Effectiveness, acceptability and usefulness of mobile applications for cardiovascular disease self-management: systematic review with meta-synthesis of quantitative and qualitative data.

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Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. GMC is supported by a National Heart Foundation Health Professional Scholarship (101544). JR is funded by a Career Development and Future Leader Fellowship co-funded by the National Health and Medical Research Council and the National Heart Foundation (APP1061793).

Competing interests: None.

Ethical approval: Not required.

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Word count (including references): 7662

ABSTRACT

Background: Mobile technologies are innovative, scalable approaches to reducing risk of cardiovascular disease (CVD) but evidence related to effectiveness and acceptability remains limited. We aimed to explore the effectiveness, acceptability and usefulness of mobile applications (apps) for CVD self-management and risk factor control.

Design: Systematic review with meta-synthesis of quantitative and qualitative data.

Methods: Comprehensive search of multiple databases (Medline, Embase, CINAHL, SCOPUS, and Cochrane CENTRAL) and grey literature. Studies were included if the intervention was primarily an app aimed at improving at least two lifestyle behaviours in adults with CVD. Meta-synthesis of quantitative and qualitative data was performed to review and evaluate findings.

Results: Ten studies of varying designs including 607 patients from 5 countries were included. Interventions targeted hypertension, heart failure, stroke and cardiac rehabilitation populations. Factors that improved among app users were rehospitalisation rates, disease-specific knowledge, quality of life, psychosocial well-being, blood pressure, body mass index, waist circumference, cholesterol, and exercise capacity. Improved physical activity, medication adherence, and smoking cessation were also characteristic of app users. Appealing app features included tracking healthy behaviours, self-monitoring, , disease education, and personalised, customisable content. Small samples, short duration, and selection bias were noted limitations across some studies, as was the relatively low overall scientific quality of evidence.

Conclusions: Multiple behaviours and CVD risk factors appear modifiable in the shorter term with use of mobile apps. Evidence for effectiveness requires larger, controlled studies of longer duration, with emphasis on process evaluation data to better understand important system- and patient-level characteristics.

PROSPERO Registration Number: CRD42017068482

Abstract word count: 249

KEYWORDS: cardiovascular disease, mobile applications, mHealth, lifestyle behaviour, systematic review

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide, accounting for approximately one third of deaths.[1] This burden is borne unequally, with most deaths occurring in low- and middle-income countries[2] despite a trend in higher income countries towards lower age-related CVD mortality over recent decades.[1] As the major contributor to the broader burden of non-communicable disease prevalence, reducing the incidence, morbidity and mortality of CVD is a key global health priority.[3] In parallel, the World Heart Federation has initiated a '25 by 25' campaign to reduce premature mortality from CVD by 25% by 2025.[4] Central to these imperatives are innovative, cost-effective and scalable approaches that reduce behavioural and metabolic influences on CVD risk, for example physical inactivity, smoking, overuse of sodium, and medication non-adherence.[1] Long term success with such lifestyle-related decision-making is multifactorial. In modern society, this likely includes the array of personal mobile-based technologies aiming to support patients living with CVD.[5-8]

The prevalence of mobile technology offers an obvious delivery medium for expanding the reach of secondary prevention. Smartphone ownership among adults was reported in 2015 at 60% and 72% in Europe and the United States, respectively,[9] far exceeding the global median of 45%. Worth noting is that the usage rate of 37% across emerging/developing economies,[9] for example in sub-Saharan Africa, South Asia and parts of Central America, lessens the reach of this potentially beneficial technology. In 2016, mobile health app downloads were estimated at 3.2 billion.[10] Recent figures suggest that mobile devices (smartphones and tablets) account for 49% of Internet traffic,[10] underscoring their convenience and practicality. Mobile technologies are increasingly recognised for other benefits, such as bridging time and distance barriers to clinical oversight, and expanding accessibility to care that is traditionally delivered face-to face, thereby reducing evidence-practice gaps.[11, 12] Recent systematic reviews have

studied the effectiveness of multi-component technology-based interventions in CVD prevention. Typically these comprise two or more of: interactive web sites, email, tele-monitoring, video, one- or two-way text messaging, phone-based applications (apps), and non-phone devices for data acquisition prior to wireless upload to a central monitoring hub.[13-15] Other reviews have targeted a single delivery format, for example web sites[16] or text messaging[17]; or have targeted a population with a specific diagnosis, for example heart failure[18] or coronary heart disease.[19] Multi-component interventions often incur greater resource needs, especially if linked into a centralised clinical hub. On the other hand, text-messaging alone under-utilises the range of interactive capabilities within modern mobile devices. The interactive traits that patients feel are essential may not only be those that facilitate contact with health professionals. At present, there is a lack of qualitative research data about which mobile app features and functions are engaging and interesting over time for the goal of changing multiple behaviours.[13] Moreover, determining patient groups for whom the content or other components require modification in order to be more effective requires further investigation.[19]

Overall, more research about mobile apps is needed to address the gaps emerging from recent reviews in which mobile-based apps are under-represented. Therefore, the aim of this study was to review the potential effectiveness, acceptability and usefulness of patient-directed applications for CVD self- management that are delivered and used primarily on a smartphone or tablet device. Of interest is: (1) whether chiefly standalone apps with low reliance on day-to-day clinician involvement can improve risk factor control and disease self-care; and (2) patients' perspectives on preferred app features and perceived utility for supporting treatment adherence and healthier lifestyle behaviour.

METHODS

Study Design

Systematic review with meta-synthesis of quantitative and qualitative data. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[20]

Search strategy

A comprehensive database search for randomised and non-randomised studies to 29th April 2017 was carried out in the Cochrane Central Registry of Controlled Trials (CENTRAL), Medline, Embase, CINAHL and SCOPUS. Relevant studies were also sought from two trial registers: www.clinicaltrials.gov and www.anzctr.org.au (Australian New Zealand Clinical Trials Registry). Reference lists of other reviews and meta-analyses were manually searched to find additional studies. The following terms were searched: mobile communication, mobile applications, cell phone, mobile health, mHealth, mobile app, internet app, web app, smart phone, iPhone, android, cardiovascular disease. The full search strategy is provided as a supplementary file. No language or date restrictions were applied.. Where possible, authors were contacted to obtain full text publications of relevant abstracts; studies published only as an abstract were excluded.

Study inclusion criteria

Eligible studies were those which assessed an intervention comprising a patient-directed app primarily delivered and used on a smartphone or tablet device, with the aim of: (1) improving adoption and/or maintenance of at least two lifestyle behaviours, such as medication adherence, increased physical activity, or smoking cessation; (2) improving treatment adherence and disease self-care behaviour, for example through use of interactive self-monitoring and

information resources. The focus was mobile applications as either a stand-alone intervention or as the central component for the intervention. Studies were excluded if the intervention was one- or two-way short message service only; video conferencing; real-time, remote monitoring (telehealth); telephone calls between patient and health professional; a web site alone; or recording and uploading measurements alone.

The target population was adults aged eighteen years or older with diagnosed CVD requiring pharmacologic and non-pharmacologic treatment and risk factor reduction to prevent disease recurrence or complications (termed secondary prevention).[21]. Primary prevention populations were excluded. Both quantitative and qualitative data were sought for evaluation and synthesis; therefore, randomised, non-randomised and qualitative-only study designs were accepted. No restrictions on sample size or follow-up duration were applied; however, studies were excluded if the app intervention was not used by participants in their home setting.

Quantitative outcomes of interest included the following measures, where available at baseline and last reported follow up: blood pressure (BP), weight, body mass index (BMI), exercise capacity, physical activity (PA) level, dietary improvement, smoking cessation, medication adherence, participation in cardiac rehabilitation, change in quality of life (QoL), glycated haemoglobin (HbA1c), total and low-density lipoprotein (LDL) cholesterol, rehospitalisation, cardiovascular event rates, and app usage metrics. Qualitative evaluation outcomes of interest were patient perspectives on utility, preferences, benefits and drawbacks of app interventions.

Study selection process

Titles and/or abstracts of all studies identified using the search strategy and additional sources were screened by one reviewer (GMC) to identify those that potentially met the inclusion

criteria. The full texts of relevant studies were obtained and independently assessed for inclusion or exclusion by two reviewers (GMC and JM). Disagreements about eligibility of studies were resolved through discussion between reviewers or by a third reviewer (JR) until consensus was reached.

Assessment of study quality

The quality appraisal of included studies was undertaken using one of three instruments, depending on study design. GMC assessed each study; LN appraised 30% of studies to ensure assessments were consistent. Using the Cochrane Risk of Bias Tool,[22] the main sources of systematic bias in randomised trials were assessed: selection bias, performance bias, detection bias, attrition bias and reporting bias. Before and after studies were assessed (but not excluded) using the nine-item Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental Studies (non-randomised experimental studies).[23] Notably, five of the ten domains in this tool concern a comparison group, which was absent in three of the four included studies of this type. Qualitative/observational studies were assessed using the Critical Appraisal Skills Programme (CASP) tool.[24]

Data extraction, synthesis and analysis

Meta-analysis was not possible due to the variation in study designs and/or insufficient data within studies. Therefore, a narrative synthesis was undertaken after the results of each individual study were analysed and summarised. A customised data extraction form was used to extract data for assessment of study quality and evidence synthesis. One author (GMC) extracted the following details from each included study: location and setting, methodology, participant characteristics, description of the intervention and comparator, duration of follow-up, outcome data, and methodological quality. A second author (LN) verified a random

selection of extracted details. Quantitative findings were categorised as follows into nine outcome areas from the range of findings reported in the studies: hospital readmissions, QoL, psychosocial wellbeing, CVD risk factors, medication adherence, cardiac rehabilitation uptake, adherence and motivation, and process evaluation measures. Not all studies reported data for all outcomes.

RESULTS

Study selection and characteristics

A total of 1354 records were screened for possible inclusion and 101 full-text manuscripts were reviewed for eligibility (Figure 1). All reviewed manuscripts were in English. One abstract published in English was from a non-English journal and the full text was unobtainable. Ten papers representing nine studies from five countries (655 recruited participants) were eventually included (Table 1). Two studies reported different data from the same study cohort, with one detailing quantitative results[25] and the other describing a qualitative evaluation.[26] CVD populations targeted in each of the included studies were as follows: cardiac rehabilitation or acute myocardial infarction (AMI) or acute coronary syndromes (ACS);[27-30] hypertension;[25] heart failure (HF);[31] stroke;[32] coronary heart disease (CHD) or HF;[33] hypertension, angina or AMI.[34] The 10 included studies were of different designs: three uncontrolled before-after studies[25, 32, 33]; one controlled before-after study;[30] three RCTs;[28, 29, 31] two observational pilot studies;[19, 34] and one qualitative-only study.[26] Follow-up duration ranged from two weeks to six months; participant drop-out was high in several studies. Mean participant age across nine studies was 59.8±6.9 years and one study[34] did not report participant age. All studies reported sex of the participants and overall 27% were female. Although the number of participants recruited across all studies was 655 (sample size range 10-166), baseline data indicated there were 607 participants at this time-point due to withdrawals prior to baseline

assessments.

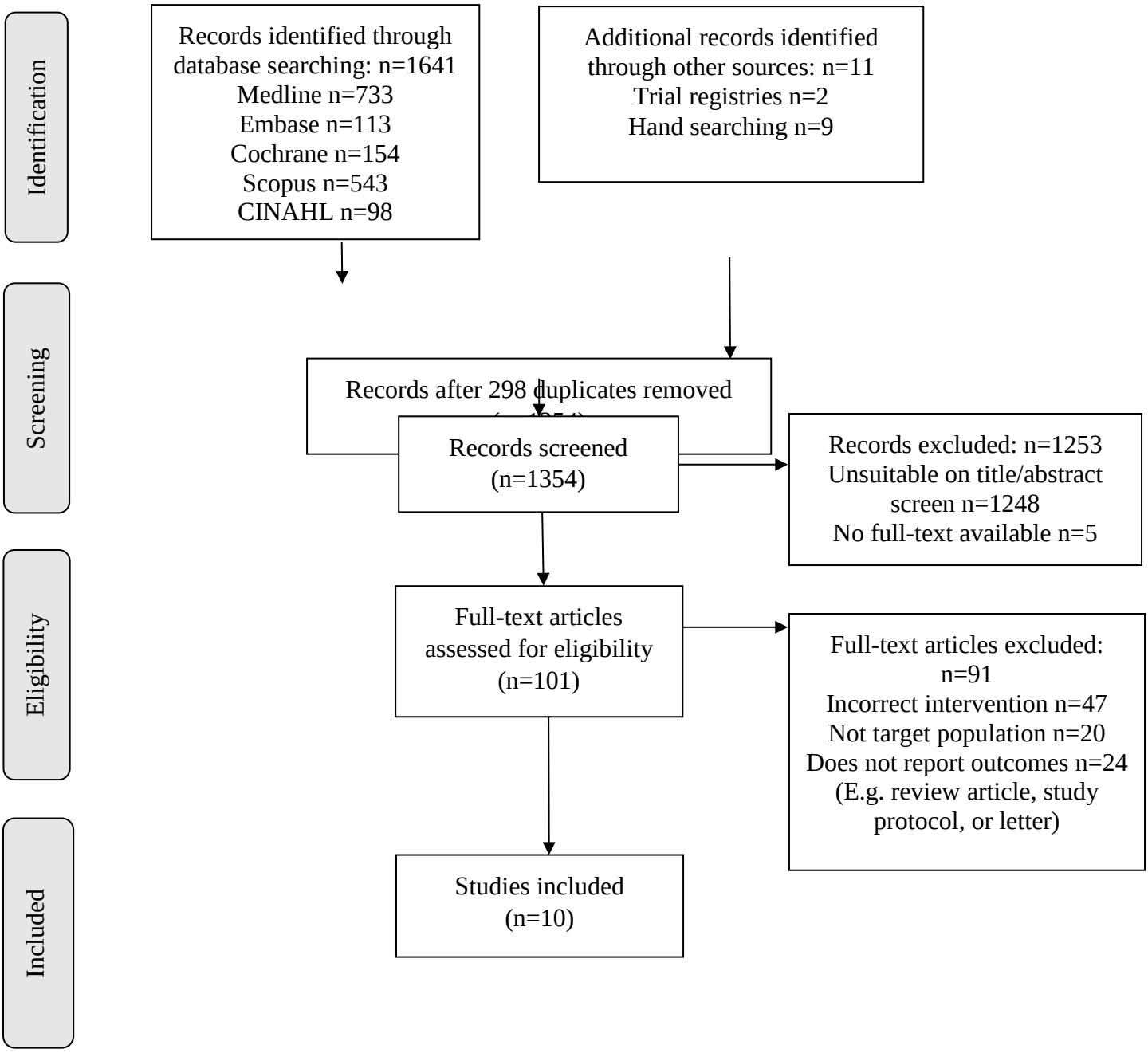

Figure 1. Flow diagram of included studies

Study quality

Methodological quality varied within the different study designs included in this review (supplementary file). In the three RCTs, assessed using the Cochrane Risk of Bias tool,[22] blinding of participants was impossible due to the nature of the interventions and blinding of outcome assessors was unclear. Only one RCT described random sequence generation and allocation concealment procedures.[29] Attrition bias was assessed as high in one study[29] and low in two studies.[28, 31] Reporting bias across the three trials was assessed as unclear,[28] low,[31] and high.[29]

The four non-randomised before-after studies were appraised against the Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental Studies (non-randomised experimental studies).[23] Three studies[25, 32, 33] had no comparison/control group so the appraisal domains related to between-group comparisons were least well fulfilled. No studies reported multiple pre-exposure measurements of the outcomes but two studies reported multiple post-exposure measurements.[25, 32] The domain of follow up completion, description and analysis was most fully met by one study.[25] All four studies described appropriate statistical measures.

Three qualitative studies[26, 27, 34] were evaluated using the CASP instrument.[24] Each one met four of the ten quality domains. The domains of recruitment strategy and consent were unclear in one study,[34] and in all three studies the relationship between researcher and participants was deemed uncertain. The domains of data analysis and statement of findings were partially fulfilled across the three studies.

Table 1: Characteristics of included studies

Author, year & country	CVD population; treatment setting	Inclusion criteria	Sample size	Mean age range)	% Female	Key components of intervention (and comparator where applicable) Operating system and development	Study design; duration of follow-up
*Bengtsson et al. 2016 Sweden	HT Primary health care	Medically treated for HT; age >30; Internet access on mobile phone; Swedish literacy.	50	59 (33-81)	48	Interactive Self-Management Support System: self-reporting BP, pulse, symptoms, side effects, medication intake and lifestyle/well-being support; graphical data displayed on companion web site. Timing of reminders determined by patient. App operating system: not specified App development: researchers, patients and clinicians involved but details not described in this paper; communication platform developed by Circadian Questions 21st Century Mobile.	Uncontrolled before-after study. 8 weeks

Dithmer et al. 2016 Denmark	MI/angina/ HT Outpatients	Not specified - stated as 'heart patients'.	10	48-89 (mean not reported)	40	Tablet-based Heart Game built for Android OS; aimed as adjunct to rehabilitation; patient and team mate complete challenges related to healthy lifestyle; accumulate points; leader board, medals, comparison of scores across teams. App operating system: Android App development: prototype built using data from workshops, field observation and interviews with patients and nurses	Single group observational pilot; no before-study data. 2 weeks
Forman et al. 2014 USA	CR Outpatients	Currently enrolled in or recently completed phase II CR; User of iPhone, iPad or iPod; English-speaking.	26	59 (43-76)	23	Heart Coach mobile app; daily task list based on behavioural goals and educational CR content. Text and video educational material; prompts were both standard (e.g. walking) and personalised (e.g. medication); activity tracking, biometric screening and surveys. Monitoring of task completion by CR staff. Feedback messages were in-app and from CR staff.	Single group observational pilot; no before-study data. 30 days

						App operating system: iOS for the study; now available on Android devices. App development: app built on 'Wellframe' (Boston, MA) platform using content from the hospital CR protocol and then verified by CR providers	
Hägglund et al. 2015 Sweden	HF Outpatients (readmitted patients could keep using app).	Hospitalised for HF; discharged to primary care; no participation in nurse-led HF clinic. Treated with regular dose or PRN diuretic.	72	75 (range not reported)	32	Intervention: Home Intervention System comprised of tablet wirelessly connected to weigh scales; also, HF info & lifestyle advice. Activities: monitor weight and symptoms, self-titrate diuretic dose, complete daily tasks; view graphical displays, visual analogue scale for evaluating perceived health status. Clinic and tech support contact details. Control: HF info and clinic phone number. App operating system: not specified	Multicentre RCT. 3 months

						App development: not described; software provided by Care Ligo Optilogg Systems.	
*Hallberg et al. 2016 Sweden	HT Primary health care	Medically treated for HT; age >30; Internet access on mobile phone; Swedish literacy.	49	60 (37-81)	47	Interactive Self-Management Support System: self-reporting BP, pulse, symptoms, side effects, medication intake and lifestyle/well-being support; Companion web site offers graphed feedback of data. Timing of reminders determined by patient. App operating system: not specified App development: researchers, patients and clinicians involved but details not described in this paper; communication platform developed by Circadian Questions 21st Century Mobile.	Qualitative. Single time-point
Johnston et al. 2016 Sweden	MI Outpatients	Diagnosis of MI; prescribed ticagrelor during hospitalisation and pre-	166	58 (range not reported)	19	In addition to standard CR: Intervention: web-based smartphone app with extended drug adherence e-diary plus secondary prevention education modules on exercise, weight and smoking cessation; self-entry of BP, LDL-C,	Multicentre RCT. 6 months

		randomisation; >18 years; access to & skill with a smartphone; Swedish literacy; willing to attend follow-up visits.				BGL data; personalised educational in-app messages; traffic light system for feedback about adherence status. Control: simplified drug adherence e-diary alone. App operating system: not specified App development: AstraZeneca and ScientificMed Tech.	
Layton et al. 2014 USA	HF/CAD Outpatients	Inpatient but eligible for discharge within 3 days.	16 HF=6 CAD=10	55 (26-84)	25	Smartphone (iOS) app to supplement outpatient discharge instructions. Daily 'to-do' list with educational info, appointment & medication reminders, PA prompts consistent with CR program, symptom monitoring; weekly phone survey with study personnel re rehospitalisation, symptoms, outpatient program use. Study team monitors uploaded biometric data and sends 1-2 messages/week. App operating system: iOS	Uncontrolled before-after study. 60 days

						App development: Wellframe Inc. Cambridge, MA; states provider dashboard is compliant with US Health Insurance Portability and Accountability Act (HIPAA) medical data privacy and security provisions.	
Seo et al. 2015. Korea	Stroke Outpatients	Previous stroke + ≥1 vascular risk factors; Able to use an Android smartphone	48	52 (range not reported)	25	Korea University Health Monitoring System for Stroke (KUHMS) mobile app; patient enters BP, waist circumference, BGL, smoking, exercise and medication adherence data. Data that exceed predefined levels trigger a message alarm to patient. App operating system: Android App development: Korea University	Uncontrolled before-after study. 6 months
Varnfield et al. 2014 Australia	MI Outpatients	Post-MI referred to CR; able to attend CR. Experience with a smartphone.	94	55 (range not reported)	13	Intervention: Care Assessment Platform of Cardiac Rehabilitation (CAP-CR) used instead of clinic-based CR: smartphone app with health and exercise monitoring (step counter, BP monitor, weight), text messages, audio and video educational and	Multicentre RCT 6 weeks

						motivational content, wellness diary (e.g., sleep, smoking, alcohol consumption, stress); web portal for uploaded data to be viewed by mentor prior to weekly progress call with patient. Control: traditional clinic-based CR App operating system: not specified App development: not described but multiple vendors listed for provision of the various monitoring apps and diary components installed on the smartphone; content aligned with national CR guidelines.	
Widmer et al. 2015 USA	ACS Outpatients	Post-PCI. Pre-CR or 3 months post-CR.	76	66 (range not reported)	27	Intervention: Standard CR plus Personal Health Assistant (PHA) online or smartphone-based app: daily tasks based on CR guidelines for healthy lifestyle behaviour; track progress, log weight, BP, lab values, daily PA, diet. Interactive health status	Controlled, non-randomised before-after study. 3 months

						info; educational CR info, email reminders, graphical displays. Comparison groups (2): standard CR alone. App operating system: Android and iOS App development: Mayo Clinic and Healarium, Inc.	

Abbreviations: CVD, cardiovascular disease; HT, hypertension; BP, blood pressure; MI, myocardial infarction; CR, cardiac rehabilitation; HF, heart failure; PRN, pro re nata; RCT, randomised controlled trial; LDL-C, low density lipoprotein cholesterol; BGL, blood glucose level; CAD, coronary artery disease; PA, physical activity; ACS, acute coronary syndromes; PCI, percutaneous coronary intervention.
*Linked studies.

Quantitative outcomes

Primary endpoints differed between studies from user engagement and satisfaction with the mobile application,[27] the extent of cardiac rehabilitation uptake and completion,[29] and reduction in risk factors.[32] As a result, studies were less amenable to direct comparison of app effectiveness. No studies reported on new CVD event rates. Selected outcomes are summarised in Table 2. Detailed synthesis of results for hospital readmissions, QoL and wellbeing, CVD risk factors, medication adherence, cardiac rehabilitation uptake and adherence, and process evaluation measures are detailed below.

Hospital readmissions

One RCT[31] and one non-randomised study[30] reported lower hospital readmission associated with the intervention. Hägglund et al[31] reported that hospital days per patient for heart failure were 1.3 and 3.5 in the intervention and control groups, respectively; 62% reduction in the intervention group (risk ratio 0.38; 95% confidence interval: 0.31-0.46, $p<0.05$). Heart failure hospitalisations were 34% of all hospital days for the intervention group but 68% for the control group. Similarly, Widmer et al[30] noted significantly reduced re-hospitalisations in the patients using the intervention concurrently with standard cardiac rehabilitation (5/25 (20%) vs 11/19 (58%), $p=0.01$), and in those using it post-rehabilitation (-28%, $p=0.04$). In the data review, we noted incongruence between the denominators in the table describing the study group assignments and the authors' data description in the text, making interpretation of their data difficult.

Quality of life and psychosocial well being

QoL was assessed in four studies[29-31, 35] using one of three different instruments (the EQ-5D, the Dartmouth QoL Survey, and the SF-36). In three RCTs, results were mixed: Johnston et al[28] reported no statistically significant difference between allocation groups with AMI; the increase in QoL scored on the EQ-5D in the intervention group was higher than for the control group but the difference was not statistically significant. In contrast, Varnfield et al[29] found that after six weeks, AMI participants in the intervention group improved their scores on the EQ-5D significantly more than the control group ($p<0.05$), noting that the convenience of home-based rehabilitation may have contributed to this result. In a controlled before-after study[30] within-group and between group Dartmouth QoL survey scores significantly improved in ACS patients using the intervention concurrently with standard cardiac rehabilitation, compared with controls ($p=0.009$ and $p=0.04$, respectively). In the third RCT,[31] mental and physical scores for HF patients on the SF-36 were comparable between intervention and control groups. However, when heart failure-specific self-care and health-related QoL were assessed, the intervention group significantly improved scores on the European Heart Failure Self-Care Behaviour Scale, $p<0.05$; and achieved significantly higher clinical mean summary score ($p<0.05$) and improved physical limitation ($p<0.05$) on the health-related QoL Kansas City Cardiomyopathy Questionnaire. Thus, the general QoL improvement, where apparent, appeared to be more evident in the shorter term in CHD patients. Disease-specific QoL improved in a HF population over three months.

One RCT[29] and one controlled before-after study[30] assessed psychosocial wellbeing and found improvements in patients using the mobile apps. Varnfield et al[29] reported that cardiac rehabilitation patients in the intervention group demonstrated significantly reduced DASS-

Depression score (p<0.001) and DASS-Anxiety score (p=0.003) from baseline to week six, although the between group difference was not significant. Interestingly, the K10 psychological distress score that improved in the intervention group in the shorter-term follow-up at week six (p=0.001) remained significantly improved at month six. Widmer et al[30] reported that stress scores significantly improved in ACS patients using the intervention concurrent with standard cardiac rehabilitation (-1.3±1.3, p=0.008).

CVD risk factors

One non-randomised study and two RCTs assessed aspects of lipid profile, with mixed results. In a controlled before-after study[30] the intervention group had significant reduction in total cholesterol (-46.9±38.3 mg/dL, p<0.0001), LDL cholesterol (-36.7±35.7 mg/dL, p=0.0004), and triglycerides (-39.3±69.1 mg/dL, p=0.03) compared with baseline. Patients in the control group had a significant reduction in LDL cholesterol, however the between group difference was not reported. Two RCTs[28, 29] assessed LDL cholesterol. Meta-analysis was not possible with the way the data were reported. Johnston et al[28] reported no mean change in LDL cholesterol between treatment groups. Varnfield et al[29] reported that the imputed lipid profile data exceeded 21% for six-week data; no six-month values are shown. The intervention group showed no difference in LDL cholesterol at week six. It was possible to calculate between-group differences in mean LDL-cholesterol; however, no difference was seen.

Change in BP was assessed in three before-after studies[25, 30, 32] and one RCT,[29] with improvements from baseline reported in each study. In one uncontrolled before-after study, a statistically significant decrease was reported between the baseline mean systolic BP and mean diastolic BP and the mean values at week eight (SBP, 7 mmHg; SD 18; 95% CI, 1.94-12.25;

t[48]=2.77 [p=.008]) and (DBP, 4.9 mmHg; SD 10; 95% CI, 1.95-7.8; t[48]=3.35 [p=.002]).[25] In the second study, 68.8% of participants reached BP target and the change from baseline was both significant (p=0.031) and sustained at 180 days.[32] A controlled before-after study reported systolic BP significantly improved in the patients using the intervention (-10.8±13.5 mmHg, p=0.0009); also, systolic BP decreased significantly (p=0.01) compared with the control group.[30] One RCT found a significant between-group difference in adjusted mean diastolic BP at week six (p=0.03); however, BP results were not reported for the later data point at month six.[29]

Two studies reported change in waist circumference. A slight but significant within-group reduction was observed in the intervention group of an RCT.[29] Target waist circumference was achieved in 77.1% of patients in an uncontrolled before-after study.[32] Four studies reported change in BMI and/or weight, with mixed results. Across two RCTs, there was no change in BMI between groups reported by Johnston et al[28] however, slight but significant improvement in weight in the intervention group was observed by Varnfield et al[29] Two before-after studies reported significant improvement in baseline BMI.[30,32]

One uncontrolled before-after study[32] assessed change in HbA1c, reporting that 54.2% of participants with diabetes mellitus at baseline achieved significant improvement in this indicator at end of study (p=0.012). Three studies that reported change in participant self-reported smoking status[28, 30, 32] found positive changes but not statistically significant results. In one RCT, the intervention group showed more quitters than the control group.[28] In an uncontrolled before-after study[32] smoker rate reduced in those who used the app longer compared with those who used the app less often. Also, a controlled before-after study[30]

reported all smokers at baseline were non-smokers at end of study, regardless of allocation group.

Self-reported physical activity behaviour was assessed in five studies[28-30, 32, 33] and overall, users of the applications improved on this indicator. Two RCTs reported increased PA in the intervention participants although not statistically significant[28, 29] and 89% of intervention patients who adhered to the intervention self-entered a record of daily exercise and/or used the step counter to reach their exercise goals.[29] Two uncontrolled before-after studies had limited data: Layton et al[33] reported that patients who used the intervention up to 60 days performed the recommended PA 42% of the time compared with 25% in those who used the intervention for 1-30 days. Seo[32] reported that at 180 days, adherence in the previous month to moderate-intensity exercise was 10.40±9.92 days but this was not assessed at baseline to compare the potential change. In a controlled before-after study[30] the intervention group significantly improved minutes of weekly exercise (148.1±78.5 mins/week, $p<0.0001$) but the between group difference was not significant.

Two studies that focused on cardiac rehabilitation assessed change in exercise capacity. An RCT[29] reported that both study groups improved the six-minute walk test from baseline to week six and maintained this improvement to month six. Participant dropouts reduced sample size such that significant between-group differences were not demonstrated. The Bruce Protocol treadmill test was used in a controlled before-after study[30] in which the intervention group significantly improved exercise capacity (2.5±2.7 ml O_2/min/kg, $p=0.004$); between group difference was not reported.

Medication adherence

Three studies[25, 28, 32] assessed medication adherence by different methods and reported an overall positive impact. In one of two uncontrolled before-after studies,[25] adherence was self-reported and responses were checked against National Prescription Repository data. The percentage of filled prescriptions corresponded to at least 80% of the prescribed doses during the study period. In the second study,[32] patients reported days of medication adherence in the last 30 days at 29.25, however no baseline data were reported with which to compare. In a RCT,[28] self-reported drug non-adherence at six months using the e-diary app intervention was significantly lower in the intervention group compared with the control group (p=.025).

Cardiac rehabilitation uptake, adherence and motivation

Several studies used a cardiac rehabilitation population for the research, but only two studies[27, 29] had attitudes towards, and participation in, rehabilitation as an outcome focus. Forman et al[27] reported that users of the smartphone app in cardiac rehabilitation phase II had a 42% lower visit cancellation rate compared with non-users. Furthermore, users in phase III cardiac rehabilitation reported improved sense of connection to clinic staff and sustaining goals around wellness behaviours. In a RCT,[29] cardiac rehabilitation uptake was defined as attending baseline assessment and at least one gym session (control group) or one upload of exercise data (intervention group using app-based cardiac rehabilitation). Uptake was higher in the intervention group: (48/60, 80% vs 37/60, 62%) (RR 1.30; 95% CI 1.03-1.64; $p<0.05$). Adherence was defined as clinic cardiac rehabilitation attendance to four weeks (control group) or uploading four weeks' exercise data (intervention group, and attending the six-week assessment (both groups). Intervention participants were 1.4 times more likely to adhere (RR 1.4; 95% CI 1.13-1.70; $p<0.05$). Completion was defined as attendance at six-week assessment and was 33% higher in intervention participants (RR 1.71; 95% CI 1.30-2.27; $p<0.05$).

Table 2. Summary of selected outcomes by study design

Outcome	Number of studies that assessed this outcome	Open label randomized controlled trial		Quasi-experimental studies			
				Controlled before-after study		Uncontrolled before-after study	
		Study	Effect	Study	Effect	Study	Effect
Hospital readmissions	2	Hägglund et al, 2015	+++	Widmer et al, 2015	+++		
QoL	4	Johnston et al, 2016	++	Widmer et al, 2015	+++		
		Varnfield et al, 2014	+++				
		Hägglund et al, 2015	+++				
Psychosocial well-being	2	*Varnfield et al, 2014	+++	Widmer et al, 2015	+++		

Total cholesterol	2	Varnfield et al, 2014	x	Widmer et al, 2015	+++		
LDL cholesterol	3	Johnston et al, 2016	-	Widmer et al, 2015	+		
		Varnfield et al, 2014	x				
BP	4	Varnfield et al, 2014	+++	Widmer et al, 2015	+++	Bengtsson et al, 2016	+++
						Seo et al, 2015	+++
BMI and/or weight	4	Johnston et al, 2016	-	Widmer et al, 2015	+++	Seo et al, 2015	+++
		Varnfield et al, 2014	+++				
Smoking	3	Johnston et al, 2016	++	Widmer et al, 2015	+	Seo et al, 2015	^
Exercise capacity	2	Varnfield et al, 2014	+	Widmer et al, 2015	+++		

Physical activity	5	Johnston et al, 2016	++	Widmer et al, 2015	+++	Layton et al, 2014	∫
		Varnfield et al, 2014	∫			Seo et al, 2015	∫
Medication adherence	3	Johnston et al, 2016	+++			Bengtsson et al, 2016	∫
						Seo et al, 2015	∫
CR uptake	2	Varnfield et al, 2014	+++			Forman et al, 2014[2]	∫

Abbreviations: QoL, quality of life; LDL, low density lipoprotein; BP, blood pressure; BMI, body mass index; CR, cardiac rehabilitation.

Key: +++ statistically significant effect; ++ greater improvement in intervention group than control but between group difference not significant; + significant improvement in both groups but between group difference not reported or not significant; - no reported change between treatment groups; × imputed data and/or data not shown; ^ within-group improvement not significant; ∫ adherence improvement data from participant survey.

*Anxiety and psychosocial distress scores.

Process measures and qualitative outcomes

User engagement

Intervention uptake was defined and reported differently in each of eight studies[25, 27, 28, 30-34] that described metrics such as app usage frequency, duration, data registration, or responsiveness of the user to daily tasks. Combined with often low participant numbers, drop outs and short exposure duration, conclusions about engagement are difficult to draw. Completion of tasks within the app (for example, an educational module) was a typical indicator of use in studies with an overall healthy lifestyle focus.[27, 33, 34] In others, emphasis was on logging medication intake or physical measurements.[25, 28, 30-32] Forman et al[19] gauged engagement by patient completion of at least one prescribed daily task from an average of 6.3 tasks per day. Overall, patients completed on average 78% of 189 tasks set over 30 days; but the proportion of patients completing specific tasks varied by type of task, for example PA or disease education. Layton et al[33] reported that ten of sixteen study participants withdrew prior to day sixty but patients who completed 31-60 days used various interactive aspects of the app overall more than those who withdrew prior to day 31. Self-reported health status on day of hospital discharge, as well as breath sounds by physical exam, were reported correlates of application use, with lower uptake in more medically unwell patients. The authors did not comment on specific differences by diagnostic group of the study participants (CHD or HF). In a short study with patients of mixed CVD diagnoses,[34] eight of the 10 participants used the game-style app challenges daily for 14 days but used the leader board feature third-daily.

In one RCT, the proportion of patients who prematurely stopped using the e-diary app was reported as low but the actual figure was not stated.[28] In another RCT,[31] adherence was defined as the number of days the patient interacted with the system, divided by the number of days

equipped with the system. Median adherence was 88% and suggested to be a proxy indicator of system usability. Seo et al[32] defined app usage as days with risk factor data entry into the app. Days entering data averaged 60.4 (range 1-180). Participants were dichotomized as compliant (entered data on ≥47 days) and non-compliant (entered data on <47 days); however, achievement rates for the assessed outcomes – achieved within the first three months and maintained over the next three months - did not differ between 'compliant' and 'non-compliant' groups. Therefore, higher frequency of data entry may not equate with achieving improvements and other factors are likely to contribute.

In an uncontrolled before-after trial[25] participants were required to log daily BP measurements for 55 days; however, it was not clear whether all patients logged BP on each of 55 days. Widmer et al[30] assessed usage frequency by number of log-in days divided by total number of active days and counted frequency of log-ins per week. Factors associated with usage frequency were minutes of weekly exercise at 90 days (r^2=0.24, p=0.04), reduction in BP (r^2=0.38, p=0.04) and stress scores (r^2=0.32, p=0.02), and improvement in diet score (r^2=0.41, p=0.007). Thus, data entry as an indication of app engagement is a common metric, but requires high user motivation. It may underestimate other ways patients use app features that do not register data in a central record under research conditions.

User preferences and feedback

Five studies[26-28, 33, 34] explored patient preferences (Box 1) and one study reported feedback from cardiac rehabilitation staff.[27] Patients in one small study of both HF and CHD participants[33] liked medication reminders and PA information. However, they disliked being unable to self-enter appointments and other reminders (study team initiated these or they were

system-generated), and felt daily requirements for data entry or other responses were inconvenient. In a second small qualitative study[34] however, daily reminders and challenges about required exercise and lifestyle changes were well-received but participants would have liked puzzle-style, memory and psychological challenges alongside the standard dietary and exercise focus.

Motivational messages were varyingly received with some patients describing them as stimulating and encouraging, whilst others opted to not receive them. Preferred features were to be able to formulate one's own messages, or receive messages that more closely reflect goal achievements or non-achievements. An example would be for a message to reinforce benefits of having achieved their goal, or motivate them to increase their effort if required.[26] Software needs would thus be more sophisticated than currently used, wherein a bank of prepared messages is employed and in-app modification of the messages in response to user data entry does not occur. The app used in one RCT[28] did have a version of more tailored responsiveness of the messaging system according to input from the patient. That study reported patient satisfaction feedback but not specifically how this adaptable message logic was rated.

Patients with hypertension found the smartphone format more convenient than a computer-based app for self-reporting data or responding to learning tasks.[26] They suggested an editing option for self-entered data; also, to insert comments beside measurements so that any irregular readings could be seen in the context of other things happening in their lives that day/week. This is important for helping patients understand the relationship between lifestyle and general health, and their BP, and thus helps them address day to day influences on BP. Mixed responses were obtained to ease of reading and interpreting the graphical BP data. Some patients relied

on viewing these with nursing staff during a routine clinic visit,[26] so preferred that graphs be viewable on a smartphone, not just on an optional secure web site.

Where apps were used as an adjunct to clinic-based care, patients valued personalisation and flexibility. Feedback from one small study identified that cardiac rehabilitation content would ideally be adaptable to the patient's stage of rehabilitation and overall health, rather than identical for each patient.[34]

Impact on disease knowledge and participation in treatment

In a small observational study of patients in cardiac rehabilitation, 96% of participants felt that using the app supported their participation by helping them identify personal lifestyle challenges and goals such as healthier eating or smoking cessation.[27] Further, it helped them adhere to rehabilitation (93%) and improved the quality of clinic visits (71%). Overall, 83% of patients had a positive experience with the app. This same study reported app feedback from staff. Among the benefits identified were reduced cardiac rehabilitation barriers, better patient participation, improved between-visit communication and better attendance.[27] Participants in a small study using gamification design[34] felt the team-based approach to rehabilitation was effective for relatives wishing to provide emotional support. Ideally the app should allow communication between teams, perhaps underscoring the value placed on peer support between those with shared conditions.

Patients using a hypertension management app reported greater insight into their condition, evidenced by (1) adhering to treatment even when feeling well and their BP was controlled; (2) making lifestyle changes to positively affect BP, for example losing weight, quitting smoking and increasing PA; and (3) being more active in discussions with their doctor.[26]

Limited participant feedback was reported in two of the RCTs. Johnston et al[28] used a self-reported system usability score (not shown) that was reported higher at study visit two and end of study (p.001). Of the intervention participants, 97.5% would recommend the app to others; 68.4% were willing to continue using the app; and 80% felt the app was relevant and helpful for motivation. In a second RCT,[29] feedback questionnaires at week six and month six about cardiac rehabilitation exercise adherence noted that more than 85% of intervention patients found the step counter to be motivational. More extensive feedback about using an app to undertake the rehabilitation was not reported.

Box 1. Preferred app features from qualitative data in the included studies.

- Healthy eating and exercise goal setting
- Recognition of achievements
- Memory and psychological tasks
- Enable user editing of self-entered numeric data, reminders and appointments
- Motivational messages with:
    - Opt-out option
    - User-created and system-generated content
    - Content responsive to user input to app
- Game-based design techniques
- Enable textual data to be entered with numeric data
- Ensure graphical data displays are viewable on a smartphone
- Tailor content of cardiac rehabilitation-related apps to stage of recovery
- Offer team-based competition options
- Remove requirement for daily data entry
- Provide in-app “how to” guides.

DISCUSSION

This study reveals mixed findings for the effectiveness of patient-focused apps across a range of outcomes for disease self-management and risk factor control. Factors that improved among users of the apps were hospital readmission rates, disease-specific knowledge, general and health-related QoL, psychosocial well-being, BP, BMI, waist circumference, cholesterol, and exercise capacity. Improved daily PA, medication adherence (including medication self-titration), and smoking cessation were also characteristic of app users. One uncontrolled

before-after study attributed improvements to possible Hawthorne effect rather than use of the intervention.[32] Not all reported improvements were of statistical significance; others occurred within but not between treatment groups; and in several controlled studies, observer effect may have accounted for improvements seen in non-app users.[36]

This review revealed appealing app features were tracking daily healthy behaviours, self-monitoring measurements and symptoms, appointment reminders, disease education, and managing communication with providers. As apps become integrated into usual health care, studies indicate that patients want more flexible options in terms of entering, editing and viewing data. They also value customisable app features that are typically system-generated, such as notifications and motivational messages. Further noted was the appeal of optional interaction with other people in the game-based apps. In this review, digital products that are targeted to self-management were viewed as increasingly routine.

Understanding and optimising enablers to uptake of self-care tools offered via mobile platforms will continue to widen their appeal, relevance and utility. For example, within this review, the mean age of participants was $\leq$ 60 years in seven of the studies. The appeal of mobile app use in these studies could possibly be ascribed to younger age, indicating a selection bias. Although often assumed to be a predictor of technology appeal, age per se is not a barrier to app use. Simple navigation that is visually clear and personalised are among the appealing features for older app users.[37] Ongoing promotion of apps to adults with CVD must adopt such core design features. Addressing other issues such as outdated devices, service connectivity and affordability, and tailoring cultural and linguistic adaptations where appropriate, will continue to remove practical barriers to uptake. Notably, no studies in this review reported sub-analyses

based on, for example, sex or age. Further research focused on efficacy of smartphone-based programs relative to sociodemographic variables would thus broaden and strengthen the insights found in this review.

Several implications emerged from this review relating to the future use of mobile device-based apps in CVD populations. In a point of difference to many apps with even nominal interaction with health staff, an app whose design excluded this feature improved self-care across a range of important outcomes in patients with heart failure.[31] In a second example, patients who undertook home-based cardiac rehabilitation using a smartphone app in lieu of, not as an adjunct to, clinic-based cardiac rehabilitation, did at least as well in terms of key outcomes of healthier diet, increased functional capacity and lowered depression scores.[29] A stand-alone app that expands the reach of evidence-based treatment, improves disease self-management, and lowers human resource needs has great appeal. Interestingly, user perception of human-like attributes in technology-based interventions may be what is important. In a recent RCT of a text-message-based intervention for patients with CHD in which message content was entirely automated, participants felt a sense of personal connection with health staff simply due to a familiar hospital as the sender identity and having met the research staff at recruitment, although not thereafter.[38] In a review of CVD app personalisation strategies,[39] avatars that match the user's culture and literacy level were another appealing medium for game-based heart health programs without human communication. Further research could explore the role of personalisation or attribution of human qualities (known as anthropomorphism[40]) to stand-alone mobile apps. Cost-effectiveness was not examined in any of the studies in this review but warrants further research in larger studies of CVD in more diverse economies to better understand the role of an intervention requiring fewer clinical resources.

The timing of app introduction relative to hospital discharge merits further investigation. App usage as an adjunct to clinic-based cardiac rehabilitation, for example, appears to have a reinforcing effect on adherence to secondary prevention behaviours. This suggests that app uptake may be time-sensitive, with proximity to starting rehabilitation driving some of the interest. Short, easily-achievable, minimally stressful tasks for patients commencing cardiac rehabilitation may help establish and maintain ongoing commitment, compared with more demanding challenges for those further along from hospital discharge.[34] As constrains most interventions of this nature, little is known of long-term effectiveness on hard CVD endpoints. Clearer perhaps is that multiple behavioural domains and risk factors are potentially modifiable, at least in the shorter term, by the dynamics of mobile-based programs.

Attrition rates are commonly high over time for apps targeted to management of disease risk factors[41] or long term conditions, generally.[42] The inconvenience of daily data entry was cited as a factor in lower app usage and data gaps in at least one of the included studies with a comparatively long follow-up (six months).[32] App acceptability and usefulness may be hindered by other factors, for example patient and/or clinician confidence in the reliability of measurements obtained by app-based software. A recent study of smartphone-based commercial heart rate monitors, for example, revealed mixed results for accuracy between apps, particularly as heart rate increased, highlighting that perceptions of data unreliability may undermine adoption or continuance of app use for biometric monitoring purposes.[43] Another potential barrier to engagement is user trust in data security and privacy.[11] In this review, only one study[33] reported on app compliance with national confidentiality laws; no study evaluated patient or provider views about this issue. Reporting data security/privacy protocols in relation

to mHealth is therefore recommended.[35] Integrating gamification principles into mobile apps may increase motivation for sustaining essential but repetitive, routine lifestyle tasks over the longer term.[11, 34] In non-health gaming, priority is given to incentives and engagement[44] but core gaming principles such as a requirement for strategic thinking, providing motivational feedback and voluntary participation could be applied for a disease-specific context. Hence, further evaluation research may elucidate the crucial time point(s) from the index CVD diagnosis or event at which a particular style of mobile app most effectively impacts lifestyle decision-making and longer-term self-care behaviour.

This review has several limitations. Although every attempt was made to locate potentially suitable studies in languages other than English, all retrieved studies for which the full text was available were in English. The included studies are from high income countries and therefore do not represent the diversity of settings for which CVD prevention programs delivered via mobile apps could be beneficial. Drawbacks were identified related to the relatively low quality of the included studies across various items within the respective appraisal instruments used; the implications of this for the strength of evidence for app effectiveness on many reported outcomes is acknowledged. Sample sizes were small (six of the studies had 50 or fewer participants), compounded by significant dropouts. Only two studies were of six months duration; five of the studies were of eight weeks duration or less. Thus, longer term impact on risk factor control or health service use cannot be appraised and remains a need for future research. Biases, especially selection bias, are inherent in the non-randomised designs. Studies lacking a control group further limits association between the identified improvements in outcomes and the app intervention. Self-report may have over-estimated effects on health behaviour outcomes, such as smoking and physical activity. RCTs of patient-directed apps are unavoidably open label and inconsistencies across reporting of outcomes precluded statistical

comparisons. Single centre studies may have further limited representativeness. User acceptance data were in some cases reported even where studies otherwise excluded, or were underpowered for, clinical endpoints. However, some studies that reported clinical measures reported no user feedback; hence there may be gaps in data about patient preferences for features of apps .App development, implementation and maintenance cost considerations were not routinely reported, nor whether the interventions have been adopted into routine practice. Accounts of both could be an instructive adjunct to outcomes data. Future reviews in this dynamic area would therefore be aided by more systematic reporting of research. A standardised reporting format, such as the sixteen-item mobile health evidence reporting and assessment checklist[35] would help overcome variations and aid information synthesis in future reviews.

Notwithstanding these limitations, the range of outcomes for which improvements were seen suggests a place for mobile-based apps in CVD self-management. Mobile technologies are recognised for their potential to improve reach, efficiency and affordability.[5, 11] Those who depend on a smartphone as their only online device, for example, may stand to benefit from otherwise inaccessible material. Apps are broadly acceptable to consumers, in part because they employ a familiar device interface; however, by design and intention they place greater emphasis on patient agency. Accordingly, pragmatic patient selection for such apps may prove the more judicious approach to ensure that those most likely to benefit do so. A randomised trial with patient preference arms for home- or clinic-based cardiac rehabilitation[45] demonstrated similar effectiveness between groups, suggesting that patient-preferred allocation may more realistically predict success with home-based CVD self-care. Therefore, routine process evaluation of intervention studies could also elucidate characteristics of patients for whom mobile apps are likely to be suitable and successful as an adjunct to, or a substitute for, clinic-based management.

CONCLUSIONS

Mobile-based applications with low clinician involvement are promising strategies to help selected patients succeed with improving risk factor control and disease self-care. At service level, they may offer a sustainable, credible, low-resource approach within the wider technology-enabled health care environment. At the patient level, uncertainty about longer-term program interest and impact needs to be addressed by studies of higher scientific quality to more reliably determine whether reported improvements are app-related, and which other factors contribute. Analyses by sociodemographic variables would improve interpretation of outcomes. Future research should routinely encompass process evaluation data to further refine optimal system-side features, including personal data privacy and safety; resources needed to manage patient-generated data; and inclusion of relevant provider perspectives. Taken together, such data inform translation and scale-up of personal technologies to enhance CVD self-management and reduce evidence-practice gaps.

Author contributions: GMC, LN and JR contributed to the conception or design of the work. GMC, LN and JM contributed to the acquisition, analysis, or interpretation of data for the work. GMC drafted the manuscript. LN, JM and JR critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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