

Chapter 18

Quality Improvement in Cardiovascular Disease Care

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INTRODUCTION

This chapter reviews the diagnosis and treatment of cardiovascular disease in low- and middle-income countries (LMICs) with a view to improving the quality of care. In keeping with the Institute of Medicine's definition of quality as the “degree to which health services for individuals and population increase the likelihood of desired health outcomes and are consistent with current professional knowledge” (Lohr 1990, 4), the focus is on studies of specific interventions and measurable health outcomes. Because the resources available to support health care delivery in LMICs are scarce, this chapter seeks to improve clinical quality by getting the most out of known effective interventions within the limits of available resources rather than recommending unproven interventions that require early-phase studies or substantial investment to scale up. Clinical quality can be improved anywhere and at any time and doing so need not be expensive.

Quality standards and measures contain principles that can be compared and shared across countries and local settings. However, quality care delivery in low-resource settings does not necessarily mean dissemination and implementation of a universal set of standards—especially those formulated for cardiovascular diseases in

high-income countries (HICs). Standards and interventions should be dictated by context and community capacity. Adaptation to the local setting is necessary for achieving optimal clinical outcomes and patient satisfaction.

A conceptual framework guided this chapter. The authors specified four domains, cutting across two distinct phases of cardiovascular disease (acute versus chronic) and two levels of intervention (health system versus patient-provider) (table 18.1). Health system-level interventions include those directly targeting one or more of the six “building blocks of a health system” as defined by the World Health Organization (2007). Patient-provider-level interventions are focused on influencing patient or provider behavior. Acute phases of cardiovascular disorders, such as acute myocardial infarction, stroke, and limb ischemia, occur unpredictably. Good outcomes demand timely clinical responses, which require adequate and accessible facilities, functional transportation networks, providers prepared to treat cases that present at all hours, and patient awareness of when and how to seek medical attention. In contrast, chronic phases of cardiovascular disorders, such as diabetes mellitus, hypertension, and congestive heart failure, require screening for preclinical risk factors, systematic monitoring for complications, and substantial

Table 18.1 Conceptual Framework for Quality of Care for Cardiovascular Diseases

Level	Acute phase	Chronic phase
Health system	<ul style="list-style-type: none"> • Strategically locate hospitals to reduce treatment delays. • Improve provider skills to deliver high-quality care; provide salary support for health care providers. • Improve access to revascularization services. • Improve transportation to hospital. • Improve population awareness of acute symptoms and means to access acute care. • Formulate and disseminate clinical practice guidelines and standards. 	<ul style="list-style-type: none"> • Formulate and disseminate clinical practice guidelines and standards. • Improve access to health care and medicines. • Train health care providers. • Provide financial support for quality improvement. • Improve infrastructure, including health care facilities and electronic and telephonic communication.
Patient-provider	<ul style="list-style-type: none"> • Implement clinical practice guidelines using clinical pathway algorithms. • Improve hospital discharge planning and transition to chronic care. 	<ul style="list-style-type: none"> • Educate providers and patients. • Implement clinical practice guidelines. • Improve risk factor monitoring. • Improve treatment adherence.

patient self-care and engagement to initiate and maintain treatment adherence. Good-quality, chronic-phase care may prevent or delay onset of acute-phase manifestations, thereby preventing or delaying disability or death.

Quality interventions are examined at the health care system and patient-provider levels. The authors populated the four domains of this two-by-two framework with potential quality improvement levers based on previous knowledge of the field and examples gleaned from other chapters in this volume. Once the framework was established, a systematic literature review was conducted to identify evidence supporting specific interventions within it. The results are accompanied by detailed narratives of clinical quality improvement efforts for cardiovascular diseases, including the story of a comprehensive community-based cardiovascular disease primary prevention program in Kenya, the experience of an acute coronary syndrome (ACS) clinical pathways intervention in China, and a spotlight on mobile health (m-health) applications around the world.

METHODOLOGY

The methodology for the systematic review, including the electronic search terms used, is detailed in annex 18A. In brief, an electronic search was conducted of the MEDLINE and EMBASE databases to capture published reports of English-language studies on cardiovascular disease care quality improvement studies carried out in LMICs from January 2000 to June 2014. The review identified 49 full text papers that reported on completed, population-based studies with clinically meaningful outcomes. These studies were selected for the review and

assigned to one or more categories in the chapter framework. The chapter highlights 32 of these studies.

SYSTEM-LEVEL INTERVENTIONS

Acute Phase

Timely intervention can dramatically improve the outcomes of acute cardiovascular disease, while delays may result in unnecessary death or disability. System-level factors affect the time to treatment in both the prehospital and hospital phases of an acute event. Before arriving at a hospital, patients educated about the cardinal symptoms of cardiac disease will seek care more quickly and be aware of nearby hospitals or ambulance transport to regional centers. Hours of service availability are critically important. For example, if a patient with an acute cardiovascular event arrives in the middle of the night at a hospital with revascularization services, staff must be available to provide those services. Lack of awareness, lack of acceptability, lack of affordability, and lack of availability are all common barriers that can delay treatment of acute events (see chapter 16 on surgery volume quality in volume 1, Weiser and Gawande 2015).

System-wide planning can overcome barriers to timely and appropriate care for acute cardiovascular disease. The systematic review found limited evidence of interventions to improve system-level, acute-phase care (table 18.2). Poor underlying infrastructure in low-resource settings perhaps presents daunting challenges to reorganizing complex health care delivery systems (Macharia and others 2009). Just as likely, government, nongovernmental, and private sector organizations often introduce system improvements without rigorous systematic study; therefore, the health

Table 18.2 Selected Studies on System-Level, Acute-Phase Quality Improvement Interventions

Quality improvement intervention	Study	Country	Study design	Sample	Observation interval	Quality measures	Results
National health care reform	Nazzal and others 2008	Chile	Retrospective, multicenter	STEMI patients from 10 hospitals that perform thrombolysis as main perfusion therapy	Not reported	Global in-hospital mortality; evidence-based prescribing for patients treated with thrombolysis	10 percentage point absolute increase in use of thrombolysis (50.0% vs. 60.5%); 3.8 percentage point absolute reduction in in-hospital mortality of patients treated with thrombolysis (10.6% vs. 6.8%); 3.4 percentage point absolute reduction in global in-hospital mortality (12.0% vs. 8.6%); adjusted odds ratio for in-hospital mortality, 0.64
Organization of hospitals in hub-and-spoke model	Alexander and others 2013	India	Prospective, multicenter, community-based study	Plan to enroll 1,500 consecutive STEMI patients at participating institutions	Patients to be enrolled over 9 months and followed for 1 year	Before-and-after study of the use of reperfusion therapy, time to reperfusion	Not yet available
Community education program regarding ACS symptoms and treatments	Prabhakaran and others 2008	India	Prospective, nonrandomized study	1,033 ACS patients in 34 hospitals; mean age, 58; males, 71%–78% of total	Follow-up: inpatient hospitalization	No specific outcomes related to community education program	No specific outcomes related to community education program

Note: ACS = acute coronary syndrome; STEMI = ST-elevation myocardial infarction.

effects of system-level changes may go unmeasured or unreported. Randomized comparison studies in low- and middle-income settings may not be conducted because of lack of research capacity, perception of causing unwanted delay in care delivery, “contamination” between intervention and control sites, and ethical concerns.

Alexander and others (2013) reported on a project being launched in the rural region within Tamil Nadu, India, which plans to implement a hub-and-spoke model using existing health care resources to improve the acute ST-elevation myocardial infarction (STEMI) care delivery system. Hub hospitals are capable of delivering timely percutaneous catheter-based reperfusion therapy, while spoke hospitals are primary health care facilities with or without capacity to deliver thrombolytic reperfusion therapy. Hubs and spokes are linked by privately owned professional ambulance services. After an observation phase, the hub-and-spoke program will be implemented, and primary outcomes are expected to change in response to rates of reperfusion therapy and time to coronary reperfusion.

Community-based education initiatives can prime the public by increasing awareness of clinical signs of

ACS, stroke, and heart failure and enhance acceptability of acute care solutions in the community. The Kerala Acute Coronary Syndrome Program included community-based health education programs that promoted self-detection of acute coronary disease symptoms, rapid self-referral for treatment, and timely self-administration of aspirin (Prabhakaran and others 2008). The investigators concluded that improved patient awareness contributed to reductions in time-to-thrombolysis achieved by the multicomponent intervention.

No studies were found on the impact of improved geographic and temporal coverage of acute care services, including the impact of building more hospitals within underserved areas or making revascularization more widely available.

Chronic Phase

Most studies in the system-level, chronic-phase category examined the expansion of health insurance coverage (table 18.3). Two studies evaluated the health impact of the Seguro Popular insurance that was rolled out in

Table 18.3 Selected Studies on System-Level, Chronic-Phase Quality Improvement Interventions

Quality improvement intervention	Study	Country	Study design	Sample	Observation interval	Quality measures	Results
Enrollment in Seguro Popular	Bleich and others 2007	Mexico	Cross-sectional, 2005 Mexican national survey	Adults with hypertension; 1,065 uninsured matched with 1,065 insured	Not reported	Self-reported hypertension treatment and control	Adults enrolled in Seguro Popular had higher rates of hypertension treatment (odds ratio 1.5) and controlled blood pressure (odds ratio 1.49)
Enrollment in Seguro Popular	Sosa-Rubi, Galarraga, and Lopez-Ridaura 2009	Mexico	Cross-sectional, 2005–06 Mexican national survey	Adults with diabetes; 425 insured matched with 1,029 uninsured	Not reported	Process outcomes and biological outcomes (hemoglobin A1c)	Adults enrolled in Seguro Popular more likely to have appropriate glucose control (average treatment effect 0.056)
Community-based health insurance	Hendriks and others 2014	Rural Nigeria	Prospective, nonrandom, nonblind; one geographic area with intervention, one control area	Adults with hypertension	Intervention and follow-up for one year	Blood pressure, measured by trained interviewers	Systolic blood pressure decreased by 10.4 mmHg vs. 5.2 mmHg and diastolic blood pressure decreased by 4.3 mmHg vs. 2.2 mmHg in intervention group
Medication subsidy program providing full coverage of antihypertension medications	Yu, Zhang, and Wang 2013	Rural China	Prospective cohort study with propensity-score-matched controls	Low-income, hypertensive adults taking more than one antihypertensive medication (93% taking more than three)	Intervention and follow-up for 18 months	Blood pressure, medication adherence, and health care costs	Intervention arm had a 9 percentage point absolute increase in medication adherence (75% vs. 66%) and lower annual out-of-pocket medical costs overall

Note: mmHg = millimeter of mercury, a measure of pressure.

2002 as part of Mexico's national universal health insurance plan. Seguro Popular covered approximately 50 million low-income people who had no formal health insurance—often because working family members participated in the informal economy. Based on data gathered in Mexican national health and nutrition surveys, Bleich and others (2007) found that, compared with matched hypertensive adults without insurance, Seguro Popular enrollees had 1.5-fold higher odds of receiving hypertension treatment and 1.4-fold higher odds of having controlled blood pressure. A similar study of low-income diabetic patients found those with Seguro Popular insurance were more likely to receive regular blood glucose control monitoring and maintain adequate glucose control compared with their matched, uninsured counterparts (Sosa-Rubi, Galarraga, and Lopez-Ridaura 2009). In rural Nigeria, hypertensive patients living in a district where community-based health insurance was available had significantly lower systolic and diastolic blood pressures, changes not

observed in the control group without insurance (Hendriks and others 2014). In rural China, hypertensive patients receiving subsidies to defer medication costs had a 9 percent absolute increase in medication adherence and significantly lower annual out-of-pocket medical costs (Yu, Zhang, and Wang 2013).

System-level quality improvement efforts can lead to measurable improvements in health status in patients with chronic cardiovascular disease. These studies also demonstrate that the health impact of system-level changes can be rigorously evaluated. Researchers can simulate randomization through natural experiments, propensity score matching, or comparison of geographic areas or facilities with and without the intervention. Stepped-wedge trials introduce interventions to couple stepwise active and systematic program implementation with evaluation (Hemming and others 2015). As in the Seguro Popular studies, repeated population-based surveys can be leveraged to measure changes in chronic cardiometabolic disease risk factors and outcomes.

Quality improvement studies will be most feasible where key outcomes are part of, or added to, ongoing surveys.

Many cardiovascular disease patients remain untreated or incompletely treated with standard oral medications for secondary prevention (Yusuf and others 2011). System-level policies to improve the availability and reduce the costs of essential preventive medicines have the potential to extend effective prevention to many more of these patients. No studies were found on the impact of essential medicines designations or pharmaceutical market regulations on the quality of clinical care for

cardiovascular diseases (see chapter 8 in this volume, Dugani and others 2017).

In Sub-Saharan Africa, the substantial infrastructure investment that turned the tide of the human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) epidemic is now being leveraged for chronic noncommunicable disease management. Groups like the Kenya-based Academic Model Providing Access to Healthcare (AMPATH) have leveraged the infrastructure established for chronic care to improve hypertension control in the communities they serve (box 18.1).

Box 18.1

Systems and Individuals: The AMPATH Chronic Disease Management Experience in Kenya

In Sub-Saharan Africa, cardiovascular disease (CVD) is the leading cause of death among individuals older than age 30 years (Gaziano and others 2006). In Kenya, atherosclerotic CVD, particularly stroke (Etyang and others 2014), and CVD risk factors, particularly hypertension (Kayima and others 2013), are increasing. To address the rise in noncommunicable diseases, Kenya formed the Division of Noncommunicable Diseases in the Directorate of Preventive and Promotive Health Services within the Ministry of Health. This division has developed a strategic plan for noncommunicable diseases, including hypertension; designated clear targets; and recommended evidence-based interventions.

However, widespread implementation of programs is still lacking. The infrastructure for hypertension management is challenging. Human resources for health are insufficient (WHO 2013), and physicians have traditionally managed hypertension. Stockouts of even the essential medicines on the national formulary are frequent (Manji and others 2012). The availability of hypertension medicines is even less reliable, especially in rural areas. In addition, there is a profound lack of facilities, supplies, and equipment, including sphygmomanometers.

The Academic Model Providing Access to Healthcare (AMPATH)—a collaboration between the Moi University College of Health Sciences, the Moi Teaching and Referral Hospital, and a consortium of North American universities led by Indiana

University—has sought to address both system-level and individual-level factors in an attempt to improve access to high-quality, comprehensive, coordinated, and sustainable care for CVD risk factors such as hypertension and diabetes. AMPATH has established a human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) care system in western Kenya that has served more than 160,000 patients (AMPATH 2015; Einterz and others 2007). It has also developed a comprehensive chronic disease management program, focusing initially on hypertension and diabetes (Bloomfield and others 2011). The program has several goals:

- Achieve population-wide screening for hypertension and diabetes
- Engage community resources and governance structures
- Achieve geographic decentralization of care services
- Redistribute tasks
- Ensure a consistent supply of essential medicines
- Improve the physical infrastructure of rural health facilities
- Develop an integrated health record to be used at all levels of the health system
- Use mobile health initiatives strategically.

Bringing together all of these components, AMPATH has created an integrated system of chronic disease treatment and prevention services. Nurses in rural dispensaries have received

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Box 18.1 (continued)

specialized training and simple clinical algorithms to manage uncomplicated cases of hypertension and diabetes. Community health workers have received structured training to provide health education, link patients to hypertension and diabetes care, and improve retention. Rural clinicians and community health workers are using handheld devices, equipped with clinical decision support and record-keeping functions, to improve the quality of care and the efficiency of follow-up. Novel community-based,

revolving-fund pharmacies (Manji and others 2012) and provider supply networks have been developed to increase the availability of chronic disease medications. The program has also launched a community-based outpatient health insurance program to improve affordability. Finally, implementation research is being conducted to determine which components are or are not working and why to generate lessons for the program and for programs in other low-resource settings worldwide.

PATIENT-PROVIDER-LEVEL INTERVENTIONS

Acute Phase

ACS and acute stroke care have a remarkably strong evidence base, supported by randomized controlled trials of life-saving medications and reperfusion procedures (table 18.4). Professional societies have endorsed clinical practice guidelines that propose to set international quality standards for acute care. However, these quality standards are incompletely implemented even in high-income settings (Aliprandi-Costa and others 2011; Berwanger and others 2012; Cabana and others 1999; Du and others 2014; Fox and others 2002; Hoekstra and others 2002; Pearson, Goulart-Fisher, and Lee 1995). For years, the case for initiatives to improve the quality of ACS care was based on observations of quality gaps in registry studies; only recently has evidence emerged from randomized controlled trials (Flather and others 2011; Tu and others 2009).

Modeling studies have projected that treating ACS patients according to the recommendations of clinical guidelines is cost-effective in LMICs (Megiddo and others 2014; Wang and others 2014; see chapter 8 in this volume [Dugani and others 2017]). However, the gap between current and optimal ACS care appears to be even wider in LMIC hospitals than in HIC hospitals (Berwanger and others 2012; Du and others 2014; Wang and others 2012; Wang and others 2014; Xavier and others 2008). The Kerala Acute Care Syndrome Registry, which studied 25,748 consecutive ACS admissions in hospitals in Kerala, India, over two years, found that 41 percent of STEMI patients reached the health care facility six hours or more after symptom onset (Mohanan and others 2013). Only 41 percent and 13 percent of STEMI patients received reperfusion therapy using thrombolytics or percutaneous

coronary interventions, respectively. The study also demonstrated that optimal in-hospital and discharge medical care were delivered in only 40 percent and 46 percent of admissions, respectively, with rural hospitals performing worse than urban ones (Huffman and others 2013). Patients receiving optimal in-hospital medical therapy reported a 21 percent lower rate of major adverse in-hospital cardiovascular events.

Adopting HIC guidelines for LMICs offers a great opportunity both for implementing quality improvement standards and for benchmarking significant improvements in practice and outcomes. The ACS quality improvement studies identified in the review showed some improvements in measures of clinical process, but, like studies in HICs, only equivocal clinical improvements were found.

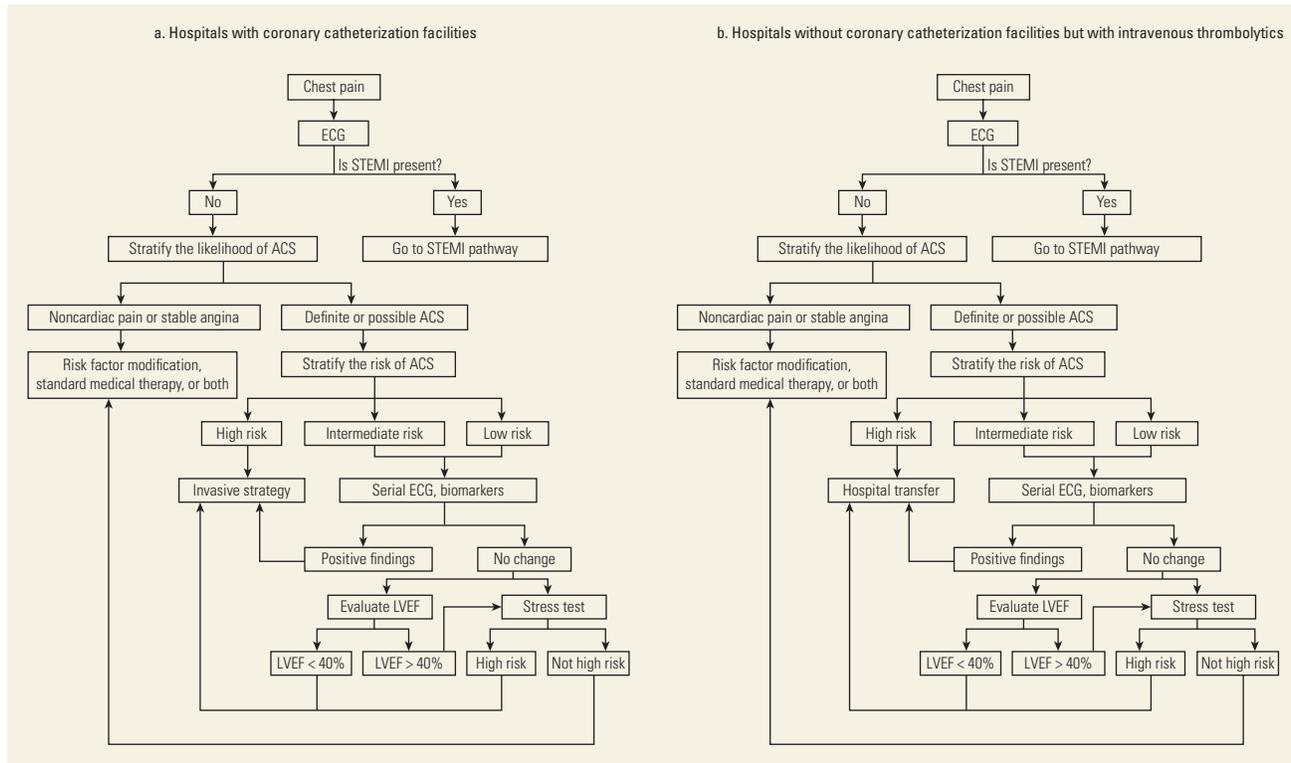
Berwanger and others (2012) randomized large urban hospitals in Brazil into those offering a multifaceted quality improvement program with educational material, reminders, algorithms, and training visits and those offering usual care. The intervention group had 2.64 higher odds of receiving evidence-based ACS therapy within the first 24 hours following symptom onset. There were no changes, however, in 30-day mortality or in-hospital cardiovascular events. Du and others (2014) randomized large urban Chinese hospitals to implement a U.S.-guidelines-based ACS pathway, along with periodic clinical performance audits and feedback throughout the intervention period (figure 18.1). Hospitals in the intervention arm showed higher rates of discharge for recommended therapies, but no difference in other indicators, including reperfusion in STEMI cases within 12 hours of symptom onset, door-to-needle time, door-to-balloon time, or high-risk patients undergoing angiography. As in Berwanger and others (2012), there were

Table 18.4 Selected Studies of Patient-Provider-Level, Acute-Phase Quality Improvement Interventions

Quality improvement intervention	Study	Country	Study design	Sample	Observation interval	Quality measures	Results
ACS							
Multifaceted quality improvement intervention with educational materials, reminders, algorithms, and training visits	Berwanger and others 2012	Brazil	Prospective, cluster randomized controlled, multicenter study; 17 hospitals randomized to intervention and 17 to routine practice	1,150 ACS patients in 34 public hospitals; mean age, 62	Follow-up of 30 days	Evidence-based therapy (aspirin, clopidogrel, anticoagulants, and statins) for ACS within first 24 hours	Intervention group more likely to receive all eligible acute and discharge medications and higher adherence; no change in 30-day all-cause mortality or in-hospital cardiovascular events
Clinical pathways approved by the American College of Cardiology and American Heart Association	Du and others 2014	China	Prospective, cluster randomized controlled, multicenter study; regional and tertiary urban hospitals with more than 100 ACS patients annually; 32 hospitals in early intervention and 38 hospitals in late intervention	3,500 ACS patients; mean age, 64; males, 67%–72% of total	Follow-up: inpatient hospitalization	Primary outcomes were correct final diagnosis, thrombolysis or angioplasty within 12 hours, door-to-needle time, door-to-balloon time, high-risk patients undergoing angiography, low-risk patients undergoing functional testing, discharge on correct medications, and length of hospital stay	11.6 percentage point absolute increase in discharge rates on recommended therapies (relative risk 1.23); no difference in other primary outcomes, death, or major cardiovascular events
Education program for physicians and community members in detection and optimal management of ACS	Prabhakaran and others 2008	India	Prospective, nonrandomized study; 34 hospitals treating ACS patients in Kerala region	1,033 ACS patients; mean age 58; males, 71%–78% of total	Follow-up: inpatient hospitalization	Use of aspirin, heparin, beta blockers, lipid-lowering agents, calcium channel blockers, time to thrombolysis	Absolute decreases of 43 minutes in symptom-to-door time, 11 minutes in door-to-thrombolysis, and 55 minutes in time-to-thrombolysis; significant increase in use of aspirin, heparin, beta blockers, lipid-lowering agents; reduction in use of calcium channel blockers
Stroke							
Guideline-based structured case program for secondary stroke prevention	Peng and others 2014	China	Prospective, cluster randomized controlled, multicenter study; large regional or tertiary hospitals; 23 hospitals in intervention and 24 in control	1,287 inpatient stroke patients; mean age, 60–61; males, 67%–69% of total	Follow-up of one year	Medication adherence to secondary prevention	Higher adherence to statins (56% vs. 33%); no difference in antiplatelet, antihypertensive, or diabetes mellitus drugs; no difference in composite endpoint (new stroke, ACS, and all-cause death)

Note: ACS = acute coronary syndrome.

Figure 18.1 Clinical Pathways for Acute Coronary Syndrome in Hospitals with and without Catheterization Facilities in the Phase 2 CPACS-2



Source: Du and others 2014 (Supplementary Material).

Note: CPACS = Clinical Pathways for Acute Coronary Syndromes; ECG = electrocardiogram; ACS = acute coronary syndrome; STEMI = ST-elevation myocardial infarction; LVEF = left ventricular ejection fraction.

no significant differences in mortality or cardiovascular events. Prabhakaran and others (2008) enrolled 34 hospitals in the Kerala region of India to serve as their own controls in a pre- and postintervention design. After the multifaceted quality improvement intervention, there was a significant median reduction in time-to-thrombolysis of 54 minutes—from 193 to 139 minutes—and a significant increase in the use of evidence-based medications.

In sum, selected studies of quality improvement programs for ACS and stroke care found improvements in some measures of clinical process, but not in clinical outcomes—similar to the pattern commonly found in programs in HICs. Even regarding surrogate measures of process, quality improvement studies yielded variable results. It may be that success depends on the support of health care providers and administrators and tailoring to the specific context of the participating health care system (that is, the availability of treatments and financial protection for patients). Lessons learned from these

programs may be helpful for the design of future patient-provider-level studies on cardiovascular disease (box 18.2). Despite their limitations, these ambitious studies demonstrated that complex quality improvement programs can be implemented in the hospital setting in middle-income countries. No studies were found measuring the impact of physician education on diagnostic accuracy or clinical decision making related to acute cardiovascular disorders.

Chronic Phase

Adherence to life-saving medications and lifestyle changes is suboptimal worldwide, regardless of country income level (Yusuf and others 2011). Since the overwhelming majority of chronic-phase cardiovascular disease patients live in LMICs, where health care resources are limited, optimizing low-cost primary and secondary prevention interventions is critical. Numerous studies have been conducted on a variety of

Box 18.2

Acute Care Quality Improvement in Middle-Income Countries: Lessons from the CPACS Study in China

Three acute coronary syndrome (ACS) clinical quality improvement programs were identified, including the second phase of the Clinical Pathways for Acute Coronary Syndromes (CPACS) study conducted in China (Berwanger and other 2012; Du and others 2014; Prabhakaran and others 2008). Following the intervention, CPACS collected data from structured health care provider surveys in all 75 hospitals participating in the initiative and from in-depth semistructured interviews with study coordinators and leaders in 10 of the hospitals. These data were analyzed using quantitative and qualitative methods. The analysis found that provider-level, system-level, and patient-level factors—government and administrative support, hospital resources, and patient health insurance coverage and lack of financial protection—all limited the intervention's impact. Several lessons emerged from the CPACS experience.

Engaging health care providers and hospital administrators. Not all diagnostic and clinical practice guidelines formulated in high-income countries will apply to the local context in low- and middle-income countries. CPACS engaged providers in study hospitals early in the process of planning to involve them as stakeholders and incorporate their recommendations. More than 80 percent of providers attended

program training sessions and reported using the ACS pathways in clinical practice, and providers had a generally positive view of the program's objectives. In China, hospital administrators and local governments are powerful arbiters of hospital priorities. Failure to gain support from these high-level officials limited successful implementation of the clinical pathways in some hospitals. For example, hospitals with less administrative buy-in assigned responsibility for collecting and analyzing CPACS data and for following up with patients to students and junior physicians without scaling back their regular academic and administrative obligations.

Overcoming patient-level obstacles. Community education about the signs, symptoms, and treatment of acute cardiovascular disease may be difficult to carry out in large-scale, multisite, hospital-based studies. CPACS found that patient factors limited the effectiveness of the intervention. Patients' insurance circumscribed the treatments reimbursed, and many patients were underinsured or uninsured and found it difficult or impossible to pay out of pocket for treatments considered part of the quality care program. Limited knowledge of coronary heart disease negatively affected patients' participation in discussions regarding informed consent and limited their willingness to pursue long-term secondary prevention after being discharged from the hospital.

interventions to improve the quality of chronic-phase cardiovascular diseases in LMICs (table 18.5). Because patients are ideally prescribed several standard daily oral medications for primary or secondary prevention of cardiovascular disease, achievement of medication adherence, sometimes lifelong, is a key challenge for quality health care worldwide (figure 18.2). Most of the interventions reviewed were related to chronic medication adherence, specifically the use of fixed-dose combination pills, health care delivery supported by mobile communication technology, and task-shifting.

Combination Pills

Many patients with cardiovascular disease are prescribed multiple daily medications. As the number of medications

increases, the probability that patients will take all of the prescribed pills declines. For this reason, combining multiple medications into a single pill can improve adherence. Combined low doses of multiple medications in place of higher doses of a single medication also should lower the frequency of side effects.

Thom and others (2013) randomized persons at high risk of cardiovascular disease (CVD) living in India (one of four countries studied) to receive combination pills or the usual multiple-pill therapy. After a mean follow-up of about 15 months, participants taking the combination pills had 25 percent higher absolute adherence and small but significant reductions in both systolic blood pressure and low-density lipoprotein compared with participants randomized to receive

Table 18.5 Selected Studies of Chronic-Phase, Patient-Provider-Level Interventions

Quality improvement intervention	Study	Country or region	Disease	Study design	Sample	Observation interval	Quality measures	Results
<i>Combination pills</i>								
Fixed-dose combination medications	Thom and others 2013	India	CVD, secondary prevention	Prospective, randomized, open-label, multicenter, multinational, blind endpoint trial; 501 patients in intervention, 499 in usual care	Participants with CVD or five-year CVD risk of at least 15%; in all population, mean age, 62 years; males, about 80% of total	Median intervention and follow-up of 15 months	Self-reported adherence to all of aspirin, statin, and two or more medications	25% absolute higher adherence to all four medications (ratio of 1.4); small but statistically significant decreases in systolic blood pressure (−2.6 mmHg) and LDL (6.7 mg/dL)
CVD prevention protocol, including low-dose combination pill with lifestyle modification	Zou and others 2014	Rural China	CVD, secondary prevention	Prospective, nonrandomized, single-center study; pilot before RCT; 153 patients in intervention, no control	Subjects ages 40–74 years with a calculated 10-year CVD risk of 20% or more; mean age 71 years; males, 71% of total	Intervention and follow-up for 3 months	Blood pressure, percent taking CVD medications, self-reported adherence to smoking cessation and salt intake, appointment rates	Significantly higher rates of subjects taking CVD preventive drugs (73% vs. 84%) and reduction in smoking rates (38% vs. 35%); no changes in salt intake or measured blood pressure
Low-dose combination pill, “polycap”	Yusuf and others 2009	India	CVD	Prospective, double-blind, multicenter trial; 2,053 individuals randomized to eight groups; 412 in intervention, about 200 in each of eight groups	Subjects ages 45–80 years without previous CVD but one risk factor	Intervention for 12 weeks; follow-up for 4 weeks post-intervention	Blood pressure, LDL, heart rate, urinary 11-dehydrothromboxane B2	Significant reductions in systolic and diastolic blood pressure (by 7.4 and 5.6 mmHg, respectively) compared with groups not receiving antihypertensives; significant reduction in LDL (by 0.7 millimole per liter) compared with groups not taking simvastatin
Full-dose pills with potassium vs. low-dose combination pills	Yusuf and others 2012	India	CVD	Prospective, randomized, multicenter trial; 257 patients in full-dose group, 261 in low-dose group	Subjects older than age 40 years with blood pressure higher than 130/90 on two consecutive occasions or on antihypertensive medications and with cardiovascular disease or high-risk diabetes	Intervention for 8 weeks; follow-up for 4 weeks postintervention	Blood pressure, heart rate, serum lipids, serum and urinary potassium, and tolerability	Significant reductions in systolic and diastolic blood pressure (by 2.8 mmHg and 1.7 mmHg, respectively); significant reductions in both total cholesterol and LDL; similar rates of discontinuation

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Table 18.5 Selected Studies of Chronic-Phase, Patient-Provider-Level Interventions (continued)

Quality improvement intervention	Study	Country or region	Disease	Study design	Sample	Observation interval	Quality measures	Results
<i>Mobile health</i>								
Mobile phone messaging intervention	Ramachandran and others 2013	India	Diabetes	Prospective, multicenter, RCT; 271 subjects in intervention, 266 in control	Men with impaired glucose tolerance; mean age 45–46 years	Mean intervention and follow-up for 20.2 months	Progression to diabetes	9 percentage point absolute reduction in progression to diabetes (18% vs. 27%, hazard ratio 0.64); improved dietary adherence (hazard ratio 0.48)
SMS message about diet, exercise, medication	Goodarzi and others 2012	Iran, Islamic Rep.	Diabetes	Prospective, RCT; 43 subjects in intervention, 38 in control	Subjects with type 2 diabetes; mean age, 51–56 years; males, 21%–24% of total	Intervention and follow-up for 3 months	Laboratory results and questionnaire	0.9 percentage point absolute decrease in hemoglobin A1c; significant decreases in total cholesterol and microalbumin; significant improvement in knowledge, attitude, practice, and self-efficacy
SMS regarding medications and healthy lifestyle changes	Shetty and others 2011	India	Diabetes	Prospective, RCT; 110 subjects in intervention, 105 in control	Subjects with diabetes; mean age, 50 years	Intervention and follow-up for 1 year	Hemoglobin A1c, fasting plasma glucose, lipids	Significant improvement in fasting plasma glucose (185 vs. 166); no significant difference in hemoglobin A1c
Automated phone calls and home blood pressure monitors; e-mail alerts to providers	Piette and others 2012	Honduras; Mexico	Hypertension	Prospective, RCT; primary care clinics; 99 subjects in intervention, 101 in control	Subjects with uncontrolled hypertension; mean age, 58 years; males, 33% of total	Intervention and follow-up for 6 weeks	Blood pressure	No significant effect on systolic blood pressure, but in subgroup analysis, reduction in systolic blood pressure (by 8.8 mmHg) in low-literacy group
Education, counseling, and medical adjustment by nurses via phone calls	Ferrante and others 2010; GESICA Investigators 2005	Argentina	Congestive heart failure	Prospective, multicenter, RCT; 760 patients in intervention, 758 in usual care	Outpatients with stable chronic heart failure; mean age, 65 years; males, 71% of total	Intervention for 1 year; follow-up for 4 years	All-cause mortality and heart failure hospitalization	2 percentage point absolute reduction in composite outcome of mortality or heart failure hospitalization at 3 years (relative risk 0.88); mostly driven by 7 percentage point absolute reduction in heart failure hospitalization at 3 years (relative risk 0.72)

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Table 18.5 Selected Studies of Chronic-Phase, Patient-Provider-Level Interventions (continued)

Quality improvement intervention	Study	Country or region	Disease	Study design	Sample	Observation interval	Quality measures	Results
Automated SMS message reminders	Khonsari and others 2014	Malaysia	CVD, secondary prevention	Prospective, open-label, single-center, RCT; ACS patients at tertiary teaching hospital; 31 patients in intervention, 31 in control	Participants admitted for ACS; mean age, 58 years; males, 86% of total	Intervention and follow-up for 2 months	Adherence to cardiac medications	Higher medication adherence rate (64.5% vs. 12.9%); intervention group trended toward lower hospital readmission rates (0 vs. 12.9%)
Telephone-based peer support	Rotheram-Borus and others 2012	South Africa	Diabetes	Prospective, single-center, nonrandomized, clinical trial; 22 subjects in intervention	Subjects with diabetes; mean age, 53; all females	Intervention for 3 months; follow-up at end of study and at 3 months postintervention	Blood glucose, body mass index, coping and social support	No significant improvements in clinical measures; blood glucose and diastolic blood pressure increased; social support and coping abilities increased
<i>Task-shifting</i>								
Counseling by pharmacists, telephone reminders	Ramanath and others 2012	India	Hypertension	Prospective, RCT; 26 subjects in intervention, 26 in control	Subjects with hypertension; males, 62%–81% of total	Intervention and follow-up for 1 month	Blood pressure, self-reported medicine adherence	No significant effect on blood pressure; increased self-reported medication adherence
Nurse-led clinic	Kengne and others 2009	Sub-Saharan Africa	Hypertension	Prospective, nonrandomized, no-control study; 5 urban and rural clinics; 454 subjects	Subjects with hypertension; mean age, 53–58 years; males, 41%–55% of total	Median intervention and follow-up for 6 months	Blood pressure	Decrease in systolic and diastolic blood pressure (by 11.7 mmHg and 7.8 mmHg, respectively)
Pharmacist-led hypertension clinic	Erhun, Agbani, and Bolaji 2005	Nigeria	Hypertension	Prospective, randomized cohort trial; state comprehensive health center; 51 subjects	Subjects with uncontrolled hypertension; mean age, 61; males, 29% of total	Intervention and follow-up for 1 year	Blood pressure	Decrease in mean blood pressure from 168/103 at enrollment to 126/80 at fifth visit; no control group
Home visits	Adeyemo and others 2013	Nigeria	Hypertension	Prospective, RCT; rural and urban populations; 280 subjects in intervention, 264 in control	Subjects with hypertension; mean age, 63 years; males, 51%–53% of total	Intervention and follow-up for 6 months	Medication adherence via pill counting or urine test	No difference in adherence

table continues next page

Table 18.5 Selected Studies of Chronic-Phase, Patient-Provider-Level Interventions (continued)

Quality improvement intervention	Study	Country or region	Disease	Study design	Sample	Observation interval	Quality measures	Results
Family-based home health education for patients and training of general practitioners	Jafar and others 2009	Pakistan	Hypertension	Prospective, cluster RCT; geographic census-based clusters; 629 subjects in intervention, 640 in control	Subjects with hypertension; mean age, 54 years; males, 37% of total	Intervention and follow-up for 2 years	Systolic blood pressure	Decrease in systolic blood pressure (by 10.8 mmHg vs. 5.8 mmHg)
Follow-up by nurses	Nesari and others 2010	Iran, Islamic Rep.	Diabetes	Prospective, RCT	Subjects with diabetes; mean age, 51 years; males, 20% in control and 37% in intervention	Intervention and follow-up for 3 months	Hemoglobin A1c	1.87 percentage point absolute decrease in hemoglobin A1c in intervention group; no change in control group; intervention group also saw significantly higher adherence to diet, exercise, and glucose monitoring
<i>Guideline implementation</i>								
Training general practitioners in hypertension management	Qureshi and others 2007	Pakistan	Hypertension	Prospective, cluster RCT; communities in Karachi; 100 subjects in intervention, 100 in control	Subjects with hypertension; mean age, 55 years; males, 38% of total	Intervention and follow-up for 6 weeks	Medication adherence	16 percentage point absolute increase in patient medication adherence (48.1% vs. 32.4%)
Clinical decision support system	Anchala and others 2015	India	Hypertension	Prospective, cluster RCT; eight primary health clusters in each arm; 845 subjects in intervention, 793 in control	Subjects with hypertension; mean age, 54 years; males, 49%–52% of total	Intervention and follow-up for 12 months	Systolic blood pressure, cost-effectiveness	Absolute decrease in systolic blood pressure (by 6.59 mmHg); cost-effectiveness ratio of US\$96.01 per systolic blood pressure reduction in intervention and US\$36.57 in control

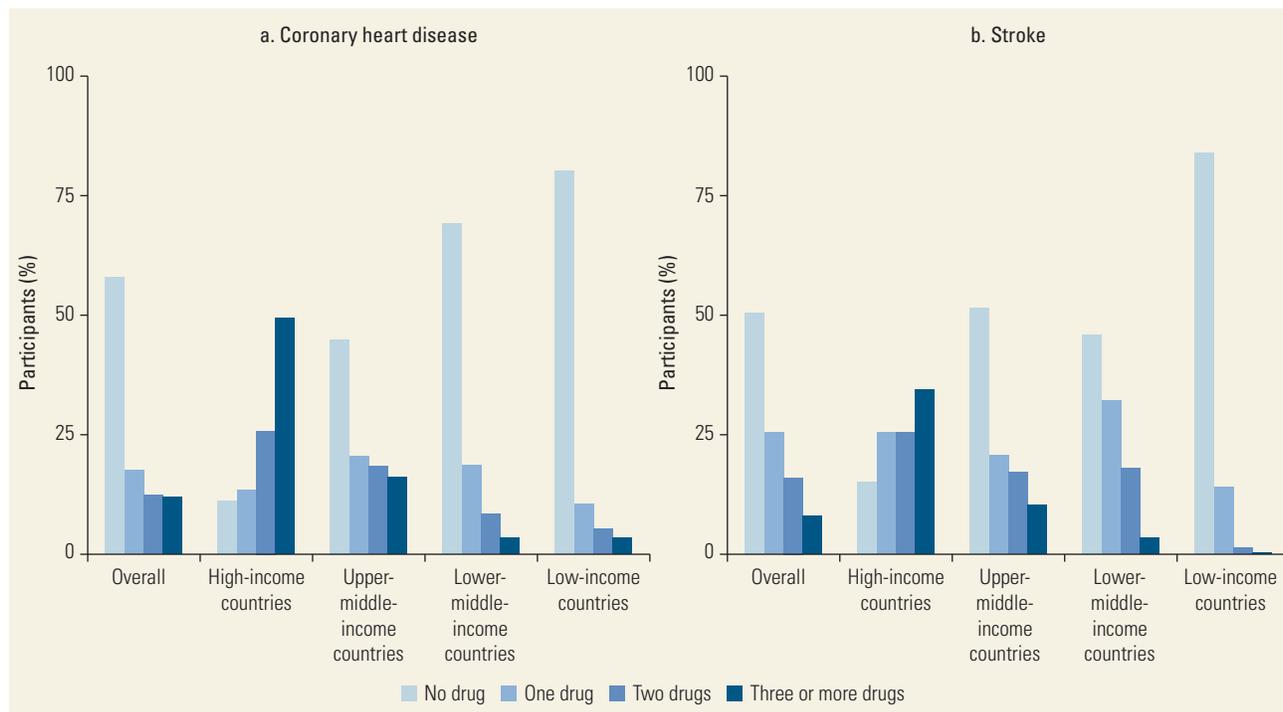
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Table 18.5 Selected Studies of Chronic-Phase, Patient-Provider-Level Interventions (continued)

Quality improvement intervention	Study	Country or region	Disease	Study design	Sample	Observation interval	Quality measures	Results
Education of general practitioners regarding management guidelines including meetings, reminders, medical record summary, and patient result cards	Reutens and others 2012	Asia	Diabetes	Prospective, multinational, cluster RCT; 50 subjects in intervention, 49 in control	Asia-Pacific general practitioners; mean age, 44 years; males, 50%–57% of total	Intervention and follow-up for 12 months	Patient hemoglobin A1c, blood pressure, lipids	No significant difference in hemoglobin A1c or other glycemic indexes
Guidelines for diabetes and hypertension incorporated into each chart for providers	Steyn and others 2013	South Africa	Diabetes	Prospective, multicenter, RCT; public sector community health centers; nine centers in intervention, nine in control	Subjects with diabetes or hypertension; 690 in intervention, 686 in control; mean age 58–61 years; males, 72%–83% of total	Intervention and follow-up for 1 year	Blood pressure, A1c	No effect; fewer than 60% of guideline forms used

Note: ACS = acute coronary syndrome; CVD = cardiovascular disease; LDL = low-density lipoprotein; mg/dL = milligram per deciliter; mmHg = millimeters of mercury, a measure of pressure; RCT = randomized controlled trial; SMS = short message service.

Figure 18.2 Number of Drugs Taken for Coronary Heart Disease and Stroke by Individuals in the PURE Study, by Country Income Level, 2003–09



Source: Yusuf and others 2011.

Note: PURE = Prospective Urban Rural Epidemiology.

multiple-pill treatment. Yusuf and others (2009) also found small but significant improvements among Indian subjects at risk for CVD when randomized to receive a combination pill containing multiple blood pressure medications, statins, and aspirin. A follow-up study by Yusuf and others (2012) showed that high-dose combination pills improved blood pressure and lipid control in high-risk Indian subjects compared with low-dose ones with similar rates of tolerability. Zou and others (2014) found that starting high-risk rural Chinese participants on combination pills achieved an 11 percent higher absolute adherence rate.

These trials show that combination pills can improve medication adherence and improve risk factor control in high-risk CVD patients. For this reason, efforts to approve and manufacture combination medications are underway (FDA 2014).

Mobile Communication Technology

Mobile technologies such as cell phones are becoming increasingly available in LMICs and are playing an important role in health promotion (box 18.3). Twelve studies were identified on the role of m-health in the

prevention and treatment of diabetes, hypertension, heart failure, and coronary artery disease. Although not every study demonstrated a significant improvement in clinical care quality, these studies suggest that m-health via text messages and phone calls can be a useful tool for managing chronic cardiovascular conditions in LMICs.

Task-Shifting

Task-shifting refers to the rational redistribution of tasks among health care teams, often from a few highly trained health providers to a larger contingent of providers with less training (see chapter 17 in this volume, Joshi and others 2017; WHO 2008). Six studies were identified evaluating task-shifting for improving patient adherence to prescribed medications. Some studies coupled task-shifting with increased access to affordable or free medications (Erhun, Agbani, and Bolaji 2005; Kengne and others 2009), or family-based home health education and supplemental training of general practitioners (Jafar and others 2009).

Five task-shifting studies targeted hypertensive patients. Kengne and others (2009) carried out a large

Box 18.3

Mobile Health: Harnessing the Communication Revolution in LMICs

Mobile health, also known as *m-health*, uses cell phones and other devices to support public health and clinical care (Kahn, Yang, and Kahn 2010). The number of mobile phone subscriptions reached almost 7 billion by the end of 2014, nearly equaling the number of people in the world, and penetration rates are now 69 percent in Africa, 89 percent in Asia and Pacific, and 90 percent in low- and middle-income countries (LMICs) overall (ITU 2013).

Access to health care providers is a significant challenge in LMICs, especially in rural areas. Kinfu and others (2009) found that it would take 36 years for physicians and 29 years for nurses and midwives to reach the World Health Organization's workforce targets, given current training levels. Voice and short message system (SMS) communication—telemedicine—allows providers to interact with more patients over a wider geographic area, increasing cost efficiency.

Ferrante and others (2010) conducted a multicenter, randomized controlled trial of patients with chronic congestive heart failure in Argentina. Nurses called patients, adjusting their medications depending on their symptoms and providing counseling and education. Patients in the intervention arm had a 20 percent relative risk reduction in all-cause mortality and heart failure hospitalizations at the end of the study (GESICA Investigators 2005). After three years, they continued to have fewer heart failure hospitalizations, higher medication adherence rates, and better quality-of-life scores (Ferrante and others 2010). Similarly, Nesari and others (2010) found that nurse phone calls to Iranian diabetic subjects led to significant improvements in hemoglobin A1c and healthy lifestyle changes.

LMICs often have limited postal and landline capabilities. Landlines require physical wires or fiber optic cable networks, which are prohibitively expensive to build without significant capital investments, and mobile technology allows LMICs to catch up to high-income countries without significant investments.

Affordable and reliable communication channels can be leveraged to better manage chronic conditions. Automated SMS messages led to improved glycemic

control in Indians with prediabetes and diabetes (Ramachandran and others 2013; Shetty and others 2011), lower hemoglobin A1c in Iranian diabetics (Goodarzi and others 2012), and higher medication adherence rates in Malaysian ACS patients after hospital discharge (Khonsari and others 2014). All four studies included only participants with access to mobile phones with SMS-receiving capabilities.

Telemonitoring refers to remotely monitoring patients who are at different locations from the health provider. This field has grown dramatically since medical devices, such as blood pressure machines and glucometers, have become more affordable and capable of sending data to health providers over the Internet.

Piette and others (2012) studied the effect of automated phone calls and home blood pressure monitors in Hondurans and Mexicans with uncontrolled hypertension. While persons in the general intervention group did not show any improvement, those with low literacy had significantly lower blood pressure after the intervention. The Minerva Telecardio Project is researching the effect of electrocardiogram machines in remote towns in Brazil. These machines can record and send information to a cardiologist for interpretation. Andrade and others (2011) found that using these machines is more cost-effective than referring patients to another city.

Technological advances are not without inherent risks. Technology has made information vastly more accessible and shareable, but connectivity creates opportunities for abuse. Developed countries, such as the United States, have strict laws regarding health information that are enforced by government institutions and courts. Such legal precedents and infrastructure have not yet been set up in many LMICs.

M-health is not a replacement for patient-provider encounters but a facilitator of existing relationships. LMICs need to continue investing in their networks of medical providers and hospitals for m-health to be effective. Overall, m-health is a promising field of innovation for managing cardiovascular disease and will grow even more rapidly once smartphones with broadband capability become more prevalent in LMICs.

trial of hypertensive participants enrolled in a nurse-led clinic in Cameroon. Erhun, Agbani, and Bolaji (2005) evaluated the role of pharmacist-led clinics for patients with hypertension in Nigeria. Adeyemo and others (2013) randomized Nigerian participants with hypertension to clinic-based care with home visits or to clinic-based care only. Jafar and others (2009) conducted a cluster, randomized controlled trial of two interventions—home health education provided by health aides and training of general practitioners—in a population of Pakistani patients with hypertension. Regardless of the approach, intensified team-based care led to improved hypertension control.

Nesari and others (2010), the single study on diabetes, showed that having nurses call patients regularly to reinforce lifestyle changes and adjust medication doses led to a significant decrease in hemoglobin A1c. The intervention group increased adherence to lifestyle changes and glucose monitoring.

Guideline Implementation or Provider Education

Health care provider education and implementation of guidelines have the potential to standardize, improve, and sustain quality of care for cardiovascular and other conditions in LMICs. Studies of the impact of physician education and guideline dissemination yielded mixed results. Qureshi and others (2007) found that physician education through workshops and guideline dissemination led to significant improvements in patient care. Anchala and others (2015) revealed that providing physicians with a clinical decision support system for undertaking guideline-based hypertension management led to significant reductions in systolic blood pressure. However, Reutens and others (2012) and Steyn and others (2013) showed conflicting results and highlighted that guideline dissemination alone did not lead to actual implementation. Imposing guidelines without first gaining buy-in from providers may be a recipe for failure. Allocating time for education and feedback and strategically inserting guideline information into the flow of clinical practice may increase the chance that guidelines are actually implemented.

CONCLUSIONS

This chapter surveys the evidence on quality improvement in cardiovascular disease care at the system and patient-provider levels. An impressive amount of research on quality improvement has been carried out in LMICs—although not all approaches reviewed were consistently effective (figures 18.3 and 18.4). The innovative approaches taken by these programs demonstrate

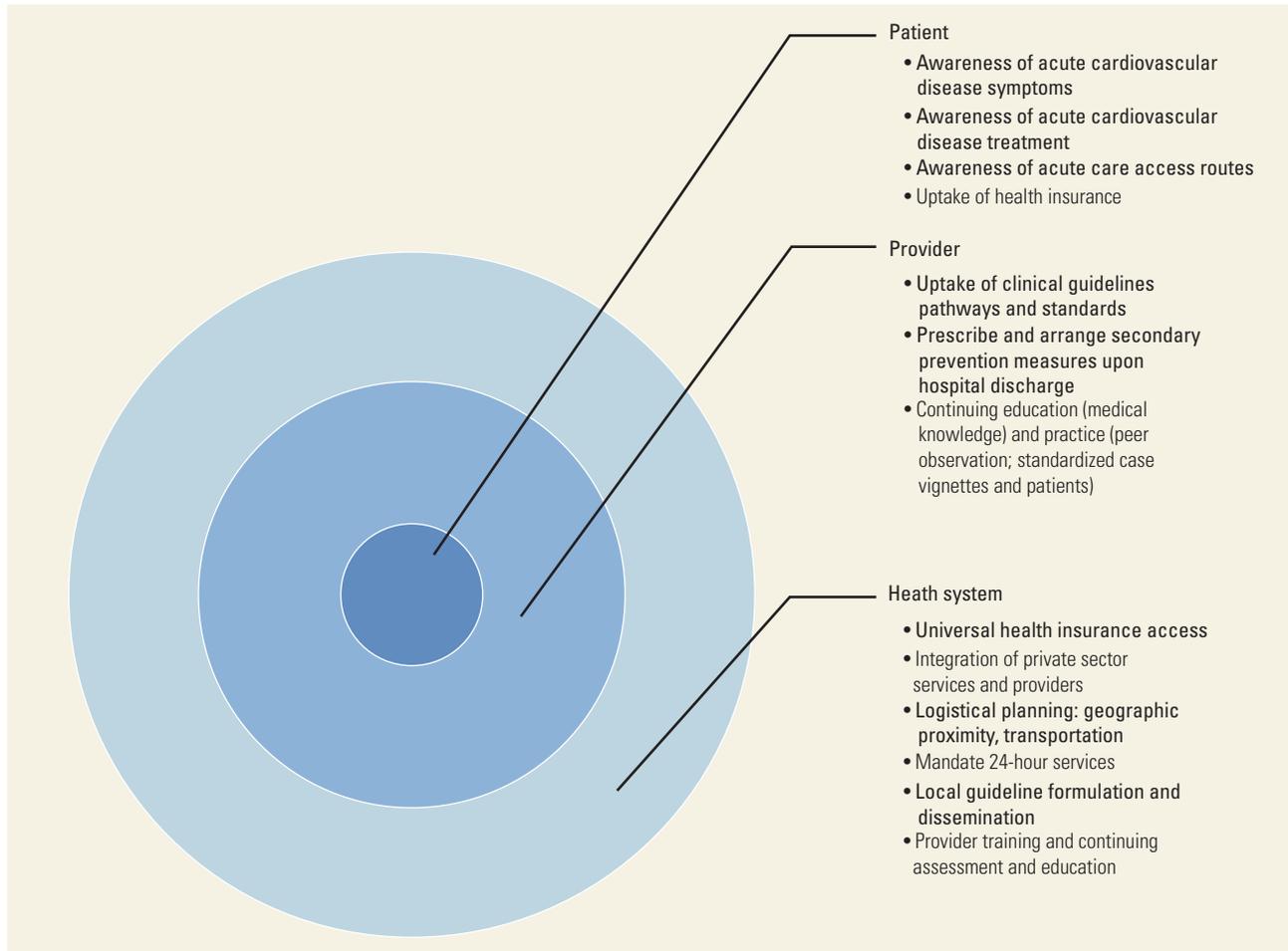
that it is not simply a matter of adapting HIC programs to LMICs: innovations to improve the quality of clinical care may originate precisely in low-resource environments. For example, the concept of shifting health care tasks to lay health workers originated in LMICs as a means to address the limited supply of medical doctors. As the AMPATH experience demonstrates (box 18.1), implementing a comprehensive approach to quality improvement, at both the system and patient-provider levels, is feasible in LMICs.

The majority of studies in this review focused on chronic cardiovascular disease and chronic risk factors such as hypertension and diabetes. At the system level, expanded health insurance coverage was found to improve the control of hypertension and diabetes. These powerful findings likely stem from improved access to care and financial protection from out-of-pocket health expenditures. Pharmaceutical supply regulation, drug price regulation, and essential medication designations are all potentially powerful system-level interventions, but their impact on cardiovascular disorders has yet to be studied.

At the patient-provider level, increased intensity of care—however delivered or by whom—was consistently found to improve chronic disease or risk factor outcomes. Intensification involved a team-based approach that included extra health care provider input, such as shifting tasks to pharmacists, dietitians, or nurses; phone counseling; smartphone-based reminders; or home visits. There were no head-to-head comparative effectiveness studies between these approaches, and multiple approaches often were combined (for example, implementing both task-shifting and patient education), so no one approach stands out as better than the others. Care intensification inevitably requires up-front investment, but this investment may be offset by improved downstream health outcomes for cardiovascular disease. A modeling study by Gaziano and others (2014) projected that, despite the added costs of hiring community health workers to manage hypertension in South Africa, increased intensity of care may offset this investment by averting expensive hospital admissions and chronic disease complications.

The studies reviewed for this chapter were often limited in ways that require cautious interpretation of their results. Because of the diversity of interventions and conditions, effect sizes could not be summarized in a meta-analysis. First, it is possible that the studies were published because of their positive results, and, because of the heterogeneity of interventions and targets, it was not possible to evaluate evidence of publication bias. Second, most studies were very short term (less than 12 months), and sustaining intervention effects may be

Figure 18.3 Examples of Acute-Phase Cardiovascular Disease Quality Improvement Interventions Identified in the *DCP3* Systematic Review



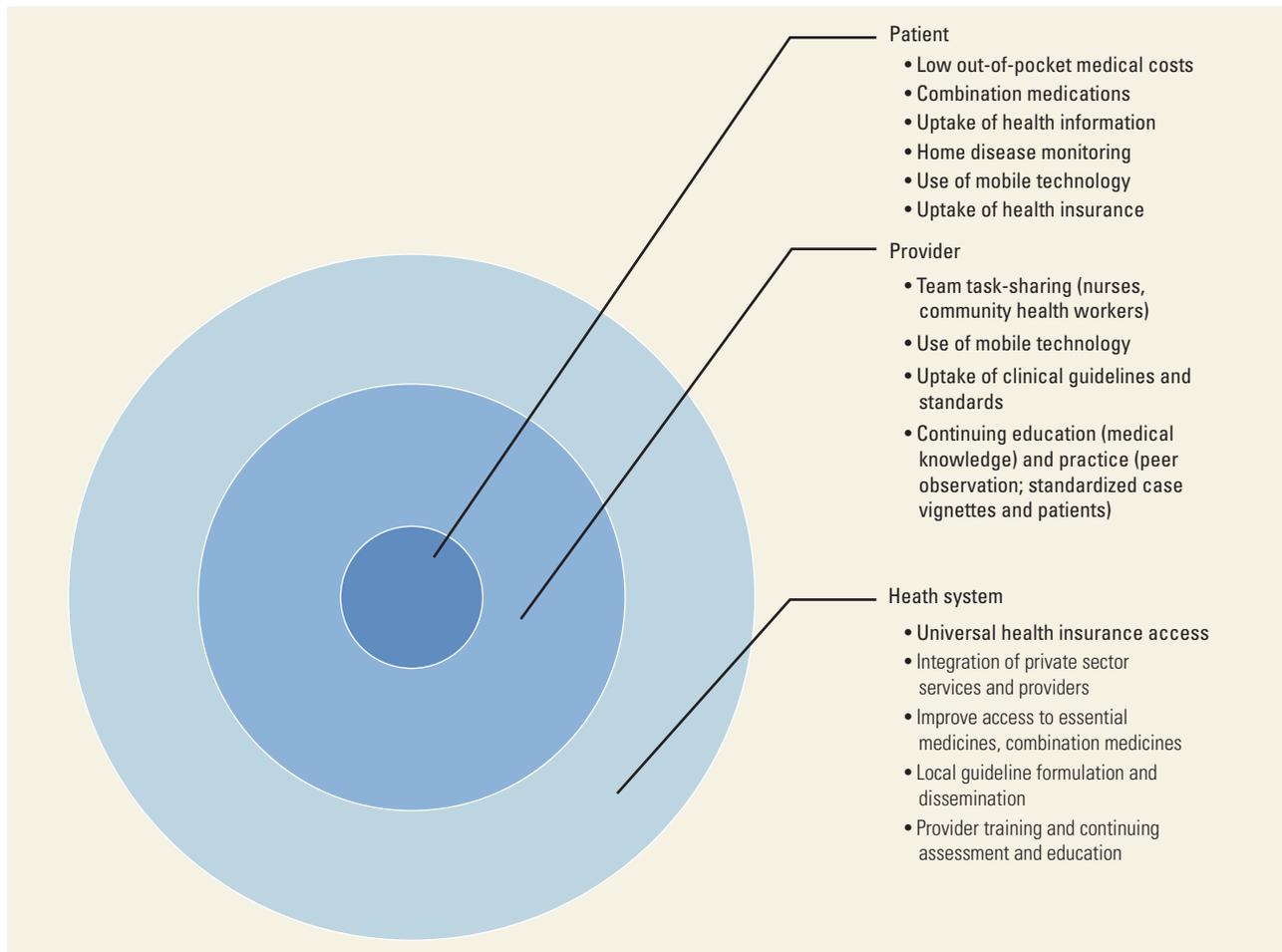
Note: *DCP3* = *Disease Control Priorities* (third edition). Types of interventions targeting three levels of acute-phase cardiovascular disease prevention and management. Bulleted items in bold type were supported by evidence from the review. Bulleted items not in bold type indicate that no supporting evidence was found in the review and these interventions are potential areas for further research.

difficult in real clinical settings. As in HICs, most investigators studied clinical process measures and did not report on hard clinical outcomes, which may lead to gaming the system (via an inappropriately strong focus on reaching surrogate targets to the neglect of measures that improve meaningful outcomes) and other unintended consequences when these interventions are introduced into routine practice.

Although all of the studies measured some change in the quality of care, and some reported on the number of provider contacts and specified the technology or medications used, none reported on the costs or cost-effectiveness of these interventions. When resources are limited, the call to improve or restructure existing services may be tempered by the perception that implementation will be costly and not worth the effort—or at least not as attractive as an alternative policy with more immediate returns on investment.

Cost and quality-of-life measurement and cost-effectiveness analyses can be important guides in assessing the net benefits of quality improvement programs in limited-resource contexts. Modeling studies can extend the results of short-term interventions and surrogate clinical measures by simulating a range of likely downstream disease outcomes. At the very least, future studies need to report on intervention inputs as measured by “units”—including the number of providers, contacts between patients and providers, medications, and education classes and teachers—so that clinics and health organizations can “cost out” interventions when seeking the best ones for their settings. Collecting data elements common to implementation research, such as acceptability, sustainability, local context, and affordability, will help ensure that both positive and negative studies will guide implementation and future research.

Figure 18.4 Examples of Chronic-Phase Cardiovascular Disease Quality Improvement Interventions Identified in the *DCP3* Systematic Review



Note: *DCP3* = *Disease Control Priorities* (third edition). Types of interventions targeting three levels of chronic-phase cardiovascular disease prevention and management. Bulleted items in bold are supported by evidence from the review. Bulleted items not in bold type indicate that no supporting evidence was found in the review and these interventions are potential areas for further research.

The majority of cardiovascular disease patients now live in LMICs, and demographic trends virtually guarantee that the number and proportion will grow in coming decades. To ensure that each of these patients receives long-term treatment and control, it is essential to draw on promising research on clinical quality improvement and make the most of the resources directly at hand.

ANNEX

The annex to this chapter is as follows. It is available at <http://www.dcp-3.org/CVRD>.

- Annex 18A. Systematic Review Methods and Complete Search Results

NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046 to US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126 to US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

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