Effectiveness of Cardiac Rehabilitation on Health-Related Quality of Life in Coronary Artery Disease Patients in Low and Middle-Income Countries

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ABSTRACT

This meta-analysis of published studies was conducted to determine the effectiveness of cardiac rehabilitation (CR) in terms of health-related quality of life (HRQoL) in post-coronary artery disease (CAD) patients in low- and middle-income countries (LMICs). Eighteen studies were identified from six countries (Malaysia, Iran, Brazil, Turkiye, China, and Pakistan) totalling 2,620 study participants with a mean age of 57.43 ± 7.9 years. Significantly higher mean physical (13.48, 95% CI: 7.75 to 19.21, p <0.001) and mental (11.52, 95% CI: 4.44 to 18.60, p <0.001) component scores were observed in the CR group compared to the usual group. The myocardial infarction- specific MacNew QLMI domains also showed significant mean differences (1.59, 95% CI: 0.97 to 2.21, p <0.001). This systematic review and meta-analysis showed significant improvements in physical and mental HRQoL in the CR group compared to the control group among post-CAD patients in LMIC. Furthermore, the myocardial infarction-specific MacNew QLMI global domain shows significant improvement in the CR group compared to the usual care group.

Key Words: Acute coronary syndrome, Cardiac rehabilitation, Quality of life, Short-form 36, MacNew quality of life after myocardial infarction.

How to cite this article: Hisam A, Haq ZU, Khan Z, Masood S, Pell JP, Doherty P. Effectiveness of Cardiac Rehabilitation on Health-Related Quality of Life in Coronary Artery Disease Patients in Low and Middle-Income Countries. *J Coll Physicians Surg Pak* 2025; **35(02)**:221-228.

INTRODUCTION

Coronary artery diseases (CADs) are the most common cause of death around the world. In 2019, CADs claimed the lives of 17.9 million individuals worldwide, accounting for 32% of all premature deaths. Low-and middle-income countries (LMIC) account for about three-quarters of this CAD mortality.¹ CAD has also been identified as both a risk factor for and a sequela of COVID-19 infection.²

People with CAD now live longer, attributed to advancements in diagnostics, therapeutics, and secondary presentation over the last 30 years.³ Although these patients have a longer life expectancy, their overall well-being may still be compromised. CAD can negatively impact an an individual's perception of health and subjective well-being, known as health-related quality of life (HRQoL).^{4,5}

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Received: January 10, 2024; Revised: May 31, 2024; Accepted: July 10, 2024 DOI: https://doi.org/10.29271/jcpsp.2025.02.221 Cardiac rehabilitation (CR) is one of the secondary preventive measures for CAD patients to decrease premature mortality and morbidity and improve HRQoL. CR is a multidisciplinary programme that has several components such as exercise training, risk factor education, psychological support, lifestyle and behaviour modifications, and the reduction of common risk factors.⁶⁻⁸ To achieve sustainable development goal 3 and attain a 30% decrease in early mortality attributable to CADs, countries must focus on adapting the existing cost-effective policies and initiatives.¹ CR is one such cost-effective strategy that may mitigate the CAD burden.⁹

In the developed countries, CR is now an essential component of post-CAD care but developing countries, being already resource-constrained, are lagging in effectively deliveringproven interventions to the CAD patients.^{6,10,11} A few systematic reviews and meta-analyses have been published, documenting the effectiveness of CR in terms of HRQoL among CAD patients, but none have been conducted in LMIC specifically.¹² CR availability and effectiveness in LMIC have not been assessed systematically.⁹ Therefore, the results of existing meta-analysis cannot be generalised to LMIC as these countries are scientifically unfledged and resources constrained. The objective of this systematic review and meta-analysis was to analyse the data from published clinical trials conducted in LMICs to determine whether CR programmes can improve the HRQoL in patients with CAD or not.

METHODOLOGY

The systematic review and meta-analysis were conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.¹³ This systematic review was registered with PROSPERO (Registration Number: CRD42018099290).¹⁴

The search was undertaken by the principal author (AH) and by consulting an information science specialist till May 6, 2021. The search strategy included using electronic databases and a reference crosschecking process. The studies were identified using four databases, i.e. PubMed, Web of Sciences, Embase (*via* Ovid), and Cochrane (*via* Wiley), using different combinations of MeSH terms and keywords. Filters and language restrictions were applied. There was one study in the Persian language which was translated into English language to decrease the language bias. Studies having human subjects were identified. The eligibility criteria for considering studies for this review are described in Table I.

Table I: Population, intervention, control, outcome, study design, and period (PICOST).

Population Age Time of index events The minimal standard of acute treatment	Participants of any age group from any gender. At least one month. Standard care in-patient and outpatient.
Location	LMICs.
Intervention (CR) Start Multi-component CR supervision CR setting	At least one month after the index event. At least having three CR components, e.g., exercise, dietary advice, and smoking cessation. In-patient, out-patient, both.
Control Usual care	Patient with index case but not participating in CR.
Outcomes Primary outcomes Observational period	Short form: 36 and MacNew QLMI. One month or more.
Study design Study design included	Randomised clinical trial (prospective and retrospective) and Quasi-experimental trial.
Period Searched till Exclusion criteria	May 6, 2021 Where full-text articles could not be retrieved. Studies that were conducted without using a validated measure of HRQoL. Duplicate publication Studies not specifying all the relevant measures of HRQoL Studies that were not available in English could not be translated into the English language at all.

The studies were selected according to their adherence to the eligibility criteria, including the need for them to have been conducted in an LMIC. Where studies had three groups, they contributed two comparisons to the meta-analysis. The control group was compared twice with the two intervention groups to analyse individual group impact. The study selection process is described in detail through a PRISMA flow diagram (Figure 1).

The first author, after running the electronic search in the databases, exported the references to EndNote reference management software,¹⁵ and removed duplicates. The same author scanned titles and abstracts to retrieve articles according to the eligibility criteria. The selected studies were then scanned for their location, and those studies conducted in

LMICs were selected for further evaluation. All retrieved articles were saved in a separate folder on the principal author's laptop. The second author (SM) also independently reviewed the titles and abstracts for the eligibility of the studies and selected the relevant ones. Both authors then compared their selected articles. In case of disagreement between the two reviewers (AH and SM) regarding the article selection decision, a consensus was reached following discussion, or a third reviewer (ZUH) was consulted for a final decision.

General characteristics of the studies, e.g., title, author name, publication year, country, study period, study design, sample demographics, type of cardiac rehabilitation, and HRQoL parameters, were recorded on a predesigned data extraction Excel spreadsheet. For any relevant missing data, the corresponding authors of those articles were approached through email. In case of an author not replying, reminder emails (maximum two) were sent and, if the author still did not respond, the article was excluded from the review.

As part of the data extraction procedure, quality assessment was performed using the Cochrane criteria of bias assessment in random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, inadequate outcome data, and selective reporting.¹⁶ Quality assessment of the selected studies was performed independently by the first author (AH) and then checked by the second author (SM) following the Cochrane guidelines.

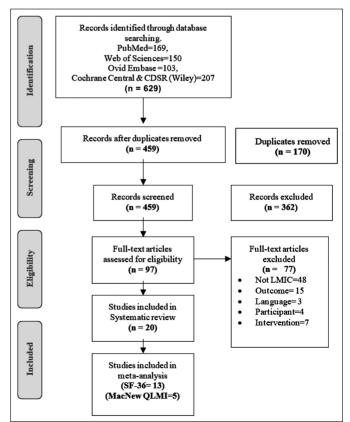


Figure 1: PRISMA flow diagram.

Table II: Summary of selected studies: Cardiac rehabilitation effectiveness compared with usual care among post-CAD patients.

Author year country	Age (years_ male n (%) female	Sample size (n)	Follow-up (weeks)	HRQoL tool	Cardiac rehabilitation interventions
Anchah <i>et al.</i> ²⁸ 2017 Malaysia	55.83 ± 10.13 99, 88.3%	112	24, 48	SF-36	MRCP: Clinical pharmacist services are added into routine CR protocol. Lifestyle modification counselling and pharmacological medicine therapy followed by post-discharge CR. At least 1 hour was spent by the clinical pharmacist with one patient. Then multidisciplinary talks and exercise sessions in the hospital were scheduled. CCRP: A four-week educational programme conducted through group classes, and slide presentations covering pharmacotherapy, cardiovascular risk factors, exercise, and medicine-related diet intake.
Azimi <i>et al.</i> ²⁵ 2016 Iran	61.40 ± 12.83 46, 65.7%	70	24, 48, 96	SF-36	FCEM: Standard in-patient CR and an outpatient CR using FCEM strategy. A group approach was used using a multidisciplinary team along with family members. After discharge, any illness was reported to the nurse every two days: Weekly cardiologist evaluated the patient. Daily exercise for 0-2 h/day from 0800 to 10:00. A designee (family member) attended the patient secsions and continued all CR with the patient as one unit. After 90 days post-intervention: Patient's durability, stability of empowerment, and knowledge attitude and practice (KAP) were assessed over eight follow-up sessions at an interval of three months A 21 support-group webinars were attended throughout 24 months of follow-up interviews using home visits or Skype, Viber, or WhatSApp.
Benetti <i>et al.</i> ²⁹ 2010 Brazil	57.7 ± 6.1 100%	87	12	MacNew QLMI	High-and moderate-intensity aerobic exercise programme, five times a week for 45 minutes, followed by stretching and muscle- strengthening exercises.
Dorri <i>et al.</i> ¹⁸ 2016 Iran	NA	50	04	SF-36	NA as the Persian language.
Firouzabadi et al. ³⁰ 2014 Iran	59.01 ± 8.37 NA	70	04, 16	SF-36	A 24-32 sessions of physical activity, three times a week for one-to-one and a half hours, respectively under the supervision of medical and CCU nurses, including 20 minutes of warm-up, 20-40 minutes of aerobic exercise (such as bikes and treadmills), 5 minutes cooling, and 20 minutes relaxation.
Haq <i>et al.</i> ³¹ 2019 Pakistan	53.6 ± 8.3 150, 76.92%	195	08	MacNew QLMI	Structured exercise programme by the multidisciplinary team provided in hospital premises for eight weeks period. While the participants were still in-patient, Phase one was administered for the first one-two weeks. Phase two began directly after phase one and consisted of a standardised workout routine lasting 6-7 weeks.
Karapolat <i>et al.</i> ³² 2009 Turkey	44.6 ±12.53 43, 63.88%	74	08	SF-36	Under the physician's supervision, three exercise sessions per week for eight weeks: 45-60 min. Exercises included flexibility exercises, aerobic exercises, and breathing exercises. Also, motivational calls and follow-ups on a weekly schedule.
Peixoto <i>et al.</i> ²⁴ 2015 Brazil	56.4 ± 10.2 62, 54.56%	100	04	MacNew QLMI	A supervised early mobilisation exercise programme twice a day, beginning 12 hours after the AMI for the month after hospital discharge.
Saeidi <i>et al.</i> ²⁰ 2013 Iran	61.7 ± 6.4 69, 69%	100	08	SF-36	Twenty-four sessions (3/week) of exercise training; consisted of 10-20 minutes of warm-up, 20-40 minutes of aerobic training using a treadmill, arm ergometer, and stationary bicycle, 10 minutes of cool-down and 20 minutes of relaxation as well as eight education sessions (weekly) were conducted: Which were supervised by a team (physician, cardiologist, trained nurse, and physiotherapist).
Salavati et al. ²¹ 2016 Iran	5.25 ± 2.47 55, 50%	110	08	MacNew QLMI	Four sessions a week in the hospital (and three days left at home-based on the training given at the hospital) for five weeks and 20 sessions. In between the visits (three home visits included: Days 7, 27, and 47 after discharge. The nurses made a telephone call to resolve any questions. A simplified booklet about the illness was given.
Salvetti <i>et al</i> . ³³ 2008 Brazil	53.5 ± 8.5 29, 74.35%	39	12	SF-36	The home group attended two classes in a gymnasium under the physiotherapist's supervision. (10-minute warm-up consisting of walking and stretching exercises, 40 minutes of aerobic). After two classes, patients were submitted to individualised training including standard stretching exercises, and walking three times per week for 30 minutes on non-consecutive days for three months. Patients were given a weekly logbook. Two weekly telephones by the doctor were conducted to monitor progress, assess adherence and provide support.
Uysal <i>et al.</i> ³⁴ 2012 Turkey	NA 70, 77.8%	90	12	SF-36	Individualised training on the fifth-seventh days before discharge for an hour by the content of 'desktop training and counselling guide for post-MI patients was given. Information was given on MI, medication, stress management, the effect of smoking and alcohol consumption, blood pressure control, hypertension management and the importance of physical activity, weight control, healthy eating, and diabetes control. Telephone counselling in the fourth and eighth weeks following discharge was conducted.
Wang <i>et al.</i> ²³ 2012 China	57.8 ± 9.5 111, 83.45	160	6,12,24	SF-36	A six-week, home-based rehabilitation programme was introduced using a self-help heart manual. The fitness plan included a home exercise and relaxation plan to practise at home week by week. An exercise self-evaluation form was included in the manual.
Yousefy et al. ¹⁹ 2009 Iran	50-60 years. 90, 74.38%	140	NA	MacNew QLMI	No intervention, in groups based on whether received CR or not and two different questionnaires were filled out by all participants.
Yu <i>et al.</i> ²⁶ 2003 China	61.75 ± 10.7 89, 79.46	112	2, 8, 24, 96	SF-36	An in-patient ambulatory programme for 7 to 14 days. For eight weeks, twice-weekly sessions, outpatient exercise and education programme. Each session included one hour of education class followed by two hours of exercise training (aerobic cardiovascular training) by a physiotherapist. The next hour, an occupational therapist conducted a domiciliary or vocational environment-focused training. For another six months, a community-based home exercise programme. They followed a long-term follow-up programme for two years, including half-yearly monitoring lipid profiles monitoring regular exercise and risk factor modification counselling.
Yu et al. ²⁷ 2004 China tril	64 ± 11 204, 75.83%	269	2, 8, 24, 96	SF-36	An in-patient ambulatory programme for 7 to 14 days. For eight weeks, twice weekly, an outpatient exercise and risk factor modification education programme was conducted. Each session included one hour of education class followed by two hours of exercise training (aerobic cardiovascular training) conducted by a physiotherapist. The next hour, an occupational therapist conducted a domiciliary or vocational environment-focused training. Also, telemetry for high risk. They followed a long-term follow-up programme for two years, including half- yearly monitoring [lipid profiles monitoring regular exercise and risk factor modification counselling.
Zadeh <i>et al.</i> ³⁵ 2015 Iran	NA 27, 54%	50	04	SF-36	Physical rehabilitation interventions for five straight days under the researchers' and a cardiologist's supervision in the hospital for four weeks. At the time of patients' discharge, for four weeks, a rehabilitation programme by simulation of rehabilitation activities based on MET, with the cooperation of a cardiologist, a CCU nurse, and one of the academic members in the nursing school teaching cardiology subjects was conducted.
Zhang et al. ³⁶ 2017 China	63.9 ± 7.25 116, 79.45%	146	24	SF-36	A team of trained community physicians or nurses conducted first home visits after discharge for counselling and designing a community- based exercise individualised training plan. Then three additional visits, at intervals of three weeks, two and six months, for training plan maintenance. In between the visits, community physicians or nurses made two - three phone calls to resolve issues if any. J-based exercise group; home. G: Home-based exercise group; NA: Not available; MCRP: Modified cardiac rehabilitation programme; CCRP:

CR: Cardiac rehabilitation; IG: Intervention group; CG: Control group; hosp. G: Hospital-based exercise group; home. G: Hospital-based exercise group; hospital-based exercise group; home. G: Hospital-based exercise group; home. G: Hospital-based exercise group; hospital-based e

Afterwards, the data were entered and analysed in Stata version 14.17 A random-effect meta-analysis was carried out to determine the weighted mean differences with 95% CI of the HRQoL tools: SF-36 (physical and mental component score) MacNew QLMI (social, emotional, physical, and global domains) among the usual and CR groups. Results are presented as a forest plot. Sub-group analysis was examined to explore all possible causes of heterogeneity between the studies. Heterogeneity between the studies was quantified using I^2 statistics. I² values of less than 30% represent low levels, 30 -60% represent moderate levels, and more than 60% represent a high level of heterogeneity. A funnel plot of the mean differences of the primary outcome measure (HRQoL) against their standard errors was plotted for assessing publication and small study biases. Publication bias was assessed visually from the asymmetry of funnel plots and formally by Egger's test.

Cumulative meta-analyses were used to explore the changes over time in the pooled estimates of study effect sizes. Metainfluence plots were used to examine the influence of individual studies. Narrative analysis was conducted where meta-analysis was not possible. Funnel plots, cumulative meta-analysis, and meta-influence plots were constructed.

RESULTS

The electronic search was carried out till May 6, 2021, with the identification of 629 studies published in PubMed (n = 169), OVID Embase (n = 103), Web of Science (n = 150), and Cochrane Central and CDSR = 207. After 332 duplicates were removed, the titles and abstracts of the remaining 459 articles were screened, and 77 additional articles were excluded, with 97 articles remaining for full-text review.

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	Card	liac Rel	nab	Us	ual Car			Mean Difference	Mean Difference
Study or Subgroup	Mean		Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Physical Compone									
Anchah L 2017a		20.73		44.15		62		37.96 [28.91, 47.01]	
Anchah L 2017b	47.19	10.45	28		10.15	62	2.3%	3.04 [-1.58, 7.66]	-
Azimi AV 2016a	88.37	3.42	35	20.1	4.65	35		68.27 [66.36, 70.18]	
Azimi AV 2016b	85.21	4.65			4.87	35	2.4%	62.20 [59.97, 64.43]	-
Dorri S 2016	40.9	9.9	25	46.9	8.6	25	2.3%	-6.00 [-11.14, -0.86]	
Firouzabadi MG 2014a	47.14	20.7		47.42	18.8	35	2.1%	-0.28 [-9.54, 8.98]	
Firouzabadi MG 2014b	69.85	17.46	35	47.52	16.07	35	2.2%	22.33 [14.47, 30.19]	
Karapolat H 2009	59.39			69.57		37	2.1%		
Saeidi M 2013	68.2	22.3	50	61.05	23.3	50	2.2%	7.15 [-1.79, 16.09]	<u>+</u>
Salvetti XM 2008	97.32	2.63	19	78	23.81	20	2.1%	19.32 [8.82, 29.82]	
Uysal H 2012	87.5	10.9	45	77.1	14.1	45	2.3%	10.40 [5.19, 15.61]	
Wang W 2012a	80.8	13.7	68	73.2	13	65	2.3%	7.60 [3.06, 12.14]	
Wang W 2012b	78	18.8	68	70.3	17.9	65	2.3%	7.70 [1.46, 13.94]	
Wang W 2012c	70.8	23.3	68	62.7	20.7	65	2.2%	8.10 [0.62, 15.58]	<u> </u>
Yu CM 2003a	88	13	72	87	9	40	2.3%	1.00 [-3.10, 5.10]	+
Yu CM 2003b	88	12		82	17	40	2.3%	6.00 [0.05, 11.95]	<u> </u>
Yu CM 2003c	87	12		82	14	40	2.3%	5.00 [-0.15, 10.15]	<u>+</u>
Yu CM 2004a	85	1	181	76	2	88	2.4%	9.00 [8.56, 9.44]	
Yu CM 2004b	87	1	181	84	3	88	2.4%	3.00 [2.36, 3.64]	-
Yu CM 2004c	86	1	181	79	2	88	2.4%	7.00 [6.56, 7.44]	-
Zadeh AK 2015	80.6	17.3	25	66.4	17.9	25	2.1%	14.20 [4.44, 23.96]	
Zhang L 2017	47.4	8.5	57	37.4	8.2	69	2.4%	10.00 [7.07, 12.93]	-
Subtotal (95% CI)			1411			1114	49.9%	13.48 [7.75, 19.21]	
Heterogeneity: Tau ² = 1 Test for overall effect: Z :				1 = 21 ()	^y < 0.00	1001); I-	= 100%		
1.1.2 Mental Componen	nt Score								
Anchah L 2017a	81.89	17.71	22	47.57	11.2	62	2.2%	34.32 [26.41, 42.23]	
Anchah L 2017b	50.39	8.52		47.57	11.2	62	2.3%	2.82 [-1.39, 7.03]	+-
Azimi AV 2016a	85.17			25.25	6.34	35		59.92 [57.55, 62.29]	-
Azimi AV 2016b	83.86	3.81	35	20.44	5.48	35	2.4%		-
Dorri S 2016	37.7	10.4	65	45.3	10.6	65	2.4%	-7.60 [-11.21, -3.99]	
Firouzabadi MG 2014a		22.07	35		22.58	35	2.1%	0.80 [-9.66, 11.26]	
Firouzabadi MG 2014b		15.88	35		22.07	35	2.1%	14.17 [5.16, 23.18]	
Karapolat H 2009		19.04		70.52		37	2.1%	-5.85 [-14.83, 3.13]	
Saeidi M 2013	67.04	20.1	100	65.28	21.3	100	2.3%	1.76 [-3.98, 7.50]	+
Salvetti XM 2008		16.03	19		13.11	20	2.1%	7.49 [-1.73, 16.71]	<u> </u>
Uysal H 2012	77.8	15.5	45	53	10.6	45	2.3%		
Wang W 2012a	73.5	17.1	80	65.4	20.7	80	2.3%	8.10 [2.22, 13.98]	
Wang W 2012b	74.2	16.4	80	64.9	21	80	2.3%	9.30 [3.46, 15.14]	
Wang W 2012c	73.5	16.6	80	66.3	20.9	80	2.3%	7.20 [1.35, 13.05]	
Yu CM 2003a	85	14	72	85	12	40	2.3%	0.00 [-4.93, 4.93]	+
Yu CM 2003b	84	16	72	80	15	40	2.3%	4.00 [-1.94, 9.94]	<u>†</u> –
Yu CM 2003c	82	15		83	15	40	2.3%	-1.00 [-6.80, 4.80]	-+
Yu CM 2004a	82	2		81	3	88	2.4%	1.00 [0.31, 1.69]	r
Yu CM 2004b	83	2		81	3	88	2.4%	2.00 [1.31, 2.69]	-
Yu CM 2004c	83	2		78	4	88	2.4%	5.00 [4.11, 5.89]	-
Zadeh AK 2015	61.1	17.1	25	46.9	19.8	25	2.1%	14.20 [3.94, 24.46]	
Zhang L 2017	52.1	9.7	69	46.4	9.5	62	2.4%	5.70 [2.41, 8.99]	
Subtotal (95% CI)			1549			1242	50.1%	11.52 [4.44, 18.60]	
Heterogeneity: Tau ² = 2 Test for overall effect: Z				f= 21 (F	° < 0.00	1001); I 2	= 100%		
Total (95% CI)			2960				100.0%	12.52 [8.42, 16.61]	•
Heterogeneity: Tau ² = 18		ni² = 116 ≺ 0.000		df = 43	(P < 0.0	0001);	I ² = 100%		-50 -25 0 25 50 Favours UC Favours CR

Figure 2: Physical and mental component score of the selected studies.

	ab	Usu	al Car	e		Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.2.1 Social Domain									
Benetti M 2010b	6.7	0.97	29	4.9	1.1	29	5.5%	1.80 [1.27, 2.33]	-
Peixoto TCA 2015	5.7	0.97	45	5.2	1.2	43	5.5%	0.50 [0.04, 0.96]	-
Salavati M 2016	60	0.97	27	53	1.08	30	5.5%	7.00 [6.47, 7.53]	→
Yousefy A 2009	2.87	1.14	57	3.15	0.96	64	5.6%	-0.28 [-0.66, 0.10]	-
Subtotal (95% CI)			158			166	22.0%	2.25 [-0.81, 5.31]	
Heterogeneity: Tau ² = Test for overall effect				f= 3 (P	< 0.00	1001); P	²= 99%		
1.2.2 Emotional Dom	nain								
Benetti M 2010a	6.91	0.71	29	5.8	0.97	29	5.5%	1.11 [0.67, 1.55]	+
Benetti M 2010b		0.71	29		0.97	29	5.5%	0.91 [0.47, 1.35]	-
Peixoto TCA 2015	6	0.7	45		1.2	50	5.6%	1.10 [0.71, 1.49]	+
Salavati M 2016		0.71	27		0.97	30	5.5%	5.00 [4.56, 5.44]	-
Yousefy A 2009		0.77	57		0.74	64	5.6%	-0.18 [-0.45, 0.09]	4
Subtotal (95% CI)	0.0		187	0.10	24	202		1.58 [-0.11, 3.28]	
Heterogeneity: Tau ² = Test for overall effect				f= 4 (P	< 0.00	1001); P	²= 99%		
1.2.3 Physical Doma	ain								
Benetti M 2010a	6.18	0.62	29	5.12	0.84	29	5.6%	1.06 [0.68, 1.44]	+
Benetti M 2010b	6.18	0.62	29	5.12	0.84	29	5.6%	1.06 [0.68, 1.44]	+
Peixoto TCA 2015	6.1	0.7	45	4.9	0.9	50	5.6%	1.20 [0.88, 1.52]	+
Salavati M 2016	30	0.62	27	28	0.84	30	5.6%	2.00 [1.62, 2.38]	-
Yousefy A 2009 Subtotal (95% CI)	3.51	0.55	57 187		0.78	64 202	5.6% 28.0%	0.57 [0.33, 0.81] 1.17 [0.70, 1.64]	-
Heterogeneity: Tau ² = Test for overall effect					0.000	101); I ^z :	= 90%		
1.2.4 Global Domain									
Benetti M 2010a	6.72	1	29	5.15	1	29	5.5%	1.57 [1.06, 2.08]	-
Benetti M 2010b	6.8	1	29	5.15	1	29	5.5%	1.65 [1.14, 2.16]	-
Hag ZU 2019	5.6	0.5	99	3.8	0.5	96	5.7%	1.80 [1.66, 1.94]	-
Peixoto TCA 2015	6.1	0.6	45	5.2	1	50	5.6%	0.90 [0.57, 1.23]	+
Subtotal (95% CI)			202			204	22.2%	1.48 [1.00, 1.96]	•
Heterogeneity: Tau ² = Test for overall effect					0.000	I1); I²=	88%		
Total (95% CI)			734			774	100.0%	1.59 [0.97, 2.21]	•
Heterogeneity: Tau ² =	= 1.76: CI	hi² = 10		df = 17	(P < 0				
Test for overall effect Test for subgroup dif	t: Z = 5.03	(P < 0	00001)				-	-10 -5 0 5 Favours UC Favours CR

Figure 3: MacNew QLMI.

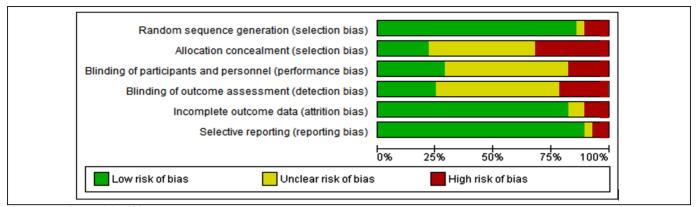


Figure 4: Cochrane risk of bias assessment.

Table III: Trial, patients, and intervention characteristics summary.

Parameters	No. of studies
Published year	2003-2019
Study location	
Malaysia	1
Iran	7
Brazil	3
Turkiye	2
China	4
Pakistan	1
Population characteristics	
Gender	
Male	1266
Female	529
Not reported	1795
Age in years	57.43 ± 7.9 years
Diagnosis	
Acute coronary syndrome	12
Heart failure	1
Coronary artery disease	5
Setting	
In-patient	4
Outpatient	7
In and out-patient	7
Post-cardiac event intervention	
CABG	2
PCI	3
CABG and PCI	5
Not mentioned	8
CR approach	
Individual	10
Group	7
Both	1
Follow-up duration, weeks	
Less than 24 weeks	12
More than 24 weeks	6
HRQoL tools	
Short form-36	13
MacNew QLMI	5

Parameters	Pooled estimate	Heteroge	Heterogeneity		
	WMD (95% CI)	p-value	1 ²	p-value	
Physical component score	13.48 (7.75, 19.21)	< 0.001	100%	< 0.001	
Mental component score	11.52 (4.44, 18.60)	< 0.001	100%		
Overall (PCS + MCS)	12.52 (8.42, 16.61)	< 0.001	100%		
Social domain (S)	2.25 (-0.81, 5.31)	0.15	99%		
Emotional domain (E)	1.58 (-0.11, 3.28)	0.07	99%		
Physical domain (P)	1.17 (0.70, 1.64)	< 0.001	99%		
Global domain (G)	1.48 (1.00, 1.96)	< 0.001	88%		
Overall (S, E, P, and G)	1.59 (0.97, 2.21)	< 0.001	98%		

The eligibility criteria were applied to those 97, and 20 studies were found to fulfil the eligibility criteria. Two studies were further excluded, and therefore 18 studies were able to be included in the quantitative analysis. The PRISMA flow diagram provides details of the study selection process (Figure 1).

The included 18 studies were published between 2003 and 2019. The total sample size of these studies was 2,620 (CR: 1697, UC: 923), with the individual study sample size ranging from 39 to 269 participants. These studies were conducted in six countries; Malaysia, Iran, Brazil, Turkiye, China, and Pakistan. The mean duration of these studies was 24 weeks. The mean age of the participants was 57.43 ± 7.9 years. The majority of studies included a higher proportion of men, presumably due to their higher incidence of cardiovascular diseases. All studies were published in the English language except one in Persian which was translated.¹⁸

All studies were randomised controlled trials except for three studies,¹⁹⁻²¹ that were non-randomised quasi-experimental designs.^{22,23} In one study, there was no explicit mention of the study design.¹⁹

Follow-up period varied from four weeks to 96 weeks with 24 weeks as the mean follow-up period with the average outcome collected three times. $^{18,24-27}$

Cardiac rehabilitation: The question of which core components of the CR are most effective in improving the HRQoL of CAD patients is difficult to answer in the presence of such large heterogeneity among the studies' CR interventions. The CR intervention of the included studies varied in the follow-up period, number, duration and content (physical activities, dietary modifications, behavioural change therapies, and stress management), provision or not of supervision, setting (in-or out-patient), approach (individual or group), and mode of delivery (with or without telecommunication).

CR delivery may involve a multidisciplinary team focusing on counselling, education programmes on risk modification, diet and medicine advice, support teams, and calls. Most of the studies' primary intervention was CR lifestyle modification counselling along with physical activity. In eight studies, patients were counselled individually,^{20,21,23,24,29,30,32,34} while in ten studies, there was group counselling.^{18,19,21,25-27,30} In one study, there was no mention of the type of counselling,³⁵ while one study had both types of approach, the individual and the group.²⁸ The physical activity component was heterogeneous

in terms of the number of sessions, duration of sessions, setting, supervision, and type of activity. Also, dietary modifications comprised advice to follow a healthy diet, with low salt intake. There were studies in which patients were part of an educational programme to discuss their problems and coping strategies to resolve them (Table II and III).^{19,21,28,37}

Health-Related Quality of Life: HRQoL tools most commonly used were short form 36³⁸ (SF-36, a generic tool), used in thirteen studies and MacNew quality of life after myocardial infarction (MacNew QLMI, a specific tool),³⁹ used in five studies.

Short Form 36: The SF-36 used by 15 studies^{18,20,23,25-28,30,32-36,40,41} showed significant differences in mean HRQoL improvement (PCS: 13.48, 95% CI: 7.75, 19.21, p <0.001, MCS: 11.52, 95% CI: 4.44, 18.60, p <0.001) as measured by generic SF-36. The overall specific quality of life using SF-36 showed a significant mean difference between the groups (12.52, 95% CI: 4.44, 18.60, p <0.001, Figure 2). Point estimates favoured the CR arm in improving HRQoL. However, there was a significant heterogeneity between studies (I² 100%, p <0.001) and hence a random-effects meta-analysis was used. The subgroup analysis also showed significant improvement and is shown in Figure 3 and 4.

MacNew QLMI: The five studies reporting MacNew QLMI, 19,21, ^{24,29,31} showed significant differences in mean physical (1.17, 95% CI: 0.70, 1.64, p < 0.001) and global (1.48, 95% CI: 1.00, 1.96, p < 0.001) scores among the CR group compared to the usual care group but there were non-significant mean differences in the social (2.25, 95% CI: -0.81, 5.31, p = 0.15), and emotional domains (1.58, 95% CI: -0.11, 3.28, p = 0.07). The overall myocardial infarction-specific MacNew QLMI also showed a significant mean difference between the groups (1.59, 95% CI: 0.97, 2.21, p <0.001, Figure 3). Two studies,^{19,21} did not compute global domain scores and were excluded from the global domain analysis only. One study³¹ reported only the global domain, so it was included in the analysis of the global domain only. Heterogeneity was significant between the studies ($I^2 = 96\%$, p < 0.001), hence a random effect model was used. The pooled estimate of weighted mean differences and their heterogeneity is shown in Table IV.

The Cochrane risk of bias assessment showed a low risk of bias for the majority of the studies. Most of the studies had reported sufficient information, and hence altogether, the risk seemed low. The funnel plot was a symmetrical, showing no publication bias, which was confirmed through Egger's test (p = 0.190). Details of the quality and risk assessment are shown in Figure 4.

DISCUSSION

A systematic review and meta-analysis of CR were conducted to determine the effectiveness of CR in LMICs. The studies selected for review were conducted between 2003 and 2019 with a mean participant age of 57.43 ± 7.9 years. The individual studies sample size varied from as few as 39 participants to as large as 269 participants. The studies were conducted in six countries: Malaysia, Iran, Brazil, Turkiye, China, and Pakistan. The mean duration of these studies was 24 weeks.

CR in these studies involved a multidisciplinary team focusing on counselling, education programmes on risk modification, diet and medicine advice, and support teams and calls. The primary components of the CR intervention were lifestyle modification counselling along with physical activity. Generic HRQoL physical component and mental component scores significantly improved in the CR group due to CR. The myocardial infarction-specific MacNew QLMI physical and global domains were also significantly improved among the CR group. The subgroup analyses of the SF-36 and MacNew physical and global domains by mean study duration, approach, setting, and country showed consistently significant improvement among the CR group compared to the UC.

Other systematic reviews and meta-analyses of CR among CAD, conducted in developed countries, have shown significant improvement in HRQoL, which are consistent with the current review findings. In 2019, Francis *et al.* analysed 49 studies including forty-one randomised trials involving a total of 11,747 patients. The findings confirmed that engaging in physical activity, non-physical activity, or mentally and emotionally based CR is effective in not only reducing the risk of fatalities and future hospital admissions but also help in enhancing HRQOL when compared to usual care.^{41,42} The mean age was 57.43 \pm 7.9 years; the lower age can be explained because of the lower life expectancy in developing countries compared to developed countries.

The CR components, mode of delivery, approach, and followup techniques varied widely between different studies. Therefore, it is difficult to point out which aspect of CR is most effective in improving the HROoL among post-CAD patients. In developing countries, the CR component, mode of delivery, setting, approaches, and demographics of the people receiving and not receiving CR impact the CAD outcomes. The reassurance given in the CR lifestyle modification counselling and knowledge regarding the risk factor modification may have impacted the individual behaviours that may have improved their HRQoL outcomes. Standard CR can be devised after more extensive trials for LMICs, keeping in mind the low resource settings and cost-effectiveness.⁴² The subgroup analysis of this review has shown persistent improvement in the CR group compared to usual care. HRQoL component scores were improved at the mean study duration of 24 weeks. The country-specific analysis of the eighteen studies also showed significant improvements in the HRQoL outcome. The HRQoL improve-ment was seen for both individual and group approaches as well.

CONCLUSION

All the domains of the generic HRQoL tool (SF-36) showed significant improvement among the CR group compared to the control group. The myocardial infarction-specific MacNew QLMI physical and global domains also showed significant improvement in the CR group compared to the usual care group.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

AH, ZUH: Perception of the study, design, and working on methodology, results in write-up, data analysis, discussion, and final drafting of the manuscript.

SM: Literature review, collecting and analysing data, quality assessment, and result analysis.

ZK, JPP, PD: Drafting of the manuscript and critical analysis for the important intellectual content.

All authors approved the final version of the manuscript to be published.

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