Global Burden of Cardiovascular Disease

Mobile Health Devices as Tools for Worldwide Cardiovascular Risk Reduction and Disease Management

John D. Piette, PhD; Justin List, MD; Gurpreet K. Rana, MLIS; Whitney Townsend, MLIS; Dana Striplin, MHSA; Michele Heisler, MD, MPA

Abstract—We examined evidence on whether mobile health (mHealth) tools, including interactive voice response calls, short message service, or text messaging, and smartphones, can improve lifestyle behaviors and management related to cardiovascular diseases throughout the world. We conducted a state-of-the-art review and literature synthesis of peer-reviewed and gray literature published since 2004. The review prioritized randomized trials and studies focused on cardiovascular diseases and risk factors, but included other reports when they represented the best available evidence. The search emphasized reports on the potential benefits of mHealth interventions implemented in low- and middle-income countries. Interactive voice response and short message service interventions can improve cardiovascular preventive care in developed countries by addressing risk factors including weight, smoking, and physical activity. Interactive voice response and short message service–based interventions for cardiovascular disease management also have shown benefits with respect to hypertension management, hospital readmissions, and diabetic glycemic control. Multimodal interventions including Web-based communication with clinicians and mHealth-enabled clinical monitoring with feedback also have shown benefits. The evidence regarding the potential benefits of interventions using smartphones and social media is still developing. Studies of mHealth interventions have been conducted in >30 low- and middle-income countries, and evidence to date suggests that programs are feasible and may improve medication adherence and disease outcomes. Emerging evidence suggests that mHealth interventions may improve cardiovascular-related lifestyle behaviors and disease management. Next-generation mHealth programs developed worldwide should be based on evidence-based behavioral theories and incorporate advances in artificial intelligence for adapting systems automatically to patients’ unique and changing needs. (Circulation. 2015;132:2012-2027. DOI: 10.1161/CIRCULATIONAHA.114.008723.)

Key words: computational biology ■ developing countries ■ telemedicine

Cardiovascular disease is the leading cause of death and disease globally, responsible for 30% of all deaths worldwide. Improved cardiovascular outcomes depend largely on how well affected people manage these conditions between face-to-face office visits with their healthcare providers. Self-management is often challenging because of the complexity of patients’ medication regimens; the importance of self-monitoring for signs of emerging complications; and the need for lifestyle behavior change including physical activity, healthy diet, smoking cessation, and weight loss. Especially in resource-constrained settings, healthcare providers have limited opportunity to interact directly with patients between in-person encounters. The effective use of patient-centered health communication technology thus represents a promising approach to extend the reach of health systems to provide ongoing support.

Limitations of Health Systems in Low- and Middle-Income Countries

Providing patients with the tools to take an active, participatory role in their cardiovascular disease prevention and management is particularly important in low- and middle-income countries (LMICs). Patients with chronic diseases in less developed countries often face out-of-pocket healthcare costs that are prohibitive given limited household budgets. A World Health Organization survey of >256 000 respondents in 70 countries found that health care accounted for 13% to 32% of household expenditures, and cost barriers were a frequently cited reason for inadequate chronic illness care. Even when patients can afford it, health services in LMICs for lifestyle behavior change and disease management are often unavailable or of low quality. According to the World Health Organization, the global deficit of health professionals

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exceeds 4 million, with severe shortages in 57 countries. The number of health professionals who leave LMICs to practice elsewhere has never been higher, and providers who stay in LMICs are often poorly trained for the growing challenge of preventing and managing cardiovascular health problems.

Mobile Health as a Partial Solution

Innovations in mobile health technology may help to address the barriers to cardiovascular disease prevention and management. There are >6 billion mobile phone users worldwide with almost three-quarters living in LMICs. The explosion in cell phone use represents an important resource for lifestyle behavior change and disease management, because abundant evidence has demonstrated that telephone follow-up improves the quality and outcomes of care. Although most trials of telephone care have been conducted in high-income countries (HICs), investigators in Chile reported that low-income diabetic patients randomly assigned to telephone nurse counseling had better glycemic control than patients receiving usual care, and postdischarge telephone support for patients with heart failure in Argentina significantly reduced readmission rates relative to randomly assigned controls.

Unfortunately, telephone care management programs often fail to demonstrate the cost savings that decision makers look for to justify the investment in human capital. In a review of 15 randomized care management trials including >18 000 chronically ill patients, investigators found that only 2 studies showed significant reductions in healthcare costs. Other studies including data on hundreds of thousands of patients receiving care management with telephone follow-up also have found that improving quality through care management while reducing costs is extremely difficult. To meet the dual goals of improving cardiovascular outcomes while minimizing the costs associated with clinician follow-up, health systems, and payers increasingly look to mobile health technologies that can deliver health information and improve patient monitoring between visits, a field now widely known as mobile health or mHealth (a specialized offshoot of the more established field of health informatics known as eHealth). Previous reviews report generally positive impacts of mHealth on chronic disease treatment and outcomes, although significant barriers to implementation remain in LMICs.

mHealth interventions take a variety of forms, each with its own benefits and limitations in terms of the specific modality’s reach and the richness of the information exchange (see Table 1 and Figure). Interactive voice response (IVR) calls allow patients to receive information and communicate with others asynchronously using their mobile or landline telephone. Using IVR, patients interact with a structured series of recorded message components and respond to queries using their touch-tone keypad or voice-recognition technology. Based on their responses, patients can receive recorded messages tailored to their individual needs. Clinicians can receive automated updates based on patients’ responses during IVR calls, along with structured feedback about how to improve disease management. Patient-directed short message service (SMS) or text messaging interventions are designed to improve disease management primarily through reminders that improve adherence to behavioral goals such as medication taking, and through educational or supportive messages that increase motivation for changes in lifestyle behaviors or self-care. SMS messages can be triggered automatically or by clinicians, and some services use bidirectional communication with patients to increase program engagement and service impact. More recent advances in mHealth include smartphones and other mobile communication tools enabled with graphical screens, video, audio, and Internet access. An advantage of smartphones is that structured information from patients can be collected through a touchscreen or voice recognition system, thereby allowing more accurate and extensive patient reporting than is possible with SMS. Global positioning systems and physiological sensors can be added to further tailor health communication and monitor patients’ status. The widespread and growing use of social media such as social network sites, blogs, wikis, Twitter chats, photo/video sharing services, and virtual worlds represent additional opportunities for engaging patients via their smartphone. In particular, new social media can extend the reach and impact of social networks, enable sharing of knowledge and information, and integrate real-time personal health data to leverage peer support.

Scope of the Review

We conducted a state-of-the-art review and synthesis of the evidence regarding the potential benefits of mHealth interventions for improving the quality and outcomes of services targeting lifestyle behavior change and management of cardiovascular diseases. Key innovations are described for interventions using IVR and SMS that are accessible from almost any cell phone, and interventions using Web-enabled communication tools such as smartphones, as well. Given the large volume of literature in this field and limits on the length of the review, studies of interventions using specialized devices (eg, electronic scales for assessing patients’ weight or automatically uploading blood pressure monitors) were not included. Although much less research has been conducted on the use of social networking tools to address the needs of patients with chronic diseases, we also report on the use of those approaches when evaluations have been reported in the literature. Our review of the evidence focused primarily on randomized trials, although other studies were included when they represented the strongest evidence available for an important topic. Most research on mHealth has been conducted in a small number of HICs; however, we highlight studies that have been conducted in less represented regions of the world, including LMICs.

Methods

Literature Search Methods

Using an accepted typology for reviews, we conducted a state-of-the-art review and literature synthesis. These reviews are appropriate for situations such as this one in which the purpose is to identify future areas of research in a new and rapidly evolving field of evidence. The literature search was conducted in March 2014 by the informationists (G.K. Rana and W. Townsend) to identify scholarly research and industry reports related to eHealth and social media interventions for cardiovascular disease lifestyle behavior change and management. A broad net was cast to find potentially relevant literature that could be applicable to cardiovascular disease. Discrete systematic searches were conducted in the

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Medline, Scopus, Embase, Global Health (Centre for Agriculture and Biosciences International), and Health Policy Reference Center literature databases. Separate searches were also run in each database to identify mHealth interventions in the areas of infectious disease management and maternal health services to identify effective interventions that could be adapted and applied to populations affected by cardiovascular diseases. Searches used controlled vocabulary terminology and keywords representing search concepts in mHealth in LMICs, including: mHealth and social networking; cardiovascular disease and eHealth programs; eHealth strategies in vector-borne and infectious disease management; and use of eHealth/mHealth in maternal and reproductive health services. A sample Medline search strategy using the Ovid interface is included in the online-only Data Supplement. Additional search details are available from the authors on request.

To identify gray or potentially unpublished literature, general Web searches and searches of business resources for mobile industry–specific reports and reports from global public health organizations including the World Health Organization were conducted. Searches were limited to articles published in English in the past 10 years. Hand searching and the initial appraisal of search retrieval were conducted by the informationists, with final screening and assessment for relevance conducted by other authors. A secondary subsearch was limited to English-language randomized controlled trials and clinical studies published in the past 5 years. Citations of identified articles were hand searched for relevant references.

## Results

### mHealth Interventions for Lifestyle Behavior Change

#### Interactive Voice Response

Trials conducted in HICs have shown that IVR-based interventions can be effective in promoting physical activity, improved dietary behavior, and smoking cessation (Table 2).\(^3^7,59,40,46^\) A trial of 337 blacks with hypertension found that 32 weekly IVR calls improved overall dietary quality and energy expenditures relative to controls who also received a resource manual and a 20-minute in-person health education session focused on lifestyle behaviors.\(^3^7^\) A study of an IVR-delivered intervention focused on family goal setting and changes in the home environment showed improvements in obese children’s level of physical activity, dietary behaviors, and body mass index.\(^4^4^\) In a diverse low-income sample of patients with diabetes mellitus, investigators found that an IVR service coupled with nurse care management achieved physical activity objectives at modest cost.\(^3^6^\)

### SMS or Text Messaging

With 5800 participants, the SMS smoking cessation program (txt2stop) trial sought to improve smoking cessation rates in the United Kingdom through a series of motivational messages.\(^4^5^\) Patients were randomly assigned to receive motivational SMS messages or messages unrelated to smoking. Txt2stop more than doubled biochemically confirmed quit rates at 6 months relative to controls. Studies of SMS interventions focused on promoting a more healthy diet, weight loss, and physical activity in HICs have shown mixed results. One US trial using daily SMS messages focused on tailored dietary goal setting and showed significant improvements at 4 months in eating...
Table 2. Trials Using mHealth Interventions for Lifestyle Behavior Change

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Sample Characteristics</th>
<th>Country</th>
<th>mHealth Tool</th>
<th>Intervention Components</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chow et al (2012)</td>
<td>720 adults with coronary artery disease</td>
<td>Australia</td>
<td>SMS (4 messages per wk for 24 wk)</td>
<td>Messages to reduce CVD risk factors: motivation to quit smoking, follow a healthy diet, and exercise</td>
<td>RCT: SMS vs usual care 6 mo follow-up</td>
<td>Ongoing trial</td>
</tr>
<tr>
<td>Handley et al (2008)</td>
<td>226 adults with type 2 diabetes mellitus</td>
<td>USA</td>
<td>Weekly IVR</td>
<td>IVR patient education and nurse phone counseling</td>
<td>RCT: IVR vs usual care 12 mo follow-up</td>
<td>Per-patient cost of $65K per QALY, 14% increase in the proportion of patients achieving vigorous activity relative to controls</td>
</tr>
<tr>
<td>Migneault et al (2012)</td>
<td>337 urban black adults with hypertension</td>
<td>USA</td>
<td>32 weekly IVR counseling sessions</td>
<td>Patient reported health information collected on study-issued home measurement devices with motivational and behavior-change messages targeting medication adherence, physical activity, and diet</td>
<td>RCT: IVR vs usual care 8 mo follow-up</td>
<td>Significant improvement in overall diet quality score (P&lt;0.03), fiber intake (P&lt;0.02), and energy expenditure (P&lt;0.02) in the intervention group; no significant differences in medication adherence</td>
</tr>
<tr>
<td>Newton et al (2009)</td>
<td>78 adolescents from 4 regional diabetes services</td>
<td>New Zealand</td>
<td>Weekly SMS messages</td>
<td>Motivational reminder messages to wear a pedometer and be active</td>
<td>RCT: SMS vs usual care 12 wk follow-up</td>
<td>No improvement in physical activity</td>
</tr>
<tr>
<td>Nolan et al (2011)</td>
<td>680 adults at high risk of CVD or with CVD diagnoses</td>
<td>Canada</td>
<td>6 weekly 1-h group teleconferences with lifestyle counseling sessions</td>
<td>Baseline advice and education for both groups plus 6 weekly 1-h teleconference lifestyle counseling sessions</td>
<td>RCT: teleconferencing on lifestyle vs active control (risk factor feedback, brief advice, handouts) 6 mo follow-up</td>
<td>Significant improvements in exercise and diet in teleconference group (P&lt;0.001) and in systolic and diastolic BP relative to control (P&lt;0.001)</td>
</tr>
<tr>
<td>Reid et al (2007)</td>
<td>99 adult smokers recently hospitalized with CVD</td>
<td>Canada</td>
<td>IVR posthospital discharge calls on days 3, 14, and 30</td>
<td>Questions about smoking status, confidence in stopping smoke-free, use of pharmacotherapy, and self-help information with feedback to a nurse who set up phone counseling sessions for those reporting smoking-abstinence problems</td>
<td>RCT: IVR vs usual care 12 mo follow-up</td>
<td>Greater proportion abstinent (odds ratio, 2.34; 95% CI, 0.92–5.92; P=0.07)</td>
</tr>
<tr>
<td>Wong et al (2013)</td>
<td>105 professional drivers with prediabetes</td>
<td>Hong Kong</td>
<td>SMS 3 times/wk for 3 mo, then weekly, then monthly</td>
<td>Messages regarding diabetes knowledge and lifestyle modification</td>
<td>RCT: SMS vs usual care 24 mo follow-up</td>
<td>Risk of DM onset 5.6% vs 16% at 12 mo (RR, 0.35; 95% CI, 0.10–1.24) but nonsignificant results at 24 mo</td>
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<tr>
<td>Other participants</td>
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<tr>
<td>Appel et al (2011)</td>
<td>415 obese adults with at least 1 cardiovascular risk factor</td>
<td>USA</td>
<td>Weekly website learning modules</td>
<td>Website learning modules (self-monitoring weight, calorie intake, exercise) with monthly e-mail messages summarizing progress</td>
<td>RCT: remote weight loss support, vs remote support plus in-person support, vs self-directed behavior change control group 24 mo follow-up</td>
<td>Greater weight loss at 24 mo with remote support (~4.6 kg) and remote plus in-person support (~5.1 kg) in comparison with control (~6.8 kg, P&lt;0.001)</td>
</tr>
<tr>
<td>de Niet et al (2012)</td>
<td>141 overweight or obese children</td>
<td>Netherlands</td>
<td>Weekly SMS messages</td>
<td>Patient-reported data on exercise and diet with tailored behavior-change feedback</td>
<td>RCT: SMS vs usual care 12 mo follow-up</td>
<td>No improvement in weight, eating behavior, or well-being</td>
</tr>
<tr>
<td>Estabrooks et al (2009)</td>
<td>22 parent-child dyads with overweight children</td>
<td>USA</td>
<td>10 weekly IVR counseling sessions</td>
<td>Tailored messages regarding changes in home environment to promote activity and healthy eating</td>
<td>RCT: IVR vs individual workbook education vs group counselling 12 mo follow-up</td>
<td>Greater improvement in child BMI in the IVR group than the other 2 groups (P&lt;0.01)</td>
</tr>
<tr>
<td>Free et al (2011)</td>
<td>5800 adult smokers willing to make a quit attempt</td>
<td>United Kingdom</td>
<td>SMS messages (5 per day first 5 wk, 3 times/d last 26 wk)</td>
<td>Motivational and behavior-change messages</td>
<td>RCT: SMS messages vs SMS attention control 6 mo follow-up</td>
<td>Increase in biochemically-confirmed quit rates (10.7% vs 4.9%; P&lt;0.0001)</td>
</tr>
<tr>
<td>King et al (2014)</td>
<td>127 inactive midlife and older adults</td>
<td>USA</td>
<td>IVR counseling sessions (=15 delivered over a year)</td>
<td>Instructional sessions emphasizing cognitive and behavioral skills, based on current stage of motivational readiness to change, for moderate-intensity physical activity adoption</td>
<td>RCT: IVR vs human counselling 18 mo follow-up</td>
<td>No difference in moderate-to-vigorous physical activity levels or percentage meeting national physical activity guidelines</td>
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</tbody>
</table>

(Continued)
behavior and body weight. However, an SMS intervention incorporating pedometer step-count feedback among adolescents with diabetes mellitus did not increase physical activity. A trial focusing on promoting weight maintenance after a 3-month behavioral weight loss program through bidirectional and tailored SMS messages found no overall benefit over the subsequent 9 months in weight, eating behavior, or psychological mediators of behavior change. Despite relatively high adherence among adult participants in an interactive and personalized weight management program, investigators found no between-group difference at 6 and 12 months in weight or obesity scores (all P<0.05); weight loss 5.4 lbs in comparison with 1.4 in controls (P<0.006).

Research currently underway may further elucidate the potential of SMS for promoting meaningful lifestyle behavior changes that are important for cardiovascular risk reduction.

Studies including SMS interventions have been conducted in >30 countries, including several LMICs. A trial conducted in Hong Kong found that SMS messages focused on diabetes mellitus–related lifestyle modification reduced rates of progression from prediabetes to diabetes mellitus over 12 months. Many mHealth studies in LMICs have focused on human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS); 2 large randomized trials in Kenya found that SMS reminders improved adherence to antiretroviral therapy, and 1 trial also reported reductions in viral load among patients receiving SMS adherence reminders relative to randomly assigned controls. (See online-only Data Supplement Table I for a summary of HIV/AIDS trials.)

Other mHealth Approaches

The use of multiple mHealth communication modalities together may improve their impact on cardiovascular disease–related lifestyle behaviors. For example, a quasi-experimental study in Korea evaluated a combined SMS plus Internet intervention among overweight and obese women and demonstrated significant reductions in waist circumference, body weight, total cholesterol, and low-density lipoprotein cholesterol. In another trial, investigators found that remote weight-loss support by using a combination of telephone, Internet, and email resulted in improvements in weight at 24 months in comparison with what was achieved with an in-person weight loss intervention. Especially because of their widespread use among younger adults, social media technologies including podcasts, apps, and Twitter represent promising channels for communicating about cardiovascular disease prevention. In 1 trial, overweight adults were randomly assigned to multiple motivational podcasts per week or podcasts plus additional behavior change support via a specialized app on users’ smartphones and interaction via Twitter with behavioral counselors. Although the enhanced communication group was more engaged with online health information resources, there was no incremental benefit in weight loss at 6 months relative to participants receiving podcasts alone.
**mHealth Interventions for Cardiovascular Disease Management**

**Interactive Voice Response**

IVR monitoring can provide reliable and valid information about patients’ status between outpatient encounters, including information about socially stigmatizing behaviors (Table 3). Non–English-speaking patients are willing and able to use IVR as part of their disease management. In a study of 464 underserved patients with home blood pressure monitors, patients were able to accurately report their blood pressure values via IVR, obviating the need for more costly automatically uploading blood pressure devices.

IVR-based interventions can improve outcomes for patients with chronic illnesses. In a quasi-randomized study including >3000 Medicare patients, IVR-supported postdischarge care management was associated with a 44% reduction in 30-day readmission rates in comparison with care management without IVR support. Other studies using IVR to improve adherence to self-care plans have shown improvements in outcomes for patients after cardiac surgery or with hypercholesterolemia. One trial among patients with poorly controlled hypertension showed improvements in diastolic blood pressures and medication adherence at 6 months. A separate hypertension trial demonstrated greater improvements in systolic blood pressures among patients receiving IVR-supported care management than randomly assigned controls.

A number of trials have demonstrated benefits of IVR-supported diabetes care. In a trial of lower-income patients with diabetes mellitus in the United States, participants receiving IVR calls with nurse follow-up experienced significant improvements at 12 months relative to randomly assigned controls in glycemic control, self-care behaviors, and patient-centered outcomes such as depressive symptoms. A similar intervention among patients receiving care in the US Department of Veterans Affairs health system had similar 12-month findings. Intervention patients receiving IVR-supported diabetes management in Australia had improvements at 6 months in glycemic control and mental health functioning relative to randomly assigned controls.

Not all trials of IVR-supported diabetes care have shown benefit. One trial of women with gestational diabetes mellitus found no impact on maternal blood glucose levels. A trial of IVR use to promote diabetes mellitus–related retinopathy testing among 1200 health plan members showed low uptake of the intervention and no improvement in testing rates relative to randomly assigned controls. Finally, a US trial of IVR augmentation to a successful peer-support model for promoting care management among Spanish speakers with diabetes mellitus found no incremental benefit of the IVR booster intervention.

To our knowledge, only 2 published studies have examined the impact of IVR-supported disease management in LMICs. In 1 prepost study, investigators tested the feasibility of delivering IVR diabetes management calls to patients in Honduras using a cloud computing approach with the IVR infrastructure maintained in the United States, and calls sent using Voice over IP. Despite very low levels of educational attainment, at the 6-week follow-up, participants reported high levels of intervention satisfaction and improvements in their self-care. Hemoglobin A1c levels improved significantly, and patients reported improvements in their perceived health. In a randomized trial, 200 patients with poorly controlled hypertension were enrolled in clinics in Honduras and Mexico. Intervention patients received weekly IVR monitoring and self-care support calls, and structured notifications based on patients’ IVR-reported information were sent automatically to the clinical team. At follow-up, intervention patients had systolic blood pressures that were on average 4.2 mm Hg lower than control patients, and in a preplanned subgroup analysis among patients with high information needs, intervention patients had an average 8.8 mm Hg reduction in systolic blood pressure relative to controls. Intervention patients at follow-up also had fewer depressive symptoms, fewer medication problems, better overall perceived health, and greater satisfaction with their hypertension care. Because literacy rates are lower in LMICs, patients may prefer IVR to SMS adherence reminders. However, IVR call completion rates are lower in LMICs than they are in more developed countries, particularly among older adults.

**SMS or Text Messaging**

A 2012 Cochrane review evaluating the evidence on SMS messaging for facilitating chronic disease self-management found only 4 randomized trials that met their quality criteria (2 diabetes mellitus trials, 1 hypertension trial, and 1 asthma trial). The authors cautiously concluded that there were some indications across all the studies that mobile phone messaging interventions may improve chronic disease self-management. However, they also noted significant information gaps regarding long-term effects, acceptability, costs, and the possible risks of such interventions.

A recent quasi-experimental study found that SMS program participation resulted in improved glycemic control, high patient satisfaction with care, and a net cost saving of 8.8% in comparison with the same time period before the program. Over 6 months, adults with diabetes mellitus received automated text messages, including educational modules on diabetes self-care and prompts to engage in specific behaviors (eg, “Do you need refills of any of your medications?”). Patients were asked to respond to messages via a reply text, and patient reports exceeding predefined thresholds triggered a response from a nurse. To increase patient engagement and message relevance, the contents of the messages were modified every 2 weeks based on users’ interactions with the system. With program costs estimated at $375 per patient, net cost savings in outpatient, emergency department, and inpatient care were $437 per patient. In another US trial among English- and Spanish-speaking patients with diabetes mellitus presenting to a safety net emergency department, the intervention group received 2 daily SMS messages and had improvements in medication adherence and decreased emergency department use over the subsequent 6-month period. Intervention effects were particularly pronounced among Spanish speakers.

A 2014 trial examined antiplatelet and statin medication adherence among recently discharged patients hospitalized for a myocardial infarction or cardiac procedure. Patients were
Table 3. Trials Using mHealth Interventions for Cardiovascular Disease Management

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Participants identified with HTN</th>
<th>Sample Characteristics</th>
<th>Country</th>
<th>mHealth Tool</th>
<th>Intervention Components</th>
<th>Design</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Contreas et al (2004)&lt;sup&gt;27&lt;/sup&gt;</td>
<td>67 adults with HTN</td>
<td>Spain</td>
<td>Twice/wk SMS</td>
<td>Information and adherence reminders</td>
<td>Cluster RCT: SMS vs usual care 6 mo follow-up</td>
<td>No significant differences in adherence to HTN therapy</td>
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<tr>
<td>Friedman et al (1996)&lt;sup&gt;16&lt;/sup&gt;</td>
<td>267 adults with HTN</td>
<td>USA</td>
<td>Weekly patient-initiated IVR calls</td>
<td>IVR-reported BP, medication understanding, adherence, and symptoms; IVR provided education and motivation and transmitted patient reports to provider</td>
<td>RCT: IVR vs usual care 6 mo follow-up</td>
<td>Significantly improved medication adherence (17.7% IVR adherence in comparison with 11.7% in controls; P=0.03), BP improved more in IVR group if medication adherence improved (diastolic BP mean decrease of 5.5 mm Hg in comparison with 0.6, P=0.03)</td>
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<tr>
<td>Magid et al (2011)&lt;sup&gt;19&lt;/sup&gt;</td>
<td>283 adults with HTN taking ≤4 antihypertensive meds</td>
<td>USA</td>
<td>Weekly IVR</td>
<td>Self-reported home BP monitoring with pharmacist follow-up</td>
<td>RCT: IVR vs usual care 6 mo follow-up</td>
<td>Systolic BP reductions significantly greater in intervention group (~13.1 mm Hg in comparison with ~7.1 mm Hg, P=0.006)</td>
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<tr>
<td>Margolis et al (2013)&lt;sup&gt;30&lt;/sup&gt;</td>
<td>450 hypertensive adults with uncontrolled BP</td>
<td>USA</td>
<td>BP transmitted 6 times/wk via modem to Telemonitoring (TM) website</td>
<td>Home BP telemonitoring with BP readings transmitted to pharmacist for medication adjustment</td>
<td>Randomized 2-group cluster: TM vs usual care 12 mo follow-up</td>
<td>Significantly more TM patients with controlled BP at follow-up (71.8% in comparison with 45.2% in controls, P&lt;0.001)</td>
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<tr>
<td>Piette et al (2012)&lt;sup&gt;21&lt;/sup&gt;</td>
<td>200 Spanish-speaking adults with systolic BP ≥140 mm Hg (non diabetic) or ≥130 mm Hg (diabetic)</td>
<td>Honduras and Mexico</td>
<td>Weekly IVR</td>
<td>Weekly automated monitoring and behavior-change calls plus home BP monitoring</td>
<td>RCT: IVR vs usual care 6 wk follow-up</td>
<td>IVR significantly improved depressive symptoms, medication problems, general health, and satisfaction with care (P≤0.004), systolic BP 4.2 mm Hg lower (P=0.09), improved systolic BP among patients with low literacy (~8.8 mm Hg, P=0.002)</td>
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<tr>
<td>Arora et al (2014)&lt;sup&gt;25&lt;/sup&gt;</td>
<td>128 adults with poorly controlled diabetes mellitus</td>
<td>USA</td>
<td>Daily SMS messages</td>
<td>Education and motivational texts plus reminders; trivia questions with answers delivered 1 h later</td>
<td>RCT: SMS vs usual care 6 mo follow-up</td>
<td>No significant difference in HbA1c improvement, although SMS group improved in medication adherence and emergency department use relative to controls</td>
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<tr>
<td>Homko et al (2012)&lt;sup&gt;20&lt;/sup&gt;</td>
<td>80 women at least 33 wk gestation with gestational diabetes mellitus</td>
<td>USA</td>
<td>Up to 3 IVR reminders (a day apart)</td>
<td>Asynchronous 2-way communication between patients and providers plus automated patient reminders to transmit health data to providers</td>
<td>RCT: IVR vs usual care, duration from enrollment to delivery: average 2 mo</td>
<td>No improvement in maternal glucose control or infant birth weight</td>
<td></td>
</tr>
<tr>
<td>Lorig et al (2008)&lt;sup&gt;44&lt;/sup&gt;</td>
<td>533 Spanish-speaking adults with diabetes mellitus</td>
<td>USA</td>
<td>Monthly IVR</td>
<td>IVR reinforcement calls to patients participating in a 6-wk community-based peer-led program of self-management support</td>
<td>RCT: IVR vs usual care 18 mo follow-up</td>
<td>Increases in glucose monitoring for patients receiving IVR (P=0.001) but no improvement in HbA1c, symptoms, or other outcomes</td>
<td></td>
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<tr>
<td>Nundy et al (2014)&lt;sup&gt;26&lt;/sup&gt;</td>
<td>67 adults with type 1 or type 2 diabetes mellitus</td>
<td>USA</td>
<td>2–6 SMS messages/d</td>
<td>Messages provided self-management support with approximately monthly nurse calls and facilitated team-based care</td>
<td>Quasi experiment with health plan members who were not enrolled serving as controls</td>
<td>Pre-post improvement in glycemic control (P=0.01, no glycemic change in controls), costs decreased in both groups pre/post (8.8%, P=0.02)</td>
<td></td>
</tr>
<tr>
<td>Piette et al (2000)&lt;sup&gt;9,37&lt;/sup&gt;</td>
<td>248 adults with diabetes (English or Spanish speaking)</td>
<td>USA</td>
<td>Biweekly IVR</td>
<td>IVR behavior and symptom assessment with tailored patient feedback and telephone follow-up by a nurse care manager</td>
<td>RCT: IVR vs usual care 12 mo follow-up</td>
<td>IVR increased proportion of patients with normal HbA1c by 9% (P=0.04), decreased serum glucose by 41 mg/dL (P=0.002), decreased depressive symptoms and sick days (both P&lt;0.03)</td>
<td></td>
</tr>
<tr>
<td>Piette et al (2001)&lt;sup&gt;28&lt;/sup&gt;</td>
<td>272 VA diabetic patients on hypoglycemic medication</td>
<td>USA</td>
<td>Weekly IVR</td>
<td>IVR assessment and self-care education with follow-up by a nurse care manager</td>
<td>RCT: IVR vs usual care 12 mo follow-up</td>
<td>Increased frequency of patient monitoring of blood glucose (P=0.05) and feet inspection (P=0.05)</td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
Table 3. Continued

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Sample Characteristics</th>
<th>Country</th>
<th>mHealth Tool</th>
<th>Intervention Components</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piette et al (2011)78</td>
<td>85 Spanish-speaking adults with diabetes mellitus</td>
<td>Honduras</td>
<td>Weekly IVR</td>
<td>Weekly self-management support calls with concerning patient reports forwarded to participants clinical team</td>
<td>Single-group, pre-post study with 6-wk follow-up</td>
<td>HbA1c improved from 10% at baseline to 8.9% at follow-up (P&lt;0.01). High intervention satisfaction and participation in IVR calls, and improved perceived health</td>
</tr>
<tr>
<td>Quinn et al (2008)79</td>
<td>32 adults with type 2 diabetes mellitus</td>
<td>USA</td>
<td>Monthly cell phone transmission via WellDoc</td>
<td>Cell phone software delivered real-time feedback on HbA1c levels; both groups received blood glucose monitors</td>
<td>RCT: Cell phone-delivered feedback vs usual care 3 mo follow-up</td>
<td>Significant improvement in HbA1c (decrease of 2.03% in comparison with 0.68% in controls, P&lt;0.02)</td>
</tr>
<tr>
<td>Quinn et al (2011)80</td>
<td>126 adults with type 2 diabetes mellitus from 26 primary care practices</td>
<td>USA</td>
<td>Mobile coaching and patient/provider Web portals</td>
<td>Automated medication management and lifestyle behavior messages in response to patient-reported blood glucose values with quarterly reports to providers</td>
<td>Cluster-randomized trial: 3 stepped treatment groups vs usual care 12 mo follow-up</td>
<td>Significantly greater improvement in HbA1c in maximal treatment group at follow-up (1.9% in comparison with 0.7% in controls, P=0.001)</td>
</tr>
<tr>
<td>Schillinger et al (2008)81</td>
<td>339 English-, Spanish-, or Cantonese-speaking adults with diabetes mellitus</td>
<td>USA</td>
<td>Weekly IVR</td>
<td>Evaluating the reach of self-management support strategies in 2 intervention groups: those receiving IVR and those in the monthly Group Medical Visit (GMV) group</td>
<td>Effectiveness study within RCT: IVR or GMV vs usual care 9 mo follow-up</td>
<td>IVR arm yielded higher engagement, especially among those with limited English proficiency and literacy, than the GMV arm (93.8% IVR in comparison with 69.6% GMV)</td>
</tr>
<tr>
<td>Simon et al (2010)82</td>
<td>232 adults with diabetes mellitus overdue for diabetes-related screening</td>
<td>USA</td>
<td>3 IVR calls</td>
<td>IVR reminders to encourage dilated eye examinations and laboratory tests, with offer of token gifts</td>
<td>RCT: IVR vs usual care 30 day follow-up</td>
<td>No difference in time to completion of eye examinations, or testing of HbA1C, LDL, or microalbumin</td>
</tr>
<tr>
<td>Williams et al (2012)83</td>
<td>120 adults with type 2 diabetes mellitus and HbA1c ≥7.5%</td>
<td>Australia</td>
<td>Weekly IVR call-in</td>
<td>Assessments of patients' health and self-care with tailored feedback; email alerts sent to study team if any concerning issues reported during the call</td>
<td>RCT: IVR vs usual care 6 mo follow-up</td>
<td>Significantly improved HbA1c (IVR: 8.7%–7.9%; controls: 8.9%–8.7%, P=0.002); relative improvement in mental HRQL (P=0.007)</td>
</tr>
</tbody>
</table>

Participants identified with other/multiple cardiovascular risks

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Sample Characteristics</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Boriani et al (2013)84</td>
<td>148 adults with heart failure and implanted CRT-D devices</td>
<td>France, Hungary, Israel, Italy, Spain, Switzerland</td>
<td>Remote monitoring with alerts triggered by device</td>
<td>Remote follow-up and wireless automatic alerts to clinic nurses or physicians for lung fluid overload</td>
<td>RCT: Remote monitoring vs usual care 12 mo follow-up</td>
<td>Significantly shorter delay in clinical follow-up (2 days in comparison with 29 days in control group, P=0.004) and significantly reduced inpatient stays (P&lt;0.001)</td>
</tr>
<tr>
<td>Glozier et al (2013)85</td>
<td>487 adults with depression and CVD</td>
<td>Australia</td>
<td>Weekly Internet-based CBT</td>
<td>Internet-based CBT (E-Couch) compared with online attention control (HealthWatch)</td>
<td>RCT: Internet-based CBT vs attention control 12 wk follow-up</td>
<td>Significantly greater improvement in depression scores (P=0.012), self-reported medication adherence, and health behaviors</td>
</tr>
<tr>
<td>Graham et al (2012)86</td>
<td>3295 Medicare case-managed adults</td>
<td>USA</td>
<td>Weekly IVR for 30 days</td>
<td>Geisinger Monitoring Program (GMP) IR protocol to reduce 30-day readmission rates with case management</td>
<td>Pre-post parallel quasi-experimental study, GMP IVR vs matched controls 30 day follow-up</td>
<td>Patients in IVR monitoring plus case management were 44% less likely to have a 30-day readmission than the case management alone group (P=0.0004)</td>
</tr>
<tr>
<td>Park et al (2014)87</td>
<td>90 adults with CVD</td>
<td>USA</td>
<td>At least daily SMS messages, educational messages 3 times/wk</td>
<td>Messages to improve adherence to antplatelet and statin meds. with personalized 2-way reminders correlated with medication schedule and 1-way educational messages</td>
<td>RCT: SMS educational messages only, vs SMS medication reminders plus educational messages, vs usual care 30-day follow-up</td>
<td>SMS medication reminders improved antplatelet medication adherence (P=0.02), and percentage of doses taken on schedule (P=0.01), no significant differences in clinical outcomes between SMS groups</td>
</tr>
</tbody>
</table>
A 2010 systematic review of behavior change interventions for chronic disease management and prevention delivered through SMS examined 9 studies that were sufficiently powered to detect a difference in the specific characteristics of the intervention.26 Eight of the 9 studies found evidence to support text messaging as a tool for behavior change. Noting that previous research has shown that messaging interventions designed based on behavioral theory are more likely to be successful, the authors observed that few studies they reviewed specified a theoretical rationale for the intervention design. In a 2011 systematic review of mHealth intervention trials, Riley and colleagues88 also found that most studies did not report on whether the intervention was informed by behavioral theories.

### Smartphone and Internet-Enabled Applications

A large body of evidence has demonstrated the effectiveness of remote monitoring of clinical parameters for cardiovascular diseases including heart failure, hypertension, and diabetes mellitus.60,75,89 In 1 trial of adults with diabetes mellitus,70 investigators evaluated a cell phone–based software system with Web-based data analytics and therapy optimization tools. The application provided real-time feedback to patients on their blood glucose levels, displayed the patient’s medications, and prompted patients for additional information useful

#### Table 3. Continued

<table>
<thead>
<tr>
<th>Authors (Year)</th>
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<th>Intervention Components</th>
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<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santamore et al (2008)79</td>
<td>464 adults with heightened 10-y risk of CVD</td>
<td>USA</td>
<td>Telemedicine System (Internet Server with database)</td>
<td>Both groups were given BP monitors; Telemedicine Group (TG) entered their BP readings weekly, which were downloaded at clinic visits</td>
<td>RCT: TG vs usual care 8 mo follow-up</td>
<td>Significantly more blood pressure monitoring (92% in comparison with 49% in controls, P&lt;0.0001), readings accurate in comparison with office BP measurements</td>
</tr>
<tr>
<td>Sherrard et al (2009)80</td>
<td>331 adults post cardiac surgery</td>
<td>Canada</td>
<td>IVR postdischarge calls at 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, and 24 wk</td>
<td>Questions addressed medication compliance and reporting of adverse events, and provided medication information and general medication safety tips</td>
<td>RCT: IVR vs usual care 6 mo follow-up</td>
<td>Significantly greater medication adherence with no adverse events (51% vs 38% in controls, P&lt;0.04)</td>
</tr>
<tr>
<td>Stacy et al (2009)81</td>
<td>497 adults with hyperlipidemia who recently filled a statin prescription</td>
<td>USA</td>
<td>Up to 3 IVR calls</td>
<td>Motivational messages and tailored feedback reinforcing adherence/ persistence with meds; enhanced usual care controls received 1 IVR call with message to contact doctor if they had questions</td>
<td>RCT: IVR vs enhanced usual care 6 mo follow-up</td>
<td>Significantly greater persistence in taking statins (67% in comparison with 37% in controls, P&lt;0.05)</td>
</tr>
<tr>
<td>Vernooij et al (2012)82</td>
<td>330 adults with vascular disease</td>
<td>Netherlands</td>
<td>Website with biweekly participant submission of weight, blood pressure, smoking status, and cholesterol</td>
<td>Internet-based, nurse-led treatment program with website personalized for participant based on risk factors</td>
<td>RCT: Internet-based nurse management vs usual care 12 mo follow-up</td>
<td>Small nonsignificant improvement in CVD risk. Relative change of –14% in Framingham heart risk score, in comparison with control group (95% CI, –25% to –2%)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; CBT, cognitive behavioral therapy; CI, confidence interval; CRT-D, cardiac resynchronization therapy device; CVD, cardiovascular disease; GMV, group medical visits; HbA1c, glycosylated hemoglobin; HRQL, health-related quality of life; meds., medications; HTN, hypertension; IVR, interactive voice response; LDL, low-density lipoprotein; RCT, randomized controlled trial; and SMS, short message service.
for feedback on their diabetes management. The system also
sent computer-generated trend reports to the patient’s pro-
vider team along with suggested modifications to the treat-
ment plan. The intervention group had significantly improved
glycemic control and medication adjustments at 3 months in
comparison with randomly assigned controls. In addition to
improving diabetic patients’ glycemic control, such applica-
tions show promise for enabling more effective monitoring
of other cardiovascular risk factors such as blood pressure,
physical activity, and weight.

A 2012 review of diabetes self-management interven-
tions using mobile monitoring technologies reported that 10
of the 13 reviewed studies led to improved glycemic control
in comparison with usual care.29 Similarly, a 2012 review of
mHealth in diabetes management30 reviewed 28 intervention
studies, most of which included specialized features designed
for use with smartphones or other communication tools that
have graphical displays. The focus of those communication
tools included electronic trend reports about data such as
blood pressures, blood glucose, or physical activity; remind-
ers; and tailored information for the patient. Eighty-five per-
cent of studies with hemoglobin A1c as an outcome reported
improvements. Forty-eight percent of the studies reported on
patient satisfaction, and 90% of those trials reported high satis-
faction with the mobile disease management support.

Several studies, including a recent meta-analysis, have
shown that Internet-based interventions can be effective and
that most of the features used could be adapted for mobile
phones or tablets.31 A number of these trials have used mul-
tiple modalities to reach patients and provide a more flexible
platform for monitoring and self-care education. A trial con-
ducted in Australia evaluated an Internet-delivered cognitive
behavioral therapy intervention among patients at high risk
for cardiovascular disease who had comorbid depression and
found improvements relative to randomized controls in psy-
chological symptoms, self-reported medication adherence, and
health behaviors.76 In a 2011 cluster-randomized trial among
26 primary care practices, investigators evaluated a mobile-
and Web-based self-management program for diabetic patient
coaching and provider decision support.32 Patients received
automated real-time educational and behavior change mes-
sages in response to their reported blood glucose values, with
messages focusing on medication management and lifestyle
behaviors. Providers received quarterly reports summarizing
patients’ glycemic control, medication management, life-
style behaviors, and evidence-based treatment options. At the
12-month follow-up, mean hemoglobin A1c levels declined
relative to baseline in the intervention group more than twice
as much as among patients randomly assigned to usual care.

Over the past decade there has been an explosion of new
social media sites offering users opportunities to interact vir-
tually with peers and health professionals, sharing written
information, graphical displays, videos, photographs, and
other forms of communication. Online community resources
include social networking sites such as Facebook, blogs,
wikis, Twitter chats, photo and video sharing sites, and vir-
tual worlds. A number of interventions are being evaluated
that seek to leverage social media for improving chronic
disease management. However, so far, few results from such
intervention trials have been published. One 2013 review
examined studies on social media use by adults with chronic
disease,33 including cardiovascular disease. The most salient
finding was the paucity of rigorous studies and the variability
of study methodologies. Only 3 of the 19 studies reviewed
were randomized trials, and only 7 reported on social media
with Web 2.0 platforms. Although highlighting the potential
of this growing and diverse set of tools for cardiovascular life-
style behavior change and disease management, the review
drew no conclusions about the effectiveness of different
approaches to improving health outcomes.

Discussion

Summary of Findings

Although not all studies have had positive outcomes, a num-
ber of randomized controlled trials, including 2 studies from
LMICs, have shown that IVR interventions can improve
lifestyle risk factors for cardiovascular disease and disease
management, as well. An advantage of IVR self-management
support programs is that they can be used with any standard cell
or landline phone. Because no reading or writing is required,
IVR interactions are accessible to low-literacy populations,
and to those with vision problems. Patients can use IVR to
report detailed information about their status and receive tai-
lored feedback about their health and self-care. However, IVR
interactions typically require patients to participate when the
call is placed or to call in to the system. Although patients
sometimes can specify when they are likely to be available,
changes in their schedule may be difficult to accommodate.
Unlike texts, images, or website links sent to patients via a
smartphone, patients using IVR cannot review information
after the fact. Unfortunately, because of the diversity of study
populations, outcomes, and IVR system designs, we still can-
not identify the characteristics of interventions that are associ-
ated with greater behavior change and health improvements.

Evidence also is growing about the effectiveness of SMS
interventions in improving behavioral risk factors and car-
diovascular disease management, especially interventions
enabling real-time feedback, exchange, and support. Most
randomized trials of SMS interventions for chronic disease
behavior change have been conducted in HICs, however,
and little work to date has examined different behavioral
approaches to intervention design or content development.
Also, there is little known about the optimal dosing, frequency,
and content of text messages, the duration of interventions,
or the individual and group characteristics that may identify
patients most likely to benefit. An advantage of SMS interven-
tions is that they can be used with almost all mobile phones,
and they take advantage of the widespread use of texting both
in HICs and LMICs.28,31,32 However, SMS services are difficult
for individuals with limited vision, dexterity, or literacy, all of
which are more common in poor communities. SMS self-care
supports tend to be less interactive than counseling by a clini-
cian, but when patients are asked to confirm receipt of texts,
interventions may have increased engagement and impact.
More complex 2-way SMS messages may boost engagement
and effectiveness, but this may require a clinician or other live
person to be in the loop, because computers are challenged by the nonstandard spelling and grammar from patients’ texts.

Newer mHealth interventions hold considerable promise, but the research base on interventions delivered via smartphones or social media is still small. In the next few years, results from ongoing trials will help to develop the evidence in this important area.

**Challenges and Future Directions**

Given this rapidly evolving field with heterogeneous intervention characteristics, populations, and study end points, it was not possible to conduct a definitive, systematic review with clearly defined questions regarding whether mHealth works for cardiovascular behavior change and disease management. Similarly, this field is still too new to allow definitive conclusions about which components of successful interventions most contribute to their effectiveness. As such, in this review we have sought to highlight major advances and suggest important unanswered questions for moving the field forward (Table 4). For example, the content of mHealth messages is unstandardized across studies (see examples in Tables 5 and 6). Although this may be appropriate given the state-of-the-science, it currently makes it impossible to say with certainty whether differences in content, mode of delivery (eg, IVR versus SMS), or other factors are responsible for variation in intervention effects across studies.

Problems in the dissemination of mHealth services within LMICs mirror those seen in LMIC medical care, ie, services are limited in scope, unevenly distributed across geographic areas, and of variable quality when they are available. In a systematic review of health data quality in LMICs, investigators identified multiple critical weaknesses, including missing data, unreliable clinical information entered into electronic records, problems with timeliness, and limited accessibility.92 One important challenge to the development of scalable, sustainable mHealth services is the limited infrastructure for training and supporting the workforce in LMICs with skills in health informatics.93 Several programs for building the needed human capital have been launched, with support by the US Fogarty International Center, the Bill and Melinda

<table>
<thead>
<tr>
<th>Gaps in Knowledge and Future Directions for Research</th>
<th>Next Steps</th>
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<tbody>
<tr>
<td><strong>Technology</strong></td>
<td></td>
</tr>
<tr>
<td>Best combinations of features for monitoring and self-care behavior change support (animations, graphics, video, text-to-speech), given the varying levels of literacy and technology access in LMICs</td>
<td>Process studies and trials examining what features best promote engagement and effectiveness for different behaviors and patients</td>
</tr>
<tr>
<td>Optimal duration of interventions and frequency of patient contacts</td>
<td>Compare different durations and frequencies of contact, both in traditional randomized trials and patient-preference trials</td>
</tr>
<tr>
<td>Relative advantages of different types of end user participation (eg, required user responses to messages and bidirectional interaction with providers)</td>
<td>Usability testing and qualitative interviews, plus trials comparing levels and types of end user active participation within and across cultures</td>
</tr>
<tr>
<td>When and how to integrate mHealth interventions with electronic health records or patient portals</td>
<td>Testing of different models of integration, including studies of the budget impact and cost-effectiveness of greater integration</td>
</tr>
<tr>
<td>Optimal balance between automated communication and self-management support delivered by community health workers and other providers</td>
<td>Comparative effectiveness trials of different levels of live vs mHealth support</td>
</tr>
<tr>
<td>Use of adaptive techniques in the field of artificial intelligence to design more patient-centered systems</td>
<td>Laboratory-based engineering studies to determine when and how mHealth services can adapt to patients’ characteristics and changing context. Trials comparing adapted with more regimented message delivery strategies in real-world LMIC settings</td>
</tr>
<tr>
<td><strong>Behavior change</strong></td>
<td></td>
</tr>
<tr>
<td>Best ways to mobilize social networks and online communities for behavior change</td>
<td>Network analysis of influencers in social media networks. Studies to better understand what information patients are willing to share in networks given their sociodemographics and cultural context</td>
</tr>
<tr>
<td>What patient characteristics to use in tailoring messages (eg, level of self-efficacy, source of motivation, values/ life goals, demographic characteristics) for behavior change</td>
<td>Fractional factorial studies examining most effective tailoring approaches for behavior change</td>
</tr>
<tr>
<td>Most effective behavioral theories to underpin intervention design</td>
<td>Fractional factorial studies and careful analysis of mediators of intervention effects to refine behavioral theory</td>
</tr>
<tr>
<td><strong>Settings and populations</strong></td>
<td></td>
</tr>
<tr>
<td>Most effective approaches to adapt technologies found effective in high-income settings for LMIC settings and for populations in which low health literacy and limited electronic literacy are common</td>
<td>Development processes incorporating input from end users in different settings and careful piloting of mHealth interventions for feasibility and acceptability in various populations and LMICs</td>
</tr>
<tr>
<td>Most effective behavioral theories to underpin different interventions</td>
<td>Include mediator analyses in evaluations of mHealth interventions to test mechanisms by which the interventions influence outcomes. Explicitly outline behavioral theories motivating different intervention components and messages</td>
</tr>
<tr>
<td>Characteristic of populations that benefit most from various mHealth approaches</td>
<td>Include moderator analyses (specifically focusing on variation in culture and socioeconomic status within and across countries) in evaluations of interventions</td>
</tr>
</tbody>
</table>

LMICs indicates low- and middle-income countries; and mHealth, mobile health.
Table 5. Examples of Message Content for Interventions Targeting Disease Prevention

<table>
<thead>
<tr>
<th>Reference</th>
<th>Examples</th>
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</thead>
<tbody>
<tr>
<td>IVR</td>
<td>“Be consistent in limiting the amount of television your child watches this week to 2 h/d.” “Set a goal to take your family to a new park or trail that you haven’t visited before.”</td>
</tr>
<tr>
<td>de Neit (2012)</td>
<td>“Well done with your exercise! Keep going! Find distractions when you cannot resist unhealthy food. Good luck, you can do it!” “Hi Bart! Well done with your exercise! Keep going! Great that you exercised with your friends! Find distractions when you cannot resist unhealthy food.”</td>
</tr>
<tr>
<td>SMS</td>
<td>“Why not write an action list of your reasons why you want to quit [smoking]. Use it as your inspiration.” “TXT2STOP: Think you’ll put on weight when you quit? We’re here to help - We’ll TXT weight control and exercise tips, recipes, and motivation tips.” “Cravings last &lt;5 min on average. To help distract yourself, try sipping a drink slowly until the craving is over.”</td>
</tr>
<tr>
<td>Free (2011)</td>
<td>“Writing down what you ate and how you felt when you ate it will help you stay on track with your goals.” “Organize your pantry so that healthier foods are facing forward and less healthy items are in the back and out of sight.” “Find friends who share similar weight loss goals and support each other. It’s fun to exchange healthy recipes too!”</td>
</tr>
<tr>
<td>Shapiro (2012)</td>
<td>“Here’s a tip: put your workout clothes in front of your door this evening so you don’t forget to work out tomorrow.” “Remember to weigh yourself tomorrow morning.” “Peaches are a great source of carotenes, potassium, and flavonoids. Try one for 70 calories and 2.6 g of fiber.”</td>
</tr>
<tr>
<td>Chow (2012)</td>
<td>“Are you taking daily aspirin? If not discuss it with your doctor.” “Try steaming, baking or BBQ to reduce the need for excess oil when cooking.” “If you crave a cigarette, try and distract yourself by going for a walk or doing something creative.”</td>
</tr>
<tr>
<td>Wong (2013)</td>
<td>“Diabetic complications include eye problems and feet problems.” “Should choose lean meat with skin and fat trimmed off.” “Smoking is old fashioned, quit smoking is the trend.”</td>
</tr>
<tr>
<td>Other/Multiple Channels</td>
<td>Web based diary with recommendations on diet and exercise through cell phone and internet “New week is beginning, let’s exercise.” “Walking as aerobic exercise can reduce abdominal fat.”</td>
</tr>
<tr>
<td>Turner-McGrievy (2011)</td>
<td>Social network posts via Twitter “Got an insulated lunch bag? Sure helps w/healthy eating at work. Good lunch bags are available at kitchen stores at the mall.”</td>
</tr>
</tbody>
</table>

IVR indicates interactive voice response; and SMS, short message service.

Gates Foundation, and the American Medical Informatics Association. Web-based distance learning programs will be important, and multiple models have been described. Internationally shared platforms such as the Virtual Campus of Public Health supported by the Pan America Health Organization also will facilitate the transfer of knowledge from HICs to LMICs.

The mHealth Alliance is an international leader in promoting research and dissemination on effective models of mHealth globally, through work on strategies for sustainable funding, the development of supportive governmental policies, and workforce development. In 2013, the Alliance published an important review with recommendations on standards and interoperability for mHealth services in LMICs. The report found that investment in standards for compatibility of systems is among the greatest challenges, although systems currently in use in some LMICs could serve as models for scaling programs transnationally. Alignment of market incentives to promote pooling of resources and expertise will be critical to establishing mHealth systems as tools for cardiovascular disease prevention and management around the globe.

Next-Generation Systems

Regardless of whether communication is via IVR, SMS, Internet-enabled devices, or a combination of these modalities, almost all automated mHealth patient interactions use algorithms for determining what information to push out to patients, what information to request, and how to determine what additional actions should be taken based on patients’ responses (eg, feedback to the clinical team). Those algorithms typically reflect decisions made by experts that are codified in tree-structured protocols for identifying problems and giving advice. Regardless of the rigor of the development process and the complexity of the underlying conversation map, interactions based on expert systems inevitably represent developers’ best guess regarding the information exchanges that will be most useful in supporting patients’ self-management. Limited experience with users can mean that, on average, patients’ needs are different than what the experts expected. Even if the system targets an average patient well, variations around that average can result in a poor fit between individual messages and users’ unique needs and learning styles. Unpredictable changes in a patient’s health status or self-management support needs, eg, a recent cardiovascular event, cannot be accommodated easily given that the underlying structure is often limited in its ability to listen to patients and adapt to important events. Finally, as patients’ health declines or they master a given self-management task, their need for information support will evolve, and an expert system that worked in the past may become increasingly unhelpful after multiple interactions. Because expert systems often do a poor job of adapting to individual patients’ needs, they can lack the credibility that patients and clinicians expect to adopt and maintain an mHealth service over the long term.

Well-established informatics strategies are available for improving on these deterministic mHealth programs so that
they can provide a more patient-centered experience and adapt to users’ unique learning styles, preferences, and needs. Many of these strategies have been developed for use through Web-based applications such as Amazon.com, Netflix, or Pandora.com. These intelligent systems automatically learn from users what works for them, adapt to users’ preferences (eg, by watching what they buy online), and recommend options based on the ways in which 1 user is similar in their behavior to others. More adaptive mHealth systems using artificial intelligence and machine learning principles may represent a substantial improvement in our ability to monitor patients’ status and provide relevant behavior change messages related to cardiovascular disease prevention and management.

More evidence is needed on the impacts of mHealth in LMICs. Development of mHealth services for language minority patients, eg, the many indigenous communities in Latin America, is an important priority. Highly controlled studies fail to answer questions about the reach of mHealth in vulnerable communities or whether such systems can be adopted, scaled, and maintained outside the environments in which they are originally tested. New approaches to implementation science, emphasizing both qualitative and quantitative methods, community-based participatory research, and organizational theory can complement controlled trials and ensure that mHealth systems are relevant and flexible enough to adapt to multiple environments.

Traditionally designed large multisite trials are expensive and can take years to produce information. Investment in such studies should be carefully weighed against funding larger numbers of smaller and innovative (albeit less definitive) studies of solutions adapted to different cultures and settings. As this field matures, more focused, systematic reviews and meta-analyses will be possible to determine whether specific intervention types improve clearly defined outcomes across multiple studies. Given the current state of the science and the heterogeneity of interventions, intervention targets, and populations, that type of review currently is not possible, particularly with respect to the efficacy of mHealth solutions in LMICs. Finally, to overcome the field’s pilot-itis (chronic proliferation of small, short-term studies without a clear path toward scalability and sustainability), future research will need to address financing and examine

### Table 6. Examples of Message Content for Interventions Targeting Disease Management

<table>
<thead>
<tr>
<th>Reference</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Sherrard (2009)⁴⁶</td>
<td>“Did you fill the prescriptions given to you at discharge?”</td>
</tr>
<tr>
<td>Reid (2007)⁴³</td>
<td>“Have you smoked any cigarettes, even a puff, since you left the hospital?” “On a scale of 1–10, with 10 being the most confident, how confident are you that you will remain a nonsmoker?”</td>
</tr>
<tr>
<td>Pilette (2011)⁴⁰</td>
<td>“During the past week, did you have any symptoms of low blood sugar? This is sometimes called a ‘hypoglycemic reaction and can cause symptoms such as sweating or trembling. Another symptom may be feeling weak to the point that a person feels like they’re going to fall down or does fall down.”</td>
</tr>
<tr>
<td>Nundy (2014)⁴⁶</td>
<td>“Time to check your blood sugar.” “Do you need refills of any of your medications?”</td>
</tr>
<tr>
<td>Arora (2014)⁴²</td>
<td>“Having diabetes can lead to a heart attack or stroke—but it doesn’t have to.” “Medication reminder! Don’t leave home without your medications.” “Challenge! Don’t drink any soda or juice today. Only drink water or milk.”</td>
</tr>
<tr>
<td>Park (2014)³⁸</td>
<td>“John, take Plavix 75 mg at 9:00 AM. Respond with 1.” ‘‘Remember to see your cardiologist and/or primary physician 1–2 wk after your hospitalization.’’</td>
</tr>
<tr>
<td>Mbuagbaw (2012)⁴⁸</td>
<td>“You are important to your family. Please remember to take your medication. You can call us at this number: xxx-xxx-xxxx.’’</td>
</tr>
<tr>
<td>Pop-Ecleches (2011)⁴⁵</td>
<td>“This is your reminder.” “This is your reminder. Be strong and courageous, we care about you.”</td>
</tr>
<tr>
<td>Contreras (2004)³⁷</td>
<td>“Always take your blood pressure pill when you get up in the morning.” “A little exercise each day will help make your treatment more effective.” “A healthy, balanced diet is the best guarantee for controlling your blood pressure.”</td>
</tr>
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<td>Sidney (2012)⁴⁶</td>
<td>IRV and SMS</td>
</tr>
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<td>Haberer (2010)⁶⁶</td>
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IRV indicates interactive voice response; and SMS, short message service.
the cost-effectiveness of different mHealth interventions from the perspective of large payers.

**Conclusions**

People with cardiovascular diseases and their risk factors – like the rest of the societies in which they live – are increasingly mobile, and mobile patients require mhealth support to meet their ongoing needs for assistance with self-management. A solid body of evidence has shown that telehealth delivered by trained clinicians can improve cardiovascular outcomes, but cost constraints will continue to limit the availability of these services. mHealth tools could fill the gap between what patients need and what their health systems can provide given cost constraints. IVR, SMS, smartphones, and social media each provide a unique platform for developing mHealth services, and a variety of trials indicate that such tools may provide a low-cost and effective solution to the challenges of providing ongoing patient care at a distance. Research on new models of mHealth should emphasize creative approaches to addressing the epidemic of cardiovascular diseases in LMICs. In addition, researchers should develop new systems that take advantage of the advances in artificial intelligence, and behavioral theory, as well, to ensure that mHealth services are as personalized and effective as possible.

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**Disclosures**

None.

**References**


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