# Effect of comprehensive cardiac telerehabilitation on one-year cardiovascular rehospitalization rate, medical costs and quality of life: A cost-effectiveness analysis

Ines Frederix<sup>1,2</sup>, Dominique Hansen<sup>2</sup>, Karin Coninx<sup>3</sup>, Pieter Vandervoort<sup>2,4</sup>, Dominique Vandijck<sup>2</sup>, Niel Hens<sup>5,6</sup>, Emeline Van Craenenbroeck<sup>7</sup>, Niels Van Driessche<sup>2</sup> and Paul Dendale<sup>1,2</sup>



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#### Abstract

Background: Notwithstanding the cardiovascular disease epidemic, current budgetary constraints do not allow for budget expansion of conventional cardiac rehabilitation programmes. Consequently, there is an increasing need for costeffectiveness studies of alternative strategies such as telerehabilitation. The present study evaluated the costeffectiveness of a comprehensive cardiac telerehabilitation programme.

Design and methods: This multi-centre randomized controlled trial comprised 140 cardiac rehabilitation patients, randomized (1:1) to a 24-week telerehabilitation programme in addition to conventional cardiac rehabilitation (intervention group) or to conventional cardiac rehabilitation alone (control group). The incremental cost-effectiveness ratio was calculated based on intervention and health care costs (incremental cost), and the differential incremental quality adjusted life years (QALYs) gained.

**Results:** The total average cost per patient was significantly lower in the intervention group  $(\infty156 \pm \in 126)$  than in the control group (€2720  $\pm$  €276) (p = 0.01) with an overall incremental cost of €–564.40. Dividing this incremental cost by the baseline adjusted differential incremental QALYs (0.026 QALYs) yielded an incremental cost-effectiveness ratio of  $\epsilon$ –21,707/QALY. The number of days lost due to cardiovascular rehospitalizations in the intervention group (0.33  $\pm$  0.15) was significantly lower than in the control group (0.79  $\pm$  0.20) (p  $=$  0.037).

Conclusions: This paper shows the addition of cardiac telerehabilitation to conventional centre-based cardiac rehabilitation to be more effective and efficient than centre-based cardiac rehabilitation alone. These results are useful for policy makers charged with deciding how limited health care resources should best be allocated in the era of exploding need.

#### Keywords

Telerehabilitation, telemonitoring, telecoaching, cost-effectiveness

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6 Centre for Health Economic Research and Modelling Infectious Diseases, Vaccine and Infectious Disease Institute, University of Antwerp, Belgium

<sup>7</sup>Department of Cardiology, Antwerp University Hospital, Belgium

#### Corresponding author:

Ines Frederix, Beatrijslaan 105, 3110 Rotselaar, Belgium. Email: ines.frederix@gmail.com

<sup>&</sup>lt;sup>1</sup>Department of Cardiology, Jessa Hospital, Hasselt, Belgium <sup>2</sup>Faculty of Medicine & Life Sciences, Hasselt University, Belgium <sup>3</sup>Faculty of Sciences, Expertise Centre for Digital Media, Hasselt University, Belgium

<sup>4</sup> Department of Cardiology, Hospital East-Limburg, Genk, Belgium <sup>5</sup>Interuniversity Institute of Biostatistics and Statistical Bioinformatics, Hasselt University, Belgium

# Introduction

According to the European Heart Network's statistics (2012), each year cardiovascular disease (CVD) causes over four million deaths in Europe and over 1.9 million deaths in the European Union, accounting for, respectively, 47% and 40% of all deaths.<sup>1</sup> Following a cardiac event, secondary prevention by means of cardiac rehabilitation is a Class IB recommendation by the European Society of Cardiology (ESC). $<sup>2</sup>$  For heart fail-</sup> ure patients, regular aerobic exercise is encouraged to improve functional capacity and symptoms (Class IA recommendation).<sup>3</sup> Despite the proven clinical effectiveness of conventional centre-based cardiac rehabilitation programmes, $4 \text{ long-term benefits}$  are often disappointing, mainly due to low cardiac rehabilitation uptake and adherence rates. $5$  The escalation of health care costs over the past years, however, has restricted the budget for expansion of cardiac rehabilitation programmes and prompted the need for alternative care strategies. Innovations in telecommunication technologies enabled the advent of cardiac telerehabilitation programmes, in which patients rehabilitate remotely using telemonitoring, telecoaching and e-learning. Two recent systematic reviews on the feasibility, safety and effectiveness of cardiac telerehabilitation showed non-inferiority and/or superiority of this approach, compared with centre-based cardiac rehabilitation. $6,7$  The majority of reviewed studies, however, did not include cost-effectiveness assessment. The Telerehab III trial was a multi-centre prospective, randomized, controlled trial investigating the long-term effectiveness of a patient-specific, comprehensive cardiac telerehabilitation programme, focusing on telemonitoring and telecoaching. As part of this study, cost-utility analysis based on intervention costs, cardiovascular disease related health care costs and healthrelated quality of life was performed. We hypothesized the addition of telerehabilitation to standard cardiac rehabilitation to be cost-effective, when compared with standard cardiac rehabilitation alone. This paper reports on the results from the cost-utility analysis.

# Methods

# Study design

The present study was part of Telerehab III, a multicentre, prospective, randomized, controlled clinical trial, investigating the long-term effectiveness of a comprehensive cardiac telerehabilitation programme at Jessa Hospital (Hasselt), Ziekenhuis-Oost Limburg (Genk) and St Franciscus Hospital (Heusden-Zolder) in Belgium. The study was conducted in accordance with the principles stated in the Declaration of Helsinki (reviewed version of 2008), local and national regulations. All patients provided written informed consent prior to study enrolment. The study protocol was approved by Jessa Ethics Committee (reference number: B243201216043). The protocol has been described in detail elsewhere.<sup>8</sup>

# Study population and randomization

The sample size calculation, based on a 20% effect size for the primary outcome measure with a power  $(1 - \beta)$  of 95%, an  $\alpha$ -error probability of  $< 0.05$  and an expected dropout rate of 30%, resulted in 140 patients being included. Patients were eligible for participation in the study when they entered cardiac rehabilitation for (i) coronary artery disease (CAD) and were treated conservatively, with a percutaneous coronary intervention or with coronary artery bypass grafting; (ii) chronic heart failure (CHF) with reduced ejection fraction (New York Heart Association (NYHA) I, II and III) or (iii) CHF with preserved ejection fraction (NYHA I, II and III) (as defined in the ESC guidelines). Patients were required to have a computer at home with internet access. The main exclusion criteria were (i) CHF NYHA class IV, (ii) symptomatic and/or exercise induced cardiac arrhythmia within the previous six months, (iii) physical disability related to musculoskeletal or neurological problems and (iv) severe cognitive impairment. Eligible patients were randomly assigned (1:1) to internet-based telerehabilitation in addition to centre-based rehabilitation (intervention group) or centre-based rehabilitation alone (control group). A central computerized randomization system, using block randomization, ascertained equal distribution of patients in the different recruiting hospitals for both treatment arms.

# Study intervention

Centre-based cardiac rehabilitation programme. Both groups participated in the 12-week conventional centre-based cardiac rehabilitation programme, including 45 pluridisciplinary rehabilitation sessions with at least two training sessions per week.<sup>9</sup> Patients were instructed to exercise for 45–60 min per session at a target heart rate and/or workload corresponding to an intensity between their first ventilatory threshold  $(VT_1)$  and respiratory compensation point (RCP).<sup>10</sup> Endurance training consisted of walking/running, and/or cycling and arm cranking.

Telerehabilitation programme. Intervention group patients received a 24-week internet-based, comprehensive telerehabilitation programme in addition to the conventional centre-based cardiac rehabilitation.

The telerehabilitation programme started at week six of the centre-based cardiac rehabilitation, allowing the intervention group patients to become familiarized with the telerehabilitation's motion sensor (Yorbody accelerometer) and associated web service during the six-week overlap period. The programme focused on multiple cardiac rehabilitation core components and used both physical activity telemonitoring and dietary/smoking cessation/physical activity telecoaching strategies. For the telemonitoring part, intervention group patients were prescribed with patient-specific exercise training protocols, based on achieved peak aerobic capacity ( $VO<sub>2</sub>$  peak) during initial maximal cardiopulmonary exercise testing  $(CPET)^{11}$  and calculated body mass index  $(BMI)$ .<sup>7</sup> Intervention group patients were instructed to continuously wear the accelerometer and to weekly transmit their registered activity data to the telerehabilitation centre's local server. These data enabled a semi-automatic telecoaching system to provide the patients with feedback, encouraging them to gradually achieve predefined exercise training goals. In addition patients received e-mails and/or SMSs (text messages) with tailored dietary and smoking cessation recommendations, based on cardiovascular risk factor profiling at study start.

#### Cardiovascular rehospitalizations

Rehospitalizations were defined as both emergency visits  $( $24h$ ), hospital admissions ( $> 24h$ ) and day$ procedures. All rehospitalizations (both cardiovascular and non-cardiovascular) were retrieved from the patients' electronic medical files in the recruiting hospitals by the study investigators. They were cross-checked with those on file in the patients' medical insurance records to ascertain accurateness. A Clinical Endpoint Committee (CEC), composed of three independent cardiologists blinded to treatment allocation, classified all rehospitalizations to (non-) cardiovascular and provided physician reported diagnoses. The time to first cardiovascular rehospitalization was calculated as were the number of days lost due to cardiovascular rehospitalizations and the proportion of actual to theoretical maximal days alive and out of hospital.

# Cost-effectiveness

The cost-effectiveness evaluation was conducted from a society and patient perspective, taking into account both intervention and health care resource costs. As the majority of patients was retired, productivity losses due to illness-related absence from the workplace were not estimated.

Intervention costs were those associated with delivering the centre-based cardiac rehabilitation and

telerehabilitation programme. The National Sickness and Invalidity Insurance Institution (INAMI/ RIZIV)'s (dated January 2015) nomenclature-based tariffs were employed to quantify the centre-based cardiac rehabilitation costs (code no. 771212). Expenditure records were used to determine the equipment and consumable resources for telerehabilitation. Health care costs were the aggregated costs of emergency visits, hospital admissions and day procedures for cardiovascular reasons (combined cardiovascular rehospitalizations) and also specialist visits and associated diagnostics. The cardiovascular rehospitalizations' related costs were derived from invoices retrieved from the recruiting hospitals' financial departments. INAMI/RIZIV's nomenclature-based tariffs defined specialist visits and diagnostics denominations.

Quality adjusted life years (QALYs) were used as a generic measure of effectiveness. Estimates of QALYs were derived from the EQ-5D questionnaire,<sup>12</sup> which was completed by participants at baseline, at six weeks and at 24 weeks of follow-up period. The EQ-5D scores were converted to utility scores. The utility estimates were converted to adjusted mean QALYs by calculating the area under the curve (AUC) utility estimates for all time intervals for each patient, weighted by the length of follow-up at that time interval. The change from baseline utility (adjusted differential incremental QALYs) was then calculated, using the multiple regression model to control for baseline utility differences.<sup>13</sup>

The incremental cost-effectiveness ratio (ICER) was calculated  $(ICER = (Cost_{\text{intervention group}} - Cost_{\text{control}}))$ group)/(Effectiveness intervention group – Effectiveness control group)) to compare costs and outcomes (effectiveness) across both treatment groups. The incremental cost was determined by the difference in total average cost per patient between the intervention group and control group. The incremental effectiveness was estimated by the adjusted differential incremental QALYs.

## Statistical analysis

Data analysis was performed using SPSS v. 22 according to the intention-to-treat principle, by assigned treatment group. The Shapiro–Wilk test was used to assess normality. Independent  $t$ -tests and Man– Whitney U tests compared normally and not normally continuous variables between treatment groups respectively. Chi-square tests compared categorical variables between groups, Fisher's exact tests were used when expected frequencies were small. Cumulative survival curves for the time-to-first rehospitalization analyses were made according to the Kaplan–Meier method; the log-rank statistic evaluated the difference between the curves. The Cox regression model was used to estimate the hazard ratio (HR); treatment was the only



Figure 1. Diagram of participant flow through the study.

covariate. Censoring was applied in the case of dropout and when the study terminated before the first event of interest occurred. For the proportion of actual versus theoretical maximal days alive and out of hospital, the theoretical maximal days value was defined from randomization to one year after study completion. In the case of premature dropout, theoretical maximal days were defined up to the censoring date. The significance level for tests was two-sided  $\alpha$  of 0.05.

## Results

A total of 140 patients were enrolled in Telerehab III (.Figure 1). The numbers and reasons for dropout during study period were similar for both treatment groups, with the exception of one intervention patient (diagnosed with non-cardiac related pathology, i.e. lung cancer) who was excluded from final analysis. Baseline demographics, clinical characteristics and cardiovascular medication use were similar between the two groups (Table 1).

## Cardiovascular rehospitalizations

The proportional hazards assumption was valid as assessed using the log–log plot and comparing curves for the different strata. One year after study termination, 23 participants were rehospitalized for cardiovascular reasons (seven in the intervention group, 16 in the control group). The reasons for rehospitalization were in-stent restenosis ( $n = 2$ ), atypical thoracic pain ( $n = 1$ ), ventricular arrhythmia  $(n = 1)$ , supraventricular arrhythmia  $(n = 1)$ , pericarditis  $(n = 1)$  and peripheral artery disease  $(n=1)$  for the intervention group. In the control group, rehospitalizations were due to in-stent restenosis  $(n = 1)$ , acute coronary syndrome  $(n = 2)$ , stable angina  $(n = 6)$ , atypical thoracic pain  $(n = 2)$ , ventricular arrhythmia  $(n = 1)$ , supraventricular arrhythmia  $(n = 1)$ , atrial fibrillation ablation  $(n = 1)$ , cardiac resynchronization therapy – defibrillator (CRT-D) replacement  $(n = 1)$  and peripheral artery disease  $(n = 1)$ . The average (95% confidence interval (CI)) time to first cardiovascular rehospitalization was 502 (469–535) days for the intervention group and 445 (400–491) days for the control group ( $p = 0.045$ ; HR 0.415 (0.170–1.009)) (.Figure 2). The number of days lost due to cardiovascular rehospitalizations in the intervention group  $(0.33 \pm 0.15)$  was significantly lower than in the control group  $(0.79 \pm 0.20)$ ,  $U = 2127$ ,  $z = -2.084$ ,  $p = 0.037$ ,  $r = -0.18$  (i.e. small to medium effect). The proportion of actual to theoretical maximal days alive and out of hospital was significantly higher in the intervention group, compared with the control group,  $U = 2765$ ,  $z = 2.038$ ,  $p = 0.042$ ,  $r = 0.17$  (i.e. small to medium effect).

# Cost-effectiveness

The total average cost per patient (intervention plus health care costs) was significantly lower in the

Table 1. Baseline demographics, clinical characteristics and medication use.

	Intervention group ( $n = 69$ )	Control group $(n = 70)$	Þ
Age, years	$61 \pm 9$	$61 \pm 8$	0.95
Gender			0.38
Female	$14%$ (10)	$21\%$ (15)	
Male	86% (59)	79% (55)	
Type of cardiac pathology			0.53
CAD	94% (65)	93% (65)	
Primary presentation			0.69
<b>STEMI</b>	$31\% (20)$	26% (17)	
<b>NSTEMI</b>	$17%$ (11)	23% (15)	
UA	12% (8)	$8\%$ (5)	
SA	40% (26)	43% (28)	
Primary intervention			0.23
PCI	73% (47)	82% (53)	
CABG	26% (17)	14% (9)	
Conservative therapy	$1\%$ (1)	$4\%$ (3)	
Single/multiple vessel disease			0.50
Single	54% (35)	55% (36)	
Multiple	46% (30)	45% (29)	
Vessel(s) involved			
<b>RCA</b>	57% (37)	52% (34)	0.40
<b>LCA</b>	63% (41)	68% (44)	0.31
Cx	51% (33)	42% (27)	0.21
Main trunk	$9\%$ (6)	$6\%$ (4)	0.36
<b>HFrEF</b>	3% (2)	$6\%$ (4)	
<b>HF<sub>P</sub>EF</b>	3% (2)	$1\%$ (1)	
NYHA class			0.10
NYHA I	78% (54)	87% (61)	
NYHA II	18% (12)	$6%$ (4)	
NYHA III	$4\%$ (3)	7% (5)	
EF			0.32
$EF > 50\%$	75% (52)	71% (50)	
EF 35-50%	$0\%$ (0)	$4\%$ (3)	
EF < 35%	25% (17)	24% (17)	
Atrial fibrillation	$7.2%$ $(5)$	9% (6)	0.99
Diabetes mellitus	24.6% (17)	27% (19)	0.85
Hyperlipidaemia	76.8% (53)	79% (55)	0.84
Arterial hypertension	60.0% (40)	63% (44)	0.61
Family history	49.3% (34)	51% (36)	0.87
Smoking			0.99
Current smoker	26% (18)	26% (18)	
Prior smoker	32% (22)	33% (23)	
Non-smoker	42% (29)	41% (29)	
BMI	$28\pm5$	$28 \pm 4$	0.54
Peripheral artery disease	$12\%$ (8)	$16\%$ (11)	0.62
On beta-blocker	77% (53)	$81\%$ (57)	0.61
On ACE-inhibitor	64% (44)	69% (48)	0.72

(continued)

#### Table 1. Continued



Note that continuous variables are expressed as mean $\pm$ SD. Categorical variables are expressed as proportion in % (n). CAD: coronary artery disease; STEMI: ST-elevation myocardial infarction; NSTEMI: non ST-elevation myocardial infarction; UA: unstable angina; SA: stable angina; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; RCA: right coronary artery; LCA: left coronary artery; Cx: circumflex artery; HFrEF: heart failure with reduced EF; HFpEF: heart failure with preserved EF; NYHA: New York Heart Association; EF: ejection fraction; BMI: body mass index; ACE: angiotensin-converting enzyme; DAPT: dual antiplatelet therapy



Figure 2. Time to first cardiovascular rehospitalization after randomization.

intervention group ( $\text{\textsterling}2156 \pm \text{\textsterling}126$ ) than in the control group  $(\text{ } \in 2720 \pm \text{ } \in 276, \text{ } U = 3068, \text{ } z = 2.582, \text{ } p = 0.01,$  $r = 0.22$  (i.e. small to medium effect) (Table 2). In the intervention group quality of life improved (average  $\Delta QALY$  0.06); in the control group quality of life deteriorated (average  $\Delta \text{QALY}$  -0.09) during the study period. The cost-effectiveness analysis demonstrated that, overall, the addition of the telerehabilitation programme to centre-based cardiac rehabilitation (intervention group) was both cost-saving and more effective than the centre-based cardiac rehabilitation alone (control group). Dividing the overall incremental average cost per patient ( $\epsilon$ –564.40) by the baseline adjusted differential incremental QALYs (0.026 QALYs) yielded an ICER of  $\epsilon$ –21,707/QALY. The distribution of the points in the cost-effectiveness scatter plot (.Figure 3) further illustrate the aforementioned findings.

#### **Discussion**

This cost-effectiveness study showed that overall, the addition of the cardiac telerehabilitation programme to conventional centre-based cardiac rehabilitation was more effective and efficient as compared with centre-based cardiac rehabilitation alone. The additional health benefits provided by the telerehabilitation programme, reflected in the intervention group's reduced cardiovascular rehospitalization rate, may have been responsible for the additional quality of life gained over the trial period.

As reported by several recently published clinical trials, including the TIM-HF trial, $^{14}$  the Telerehab II trial,<sup>15</sup> the CHOICE trial,<sup>16</sup> the COACH trial,<sup>17</sup> the eOCR trial, $^{18}$  the TeleIntermed trial<sup>19</sup> and the TEMA-HF trial, $^{20}$  cardiac tele-interventions showed favourable results regarding feasibility, safety and effectiveness (such as effect on adherence to physical activity guidelines,  $VO<sub>2</sub>$  peak). However, trials including profound cost-utility assessment are less prevalent. Körtke et al. $^{21}$  were one of the first groups to report on cost-effectiveness in a non-randomized controlled trial assessing a transtelephonic guide for ambulatory rehabilitation in cardiac surgery patients. They concluded the total cost of an ambulant telemedicine cardiac rehabilitation programme to be lower compared with conventional in-hospital cardiac rehabilitation.



°QALYs calculated using 'area under the curve method'. <sup>b</sup>Adjusted for baseline differences in QALYs between intervention and control group. CR: cardiac rehabilitation; RIZIV/INAMI: The National Sickness<br>and Invalidity Ins aQALYs calculated using 'area under the curve method'. bAdjusted for baseline differences in QALYs between intervention and control group. CR: cardiac rehabilitation; RIZIV/INAMI: The National Sickness and Invalidity Insurance Institution; CV: cardiovascular; I: intervention; C: control; QALY: quality adjusted life year; ICER: incremental cost-effectiveness ratio



Figure 3. Cost-effectiveness plane scatter plot of the incremental cost (euros) and incremental quality-adjusted life years (QALYs) gained, based on the bootstrap resampling method. Each point in the scatter plot represents one bootstrap iteration; 1000 bootstrap iterations were carried out. CR: cardiac rehabilitation

It is clear, however, that, from an economic point of view, current restrictions on health care budgets impose great difficulties for cardiac rehabilitation centres to expand centre-based cardiac rehabilitation services in order to cope with the increasing CVD epidemic. There is a need for alternative care strategies, exemplified by remote cardiac tele-intervention programmes, that prove to be cost-effective. This paper provides promising cost-utility assessment results, but, given the contradicting findings with other trial(s), also indicates the necessity for future large clinical randomized controlled trials to further assess the potential costeffectiveness of cardiac telerehabilitation programmes.

Strengths of this study were that data on use of health care services were derived from administrative records, rather than patient self-report, thereby eliminating recall bias. The quality of life data were collected directly from participants by using a tool validated in a cardiac patient population<sup>11</sup> similar to the one in this trial. The follow-up period of one year allowed a reasonable time frame to assess cardiovascular rehospitalization rate. A limitation of this study is that it did not take into account a full societal approach, potentially resulting in an underestimation of productivity gains for those patients still professionally active. However, given that the study population was mostly retired, any such underestimation is likely to be minimal. This study compared the addition of a cardiac telerehabilitation programme to conventional cardiac rehabilitation with conventional centre-based cardiac rehabilitation alone. A comparative study between cardiac telerehabilitation per se and conventional cardiac rehabilitation would enable a more direct cost-effectiveness analysis of the tele-intervention programme. Lastly, the Telerehab III trial was initially designed to assess the effectiveness of the implemented intervention on physical fitness improvement (as defined by improved peak oxygen uptake  $(VO<sub>2</sub>$  peak) on maximal cardiopulmonary exercise testing (CPET)), rather than cost-utility possibly underestimating current findings.

## Conclusion

This paper shows the addition of a cardiac telerehabilitation programme to conventional centre-based cardiac rehabilitation to be more effective and efficient than centre-based cardiac rehabilitation alone. At one year follow-up, it resulted in a reduced number of days lost due to cardiovascular rehospitalizations and an increased proportion of actual to theoretical maximal days alive and out of hospital. These results are useful for policy makers charged with deciding how limited health care resources should best be allocated in the era of an ever increasing CVD epidemic.

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trial were presented at Europrevent 2015 (Lisbon) in the Rapid Fire Abstract Session II – Cardiac Rehabilitation & Exercise Basic & Translational Research. Title: Investigating the effectiveness of an internet-based telerehabilitation programme on coronary artery disease and heart failure patients' physical activity level and physical fitness. This trial has been registered at the ISRCTN registry with registration number ISRCTN29243064.

#### Declaration of conflicting interests

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