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Optimizing Value From Cardiac Rehabilitation: A Cost-Utility Analysis Comparing Age, Sex, and Clinical Subgroups

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Abstract

Objective: To assess the cost utility of a center-based outpatient cardiac rehabilitation program compared with no program within patient subgroups on the basis of age, sex, and clinical presentation (acute coronary syndrome [ACS] or non-ACS).

Methods: We performed a cost-utility analysis from a health system payer perspective to compare cardiac rehabilitation with no cardiac rehabilitation for patients who had a cardiac catheterization. The Markov model was stratified by clinical presentation, age, and sex. Clinical, quality-of-life, and cost data were provided by the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease and TotalCardiology.

Results: The incremental cost per quality-adjusted life-year (QALY) gained for cardiac rehabilitation varies by subgroup, from \$18,101 per QALY gained to \$104,518 per QALY gained. There is uncertainty in the estimates due to uncertainty in the clinical effectiveness of cardiac rehabilitation. Overall, the probabilistic sensitivity analysis found that 75% of the time participation in cardiac rehabilitation is more expensive but more effective than not participating in cardiac rehabilitation.

Conclusion: The cost-effectiveness of cardiac rehabilitation varies depending on patient characteristics. The current analysis indicates that cardiac rehabilitation is most cost effective for those with an ACS and those who are at higher risk for subsequent cardiac events. The findings of the current study provide insight into who may benefit most from cardiac rehabilitation, with important implications for patient referral patterns.

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Patients who experience a cardiac event are at high risk of death and subsequent cardiac events.^{1,2} Cardiac rehabilitation is a multidisciplinary intervention with the overarching purpose of improving the health and quality of life of people who have had a cardiac event.³ Several meta-analyses of randomized clinical trials revealed that completion of a cardiac rehabilitation program may reduce cardiovascular mortality,^{1,4,5} all-cause mortality,^{4,5} the risk of a second cardiac event,⁴ and hospital readmission.¹ However, these analyses do not unilaterally support the effectiveness of cardiac rehabilitation in all clinical situations, with the 95% CIs of the relative risks (RRs)

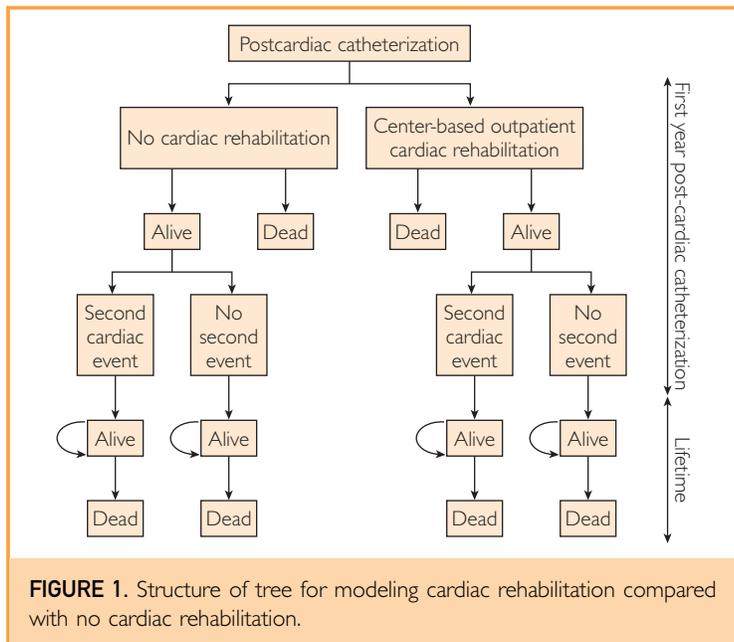
sometimes approaching or including 1.0 (no effect).^{1,4,5}

As with the clinical effectiveness, the cost-effectiveness of cardiac rehabilitation remains equally unclear. In a recent systematic review,⁶ 16 economic evaluations were identified (14 cost-effectiveness studies and 2 cost-utility studies), with some reporting high incremental cost-effectiveness ratios and some reporting cost savings. The 2 existing cost-utility analyses (the most appropriate design to assess the value of cardiac rehabilitation because it measures benefit incorporating both length and quality of life^{7,8} using quality-adjusted life-years [QALYs]) also report conflicting findings. However, they



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adopted different perspectives (societal vs health care payer), were performed in different contexts (Canada vs Hong Kong), were performed on the basis of small sample sizes, are out of date, and do not broadly explore the costs and benefits of rehabilitation in a variety of cardiac population subgroups.

The objective of this study was to assess the cost-utility of a center-based outpatient cardiac rehabilitation program compared with no program in patients who have undergone a cardiac catheterization. The secondary objective was to determine the cost utility of a center-based outpatient cardiac rehabilitation within patient subgroups on the basis of age, sex, and clinical presentation (with or without acute coronary syndrome [ACS]).

METHODS

Study Design

The cost per QALY gained was the primary outcome. A Markov model compared center-based outpatient cardiac rehabilitation (hereafter referred to as *cardiac rehabilitation*) vs no cardiac rehabilitation for patients who have undergone a cardiac catheterization (Figure 1). A cycle length of 1 year was used. The model was stratified by age (<65, 65-74, >75 years), clinical presentation (with or without ACS), and sex to capture

the differential risks of clinical events across the patient population. A health system payer perspective and a lifetime horizon were adopted. A discount rate of 5% was used for all cost and effectiveness estimates.⁹ The cost per QALY was calculated using the standard approach: $(\text{cost}_1 - \text{cost}_2) / (\text{effectiveness}_1 - \text{effectiveness}_2)$. STATA software, version 12 (StataCorp), was used for all statistical analysis, and TreeAge Pro 2012 (TreeAge Software Inc) was used for economic modeling.

Target Population and Data Sources

The Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) database provided short- and long-term clinical and quality-of-life data. APPROACH was established in 1995 as a prospective, ongoing data collection initiative. This database captures data from all patients undergoing cardiac catheterization in Alberta, a province in Canada of approximately 4 million people.¹⁰ APPROACH uses a rigorous protocol for data collection and verification that ensures the highest quality of data is maintained. In routine comparison with medical record reviews, APPROACH has an error rate of less than 5%, and data are missing less than 1% of the time. Alberta has a relatively stable population, with less than 1% outmigration each year, so patients are generally not lost to follow-up. Full methodologic details of the APPROACH database are reported in the article by Ghali et al.¹⁰ APPROACH data on all patients undergoing a cardiac catheterization for myocardial infarction or stable or unstable angina from January 1, 2002 to January 1, 2013 were used in this analysis.

RISK OF DEATH AND SECOND EVENT

The probability of death and the probability of having a second cardiac event in the year after cardiac catheterization were calculated for each age, sex, and clinical presentation subgroup, using the APPROACH database. A second event was defined as any percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), or catheterization completed between 90 and 365 days after the index catheterization. Kaplan-Meier survival analysis was used to calculate the long-term annual risk of death for each age, sex, and clinical presentation subgroup. The RR of death (0.82; 95% CI, 0.67-1.01) and the RR of second event (0.97; 95% CI,

0.77-1.23) reported in a recent meta-analysis¹ were applied to the death and second event rates to simulate the effect of cardiac rehabilitation.

Utility Estimates

For each subgroup, 1-year postcatheterization utility scores were calculated using the EuroQol-5D-3L (EQ-5D) collected routinely through the APPROACH database at 1, 3, and 5 years after catheterization. The EQ-5D includes 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety and depression.¹¹ These domains are combined using an algorithm¹² to produce an overall utility index score on a scale of 0 (very poor health) to 1 (full health).¹¹

Costs

Cost of providing cardiac rehabilitation, cost for the first year after cardiac catheterization for those who do and those who do not have a second cardiac event, subsequent annual cost of care, and the cost of treating patients who die were included. All of these costs were obtained from previously published estimates.¹³ Cost per patient of providing cardiac rehabilitation was obtained from the TotalCardiology Rehabilitation and Risk Reduction program, which is a functioning cardiac rehabilitation facility that provides cardiac rehabilitation to approximately 1000 patients per year. Costs such as those attributed to salaries, employee benefits, professional development, office supplies, medical supplies, and exercise equipment, as well as overhead costs, such as annual facility, advertising, technology, insurance, and electricity costs were included. Annual costs from 2005 to 2009 were averaged to obtain a robust estimate of the mean cost of cardiac rehabilitation per patient. All costs were inflated to 2012 Canadian dollars using the *Consumer Price Index*.¹⁴

Uncertainty

To investigate areas of uncertainty in the model, 1-way sensitivity analyses, scenario analyses, and probabilistic sensitivity analyses were conducted. The 1-way sensitivity analyses varied rehabilitation program costs, RRs, discount rates, duration of effect, and time to commencing cardiac rehabilitation. Rehabilitation program costs were varied within $\pm 50\%$ of the mean value observed by TotalCardiology (lower: \$1216,

upper: \$3650) to reflect differences on the basis of staffing, equipment, setting, and location. The RRs of death and second event were varied within the 95% CIs. Discount rates were varied from 0% to 3%. Given the uncertainty in the duration of effectiveness of cardiac rehabilitation, the length of effectiveness was varied from 1 year in the base case to 5 years in a patient's lifetime. The time from referral to program commencement is likely to vary. Thus, we completed sensitivity analyses considering commencement of cardiac rehabilitation 30 days after the event (risk of death excluded deaths within 30 days of initial catheterization), 60 days after the event (risk of death excluded deaths within 60 days of initial catheterization), and 90 days after the event (risk of death excluded deaths within 90 days of initial catheterization).

In addition, a scenario analysis was completed to model the cost utility of a functioning cardiac rehabilitation program. The same linked and propensity-matched data set as previously reported in the article by Martin et al¹⁵ was used to calculate the RRs of death and second event on an observational cohort of patients undergoing cardiac rehabilitation propensity matched to those who did not undergo cardiac rehabilitation obtained from TotalCardiology. Briefly, using a nonparsimonious regression model, patients undergoing cardiac rehabilitation were matched 1 to 1 to those who did not participate in cardiac rehabilitation on the basis of age, sex, chronic obstructive pulmonary disease, cerebrovascular disease, elevated creatinine level, congestive heart failure, dialysis, hypertension, hyperlipidemia, diabetes mellitus, malignant tumor, current smoking status, former smoking status, prior myocardial infarction, prior PCI, prior CABG, peripheral vascular disease, liver or gastrointestinal disease (any), Duke jeopardy score, ejection fraction, coronary anatomy, interventions (PCI within 1 year of referral, CABG within 1 year of referral), and socioeconomic status (quintile of income). Balance was achieved in the matched groups with a standardized differences between groups for less than 10%.¹⁵

Last, a probabilistic sensitivity analysis was conducted. In this analysis, sensitivity analysis, costs, clinical risks, RRs, and utilities for all subgroups were simultaneously varied. Following best practice guidelines, log-normal distributions

TABLE 1. Cost-Utility Results Comparing Cardiac Rehabilitation and No Cardiac Rehabilitation

| Group | Cost (\$) | Incremental cost (\$) | Effectiveness (QALYs) | Incremental effectiveness (QALYs) | Incremental cost-effectiveness ratio (\$/QALY) |
|---|-----------|-----------------------|-----------------------|-----------------------------------|--|
| Overall | | | | | |
| No rehabilitation | 43,179.57 | ... ^a | 9.70 | ... | ... |
| Rehabilitation | 45,792.91 | 2613.34 | 9.77 | 0.07 | 37,662.00 |
| All patients with ACS | | | | | |
| No rehabilitation | 42,310.08 | ... | 9.51 | ... | ... |
| Rehabilitation | 44,975.61 | 2665.53 | 9.59 | 0.08 | 32,178.75 |
| All men with ACS | | | | | |
| No rehabilitation | 42,759.39 | ... | 9.90 | ... | ... |
| Rehabilitation | 45,398.13 | 26,398.74 | 9.98 | 0.08 | 32,949.38 |
| Men with ACS younger than 65 years | | | | | |
| No rehabilitation | 45,852.59 | ... | 11.26 | ... | ... |
| Rehabilitation | 48,390.01 | 2537.42 | 11.31 | 0.05 | 50,237.56 |
| Men with ACS 65-74 years old | | | | | |
| No rehabilitation | 40,136.19 | ... | 8.75 | ... | ... |
| Rehabilitation | 42,845.39 | 2709.20 | 8.85 | 0.10 | 26,082.83 |
| Men with ACS 75 years or older | | | | | |
| No rehabilitation | 34,377.52 | ... | 6.22 | ... | ... |
| Rehabilitation | 37,315.54 | 2938.01 | 6.38 | 0.16 | 18,101.74 |
| All women with ACS | | | | | |
| No rehabilitation | 41,220.82 | ... | 8.57 | ... | ... |
| Rehabilitation | 43,951.31 | 2730.49 | 8.66 | 0.09 | 30,507.15 |
| Women with ACS younger than 65 years | | | | | |
| No rehabilitation | 45,049.92 | ... | 10.07 | ... | ... |
| Rehabilitation | 47,610.47 | 2560.55 | 10.12 | 0.05 | 49,044.73 |
| Women with ACS 65-74 years old | | | | | |
| No rehabilitation | 40,666.94 | ... | 8.52 | ... | ... |
| Rehabilitation | 43,379.58 | 2712.64 | 8.62 | 0.10 | 27,519.07 |
| Women with ACS 75 years or older | | | | | |
| No rehabilitation | 35,211.31 | ... | 6.05 | ... | ... |
| Rehabilitation | 38,255.82 | 3044.51 | 6.20 | 0.14 | 21,151.82 |
| All individuals without ACS | | | | | |
| No rehabilitation | 44,809.12 | ... | 10.04 | ... | ... |
| Rehabilitation | 47,324.64 | 2515.52 | 10.09 | 0.04 | 56,925.48 |
| All men without ACS | | | | | |
| No rehabilitation | 44,861.93 | ... | 10.23 | ... | ... |
| Rehabilitation | 47,372.95 | 2511.01 | 10.28 | 0.05 | 55,174.42 |
| Men without ACS younger than 65 years | | | | | |
| No rehabilitation | 47,049.88 | ... | 11.25 | ... | ... |
| Rehabilitation | 49,517.43 | 2467.56 | 11.28 | 0.03 | 75,753.43 |
| Men without ACS 65-74 years old | | | | | |
| No rehabilitation | 43,464.19 | ... | 9.56 | ... | ... |
| Rehabilitation | 45,987.45 | 2523.26 | 9.61 | 0.05 | 49,471.90 |
| Men without ACS 75 years or older | | | | | |
| No rehabilitation | 39,105.33 | ... | 7.63 | ... | ... |
| Rehabilitation | 41,763.95 | 2658.62 | 7.71 | 0.09 | 31,099.69 |
| All women without ACS | | | | | |
| No rehabilitation | 44,675.27 | ... | 9.56 | ... | ... |
| Rehabilitation | 47,202.21 | 2526.94 | 9.61 | 0.04 | 61,870.91 |
| Women without ACS younger than 65 years | | | | | |
| No rehabilitation | 47,081.06 | ... | 10.55 | ... | ... |
| Rehabilitation | 49,550.34 | 2469.728 | 10.58 | 0.02 | 104,518.61 |
| Women without ACS 64-74 years old | | | | | |
| No rehabilitation | 44,180.38 | ... | 9.50 | ... | ... |

Continued on next page

TABLE 1. Continued

| Group | Cost (\$) | Incremental cost (\$) | Effectiveness (QALYs) | Incremental effectiveness (QALYs) | Incremental cost-effectiveness ratio (\$/QALY) |
|--|-----------|-----------------------|-----------------------|-----------------------------------|--|
| Women without ACS 64-74 years old, continued | | | | | |
| Rehabilitation | 46,710.37 | 2529.99 | 9.54 | 0.04 | 56,335.14 |
| Women without ACS 75 years or older | | | | | |
| No rehabilitation | 39,304.39 | ... | 7.12 | ... | ... |
| Rehabilitation | 41,974.86 | 2670.47 | 7.20 | 0.08 | 34,065.37 |

^aEllipses indicate data not applicable.

ACS = acute coronary syndrome; QALY = quality-adjusted life-year.

were used for costing estimates and RRs, whereas normal distributions were used for utilities, survival estimates, and clinical probabilities.¹⁶ A total of 5000 simulations were completed.

RESULTS

Model Validity

The validity of the decision model was assessed in accordance with published guidelines.⁹ Technical accuracy and internal validity was assessed by systematically modifying each input using extreme and null values to ensure the model was responding properly. Outcomes were assessed for external validity by comparing the costs per QALY found in this analysis with the costs per QALY reported in existing cost-utility analyses.^{17,18}

Patient Cohort

The clinical inputs were calculated using a cohort of myocardial infarction or stable or unstable angina patients (n=121,763) captured in the APPROACH database (total N=139,866), 71.1% of whom were male. The mean (SD) age of the cohort was 62.9 (11.9) years. This cohort is composed of 65.2% of patients with ACS and 34.8% of patients without ACS.

Clinical probabilities, utility inputs, and costs are presented in Supplemental Tables 1 and 2, respectively (available online at <http://www.mayoclinicproceedings.org>). The long-term survival, by subgroup, is presented in Supplemental Figure 1 (available online at <http://www.mayoclinicproceedings.org>). As expected, the probability of death 1 year after a cardiac event was higher for older patients, and individuals with ACS were more likely to die than those without ACS conditions

(7.0% vs 3.3%). Similarly, the survival analyses reveal that older persons are more likely to die (10-year risk of death: 12.7% for those <65 years old, 27.0% for aged 65-75 years, and 48.1% for >75 years old). The utility scores were higher for individuals who did not have a second event compared with those who did (0.82 vs 0.78).

Base-Case Results

The results from the base-case analysis are presented in Table 1. Overall, the cost for patients who do not participate in cardiac rehabilitation is \$43,180 compared with \$45,793 for the same population who go through a rehabilitation program (a cost differential of \$2613). Although the cardiac rehabilitation program strategy is more expensive, it results in more QALYs gained (9.77 vs 9.70), producing an incremental cost of \$37,662 per QALY gained.

The cost and utility of cardiac rehabilitation varied within the sex, age, and clinical presentation subgroups; the incremental cost per QALY gained ranged from \$18,102 for men with ACS older than 75 years to \$104,519 for women without ACS younger than 65 years. Broadly, cardiac rehabilitation was more economically attractive for individuals with ACS when compared with those without ACS and individuals who were older (Table 1).

The results of the 1-way sensitivity analysis are presented by subgroup in Table 2. When program costs were varied from \$1216 to \$3650, the cost-effectiveness ranged from \$10,602 to \$156,023 cost per QALY gained. As expected, higher cost per QALYs were associated with higher program costs. When all utilities were

TABLE 2. One-Way Sensitivity Analysis Results Comparing Cardiac Rehabilitation and No Cardiac Rehabilitation

| Variable | Costs for patients with ACS by age (y) and sex, CAN \$ | | | | | | Costs for patients without ACS by age (y) and sex, CAN \$ | | | | | |
|--|--|---------|--------|--------|--------|--------|---|-----------|--------|--------|--------|--------|
| | <65 | | 65-75 | | >75 | | <65 | | 65-75 | | >75 | |
| | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| Base case | 50,237 | 49,044 | 26,082 | 27,519 | 18,101 | 21,151 | 75,753 | 104,518 | 49,471 | 56,335 | 31,099 | 34,065 |
| Program costs | | | | | | | | | | | | |
| High | 74,328 | 72,351 | 37,797 | 39,863 | 25,598 | 29,605 | 113,108 | 156,022 | 73,328 | 83,429 | 45,333 | 49,587 |
| Low | 26,138 | 25,730 | 14,364 | 15,170 | 10,602 | 12,695 | 38,385 | 52,997 | 25,607 | 29,231 | 16,861 | 18,538 |
| RR of death | | | | | | | | | | | | |
| Upper 95% CI | Dominated | | | | | | | | | | | |
| Lower 95% CI | Dominated | | | | | | | | | | | |
| RR of 0.82 sustained for 5 years | Dominated | | | | | | | | | | | |
| RR of 0.82 sustained for lifetime | Dominated | | | | | | | | | | | |
| Probability of death within 1 year | Dominated | | | | | | | | | | | |
| Probability of death 30-365 days after catheterization | 103,524 | 90,478 | 46,086 | 49,745 | 33,873 | 37,048 | 86,325 | 122,543 | 60,324 | 66,820 | 35,277 | 40,827 |
| Probability of death 60-365 days after catheterization | 118,151 | 103,546 | 56,536 | 60,366 | 36,169 | 46,050 | 93,693 | 142,804 | 66,549 | 74,748 | 39,757 | 47,379 |
| Probability of death 90-365 days after catheterization | 132,103 | 113,491 | 66,679 | 70,628 | 43,500 | 55,434 | 104,517 | 157,361 | 73,897 | 82,439 | 47,570 | 54,685 |
| RR for second event | | | | | | | | | | | | |
| Upper 95% CI | 100,036 | 95,282 | 28,157 | 28,645 | 17,512 | 23,018 | 98,1996 | Dominated | 64,011 | 79,258 | 32,342 | 34,343 |
| Lower 95% CI | 34,463 | 34,307 | 24,438 | 26,587 | 18,648 | 19,769 | 38,509 | 48,698 | 39,363 | 43,854 | 29,882 | 33,799 |
| Discount | | | | | | | | | | | | |
| None | 29,255 | 28,944 | 17,040 | 17,788 | 12,513 | 14,540 | 43,978 | 57,993 | 31,285 | 33,559 | 20,329 | 23,137 |
| 3% rate | 41,194 | 40,402 | 22,271 | 23,401 | 15,778 | 18,398 | 62,090 | 84,304 | 41,813 | 46,611 | 26,612 | 29,510 |
| 6% rate | 55,010 | 53,596 | 28,056 | 29,658 | 19,287 | 22,560 | 82,957 | 115,265 | 53,439 | 61,421 | 33,395 | 36,405 |
| Utilities | | | | | | | | | | | | |
| Set to 1.0 | 45,643 | 40,615 | 22,985 | 22,716 | 15,069 | 15,540 | 71,264 | 87,518 | 44,261 | 45,729 | 26,114 | 26,231 |

ACS = acute coronary syndrome; RR = relative risk.

set to 1 (full health), the cost per life-year gained ranged from \$15,069 to \$87,518.

When the lower 95% CI for RR of death (0.67) was used, the cost per QALY gained decreased compared with the base case (range, \$11,291-\$62,432). When the upper 95% CI was used with the RR of death (1.01), cardiac rehabilitation was less effective and more costly than no cardiac rehabilitation (dominated) in 10 of the 12 subgroups. Only in non-men with ACS younger than 65 years and women did cardiac rehabilitation remain a more effective option, although with substantially higher costs per QALYs gained. Incorporating the RR of death (0.82) for 5 years in patients who underwent cardiac rehabilitation resulted in a decreased cost per QALY gained (range, \$6409-\$24,800) compared with the base case. When the RR of death was incorporated throughout the lifetime of those who underwent cardiac rehabilitation, the cost per QALY gained lowered further (range, \$5169-\$11,515).

When the RR of the second event was reduced to the lower 95% CI bound (0.77), the cost per QALY gained decreased compared with the base case (range, \$18,648-\$48,698). When the RR of the second event was increased to the upper 95% CI bound (1.23), in women without ACS younger than 65 years cardiac rehabilitation was dominated, and the other groups ranged from \$17,512 to \$100,036.

When deaths 30, 60, and 90 days after cardiac catheterization were excluded to simulate different time-to-referral patterns, cardiac rehabilitation became less economically attractive. The cost per QALY gained varied from \$33,874 to \$122,543 with a 30-day referral, \$36,169 to \$142,805 with a 60-day referral, and \$43,501 to \$157,362 with a 90-day referral.

For the scenario analysis simulating a real-world cardiac rehabilitation program, the propensity matched RR of the second event was 0.67 (95% CI, 0.54-0.81), and the RR of death was 0.99 (95% CI, 0.86-1.18). Compared with no rehabilitation, cardiac rehabilitation had an incremental cost per QALY gained of \$22,481. Cardiac rehabilitation was most economically attractive in men with ACS older than 75 years (cost of \$11,294 per QALY gained), whereas women without ACS younger than 65 years had the highest cost per QALY gained (\$67,055). Similar to the base case, cardiac rehabilitation was a more economically

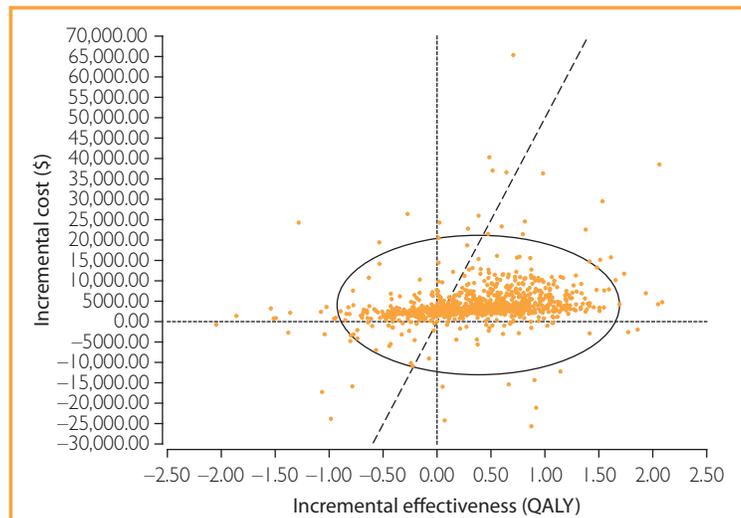


FIGURE 2. Monte Carlo incremental scatterplot showing the probabilistic sensitivity analysis of cardiac rehabilitation compared with no cardiac rehabilitation. QALY = quality-adjusted life-year.

attractive option for those with ACS and for older individuals.

Probabilistic Sensitivity Analysis

The incremental-effectiveness scatterplot of cardiac rehabilitation vs no cardiac rehabilitation is presented in Figure 2, with each point representing one simulation. This analysis reveals that cardiac rehabilitation will be more effective and more expensive 74.8% of the time. Cardiac rehabilitation will be more expensive and less effective 18.6% of the time, more effective and less expensive 3.5% of the time, and less expensive and less effective 3.1% of the time.

DISCUSSION

We found that cardiac rehabilitation resulted in greater cost but improved clinical outcomes compared with no cardiac rehabilitation for patients who have undergone cardiac catheterization. Considering a health system payer perspective, the overall cost per QALY gained associated with cardiac rehabilitation was \$37,662. Among the subgroups assessed in the current study, this cost varied widely: from \$18,102 to \$104,519 per QALY gained, depending on age, clinical presentation and sex. Broadly, cardiac rehabilitation provides better value for money for individuals who had an ACS and are older.

Program costs, RR of death, RR of second event, discount rates, probability of death in the first year, and utility estimates affected the cost-effectiveness of cardiac rehabilitation in the 1-way sensitivity analysis. Notably, when RR of death and second event were varied, cardiac rehabilitation became dominated in some subgroups; when the RR is greater or equal to 1.0, cardiac rehabilitation was more costly but no more effective than no cardiac rehabilitation. Given that the 95% CIs associated with both the RR of death and second event include 1.0, cardiac rehabilitation may represent an investment that does not offer additional clinical benefit to all patients. The probabilistic sensitivity analysis reveals this is the likely case 18.6% of the time for patients overall.

The scenario analysis modeling the cost utility of an operational real-life cardiac rehabilitation program found cardiac rehabilitation to have an incremental cost-utility ratio of \$22,482 per QALY gained. Subgroups in the scenario analysis ranged from \$11,294 to \$67,055 per QALY gained, on the basis of age, sex, and clinical presentation. This analysis provides confidence that our results are not limited to experimental settings and are generalizable to practice.

It has been documented that older individuals are the less likely to attend cardiac rehabilitation.¹⁹⁻²² Given that our study indicates that cardiac rehabilitation is more economically attractive in older patients, continued efforts to increase the referral and participation of older adults is required. This will require an understanding of the barriers to participation and innovative patient-focused approaches to overcome the identified barriers for this subgroup.

Our analysis is the largest to date, uses the longest follow-up, and uniquely incorporates subgroups to identify patients who may benefit most from cardiac rehabilitation. Compared with the 2 other cost-utility analyses in the literature, by Yu et al¹⁸ and Oldridge et al¹⁷, we found a higher cost per QALY gained. Because of differences in sample size, perspective, currency, included costs, and year, the estimates of the previous cost-utility analyses are not easily comparable to the results of this cost-utility analysis. For example, when the cost per QALY gained found by Oldridge et al is adjusted for inflation, it becomes similar to the cost per QALY gained in the current analysis (\$9200 in 1993 Canadian

dollars, inflated to approximately \$13,500 in 2012 Canadian dollars).¹⁷ In addition, the current analysis includes overhead costs (eg, electricity, rent), unlike previous cost-utility analyses on cardiac rehabilitation, which could account for the higher cost per QALY gained.

Like most health care interventions, cardiac rehabilitation requires an investment to improve clinical outcomes; rarely does a health care intervention improve outcomes and save money. However, the cost per QALY gained for cardiac rehabilitation compared with no intervention is similar to that of other technologies that are funded within many health care systems. For example, published estimates for coronary artery bypass surgery range from CAN \$13,200 to \$100,000 per QALY gained,^{23,24} and cardiac defibrillators when implanted in cardiac arrest survivors with a low ejection fraction are an estimated CAN \$75,000 per QALY gained.²⁵

Others have argued that cardiac rehabilitation in its current form is unsustainable because of, among other barriers, affordability.²⁶ Within the context of a fixed health care budget, it is important to consider the opportunity cost (the health benefit that could have been derived from funding the next best alternative) associated with programs.²³ There is an increasing body of literature documenting that factors other than the cost per QALY are valued in funding decisions. These factors include (1) whether an intervention is immediately lifesaving and, less so, the expected gain in life expectancy, (2) the effect on quality of life, (3) the number of people eligible for treatment, (4) the age of the potentially treatable patients (younger vs older), (5) whether the treatment was for people with good or poor underlying baseline health, (6) the likelihood of the treatment being successful, and (7) its effect on equality of access to therapy.²⁷⁻²⁹ Applying this checklist to cardiac rehabilitation, one could make the case that increasing the focus of cardiac rehabilitation toward those with ACS and those at higher risk of subsequent events is an attractive option because it would direct resources toward those likely to achieve the greatest effect on quality of life, those with lower underlying health, and those with the greatest capacity to benefit.

Several limitations merit comment. Our model simulates the effect of cardiac rehabilitation on patients undergoing cardiac catheterization, a subset of patients who may undergo cardiac rehabilitation. Our findings may not apply to other

subgroups of patients, such as those with congestive heart failure or myocardial infarction who do not undergo catheterization, because they may benefit differentially from cardiac rehabilitation. We chose to examine the effect of cardiac rehabilitation on second cardiac events and death. This model, therefore, does not intend to capture all the benefits that may be associated with cardiac rehabilitation. Any other effects on quality of life are not directly included in the model. For example, the effect of cardiac rehabilitation on other possible comorbidities, such as diabetes or obesity, was not modeled directly. However, some of the effect on these other comorbidities will have been indirectly modeled because the patients enrolled in the randomized clinical trials, which informed the estimate of clinical effect, may have also had comorbidities. We are unable to distinguish those who underwent cardiac rehabilitation and those who did not within the cohort of APPROACH patients used to calculate the clinical probabilities in the base-case analysis. Thus, the clinical probabilities of death, second event, and quality of life may be overestimates of the true values for patients who do not undergo cardiac rehabilitation. In addition, age, sex, and ACS or non-ACS are fundamental and necessary subgroups to consider; however, other elements, such as comorbidities, self-efficacy, adherence, and attitude toward cardiac rehabilitation, may also affect the effectiveness of cardiac rehabilitation.^{30,31} These were not modeled directly in the current analysis. Last, we did not examine other perspectives that include patient-related health costs; no recent comprehensive patient-related costing data were found in the literature. Future research on patient-related costing data would facilitate the development of models capturing these broader costs.

CONCLUSION

Cardiac rehabilitation appears to be an economically attractive intervention for individuals who have had a cardiac event. The cost per QALY of cardiac rehabilitation is in line with other technologies that are funded within many health care systems. Our findings particularly support the use of cardiac rehabilitation for those older than 75 years and those with ACS. Although reasonable value for money, this intervention does not save costs and does represent an opportunity cost. The

provision of cardiac rehabilitation incurs an up-front investment and is therefore dependent on the availability of additional resources.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at: <http://www.mayoclinicproceedings.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

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