ORIGINAL RESEARCH gSCIENCE

Availability, Use, and Barriers to Cardiac Rehabilitation in LMIC



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Background: Cardiac rehabilitation (CR) is a cornerstone of secondary prevention of ischemic heart disease. It is critically important in low- and middle-income countries (LMIC), where the burden of ischemic heart disease is substantial and growing. However, the availability and utilization of CR in LMIC is not systematically known.

Objectives: This study sought to characterize the availability, use, and barriers to the use of CR.

Methods: Electronic databases (Cochrane Library, EMBASE, PubMed, Web of Science) were searched from January 1, 1980 to May 31, 2013 for articles on CR in LMIC. Citations on availability, use, and/or barriers to CR were screened for inclusion by title, abstract, and full text. Data were summarized by region or country to determine the characteristics of CR in LMIC and gaps in the peer-reviewed biomedical publications.

Results: Our search yielded a total of 5,805 citations, of which 34 satisfied full inclusion and exclusion criteria. The total number of CR programs available ranged from 1 in Algeria and Paraguay to 51 in Serbia. Referral rates for CR ranged from 5.0% in Mexico to 90.3% in Lithuania. Attendance rates ranged from 31.7% in Bulgaria to 95.6% in Lithuania, and CR attendance was correlated with higher educational background. The most commonly cited barrier to CR in LMIC was lack of physician referral.

Conclusions: Our results illustrate that the published reports reflects heterogeneity of CR availability and use in LMIC. Overall, CR is insufficiently available and underutilized. Further characterization of CR in LMIC, especially in Asia and Africa, is necessary to develop targeted strategies to improve availability and utilization. Patient, physician, and systems factors must be addressed to overcome barriers to participation in CR in LMIC.

Cardiovascular disease (CVD) is the leading cause of death worldwide, and >80% of CVD deaths occur in low-and middle income countries (LMIC) [1,2]. In 2010, 62.5 million new cases of CVD were reported, of which 24.2 million were attributed to ischemic heart disease [3]. Age-standardized ischemic heart disease mortality is substantially higher in LMIC [1]. In addition to the global health burden, CVD will exert a significant economic burden, on the order of approximately \$15 trillion over the next 20 years [3].

Given the burden of CVD globally, and in particular in LMIC, secondary prevention strategies are vitally important to stemming this growing epidemic. Over the last several decades, cardiac rehabilitation (CR) has become established as a cornerstone for a comprehensive secondary prevention strategy [4]. CR is a multidisciplinary program of supervised exercise, education, and behavior modification designed to return the patient to optimal physical, emotional, psychosocial, and vocational function. CR for patients experiencing myocardial infarction (MI), acute coronary syndrome, coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), chronic stable

angina, or heart failure is a Class I recommendation from the European Society of Cardiology, American Heart Association, and American College of Cardiology [5,6].

In high-income countries, CR has been shown to reduce mortality by 25%, reduce MI by 17%, decrease recurrent hospitalizations, as well as reduce health care expenditures [5,7,8]. In a recent Cochrane meta-analysis of exercise-based CR, it was shown to reduce pooled cardiovascular mortality from 10.4% to 7.6%, and to reduce hospital admission from 30.7% to 26.1% [9]. CR is associated with improved outcomes in LMIC as well [10]. Despite strong recommendations for CR, CR services are underutilized even in high-income countries [11,12]. In LMIC, the availability and use of CR programs is not systematically known. The purpose of this study, therefore, is to perform a systematic review of peer-reviewed publications on CR in LMIC in order to characterize the availability, use, and barriers to use of CR.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and The authors report no relationships that could be construed as a conflict of interest.

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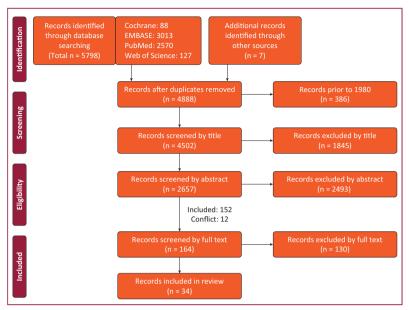


FIGURE 1. Flow diagram indicating the number of articles at each stage of the systematic review.

Meta-Analyses. It is registered (#CRD42014010449) on PROSPERO, an international prospective register of systematic reviews.

Electronic databases (Cochrane Library, EMBASE, PubMed, Web of Science) were searched for articles on CR in LMIC published from January 1, 1980, to May 31, 2013, correlating with the formalization of CR programs in the 1980s [4]. LMIC were identified as defined by the World Bank in 2013 [13]. The detailed search strategy for PubMed is given in Online Appendix 1, and similar search strategies were used for the other databases. Articles were screened in 3 sequential phases: 1) by title by 1 reviewer (L.R.); 2) by abstract by 2 reviewers (L.R., R.V.), with nonresolvable disagreements between the 2 reviewers included for the next phase of screening; and 3) by full text by 2 reviewers (L.R., R.V.). There were no disagreements by the final phase of screening. Additional potential references were identified by review of reference lists of the included articles and were subject to the same screening process. Foreign language articles that were included for full text review were summarized in English by translators (see Acknowledgments) and were also reviewed by 2 reviewers (L.R., R.V.).

The components of CR as outlined by the American Heart Association include patient assessment, nutritional counseling, weight management, blood pressure management, lipid management, diabetes management, tobacco cessation, psychosocial management, physical activity counseling, and exercise training. Articles were included in the review if they described ≥ 1 component of CR, in ≥ 1 category of patients for which CR is indicated [6], and if they reported on ≥ 1 of the following: availability; use; or

barriers to CR in ≥ 1 LMIC. Articles of any study design, systematic reviews, meta-analyses, nonsystematic reviews, and editorials were all eligible for inclusion. Articles of any language were included. Articles and abstracts that were published or in press were included, and authors of 2 studies were contacted for more detailed data than had been originally published (see Acknowledgments).

Qualitative and quantitative data were extracted and organized by region or country. Due to heterogeneity of the data, meta-analysis was not conducted. Descriptive statistics related to availability, use, and barriers were calculated when possible. When only qualitative information was available, those data were summarized.

Availability of CR

Data on the number of centers of CR by country were standardized by total population and number of deaths due to CVD as of 2012 [14]. Ideally, standardization of the number of CR programs by the number of patients indicated for CR would provide the optimal measure of CR density. However, those data are not available, so the number of CVD deaths was used as a surrogate marker to estimate patients who would be eligible for CR. Data were extracted regarding the diagnoses accepted by CR centers, the services offered, and the type of health care personnel available, as per the core components of CR as outlined by the American Association of Cardiovascular and Pulmonary Rehabilitation [15].

Use of CR

The use of CR was defined in 2 ways: 1) referral rates to CR programs by health care professionals; and 2) attendance rates at CR programs by patients. All demographic data on patients who attended CR programs were extracted when available.

Barriers to CR

The barriers to CR were categorized broadly into physician, patient, and systems factors. Qualitative and quantitative information on perspectives from patients and health care providers were extracted.

RESULTS

Our search yielded a total of 5,805 citations, of which 34 satisfied full inclusion and exclusion criteria. Figure 1 summarizes the number of articles involved at each stage of the systematic review process. Online Appendix 2 summarizes the reasons for exclusion of articles at the abstract and full-text levels of screening. At the full-text screening level, the majority of articles were excluded due to a lack of information on availability, use, or barriers to CR. A total of 34 articles were included in this review, with information on 31 LMIC—2 in Africa, 7 in Asia, 7 in Europe, and 15 in Latin America/Caribbean, as

summarized in Table 1, with references provided in Online Appendix 3.

Availability of CR

The total number of CR centers in LMIC was reported from 1986 to 2013 and varied considerably across countries (Figure 2, see Online Appendix 3 for exact results). The lowest density of CR programs was reported in Algeria, where only 1 CR program was functioning in 2008. The highest absolute number of CR centers was 51 and was reported in Serbia. The highest density of CR centers was reported in Lithuania, with 348 CR centers per 100,000 annual CVD deaths, and the lowest density was found in Algeria, with 1 CR center per 100,000 annual CVD deaths. In addition to this quantitative information, qualitative information on CR availability was reported in editorials, review articles, and surveys of health professionals (references [7-9] cited in Online Appendix 3). Overall, India and China were reported to have low availability of dedicated CR programs. In Indonesia, the first CR program began in 1978, and subsequently expanded to many cities (exact number not specified), with CR being provided by both community-based organizations as well as the National Heart Organization.

The indications accepted for CR, the CR services offered, and the type of personnel available varied significantly across countries (Figure 3, Online Appendix 4). The most commonly accepted indications for CR were following MI, PCI, or CABG. Exercise training and physical activity counseling were offered in the vast majority of programs. Overall, a broader array of services was offered in Latin American and Caribbean countries than in Africa, Asia, and Europe. The personnel involved in CR were heterogeneous across countries; however, the majority of programs involved a cardiologist.

Use of CR

Referral rates to CR were available for 6 European countries and for Mexico from 2013 and 2009, respectively. There was a high degree of variability in CR referral rates, from 5% in Mexico to 90% in Lithuania (Figure 4). Most countries had a referral rate <40% (references [16,31] cited in Online Appendix 3).

Those countries reporting CR attendance, defined by the number of CR attendees as a fraction of number referred to CR, are summarized in Figure 5 (full results for CR attendance rates are given in Online Appendix 5). Overall, CR attendance was reported in studies published from 1984 to 2012; among patients referred for CR, CR attendance rates ranged from 32% in Bulgaria to 96% in Lithuania. Among patients eligible for CR, CR attendance rates were 40% in Belarus, 90% in Lithuania, and 10% in Romania. In Johannesburg, a 50% completion rate of CR was observed at a single center between 1986 and 1990. In Russia, the rate of CR attendance among patients who were referred was 12% in 1984 and was subsequently

reported as 42% in 2011. In Iran, the rate of CR attendance among all patients with PCI and CABG was 4%; however, there was 87% attendance among patients who were referred to CR. Additionally, the first and only Algerian CR center as of 2008 reported a population of 158 patients enrolled per year (reference [1] cited in Online Appendix 3).

Information regarding the characteristics of patients referred for CR was available from Brazil, Iran, Pakistan, and Romania and is summarized in Table 2. In all studies, males made up >65% of patients who were referred for CR. In Iran, Pakistan, and Romania, those who did not attend CR were more likely to be male, whereas in Brazil, those who did not attend CR were more likely to be female. CR participants had higher levels of education; their employment status was variable. In Iran and Romania, a greater proportion of those who did not attend CR were smokers, whereas in Pakistan, a greater proportion of CR attendees were smokers. The indications for CR were variable.

Barriers to CR

Barriers to CR were reported in surveys of CR programs, and, in 1 article, by patients who had dropped out of CR programs (Table 3). The most commonly reported barrier to CR was the lack of physician referral to CR, cited by 45% to 93% of CR programs and health professionals. Patient-related factors cited were affordability, particularly due to lack of insurance coverage; transportation difficulties, primarily driven by long distances to CR centers; an unwillingness to attend CR; and competing priorities on patients' time. The most frequently reported systems factor was a lack of personnel and resources.

DISCUSSION

In this systematic review, we found substantial geographic variability in the availability, use, and barriers to CR in LMIC. In general, the availability of CR was low relative to the burden of CVD in LMIC. Referral rates for CR were also variable and were <40% in a majority of countries. Attendance rates varied across geography and were also suboptimal. Among those referred for CR, higher attendance was generally correlated with certain patient characteristics—higher educational background and nonsmoking status. The most commonly cited barrier to CR in LMIC was lack of physician referral.

The overall goals for rehabilitative care among cardiac patients in LMIC were laid out by the World Health Organization Expert Committee on Rehabilitation after CVD in 1993. These included availability of CR to all patients with CVD, awareness of health care providers and the public for the need for CR, patient and provider education on CR, and integration of CR into the health system, with the type of program matched to the needs of the community [16]. Progress toward these goals has proven to be suboptimal in LMIC, as evidenced by the findings of this

TABLE 1. Summary information of articles included in systematic review

Reference (Cited in Online							
Appendix 3)	Region	Country	Year	Availability	Use	Barriers	Type of Article
1]	Africa	Algeria	2008	Х	х		Single institution; prospective survey or patients
2]	Africa	Johannesburg, South Africa	1991	q	q		Single institution; prospective survey of patients
3]	Africa	Johannesburg, South Africa	1992		x		Single institution; prospective survey of patients
4]	Asia	China	1995	q	q		Survey of health professionals
5]	Asia	China, Philippines, Thailand	2001	q		х	Review
6]	Asia	China	2007			q	Review
7]	Asia	Xi'an, China	2009	q		q	Survey of health professionals
8]	Asia	India	2007	q			Review
9]	Asia	Indonesia	2009	q		q	Review
10]	Asia	Isfahan, Iran	2007		x		Single institution; prospective survey of patients
11]	Asia	Tehran, Iran	2009		х		Single institution; prospective survey of patients
12]	Asia	Iran	2011			Х	Survey of health professionals
13]	Asia	Tehran, Iran	2011	q	х	x	Single institution; cross-sectional survey of patients
14]	Asia	Karachi, Pakistan	2012		х		Single-institution; cross-sectional stud of patients
15]	Asia	Thailand	2001	Х			Review
16]	Europe	Bulgaria, Latvia, Lithuania, Romania, Russia, Turkey	2011		x		Multi-institution; cross-sectional study of patients
17]	Europe	Lithuania, Romania, Russia, Serbia	2010	х	х		Survey of CR centers
18]	Europe	Moscow, Russia	1984	q	х		Single institution
19]	Europe	Russia	1988	q	q		Review
20]	Europe	Timisoara, Romania	2010	,	x		Single institution; prospective survey of patients
21]	Europe	Romania	2011		х		Multi-institution; retrospective study of patients
22]	Europe	Turkey	2000			q	Review
23]	Europe	Turkey	2011		х	·	Multi-institution; cross-sectional study of patients
24]	Latin America/ Caribbean	Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, Mexico, Peru, Puerto Rico,* Venezuela	2009	X	X	X	Survey of CR centers
[25]	Latin America/ Caribbean	Argentina, Brazil, Colombia, Chile, Ecuador, Paraguay, Peru, Uruguay, Venezuela	2013	х	x	x	Survey of CR centers
26]	Latin America/ Caribbean	Brazil	2013		x		Multi-institution; cross-sectional study of patients
27]	Latin America/ Caribbean	Chile	2012	х	X	x	Survey of CR centers
28]	Latin America/ Caribbean	Colombia	1999	х	X	q	Survey of CR centers
29]	Latin America/ Caribbean	Colombia	2009	х	х		Survey of CR centers
30]	Latin America/ Caribbean	Colombia	2010	х	х	х	Survey of CR centers

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TABLE 1. Continued

Appendix 3)	Region	Country	Year	Availability	Use	Barriers	Type of Article
[31]	Latin America/ Caribbean	Mexico	2009	х	х	х	Survey of CR centers
[32]	Latin America/ Caribbean	Uruguay	2011	X	х	x	Survey of CR centers
[33]	Latin America/ Caribbean	Venezuela	2010		x	q	Single institution
[34]	Latin America/ Caribbean	Brazil, Venezuela	1986	х	х	q	Survey of CR centers

systematic review, including the low density of CR programs in the majority of LMIC, low referral rates, and low

rates of participation by patients in CR.

*Data from Puerto Rico could not be separated out.

A recent review of the global availability of CR reported CR availability in 68% of high-income countries, 28% of middle-income countries, and 8% of low-income countries [17]. Based on 2003 estimates [18], in the United States, there were 721 CR programs per 100,000 CVD deaths, which is significantly higher than the highest estimate in LMIC from our study, found in Lithuania. Overall, we found significant geographic variability in the amount of published data describing the availability of CR services in LMIC. The most comprehensive data are available from Latin America/Caribbean and Europe, whereas updated publications are lacking in Asia and Africa.

Use of CR worldwide, even in high-income countries, is suboptimal; both CR referral and participation in CR can be improved. In the United States, referral to CR following MI was established as a hospital performance measure in 2007; however, CR referral remains suboptimal [19,20]. Data from Medicare beneficiaries in the United States show that only 13.9% of MI survivors and 31.0% of patients following CABG participate in CR [21]. A 2012 Canadian study of ischemic heart disease patients referred for CR found a 49.3% completion rate of CR [22].

Our data from LMIC are generally consistent with those figures from high-income countries. For example, in Iran, the rate of CR attendance among all patients with PCI and CABG was only 3.6%, despite nearly 86.5% attendance among patients who were referred to CR, likely reflecting inadequate referral to CR [23,24]. Most other

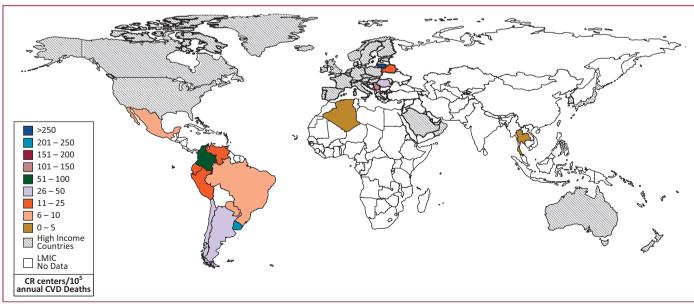


FIGURE 2. Cardiac rehabilitation availability in low- and middle-income countries (LMIC). CR, cardiac rehabilitation; CVD, cardiovascular disease.



FIGURE 3. Cardiac rehabilitation in low- and middle-income countries: accepted indications. CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention.

LMIC in our study had low referral and attendance rates, with notable exceptions such as Colombia, Latvia, and Lithuania, which were characterized by high referral and participation rates. Literature on completion rates of CR in LMIC were lacking in the retrieved articles, and consistency of CR attendance needs further evaluation in LMIC; a recent review indicates that CR dropout rates have been reported at over 80% in Iran [25].

Part of the heterogeneity in CR utilization may be explained by health systems in each country. As with in high-income countries, health care utilization is linked closely to cost and payment structures. CR referral rates in the United States are highest among patients with private insurance carriers [19]. In Lithuania, where CR availability and utilization were exceptionally high, health care is a state-funded industry with referral to CR embedded into

care metrics [26]. In contrast, many parts of South Asia, Southeast Asia, and Africa rely on out-of-pocket payment systems. In addition to payment systems for CR, access to cardiac interventions leading to CR referral are also heterogeneous among LMIC, which would also lead to variability in CR availability and use as a secondary prevention strategy [2].

Efforts to improve on the suboptimal availability and use of CR in LMIC require a careful analysis of the barriers to implementation and utilization of this service, particularly given the resource scarcity to make changes in health care delivery. Barriers to CR in high-income countries include lack of referral, low knowledge and insight into services, beliefs about heart disease, negative views of the health care system, financial and work constraints, long distance to services, hours of operation, lack of family

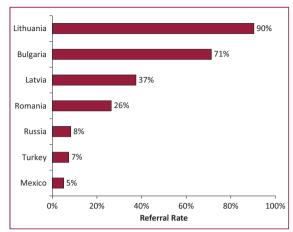


FIGURE 4. Rates of referral to cardiac rehabilitation (references [16,31] cited in Online Appendix 3).

support, and medical comorbidities. Female sex, older age, lower socioeconomic status, and low educational attainment have been correlated with poor CR attendance [11]. Whereas our results were generally consistent with barriers reported from high-income countries, we found additional patient-related barriers to CR specific to LMIC, including lack of resources and poor affordability of CR programs. Conversely, medical comorbidities were not reported as a barrier to CR in LMIC in our review.

In the United States, solutions to overcome barriers to CR have been proposed; these target patient-centeredness of CR programs, systematization of CR referral, improved accessibility, and data-driven performance improvement [27,28]. In LMIC, the solutions to improve utilization of CR must be tailored to the unique barriers faced by resource scarcity, and novel strategies for the

implementation of secondary prevention programs may be necessary. A recent consensus statement on CR delivery in low-resource settings outlined the essential components of CR, and low cost alternatives to CR delivery methods practiced in high-income countries. These include improved risk stratification of patients to enable decreased supervision of patients at low risk for ischemic/arrhythmic events and the use of low-cost exercises and equipment [29].

Based on the barriers to CR in LMIC identified in this review, we have proposed solutions for this setting in Figure 6, based on several studies evaluating novel CR strategies. A recent Cochrane systematic review and metaanalysis, which included studies from Iran and Turkey, concluded that home-based CR was as effective as centerbased CR [30]. Subsequently, another study of homebased CR in Xi'an, China, found that home-based CR, in comparison with usual care (i.e., no CR), improved healthrelated quality of life [31]. Indeed, the use of innovative non-center-based CR in LMIC may improve adherence and overall outcomes after cardiovascular events. In addition, in India, yoga-based CR has been shown to improve left ventricular ejection fraction, blood glucose control, and body mass index, in comparison with standard CR [32]. Mobile technology is emerging as a tool for increasing patient-centeredness of CR and addressing the issue of distances and time [33]. A virtual world-based CR program with features of social interactivity and active learning is currently being evaluated for feasibility and effectiveness; this would additionally address issues of motivation [34].

Completion of CR programs has been shown to be associated with a lower risk of death, lower risk of MI, all-cause hospitalization, and cardiac hospitalization [22]. In LMIC, CR has also been demonstrated to improve CVD risk factors [25]. In high-income countries, CR has been

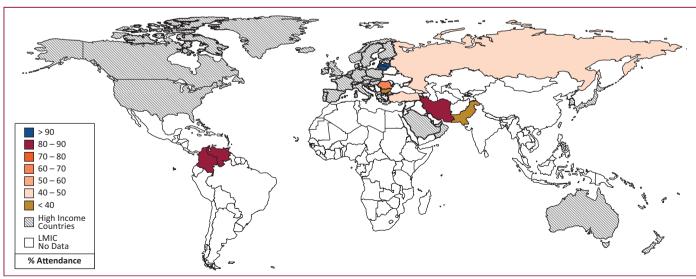


FIGURE 5. Cardiac rehabilitation program attendance rates in low- and middle-income countries (LMIC) among patients who were referred.

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TABLE 2. Characteristics of patients referred for cardiac rehabilitation

Location	Isfahan,	Iran	Tehran	, Iran	Tehran,	Iran	Karachi,	Pakistan	Timisoara, I	Romania*	В	razil*	
Year	200	7	200	9	201	1	20	12	201	10	2	2013	
Reference (Cited in Online Appendix 3)	[10	1	[11	1	[13]	1	[1	41	[20	n1		[26]	
Appendix 5)					[13]				[20	<u> </u>			
	Completed CR	Dropped Out of CR	Completed CR	Dropped Out of CR	Completed CR	Dropped Out of CR	Attended CR	Did Not Attend CR	Attended CR	Did Not Attend CR	Attended CR	Did Not Attend CR	
Patients, n (%) Age, yrs, mean \pm SD	499 (44.8) 56.2 ± 0.4		361 (18.2) 57.8 ± 10.4	1,625 (81.8) 56.8 ± 10.7	40 (31.3) 54.2 ± 11.1	. ,	151 (36.3) 56.1 ± 10.3	265 (63.7) 57.2 ± 10.7	81 (58.7)	57 (41.3)	, ,	98 (41.4) 64.09 ± 14.4	
Male Employed	72.3 21.4	80.9 26.4	71.5	73.0	79.6 74.6	84.1 70.5	78.1 58.9	81.9 72.1	75.0	89.0	100.0	65.8	
Education level Less than secondary											24.5	62.2	
Secondary Post-secondary	30.0 11.7	32.3 11.7	70.1	53.7	71.0	49.8					15.1 60.4	15.3 22.4	
Risk factor profile	11.7	11.7			71.0	45.0					00.4	22.7	
Diabetes Hyperlipidemia Hypertension Obesity	22.5 52.1 32.4 40.2	25.1 49.8 29.8 40.8	23.3 51.8 41.3	23.6 47.1 36.4			56.3 57.0 74.8	40.8 49.1 62.3	20.0 53.0 68.0 31.3	19.3 59.7 68.4 35.1	29.5 26.6 43.2 5.8	21.4 28.6 56.1 2.0	
Smoking Left ventricular	12.9 52 ± 1	25.5 51 ± 1	21.6 52 ± 10	23.9 51 ± 11	45 ± 13	35 ± 10	41.7	36.6	4.9	15.8	5.6	2.0	
ejection fraction, mear \pm SD	1	31 ± 1	32 ± 10	31 ± 11	45 ± 15	33 ± 10							
Indication for cardiac rehabilitation													
MI PCI	27.8 9.3	38.0 8.5			7.5 25.0	1.1 45.5	9.9 20.5	25.7 44.9	1.0 49.0	7.0 61.0			
CABG	51.8	40.5			45.0	44.3	69.5	29.4	48.0	30.0			
Other	11.1	13.0			22.2	29.6							

Values are % unless otherwise indicated. Values in **bold and italic** represent statistically significant differences, as reported by study authors. Blank cells represent unavailable data. CABG, coronary artery bypass graft; CR, cardiac rehabilitation; MI, myocardial infarction; PCI, percutaneous coronary intervention.

^{*}Statistical significance not reported.

TABLE 3. Barriers to cardiac rehabilitation

	Reference (Cited in														
	Online Appendix 3)	[7]	[9]	[12]	[13]	[5]	[5]	[22]	[24]	[25]	[34]	[27]	[30]	[31]	[32]
	Location	China	Indonesia		Tehran,	Philippines			South/ Central	South/ Central America	Brazil	Chile	Colombia	Mexico	Uruguay
	Year	2009	2009	2011	2011	2001	2001	2000	2009	2013	1986	2012	2010	2009	2011
		Health Care	÷		Patients: CR			. +	CR	CR Program	CR	CR	CR	CR	CR
		Professionals*		Cardiologists	Dropouts	Editorial*	NA		Programs		Programs [†]				
Physician factors	Lack of referral		Υ	91%				Υ	45%	70%		56%	66%	93%	83%
	Lack of CR as part of cardiology training	Υ													
Patient factor	Transportation		Υ	5%	70%		88%		15%	3%		28%	5%		17%
	Affordability	Υ	Υ						9%		Υ				17%
	Time		Υ				13%				Υ				
	Motivation			3%	7%			Y			Υ				
	Lack of awareness							Υ							
System factor	Lack of personnel and resources	Υ		7%	21%	Υ		Υ	21%	19%			25%	64%	17%
	Rehabilitation is not profitable enough								2%						

Blank cells represent unavailable data.

CR, cardiac rehabilitation; Y = yes.

^{*}Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, Mexico, Peru, Puerto Rico, Venezuela.

 $^{^\}dagger$ Argentina, Brazil, Chile, Colombia, Ecuador, Paraguay, Peru, Uruguay, Venezuela.

[‡]Quantitative data not available.

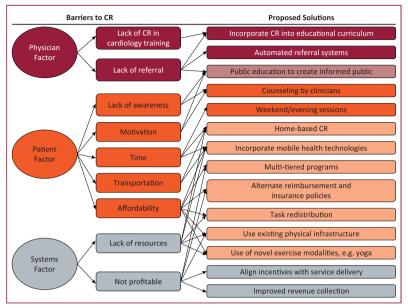


FIGURE 6. Proposed solutions to barriers to cardiac rehabilitation (CR) in lowand middle-income countries. Physician, patient, and systems factors are illustrated in red, orange, and gray, respectively. Proposed solutions are similarly color-coded; additionally, solutions overlapping physician and patient factors, and patient and systems factors are illustrated in light red and light orange, respectively.

demonstrated to be cost-effective. However, the data for cost-effectiveness from LMIC are limited; studies from heart failure patients in Brazil and Columbia estimate CR to be cost-effective [35]. Cost-effectiveness and affordability analyses of CR programs, and associated efforts to develop novel CR delivery methods in LMIC, must take into account the cost savings from preventing hospitalization, as well as increasing productivity. Indeed, novel CR delivery methods may likely be a cost-effective and potentially affordable approach to improving access to CR in LMIC.

Study limitations

As a systematic review of the peer-reviewed published reports, publication bias is the foremost limitation of our results. This is most likely to affect our results on CR availability; it is likely that more CR programs exist in LMIC than we have reported, and our results do not comprise a global index of CR programs. However, our goal was to assess the status of the published data on this topic, and we would argue that critical assessment of CR programs, including summary of peer-reviewed publications, is a necessary step toward dialogue, expansion, and improvement of the available resources.

A second limitation is that we chose to include articles since 1980, and the oldest article meeting inclusion criteria was from 1984. Given the rapid pace of health care innovation and overall health system development, we

recognize that these older data may not be relevant to the present-day situation in LMIC. However, the majority of included studies were published since 2000; therefore, we feel that our results generally represent the current status of the published data.

Finally, in this systematic review, there were varied definitions of the patient population, outcomes, and comparator groups in the data, making it unsuitable for aggregation in the form of a meta-analysis. Additionally, many of the data points collected did not include measures of imprecision, for which reason we were not able to report on this.

CONCLUSIONS

The available published data reveals a wide variability in the availability of CR in LMIC. There is overall insufficient availability of CR services in LMIC to meet the growing burden of CVD in these areas. Where CR is available, utilization rates of the services are suboptimal. Whereas many barriers to CR in LMIC are also present in highincome countries, there are some notable differences reflecting lower resources, health system deficiencies, and affordability. This study also illustrates the geographic disparity of publications on the availability, use, and barriers to CR in LMIC. Whereas this issue has been studied extensively in Europe and South America, there is a substantial deficiency in published data from Asia and Africa. Accurate enumeration of CR programs is the first step to identifying key areas for policy interventions and program development; thus, there is a significant need for systematic data gathering in these regions.

Interventions to quickly increase implementation and use of this cornerstone of secondary CVD prevention must be targeted to fit the needs of local populations and may need to deviate from the accepted practices in high-income countries. It is imperative on the global health community to incorporate novel CR delivery models into efforts directed at secondary prevention of CVD, in line with the World Health Organization's target of reducing mortality from noncommunicable diseases by 25% [36].

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APPENDIX

ONLINE APPENDIX 1. PubMed search strategy

Search Terms	Search Details	Results
(Cardiac Surgical Procedures/rehabilitation [MeSH] OR cardiac surgical procedures AND rehabilitation)) OR Thoracic Surgery/ rehabilitation[MeSH] OR (thoracic surgery AND rehabilitation) OR ((heart surgery OR cardiothoracic surgery) AND rehabilitation)	("Cardiac Surgical Procedures/rehabilitation" [Mesh] OR (("cardiac surgical procedures" [MeSh Terms] OR ("cardiac" [All Fields] AND "surgical" [All Fields] AND "procedures" [All Fields]) OR "cardiac surgical procedures" [All Fields]) AND ("rehabilitation" [Subheading] OR "rehabilitation" [All Fields] OR "rehabilitation" [MeSh Terms]))) OR "Thoracic Surgery/ rehabilitation" [Mesh] OR (("thoracic surgical procedures" [MeSh Terms] OR ("thoracic" [All Fields] AND "surgical" [All Fields] AND "procedures" [All Fields]) OR "thoracic" [All Fields]) OR "thoracic surgical procedures" [All Fields] OR ("thoracic" [All Fields]) OR "thoracic surgery" [All Fields]) OR "thoracic surgery" [MeSh Terms] OR ("thoracic" [All Fields]) OR "rehabilitation" [MeSh Terms])) OR ((("thoracic surgery" [MeSh Terms]) OR ("thoracic" [All Fields])) OR "surgery" [All Fields]) OR "thoracic surgery" [All Fields] OR ("heart" [All Fields]) AND "surgery" [All Fields]) OR "heart surgery" [All Fields] OR "cardiac surgical procedures" [MeSh Terms] OR ("cardiac" [All Fields]) OR "cardiac surgical" [All Fields] AND "procedures" [All Fields]) OR "cardiac surgical procedures" [All Fields] AND "surgery" [All Fields]) OR "cardiac surgical procedures" [All Fields] OR "surgery" [All Fields]) OR "surgery" [All Fields]) OR "surgery" [All Fields] OR "surgery" [All Fields]) OR "surgery" [All Fields] OR "surgery" [All Fields]) OR "surgery" [All Fields] O	6,32
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	"vietnam"[All Fields]) OR ("middle east"[MeSH Terms] OR ("middle"[All Fields] AND "east"[All Fields]) OR "middle east"[All Fields] OR ("west"[All Fields] AND "bank"[All Fields]) OR "west bank"[All Fields]) OR ("yemen"[MeSH Terms] OR "yemen"[All Fields]) OR ("zambia"[MeSH Terms] OR "zambia"[All Fields]) OR ("zimbabwe"[MeSH Terms] OR	
central asia OR east asia OR southeast asia OR eastern europe OR southeastern europe OR middle east OR africa OR north africa OR sub- saharan africa OR pacific OR latin america OR south america OR central america OR caribbean	"zimbabwe"[All Fields]) ("asia, central"[MeSH Terms] OR ("asia"[All Fields] AND "central"[All Fields]) OR "central asia"[All Fields] OR ("central"[All Fields] AND "asia"[All Fields])) OR ("far east"[MeSH Terms] OR ("far"[All Fields] AND "east"[All Fields]) OR "far east"[All Fields] OR ("east"[All Fields] AND "asia"[All Fields]) OR "east asia"[All Fields]) OR ("asia, southeastern"[MeSH Terms]	939,42

	Search Terms	Search Details	Results
		Fields] OR ("eastern"[All Fields] AND "europe"[All Fields])) OR ("Southeast	
		Eur"[Journal] OR ("southeastern"[All Fields] AND "europe"[All Fields]) OR	
		"southeastern europe"[All Fields]) OR ("middle east"[MeSH Terms] OR	
		("middle"[All Fields] AND "east"[All Fields]) OR "middle east"[All Fields])	
		OR ("africa"[MeSH Terms] OR "africa"[All Fields]) OR ("africa,	
		northern"[MeSH Terms] OR ("africa"[All Fields] AND "northern"[All Fields])	
		OR "northern africa"[All Fields] OR ("north"[All Fields] AND "africa"[All	
		Fields]) OR "north africa"[All Fields]) OR ("africa south of the	
		sahara"[MeSH Terms] OR ("africa"[All Fields] AND "south"[All Fields] AND	
		"sahara"[All Fields]) OR "africa south of the sahara"[All Fields] OR	
		("sub"[All Fields] AND "saharan"[All Fields] AND "africa"[All Fields]) OR	
		"sub saharan africa"[All Fields]) OR pacific[All Fields] OR ("latin	
		america"[MeSH Terms] OR ("latin"[All Fields] AND "america"[All Fields])	
		OR "latin america" [All Fields]) OR ("south america" [MeSH Terms] OR	
		("south"[All Fields] AND "america"[All Fields]) OR "south america"[All	
		Fields]) OR ("central america"[MeSH Terms] OR ("central"[All Fields] AND	
		"america"[All Fields]) OR "central america"[All Fields]) OR ("west	
		indies"[MeSH Terms] OR ("west"[All Fields] AND "indies"[All Fields]) OR	
		"west indies"[All Fields] OR "caribbean"[All Fields] OR "caribbean	
		region"[MeSH Terms] OR ("caribbean"[All Fields] AND "region"[All Fields])	
-	4.00.5	OR "caribbean region"[All Fields])	2.607.406
6	4 OR 5		2,687,496
7	3 AND 6	Final search string	2,570

ONLINE APPENDIX 2. Reasons for exclusion at abstract and full text levels of screening

Level of Screening	Abstract	Full Text
Total Number of Exclusions	2,493	130
Not related to humans	11 (0.4)	_
Not related to LMIC	279 (11.2)	9 (6.9)
Not related to any component of CR, or any indication for CR	1,331 (53.4)	9 (6.9)
Not related to CR use/availability	872 (35.0)	106 (81.5)
Abstract only—full text version was included	_	2 (1.5)
Full text could not be found		4 (3.1)

334.e6

ONLINE APPENDIX 3. ARTICLES INCLUDED IN SYSTEMATIC REVIEW

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ONLINE APPENDIX 4. Cardiac rehabilitation availability in LMIC

Reference (Cited in Online Appendix 3)	Year	Country	No. of CR Centers Available	Population, Thousands (2012)*	Total CVD Deaths per 100,000 (2012)*	Total CVD Deaths (2012)	No. of CR Centers/100,000 CVD Deaths
[1]	2008	Algeria	1	38,482	397	152,620	0.7
[15]	2001	Thailand	5	66,785	184	122,751	4.1
[17]	2010	Belarus	5	9,405	464	43,658	11.5
[17]	2010	Lithuania	34	3,028	323	9,765	348.2
[17]	2010	Romania	26	21,755	364	79,166	32.8
[17]	2010	Serbia	51	9,553	360	34,391	148.3
[25]	2013	Argentina	28	41,087	192	78,764	35.5
[25]	2013	Brazil	39	199,000	214	426,258	9.1
[25]	2013	Chile	9	17,465	115	20,102	44.8
[25]	2013	Colombia	49	47,704	150	71,651	68.8
[25]	2013	Ecuador	5	15,492	149	23,130	21.6
[31]	2008	Mexico	17	121,000	148	179,443	9.5
[25]	2013	Paraguay	1	6,687	220	14,691	6.8
[25]	2013	Peru	9	29,988	123	36,765	24.5
[25]	2013	Uruguay	12	3,395	147	5,004	239.8
[34] [†]	1986	Venezuela	5	_	_	_	<u> </u>
[25]	2013	Venezuela	8	29,955	187	56,106	14.3

CR, cardiac rehabilitation; CVD, cardiovascular disease; LMIC, low- and middle-income countries.

^{*}WHO. Global Health Observatory Data Repository: Cardiovascular Diseases, Deaths per 100,000; Data by country. 2012. Available at: http://apps.who.int/gho/data/node.main. Accessed December 21, 2016.

 $^{^\}dagger$ Not included in Figure 2, as updated information was available for Venezuela from 2013.

Reference (Cited in																							
Online																							
Appendix 3)	[2]	[4]	[13]	[16]	[16]	[17]	[16]	[17]	[16]	[18]	[19]	[17]	[16]	[17]	[16]	[24]	[25]	[27]	[28]	[29]	[30]	[31]	[32]
Location	S. Africa	China	Iran	Bulgaria	Latvia	Lithuania	Lithuania	Romania	Romania	Russia	Russia	Russia	Russia	Serbia	Turkey	L. America	S. America	Chile	Colombia	Colombia	Colombia	Mexico	Uruguay
Year	1991	1995	2011	2011	2011	2010	2011	2010	2011	1984	1988	2010	2011	2010	2011	2009	2013	2012	1999	2009	2011	2009	2011
Diagnoses																							
accepted																							
by CR																							
centers (%)		v								٧				100			400				400	400	400
Post MI Post PCI	Y	Y	Y							Y	Υ			Y* N		100 97	100 99	100 100	Y		100 100	100 93	100
Post CABG	V		Y								Υ			IN Y*		97 97	99	100	Ϋ́Υ		96	93	
Heart failure			Ϋ́											N		73		85			98	76	100
Valvular disease	Y		Ÿ											N		82		85	Υ				100
Peripheral arterial														N		58	88	85			89		100
disease																							
Post heart transplant														N		21	49	42	Υ		55	14	67
Services offered (%)																							
Patient assessment										N								100	Υ	Υ	98	100	83
Nutritional counseling				48	80		68		93	Υ	Υ		43		36		91	100			93	86	100
Weight management																		100			93		
Blood pressure																		100			93		
management																							
Lipid management										N							71	62.5			93		83
Diabetes management										N								62.5			93		
Tobacco cessation				43	69		44		50	Υ	Υ		0		33	39	59	100	Υ		61	71	
Psychosocial										Υ	Υ						68	85				71	67
management										٧							400	400			400		400
Physical activity										Y	Υ						100	100			100		100
counseling Exercise training				65	85		94		79	٧	Υ		86		55		97		Υ	Υ	98		
Personnel available (%)				65	65		94		79	,	,		80		55			100	T	'			
Cardiologist						٧		v		v	v	v		v		100	85				71		100
Primary care/internal						· Y		v			· v	N		· v		100	29	14	100	86	18	100	100
med physician																							
Physiotherapist						Υ		Υ			Υ	N		Υ		94	72	85	Υ	89	91		50
Dietician											Y					91	72	85	Y	51	68	79	50
Nurse		Υ				Υ		N		Υ	Υ	N		Υ		52	50	85	75	37	64	71	83
Psychologist										Υ	Υ					48	53	42			50		
Social worker																33	15	28	Υ		9	29	
Psychiatrist																12	12		Υ	32	9	71	17

CABG, coronary artery bypass graft; CR, cardiac rehabilitation; MI, myocardial infarction; PCI, percutaneous coronary intervention. Blank cells represent unavailable data.

ONLINE APPENDIX 5. CR in LMIC: accepted indications, components, and personnel

^{*}Only those who are employed.

ONLINE APPENDIX 6. Attendance rate at CR

ppendix 3)	Ye	ear Country	Attendance (%)	Definition of Attendance In	cluded in Figure 5
[3]	1992	South Africa	50.0	# Completed CR program/# began CR program	
		(Johannesburg)			
[10]	2007	Iran (Isfahan)	86.5	# CR attendees (at least 1 session)/# referred	Yes
[13]	2011	Iran (Tehran)	3.6	# CR attendees/# of patients post PCI or CABG	
[14]	2012	Pakistan (Karachi)	36.3	# CR attendees/# referred	Yes
[17]	2010	Belarus	40.0	# CR attendees/# eligible	
[16]	2013	Bulgaria	31.7	# CR attendees (at least 1 session)/# referred	Yes
[16]	2013	Latvia	92.1	# CR attendees (at least 1 session)/# referred	Yes
[17]	2010	Lithuania	90.0	# CR attendees/# eligible	
[16]	2013	Lithuania	95.6	# CR attendees (at least 1 session)/# referred	Yes
[17]	2010	Romania	10.0	# CR attendees/# eligible	
[20]	2010	Romania	58.3	# CR attendees/# referred	
[21]	2011	Romania	61.0	# CR attendees/# referred	Yes
[16]	2013	Romania	51.5	# CR attendees (at least 1 session)/# referred	
[18]	1984	Russia	12.4	# CR attendees/# referred	
[16]	2013	Russia	42.4	# CR attendees (at least 1 session)/# referred	Yes
[16]	2013	Turkey	45.8	# CR attendees (at least 1 session)/# referred	Yes
[23]	2011	Turkey	0 (Women)	# CR attendees (at least 50% of sessions)/# elig	ible
			2.6 (Men)		
[34]	1986	Brazil	75.0	Not specified	
[28]	1999	Colombia	80.0	% Adherence	Yes
[33]	2010	Venezuela	66.0	# Participants/# referred	Yes

 ${\it CABG, coronary artery \ by pass \ graft; \ CR, \ cardiac \ rehabilitation; \ PCI, \ percutaneous \ coronary \ intervention.}$