Breaking Barriers: Mobile Health Interventions for Cardiovascular Disease

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ABSTRACT
Cardiovascular disease (CVD) is a leading global cause of death and morbidity and prevention needs to be strengthened to tackle this. Mobile health (mHealth) might present a novel and effective solution in CVD prevention, and interest in mHealth has grown dramatically since the advent of the smartphone. In this review, we discuss mHealth interventions that target multiple cardiovascular risk factors simultaneously in the context of primary as well as secondary prevention. There is some evidence that mHealth interventions improve a range of individual CVD risk factors, but a relative paucity of evidence on mHealth interventions improving multiple CVD risk factors simultaneously. The existing data suggest mHealth programs improve overall CVD risk, at least in the short term. Interpretation of the evidence is difficult in the context of poor methodology and mHealth modalities often being a part of large complex interventions. In this review we identify a number of unanswered questions including: which mode of mHealth (or combination of interventions) would be most effective, what is the durability of intervention effects, and what degree of personalization and interactivity is required.

Middle-income countries.1 Multiple nonmodifiable (age, sex, ethnicity, family history) and modifiable (lifestyle and behavioural) risk factors contribute to the lifetime risk of CVD. Modifiable risk factors such as smoking, dyslipidemia, hypertension, abdominal obesity, physical inactivity, psychosocial factors, and diet account for most of the global risk for myocardial infarction (MI).2 Thus, effective prevention programs aimed at a combination of these modifiable CVD risk factors in primary as well as secondary prevention settings are likely to yield best results. Secondary prevention of CHD, including pharmacotherapy and lifestyle modification, has been shown to reduce
morbidity, mortality, and improve functional status and quality of life. However, despite strong evidence, there is substantial underutilization of secondary prevention measures in patients with CHD. For example, the European Action on Secondary and Primary Prevention by Intervention to Reduce Events (EUROASPIRE IV) study showed that most patients who had a coronary event did not meet guideline recommendations on CHD risk factor control. The reasons for the relatively poor implementation of secondary prevention are multiple, and include health system-, community-, and individual level-factors. Changing lifestyle behaviours and maintaining medication adherence is difficult for many individuals even if they know that they have CHD, and in the primary prevention setting it is even more challenging to engender enough motivation to aggressively manage risk factors.

Mobile health (mHealth) technology has gained increasing interest as a means to improve the delivery of CVD prevention in a scalable and affordable way. It has particular potential to assist lifestyle modification and improve medical adherence. The Global Observatory for eHealth defines mHealth as "Medical and public health practices supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs) and other wireless devices." It is expected that by 2018, 50% of the global population will own a smartphone (mobile phones with a computer operating system), and total mobile phone ownership in low-income countries will almost reach ubiquitous levels.

Modes of mHealth Delivery

Smartphone applications (apps) and text messaging (short messaging service or SMS) are 2 popular means of delivering mHealth interventions (Figs. 1 and 2).

Smartphone apps

Smartphone usage has been increasing, with 39% of adults globally using a smartphone in 2012 to 61% in 2014, and this has powered the growth in apps. Health-related apps are popular, and easily accessible via the iTunes store or Google Play. Many are free, although some incur a cost to download or purchase additional features. In April 2015, there were 12,991 apps in the iTunes store and 1420 apps in Google Play targeting multiple cardiovascular risk factors. These apps might use different functions of the phone such as cameras, global positioning system, as well as sensors/accelerometers.
Many apps track and monitor cardiovascular risk factors, for example, blood pressure logs, quit smoking apps, and diet and activity logs such as MyFitnessPal (MyFitnessPal, Inc; www.myfitnesspal.com). In addition to smartphone ownership, running app-based interventions generally require an internet and data plan, which results in greater mobile phone running costs. The complexity of apps is an attractive feature, but can limit utility for the less technology-literate user.11 From a technical perspective, apps need to be specifically developed for the operating system type (eg, Android, Apple) and require regular maintenance and updates.

The utility of apps to improve health outcomes has been poorly evaluated. There is limited research evidence for their effectiveness in modifying objective measures of health, and app development and provision are largely unregulated, with Food and Drug Administration regulation being limited to those apps that transform the smartphone into a medical device.17,18 In addition many of these apps are not accessible or not well designed for use by the elderly population. The rate of use of smartphone apps is lowest in elderly individuals, who are at the highest risk of CVD.19

Text messaging

Total mobile phone (smartphone and standard) subscriptions have increased, with an estimated 96.8 subscriptions per 100 persons worldwide in 2015.16 In contrast to apps, text messages are universally available on all mobile phones. There is some research evidence supporting the utility of SMS-based approaches; most have focused on single risk factors in younger populations and have short periods of follow-up. The effectiveness of SMS-based interventions has been reported with smoking,20 weight loss,21 physical activity,22 diabetes,23 and hypertension.24,25 There are also some examples of large-scale implementation of text-message interventions particularly for smoking cessation.20

Text-message interventions are relatively inexpensive, simple to use, not reliant on internet/Wi-Fi access, and allow almost instantaneous communication. SMS can be customized and delivered via a computer algorithm, which has been shown to be more effective than generic (not customized) text messages.12 The cost of text messages can be a barrier in developing countries and literacy can also be a barrier. Importantly, the text messages offer greater simplicity because texts just arrive to the phone, obviating the need to pull information as is the usual means of interacting with an app.

Primary Prevention Strategies in mHealth Targeting Multiple Risk Factors

There have been only a few randomized controlled trials (RCTs) that have assessed the feasibility and effectiveness of mHealth approaches targeting multiple cardiovascular risk factors.
factors to improve cardiovascular risk in a primary prevention cohort (Table 1).

Text message-based interventions

The largest of these was conducted in China and was an RCT of a 12-month intervention comprising text messaging and phone calls performed among 589 Chinese workers (allocated to receive an annual medical examination) without CHD aged between 45 and 75 years.26 The intervention group received personalized text messages targeting lifestyle measures to reduce CVD risk (frequency determined according to risk assessment) in addition to a computerized CVD risk evaluation, an initial 15-minute face-to-face cardiovascular risk counselling session, follow-up phone calls, educational handbook, and a medical examination. An electronic health prescription software was developed to prescribe the program to the intervention group. The software calculated overall 10-year CVD risk, informed participants of unhealthy practices, and provided an individualized intervention plan aimed to improve their risk factors. The control group received the annual medical examination and report detailing their results. At 12 months, there was a significantly lower mean 10-year CVD risk score in the control arm (adjusted difference, −2.83%; P = 0.001). However, there was no significant reduction in the mean CVD risk at 1 year compared with baseline for the intervention group. This suggests the mean difference at 1 year (−1.05%; P = 0.096). CVD risk change between intervention and control (−2.83% (P = 0.001) statistically significant change in intervention vs controls from baseline to 1 year in SBP (−5.55 vs 6.89 mm Hg; P < 0.001), DBP (−6.61 vs 5.62 mm Hg; P < 0.001), TC (−0.36 vs −0.10 mmol/L; P = 0.005), fasting BSL (−0.31 vs 0.02 mmol/L; P < 0.001), BMI (−0.57 vs 0.29; P < 0.001), waist-hip ratio (−0.02 vs 0.01; P < 0.001).

Smartphone-based interventions

We could identify no RCTs assessing the effect of apps on total cardiovascular risk in a primary prevention cohort on reviewing the current literature. However, Zhang et al.28 recently developed a smartphone-based CHD prevention program called Care4Heart and conducted an RCT of 80 adults without CHD to assess CHD awareness and lifestyle behaviour change. The intervention comprised a 4-week
program involving a mobile app consisting of 4 learning modules covering common signs and symptoms, risk factor education, and healthy lifestyle practices including smoking cessation and stress management. Users could calculate their BMI, daily caloric intake, and assess their 10-year CHD risk. In addition, participants would have a 20-minute briefing session and daily text messages with CHD prevention advice. The control group was provided with Web site addresses to peruse at their leisure. At the end of the 4-week program, participants in the intervention group had significantly better overall CHD knowledge. However, there were no significant differences in lifestyle behaviours between the groups, except with improved behaviours related to blood cholesterol control in the intervention compared with control arm. Unfortunately, assessing the difference in total CHD risk scores at the end of the program was not part of this trial.

There is some nonrandomised evidence. For example, Widmer et al. examined the effect of using a digital health intervention (DHI) offered to a multicentre primary prevention cohort of 30,974 participants. The DHI was an online and smartphone-based portal, which contained educational material, and gave the user tasks to improve health including tracking and logging activities. It also included reminders to complete tasks in the form of text messages and e-mails. Most participants had no (14,173) or very low (defined as < 12 per year; 12,260) log-ins, and 3360 had monthly, 651 weekly, and 530 semiweekly log-ins. Changes in waist circumference, weight, BMI, blood pressure, lipids, and blood glucose were assessed at 1 year. Significant improvements in weight loss were seen with increasing DHI usage with the greatest change being in the semiweekly group compared with weekly (−3.39 ± 1.06 pounds; \(P = 0.0013\)). Older, female, Hispanic individuals with a greater number of risk factors were more likely to adhere to the DHI.

It is hard to draw conclusions at this stage from this literature, because of the few studies and varied interventions. The mixing of multiple modalities (eg, SMS and e-mail), and the considerable heterogeneity between studies in frequency of delivery and level of interaction are all challenges to synthesis of the evidence. Additionally, mHealth methods have generally been evaluated in selected settings where individuals are likely to be highly motivated, and thus the results might not be applicable across various demographic populations. We need more information on how patients interact with these interventions to identify how they work, which might assist in optimizing mHealth interventions in these populations.

**Secondary Prevention Strategies in mHealth**

**Targeting Multiple Risk Factors**

There have been a number of mHealth interventions that aim to deliver secondary prevention to patients with CVD and that target multiple risk factors simultaneously (Table 2).

**Text message-based interventions**

The Tobacco, Exercise, and Diet Messages (TEXT ME) trial was a single-centre RCT of 710 patients with CHD that examined the effect of a semipersonalized text message-based intervention compared with usual care on objective measures of cardiovascular risk factors at 6 months. The intervention comprised semipersonalized (customized to baseline risk factors) text messages (4 per week) over a 6-month period, which provided advice, motivation, and support on diet, smoking cessation if relevant, physical activity, and general cardiovascular information. The text messages were 1-way, that is a response was not encouraged and participants were told that responses would not be answered. The primary outcome of low-density lipoprotein cholesterol was significantly lower in the intervention compared with the usual care group and similarly the intervention group achieved lower SBP, lower BMI, higher rates of smoking cessation, and a greater increase in physical activity at the 6-month final follow-up (Table 2).

The Text4Heart trial performed in a New Zealand cohort was a smaller RCT (n = 123), which also addressed multiple behaviour changes (smoking cessation, physical activity, healthy diet, and nonharmful alcohol use) in those with established CHD. The trial lasted 24 weeks, and the intervention group had received 1 message per day (7 per week), which decreased to 5 messages each week from week 13, and had access to a supporting Web site and a pedometer. The study identified positive effects of adherence to healthy lifestyle behaviours at 3 months but not at 6 months. This raises the question about the durability of mHealth interventions as well as the optimal frequency of text messages.

The TEXT ME and Text4Heart trials were both non- or minimally-interactive respectively, and messages semipersonalized (eg, only smokers would receive smoking cessation messages). In contrast, Blasco et al. conducted a 12-month single-blind RCT of 203 patients who had a previous acute coronary syndrome and applied a Web-based telemonitoring service with personalized text messages on the basis of cardiovascular data sent via mobile phone. Specifically, the intervention group would send blood pressure, heart rate, weight (weekly), and glucose and lipids (monthly) results through their mobile phones following a structured questionnaire. A cardiologist would then access the data and send individualized text messages with recommendations about CVD prevention on the basis of the data received. At the 12-month follow-up, participants in the intervention group were significantly (relative risk, 1.4; 95% confidence interval, 1.1-1.7) more likely to have an improved cardiovascular risk profile than controls (69.6% vs 50.5%; \(P = 0.01\)). Furthermore, more patients achieved control for blood pressure and glycosylated hemoglobin in the intervention group compared with controls, with no difference in smoking cessation or low-density lipoprotein cholesterol.

**Smartphone-based interventions**

Effects on total cardiovascular risk or simultaneous multiple cardiovascular risk factor reduction have been less promising with other modalities of mHealth. Johnston et al. examined 174 ticagrelor-treated MI patients in a multicentre RCT. The intervention was an interactive patient support tool (app) that included 4 main modules in which patients were encouraged to actively enter data on physical activity, weight, smoking habits, and a medication adherence e-diary. Additionally, patients could enter data on blood pressure, cholesterol, and blood glucose levels. There was no significant
Smartphone-based interventions

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Chow et al.</td>
<td>N = 710 Australians with proven CHD</td>
<td>6-month duration SMS (4 per week)</td>
<td>Measured at 6 months</td>
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<tr>
<td>Pfaefli Dale et al.</td>
<td>N = 123 New Zealanders with proven CHD</td>
<td>24-week duration Daily SMS and supporting Web site.</td>
<td>Measured at 3 and 6 months</td>
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<tr>
<td>Blasco et al.</td>
<td>N = 203 Spanish ACS survivors</td>
<td>12-month duration Bidirectional personalized SMS</td>
<td>Measured at 12 months</td>
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<td>Smartphone-based interventions</td>
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<tr>
<td>Johnston et al.</td>
<td>N=174 ticagrelor-treated Swedish MI patients</td>
<td>6-month duration Smartphone app (interactive patient support tool app)</td>
<td>Measured at 6 months</td>
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<tr>
<td>Varnfeld et al.</td>
<td>N = 120 Australians post-MI</td>
<td>6-week duration 6-month self-management phase in which participants from both groups were encouraged to continue lifestyle changes</td>
<td>Measured at 6 weeks and 6 months</td>
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<tr>
<td>Widmer et al.</td>
<td>N = 80 Americans post-PCI for ACS</td>
<td>3-month duration DHI consisting of online and smartphone-based program in addition to standard CR program; 30-minute training session for the DHI Control arm was standard CR</td>
<td>Measured at 6 months</td>
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ACS, acute coronary syndrome; AOR, adjusted odds ratio; app, application; BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; CI, confidence interval; CR, cardiac rehabilitation; DHI, digital health intervention; EQ5D, quality of life score; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; K10, Kessler psychological distress scale; LDL-C, low-density lipoprotein cholesterol; MET, metabolic equivalent; mHealth, mobile health; MI, myocardial infarction; 6MWT, 6-minute walk test; PCI, percutaneous coronary intervention; RR, relative risk; SBP, systolic blood pressure; SMS, short messaging service.
change in multiple cardiovascular risk factors (smoking, physical activity) and quality of life at 6 months.

Varnfield et al.34 published the results of an unblinded RCT that recruited 120 Australian patients who had a previous MI to investigate the effect of a smartphone-based home service delivery (Care Assessment Platform) on cardiac rehabilitation. The intervention group received a 6-week program involving an app for health and exercise monitoring, SMS, and audio-visual files. The app included a step counter and exercise diary. The control group participated in a traditional centre-based cardiac rehabilitation program. After the 6-week program, participants were encouraged to maintain lifestyle changes. At the 6-month follow-up, there was a significantly higher uptake (80% vs 62%), adherence (94% vs 68%), and completion (80% vs 47%) of the rehabilitation program in the intervention vs control group (all $P < 0.05$). There were equivalent improvements in 6-minute walk test and healthy diet in both groups at 6 weeks, which was maintained at 6 months. In addition, in the intervention group at 6 weeks there was significantly improved psychological and quality of life scores, and small but significant improvements in weight and waist circumference, not maintained at 6 months. The authors concluded that smartphone-based cardiac rehabilitation programs were used more and were at least as effective as centre-based methods.34 Similarly, Widmer et al.35 recently published a small RCT ($N = 80$) using combined DHI and a traditional cardiac rehabilitation program over 3 months and compared this with traditional rehabilitation. Primary outcomes were cardiovascular-related emergency visits and rehospitalizations, and secondary outcomes were changes in cardiovascular risk factor parameters. Whereas at 90 days, compared with baseline, there was a significant difference in weight loss ($-5.1 \pm 6.5$ kg vs $-0.8 \pm 3.8$ kg; $P = 0.02$), there were no statistically significant differences in other parameters including blood pressure, glycemic control, physical activity, and medication adherence. Additionally, although there was a trend toward reduced hospital visits and admissions at 180 days, this did not reach statistical significance (8.1% vs 26.6%; $P = 0.054$). This might be because the study was underpowered to detect significant differences in the primary outcome of cardiovascular-related emergency visits and rehospitalizations.

The studies presented generally found nil or small improvements in cardiovascular risk factors, but the small trial sizes mean they are unlikely to be powered to detect small improvements in cardiovascular risk factors. The theme of a number of them also suggests the potential for reducing health service utilization and hospitalization, but further research is required to clarify this. If mHealth interventions were able to reach large numbers of people, small improvements might be impactful on a population level. Few studies discuss or examine the extent to which the interventions they propose would be efficacious if implemented into practice, and this should be addressed in future studies.

**Optimizing Medication Adherence**

Medication adherence is a challenge in chronic disease management, and mHealth strategies have also been proposed as having potential in addressing this.36,37 In a recent systematic review that included 107 articles targeting adherence for chronic diseases, most (40.2%) had used SMS-predominant interventions, and 23% used app-predominant methods.38 Of the 6 cardiovascular RCTs that assessed the effectiveness of mHealth on adherence outcomes (predominantly SMS-based), 5 showed a significantly improved medication adherence rate in the intervention vs control groups. Published after this review was the multicentre RCT published by Johnston et al., previously referenced.33 This study in addition assessed drug adherence via an interactive patient support app (described previously) in post-MI patients. They showed that self-reported medication adherence was higher in the intervention vs control arm at the 6-month follow-up (nonadherence score [lower score indicates better adherence]: 16.6 vs 22.8; $P = 0.025$).

More recently, a meta-analysis was published that assessed SMS-based interventions on medication adherence in chronic disease including CVD.39 In this study of 2742 patients across 16 RCTs, participants who received SMS-based interventions were more than twice as likely to have adequate medication adherence compared with controls (odds ratio, 2.11; 95% confidence interval, 1.52-2.93; $P < 0.001$). The median period of intervention was 12 weeks. Similarly, increased adherence to pharmacologic and nonpharmacologic therapy was shown in a recent systematic review including 27 studies (5165 patients) that compared mHealth (all modalities) with standard care.40

The studies presented have shown promise. However, most are predominantly text-message based, and of short duration. More studies are needed to assess the more appropriate medium for delivery (ie, text-message based, app-based, or combination), and long-term studies are required before translation into current health care delivery.

**Limitations of the Current Evidence and Future Implications**

It is apparent that mHealth strategies for CVD prevention have the potential to improve outcomes. The body of evidence is generally supportive of this, however, there are still a significant number of unanswered questions about how to optimize interventions, how to maintain engagement and efficacy, and information on how to quantify the effect size of these interventions is lacking.

However, there is already an overwhelming number of cardiovascular mHealth options available to consumers. Many of these available mHealth interventions have not undergone significant evaluation, and most apps have not gone through Food and Drug Administration approval. Although direct harm from an mHealth intervention might seem unlikely, a lack of benefit is a harm to public health, and the delivering of incorrect information potentially even more harmful. Implementation of high-quality and effective mHealth interventions needs to be our goal. And although the background has become increasingly complex with the range of freeware available to consumers, as clinicians and patients we still seek those interventions that are most effective.

Thus, future studies are needed to better evaluate mHealth interventions with respect to long-term outcomes, optimizing programs (including program duration, frequency of text messages, degree of complexity, degree of interactivity, and degree of personalization), and safety, effectiveness, and cost-
effectiveness. Furthermore, studies assessing mHealth pro-
grams across different socioeconomic classes, cultural groups,
and in different languages would be highly valuable in
determining the potential reach of these programs and how to
customize and optimize them for wider delivery. Importantly,
future mHealth producers should collaborate with clinicians
and regulatory agencies to ensure the interventions are safe
and effective, and outcome measures standardized.

There are important limitations to consider in our review.
Because of the paucity of RCTs evaluating mHealth on
multiple risk factor reduction, this is a narrative literature
review and not a systematic review. Additionally, we have only
included published studies.

Conclusions
mHealth interventions are a novel, exciting, and expanding
field in medicine that will potentially transform health care
delivery by improving access to treatments that would
otherwise require frequent clinic/hospital visits. In particular,
SMS-based interventions, because of their low cost and
ubiquity, could assist in achieving equity in delivery of car-
diovascular prevention programs to developed as well as
developing nations. There is evidence supporting the utility of
mHealth programs, at least in the short-term. However, there
are many unknown variables including which mode of
mHealth (or combination of) would be most efficacious. The
current challenge is ensuring patients have access to evidence-
base-based interventions that have the input of clinicians.

Funding Sources
Clara K. Chow is supported by National Health and
Medical Research Council Career Development Award
(APP1105447) co-funded by a Future Leader Fellowship
from the National Heart Foundation.

Disclosures
The authors have no conflicts of interest to disclose.

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