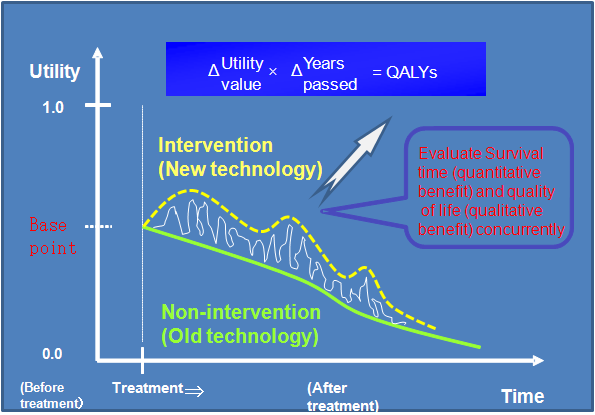
**Supplementary Material Figure 1: Concept of QALY**

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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  218.29  Equipment  48.17  Staff salaries  111.4  Community 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  776.6  Miscellaneous  4.6 | Coronary angiogram  871.8  Echocardiography  448.7  Holter 118.6  Exercise test  553.8  Electrocardiogram  140.4  Blood test  1013.1  Chest X-ray  48.7 | Admission 3553.6  PCI 4885  CABG 256.4  Private clinic visit　　　　 　　82  Public cardiac clinic visit  425.3  Public cardiac non clinic visit  146.3  ER 27.4  Drugs 1939.6 | 15291.9 | Coronary angiogram  1025.6  Echocardiography  448.7  Holter 118.6  Exercise test  553.8  Electrocardiogram  140.4  Blood test  1013.1  Chest X-ray  48.7 | Admission 2747.0  PCI 6481.2  CABG 205.1  Private clinic visit　　　　 53.5  Public cardiac clinic visit  435.2  Public cardiac non clinic visit  155.0  ER 30.0  Drugs 1836.5 | Staff salaries  415 | 15707.4 |
| Briffa, 2005 | Direct cost | 6-week package  508.23 | Imaging test  　1666.77  Biological test  　　 422.55 | Drugs  487.73  Consultation (ER, local doctor, heart specialist, etc)  297.32  Ambulance  138.41 | 3521.01 | Imaging test  1652.85  Biological test  385.2 | Drugs  573.41  Consultation (ER, local doctor, heart specialist, etc)  345.66  Ambulance  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 376.31  Secondary health care costs 1224.86  Occupational health care service costs 132.82 | 2168.73 | Not mentioned | Primary health care costs  509.13  Secondary health care costs  2613.11  Occupational 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 99 Control 102 | CR 132 Control 72 | CR 56 Control 57 | ─ | CR 109 Control 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 package 60～90 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 cost 1) 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 cost Other cost (renting space, patient-borne cost)  【Medical fee basis】 2) Cost of investigation | [Cost basis] 1) 4) Staff cost，depreciation cost 2) 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 rehabilitation  3)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 | [Cost basis] 1) 4)Staff cost，material cost  2) 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 exercise  equipment, 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** Anterior Inferior Posterior Indefinite | 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 infarction PCI | 129 (71)  52 (29) | 64 (73) 24 (27) |
| **Medications** Thrombolytic therapy Antiplatelet drugs β-blockers  Calcium channel blockers Nitrates Statins ACE inhibitors Diuretics  Oral 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** Smoking Hypertension Hyperlipidemia  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** AMI  Unstable angina Thrombolytic therapy PCI/CABG Prior AMI,PCI,CABG Prior 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** Aspirin Antiarrhythmic agent β-blocker ACE inhibitor Calcium channel blockers Long-acting nitrates Diuretic Insulin Hypolipidemic 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 disease Hypercholesterolemia Hypertension Current smoker Diabetes Obesity | 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**  NSTEMI  STEMI | 47 (48)  44 (45) | 45 (58)  28 (36) |
| **Revascularization**  PCI  Earlier CABG | 95 (87)  5 (5) | 83 (87)  8 (8) |
| **Medications**  β-blocker ACE inhibitor or ARB  Lipids  Anticoagulants  Calcium channel blockers Nitrates Diuretics | 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.