Cost-Effectiveness of Exercise-Based Cardiac Rehabilitation in Chilean Patients Surviving Acute Coronary Syndrome

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Purpose: To assess the cost-effectiveness of 3 models of exercise-based cardiac rehabilitation (CR) compared with standard care in survivors of acute coronary syndrome (ACS) within the public health system in Chile.

Methods: A Markov model was designed using 5 health states: ACS survivor, second ACS, complications, general mortality, and cardiovascular mortality. The transition probabilities between health states for standard care and corresponding relative risk for CR were calculated from a systematic review. Health benefits were measured with the EuroQol 5-dimensional 3-level (EQ-5D-3L) survey. Costs for each health state were quantified using the national cost verification study. The CR cost was estimated with a microcosting methodology. The time horizon was a lifetime and the discount rate was 3% per year for costs and benefits. Deterministic and probabilistic analyses were performed. Structural uncertainty was managed by designing 3 scenarios: CR as currently delivered in a specific Chilean public health center, CR as recommended by South American guidelines, and CR as proposed for low-resource settings.

Results: Cardiac rehabilitation versus standard care showed an incremental cost-effectiveness ratio for the standard model of $722, for the South American model of $1247, and for the low-resource model of $666. The tornado diagram showed higher uncertainty in relative risk for the complications state and for the second ACS state.

Conclusion: Considering a cost-effectiveness threshold of 1 unit of gross domestic product per capita (~$19 000), CR is highly cost-effective for the public health system in Chile.

Key Words: cardiac rehabilitation • cost-effectiveness • economic evaluation • South America

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This study was funded by Fondo Nacional de Investigación y Desarrollo en Salud FONIS—Chile (grant SA14ID0005).

The authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jcrpjournal.com).

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DOI: 10.1097/HCR.0000000000000356

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the world, of which ischemic coronary artery disease produces the highest mortality and disability-adjusted life-years.[1] In the Americas, it contributes to 34% of the total number of deaths.[2] In Chile, CVD accounts for 67% of diseases, making it the second most common condition for which the most life years are lost due to premature death.

Once heart disease has been established, the fundamental objective is to reduce mortality and new CVD events through secondary prevention programs that include drug therapy, healthy lifestyle intervention, and control of hypertension, cholesterol, and diabetes mellitus.[3] While these recommendations are widely known, their impact is not as expected, as evidenced by a global study which reported that only 35% of patients with a CVD event maintain high levels of physical activity, 39% follow a healthy diet, and 18% continue smoking. The achievement of such healthy goals is even lower in low-income countries.[4]

Cardiac rehabilitation (CR) programs are long-term programs that include medical evaluation, education, and counseling, with the prescription of exercise being one of the key components.[5] To achieve the secondary prevention goals, the interventions currently in use must be complemented by a CR program, as recommended by international guidelines.[6] Guidelines exclusively for CR strongly recommend supervised exercise or controlled physical activity based on high-level evidence.[7] Nevertheless, CR programs are underutilized compared with other interventions, such as medications. Worldwide, 68% of high-income and 23% of low-/middle-income countries offer CR programs to patients with CVD.[8] Specifically, in Chile the existing CR programs cover only 5% of patients who need them, and these are mainly in the private system and in the country's capital.[9] This is a very similar situation to that of other Latin American countries,[10] revealing major inequalities of access. The barriers to implementation of CR programs may be lack of knowledge and scarcity of specialists in the area, but one of the most recurrent explanations is the associated cost. However, cost should not be the only input for decision making. One appropriate way to realize the impact of health technology is by conducting an economic analysis that integrates the benefit of interventions and their associated costs into one indicator.

Economic evaluations that support the implementation of CR have been conducted in other countries,[11,12] but the wide variability in CR design and delivery added to the economic specificities of each country make them difficult to generalize and transfer. This study aimed to assess the cost-effectiveness of 3 models of exercise-based CR compared with standard care received by survivors of acute coronary syndrome (ACS) within the public health system in Chile.

METHODS

A cost-utility analysis was conducted. A Markov model was designed to compare exercise-based CR and standard care. Five health states and 1-y cycles were considered. The hypothetical cohort included patients who had survived their first ACS at an initial age of 63 y,[13] with a time horizon of life expectancy. The discount rate used was 3% per year for both costs and benefits. The data analysis was performed using the TreeAge Pro software. A sensitivity analysis was performed with a tornado graph, where variables related to the benefits, costs, and transition probabilities were entered. The probabilistic sensitivity analysis was conducted using 1000 iterations, in which a triangular distribution for relative risk (RR), gamma for the costs, and beta for the benefits were considered. The main outcome was expressed through the incremental cost-effectiveness ratio (ICER), which is defined as the ratio of the difference in costs between 2 competing strategies to the difference in effectiveness.[14]

ALTERNATIVES FOR COMPARISON

The standard care of patients with ACS who have been discharged includes drug therapy and, for patients with myocardial infarction with ST elevation, advice on physical activity from treating physicians and a cardioprotective diet according to current clinical guidelines in Chile.[15]

The alternative being assessed in this study is exercise-based CR, defined as an intervention in the period after hospital discharge for patients who have survived ACS. Its main component is exercise at a pre-established intensity, frequency, duration, and modality, which is supervised by a competent professional and based on a suitable evaluation of their physical capacity. In addition to exercise, this program includes education about a healthy lifestyle.[16] To manage structural uncertainty and considering that different CR structures generate different costs, 3 CR models (see Supplemental Digital Content 1, available at: http://links.lww.com/JCRP/A80) were defined for this economic analysis. The Standard Model was based on the program delivered by one of the centers in the Chilean public health system, the South American Model on the South American consensus on CR,[17] and the Low-Resource Model on the International Council of Cardiovascular Prevention and Rehabilitation Consensus Statement.[18]

HEALTH STATES AND TRANSITIONS IN THE MODEL

The Markov model and the transitions between states are shown in Figure 1. The initial post-ACS state includes patients who survive an initial ACS; are treated with thrombolytic therapy, angioplasty, or revascularization surgery; and who are discharged from hospital. These patients can remain in this state, suffer a second nonfatal ACS, develop complications arising from this first event, or die from CVD or other causes. The second nonfatal ACS state includes patients with a new ACS within 1 y following the first ACS, are treated with thrombolysis or angioplasty, and who are subsequently discharged from the hospital. These patients can remain in this state or die because of CVD or other causes. The nonfatal complications state includes patients who, after the initial ACS, develop complications that require hospitalization due to CVD (heart failure, stroke, or revascularization surgery to treat the initial ACS). These patients return, in the next cycle, to the post-ACS state or may die from general causes. Specific death is defined as death by CVD, including ACS, stroke, heart failure, or death during or immediately after a revascularization procedure. General death includes patients who die from any cause other than CVD. The death states are absorbent states.

The transition probabilities between health states in the model were obtained from the literature. The probability that a patient had a second ACS after receiving standard care was taken from a cohort study.[19] The probability that a patient died of non-CVD causes was taken from national indicators. Specific data from a Cochrane systematic review[20] about exercise-based CR for coronary heart disease were used to determine the rest of the probabilities in the standard care arm. The difference in probabilities in the exercise-based CR arm[20] were determined by a meta-analysis conducted with data from some individual clinical trials included in same systematic review. These involved patients who had an ACS, and the trials were conducted after 1990, when thrombolytic therapy became available.[21–43]

The assumptions of the model were the following:

- Patients may present with a maximum of 2 ACSs.
- The complications are derived from only the initial ACS.
- The probability of CVD death after the second ACS is the same as for CVD death after the first ACS.

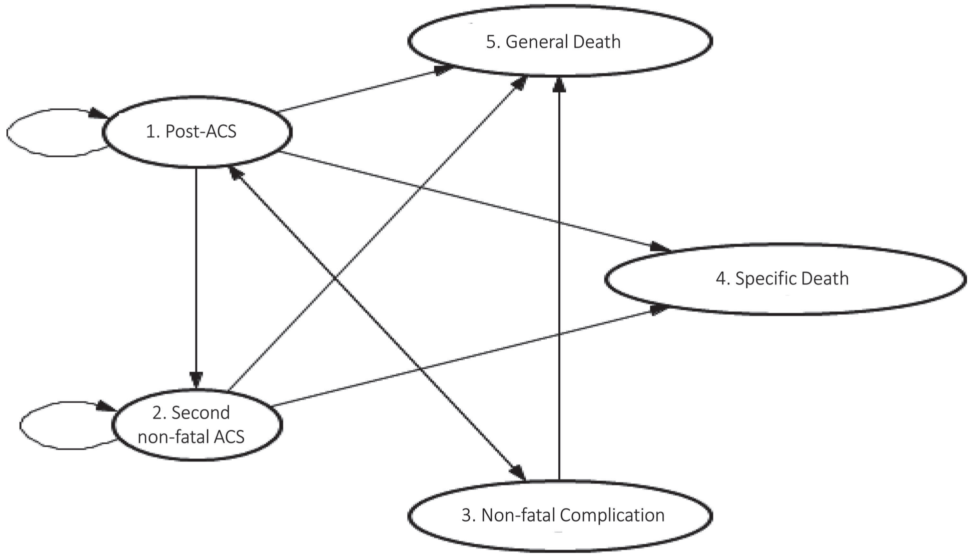

Figure 1. Health states in the Markov model. ACS indicates acute coronary syndrome.

- Patients who have nonfatal complications return to the post-ACS initial state or die from other causes in the following cycle, not staying in this state for more than 1 cycle.
- The effectiveness of the intervention, expressed as RR, is the same for the first 3 y, and from the fourth year onward, there is a progressive decrease in effectiveness until a null-effect RR is reached in the tenth cycle.

The model was run several times and the survival curves were analyzed for both groups (with and without exercise-based CR) to check their plausibility.

MEASUREMENT OF HEALTH BENEFITS

The outcome was established as the subjective dimension of health-related quality of life. To estimate the benefits defined as utilities derived from transit through the health states, 95 patients who were representative of each health state were selected in the Complejo Hospitalario San José and Dr Hernán Henriquez Aravena Hospital. Trained personnel applied the EuroQol 5-dimensional 3-level (EQ-5D-3L) instrument,[44] widely used in economic evaluations. It has been validated, and the utility values have been established for the Chilean population.[45] The benefits were expressed in quality-adjusted life-years (QALYs), a specially combined metric that incorporates life expectancy and quality of life, interpreting "1 QALY" as 1 y living in perfect health.

The study protocol was approved by the Ethics Committee of the Servicio de Salud Metropolitano Norte and the Servicio de Salud Araucanía Sur.

COST DETERMINATION

Costs for each health state were estimated by considering the standardized pool of services established by Chilean clinical guidelines. The analysis was done from the perspective of the Chilean public health system. For the post-ACS state, costs covering the first year of health care after hospital discharge as well as the follow-up costs from the second year were considered differentially. They included the costs of a comprehensive consultation by a specialist, diagnostic tests, and drug therapy as stipulated by the national clinical guideline.[15] Diagnosis, treatment, and follow-up costs for the first year were included for both the second ACS and for complications. For the second ACS state, 35% of patients were considered to have received medical treatment, 50% thrombolytic therapy, and 15% angioplasty.[46] For the complications state, the average hospitalization costs due to heart failure, stroke, and bypass surgery were taken into account. For the specific death state, the weighted costs of diagnosis and treatment were included but only for the proportion of patients estimated to have died in the hospital. Local data from a cohort study showed that 100% of patients who died from cardiac failure died in the hospital; similarly, 66% of those who died from stroke, 4% of those who died undergoing bypass surgery, and 75% who died from ACS also died in the hospital. For the general death state, no cost was assumed. The costs were obtained from the 2009 or 2010 Chilean Cost Verification Study and price lists for purchases available on the Chilean Public Market platform.

Microcosting through a cost form (a strategy that collects and records cost data) was used to determine CR costs. A cost pool was constructed for each CR model. Included in each pool was the direct cost of labor (professional and administrative), depreciation of equipment and instruments, and the goods and services of normal consumption. Indirect costs were considered at a rate of 0.3239, which was obtained from the calculation of indirect structural costs as an average percentage of direct costs in the Hospital San José. Building depreciation costs were discounted at a factor of 0.02, a rate obtained from a previous study performed by the Chilean Ministry of Health that included all public hospitals.

All costs have been updated according to the consumer price index variation as of June 2016 and were converted into US dollars for this report. Its equivalence in the local currency, Chilean pesos (CL$), is indicated within parentheses in the tables, the exchange rate being USD $1 equivalent to CL $665. For additional supportive references, see Supplemental Digital Content 2 (available at: http://links.lww.com/JCRP/A81).

RESULTS

Table 1 shows the values, variability measures for the probabilities of transition between states in standard care, the respective RR used to quantify the effect size of participating in an exercise-based CR program, and the benefits and costs.

The cost of implementing an exercise-based CR program was $58 with a range of $46 to $69 in the low-resource model, $102 with a range of $82 to $122 in the standard model, and $486 with a range of $389 to $584 in the South American model (Table 2).

The total and incremental costs and QALYs are shown in Table 3. For the standard model, the exercise-based CR intervention resulted in an ICER of $722 per QALY, compared with that of standard care. For the South American model, the ICER was $1247 per QALY, and for the low-resource model, the ICER was $666 per QALY.

In the 1-way sensitivity analysis using the tornado method, the ICER was observed to be sensitive to the RR of having complications, suffering a second ACS, dying by CVD and also to the costs of the complications (Figure 2). Considering the heightened uncertainty given by the RR of having complications (as shown at the top of Tornado graph), the ICER could fluctuate between $263 and $1343 for the standard model, between $260 and $1869 for the South American model, and between $324 and $1284 for the low-resource model.

Figure 3 shows the scatter plot from the probabilistic analysis of 1000 iterations. Eighty-seven percent and 92% of these are under the threshold of willingness to pay in the standard and low-resource models and in the South American model, respectively.

DISCUSSION

The results of this study show that from the point of view of the Chilean public health system, exercise-based CR is highly cost-effective regardless of the program configuration. The ICER goes from $666 in the low-resource model to $1247 in the South American model, which has more professionals, equipment, and sessions per program. Therefore, the costs of gaining a year of life with perfect health fall well below the willingness-to-pay threshold of 1 unit of gross domestic product, approximately $19 550.

Another cost-effectiveness analysis conducted in Chile used a decision tree, incorporating the probability of dying during a time horizon of 2 y and expressing its results in life years gained after participation in a CR model program. This study determined that a life year gained costs $715.[47] The results align with the present study, but the working model of that study incorporates only premature death as an event of interest in a 2-y decision tree.

Table 1

Information Used to Populate the Model

	Probability for Usual Care		
	Probability	**Range**	**Source**
Second ACS	.053	0.47-0.59	19
Complications	.2	0.06-0.67	24, 28, 31, 33, 38, 39
Specific death	.071	0.03-0.15	24, 31, 38
General death	.0088	0.007-0.011	DEIS 2014
	Effect Size With Cardiac Rehabilitation		
	Relative Risk	**Confidence Interval**	**References**
Second ACS	0.8	0.52-1.22	28, 31, 32, 41
Complications	0.92	0.79-1.07	24, 28, 31, 33, 38, 39
Specific death	0.58	0.37-0.90	24, 31, 38
General death	1	0.89-1.12	21-25, 27-30, 32, 35, 36, 39-43
	Utilities		
	Mean	**Standard Deviation**	**Source**
First ACS	0.68752	0.2158026	Own data
Second ACS	0.712069	0.2804421	Own data
Complications	0.393875	0.4642811	Own data
	Costs		
	Weighted Mean	**Range**	**Source**
First ACS (year 1)	$120 (CL $80 043)	$108 to $132 (CL $72 039 to CL $88 047)	CVS 2009 PMS
First ACS (subsequent years)	$56 (CL $37 288)	$50 to $62 (CL $33 559 to CL $41 017)	CVS 2009 PMS
Second ACS	$1054 (CL $700 599)	$120 to $1652 (CL $80 043 to CL $1 098 854)	CVS 2009 PMS
Complications	$3539 (CL $2 353 387)	$2139 to $6289 (CL $1 422 304 to CL $4 182 268)	CVS 2009 PMS
Specific death	$1212 (CL $805 946)	$252 to $1458 (CL $167 291 to CL $969 860)	CVS 2009 PMS

Abbreviations: ACS, acute coronary syndrome; CL, Chilean; CVS, cost verification study; DEIS, Department of Statistic and Information of Health, Chile; PMS, Chilean public market system.

This study's results are similar to those reported by studies in other settings, but this does not ensure that they can be generalized to other countries in Latin America or other regions, since the structure and delivery of the programs are variables and because there are economic particularities. A systematic review that includes 16 economic evaluations supports the implementation of CR for patients with myocardial infarction and heart failure; however, it should be borne in mind that there is significant variability in the design and delivery of the programs

Table 2

Unique Cost of Exercise-Based Cardiac Rehabilitation for the 3 Models

	Standard Model	South American Model	Low-Resource Model
Professionals and administrative staff (labor cost)	$76 CL $49 801	$358 CL $237 830	$42 CL $28 138
Equipment and instrument depreciation	$0.53 CL $355	$2.42 CL $1606	$0.26 CL $171
Goods and Services	$0.16 CL $106	$0.91 CL $106	$0.16 CL $106
Total direct cost	$76 CL $50 262	$360 CL $239 542	$43 CL $28 415
Indirect cost rate	0.3239	0.3239	0.3239
Indirect cost	$25 CL $16 281	$117 CL $77 592	$14 CL $9204
Recurrent cost of hospital delivery	$100 CL $66 543	$477 CL $317 135	$57 CL $37 619
Building depreciation factor	0.0200	0.0200	0.0200
Building depreciation cost	$2 CL $1331	$10 CL $6343	$1 CL $752
Total indirect cost	$27 CL $17 612	$126 CL $83 935	$15 CL $9957
TOTAL	$102 CL $67 874	$486 CL $323 477	$58 CL $38 372

Abbreviation: CL, Chilean.

Table 3

Cost-Effectiveness Results for the 3 Models of Exercise-Based Cardiac Rehabilitation

	Total Cost	Incremental Cost	QALY Total	Incremental QALY	ICER
Standard Model					
Usual care	$4775 CL $3 175 047		5.34		
CR	$5 304 CL $3 527 015	$529 CL $351 968	6.07	0.73	$722 CL $480 360
South American Model					
Usual care	$4775 CL $3 175 047		5.34		
CR	$5688 CL $3 782 618	$914 CL $607 571	6.07	0.73	$1247 CL $829 203
Low-Resource Model					
Usual care	$4775 CL $3 175 047		5.34		
CR	$5259 CL $3 497 512	$485 CL $322 465	6.07	0.73	$666 CL $440 095

Abbreviations: CL, Chilean; CR, cardiac rehabilitation; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

evaluated.[11] Nine studies included in this review compared center-based CR versus no CR, with results ranging from $650 to $9200 per QALY in favor of CR. Another review, which includes studies of low- and middle-income countries, shows that there are few analyses available; only 2 cost-effectiveness evaluations exist in Latin America, applied to patients with heart failure. The reports from Brazil[48] and Colombia[49] show that CR is highly cost-effective, but the review authors are emphatic in concluding that given the countries' limited budgets, affordable models must be designed, especially for countries with low-income levels.[12] This conclusion is reinforced by existing reports about the low accessibility and availability of CR programs[8] and the proposal of a CR delivery model for low-resource settings,[18] which has been included in this study as an alternative to be considered.

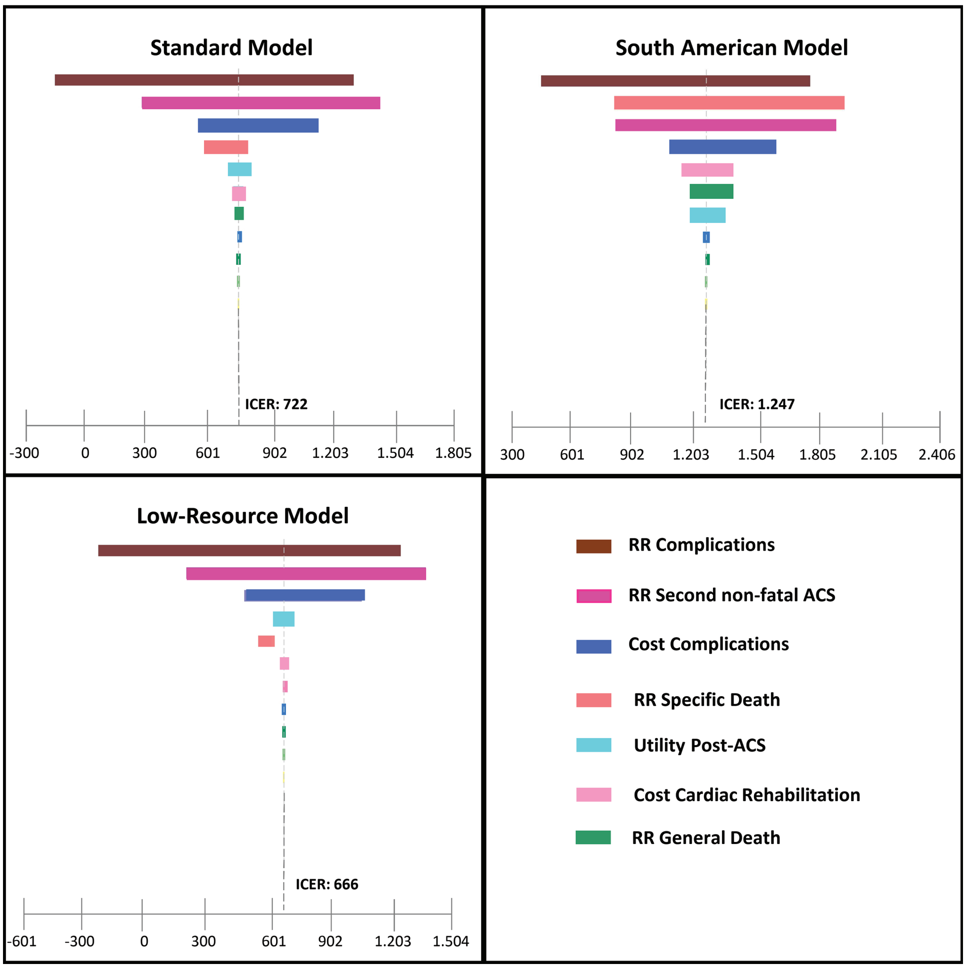

Figure 2. Tornado graph for 1-way sensitivity analysis in the 3 exercise-based cardiac rehabilitation models. ACS indicates acute coronary syndrome; ICER, incremental cost-effectiveness ratio; RR, relative risk.

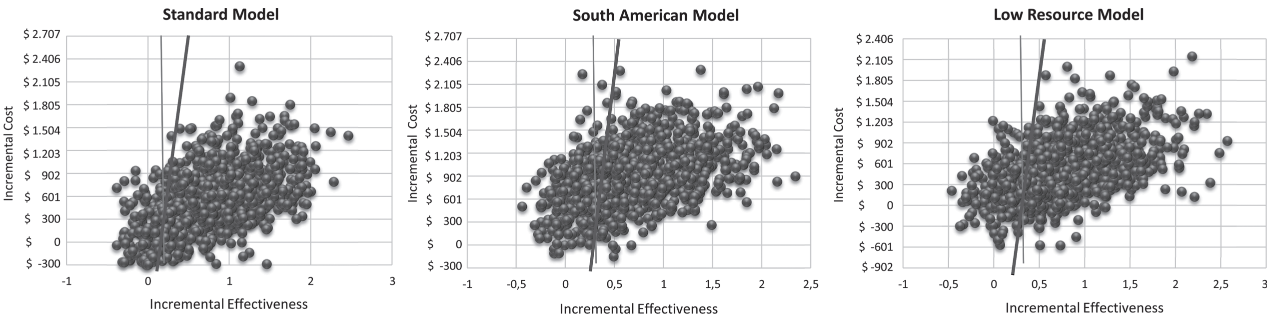

Figure 3. Incremental cost-effectiveness of exercise-based cardiac rehabilitation versus standard care. Scatter plot from the probabilistic analysis for the 3 models.

With respect to the costs estimated of 1 exercise-based CR program for 1 patient, which range from $58 in the low-resource model to $486 in the South American model, it is necessary to mention that the cost of CR delivery is widely variable around the world. According to a recent review, costs in high-income countries ranged from $294 in the United Kingdom to $12 409 in Italy, and from $146 in Venezuela to $1095 in Brazil in middle-income countries. These differences were explained principally by differences related to facilities, personnel involved, and session dose.[50] In the present economic evaluation, we did not include drug therapy in the cost determination because this is part of usual care. If drug therapy were to be included, the CR cost in the standard model could increase to almost $1500, making it comparable to programs in other countries.

In addition, it should be noted that in 2014, the per capita health expenditure in Chile was approximately $1750, equivalent to 7.8% of the gross domestic product. In this context, and given the results of this study, a budget impact analysis needs to be conducted to estimate the proportion of expenditure if exercise-based CR were incorporated into the country's health system.

This study had limitations and strengths. First, it is important to note that secondary data were combined with information obtained from the national reality in a theoretical model. The secondary data were specifically those that facilitated the probabilities of transition between the different health states of the model, for which the patient and treatment characteristics are similar to those in Chile, even though the studies were conducted out in other regions. Although the studies were clinical trials, a weakness of this study was that these inputs spread uncertainty across the model. Nevertheless, sensitivity analyses showed the forcefulness of our results. In this regard, note that given the Cochrane review on the subject, the decision was made to include only the primary studies carried out after the implementation of thrombolysis as the first-line medical treatment of ACS patients in an attempt to homogenize the study population and make the data more representative of the current medical approach to coronary events. This also made the analysis more conservative, since the studies conducted before 1990 showed greater effectiveness.

The health benefits were assessed in the local context under a rigorous selection process of representative patients for each health state and using the EQ-5D-3L. An additional advantage of utilities generated by using this questionnaire is that comparisons can be made across conditions because the measurement is not disease-specific.[51]

The cost determination for each state in the model was estimated on the basis of the country's pre-established pools of health services, and their sources were recognized in the public health network establishments. The biggest challenge was establishing the cost of exercise-based CR, since it is a complex intervention that does not have a fixed price and involves multiple professionals to include in the labor factor, along with different equipment and monitoring systems. The strength of the study was the microcosting methodology, as well as the incorporation of service implementation costs and a detailed analysis of the indirect costs.

In conclusion, considering the willingness-to-pay threshold in Chile of 1 unit of gross domestic product per capita (about $19 550), 3 CR models are highly cost-effective for the public health system in Chile and should become alternatives worth considering as part of ACS secondary prevention programs.

ACKNOWLEDGMENTS

The authors thank the physiotherapist Manuel Gálvez for coordinating and evaluating patient quality of life, and Mr José Formas, manager of the administrative office in the Complejo Hospitalario San José, for facilitating the cost data collection. Special thanks also go to Dr Ulises Garay from the Instituto de Efectividad Clínica y Sanitaria (IECS) of Buenos Aires for his advice and counsel during the study.

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