**Supplementary Material Figure 1: Concept of QALY**

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(Source) Takura T. Examining the current state of PCI application in Japan: from the standpoint of medical economics. Coronary Intervention. 2011 Aug;7(5):32-8

**Supplementary Material Table 1: Medical costs and interventional behavior of selected studies by systematic review**

|  |  |  |
| --- | --- | --- |
| 　 | **Cardiac rehabilitation (CR) arm** | **Usual care (UC) arm** |
| **Study** | **Cost (USD)****Intervention** | **Cardiac rehabilitation** | **Investigations, diagnosis** | **Treatment (admission, operation, etc)** | **Total** | **Investigations, diagnosis** | **Treatment (admission, operation, etc)** | **Others** | **Total** |
|
|
| Oldridge, 1993 | Direct cost | Renting space 218.29Equipment 48.17Staff salaries 111.4Community CR 60.22  | Not mentioned | Not mentioned | 438.09 | Not mentioned | Not mentioned | Community care 255.93 | 255.93 |
| Yu, 2004 | Direct cost | Staff salaries 776.6Miscellaneous  4.6 | Coronary angiogram871.8Echocardiography 448.7Holter 118.6Exercise test 553.8Electrocardiogram 140.4Blood test 1013.1Chest X-ray 48.7　 | Admission 3553.6PCI 4885CABG 256.4Private clinic visit　　　　 　　82Public cardiac clinic visit 425.3Public cardiac non clinic visit 146.3 ER 27.4Drugs 1939.6 | 15291.9 | Coronary angiogram 1025.6Echocardiography 448.7Holter 118.6Exercise test 553.8Electrocardiogram 140.4Blood test 1013.1Chest X-ray 48.7 | Admission 2747.0PCI 6481.2CABG 205.1Private clinic visit　　　　 53.5Public cardiac clinic visit 435.2Public cardiac non clinic visit 155.0ER 30.0Drugs 1836.5 | Staff salaries415 | 15707.4 |
| Briffa, 2005 | Direct cost | 6-week package 508.23 | Imaging test  　1666.77Biological test　　 422.55　 | Drugs 487.73Consultation (ER, local doctor, heart specialist, etc) 297.32Ambulance 138.41 | 3521.01 | Imaging test 1652.85Biological test385.2  | Drugs 573.41Consultation (ER, local doctor, heart specialist, etc) 345.66Ambulance 243.13 | Rehabilitation (details unknown) 46.14 | 3245.66 |
| Leggett,2015 | Direct cost | Program cost 1752.32 | Not mentioned | Annual cost of care after first year 2026.01 | 32981.44 | Not mentioned | Not mentioned | Not mentioned | 31099.23 |
| Hautala, 2017 | Direct cost  | Exercise-based cardiac rehabilitation costs 315.18 | Not mentioned | Primary health care costs 376.31Secondary health care costs 1224.86Occupational health care service costs 132.82 | 2168.73 | Not mentioned | Primary health care costs  509.13Secondary health care costs  2613.11Occupational health care service costs  68.52 | Not mentioned | 3376.92 |

**Supplementary Material Table 2: Summaries of selected studies by systematic review**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Year | 1993 | 2004 | 2005 | 2015 | 2017 |
| Author | Oldridge | Yu | Briffa | Leggett | Hautala |
| Country | Canada | China | Australia | Canada | Finland |
| Objective | Effectiveness of cardiac rehabilitation in patients after acute myocardial infarction  | Evaluation of long-term effects of QOL and cost-effective in the CRPP | Effects on cost and QOL by cardiac rehabilitation after acute coronary syndrome | Assess the cost utility of a center-based outpatient CR program compared with no program  | Evaluation of the cost-effectiveness of exercise-based cardiac rehabilitation  |
| Study design | RCT | RCT | RCT | Model analysis | RCT |
| Sample number | CR 99Control 102 | CR 132Control 72 | CR 56Control 57 | ─ | CR 109Control 95 |
| Target disease | Patients diagnosed with acute myocardial infarction within 6 weeks | Patients with recent acute myocardial infarction or percutaneous coronary intervention | Patients with unstable angina or treated for acute myocardial infarction | acute coronary syndrome (ACS) | CAD patients who suffered from acute coronary syndrome (ACS) |
| Age (years ± SD, intervention/control) | 53 ± 9.5/53 ± 9.5 | 64 ± 11/64 ± 11 | 61 ± 8.7/62 ± 9.4 | ─ | 60 ± 11/62 ± 9 |
| Sex（number of males, rehabilitation/control） | 87/90 | 138/66 | 42/41 | ─ | 80/67 |
| Intervention | Cardiac rehabilitation program (8 weeks)・Supervised exercise therapy ・Risk management counseling | CRPP 7 to 14 days Phase 2:outpatient education and exercise program，twice-weekly・8 weeks Phase 3:community-based home exercise program，6 months Phase 4:long-term maintenance，until the end of second years | Start within 2 weeks of leaving hospital, thrice-weekly, 6-week package60～90 minutes/time (exercise, education, counseling) | Center-based outpatient cardiac rehabilitation | During the first six months, once a week they visited our Cardiac Rehab gym, where they were individually guided in both gym and home-based exercise training by a physical therapist. Dietary counseling for each patient or a checkup by a medical doctor when appropriate. |
| Control | Usual medical treatment (includes rehabilitation in community) | Phase 1 only: inpatient ambulating program，7 to 14 days (2-hour talk with therapist, medication prescription) | Usual medical treatment (includes rehabilitation in community) | No cardiac rehabilitation | No individually tailored exercise prescriptions. |
| Subgroup analysis | ─ | ・age・sex・result of laboratory test | ─ | ・age・sex・clinical presentation(with or without ACS) | ─ |
| Evaluation period | 1 year | 2 years | 1 year | 1 year | 1 year |
| Setting of hypothesis | ─ | ─ | ─ | ─ | ─ |
| Considered cost1) CR cost (exercise therapy-relate cost)2) Additional cost (test, diagnosis and prescription for pre/post CR)3) Readmission and retreatment cost 4) Cost of other program・additional home care 5) Others (loss in income, etc) | [Cost basis]1) 4) Staff cost，depreciation costOther cost (renting space, patient-borne cost)【Medical fee basis】2) Cost of investigation | [Cost basis]1) 4) Staff cost，depreciation cost2) 3) Other medical cost Cost of investigation，admission，urgent admission，operation，medication | [Cost basis]1) 4)Staff cost，material cost【Medical fee basis】2) 3) Cost of admission, prescription，clinical examination，investigation: medical care service | [Cost basis]1)Cost of providing cardiac rehabilitation3)Cost for the first year after cardiac catheterizationfor those who do and those who do nothave a second cardiac event, subsequentannual cost of care, and the cost of treatingpatients who die | [Cost basis]1) 4)Staff cost，material cost2) 3) primary health care cost, secondary health care cost, Occupational health care service costs |
| Rationale of cost calculation | ・Rehabilitation cost: statistical data・Patient’s own expense: estimated by actual condition | ・Cost of rehabilitation, admission: published by hospital・Cost of drugs: local drug formulary ・Private practitioner: patient’s self-report | ・DRG・Schedule of Pharmaceutical Benefits・Questionnaire to patients and physicians ・Health system perspectives | ・APPROACH database・Total Cardiology Rehabilitation and Risk Reduction Program: salaries,employee benefits, professional development, office supplies, medical supplies, and exerciseequipment, overhead costs ( annual facility, advertising, technology, insurance, and electricity costs) | ・DRG・Registries・Report of the Social Insurance Institute of Finland |
| Modeling | No difference in survival rate between intervention arm and control arm | Use Kaplan-Meier survival analysis for calculation of mortality | Use Quality Adjusted Survival Analysis (QASA) for calculation of survival years (under investigation) | Markov model | Use Kaplan-Meier survival analysis to examine differences in cumulative major adverse cardiac event |
| Evidence review | ─ | ─ | ─ | ─ | ─ |
| Outcome index | ・QALY・Mortality・Work status・ICUR・Frequency of health care resource use | ・QALY・SF-36・ICUR | ・QALY・SF-36・ICUR | ・QALY・ICUR | ・QALY・15D・ICUR |
| Method of utility calculation | Time Trade-off Use mortality rate reported by meta-analysis | Time Trade-off  | UBQ-H(Utility Based Quality of life-Heart; disease-specific questionnaire that contains TTO) | EQ-5D-3L | 15D questionnaire (consists of fifteen dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity) |
| Method of cost-effectiveness analysis | ICUR | ICUR | ICUR | ICUR | ICUR |
| Discount rate of cost | 5% / year | ─ | ─ | 5% / year | ─ |
| Discount rate of outcome | 5% / year | ─ | ─ | 5% / year | ─ |
| Cost of intervention | 480 $ (1 year)※difference only | 15,291 $ (2 years) | 4,937 $ (1 year) | 45,792.91 $ (1 year) | 2168.73 $ (1 year) |
| Outcome of intervention | 0.071 (QALY, 1 year)※difference only | 0.6(QALY, survival duration)※difference only (compared with baseline) | 0.0092886 (QALY, 1 year)※difference only | 9.77 (QALY, 1 year) | 0.013 (QALY, 1 year) |
| Cost of control | ※difference only | 15,707 $ (2 years) | 4,541 $ (1 year) | 43,179.57 $ (1 year) | 3376.92 $ (1 year) |
| Outcome of control | ※difference only | ※difference only (compared with baseline) | ※difference only | 9.70 (QALY, 1 year) | -0.012 (QALY, 1 year) |
| Result of cost-effectiveness analysis | ICUR: 9,200 ($/ Δ QALY) 1 year 6,800 ($/ Δ QALY) 3 years | SF-36:Demonstrated improvement in Phase 2 in patients with CRPP ICUR: - 640 ($/ΔQALY) | ICUR: 42,535 ($/ΔQALY) | 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. | Dominant |
| Sensitivity analysis | Performed using the differences in the lower and upper 95%CI limits of utility score | ─ | Performed one-way sensitivity analysis using the differences in the lower and upper 95%CI limits of ICUR and mortality | Performed 1-way sensitivity analysis and probabilistic sensitivity analysis  | ─ |
| Conclusion | Cardiac rehabilitation is cost-effective in patients after acute myocardial infarction treatment. | Scores on the SF-36 improved from the early period. and it was highly cost-effective in patients with CRPP.  | Rehabilitation showed superiority in improvement of QOL. | Cardiac rehabilitation is most cost effective for those with an ACS and those who are at higher risk for subsequent cardiac events. | Exercise-based cardiac rehabilitation is less costly and more effective than usual care in acute coronary syndrome patients. |
| Generalization | No particular limitation | No particular limitation | No particular limitation | Generalizable to practice | No particular limitation |
| Fiscal impact analysis | ─ | ─ | ─ | ─ | ─ |

RCT, randomized controlled trial

DRG, diagnosis-related group

QALY, quality-adjusted life year

SF-36, 36-Item Short Form Survey

ICUR, incremental cost utility ratio

95%CI, 95% confidence interval

CRPP, Cardiac rehabilitation and prevention program

**Supplementary Material Table 3: Patient characteristics in selected studies by systematic review**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Item** | **CR arm****n (%)** | **UC arm****n (%)** |
| Oldridge, 1993, Canada | **AMI site**AnteriorInferiorPosteriorIndefinite | 36 (36)55 (55) 3 (3) 5 (5) | 34 (33)56 (55) 8 (8) 5 (5) |
| **Previous history**AMI | 17 (17) | 18 (17) |
| Yu, 2004, China | **Indication for CRPP**Myocardial infarctionPCI | 129 (71) 52 (29) | 64 (73)24 (27) |
| **Medications**Thrombolytic therapyAntiplatelet drugsβ-blockersCalcium channel blockersNitratesStatinsACE inhibitorsDiureticsOral hypoglycemics | 61 (49)179 (99)129 (71) 36 (20)106 (59)119 (66)119 (64) 38 (21) 69 (69) | 22 (36)87 (99)66 (75)14 (16)57 (65)49 (56)53 (60)11 (13)39 (78) |
| **Comorbidities**SmokingHypertensionHyperlipidemia Diabetes | 72 (40)84 (46)85 (47)49 (27) | 36 (42)37 (43)39 (45)26 (30) |
| Briffa, 2005, Australia | **Clinical details on index admission**AMIUnstable anginaThrombolytic therapyPCI/CABGPrior AMI,PCI,CABGPrior CR | 21(37)36 (63) 8 (14)34 (60)21 (37) 3 (5) | 27(48)29 (52)14 (25)26 (46)28 (50) 3 (5) |
| **Medications**AspirinAntiarrhythmic agentβ-blockerACE inhibitorCalcium channel blockersLong-acting nitratesDiureticInsulinHypolipidemic agent Oral hypoglycemic  | 53 (93) 3 (5)35 (61)15 (26)15 (26)32 (56) 6 (11) 2 (4)16 (28) 3 (5) | 50 (89) 5 (9)36 (64)17 (30)22 (39)34 (61) 6 (11) 4 (7)12 (21) 3 (5) |
| **Coronary risk factors**\*Family history of coronary artery diseaseHypercholesterolemiaHypertensionCurrent smokerDiabetesObesity | 13 (23)25 (44)25 (44)17 (30) 6 (11) 4 (7) | 13 (23)26 (46)29 (52)20 (36) 9 (16)12 (23) |
| Hautala, 2017, Finland | **History of AMI**NSTEMISTEMI | 47 (48)44 (45) | 45 (58)28 (36) |
| **Revascularization**PCIEarlier CABG | 95 (87)5 (5) | 83 (87)8 (8) |
| **Medications**β-blockerACE inhibitor or ARBLipidsAnticoagulantsCalcium channel blockersNitratesDiuretics | 91 (83)87 (90)95 (98)97 (100)16 (16)21 (22)13 (13) | 83 (87)67 (86)77 (99)77 (99)20 (26)22 (28)17 (22) |

Family history of coronary artery disease: first degree relative aged < 60 years with an acute coronary event

Hypercholesterolemia: total cholesterol level, ≥ 4.5mmol/L

Hypertension: blood pressure, ≥ 140/90 mmHg

Diabetes: fasting plasma glucose level, ≥ 7.8 mmol/L

Obesity: body mass index, > 30 kg·m-2

CR, cardiac rehabilitation

CRPP, cardiac rehabilitation and prevention programs

PCI, percutaneous coronary intervention

CABG, coronary artery bypass grafting

NSTEMI, non-ST segment elevation myocardial infarction

STEMI ST, segment elevation myocardial infarction.