review of mHealth in chronic disease management found that apps and other mobile tools improved adherence in a majority of the included studies, but the studies were small and often at unclear risk of bias [13]. A broader review of systematic reviews reached a similar view: positive signals on process measures and weaker support for clinical outcomes [26]. Features linked with better results include interactivity, tailored feedback and a connection to a health professional who can act on the data [13, 17]. Taken one by one, the better-designed trials tend to report that an app improved a process measure, for example the proportion of doses logged as taken, while leaving blood pressure, glycated haemoglobin or viral load only modestly changed, or not changed at all within the follow-up period [13, 17].

Electronic reminder devices occupy a middle position. These include pill bottles with lights and alarms, and connected caps that notify a relative or a pharmacist when a dose is missed. A large pragmatic randomised trial of reminder devices in patients taking chronic cardiovascular and related medicines found no meaningful improvement in adherence over the study period [27]. Earlier reviews of electronic reminders had suggested benefits for chronic medication use but flagged low study quality [16, 28]. The lesson seems to be that a device alone is not enough when the underlying barrier is not forgetting. The devices were not trivial interventions, and the trial was large, which makes the null finding more instructive than the failure of a trivial intervention would have been [27]. It also underlines how often poor adherence has causes other than forgetting.

The main findings are collected in table 1, which groups representative studies and reviews by modality. Text messaging has the most consistent positive evidence, a reasonably large number of trials and the clearest signal in HIV care. Applications and

devices show a promising but patchy record. Syntheses that cross modalities tend to agree that effects are small to moderate and that clinical translation is uncertain [13, 19, 26]. The distribution of entries by modality is shown in fig. 1, which also reflects how unevenly research effort has been spread across the available approaches. Readers who want to look more closely at any entry can follow the reference given in the last column. Many pooled estimates come with wide confidence intervals and substantial statistical heterogeneity, so the direction of effect is more reliable than its size [26, 29].

A practical point sometimes lost in the trial literature concerns integration. An app that stands alone, asks the patient to key in every dose and is unknown to the prescriber has little chance of changing care. Interventions that feed adherence data to a pharmacist or nurse, who then phones the patient, sit closer to the multicomponent strategies that have the best record in the older adherence literature [5, 6]. Such hybrids are harder to evaluate because the human contact becomes the active ingredient, and the technology serves mainly as a cheap way of deciding whom to call and when. Pharmacy-led models that combine app data with a short consultation have been described, though large controlled evaluations are still lacking [5, 6].

Table 1: Representative published evidence on mobile interventions for medication adherence

Intervention or review	Reported finding	Ref.
Weekly two-way SMS HIV, Kenya	Better self-reported adherence and viral suppression than standard care in a randomised trial.	[9]
Weekly versus daily SMS HIV, Kenya	Weekly reminders raised the proportion with high adherence on electronic monitoring; daily reminders did not.	[10]
Meta-analysis of SMS Chronic disease	Roughly doubled odds of adherence, with considerable heterogeneity between trials.	[18]
Supportive SMS Hypertension	Modest changes in some measures but no clear, lasting gain in blood pressure control.	[21]

Intervention or review	Reported finding	Ref.
Content analysis of apps	Most apps rely on reminders and self-monitoring; few use feedback or goal setting.	[23, 25]
Review of mHealth apps Chronic disease	Adherence improved in most included studies, which were small with unclear bias.	[13]
Electronic reminder devices Chronic cardiovascular therapy	No meaningful gain in adherence in a large pragmatic randomised trial.	[27]
Systematic review of reminders	Mixed benefit for chronic medication use and generally low study quality.	[28]
Review of systematic reviews	Positive process signals, weaker support for clinical outcomes.	[26]
Cochrane review of adherence strategies	Effective strategies are complex and gains in clinical outcomes are inconsistent.	[5, 6]

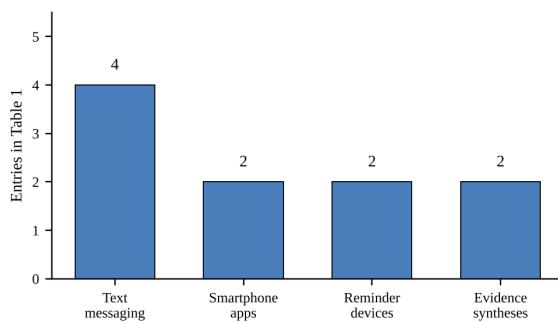


Fig. 1: Number of entries in table 1 by intervention modality

5. ENGAGEMENT, EQUITY AND PRIVACY

An intervention that patients stop using cannot change their behaviour. Eysenbach described the law of attrition in web-based trials, in which a large share of participants drop out or stop using the tool, and the pattern is familiar in mHealth [30]. Sieverink and colleagues pointed out that adherence to a digital intervention is itself a measurable concept with its own determinants, and that studies should report usage alongside outcomes [31]. In practice, many apps are installed and then forgotten within weeks. Any benefit seen at three months may reflect a motivated early-adopting subgroup. Retention strategies, such as an occasional

personal call or a small reward, have been tried, but they add cost and may bring in patients who would have adhered anyway. Better engagement is therefore a design problem as much as a delivery problem [30, 31].

Behaviour change theory offers a way to think about why some tools hold attention. The taxonomy of behaviour change techniques lists ninety-three discrete components, and the behaviour change wheel links capability, opportunity and motivation to intervention functions [32, 33]. Reminders target capability in the sense of memory, but they say little about motivation, and nothing about the physical or social opportunity to take a drug. Interventions that combine prompts with education, problem-solving and feedback address more of these levers. Reviewers have called for developers to name the techniques they use, so that effective ingredients can be identified across studies [25, 33]. Few apps report which of these techniques they deploy or why, and the lack of a shared language makes it difficult to say whether a failed app failed because of its content, its delivery or its audience [25, 32].

Patients' own views temper the technological optimism. Qualitative work with people living with several chronic conditions found that repeated reminders and data tracking can feel like a constant reminder of being ill, and that some users deliberately switch notifications off [34]. Older adults, people with low health literacy and those without a smartphone or stable data access may be least able to benefit, even though they often carry the heaviest burden of treatment. A tool designed around the habits of a young, urban, well-connected user risks widening existing inequalities in outcomes rather than closing them [7, 35]. Equity concerns extend to language and design: messages in a second language, small print on a screen or complicated log-in steps can exclude the very people who need support. Co-design with patients, including those with limited literacy, has therefore been recommended as a routine step in development [7, 35].

Privacy deserves more attention than it usually receives in effectiveness trials. An assessment of accredited health and wellness

apps found that many transmitted identifiable information without encryption or shared data with third parties [36]. Medication lists reveal diagnoses, and for conditions such as HIV or mental illness a breach could cause real harm. Regulators and professional bodies have started to publish standards for health apps, yet compliance varies. Clinicians recommending an app should ask where the data go, who can see them, and whether the app can be used without creating a permanent record. Pharmacists and nurses who suggest apps to patients should also be aware that app-store descriptions are not a guarantee of safe data handling, and that consent screens are often long, vague and rarely read [35, 36].

Cost and sustainability complete the picture. A pilot may be funded by a research grant that pays for the messaging platform and technical support, but a health service must absorb these costs for years. Platforms also change, and apps can vanish from stores when a developer stops maintaining them. Programmes that survive tend to be embedded in an existing service, such as an antiretroviral clinic or a community pharmacy, with a named person responsible for the system and for responding to the alerts it generates [8, 19]. Funding models that rely on a single grant make long-term maintenance doubtful, and few papers report what happened to a programme once the trial ended [7, 19].

There is a final human consideration. Patients differ in what they find acceptable, and the same message that reassures one person may feel intrusive to another. Offering a choice of channel, timing and tone, and letting people opt out without penalty, respects autonomy and probably improves long-term engagement. Evidence for this is mostly indirect, drawn from acceptability studies rather than head-to-head trials, but it fits with what is known about shared decision making in prescribing and with the general principle that adherence support works best when it is negotiated rather than imposed. Where choice is not offered, uptake tends to fall, and people may quietly disable the very feature that was meant to help them [31, 34]. A short explanation of why a feature exists, and how to adjust it, may reduce this kind of quiet

abandonment.

6. LIMITATIONS AND FUTURE DIRECTIONS

Several features of the evidence base restrict firm conclusions. Trials are often small, follow-up is frequently under six months, and blinding of participants is impossible. Reporting of the intervention itself is poor, so replication is difficult. Statistical heterogeneity in the pooled analyses is substantial, which weakens the meaning of any single summary effect [18, 29]. Publication bias is likely, since positive pilot studies of attractive technologies are easier to publish than null ones. Reviews, including this one, inherit these weaknesses, and the reporting standards for systematic reviews are not always followed even by authors who describe their work as systematic [37]. Added to this is the difficulty of generalising from trials run in a single clinic or country to health systems with different prescribing habits, copayments and phone coverage, a limitation that applies with particular force to results from low-income settings [8, 20].

Outcomes are the second concern. Most studies measure adherence rather than health, and the step from one to the other cannot be assumed. A small increase in the proportion of doses taken may matter greatly for an antiretroviral with a low resistance barrier and hardly at all for a drug with a long half-life and a forgiving dose-response curve. Future trials should state in advance the level of adherence needed to produce a clinical effect for the drug under study, choose a validated measure, and report clinical end points where feasible. Cost, harm and patient-reported experience should be recorded alongside. Non-adherence is also a moving target. People start well, slip, recover and slip again, and a single end-of-study snapshot misses the shape of that curve. Longitudinal analyses of dose-by-dose data from monitoring devices could describe it far more faithfully than the summary percentages used so far [15, 16].

Methodologically, the field would benefit from factorial and adaptive designs that can test components of an intervention rather than packages. Micro-randomised trials, which assign different prompts at different moments

within the same person, are well suited to identifying which message works at which time. Better reporting of engagement data, including the proportion who opened a message or used an app at each follow-up point, would make it possible to separate failure of the idea from failure of uptake [31]. Open sharing of message libraries and app content would also let others reuse what works. Careful attention to heterogeneity of treatment effect is also overdue. Subgroup findings by age, baseline adherence and digital literacy are rarely reported, even though they would tell implementers which patients are most likely to gain from a given tool and which are better served by a different approach [5, 30].

Finally, implementation research is needed. Little is known about how clinics adopt, adapt and maintain mHealth adherence tools in routine care, who pays, and what happens when staff change. Hybrid effectiveness-implementation designs could answer these questions while still testing clinical benefit. Evaluations should include the groups most at risk of non-adherence and least likely to be reached by commercial products. Without such work, mobile interventions may remain a collection of promising pilots rather than a dependable part of how pharmacists and physicians support patients who take medicines over many years. Patient involvement in setting research priorities would help here, since people who take medicines daily have good insight into what is burdensome, what is useful and what is merely noise on a lock screen. Their views have been sought in qualitative studies but seldom shape trial design [31, 34].

Regulatory and professional guidance is also lagging behind the technology. Pharmacists are increasingly asked by patients which adherence app to use, yet there is no widely accepted way to appraise one. A short checklist covering evidence of effect, behaviour change content, data protection, cost and interoperability would help. Professional bodies could maintain lists of apps that meet minimum criteria, in the way that formularies guide drug choice, so that recommendations do not rest on app-store ratings alone. Such a checklist should be

reviewed regularly, because app features and data practices change faster than a printed guideline can follow [25, 36].

7. CONCLUSION

Mobile health tools can nudge people to take their medicines, and text messaging has the most convincing record, with the clearest benefit in HIV care and a modest, variable effect in other chronic diseases [9, 18, 21]. Applications and electronic reminder devices are plausible but less well proven, and their results depend heavily on engagement, design and the barrier being addressed [25, 27]. Forgetfulness is only one of many reasons why people stop their treatment, and reminders cannot answer cost, fear of side effects or doubt about need. The size of the benefit is usually modest, and the quality of the studies means that confidence in many estimates is limited [13, 19].

For practising pharmacists and clinicians, the sensible course is selective use: offer simple messaging where forgetting is the problem, link tools to a human contact who can respond, and protect privacy and equity. For researchers, the priorities are longer trials, clinical outcomes, honest reporting of usage and active comparators [29, 31]. Until that evidence arrives, mHealth is best seen as a useful support to adherence care rather than a replacement for it. Most important is the recognition that adherence is a behaviour shaped by beliefs, costs and circumstances, and that technology succeeds when it fits these rather than ignoring them [4, 33].

8. ABBREVIATIONS

mHealth-Mobile health, SMS-Short message service, WHO-World Health Organization, HIV-Human immunodeficiency virus, RCT-Randomised controlled trial, MEMS-Medication event monitoring system, BCT-Behaviour change technique

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Nil

10. AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

11. CONFLICT OF INTERESTS

Declared none

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