Evaluating the effectiveness of mobile applications on medication adherence for chronic conditions: Systematic Review and Meta-analysis

Vaidehee Lanke, Kevin Trimm, Bettina Habib, Robyn Tamblyn

Submitted to: Journal of Medical Internet Research
on: May 22, 2024

Table of Contents

Evaluating the effectiveness of mobile applications on medication adherence for chronic conditions: Systematic Review and Meta-analysis

Vaidehee Lanke[1] BSc; Kevin Trimm[2] MSc; Bettina Habib[1] MSc, MScPH; Robyn Tamblyn[1] MSCN, MSc, PhD, CM

[1]Department of Epidemiology, Biostatistics and Occupational Health, McGill University Montreal CA
[2]Department of Experimental Medicine, McGill University Montreal CA

Corresponding Author:
Vaidehee Lanke BSc
Department of Epidemiology, Biostatistics and Occupational Health, McGill University
2001 McGill College Ave
Montreal
CA

Abstract

Background: Medication adherence is crucial in managing chronic conditions, yet only 50% of chronically ill patients take medications as prescribed, leading to poor health outcomes. Mobile applications include a variety of possible features that have the potential to support and improve medication adherence.

Objective: The purpose of this systematic review was to evaluate the effectiveness of mobile applications in promoting medication adherence for patients managing chronic conditions.

Methods: MEDLINE (Ovid), Embase (Ovid) and Cochrane Central Register of Controlled Trials databases were searched for randomized controlled trails (RCTs) evaluating the effectiveness of mobile app interventions in improving medication adherence in patients with chronic conditions. Meta-analyses were performed on medication adherence scores, categorized by adherence measurement scale, and bias assessment was conducted using the Cochrane Risk of Bias tool.

Results: This review included 14 RCTs published between 2014 to 2022, with sample sizes between 57 to 412 participants and the length of interventions ranging from 30 days to 12 months. A range of patient populations were evaluated in the included studies, including those with Parkinson’s disease, coronary heart disease, psoriasis, and hypertension, with the latter being the most common. All 14 studies reported that app interventions improved medication adherence and 10 RCTs demonstrated statistically significant improvement in medication adherence. Three separate sets of meta-analyses and difference in difference analyses were conducted on studies, categorized by the 3 scales used in individual studies: the 8-item Morisky Medication Adherence Scale, 4-item Morisky Medication Adherence Scale and percentage adherence scale. Each set of analyses demonstrated that app-based interventions improved medication adherence.

Conclusions: From the studies included in this review, mobile apps, designed for a range of conditions with a range of features, can improve medication adherence and may be a tool to successfully manage chronic conditions. Clinical Trial: PROSPERO International Prospective Register of Systematic Reviews CRD42023488188

(JMIR Preprints 22/05/2024:60822)
DOI: https://doi.org/10.2196/preprints.60822

Preprint Settings

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Evaluating the effectiveness of mobile applications on medication adherence for chronic conditions: Systematic Review and Meta-analysis

Vaidehee Lanke[1], Kevin Trimm[2], Bettina Habib[1], Robyn Tamblyn[1]

[1]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec
[2]Department of Experimental Medicine, McGill University, Montreal, Quebec

Abstract

Background: Medication adherence is crucial in managing chronic conditions, yet only 50% of chronically ill patients take medications as prescribed, leading to poor health outcomes. Mobile applications include a variety of possible features that have the potential to support and improve medication adherence.

Objective: The purpose of this systematic review was to evaluate the effectiveness of mobile applications in promoting medication adherence for patients managing chronic conditions.

Methods: MEDLINE (Ovid), Embase (Ovid) and Cochrane Central Register of Controlled Trials databases were searched for randomized controlled trails (RCTs) evaluating the effectiveness of mobile app interventions in improving medication adherence in patients with chronic conditions. Meta-analyses were performed on medication adherence scores, categorized by adherence measurement scale, and bias assessment was conducted using the Cochrane Risk of Bias tool.

Results: This review included 14 RCTs published between 2014 to 2022, with sample sizes between 57 to 412 participants and the length of interventions ranging from 30 days to 12 months. A range of patient populations were evaluated in the included studies, including those with Parkinson's disease, coronary heart disease, psoriasis, and hypertension, with the latter being the most common. All 14 studies reported that app interventions improved medication adherence and 10 RCTs demonstrated statistically significant improvement in medication adherence. Three separate sets of meta-analyses and difference in difference analyses were conducted on studies, categorized by the 3 scales used in individual studies: the 8-item Morisky Medication Adherence Scale, 4-item Morisky Medication Adherence Scale and percentage adherence scale. Each set of analyses demonstrated that app-based interventions improved medication adherence.

Conclusions: From the studies included in this review, mobile apps, designed for a range of conditions with a range of features, can improve medication adherence and may be a tool to successfully manage chronic conditions.

Trial Registration: PROSPERO International Prospective Register of Systematic Reviews CRD42023488188

KEYWORDS
Medication adherence, systematic review, mobile apps, chronic conditions, disease management

Introduction

The increasing prevalence of chronic illnesses have become a significant public health issue [1,2]. Globally, 1 in 3 adults live with more than one chronic condition and in developed countries, the estimate is closer to 3 in 4 older adults. Significant health, patient and economic impacts are associated with chronic diseases and the prevalence of these diseases is increasing substantially [3,4]. While there are a range of types of and treatments for chronic diseases, a common challenge remains the management of complex medication regimens [1], which is needed to slow disease progression, prevent further disease, and reduce the risk of adverse health outcomes [5].

Medications are an important part in the management of chronic diseases [5]. However, the effectiveness of medications depends primarily upon adherence [5], defined by the WHO as “the extent to which a person’s behaviour – taking medications, following a diet and/or executing lifestyle changes – corresponds with agreed recommendations from a health care provider” [6]. While medication adherence is clinically essential for chronic disease management [7], the WHO estimates only 50% of chronically ill patients take medications as prescribed in developed countries [8]. The causes of medication non-adherence are complex and can include insufficient information about the illness and the use of medications, adverse medication effects, inability to pay for medication and poor memory [5,8]. The clinical and economic costs of medication non-adherence are immense; for example, in the United States poor adherence causes about 33% to 69% of all medication-related hospitalizations and results in an estimated $100 billion in healthcare costs per year [9,10].

Mobile apps have the potential to meaningfully support and increase medication adherence [9,11]. Amongst many available features, apps can consolidate and provide information about all a patient’s medications in one place [9]. Mobile apps are highly accessible; an app can be downloaded for little to no cost and by anyone with a smartphone seeking to use it [9]. Because smartphones have become so ubiquitous with daily life, an app can be an easily accessible, low-cost, information-based support for medication adherence [9]. There are over an estimated 97,000 mHealth apps available on various platforms, with the 5th largest category of mHeath apps aimed at medical condition management, including medication adherence [12]. However, while the number of apps directed at medication adherence is increasing, there is a need for more research on patient use of mobile apps to improve adherence, specific app features and their effect on medication adherence [9,11].

Previous systematic reviews on the impact of mobile apps on medication adherence have predominately covered either general adherence regardless of acute or chronic conditions or focused on one specific condition, such as asthma or cardiovascular disease. They also didn’t always include accompanying meta-analyses [12 – 18]. Additionally, since the number of medication adherence apps is rapidly increasing, and advanced technical features are now possible, a review of the most up to date evidence is warranted. Therefore, the objective of this systematic review was to investigate the effectiveness of mobile apps on medication adherence in randomized controlled trials of patients with chronic conditions.

Methods

This review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for reporting. The review protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews) database (CRD42023488188).

Search Strategy

MEDLINE (Ovid), Embase (Ovid) and CENTRAL (Cochrane Central Register of Controlled Trials) databases were searched from inception to September 2023. The search strategy was developed by identifying keywords from the research question and relevant studies. The key terms in the search strategy included mobile applications, smartphones, medication adherence and medication therapy management. The search strategy was first developed for MEDLINE and then adapted for the other databases (all search strategies are presented in Multimedia Appendix 1,2,3).

Studies of interest to this review were RCTs that investigated the effectiveness of stand-alone mobile applications in improving medication adherence for those with chronic conditions. The inclusion criteria used to select studies were:

- Participants aged 18 and older with a chronic disease such as cardiovascular diseases, hypertension, diabetes, etc.
- An intervention group that was randomized to receive a mobile app designed to promote medication adherence.
- A control group that was randomized to receive usual or standard of care that did not involve any mobile application.
- The outcome, medication adherence, had to be quantitively reported for both intervention and control

groups. Medication adherence could be reported through direct (ex. Measurement of level of drug, biological marker in the blood, etc) or indirect (pill counts, self-reporting, etc) measures.
- Articles must be published in English.

The exclusion criteria used to reject studies were:
- Participants had acute conditions like myocardial infraction, stroke, etc.
- The intervention was not based on a mobile app and only involved text messaging.
- The intervention had components beyond the mobile app, such as counselling with health professionals.
- The control group received an app-based intervention or another medication adherence intervention.
- The only outcome assessed was adherence to components other than medications, such as appointment attendance, laboratory work, etc.

A two-stage screening process was employed to select studies. All studies found from the three databases were compiled in Covidence, a systematic review management web-based platform [19]. Covidence identified and subsequently removed duplicate records. In the first stage of screening, two reviewers (VL and KT) independently reviewed the title and abstract of all studies and excluded studies based on the eligibility criteria. In the second stage of screening, two reviewers (VL and KT) independently read the full text of studies and selected studies to include in the review based on whether they met the eligibility criteria. To resolve disagreements or uncertainties regarding decisions about study inclusion or exclusion, the same two reviewers met to discuss and reach a consensus.

Data Extraction and Data Synthesis

Data was extracted by one reviewer (VL) using the Cochrane data collection form for interventions. Data extracted included evidence that studies met eligibility criteria, study design and setting, participant characteristics (age, sex, medical condition(s), severity of illness), intervention and control group intervention(s), features of the mobile apps, how medication adherence was measured and medication adherence results.

Medication adherence scores were compiled and grouped by measurement method (e.g. 8 item Morisky Medication Adherence Scale MMAS-8, percentage adherence, Hill Bone compliance scales, 4 item Morisky Medication Adherence Scale MMAS-4 and self-developed scale). Meta-analyses were conducted on the mean differences of medication adherence scores at the end of the intervention between intervention and control groups. If baseline medication adherence data were available, a difference in difference meta-analysis was conducted. The meta package in R was used to run a random effects model for each metanalysis and a forest plot was created to display the results.

Quality Assessment

Two reviewers (VL and BH) independently conducted the quality assessment on each included study using the Cochrane Risk of Bias form. The following seven domains were assessed: random sequence generation, allocation concealment, selective reporting, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and other source of bias. For each domain an assessment of low, high, or unclear risk of bias was made. To discuss the assessments and resolve disagreements, the same two reviewers met and reached a consensus on the bias assessment.

Results

Search Results

The search from the three databases identified 4365 studies, of which 1365 were duplicates and removed. The remaining 3000 studies were screened by title and abstract, with 2817 studies excluded because they didn't meet the eligibility criteria. Out of the 183 studies assessed by full text for inclusion in the review, 169 were excluded for reasons including non-app intervention, acute condition, study design and comparison group. Therefore, 14 studies were included in this review. The search and study selection process are summarized in a PRISMA flowchart (Figure 1).

Study Characteristics

The studies included in this review were published between 2014 to 2022. The sample size varied from 57 [20] to 412 participants [21] and the length of intervention varied from 30 days [20, 22] to 12 months [23]. Of the 14 studies, 13 were parallel 2-arm RCTs that compared a mobile app intervention for medication adherence with a control group [20 – 32]. The remaining study was a parallel 3-arm RCT that compared two versions of an app, one with basic and one with more advanced features, with a control intervention [33]. While both versions of the app met the inclusion criteria, the basic app was most like the other apps and therefore was used in this review. Table 1 contains details about the selected studies.

Table 1. Characteristics of the selected studies.

Source; Country	RCT design	Condition	Total No. of Participants Randomized	Average Age (years)	Length of intervention	Participants recruited from
Abu-El-Noor et al. [24]; Palestine	Parallel 2-arm	Hypertension	218	56.5	3 months	Primary healthcare centers
Bozorgi et al. [25]; Iran	Parallel 2-arm	Hypertension	120	51.8	8 weeks	Tertiary medical center
Guhl et al. [22]; USA	Parallel 2-arm	Atrial Fibrillation	120	72.1	30 days	Ambulatory facilities at a medical center
Hammonds et al. [20]; USA	Parallel 2-arm	Depression	57	20.6	30 days	Campus based advertisement, flyers, and university recruitment system
Horvath et al. [26]; USA	Parallel 2-arm	HIV ART	90	37.4	4 months	Grindr, flyers and palm cards at community-based organizations and clinics that served the targeted population.
Lakshminarayana et al. [27]; UK	Parallel 2-arm	Parkinson’s disease	215	60.3	16 weeks	Health centers
Márquez Contreras et al. [23]; Spain	Parallel 2-arm	Hypertension	154	57.4	12 months	Primary healthcare centers
Mira et al.[28]; Spain	Parallel 2-arm	Multiple chronic conditions	102	71.9	3 months	Health centers
Morawski et al. [21]; USA	Parallel 2-arm	Hypertension	412	52.05	12 weeks	Online patient communities, social media, pertinent apps, and targeted advertisement
Osahon et al. [29]; Nigeria	Parallel 2-arm	Glaucoma	200	52.1	2 months	Out-patient pharmacy
Santo et al. [33]; Australia	Parallel 3-arm	Coronary heart disease	166	57.9	3 months	Hospital
Svendsen et al. [30]; Denmark	Parallel 2-arm	Psoriasis	134	48.0	4 weeks	Outpatient clinic, advertisement
Teong et al. [31]; Malaysia	Parallel 2-arm	Hyperphosphatemia	74	48.3	12 weeks	Health centers
Torkabad et al. [32]; Iran	Parallel 2-arm	Hypertension	78	46.6	3 months	Research center

Intervention and Control Arms

Table 2 describes the intervention and control arms of the selected randomized controlled trials. While control interventions differed, none of them involved a mobile application. In 4 out of 14 studies, the control group received no form of alternative intervention [21,26,28,29]. In the remaining 10 studies, control groups received various alternative interventions [20, 22 – 25, 27,30 – 33] defined as the following: usual care in 3 studies [22,27,32]; participants were encouraged to continue their daily routine in 1 study [24]; medical history, physical examinations such as blood pressure and weight measurement and laboratory tests were taken, paraclinical services offered and drug treatments prescribed according to the JNC8 recommendations in 1 study [25]; instructed to continue to take medications prescribed by their physician in 1 study [20]; received a nutrition counseling sessions with a dietitian on hyperphosphatemia management and provided an illustrated booklet in 1 study [31], received once-daily topical medication in canisters with electronic monitors to record the day and time medication applied in 1 study [30]; received standard care as determined by their doctor including cardiovascular medication, lifestyle advice and referral to cardiac rehabilitation in 1 study [33]; received the usual intervention for high blood pressure including measurement of blood pressure very 6 months, annual control of therapeutic adherence, annual analysis and biannual electrocardiogram in 1 study [23].

Table 2. Description of selected studies intervention and control arms.

Source	Intervention arm	Control arm
Abu-El-Noor et al. [24]	Mobile app	Usual care: Participants continued their daily routine.
Bozorgi et al. [25]	Mobile app	Usual care: Participants' medical history was taken, underwent physical examinations (ex. measurement of blood pressure and weight) and laboratory tests, were offered paraclinical services tailored to the individuals' conditions, and provided drug treatments according to the JNC8 recommendations.
Guhl et al. [22]	Mobile app	Usual care.
Hammonds et al. [20]	Mobile app	Usual care: Participants were instructed to continue to take medications as prescribed by their physician.
Horvath et al. [26]	Mobile app	No treatment.
Lakshminarayana et al. [27]	Mobile app	Usual care: Participants, at the 16 weeks appointment, had regular outpatient clinical assessments conducted, including symptom and medication reviews.
Márquez Contreras et al. [23]	Mobile app	Usual care: Participants received usual care for high blood pressure including control every 6 months of blood pressure, annual control of therapeutic adherence, annual analysis, and biannual electrocardiogram.
Mira et al.[28]	Tablet app	No intervention.
Morawski et al. [21]	Mobile app	No intervention.
Osahon et al. [29]	Mobile app	No intervention.
Santo et al. [33]	1) Basic app: provided simple daily reminders to take medication at correct time. 2) Advanced app: additional interactive and customisable features including medication refill reminders, adherence statistics and interactive daily reminders, etc.	Usual care: Participants received standard care, determined by their doctors, and included cardiovascular medications, lifestyle advice and referral to cardiac rehabilitation.
Svendsen et al. [30]	Mobile app	Usual care: Participants received once-daily medication of Cal/BD cutaneous foam, delivered in canisters with dispensers containing an electronic monitor that registered the day and time the dispenser was used. The canister was replaced when empty.
Teong et al. [31]	Mobile app	Usual care: Participants received usual medical care from their hemodialysis centres. Participants also received, at baseline, one 30–40-minute nutrition counseling session with a dietitian on hyperphosphatemia management covering hyperphosphatemia, dialysis removal of phosphorus, sources of dietary phosphorus (ex. animal, plant, and inorganic) with examples of foods high and low in phosphorus content, and the use of phosphate binders. Topics were accessible to the participant in a 12-page illustrated booklet available in English, Malay, and Mandarin languages.
Torkabad et al. [32]	Mobile app	Usual care.

Participant Characteristics

A range of chronic conditions were considered in this review, the most prevalent being hypertension where 5 out of 14 of the included studies targeted the condition. The other chronic conditions studied were atrial fibrillation, depression, HIV ART, Parkinson’s disease, glaucoma, coronary heart disease, psoriasis, hyperphosphatemia, and a combination of chronic conditions. The mean age of participants ranged from 20.6 years (SD 4.3) [20] to 72.1 years (SD 9.1) [22]. Studies recruited participants from a range of facilities including primary healthcare centers [23], a tertiary medical center [25], ambulatory facilities at a medical center [22], campus based advertisements [20], the university recruitment system [20], flyers [20 – 26], Grindr [26], palm cards at community based organizations and clinics serving the targeted population [26], health centers [27,28,31], online patient communities [21], social media [21], pertinent apps [21], out-patient pharmacy [29], hospital [33], outpatient clinic [30], advertisement [21,30] and a research center [32].

Adherence App Features

Overall, the apps differed in the number and type of features they offered. The characteristics of each app are provided in Table 3. Out of 14 apps, 12 had explicit medication reminder functions [20,21,23 – 30, 32,33]. These apps sent medication reminder alerts at the appropriate time and according to the number of prescribed doses. Of the remaining two apps, one featured a smartphone-based relational agent that simulated face-to-face conversations and provided education regarding adherence [22] and the second app had educational video content, including on lifestyles and responsibilities of being a dialysis patient [31]. Some apps involved users’ caregivers by sending notifications to them about critical health information like blood pressure levels, sharing monitoring of adherence to prescriptions or granting access to a patient’s medication taking history, including receiving alerts when medication doses were missed [21,25,28].

Of the 14 apps examined, 9 were specifically designed for a certain condition [21 – 27,30,31], with 4 tailored for participants with hypertension [21,23 – 25]. Six of these condition-specific apps featured educational content about the condition and how to manage it [22,24 – 27,31], 4 allowed users to record and save information about their condition (e.g recording blood pressure) [21,23 – 25], 2 allowed users to track self-monitoring measures like sleep, exercise, itching and pain [27,30], and 2 generated reports of user-inputted information like colour coded graphs of how many doses were taken in the past and current weeks [26,27]. The remaining 5 apps were general medication reminder apps, not condition specific [20,28,29,32,33].

Out of the 14 apps, 3 employed unique user engagement. The first app used a smartphone-based relation agent, Tanya, that simulated in person conversations with a health coach and provided information on atrial fibrillation, its symptoms, monitoring, and adherence [22]. The second app employed interactive storytelling where users were invited to choose what happens next to a fictional character experiencing similar health conditions as them, as a means to provide users with specific medication adherence tips [26]. Lastly, an app meant to support patients with hyperphosphatemia had a personalized diet calculator function [31], where the app’s interactive database enabled meal calculations for elements such as energy, protein and the required phosphate binder dose, titrated to the phosphate content of foods eaten for each meal by the patient.

Table 3. Features of the mobile apps from the included studies.

Source	Condition	App Features
Abu-El-Noor et al. [24]	Hypertension	The mobile application sent daily medication reminder alarms, corresponding to the number and time of prescribed doses, provided daily educational messages about hypertension, treatment, diet therapy and complications and a monthly reminder message for the next follow-up appointment and allowed participants to record blood pressure readings to show healthcare providers.
Bozorgi et al. [25]	Hypertension	The Blood Pressure Management Application allowed participants to record and save blood pressure, plotted blood pressure in a chart, received feedback on recorded blood pressure, provided reminders for time of drug consumption, next appointment date and blood pressure measurement, provided information about healthy diet, weight loss plans and the nature, control and treatment of the disease, suggested supportive programs for smoking cessation, sent notifications to patient's family members of critical blood pressure levels, sent general and specific, based on patient characteristics, motivational messages and reminders about treatment adherence and allowed participants to save health information on a portal for physicians and researchers.
Guhl et al. [22]	Atrial Fibrillation	The mobile application featured Tanya, a smartphone-based relational agent, that simulated face-to-face conversations with a health coach using speech and animated behavior. Tanya provided health and atrial fibrillation education, symptoms, monitoring, adherence and

		problem-solving for users, according to participant needs and was tailored to each user (ex. used participant name during interactions). The app referred users to the Kardia regularly to encourage use, provided instructions on how to use the device and directed users to check rhythm concomitant with reporting symptoms.
Hammonds et al. [20]	Depression	The medication reminder app provided reminders for medications and information about medications (prescriptions, doses, etc) and participants indicated whether they had taken their medication by responding to a message received by the app.
Horvath et al. [26]	HIV ART	The APP+, a mobile app, had three main components. One, it provided users a homepage with five new pieces of HIV or ART adherence content each day. The content was intended to address the informational, motivational, and behavioral skills by discussing adherence side effects, adherence and mental health, motivational messages to adhere, adherence strategies, general issues of living with HIV and tips on how to use the APP+ mobile app. Second, a story of a fictional character living with HIV, uses substances and was sexually active was presented to the user to provide specific medication adherence tips. Each installment of the storyline was available every six hours after users' response and asked participants to choose options for how to proceed and involved scenarios such as mixing drugs and HIV medications, medication side effects and not having HIV medications easily available. Third, the "My Meds" tab allowed users to self-monitor medication adherence: reminders appeared for each scheduled dose, participants reported whether they took the dose or skipped it and generated colour coded graphs of how many doses were reported taken in the current and past weeks.
Lakshminarayana et al. [27]	Parkinson's disease	The Parkinson's Tracker App allowed participants to track ten self-monitoring measures on a 5-point scale including sleep, exercise, mood, energy, movement and suppleness, had a reminder system with alerts to help participants track medications, generated a data report of information entered by participant over trial period to aid follow-up appointment, had games to track physical responsiveness and cognition and provided information about Parkinson's disease from Parkinson's UK and the Cure Parkinson's Trust.
Márquez Contreras et al. [23]	Hypertension	AlerHTA, a mobile application, allowed participants to record personal data and doctor's guidance about prescribed treatment and posology, set recommended blood pressure levels as objectives and provided reminder alarms for medications or events and recorded results of blood pressure measurement.
Mira et al.[28]	Multiple chronic conditions	ALICE, a medication tablet-based self-management app, stored details and images of prescriptions, related medication instructions and doctors recommendations, had a customized system of reminders to alert patient when to take medication, along with information about medication (name, dose, time, warnings) and enabled monitoring of adherence to prescriptions and medical advice via wireless connection to the study monitoring system, the health care provider and a caregiver if authorized by patient. The app sent the complete list of prescriptions to caregivers, along with a summary of patient's adherence behavior.
Morawski et al. [21]	Hypertension	The Medisafe app allowed patients to enter medication lists manually along with the preferred time of administration or auto-populate medications through linkage with an existing medication record, provided alerts to remind time to take medications, generated weekly adherence reports, allowed patients to track blood pressure and other biometric measurements and allowed users to assign a "Medfriend" who was granted access to the patient's medication taking history, received alerts when doses are missed and could provide peer support.
Osahon et al. [29]	Glaucoma	medPlan was a medication reminder mobile application designed to promote medication adherence.
Santo et al. [33]	Coronary heart disease	The medication reminder app allowed users to store their current list of cardiovascular medications and set and receive daily reminders at the time medication is to be taken.
Svendsen et al. [30]	Psoriasis	The medication reminder app provided daily information on amount of treatment and number of treatment applications, allowed patients to rate their symptoms (ex. Itching, pain, inflammation, dryness, stress, etc) on an interval scale and provided daily treatment reminders.
Teong et al. [31]	Hyperphosphatemia	MyKidneyDiet-Phosphate Tracker, a mobile application in three languages, English, Malay, and Mandarin, provided 6 animated education videos on hyperphosphatemia, dialysis, phosphate binders, dietary phosphorus, lifestyles, and the responsibilities of a dialysis patient. The app also had an interactive food database of more than 500 foods commonly consumed by Hyperphosphatemia patients in Klang Valley, Malaysia and had a personalized diet calculator that calculated the required phosphate binder dose, titrated to the phosphate content of foods chosen for meals by the patient.
Torkabad et al. [32]	Hypertension	DaroYab 2.1.0, a mobile application, allowed users to record name of the drug, medication dose, precautions, and time (date, day, hour) medication is to be taken, reminded participants by voice alarm and text message to take medication and provided drug information on generic drugs, herbal medicines, and their side effects.

Assessment of Adherence

Thirteen of 14 studies used continuous medication adherence measures. These medication adherence measures can be categorized into 5 categories, Hill Bone compliance scale [24,25], percentage adherent [20,23,26,30], 8-item Morisky Medication Adherence Scale (MMAS-8) [21,27,32,33], 4-item Morisky Medication Adherence Scale (MMAS-4) [28,31] and a self-made scale [29] (medication adherence scales, measurements and results are presented in Multimedia Appendix 4).

The remaining study used dichotomous medication adherence measures. The first study measured medication adherence by asking participants “Do you sometimes forget to take [name of prescribed anticoagulant medication]?” and “Over the past two weeks, were there days that you did not take [name of prescribed anticoagulant medication]?” and counting the number of yes answers at baseline and at follow-up, between control and intervention [22].

Effect of Apps on Medication Adherence

All 14 studies reported that the app improved medication adherence [20 – 33]. Ten trials showed statistically significant improvement of medication adherence [21,23 – 27, 29,30,32,33]. In the remaining 4 trials, 2 studies did not demonstrate a significant difference between comparison groups [20,31], 1 study was unclear because significance was not mentioned [28] and in 1 study, the first medication adherence measure was significant, but the second measure was not [22].

Studies that assessed medication adherence with continuous measures and had the same scales were grouped together. Three separate meta-analyses, on the mean differences of medication adherence scores at the end of the intervention, were conducted on studies using the MMAS-8 [21,27,33], MMAS-4 [28,31] and percentage adherence [23,26] scales (Figure 2,3,4).

All three meta-analyses indicate that mobile apps increased medication adherence (MMAS-8 scale: mean difference 0.57, 95% CI 0.33 to 0.80, I^2 = 0%; MMAS-4 scale: mean difference 0.15, 95% CI -0.12 to 0.42, I^2 = 0%; percentage adherence scale: mean difference 18.85, 95% CI 2.17 to 35.53, I^2 = 63%). While the MMAS-8 and MMAS-4 scale meta-analysis had low statistical heterogeneity, the percentage adherence scale had moderate statistical heterogeneity.

To further compare the changes in outcome between the app intervention and control groups, two difference in difference meta-analyses were conducted on MMAS-8 [21,27,33] and MMAS-4 [28,31], since studies within these groups reported baseline medication adherence data (Figure 5,6). Both meta-analyses demonstrated that the app intervention increased medication adherence (MMAS-8 scale: mean difference 0.38, 95% CI 0.15 to 0.62, I^2 = 0%, MMAS-4 scale: mean difference 0.55, 95% CI 0.17 to 0.93, I^2 = 33%), with low heterogeneity.

There is variation in the statistical significance and heterogeneity (I^2 ranges from 0% to 63%) among the meta-analyses. These heterogeneity statistics should be cautiously interpreted because of the small number of studies used for each meta-analysis [34].

Risk of Bias

In total, 10 out of the 14 studies reported the random sequence generation adequately [21 – 23, 25 – 27, 30 – 33] and only 3 studies reported sufficient allocation concealment [27,32,33]. While these types of interventions are difficult to blind, only 3 studies had sufficient outcome assessment blinding [21,27,33]. Nine studies had low risk of incomplete outcome data [21,23,25,28 – 33] and 13 studies had low risk of selective outcome reporting [21 – 33]. Lastly, 7 trials had an unclear risk for other biases [21, 26 – 28, 31 – 33]. Figure 7 presents the risk of bias assessments for each included study.

Discussion

Principal Results

A systematic review of 14 RCTs was conducted to evaluate the effectiveness of mobile apps on medication adherence in managing chronic conditions [20 – 33]. While the number and type of features of each app differed, 12 had explicit medication reminder functions [20,21,23 – 30, 32,33]. Nine of the 14 apps examined were specifically designed for a chronic condition [21 – 27,30,31], with 4 of them being designed for participants with hypertension [21,23 – 25]. The remaining 5 apps were general medication reminder apps applied to chronic conditions [20,28,29,32,33].

Out of the 14 RCTs, 10 trials reported that app-based interventions significantly improved medication adherence [21,23 – 27,29,30,32,33]. Meta-analyses on the mean difference in medication adherence scores between intervention and control groups and difference in difference meta-analyses of medication adherence scores, for studies using the MMAS-8, MMAS-4, and percentage adherence scales, indicated that app-based interventions can improve medication adherence [21,23,26 – 28, 31,33], with varied statistical heterogeneity and significance.

The results of this review are consistent with previous studies in this field that investigated the use of mobile apps on medication adherence. Apps have been shown to be effective in increasing medication adherence in specific chronic conditions like cardiovascular disease [17] and hypertension [15], other chronic conditions [14] and in general [16,18].

Limitations

From the results of the Cochrane Risk of Bias assessment, we can infer that the studies used in this review are of moderate quality. The bias assessment highlights blinding of participants, personnel and outcome accessors and other biases, such as sample size, unvalidated medication adherence measures and recruitment techniques, as the main concerns.

While this review purposely focused on all chronic conditions, the diversity of studies made it challenging to pool data together. For example, the age of participants in included studies ranges from 20.6 years to 72.1 years [20,22]. However, there are differences in mobile health application use by age. Younger populations, commonly defined as under 35 years old, are shown to use apps more frequently than older populations who are not as comfortable using apps [35]. The differences in mobile app comfortability and use between different age groups may mean apps impact medication adherence differentially by age, which is not captured by this review.

Another limitation was the wide variation in control interventions. Out of 14 studies, in 4 trials the control group received no alternative interventions [21,26,28,29], while the remaining 10 control groups received some form of alternative interventions, including different elements from physical examinations to nutrition counseling sessions [20,22 – 25, 27, 30 – 33]. These differences between the control arm of trials make it difficult to compare results across studies because the comparison groups aren't the same. Furthermore, the length of intervention ranged from 30 days [20,22] to 12 months [23]. This range makes it difficult to comment on the optimal duration of app use to obtain increased medication adherence. However, since chronic conditions affect different populations and have various treatments, these differences were anticipated, thereby allowing for a review to summarize effectiveness of mobile apps in managing medication adherence for chronic conditions.

Since there is no standardized way to measure adherence [36 – 38], a range of methods were used by studies included in this review, such as self-reporting with different measurement scales, pill counts and electronic monitoring. This made it difficult to pool data together to perform one meta-analysis to obtain a single summary measure of medication adherence. Instead, multiple meta-analyses based on medication adherence measure type were conducted and each demonstrated that mobile apps are effective in promoting medication adherence.

Lastly, 11 out of 14 studies used self-reporting medication adherence measures [21,22,24 – 29,31 – 33]. These measures have different questions, responses and recall periods, can be subject to social desirability and memory biases and tend to overestimate adherence compared with other assessment methods [39]. Since most of the studies analyzed used self-reported measures, the accuracy of the adherence measures might be of concern. However, self-reported measures are the most commonly used instruments to measure medication adherence in the clinical and research settings and are preferred for their speed, efficiency and low resource cost [39,40].

Future Research

Future large-scale studies with standardized medication adherence measures are needed to understand the effectiveness of apps in improving medication adherence for chronic conditions, investigate the impact of specific app features and the time of app use required to establish change in medication adherence.

Conclusion

The 14 studies included in this review have demonstrated that mobile app use is associated with higher medication adherence levels, indicating that apps can improve medication adherence for chronic conditions. The apps investigated in this review had a range of features, from simple reminder notifications to symptom trackers to a smartphone-based relation agent, demonstrating that a variety of app features can support medication adherence. There are limitations to this review including range of effect size between studies, varied control arms and self-reported adherence measures. More evidence, including larger scale trials with standardized methods of measuring medication adherence, is needed to strongly conclude that mobile apps can significantly increase medication adherence for chronic conditions.

Authors' Contributions

VL conceptualized the review and VL and RT designed the review. VL and KT developed the search strategies and completed the initial screening and the full text screening. VL completed the data extraction and data analysis. VL and BH conducted the bias assessment on each included study. VL drafted the manuscript and all authors contributed to manuscript review, revision, and final approval.

Conflict of Interest

None declared.

Multimedia Appendix 1
Search strategy: Ovid MEDLINE (1946 to September 2023).

Multimedia Appendix 2
Search strategy: Ovid Embase (1946 to September 2023).

Multimedia Appendix 3
Search strategy: Cochrane Central Register of Controlled Trials (CENTRAL, on September 13, 2023).

Multimedia Appendix 4
Medication adherence scales, measurements, and results from selected studies.

References

1. Grady PA, Gough LL. Self-Management: A Comprehensive Approach to Management of Chronic Conditions. Am J Public Health. 2014;104(8).

2. Geda NR, Janzen B, Pahwa P. Chronic disease multimorbidity among the Canadian population: prevalence and associated lifestyle factors. Arch Public Health. 2021;79(1):60. doi:10.1186/s13690-021-00583-7

3. Hajat C, Stein E. The global burden of multiple chronic conditions: A narrative review. Prev Med Rep. 2018;12:284-293. doi:10.1016/j.pmedr.2018.10.008

4. Yach D, Hawkes C, Gould CL, Hofman KJ. The Global Burden of Chronic Diseases: Overcoming

Impediments to Prevention and Control. JAMA. 2004;291(21):2616. doi:10.1001/jama.291.21.2616

5. Williams A, Manias E, Walker R. Interventions to improve medication adherence in people with multiple chronic conditions: a systematic review. J Adv Nurs. 2008;63(2):132-143. doi:10.1111/j.1365-2648.2008.04656.x

6. Henriques MA, Costa MA, Cabrita J. Adherence and medication management by the elderly. J Clin Nurs. 2012;21(21-22):3096-3105. doi:10.1111/j.1365-2702.2012.04144.x

7. Brummel A, Carlson AM. Comprehensive Medication Management and Medication Adherence for Chronic Conditions. J Manag Care Spec Pharm. 2016;22(1):56-62. doi:10.18553/jmcp.2016.22.1.56

8. Kvarnström K, Westerholm A, Airaksinen M, Liira H. Factors Contributing to Medication Adherence in Patients with a Chronic Condition: A Scoping Review of Qualitative Research. Pharmaceutics. 2021;13(7):1100. doi:10.3390/pharmaceutics13071100

9. Dayer L, Heldenbrand S, Anderson P, Gubbins PO, Martin BC. Smartphone medication adherence apps: Potential benefits to patients and providers. J Am Pharm Assoc. 2013;53(2):172-181. doi:10.1331/JAPhA.2013.12202

10. Osterberg L. Adherence to Medication. N Engl J Med. Published online 2005.

11. Hartch CE, Dietrich MS, Lancaster BJ, Stolldorf DP, Mulvaney SA. Effects of a medication adherence app among medically underserved adults with chronic illness: a randomized controlled trial. J Behav Med. Published online December 21, 2023. doi:10.1007/s10865-023-00446-2

12. Ahmed I, Ahmad NS, Ali S, et al. Medication Adherence Apps: Review and Content Analysis. JMIR MHealth UHealth. 2018;6(3):e62. doi:10.2196/mhealth.6432

13. Adunlin G, Dong J, Reeves L, Ali A, Freeman MK. A Systematic Review of the Effectiveness of Text Message Reminders on Asthma Medication Adherence. Innov Pharm. 2018;9(3):5. doi:10.24926/iip.v9i3.1370

14. Peng Y, Wang H, Fang Q, et al. Effectiveness of Mobile Applications on Medication Adherence in Adults with Chronic Diseases: A Systematic Review and Meta-Analysis. J Manag Care Spec Pharm. 2020;26(4):550-561. doi:10.18553/jmcp.2020.26.4.550

15. Mikulski BS, Bellei EA, Biduski D, De Marchi ACB. Mobile Health Applications and Medication Adherence of Patients With Hypertension: A Systematic Review and Meta-Analysis. Am J Prev Med. 2022;62(4):626-634. doi:10.1016/j.amepre.2021.11.003

16. Armitage LC, Kassavou A, Sutton S. Do mobile device apps designed to support medication adherence demonstrate efficacy? A systematic review of randomised controlled trials, with meta-analysis. BMJ Open. 2020;10(1):e032045. doi:10.1136/bmjopen-2019-032045

17. Al-Arkee S, Mason J, Lane DA, et al. Mobile Apps to Improve Medication Adherence in Cardiovascular Disease: Systematic Review and Meta-analysis. J Med Internet Res. 2021;23(5):e24190. doi:10.2196/24190

18. Pérez-Jover V, Sala-González M, Guilabert M, Mira JJ. Mobile Apps for Increasing Treatment Adherence: Systematic Review. J Med Internet Res. 2019;21(6):e12505. doi:10.2196/12505

19. Cleo G, Scott AM, Islam F, Julien B, Beller E. Usability and acceptability of four systematic review automation software packages: a mixed method design. Syst Rev. 2019;8(1):145. doi:10.1186/s13643-019-1069-6

20. Hammonds T, Rickert K, Goldstein C, et al. Adherence to Antidepressant Medications: A Randomized Controlled Trial of Medication Reminding in College Students. J Am Coll Health. 2015;63(3):204-208. doi:10.1080/07448481.2014.975716

21. Morawski K, Ghazinouri R, Krumme A, et al. Association of a Smartphone Application With Medication Adherence and Blood Pressure Control: The MedISAFE-BP Randomized Clinical Trial. JAMA Intern Med. 2018;178(6):802. doi:10.1001/jamainternmed.2018.0447

22. Guhl E, Althouse AD, Pusateri AM, et al. The Atrial Fibrillation Health Literacy Information Technology Trial: Pilot Trial of a Mobile Health App for Atrial Fibrillation. JMIR Cardio. 2020;4(1):e17162. doi:10.2196/17162

23. Márquez Contreras E, Márquez Rivero S, Rodríguez García E, et al. Specific hypertension smartphone application to improve medication adherence in hypertension: a cluster-randomized trial. Curr Med Res Opin. 2019;35(1):167-173. doi:10.1080/03007995.2018.1549026

24. Abu-El-Noor NI, Aljeesh YI, Bottcher B, Abu-El-Noor MK. Impact of a mobile phone app on adherence to treatment regimens among hypertensive patients: A randomised clinical trial study. Eur J Cardiovasc Nurs. 2021;20(5):428-435. doi:10.1177/1474515120938235

25. Bozorgi A, Hosseini H, Eftekhar H, et al. The effect of the mobile "blood pressure management application" on hypertension self-management enhancement: a randomized controlled trial. Trials. 2021;22(1):413. doi:10.1186/s13063-021-05270-0

26. Horvath KJ, Lammert S, MacLehose RF, Danh T, Baker JV, Carrico AW. A Pilot Study of a Mobile App to Support HIV Antiretroviral Therapy Adherence Among Men Who Have Sex with Men Who Use Stimulants. AIDS Behav. 2019;23(11):3184-3198. doi:10.1007/s10461-019-02597-3

27. Lakshminarayana R, Wang D, Burn D, et al. Using a smartphone-based self-management platform to support medication adherence and clinical consultation in Parkinson's disease. Npj Park Dis. 2017;3(1):2. doi:10.1038/s41531-016-0003-z

28. Mira JJ, Navarro I, Botella F, et al. A Spanish Pillbox App for Elderly Patients Taking Multiple Medications: Randomized Controlled Trial. J Med Internet Res. 2014;16(4):e99. doi:10.2196/jmir.3269

29. Osahon PT, Mote LA, Ntaji VI. Assessment of the impact of medPlan®, a medication reminder mobile application, in glaucoma patients in Benin City, Nigeria. Trop J Pharm Res. 2021;19(12):2677-2682. doi:10.4314/tjpr.v19i12.28

30. Svendsen MT, Andersen F, Andersen KH, et al. A smartphone application supporting patients with psoriasis improves adherence to topical treatment: a randomized controlled trial. Br J Dermatol. 2018;179(5):1062-1071. doi:10.1111/bjd.16667

31. Teong LF, Khor BH, Ng HM, et al. Effectiveness of a Nutritional Mobile Application for Management of Hyperphosphatemia in Patients on Hemodialysis: A Multicenter Open-Label Randomized Clinical Trial. J Pers Med. 2022;12(6):961. doi:10.3390/jpm12060961

32. Mohammadi Torkabad S, Negahban Bonabi T, Heidari S. Effectiveness of smartphone-based medication reminder application on medication adherence of patients with essential hypertension: A clinical trial study. J Nurs Midwifery Sci. 2020;7(4):219. doi:10.4103/JNMS.JNMS_16_20

33. Santo K, Singleton A, Rogers K, et al. Medication reminder applications to improve adherence in coronary heart disease: a randomised clinical trial. Heart. 2019;105(4):323-329. doi:10.1136/heartjnl-2018-313479

34. Von Hippel PT. The heterogeneity statistic I2 can be biased in small meta-analyses. BMC Med Res

Methodol. 2015;15(1):35. doi:10.1186/s12874-015-0024-z

35. Wang C, Qi H. Influencing Factors of Acceptance and Use Behavior of Mobile Health Application Users: Systematic Review. Healthcare. 2021;9(3):357. doi:10.3390/healthcare9030357

36. Pednekar PP, Ágh T, Malmenäs M, et al. Methods for Measuring Multiple Medication Adherence: A Systematic Review–Report of the ISPOR Medication Adherence and Persistence Special Interest Group. Value Health. 2019;22(2):139-156. doi:10.1016/j.jval.2018.08.006

37. Kardas P, Aguilar-Palacio I, Almada M, et al. The Need to Develop Standard Measures of Patient Adherence for Big Data: Viewpoint. J Med Internet Res. 2020;22(8):e18150. doi:10.2196/18150

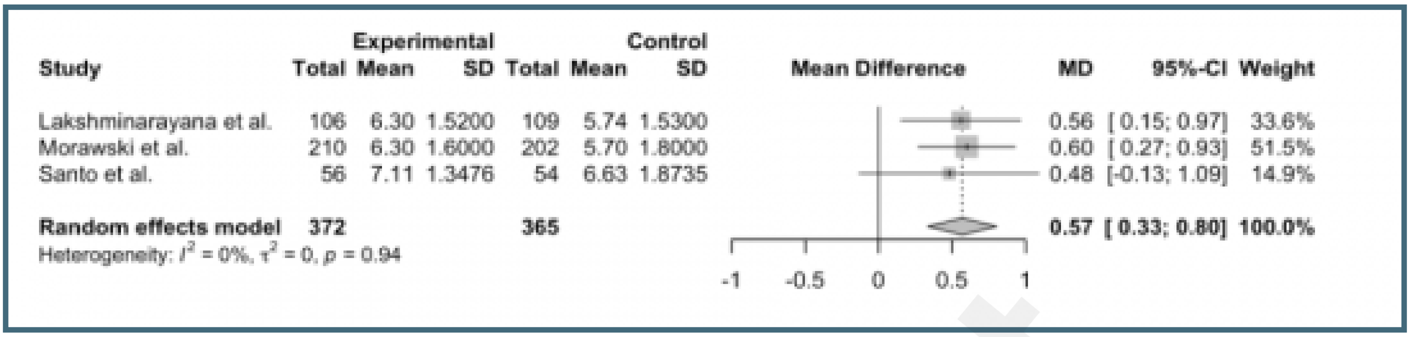
38. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Rep. Published online April 22, 2019. doi:10.15386/mpr-1201

39. Stirratt MJ, Dunbar-Jacob J, Crane HM, et al. Self-report measures of medication adherence behavior: recommendations on optimal use. Transl Behav Med. 2015;5(4):470-482. doi:10.1007/s13142-015-0315-2

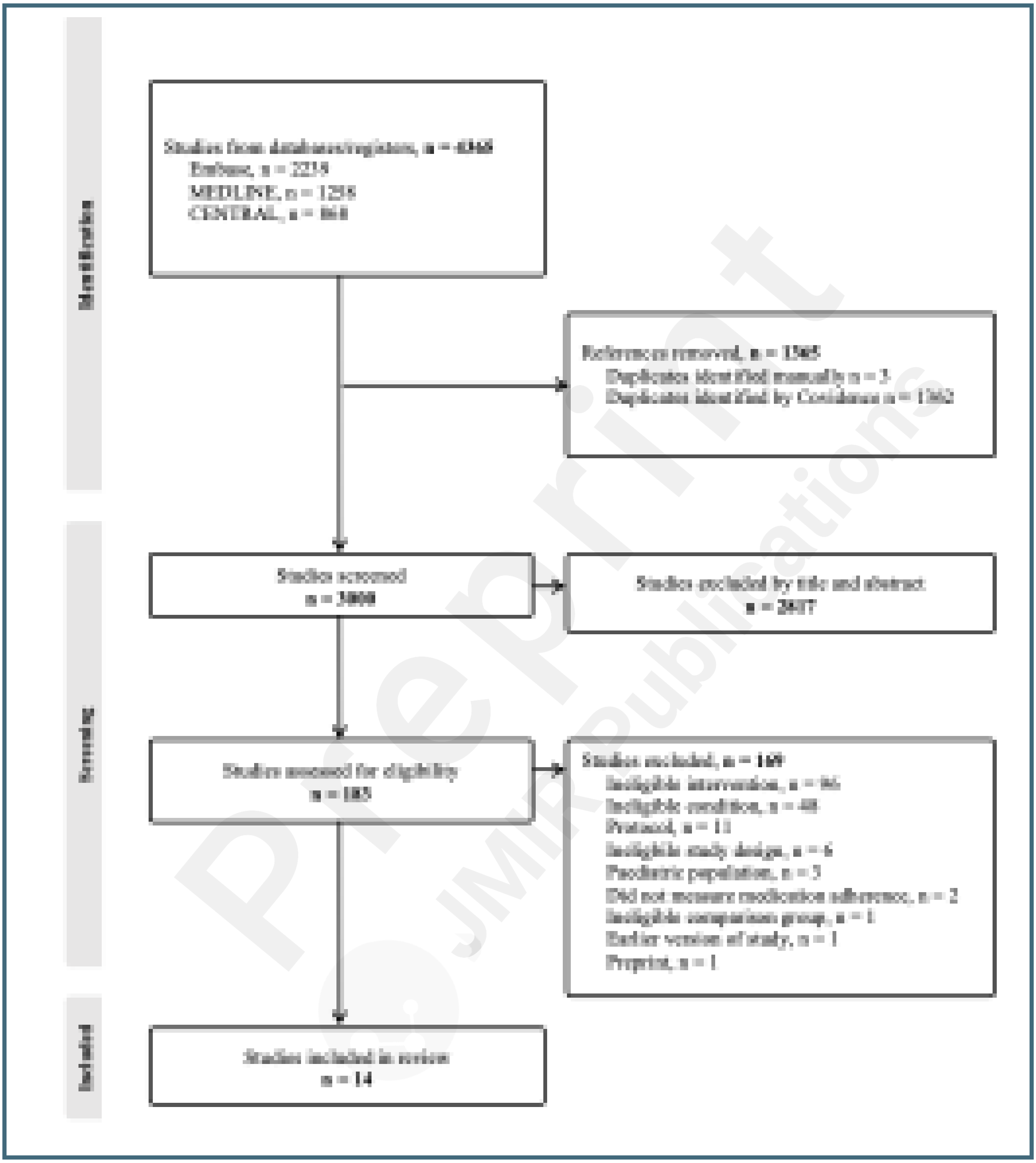
40. Khoiry QA, Alfian SD, Van Boven JFM, Abdulah R. Self-reported medication adherence instruments and their applicability in low-middle income countries: a scoping review. Front Public Health. 2023;11:1104510. doi:10.3389/fpubh.2023.1104510

Supplementary Files

Untitled.

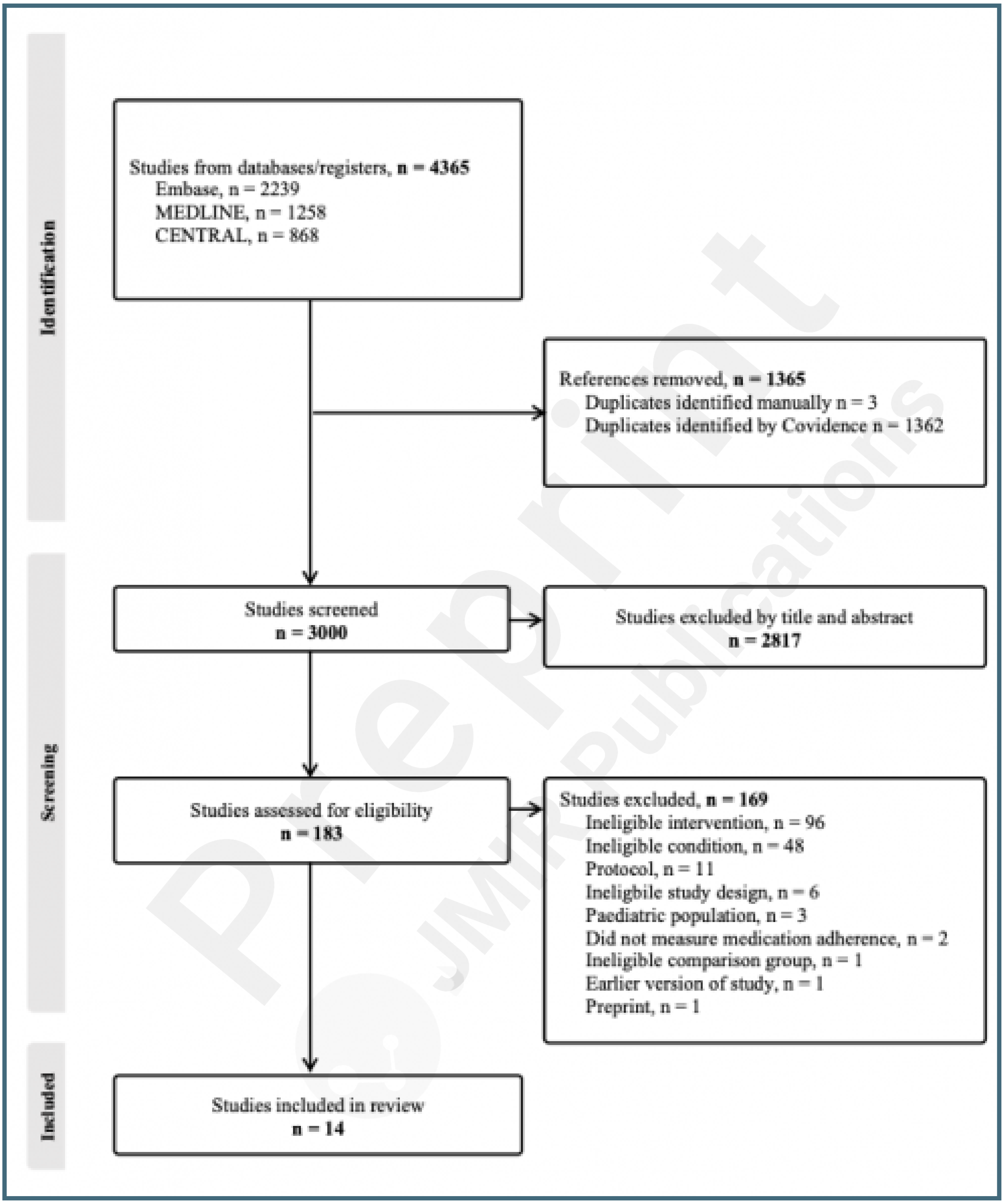

Experimental
Control
Study
Total Mean SD Total Mean SD
Mean Difference
MD 95%-CI Weight
Lakshminarayana et al. 106 6.30 1.5200 109 5.74 1.5300
Morawski et al. 210 6.30 1.6000 202 5.70 1.8000
Santo et al. 56 7.11 1.3476 54 6.63 1.8735
0.56 [0.15; 0.97] 33.6%
0.60 [0.27; 0.93] 51.5%
0.48 [-0.13; 1.09] 14.9%
Random effects model 372 365
0.57 [0.33; 0.80] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.94
-1 -0.5 0 0.5 1

Untitled.

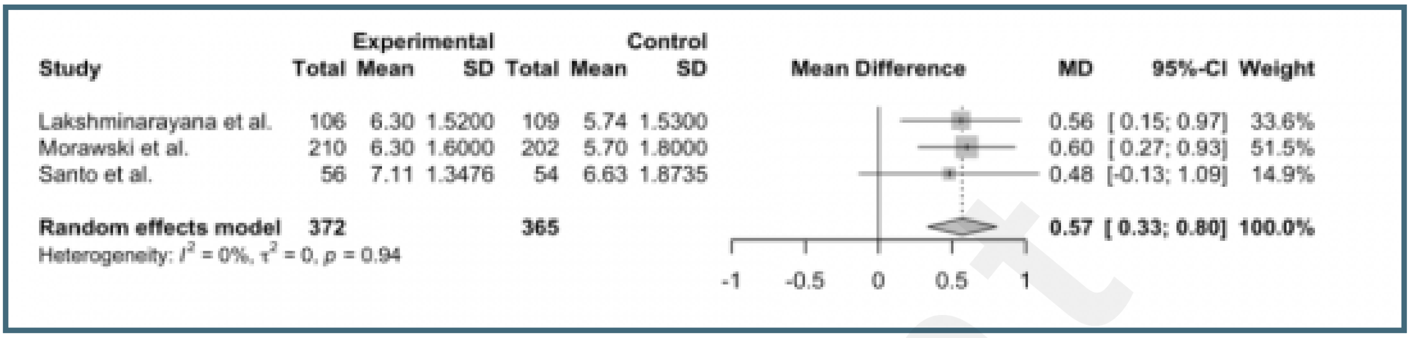

References removed, n = 1505
Duplicates identified manually n = 3
Duplicates identified by Covidence n = 1502
Studies screened
n = 3000
Studies excluded by title and abstract
n = 2817
Studies assessed for eligibility
n = 183
Studies excluded, n = 169
Ineligible intervention, n = 96
Ineligible condition, n = 48
Protocol, n = 11
Ineligible study design, n = 6
Paediatric population, n = 3
Did not measure medication adherence, n = 2
Ineligible comparison group, n = 1
Earlier version of study, n = 1
Preprint, n = 1
Studies included in review
n = 14
Included

Figures

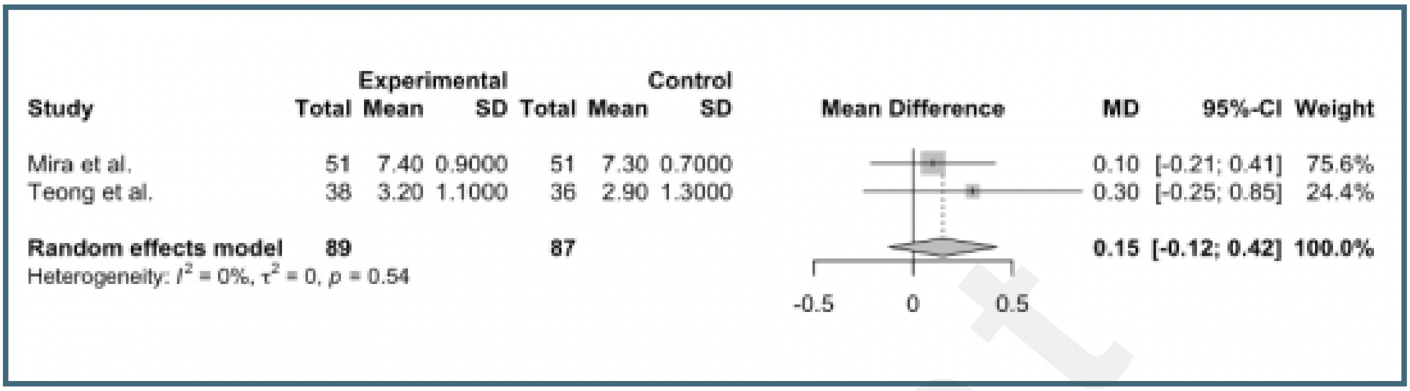
PRISMA flow diagram summarizing study search and selection process.



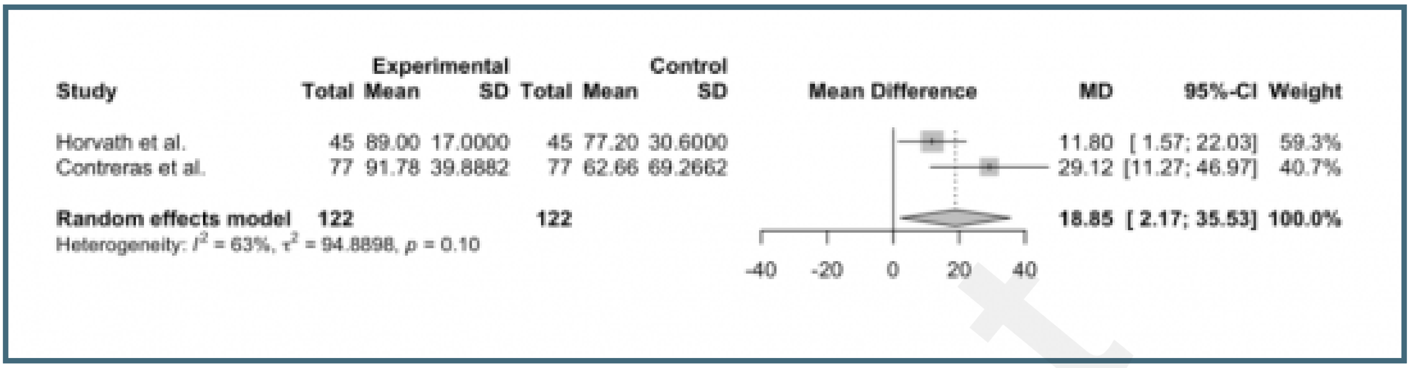
Meta-analysis results of the effect of app interventions on medication adherence for studies that used the MMAS-8 scale. The grey boxes and black lines represent mean differences and 95% CIs respectively. The grey diamond represents the combined mean difference estimate for all studies, its width signifying 95% CI bounds.



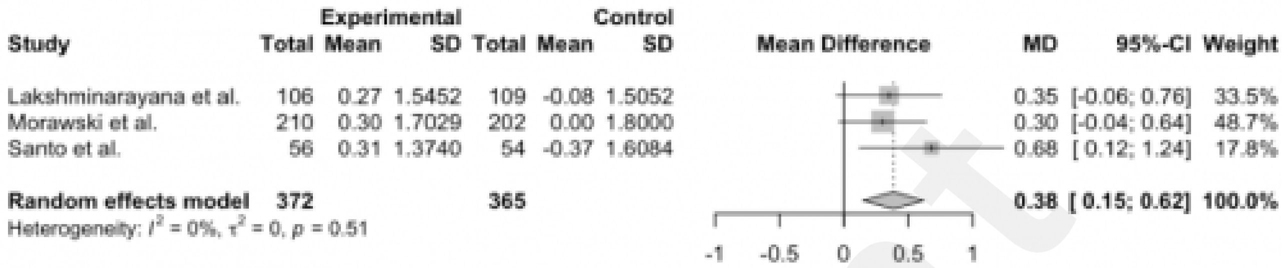
Meta-analysis results of the effect of app interventions on medication adherence for studies that used the MMAS-4 scale.



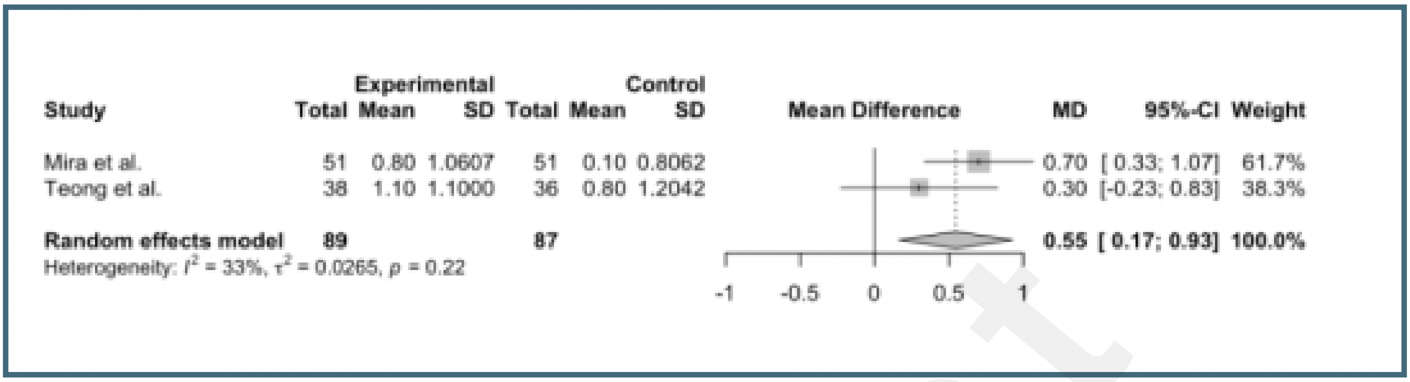
Meta-analysis results of the effect of app interventions on medication adherence for studies that used percentage adherence scale.



Difference in difference meta-analysis results of the effect of app interventions on medication adherence for studies that used the MMAS-8 scale. The grey boxes and black lines represent mean differences and 95% Cis respectively. The grey diamond represents the combined mean difference estimate for all studies, its width signifying 95% CI bounds.

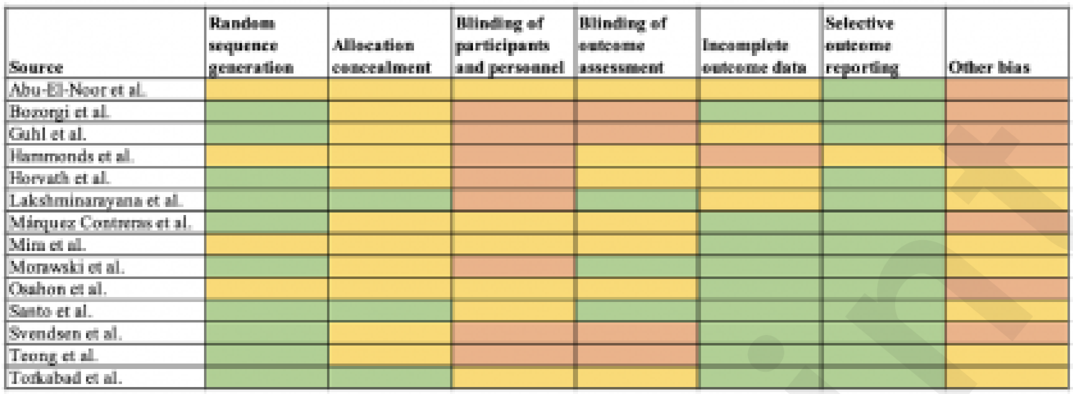


Difference in difference meta-analysis results of the effect of app interventions on medication adherence for studies that used the MMAS-4 scale.



Risk of bias assessment on 7 factors for each trial. By colour, green is low risk of bias, red is high risk of bias and yellow is unclear risk of bias.

Figure 4. Risk of bias assessment on 7 factors for each trial. By colour, green is low risk of bias, red is high risk of bias and yellow is unclear risk of bias.



Source	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other bias
Abu-El-Noor et al.							
Bozorgi et al.							
Guhl et al.							
Hammonds et al.							
Horvath et al.							
Lakshminarayana et al.							
Márquez Contreras et al.							
Mira et al.							
Morawski et al.							
Osahon et al.							
Santo et al.							
Svendsen et al.							
Teong et al.							
Torkabad et al.							

Multimedia Appendixes

Search strategy: Ovid MEDLINE (1946 to September 2023).
URL: http://asset.jmir.pub/assets/94d9f43413991256ddb70747ebcc8b8d.doc

Search strategy: Ovid Embase (1946 to September 2023).
URL: http://asset.jmir.pub/assets/0b6af9d732e0020d666c6bc32cba1be1.doc

Search strategy: Cochrane Central Register of Controlled Trials (CENTRAL, on September 13, 2023).
URL: http://asset.jmir.pub/assets/2f362574d49d658f5ed7f453b91ceef7.doc

Medication adherence scales, measurements, and results from selected studies.
URL: http://asset.jmir.pub/assets/7d511a5e498481cd63c21b1acc9004c5.doc