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Improving Medication Adherence in Coronary Heart Disease

Leah L. Zullig[1,2] · **Katherine Ramos**[3,4] · **Hayden B. Bosworth**[1,2,5,6]

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Abstract
Purpose of Review The purpose of this review was to synthesize research findings from recently published randomized controlled trials (RCTs) targeting any phase of medication adherence, from initiation to discontinuation, among patients with coronary heart disease (CHD).
Recent Findings We identified successful strategies and promising practices for improving medication adherence among patients diagnosed with CHD. Consistent intervention strategies included the following: (1) facilitating patient-provider communication, (2) using mHealth technologies with emphasis on two-way communication, (3) providing patient education in tandem with lifestyle and behavioral counseling, and (4) providing psychosocial support. Regarding medication adherence phases, all studies examined implementation (i.e., taking medications as prescribed over time) and one also addressed treatment initiation (i.e., beginning a new medication). None identified addressed discontinuation. Studies varied by use of objective, self-report, and a combination of outcome measures with a greater number reporting only subjective measures of adherence. Key findings remained mixed in supporting specific intervention designs or delivery formats.
Summary This review addresses available data of promising practices for improving CHD medication adherence. Future studies are needed to examine intervention effectiveness, scalability, and durability of observed outcome effects.

Keywords Coronary heart disease · Cardiovascular disease · Medication adherence · Randomized control trials

Abbreviations

ACE	Angiotensin converting enzyme inhibitors
CHD	Coronary heart disease
MEMS	Medication Event Monitoring System
mHealth	Mobile health

This article is part of the Topical Collection on *Psychological Aspects of Cardiovascular Diseases*

✉ Hayden B. Bosworth
hayden.bosworth@duke.edu

Leah L. Zullig
leah.zullig@duke.edu

Katherine Ramos
katherine.Ramos@va.gov

[1] Center for Health Services Research in Primary Care, Durham Veterans Affairs Health Care System, 411 West Chapel Hill Street, Suite 600, Durham, NC 27701, USA

[2] Department of Population Health Sciences, Duke University, Durham, NC, USA

[3] Geriatric, Research, Education and Clinical Center (GRECC), Durham Veterans Affairs Health Care System, 508 Fulton Street, Durham VA Health Care System, GRECC (182), Durham, NC 27705, USA

[4] Center for Aging and Human Development, Duke University, Durham, NC, USA

[5] School of Nursing, Duke University, Durham, NC, USA

[6] Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, USA

MI	Myocardial infarction
MMAS	Morisky Medication Adherence Scale
PCI	Percutaneous coronary intervention
RCT	Randomized controlled trial
SMS	short message service or text message

Introduction

Globally, coronary heart disease (CHD) is a leading cause of death and economic burden [1]. Patients with CHD are at increased risk for hospitalization, myocardial infarction, and mortality [2]. To reduce the risk of CHD-related morbidity and mortality, programs to support behavioral changes—including changes in physical activity, dietary consumption, smoking and alcohol use, and medication adherence—are urgently needed. Behavioral support interventions have the potential to significantly improve CHD prevention and treatment. The World Health Organization estimates that 80% of premature heart disease, stroke, and diabetes could be prevented through improvements in modifiable, behavioral risk factors [3].

Medication adherence is a particularly important modifiable, behavioral risk factor and is a cornerstone of CHD management. Several studies have demonstrated an association between suboptimal medication adherence and adverse clinical outcomes among patients with CHD [1, 4–6]. However, like other chronic diseases, many patients with CHD struggle to achieve optimal medication adherence. Adherence to chronic disease medications is approximately 50% worldwide [1]. Similarly, among patients with a previous myocardial infarction, adherence rates range from 13 to 61% [7]. There is an urgent need for evidence-based programs to improve medication adherence among patients with CHD.

Improving medication adherence requires acknowledging that adherence is a complex series of behaviors composed of three phases: [1] initiation, beginning a new medication; [2] implementation, taking a medication as prescribed over time; and [3] discontinuation, stopping a medication for any reason (either when not recommended or at the end of a specific course of treatment) [8]. While the barriers to adherence may differ across phases, patients with CHD and its risk factors experience adherence problems throughout this continuum. For example, at the initiation phase, one-in-five Medicare patients fail to fill their prescriptions within 7 days after a percutaneous intervention with a drug-eluting stent [9]. Regarding implementation, fewer than 50% of patients are persistent with their statins 1 year after initiation despite statins being associated with a 45% reduction in risk of mortality [9, 10]. At the discontinuation phase for patients with diabetes, hypertension, and dyslipidemia, up to 50% of patients stop their medications in the first year of prescription [11–13]. Across the phases, common barriers for medication adherence include the following: polypharmacy, low disease-related knowledge, low health literacy, barriers to obtaining medication, forgetfulness, and cost, among others [14, 15].

While there remains room for improvement in CHD-related medication adherence, there are successful strategies known to improve medication adherence [16, 17, 18••, 19••]. Many studies have been conducted with the goal of improving medication adherence among patients with CHD. Our objective was to synthesize information from recent randomized controlled trials (RCTs) to determine promising practices for improving medication adherence, from initiation to discontinuation, among patients with CHD.

Systematic Search Strategy

While this is not a systematic review, we used a systematic search strategy to identify recently published RCTs aiming to improve medication adherence among patients with CHD. We searched PubMed to identify recently published studies addressing medication adherence among patients with CHD. We limited our search to articles published in English during the previous 5 years (January 1, 2012 through May 1, 2017) and identified 77 articles [20–96]. We reviewed articles' titles and abstracts to remove articles for which CHD was not a primary focus (n = 16), those that were primarily clinical in nature (n = 3), commentaries and editorials (n = 4), and articles that described a relevant protocol but only presented baseline data or did not report study results (n = 9). In a secondary review process, we removed articles that were observational or cross-sectional (n = 25), literature reviews (n = 6), and non-randomized interventions (n = 3). After completing this search and screening process, we identified 11 RCTs. We report on the RCTs in detail below (Table 1) and reference the other identified articles for supportive, contextual information.

Synthesis of Key Findings

Approaches to Measure Adherence

There are a variety of approaches to measure medication adherence. In the absence of a gold standard measure, the best approach to measure adherence depends on the context and other factors [102•]. Among the studies identified in our review, most studies relied exclusively on patient self-reported medication adherence [30, 39, 49, 77, 86]. One study collected two methods of self-reported adherence [65]. Within these studies, a variety of specific self-report measures were used including the four- and eight-item Morisky Medication Adherence Scales in multiple languages [97, 98] and the A14-scale [99]. Only one study did not collect self-reported medication adherence, instead relying exclusively on pharmacy refill claims to measure adherence [59]. While patient self-report and pharmacy-based measures can be valuable tools to assess adherence, each measure has advantages and

Table 1 Key characteristics of RCTs addressing medication adherence among patients with CHD

Reference	Population	Sample size	Number of arms	Country	Adherence measurement approach	Outcome measures	Intervention description	Key finding	Final outcome measurement
Zhao [95]	Adults with CHD who were prescribed CHD-related medication and had phone access	90	2	China	Self-report via telephone (specific measure not noted)	Self-care ability, quality of life, patient compliance with therapy regimen, goals of treatment, heart rate, body mass index	Pharmacist support that addressed medication review, patient education, lifestyle management, discharge guidance, and telephone-follow-up	Difference between groups in drug therapy compliance was $p < 0.01$	6 months
Stamm-Balderjahm [86]	Patients with CHD undergoing cardiac rehabilitation	545	3	Germany	Self-reported MMAS-4 [97]	Health-related behavior change, subjective state of health, medication adherence, Physiological protection and risk factors, cholesterol, blood sugar, HbA1c, body mass index	Goal setting between patient and doctor, goal checking at 3 months, informational brochure, patient 'passport' to document patient-reported measures, instruction manual for doctors on standardized techniques for interviewing, goal setting, and goal checking	There were no between group differences for primary outcomes, including medication adherence.	12 months
Pfaeffli Dale [77]	Adults with CHD with access to the internet	123	2	New Zeala-nd	Self-reported MMAS-8 [98]	Self-reported adherence to recommended health guidelines using a health behaviors composite score, medication adherence, blood pressure, lipid profile, weight, body mass index, wait-to-hip ratio, psychological measures, Framingham score	24-week mHealth program sent by automated daily text messages and access to a supporting website; 1 message sent daily at first and then 5 messages weekly for weeks 13 to 24	Intervention increased adherence to recommended lifestyle behavior changes from 33% at baseline to 59% at 3 months and 53% at 6 months. The intervention group reported a significantly greater medication adherence (mean difference 0.58, 95% CI 0.19–0.97, $p = 0.04$).	6 months
Park [74, 75]	Adults with coronary heart disease who were hospitalized for non-ST elevation MI, ST elevation MI, or PCI and were	90	3	USA	MEMSSelf-reported MMAS-8 [98]Self report using two-way text message responses	Medication adherence; Medication self-efficacy	Patients received either: (1) text messages for medication reminders and education; (2) educational text	According to the MEMs, the text messaging groups had a higher percentage of correct doses taken for antiplatelets	30 days

Table 1 (continued)

Reference	Population	Sample size	Number of arms	Country	Adherence measurement approach	Outcome measures	Intervention description	Key finding	Final outcome measurement
	prescribed an antiplatelet medication and statin, and owned a mobile phone with texting capability						messages only; or (3) no text messages	(p = 0.02), percentage number of doses taken (p = 0.01), and percentage of prescribed doses taken on schedule (p = 0.01)	
Mertens [65]	Elderly patients with coronary heart disease and no prior knowledge of tablet computers	24	Crossover design with 3 se-quences	Germany	Self-reported A14-scale [99]Confirmation rate of medication intake per the app	Medication adherence	Medication Plan mobile app installed on an Apple iPad with 3 home visits to introduce the system	After each sequence there was a significant increase in subject adherence with the most pronounced increase after the interventional phase (54.0, SD = 2.01) than after the comparative phase (52.6, SD = 2.49) (for all pairs after both interventions, $p < 0.001$)	28 days
Lin [59]	Patients with poorly controlled diabetes or coronary heart disease with coexisting depression receiving care in 14 primary care clinics	214	2	USA	Pharmacy refill data [100]	Medication adherence, pharmacotherapy initiation and adjustment, patient self-monitoring of blood pressure and glucose	Multi-condition collaboration care delivered by a nurse case manager	Pharmacotherapy initiation and adjustment rates were higher for antidepressants (RR = 6.20, $p < 0.01$), insulin (RR2.97, 0 < 0.01), and antihypertensive medications (RR = 1.86, $p < 0.01$) between the intervention and control groups. Medication adherence did not different between the groups in any of the therapeutic classes examined at 5 months.	12 months
Kripalani [53]	Adults with coronary heart disease in an	435	4	USA	Pharmacy refill data using the cumulative	Cardiovascular medication refill adherence	Patients received either: usual care, refill reminder postcards,	Adherence did not differ significantly across study arms: 31.2% in	1 year

Table 1 (continued)

Reference	Population	Sample size	Number of arms	Country	Adherence measurement approach	Outcome measures	Intervention description	Key finding	Final outcome measurement
	inner-city primary care clinic				medication gap [101]Self-reported MMAS-8 [98]		illustrated medication schedules, or refill reminder postcards + illustrated medication schedules for 1 year.	usual care, 28.3% with mailed refill reminders, 34.2% with illustrated medication schedules, and 36.9% with both interventions	
Keyserling [49]	Adult patients receiving care in 5 family medicine practices with no known cardiovascular disease and at moderate to high risk for coronary heart disease based on Framingham Risk Score	385	2	USA	Self-reported MMAS-8 [98]	Framingham Risk Score, blood pressure, blood lipid levels, lifestyle behaviors, medication adherence, acceptability, cost-effectiveness	Comparative effectiveness trial. All patients received a web-based decision aid followed by tailored counseling. Counseling was received either in a counselor-delivered or web-based format.	There was a sustained reduction in Framingham Risk Score at both 4 months and 12 months for both the counselor-based and web-based groups. Both the counselor-delivered (11% to 32%, $p < 0.001$) and web-based format (8% to 28%, $p < 0.01$) improved adherence from baseline to 12 months	12 months
Fang [39]	Patients with coronary artery disease who had chronic stable angina and were prescribed beta blockers, ACE inhibitors, nitrates, or lipid-lowering medications	280	3	China	Self-reported MMAS-4 [97]	Medication adherence	Patients received health education to support lipid-lowering medication adherence via: (1) short messaging service (e.g., text message); (2) short messaging service + Micro Letter (e.g., messaging app); (3) phone only	The SMS and SMS + Micro Letter groups reported better adherence ($p = 0.001$ and $p < 0.001$, respectively) compared to the phone group	6 months
Cao [30]	Adults diagnosed with coronary heart disease and admitted for the first time	236	2	China	Self-reported MMAS-8 (Chinese version) [98]	30- and 90- day readmission rates, quality of care transitions, medication adherence, chronic disease self-efficacy	Hospital-community partnership transitional program consisting of 4 phases: (1) admission phase – cardiologist and nurse evaluate pre-admission medications; (2) hospitalization phase –	There were statistically significant differences in 30- and 90-day readmission between the study and control groups (5.1% vs. 16%, $p = 0.0004$ and 8.5% vs. 20.3%, $p = 0.005$, respectively). The	90 days after discharge

Table 1 (continued)

Reference	Population	Sample size	Number of arms	Country	Adherence measurement approach	Outcome measures	Intervention description	Key finding	Final outcome measurement
							cardiologist and nurse provide patient-specific education and self-management advice using a teach-back method; (3) pre-discharge phase – the cardiologist, nurse, patient, and caregivers cooperatively develop a written and individualized discharge plan the day before discharge; (4) post-discharge phase – hospital nurse sends the discharge plan to the home nurse in each community health care center to which each patient belonged, the family physician is sent the plan through an electronic health record (EHR), family physician and home nurse make structured calls to the patient in the first week and support continues for 4 weeks	study group has reported better medication adherence at the final time period (6.77 vs. 6.46, $p < 0.001$)	

disadvantages. Patient self-report is convenient to collect and may provide rich information about reasons for non-adherence, but is prone to over-reporting adherence. Similarly, pharmacy-based measures may be ideal for understanding adherence on a population level, but cannot provide contextual information about reasons for non-adherence and cannot assess whether patients actually consume the medication that they have filled or refilled. Thus, it is generally advised that a combination of direct and indirect measures of adherence be simultaneously collected in order to triangulate adherence behaviors [103].

There were two studies that collected adherence information from multiple data sources [53, 74, 75]. Park and colleagues collected both self-reported medication adherence and used electronic bottles (e.g., MEMS) to triangulate adherence [74, 75]. Kripalani and colleagues used both self-reported medication adherence and a pharmacy-based measure [53]. Collecting adherence information from multiple data sources may be the best practice to triangulate actual adherence behaviors. When data are available from multiple, complementary sources (e.g., self-report plus pharmacy refill), this may provide the opportunity to overcome traditional limitations of either method if used independently.

The duration of outcome measurement is also noteworthy. Optimal medication adherence requires persistence with proper medication taking over time [8]. Measuring longer-term outcomes is important to determine whether intervention effects are sustained over time and to estimate improvements in health outcomes over time. Most studies were relatively short in duration and measured shorter-term outcomes ranging from approximately 30 days [65, 74, 75], to 90 days [30], and to 6 months [39, 77, 95]. Several studies measured adherence outcomes at 1 year [49, 53, 86]. However, these assessments typically corresponded with the length of the intervention as opposed to evaluating whether treatment effects were sustained after the intervention had been withdrawn. Future studies should ideally collect outcome information after a period of time post-intervention to determine whether the intervention has a meaningful impact on medication adherence and clinical outcomes in the mid- to long-term.

Consistent Intervention Strategies

While the included studies used a variety of intervention strategies, we identified four common themes. The intervention strategy themes were as follows: (1) facilitating communication between patients and providers, (2) using mobile health (mHealth) technologies with emphasis on two-way communication, (3) providing patient education in tandem with lifestyle and behavioral management counseling, and (4) providing psychosocial support. There were several commonly used strategies that spanned across these themes. For example, medication dosing reminders were a commonly used strategy. The specific delivery of medication reminders, scripted intervention materials, and frequency of follow-up contact or appointments varied by study. Few studies (n = 3) referenced a theoretical framework or model (e.g., Social Cognitive Theory (74, 75), Goal Setting Theory [86], Leventhal's Common Sense Model of Illness [77]) to guide intervention design.

Intervention Strategy 1: Facilitating Patient and Provider Communication

Five studies addressed facilitating and/or improving provider-patient communication [30, 49, 59, 86, 95]. Interventions focused on the delivery of personalized care, use of evidence-based guidelines, and ongoing collaboration around identified patient goals and counsel. Commonly used communication strategies included the teach-back method (a communication method used by health care providers to ask patients to explain information back to them to confirm comprehension), goal setting activities, and individualized treatment planning. The teach-back method [30] was used to enhance treatment comprehension and goal setting theory among patient-provider dyads improved feedback and medication adherence [86]. Other communication improvement approaches included guiding patients through an individualized discharge plan alongside their caregiver, formally assessing patient feedback about program acceptability [49], treating patients as 'key' members of their health care management team (e.g., continued provider-patient input about maintenance and relapse prevention plans) [59], and frequent communication of heart health management [95].

The specific strategies used to improve communication between patients and providers guided the selection of the type of health care professional serving as an interventionist (e.g., pharmacists, clinical providers, nurses, health counselors). The specific strategies matched the interventionists' clinical scope of practice. Pharmacists provided the most in-depth management of medications including medication reconciliation and review, patient education for medication regimens, and lifestyle management with monthly telephone follow-up [95]. In tandem with patients, clinical providers engaged in goal setting, for example, to manage and reduce behavioral or physical risk factors at the end of rehabilitation [86]. Nurses were effective at delivering ongoing monitoring and follow-up and developing individualized care plans, but did not modify medications [59]. Like nurses, health counselors (i.e., trained health counselors who held degrees in nursing, social work, or nutrition) offered ongoing counseling sessions, but were able to do so in much less clinical detail. Content typically addressed diet, exercise, smoking cessation, and medication [49, 104]. Included in these counseling interventions were assessments of lifestyle habits and barriers to healthy living. One study used a team-based approach (i.e., a cardiologist + a hospital nurse) to facilitate transitional care across four main phases of admission to post-discharge

[30]. The team-based approach consisted of making medication adjustment, providing a diagnosis and delivering treatment.

Intervention Strategy 2: Using mHealth Technologies The use of mHealth technologies is gaining attention as a potentially lower cost, individualized health management system that, potentially, can be an effective tool to prevent and manage disease [105]. In this review, use of short message service (SMS) was the most commonly used mHealth tool, followed by use of iPads and web-based technology. A key component of successful SMS use was that the messages were personalized; they also included specific medication reminders, support, and general education [74, 75, 77]. In the included studies, SMS messages were both one- (e.g., unidirectional) and two-way (e.g., bidirectional). Unidirectional messaging was used to enable health care professionals (e.g., nurse and physician) to send medication reminders [39] as a secondary resource for patient education about cardiovascular risk [39, 74, 75]. Bidirectional SMS messages were used to not only remind patients to take their medication, but also to enable patients to report back to the research and teach and confirm their medication intake [39, 65, 74, 75, 77].

Another mHealth approach was the use of iPad applications to provide medication reminders [65]. In their study, Mertens and colleagues first conducted three home visits to introduce assistive technology, followed by the introduction of an iPad-delivered intervention, and then a use of comparative paper diary. This study was effective in encouraging elderly patients to use the iPad-delivered intervention, and results demonstrated that the app was more effective than a paper-based system for reporting blood pressure values and medication intake; however, the intensity of the in-person intervention (i.e., three home visits) may not be possible in all "real world" clinical contexts.

Web-based interventions were also used to promote medication adherence among patients with CHD. Keyserling conducted a study in five diverse family medicine practices in North Carolina [49]. Participants were randomized to either a counselor-delivered or web-based format of the intervention which involved seven, lifestyle counseling sessions and allowed patients to select their health goals with tailored content. While both delivery formats reduced CHD risk, the web-based format was less expensive. Cost may be an important consideration for scaling up successful intervention and mHealth platforms have the potential to enable wide scale delivery of interventions at a reduced cost. Another study used telephone calls and e-mail to communicate treatment and discharge planning information, provide structured calls for outpatient appointment reminders, and reinforce patient's self-management behaviors to achieve health care goals [30]. This study demonstrated short-term (e.g., at 30 and 90 days post-discharge) improvements in both medication adherence and chronic disease self-efficacy.

Across SMS interventions reported in Table 1, greater medication improvements were reported (at post-intervention through 3- and 12-month follow-up) with adherence rates ranging from 45 to 85% [49, 74, 77]. Additionally, subjective and objective measures of adherence showed significant differences in mean scores between study versus control groups. Specifically, results showed higher scores of medication adherence, chronic disease self-efficacy, and stronger adherence for mobile applications compared to paper-based versions [30, 65]. Use of mobile technology to improve medication self-efficacy was not supported [75]. While we identified SMS-driven interventions that impacted medication adherence, it should be noted that the evidence-based for texting interventions to improve medication adherence and promote chronic disease self-management is in its infancy and there are knowledge gaps regarding the long-term outcomes associated with mHealth interventions [106, 107]. However, across multiple modes of delivery, electronically delivered medication adherence interventions show promise [108].

Intervention Strategy 3: Providing Patient Education and Behavioral Counseling Most of the studies that we identified provided health education around CHD and risk reduction, in tandem with behavioral counseling to improve medication adherence. The content of health education and behavioral counseling addressed personalized care information about cardiovascular risk factors, lifestyle changes, health care management (e.g., refill reminders, medication schedules), medication adherence, and health care treatment goals [30, 39, 49, 53, 74, 75, 77, 95]. Some studies also included counseling to enhance self-care and self-efficacy to influence motivation and health-maintenance behaviors [30, 74, 75]. Counseling and education were tailored for patients based on their needs, abilities, health care goals, and caregiver desires [30]. Timing of education and health content were delivered at pre-selected times by patient's medication schedule and their personal preferences; this content was used in combination with SMS reminders [74, 75]. Behavioral counseling was associated with improvements in adherence in many of the studies that we identified. It has been suggested that telephone-based motivational interviewing may be an effective tool to improve medication adherence [109] and that behavioral interventions that reduce dosing demands and involve monitoring and feedback may be most effective [110].

Intervention Strategy 4: Providing Psychosocial Support Four studies offered psychosocial support by either direct means (e.g., therapeutic counseling by providers) or via supportive content embedded within the delivered intervention [30, 59, 77, 95]. Psychosocial support tools focused on information about coping strategies, tools to reduce stress and

improve mood. For example, pharmacists, home nurses, and nurse care managers offered direct psychosocial support to help patients manage anxiety, while also offering tools to improve depression and sleep [30, 59, 95]. Problem solving, morale boosting, and self-care strategies were also utilized, followed by formal assessment and monthly monitoring of depression [59, 111]. Alternatively, use of coping strategies to modify illness perceptions and negative emotions was offered via a supportive website [77].

Psychosocial support strategies yielded significant improvements in patient's self-efficacy to manage chronic disease [30], a six-fold increase in treatment initiation and adjustment related to antidepressant medication use by study participants compared to usual care patients [59], and greater self-care abilities and higher quality of life [95]. Only one study reported a negative effect for anxiety and found no other improvements in psychological outcomes related to depressive symptoms, self-efficacy, or illness perceptions about CHD [77]. Medication adherence rates were mixed, and effect sizes in improvements for self-efficacy and other psychological outcomes were not reported for these studies.

Conclusion

Despite general progress in CHD interventions, findings remain mixed regarding how knowledge about CHD-related health behaviors can be transformed into effective strategies to improve medication adherence and enhance patients' health [112]. Findings in this review underscore that interventions work best when they are tailored to address patients' specific barriers and engage the health care system at multiple levels (e.g., patient level, provider level, health care system level, policy level) [113]. Among the studies reviewed, most reported improvements in adherence between the intervention and control groups [30, 39, 65, 74, 75, 77, 95] or in both groups [30, 39, 49, 53, 59, 65, 74, 75, 77, 95]. Only one did not report patient-level improvements in medication adherence [86]. Findings were mixed for interventions at the health care system level with two studies showing improvements in adherence [30, 95] and two that did not [59, 86]. Notably, none of these studies intervened on a policy level. Given efforts by US Centers for Medicare and Medicaid Services (CMS) use of star ratings to gauge patient experiences [114], these study findings also underscore the importance about further clarifying how patient experiences are linked with clinical outcomes.

Additionally, to fully determine the effects of CHD interventions to increase patient's uptake of, and adherence to, cardiac rehabilitation further clarity about the intended target of adherence among CHD patients is needed. In this review, the majority studies focused on the implementation phase of medication adherence (e.g., taking a medication as prescribed over time) [77, 86] with the exception of one that identified 'initiation' as the targeted phase of adherence [59]. The studies that we identified did not address premature medication discontinuation. More work is needed across the spectrum of adherence phases, particularly to address the effectiveness of interventions aimed at improving patient engagement around the time of initiating a new therapy.

Using technology to enhance behavioral strategies present a unique, cost-effective opportunity to promote medication adherence. Benefits include reducing environmental barriers (particularly for rural populations), flexible communication with medical providers and promotion of active patient engagement in disease management. These benefits, however, must be weighed against the current paucity of high-quality evidence that would suggest mHealth as an effective medication adherence intervention [105]. Moreover, there are no current standard effect sizes in mHealth interventions that are widely accepted for medication adherence [74]. Two studies in this review report small to medium effect sizes in improving adherence [65, 74]. In the broader literature of mHealth interventions generally or SMS interventions specifically for CHD, most studies are small in scope and conducted in high-income countries making it difficult to determine intervention effectiveness [103]. These preliminary findings stress the need for sufficiently powered, high-quality RCTs that can further address equity, scalability (in real-world clinical settings), and end-user acceptability.

Personalizing care can improve patient motivation and adherence. Tailored care may include developing interventions that have modular treatment components or that use a stepped care framework and adaptive 'smart' technology to match the needs of CHD patients. Future interventions may also increase treatment adherence by greater integration of psychologically focused content that offer support and build upon mechanisms of change via use of theoretically driven frameworks. In this review, few included studies used a theory or conceptual model to address adherence. Synthesizing theory with practice will advance what is known about health behavior change and offer greater insights about the impact of CHD interventions.

Medication adherence for the management of chronic diseases broadly, and for CHD in particular, is potentially one of the largest current global public health challenges. While we highlight a few relevant RCTs targeting the improvement of CHD-related medication adherence and associated clinical outcomes, there is more work to be done. More evidence is needed about how to (1) best use multiple measurement approaches to triangulate medication adherence information, (2) design multi-level approaches to improve medication adherence, (3) determine the effectiveness of unidirectional and bidirectional SMS interventions, and (4) best tailor behavioral interventions. In summary, additional work is needed to inform evidence-based, cost-effective interventions that have been demonstrated to improve adherence and have potential for widespread implementation and scale-up.

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Compliance with Ethical Standards

Conflict of Interest Leah L. Zullig reports grants from PhRMA Foundation; a salary from the U.S. Department of Veterans Affairs, and from Duke University; and other from Novartis.

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References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Sabaté E. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003.
2. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke Statistics-2017 update: a report from the American Heart Association. Circulation. 2017;135(10):e146–603.
3. World Health Organization. Preventing chronic diseases: a vital investment. Geneva: World Health Organization; 2005.
4. Bitton A, Choudhry NK, Matlin OS, Swanton K, Shrank WH. The impact of medication adherence on coronary artery disease costs and outcomes: a systematic review. Am J Med. 2013;126(4): 357.e7-.e27.
5. Dunbar-Jacob J, Bohachick P, Mortimer MK, Sereika SM, Foley SM. Medication adherence in persons with cardiovascular disease. J Cardiovasc Nurs. 2003;18(3):209–18.
6. Ho PM, Magid DJ, Shetterly SM, Olson KL, Maddox TM, Peterson PN, et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. Am Heart J. 2008;155(4):772–9.
7. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. Circulation. 2009;119(23): 3028–35.
8. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691–705.
9. Roth GA, Morden NE, Zhou W, Malenka DJ, Skinner J. Clopidogrel use and early outcomes among older patients receiving a drug-eluting coronary artery stent. Circ Cardiovasc Qual Outcomes. 2012;5(1):103–12.
10. Mann DM, Allegrante JP, Natarajan S, Halm EA, Charlson M. Predictors of adherence to statins for primary prevention. Cardiovasc Drugs Ther. 2007;21(4):311–6.
11. Ho PM, Spertus JA, Masoudi FA, Reid KJ, Peterson ED, Magid DJ, et al. Impact of medication therapy discontinuation on mortality after myocardial infarction. Arch Intern Med. 2006;166(17):1842–7.
12. Kramer JM, Hammill B, Anstrom KJ, Fetterolf D, Snyder R, Charde JP, et al. National evaluation of adherence to beta-blocker therapy for 1 year after acute myocardial infarction in patients with commercial health insurance. Am Heart J. 2006;152(3):454.e1-8.
13. Melnikow J, Kiefe C. Patient compliance and medical research: issues in methodology. J Gen Intern Med. 1994;9(2):96–105.
14. Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. Am J Geriatr Pharmacother. 2011;9(1):11–23.
15. Schmittdiel JA, Nichols GA, Dyer W, Steiner JF, Karter AJ, Raebel MA. Health care system-level factors associated with performance on Medicare STAR adherence metrics in a large, integrated delivery system. Med Care. 2015;53(4):332–7.
16. Demonceau J, Ruppar T, Kristanto P, Hughes DA, Fargher E, Kardas P, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. Drugs. 2013;73(6):545–62.
17. Mistry N, Keepanasseril A, Wilczynski NL, Nieuwlaat R, Ravall M, Haynes RB. Technology-mediated interventions for enhancing medication adherence. J Am Med Inform Assoc: JAMIA. 2015;22(e1):e177–93.
18.•• Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2014(11) https://doi.org/10.1002/14651858. **This study reports findings from a sysetmatic review to assess the effects of interventions thtat improve both medication adherence and relevant clinical outcomes**.
19.•• van Driel ML, Morledge MD, Ulep R, Shaffer JP, Davies P, Deichmann R. Interventions to improve adherence to lipid-lowering medication. Cochrane Database Syst Rev. 2016;12: Cd004371. **This study reports findings from a systematic review to assess the effects of interventions aimed at improving adherence to lipid-lowering medications and associated clinical outcomes**.
20. Al-Foraih M, Somerset S. Factors affecting adherence to statins in Hypercholesterolemic Kuwaiti patients: a cross-sectional study. Med Princ Pract: Int J Kuwait Univ, Health Sci Cent. 2017;26(1):35–40.
21. Alsabbagh MW, Lix LM, Eurich D, Wilson TW, Blackburn DF. Multiple-domain versus single-domain measurements of socioeconomic status (SES) for predicting nonadherence to statin medications: an observational population-based cohort study. Med Care. 2016;54(2):195–204.
22. Ammenwerth E, Woess S, Baumgartner C, Fetz B, van der Heidt A, Kastner P, et al. Evaluation of an integrated Telemonitoring surveillance system in patients with coronary heart disease. Methods Inf Med. 2015;54(5):388–97.
23. Aspry KE, Furman R, Karalis DG, Jacobson TA, Zhang AM, Liptak GS, et al. Effect of health information technology interventions on lipid management in clinical practice: a systematic review of randomized controlled trials. J Clin Lipidol. 2013;7(6):546–60.
24. Ayala C, Fang J, Yuan K. Prevalence of taking actions to control blood pressure among adults with self-reported hypertension in 18 states and the District of Columbia, 2009. J Clin Hypertens (Greenwich, Conn). 2015;17(3):172–82.
25. Banerjee A, Khandelwal S, Nambiar L, Saxena M, Peck V, Moniruzzaman M, et al. Health system barriers and facilitators to medication adherence for the secondary prevention of cardiovascular disease: a systematic review. Open Heart. 2016;3(2): e000438.

26. Barker-Collo S, Krishnamurthi R, Witt E, Feigin V, Jones A, McPherson K, et al. Improving adherence to secondary stroke prevention strategies through motivational interviewing: randomized controlled trial. Stroke. 2015;46(12):3451–8.
27. Berkowitz SA, Seligman HK, Choudhry NK. Treat or eat: food insecurity, cost-related medication underuse, and unmet needs. Am J Med. 2014;127(4):303-10.e3.
28. Cai H, Dai H, Hu Y, Yan X, Xu H. Pharmacist care and the management of coronary heart disease: a systematic review of randomized controlled trials. BMC Health Serv Res. 2013;13:461.
29. Campbell DJ, Tonelli M, Hemmelgarn B, Mitchell C, Tsuyuki R, Ivers N, et al. Assessing outcomes of enhanced chronic disease care through patient education and a value-based formulary study (ACCESS)-study protocol for a 2x2 factorial randomized trial. Implement Sci: IS. 2016;11(1):131.
30. Cao XY, Tian L, Chen L, Jiang XL. Effects of a hospital-community partnership transitional program in patients with coronary heart disease in Chengdu, China: A randomized controlled trial. Jpn J Nurs Sci: JJNS. 2017 https://doi.org/10.1111/jjns.12160.
31. Chatelin J, Stathopoulou MG, Arguinano AA, Xie T, Visvikis-Siest S. Pharmacogenomic challenges in cardiovascular diseases: examples of drugs and considerations for future integration in clinical practice. Curr Pharm Biotechnol 2017;18(3):231–41.
32. Chen S, Gong E, Kazi DS, Gates AB, Karaye KM, Girerd N, et al. Development of a mobile phone-based intervention to improve adherence to secondary prevention of coronary heart disease in China. J Med Eng Technol. 2016;40(7–8):372–82.
33. Cheng HM, Chiang CE, Chen CH. The novelty of the 2015 guidelines of the Taiwan Society of Cardiology and the Taiwan hypertension Society for the Management of hypertension. Pulse (Basel, Switzerland). 2015;3(1):29–34.
34. Chowdhury R, Khan H, Heydon E, Shroufi A, Fahimi S, Moore C, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. Eur Heart J. 2013;34(38):2940–8.
35. Dale LP, Whittaker R, Jiang Y, Stewart R, Rolleston A, Maddison R. Improving coronary heart disease self-management using mobile technologies (Text4Heart): a randomised controlled trial protocol. Trials. 2014;15:71.
36. Davies AK, McGale N, Humphries SE, Hirani SP, Beaney KE, Bappa DA, et al. Effectiveness of a self-management intervention with personalised genetic and lifestyle-related risk information on coronary heart disease and diabetes-related risk in type 2 diabetes (CoRDia): study protocol for a randomised controlled trial. Trials. 2015;16:547.
37. Devi R, Singh SJ, Powell J, Fulton EA, Igbinedion E, Rees K. Internet-based interventions for the secondary prevention of coronary heart disease. Cochrane Database Syst Rev. 2015;(12) https://doi.org/10.1002/14651858.
38. Everett B, Salamonson Y, Rolley JX, Davidson PM. Underestimation of risk perception in patients at risk of heart disease. Eur J Cardiovasc Nurs: J Work Group Cardiovasc Nurs Eur Soc Cardiol. 2016;15(3):e2–9.
39. Fang R, Li X. Electronic messaging support service programs improve adherence to lipid-lowering therapy among outpatients with coronary artery disease: an exploratory randomised control study. J Clin Nurs. 2016;25(5–6):664–71.
40. Gaisenok O, Martsevich S, Tripkosh S, Lukina Y. Analysis of lipid-lowering therapy and factors affecting regularity of statin intake in patients with cardiovascular disease enrolled in the PROFILE registry. Rev Port Cardiol: Orgao Oficial Soc Port Cardiol = Port J Cardiol: Off J Port Soc Cardiol. 2015;34(2):111–6.
41. Galema-Boers JM, Lenzen MJ, van Domburg RT, Roeters van Lennep J, van Bruchem-van de Scheur GG, Sijbrands EJ, et al. Predicting non-adherence in patients with familial hypercholesterolemia. Eur J Clin Pharmacol. 2014;70(4):391–7.
42. Goss F, Brachmann J, Hamm CW, Haerer W, Reifart N, Levenson B. High adherence to therapy and low cardiac mortality and morbidity in patients after acute coronary syndrome systematically managed by office-based cardiologists in Germany: 1-year outcomes of the ProAcor study. Vasc Health Risk Manag. 2017;13:127–37.
43. Gu D, He J, Coxson PG, Rasmussen PW, Huang C, Thanataveerat A, et al. The cost-effectiveness of low-cost essential antihypertensive medicines for hypertension control in China: a modelling study. PLoS Med. 2015;12(8):e1001860.
44. Gunnell AS, Knuiman MW, Geelhoed E, Hobbs MS, Katzenellenbogen JM, Hung J, et al. Long-term use and cost-effectiveness of secondary prevention drugs for heart disease in western Australian seniors (WAMACH): a study protocol. BMJ Open. 2014;4(9):e006258.
45. Irvin MR, Shimbo D, Mann DM, Reynolds K, Krousel-Wood M, Limdi NA, et al. Prevalence and correlates of low medication adherence in apparent treatment-resistant hypertension. J Clin Hypertens (Greenwich, Conn). 2012;14(10):694–700.
46. Kalia NK, Cespedes L, Youssef G, Li D, Budoff MJ. Motivational effects of coronary artery calcium scores on statin adherence and weight loss. Coron Artery Dis. 2015;26(3):225–30.
47. Kamath DY, Xavier D, Gupta R, Devereaux PJ, Sigamani A, Hussain T, et al. Rationale and design of a randomized controlled trial evaluating community health worker-based interventions for the secondary prevention of acute coronary syndromes in India (SPREAD). Am Heart J. 2014;168(5):690–7.
48. Kang JH, Nguyen QN, Mutka J, Le QA. Rechallenging statin therapy in veterans with statin-induced myopathy post vitamin D replenishment. J Pharm Pract. 2016 https://doi.org/10.1177/0897190016674407.
49. Keyserling TC, Sheridan SL, Draeger LB, Finkelstein EA, Gizlice Z, Kruger E, et al. A comparison of live counseling with a web-based lifestyle and medication intervention to reduce coronary heart disease risk: a randomized clinical trial. JAMA Intern Med. 2014;174(7):1144–57.
50. Kim HY, Lee JA, Kim YS, Sunwoo S, Oh HJ, Kim CS, et al. Factors of compliance in patients with hypercholesterolemia using rosuvastatin in primary care. Korean J Fam Med. 2012;33(5):253–61.
51. Kim S, Shin DW, Yun JM, Hwang Y, Park SK, Ko YJ, et al. Medication adherence and the risk of cardiovascular mortality and hospitalization among patients with newly prescribed antihypertensive medications. Hypertension (Dallas, Tex : 1979). 2016;67(3):506–12.
52. Kreibig SD, Whooley MA, Gross JJ. Social integration and mortality in patients with coronary heart disease: findings from the heart and soul study. Psychosom Med. 2014;76(8):659–68.
53. Kripalani S, Schmotzer B, Jacobson TA. Improving medication adherence through graphically enhanced interventions in coronary heart disease (IMAGE-CHD): a randomized controlled trial. J Gen Intern Med. 2012;27(12):1609–17.
54. Kronish IM, Lynch AI, Oparil S, Whittle J, Davis BR, Simpson LM, et al. The association between antihypertensive medication nonadherence and visit-to-visit variability of blood pressure: findings from the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Hypertension (Dallas, Tex : 1979). 2016;68(1):39–45.
55. Kunutsor SK, Seidu S, Khunti K. Aspirin for primary prevention of cardiovascular and all-cause mortality events in diabetes: updated meta-analysis of randomized controlled trials. Diabet Med: J Br Diabet Assoc. 2017;34(3):316–27.
56. Lee WL, Abdullah KL, Bulgiba AM, Zainal AI. Prevalence and predictors of patient adherence to health recommendations after acute coronary syndrome: data for targeted interventions? Eur J

Cardiovasc Nurs: J Work Group Cardiovasc Nurs Eur Soc Cardiol. 2013;12(6):512–20.
57. Liberato AC, Rodrigues RC, Sao-Joao TM, Alexandre NM, Gallani MC. Satisfaction with medication in coronary disease treatment: psychometrics of the treatment satisfaction questionnaire for medication. Rev Lat Am Enfermagem. 2016 https://doi.org/10.1590/15188345.0745.2705.
58. Librero J, Sanfelix-Gimeno G, Peiro S. Medication adherence patterns after hospitalization for coronary heart disease. A population-based study using electronic records and group-based trajectory models. PLoS One. 2016;11(8):e0161381.
59. Lin EH, Von Korff M, Ciechanowski P, Peterson D, Ludman EJ, Rutter CM, et al. Treatment adjustment and medication adherence for complex patients with diabetes, heart disease, and depression: a randomized controlled trial. Ann Fam Med. 2012;10(1):6–14.
60. Ludt S, Wensing M, Campbell SM, Ose D, van Lieshout J, Rochon J, et al. The challenge of cardiovascular prevention in primary care: implications of a European observational study in 8928 patients at different risk levels. Eur J Prev Cardiol. 2014;21(2):203–13.
61. Malik S, Billimek J, Greenfield S, Sorkin DH, Ngo-Metzger Q, Kaplan SH. Patient complexity and risk factor control among multimorbid patients with type 2 diabetes: results from the R2D2C2 study. Med Care. 2013;51(2):180–5.
62. Marcum ZA, Zheng Y, Perera S, Strotmeyer E, Newman AB, Simonsick EM, et al. Prevalence and correlates of self-reported medication non-adherence among older adults with coronary heart disease, diabetes mellitus, and/or hypertension. Res Social Adm Pharm: RSAP. 2013;9(6):817–27.
63. Martin SS, Sperling LS, Blaha MJ, Wilson PW, Gluckman TJ, Blumenthal RS, et al. Clinician-patient risk discussion for atherosclerotic cardiovascular disease prevention: importance to implementation of the 2013 ACC/AHA guidelines. J Am Coll Cardiol. 2015;65(13):1361–8.
64. Meng K, Seekatz B, Haug G, Mosler G, Schwaab B, Worringen U, et al. Evaluation of a standardized patient education program for inpatient cardiac rehabilitation: impact on illness knowledge and self-management behaviors up to 1 year. Health Educ Res. 2014;29(2):235–46.
65. Mertens A, Brandl C, Miron-Shatz T, Schlick C, Neumann T, Kribben A, et al. A mobile application improves therapy-adherence rates in elderly patients undergoing rehabilitation: a crossover design study comparing documentation via iPad with paper-based control. Medicine. 2016;95(36):e4446.
66. Moise N, Khodneva Y, Richman J, Shimbo D, Kronish I, Safford MM. Elucidating the Association Between Depressive Symptoms, Coronary Heart Disease, and Stroke in Black and White Adults: The REasons for Geographic And Racial Differences in Stroke (REGARDS) Study. J Am Heart Assoc. 2016;5(8):e003767.
67. Molloy GJ, Messerli-Burgy N, Hutton G, Wikman A, Perkins-Porras L, Steptoe A. Intentional and unintentional non-adherence to medications following an acute coronary syndrome: a longitudinal study. J Psychosom Res. 2014;76(5):430–2.
68. Molloy GJ, Randall G, Wikman A, Perkins-Porras L, Messerli-Burgy N, Steptoe A. Type D personality, self-efficacy, and medication adherence following an acute coronary syndrome. Psychosom Med. 2012;74(1):100–6.
69. Mosleh SM, Almalik MM. Illness perception and adherence to healthy behaviour in Jordanian coronary heart disease patients. Eur J Cardiovasc Nurs: J Work Group Cardiovasc Nurs Eur Soc Cardiol. 2016;15(4):223–30.
70. Mosleh SM, Darawad M. Patients' Adherence to healthy behavior in coronary heart disease: risk factor management among Jordanian patients. J Cardiovasc Nurs. 2015;30(6):471–8.
71. Muntner P, Yun H, Sharma P, Delzell E, Kent ST, Kilgore ML, et al. Ability of low antihypertensive medication adherence to predict statin discontinuation and low statin adherence in patients initiating treatment after a coronary event. Am J Cardiol. 2014;114(6):826–31.
72. Nord JW Jr, Berry A, Stults B, Burningham Z, Beddhu S. Evaluation of the effectiveness of a patient-centered educational mailer designed to improve statin adherence: a pragmatic trial. EGEMS (Washington, DC). 2016;4(1):1256.
73. Ose D, Rochon J, Campbell SM, Wensing M, van Lieshout J, Uhlmann L, et al. Secondary prevention in patients with coronary heart diseases: what factors are associated with health status in usual primary care? PLoS One. 2012;7(12):e51726.
74. Park LG, Howie-Esquivel J, Chung ML, Dracup K. A text messaging intervention to promote medication adherence for patients with coronary heart disease: a randomized controlled trial. Patient Educ Couns. 2014;94(2):261–8.
75. Park LG, Howie-Esquivel J, Whooley MA, Dracup K. Psychosocial factors and medication adherence among patients with coronary heart disease: a text messaging intervention. Eur J Cardiovasc Nurs: J Work Group Cardiovasc Nurs Eur Soc Cardiol. 2015;14(3):264–73.
76. Pedrosa RB, Rodrigues RC. Adaptation and evaluation of the measurement properties of the Brazilian version of the self-efficacy for appropriate medication adherence scale. Rev Lat Am Enfermagem. 2016;24:e2692.
77. Pfaeffli Dale L, Whittaker R, Jiang Y, Stewart R, Rolleston A, Maddison R. Text message and internet support for coronary heart disease self-management: results from the Text4Heart randomized controlled trial. J Med Internet Res. 2015;17(10):e237.
78. Pousinho S, Morgado M, Falcao A, Alves G. Pharmacist interventions in the Management of Type 2 diabetes mellitus: a systematic review of randomized controlled trials. J Manag Care Spec Pharm. 2016;22(5):493–515.
79. Sallis R, Franklin B, Joy L, Ross R, Sabgir D, Stone J. Strategies for promoting physical activity in clinical practice. Prog Cardiovasc Dis. 2015;57(4):375–86.
80. Santo K, Kirkendall S, Laba TL, Thakkar J, Webster R, Chalmers J, et al. Interventions to improve medication adherence in coronary disease patients: a systematic review and meta-analysis of randomised controlled trials. Eur J Prev Cardiol. 2016;23(10):1065–76.
81. Schneider KI, Schmidtke J. Patient compliance based on genetic medicine: a literature review. J Community Genet. 2014;5(1):31–48.
82. Simpson RJ Jr, Tunceli K, Ramey DR, Neff DR, Kern DM, Hsieh HM, et al. Treatment pattern changes in high-risk patients newly initiated on statin monotherapy in a managed care setting. J Clin Lipidol. 2013;7(5):399–407.
83. Sin NL, Kumar AD, Gehi AK, Whooley MA. Direction of association between depressive symptoms and lifestyle behaviors in patients with coronary heart disease: the heart and soul study. Ann Behav Med: Publ Soc Behav Med. 2016;50(4):523–32.
84. Sin NL, Moskowitz JT, Whooley MA. Positive affect and health behaviors across 5 years in patients with coronary heart disease: the heart and soul study. Psychosom Med. 2015;77(9):1058–66.
85. Son YJ, Shim SK, Hwang SY, Ahn JH, Yu HY. Impact of left ventricular ejection fraction and medication adherence on major adverse cardiac events during the first year after successful primary percutaneous coronary interventions. J Clin Nurs. 2016;25(7–8):1101–11.
86. Stamm-Balderjahn S, Brunger M, Michel A, Bongarth C, Spyra K. The efficacy of goal setting in cardiac rehabilitation-a gender-specific randomized controlled trial. Dtsch Arztebl Int. 2016;113(31–32):525–31.
87. Tsoi KK, Wong MC, Tam WW, Hirai HW, Lao XQ, Wang HH, et al. Cardiovascular mortality in hypertensive patients newly prescribed perindopril vs. lisinopril: a 5-year cohort study of 15,622 Chinese subjects. Int J Cardiol. 2014;176(3):703–9.

88. Varghese T, Schultz WM, McCue AA, Lambert CT, Sandesara PB, Eapen DJ, et al. Physical activity in the prevention of coronary heart disease: implications for the clinician. Heart. 2016;102(12):904–9.
89. Vorderstrasse AA, Ginsburg GS, Kraus WE, Maldonado MC, Wolever RQ. Health coaching and genomics-potential avenues to elicit behavior change in those at risk for chronic disease: protocol for personalized medicine effectiveness study in air force primary care. Glob Adv Health Med. 2013;2(3):26–38.
90. Wald DS, Bestwick JP, Raiman L, Brendell R, Wald NJ. Randomised trial of text messaging on adherence to cardiovascular preventive treatment (INTERACT trial). PLoS One. 2014;9(12):e114268.
91. Wong MC, Tam WW, Cheung CS, Wang HH, Tong EL, Sek AC, et al. Drug adherence and the incidence of coronary heart disease- and stroke-specific mortality among 218,047 patients newly prescribed an antihypertensive medication: a five-year cohort study. Int J Cardiol. 2013;168(2):928–33.
92. Yang EY, Chambless L, Sharrett AR, Virani SS, Liu X, Tang Z, et al. Carotid arterial wall characteristics are associated with incident ischemic stroke but not coronary heart disease in the atherosclerosis risk in communities (ARIC) study. Stroke. 2012;43(1):103–8.
93. Yudi MB, Clark DJ, Tsang D, Jelinek M, Kalten K, Joshi S, et al. SMARTphone-based, early cardiac REHABilitation in patients with acute coronary syndromes [SMART-REHAB trial]: a randomized controlled trial protocol. BMC Cardiovasc Disord. 2016;16(1):170.
94. Zhao S, Zhao H, Wang L, Du S, Qin Y. Education is critical for medication adherence in patients with coronary heart disease. Acta Cardiol. 2015;70(2):197–204.
95. Zhao SJ, Zhao HW, Du S, Qin YH. The impact of clinical pharmacist support on patients receiving multi-drug therapy for coronary heart disease in China. Indian J Pharm Sci. 2015;77(3):306–11.
96. Zhu L, Xu J, Wang Q, Xu F, Chen J. Nursing care of transradial angiography and intervention in a tertiary hospital in shanghai: a best practice implementation project. JBI Database Syst Rev Implement Rep. 2016;14(5):286–94.
97. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986;24(1):67–74.
98. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich, Conn). 2008;10(5):348–54.
99. Jank S, Bertsche T, Schellberg D, Herzog W, Haefeli WE. The A14-scale: development and evaluation of a questionnaire for assessment of adherence and individual barriers. Pharm World Sci: PWS. 2009;31(4):426–31.
100. Riddle MC, Rosenstock J, Gerich J. The treat-to-target trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. Diabetes Care. 2003;26(11):3080–6.
101. Steiner JF, Prochazka AV. The assessment of refill compliance using pharmacy records: methods, validity, and applications. J Clin Epidemiol. 1997;50(1):105–16.
102.• Zullig LL, Mendys P, Bosworth HB. Medication adherence: a practical measurement selection guide using case studies. Patient Educ Couns. 2017;100(7):1410–4. **This paper uses case studies to provide examples of selecting the appropraite medication adherence measures**.
103. Lam WY, Fresco P. Medication adherence measures: an overview. Biomed Res Int. 2015;2015:217047.
104. Sheridan SL, Draeger LB, Pignone MP, Sloane PD, Samuel-Hodge C, Finkelstein EA, et al. Designing and implementing a comparative effectiveness study of two strategies for delivering high quality CHD prevention: methods and participant characteristics for the heart to health study. Contemp Clin Trials. 2013;36(2):394–405.
105. Adler AJ, Martin N, Mariani J, Tajer CD, Owolabi OO, Free C, et al. Mobile phone text messaging to improve medication adherence in secondary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2017;4:Cd011851.
106. de Jongh T, Gurol-Urganci I, Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging for facilitating self-management of long-term illnesses. Cochrane Database Syst Rev. 2012;12:Cd007459.
107. DeKoekkoek T, Given B, Given CW, Ridenour K, Schueller M, Spoelstra SL. mHealth SMS text messaging interventions and to promote medication adherence: an integrative review. J Clin Nurs. 2015;24(19–20):2722–35.
108. Cutrona SL, Choudhry NK, Fischer MA, Servi A, Liberman JN, Brennan TA, et al. Modes of delivery for interventions to improve cardiovascular medication adherence. Am J Manag Care. 2010;16(12):929–42.
109. Teeter BS, Kavookjian J. Telephone-based motivational interviewing for medication adherence: a systematic review. Transl Behav Med. 2014;4(4):372–81.
110. Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med. 2007;167(6):540–50.
111. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–13.
112. Glanz K, Rimer BK, Viswanath K. Health behavior and health education: theory, research, and practice. Hoboken: John Wiley & Sons; 2008.
113. Snyderman R. Personalized health care: from theory to practice. Biotechnol J. 2012;7(8):973–9.
114. Centers for Medicare and Medicaid Services. Choose higher quality for better health care. Available from: http://www.medicare.gov/Publications/Pubs/pdf/11226.pdf.