Is INTERdisciplinary COMmunity-based COPD management (INTERCOM) cost-effective?

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ABSTRACT: The study aimed to estimate the cost-effectiveness of interdisciplinary community-based chronic obstructive pulmonary disease (COPD) management in patients with COPD.

We conducted a cost-effectiveness analysis alongside a 2-yr randomised controlled trial, in which 199 patients with less advanced airflow obstruction and impaired exercise capacity were assigned to the INTERCOM programme or usual care. The INTERCOM programme consisted of exercise training, education, nutritional therapy and smoking cessation counselling offered by community-based physiotherapists and dieticians and hospital-based respiratory nurses. All-cause resource use during 2 yrs was obtained by self-report and from hospital and pharmacy records. Health outcomes were the St George's Respiratory Questionnaire (SGRQ), exacerbations and quality-adjusted life years (QALYs).

The INTERCOM group had 30% (95% CI 3–56%) more patients with a clinically relevant improvement in SGRQ total score, 0.08 (95% CI -0.01–0.18) more QALYs per patient, but a higher mean number of exacerbations, 0.84 (95% CI -0.07–1.78). Mean total 2-yr costs were €2,751 (95% CI -€632–€6,372) higher for INTERCOM than for usual care, which resulted in an incremental cost-effectiveness ratio of €9,078 per additional patient with a relevant improvement in SGRQ or €32,425 per QALY.

INTERCOM significantly improved disease-specific quality of life, but did not affect exacerbation rate. The cost per QALY ratio was moderate, but within the range of that generally considered to be acceptable.

KEYWORDS: Chronic obstructive pulmonary disease, community-based, cost-effectiveness, pulmonary rehabilitation, quality-adjusted life years

The importance of pulmonary rehabilitation [1] in treating chronic obstructive pulmonary disease (COPD) is increasingly recognised, as COPD is becoming more and more regarded as a systemic disease that does not only affect the lungs [2]. In patients with severe COPD, the beneficial effects of both in-patient and hospital-based outpatient pulmonary rehabilitation programmes have been well established in terms of improving exercise capacity, dyspnoea and quality of life [3]. With regard to the cost-effectiveness of pulmonary rehabilitation, the evidence is still very limited. Nevertheless, it is often stated in the literature that pulmonary rehabilitation is cost-effective, because it reduces healthcare costs [1, 4]. However, most studies only reported the programme costs or the impact on just a limited number of healthcare services, such as hospital admissions [5–10]. Only two comprehensive economic evaluations of pulmonary rehabilitation programmes have been published [11, 12].

Both studies included patients with severe COPD and were performed in the in-patient or outpatient setting of a hospital. Evidence of cost-effectiveness in less severe patients or in community settings is not available. In general, it is assumed that the substitution of hospital care by community care reduces total costs and improves cost-effectiveness. We aimed to conduct a comprehensive cost-effectiveness analysis (CEA) of a community-based multidisciplinary rehabilitation programme for COPD patients with less severe airflow obstruction than that of patients traditionally included in secondary or tertiary care pulmonary rehabilitation programmes. This CEA was performed alongside a 2-yr randomised controlled trial evaluating the effect of an INTERdisciplinary COMmunity-based COPD management programme (INTERCOM) compared with usual care. Full clinical results of this trial have been reported elsewhere [13–15]. In brief, results over the total 2-yr period showed that there were significantly better effects in the

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INTERCOM group than for usual care in St George's Respiratory Questionnaire (SGRQ) total score, Medical Research Council dysnoea score, 6-min walk distance (6MWD) and cycle endurance time in a constant work rate test at 70% of peak exercise capacity. No significant differences were found for exacerbations, muscle function and body composition. Both patient and caregiver assessment of effectiveness significantly favoured the INTERCOM programme.

METHODS

Patients and design

199 patients with Global Initiative for Chronic Obstructive Lung Disease stage 2 or 3 COPD and impaired exercise capacity (maximum work <70% predicted), recruited by respiratory physicians of two general hospitals in the Netherlands, were randomised to the INTERCOM programme (n=102) or to usual care (n=97) (fig. 1). Patients did not have prior rehabilitation or serious comorbidity that precluded exercise training. At inclusion, they were judged by their respiratory physician to be clinically stable and pharmacotherapy was optimised. The time horizon of the study was 2 yrs and disease-specific and generic quality of life and functional parameters were single-blinded evaluated at baseline and 4, 12 and 24 months. All patients gave written informed consent and ethical approval was granted by the medical ethical committees of the two hospitals.

INTERCOM programme

The core elements of the INTERCOM programme were exercise training, education, nutritional therapy and smoking cessation counselling (the latter two upon indication) [13]. During the 4-month standardised, supervised, intensive intervention phase, individual exercise training sessions were given twice a week by physiotherapists in the proximity of the patients' home. Patients were also instructed and motivated to perform the exercises at home and to walk and cycle twice a day. Smoking cessation counselling, if applicable, as well as

education to improve the knowledge of COPD and its treatments, and to teach self-management skills, was provided by respiratory nurses in the hospital (average of four sessions). Nutritionally depleted patients were scheduled to visit a local dietician four times in the first 4 months. Nutritional therapy consisted of counselling to improve nutritional intake and three oral liquid (3 × 125 mL) supplements (Respifor®; Nutricia BV, Zoetermeer, the Netherlands) per 24 h for a period of 4 months. During the less intensive, less-standardised 20-month maintenance phase, patients visited the physiotherapist once a month. In case of insufficient recovery from an exacerbation, additional training sessions (maximum of six) could be started. During the maintenance phase, patients visited the dietician four times, while they visited the respiratory nurse according to an individualised schedule.

Usual care

Patients assigned to usual care received pharmacotherapy according to accepted guidelines, a short smoking cessation advice session from their respiratory physician and short nutritional advice to eat more and better in case they were nutritionally depleted.

Perspective

The cost-effectiveness study was performed according to the good research practices for cost-effectiveness analyses alongside clinical trials [16]. The study was conducted from a societal perspective, including all COPD- and non-COPD-related healthcare costs, travel expenses and cost of productivity losses. A separate analysis was done from a third party payers' perspective. All costs related to conducting the trial and developing the intervention have been excluded.

Healthcare utilisation and unit costs

In both treatment groups, patients kept a weekly record of contacts with healthcare providers, "over-the-counter medication", medical devices, hospital admissions, time lost from

FIGURE 1. Patient disposition. INTERCOM: interdisciplinary community-based chronic obstructive pulmonary disease management programme; ITT: intention-to-treat.

paid work, hours of (un)paid household help, travel expenses and nutritional supplements using cost booklets. Each booklet covered a period of 4 weeks and was collected every 2 months. Whenever necessary, patients were contacted by telephone for further clarification. To ensure that no hospitalisations were missed, data on hospital admissions were extracted from the electronic hospital records of the two hospitals involved in the study. Information on the dispense and costs of outpatient medication was obtained from each patients' local pharmacy. For 12 patients using oxygen during exercise, the start and stop date of oxygen supply were obtained from their oxygen supplier. Resource utilisation was valued in euros using Dutch guideline prices updated to 2007 (table 1) [17]. Because of the small number of patients with a paid job and the homogeneity of this group, the weekly number of hours absent from paid work was valued with the average gross hourly earnings weighted for sex and age, €46.61 per hour. The calculation of productivity loss was based on the friction cost approach [18], using a friction period of 154 days [17]. No discounting was applied to costs or effects, because of the limited study period.

Health outcomes

It was pre-specified which of the wide range of health outcome measures applied in the clinical trial would be used in the cost-effectiveness study. These were: 1) the net proportion of patients with a clinically relevant improvement (four or more units) in disease-specific quality of life as measured by the SGRQ total score [19, 20]; 2) the total number of COPD

exacerbations (moderate plus severe); and 3) the number of quality-adjusted life years (QALYs) based on EuroQol-5D (EQ-5D) utility values [21, 22]. SGRQ and exacerbations were the co-primary outcomes of the clinical study, whereas QALYs is the outcome preferably used in economic evaluations. The SGRQ and the EQ-5D were administered at baseline and 4, 12 and 24 months, while exacerbations were measured continuously over the 2-yr period. The net proportion of patients with an improvement of four or more units in SGRQ total score was calculated as the proportion of patients with four or more units improvement between baseline and 24 months minus the proportion of patients with four or more units deterioration. A moderate exacerbation was defined as a visit to the general practitioner or respiratory physician in combination with a prescription of antibiotics and/or prednisolone or a visit to the emergency department or day care of a hospital, which according to the patient, was related to a COPD exacerbation. A severe exacerbation was defined as a hospitalisation for a COPD exacerbation. The number of QALYs for each patient was calculated by summing the days under observation weighted by their EQ-5D utilities [21, 22] using linear interpolation.

Cost-effectiveness

Cost-effectiveness was expressed as the incremental cost-effectiveness ratio (ICER), which was calculated as the difference in mean costs between the INTERCOM and usual care group divided by the difference in mean health outcome. Three different ICERs were planned: costs per additional patient with a relevant improvement in SGRQ total score, costs per exacerbation avoided and costs per QALY.

Statistical analyses

The analysis was performed according to the intention-to-treat approach. All randomised patients who had at least one outcome measurement after the start of treatment and who completed at least one cost booklet were included in the CEA. Differences in baseline characteristics of patients completing the trial and drop-outs were statistically tested using independent sample unpaired t-tests for continuous, normally distributed data, Wilcoxon Mann-Whitney U-tests for continuous non-normally distributed data and Chi-squared tests for categorical variables.

To account for costs and health outcomes that were missing after patients prematurely dropped out from the trial and the additional uncertainty that these missing values introduced, the multiple imputation technique was used [23]. Each missing value was replaced by 10 simulated values using the propensity score method in SAS V8 [24, 25]. In summary this method implied that for patients who dropped out values were imputed that were randomly drawn from the data of patients who did not drop out, but had a similar probability to have missing data given several baseline and other variables. This meant that, for patients with a worse health status that dropped out the trial, random draws of data of patients with a similar health status who did not drop out were imputed. The logistic regression to calculate the probability to have missing data (*i.e.* the propensity score) included the following independent variables: age, sex, smoking status, forced expiratory volume in 1 s (FEV1) % pred, number of comorbidities, body mass index (BMI), 6MWD, SGRQ total score and

TABLE 1 Unit costs for the most important types of resource utilisation

Type of healthcare	Unit	Unit costs € [#]
Contacts with care providers		
General practitioner	Contact	21
Medical specialist, general hospital	Contact	59
Physiotherapist	Contact	24
Dietician	Contact	31
Respiratory nurse	Contact	27
Other therapists	Contact	24–75
Hospital care		
General hospital	Day	356
University hospital	Day	502
Daycare treatment	Day	242
Emergency Department	Visit	147
Ambulance	Ride	359
Pulmonary rehabilitation centre		
Inpatient day	Day	379
Paid and unpaid help		
Home care	Hour	32
Informal care/unpaid household help	Hour	8.70
Oxygen therapy		
Respifor®	Unit	2.76
Travel expenses, public transport/car		
Productivity cost	Kilometre	0.17
	Hour	46.61

[#]: 2007 values. Respifor® is manufactured by Nutricia BV, Zoetermeer, the Netherlands.

EQ-5D utility index scores, at baseline and 4, 12 and 24 months, monthly exacerbation rates and monthly costs. Multiple imputation was carried out separately for both treatment groups and health outcomes and costs were imputed simultaneously.

Each of the 10 complete datasets was further analysed by nonparametric bootstrapping using 10,000 bootstraps per dataset [26]. The 95% confidence interval around the difference in mean costs and health outcomes was determined by taking the 2.5th percentile and the 97.5th percentile of these bootstrap replications. The bootstrap replicates were plotted in cost-effectiveness planes (CE-planes). A CE-plane is an *x-y*-diagram with the *x*-axis representing the difference in health outcome between the treatment and usual care group and the *y*-axis representing the difference in costs. By plotting all bootstrap replicates in this diagram the uncertainty around the point estimates of the ICERs was displayed. In addition, the information in the CE-planes was summarised in cost-effectiveness acceptability curves, which shows the probability that the ICER of the INTERCOM programme falls below various ceiling ratios. These ceiling ratios reflect the maximum that a decision maker would be willing to pay to have one additional patient with a relevant improvement in SGRQ, one exacerbation avoided or one additional QALY [27, 28]. All analyses were performed with either SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) or SAS V8 (SAS Institute Inc., Cary, NC, USA).

Sensitivity analyses

In addition to the probabilistic sensitivity analyses presented in the CE-planes and the acceptability curve, univariate sensitivity analyses were conducted to assess the impact of assumptions made or analytic methods used on the results. In the first sensitivity analysis (SA1), only data from patients who fully completed the trial were analysed. In addition, two sensitivity analyses on time horizon were conducted, showing the results at 4 months (SA2) and at 12 months (SA3). Finally, a sensitivity analysis was performed in which patients referred to in-patient pulmonary rehabilitation during the trial were excluded from the analyses (SA4).

RESULTS

Patients

Baseline characteristics of the 199 randomised patients did not differ between the two groups (table 2). Of the total of 199 patients, 13 dropped out after randomisation and before start of the treatment. From the 186 patients that actually started treatment, 175 patients completed the first 4 months, while 158 completed the 2-yr study period (79%), 75% in the INTERCOM group and 84% in the usual care group. Length of stay in the trial was significantly shorter for drop-outs in the INTERCOM group than in the usual care group, with mean $\pm$ SD of 262 ± 192 and 505 ± 225 days, respectively. In the INTERCOM group drop-outs were older, tended to have more comorbidities and worse scores on functional and quality of life parameters at baseline than completers, which was not the case in the usual care group. 175 patients had at least one outcome measurement after the start of treatment and completed at least one cost booklet and were, therefore, included in the CEA (fig. 1). A more detailed patient enrolment and disposition scheme is given elsewhere [13].

Resource use

Table 3 shows the mean resource use per patient as observed during the 2-yr trial. Overall, the percentages of item level missing data plus the missing data due to drop-out for the different data sources was about 5–7%, except for prescribed medication, for which this percentage was 9.2%. Missing data was primarily due to drop-out before completing the trial. To prevent bias related to differences in the length of the observation time, multiple imputation was applied to costs and health outcomes before statistically testing differences between the treatment groups.

Costs

Table 4 shows the mean 2-yr costs per patient after multiple imputation. Mean total costs, irrespective of whether they were related to COPD or not, were €13,565 for the INTERCOM group and €10,814 for the usual care group, a difference of €2,751 (95% CI -€631–€6,372). Total direct healthcare costs were €2,147 (95% CI -€1,091–€5,649) higher in the INTERCOM group. Because the INTERCOM programme is tailored to the individual patient, resulting in a variable number of contacts with the INTERCOM caregivers, the intervention costs were best estimated as the difference in costs for the physiotherapist, dietician, respiratory nurse and diet nutrition between the two groups: €1,520 per patient. Based on the study protocol the 2-yr intervention costs were €1,650 per patient, ranging from €1,350 for patients visiting the physiotherapists and the respiratory nurse to €2,500 for

TABLE 2 Baseline characteristics

	INTERCOM	Usual care
Subjects n	102	97
Females	30 (29)	28 (29)
Age yrs	66 $\pm$ 9	67 $\pm$ 9
Comorbidities	1.6 $\pm$ 1.6	1.5 $\pm$ 1.4
Exacerbations in 12 months before trial	1.2 $\pm$ 1.4	1.0 $\pm$ 1.5
COPD hospital admissions in 12 months before trial	0.2 $\pm$ 0.5	0.2 $\pm$ 0.5
Current smokers	32 (33)	22 (24)
Post-bronchodilator FEV₁ % pred	58 $\pm$ 17	60 $\pm$ 15
FEV₁/FVC %	49 $\pm$ 11	51 $\pm$ 12
W_{max} % pred	60 $\pm$ 19	61 $\pm$ 17
Fat free mass kg·m⁻²	17 $\pm$ 2	18 $\pm$ 2
SGRQ total score[#]	39 $\pm$ 15	38 $\pm$ 15
SGRQ symptom score[#]	45 $\pm$ 19	41 $\pm$ 21
SGRQ activity score[#]	55 $\pm$ 18	56 $\pm$ 19
SGRQ impact score[#]	27 $\pm$ 16	25 $\pm$ 15
EQ-5D utility index score	0.79 $\pm$ 0.21	0.79 $\pm$ 0.15
MRC dyspnoea score[†]	1.7 $\pm$ 1.0	1.5 $\pm$ 0.9

Data are presented as n (%) or mean $\pm$ SD, unless otherwise stated. COPD: chronic obstructive pulmonary disease; INTERCOM: INTERdisciplinary COMMunity-based COPD management programme; FEV₁: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; W_{max}: maximum work; SGRQ: St George's Respiratory Questionnaire; EQ: EuroQol; MRC: modified Medical Research Council. [#]: 0–100 scale; a higher score indicates a worse quality of life; [†]: 0–4 scale.

TABLE 3 Mean total healthcare utilisation and days of absenteeism per patient as observed during the trial

	INTERCOM	Usual care
Subjects n	87	88
General practitioner visits	7.2±7.0	7.9±8.1
Chest physician visits	4.4±3.1	3.5±3.6
Cardiologist visits	1.6±2.9	1.4±2.0
Internist visits	0.4±1.6	1.1±2.2
Other specialist visits	2.6±4.7	3.8±5.7
Physiotherapist visits	51±18	11±21
Dietician visits	2.1±3.4	0.6±2.1
Respiratory nurse visits	5.2±3.1	0.8±1.6
Respifor® units of 125 mL	111±314	3.6±23
Other healthcare provider visits[#]	1.3±5.7	2.1±9.1
Home care h	37±115	38±118
Paid household help h	36±103	26±73
Unpaid household help h	10±44	25±150
Ambulance rides	0.19±0.65	0.23±0.54
Hospital admissions	0.75±1.29	0.96±1.35
Hospital admissions for COPD	0.36±1.00	0.40±0.78
Total hospital days	7.8±16	9.3±15
Total hospital days for COPD	4.9±14	4.3±10
Pulmonary rehabilitation in-patient days	3.3±16	0.7±6.8
Time unable to work h	22±89	6.8±40

Data are mean±SD, unless otherwise stated. COPD: chronic obstructive pulmonary disease; INTERCOM: INTERdisciplinary COMMunity-based COPD management programme. [#]: other healthcare providers included other and alternative therapists, social workers and psychologists. Respifor® is manufactured by Nutricia BV, Zoetermeer, the Netherlands.

nutritionally depleted patients receiving additional dietary counselling and Respifor®.

Health outcomes

In the INTERCOM group 43% of the patients had an improvement of four or more units in SGRQ total score, while 29% had a deterioration of four or more units, resulting in a net improvement of 13%. In the usual care group 29% improved and 46% deteriorated more than four units, resulting in a net improvement of -17%. The difference in net proportion of patients with an improvement in SGRQ total score was significantly different between the two groups: 30% (95% CI 3–56). Over the entire 2-yr period the INTERCOM group had 3.02 exacerbations per patient compared to 2.18 in the usual care group, a not significant 2-yr difference of 0.84 (95% CI -0.07–1.78). The mean number of QALYs per patient was 1.62 and 1.54 in the INTERCOM and the usual care group respectively, *i.e.* a difference of 0.08, which was not significantly different (95% CI -0.01–0.18).

Cost-effectiveness

From a societal perspective, the ICERs of the INTERCOM programme compared with usual care were €9,078 per additional patient with a relevant improvement in SGRQ total score and €32,425 per QALY. Because the INTERCOM group

had a higher number of mean exacerbations, the costs per exacerbation avoided were negative. The CE-planes with SGRQ and QALYs as outcomes showed that the majority of bootstrap replications (>90%) fell within the upper-right quadrant, indicating that the INTERCOM programme resulted in higher costs but more patients had a relevant improvement in SGRQ and a higher gain in QALYs, respectively (fig. 2). For total exacerbations most bootstrap replications fell in the upper-left quadrant indicating higher costs and more exacerbations. The accompanying acceptability curves are shown in figure 3. The probability that the INTERCOM programme is cost-effective at a willingness-to-pay of €20,000 and €50,000 per QALY gained was 33% and 67%, respectively.

From a third party payer's perspective, the ICERs were slightly lower, *i.e.* €7,086 per additional patient with a relevant improvement in SGRQ total score and €25,309 per QALY, resulting in slightly higher probabilities that the INTERCOM programme was cost-effective.

Sensitivity analyses

Results for the sensitivity analyses (table 5) showed that when only patients that completed the trial were included in the analysis (SA1), the costs per QALY were comparable to the base case analysis. The results for the sensitivity analyses on time horizon showed that the difference in mean number of QALYs between the two groups increased over time (SA2 and SA3). It is important to note that part of the cost increase in the INTERCOM group was due to four patients who were referred to inpatient pulmonary rehabilitation, compared with one patient from the usual care group. When these five patients were excluded from the analyses (SA4), the difference in cost between the two groups reduced to €909 and the incremental costs per QALY reduced to €8,421. For all sensitivity analyses, the ICERs for total exacerbations avoided were negative as a result of a higher number of exacerbations in the INTERCOM group (data not shown).

DISCUSSION

This comprehensive CEA of an interdisciplinary community-based COPD management programme (INTERCOM) compared to usual care has shown that such a programme can significantly improve disease-specific quality of life in patients with less advanced COPD and impaired exercise performance, but the price that has to be paid is a cost increase of €2,751 per patient over 2 yrs. All other outcomes showed a consistent pattern toward better effects in the INTERCOM group compared with the usual care group and statistical significance was reached for 6MWD, cycle endurance time, dyspnoea and patient and caregiver global assessment of effectiveness [13]. These positive effects could not be explained by differences in medication use between the two groups, as this was similar. The only exception to the pattern of better effects in the INTERCOM group was the number of exacerbations that was slightly, but not significantly, higher in the INTERCOM group. Given the consistency of the outcome pattern and considering that the 2-yr costs for medication alone were €3,300 and the total 2-yr costs for usual care were €10,800, the cost increase of €2,751 per patient seems reasonable for such an intensive and comprehensive COPD management programme.

TABLE 4 Mean total 2-yr costs (in 2007 euros) per patient for different categories of resource use after multiple imputation

	INTERCOM [#]	Usual care [†]	Difference	95% CI
General practitioner	163	175	-12	-59–36
Specialist	570	610	-40	-178–101
Physiotherapist	1290	265	1025	882–1167
Dietician	70	20	50	24–77
Respiratory nurse	147	22	125	106–145
Hospital admissions	2944	3353	-408	-2084–1365
Diet nutrition	320	31	290	118–486
Prescribed medication	3532	3318	214	-239–667
Oxygen use	196	57	139	-13–304
Other direct medical costs [‡]	2911	2148	763	-1207–2909
Subtotal direct healthcare costs	12145	9998	2147	-1091–5649
Costs paid by the patient [§]	423	486	-63	-472–269
Subtotal direct costs	12568	10484	2084	-1198–5614
Productivity costs	997	330	667	-124–1566
Total costs	13565	10814	2751	-631–6372

INTERCOM: INTERdisciplinary COMMunity-based chronic obstructive pulmonary disease management programme. [#]: n=87; [†]: n=88; [‡]: other direct medical costs included costs of visits to other therapists, alternative therapists, social workers and psychologists, home care, ambulance transportation, pulmonary rehabilitation, psychiatric hospital admissions and medical devices; [§]: costs paid by the patient included costs of over the counter medication, paid and unpaid household help and travel expenses.

The incremental costs per QALY gained of the INTERCOM programme were estimated to be €32,425. This is the ratio of the additional costs of INTERCOM over usual care divided by the gain in QALYs due to INTERCOM. In the Netherlands, treatments with a cost-effectiveness ratio below €20,000 per QALY gained are generally regarded by policy makers as very cost-effective. The maximum acceptable cost per QALY ratio is the subject of ongoing debate. An advisory board of the Dutch government has recently proposed to adopt a maximum willingness-to-pay for a QALY that depends on the burden of disease for which the treatment is developed [29]. The maximum acceptable ratio in their proposal would be €80,000 per QALY gained for diseases with the highest burden of disease. With a ratio of €32,425 per QALY gained the INTERCOM programme would be considered as moderately cost-effective, although the uncertainty around this ICER was substantial. Currently, for COPD patients, the costs of the

separate components of the INTERCOM programme (*i.e.* physiotherapy, dietary counselling, counselling by a respiratory nurse and diet nutrition) are covered by the nationwide obligatory basic healthcare insurance in the Netherlands. However, this situation may change in the near future as the Dutch minister of health considers introducing one reimbursement package for “chained and integrated COPD care”, in which pre-defined types of healthcare are included. Whether a programme such as INTERCOM would be included in this package is unclear. Other healthcare interventions with comparable, but also much higher cost-effectiveness ratios [30–33] are currently reimbursed, providing an indication that a ratio of around €30,000 as found in the current study was previously considered acceptable for reimbursement. It is obvious, however, that other criteria, such as budget impact, necessity of care, own responsibility and affordability by the patient also play a role in the decision whether a healthcare

FIGURE 2. Cost-effectiveness plane: a) cost per additional patient with a relevant improvement in St George's Respiratory Questionnaire (SGRQ) total score, b) cost per exacerbation avoided and c) cost per quality-adjusted life year (QALY). [#]: difference in net proportion of patients with a relevant improvement in SGRQ total score.

FIGURE 3. Cost-effectiveness acceptability curves: probability that the INTERdisciplinary COMMunity-based chronic obstructive pulmonary disease management (INTERCOM) programme is cost-effective in relation to willingness to pay for one additional patient with a relevant improvement in St George's Respiratory Questionnaire (---), one exacerbation avoided (.....) or one additional quality-adjusted life year (—).

service should be covered by social healthcare insurance. Interpreting the costs per additional patient with a relevant improvement in SGRQ total score is more difficult, because no reference data are available and, up to now, only one study used this outcome in a CEA [34].

The estimated average intervention costs of the entire INTERCOM programme were approximately €1,500 per patient. As expected, these intervention costs were much lower than the intervention costs for in-patient rehabilitation [11]. Given the duration and intensity of the programme, the costs of our community-based intervention seemed also low compared to several outpatient programmes [7, 8, 12, 35, 36].

The increase in costs in the INTERCOM group was higher than the intervention costs. Although not significant, patients in the INTERCOM group had higher productivity costs and other direct medical costs (table 4). The latter was mainly caused by the fact that four patients in the INTERCOM group were referred to inpatient pulmonary rehabilitation during their participation in the trial, compared with only one patient in the usual care group. This difference may be coincidence, but could also be related to the frequent contact between patient and caregivers resulting in earlier signalling of insufficient improvements or significant worsening. In retrospect, it was also speculated that these patients should never have been included because their condition was so severely impaired that this community-based programme was not sufficiently intensive. However, according to the intention-to-treat principle, these patients were kept in the trial and the costs of these inpatient rehabilitation programmes were included. If the difference in referrals to inpatient pulmonary rehabilitation between the two groups indeed is an unexpected side-effect of implementing a community-based programme, including these costs in the analyses might have improved the generalisability of the results to common daily practice.

TABLE 5 Sensitivity analyses (SAs) on imputation methods for missing data and time horizon

	Difference in mean total costs €	Difference in net proportion of patients with SGRQ improvement [#]	Cost per additional patient with SGRQ improvement [#] €	Difference in mean QALYs	Cost per QALY gained €	Probability that INTERCOM is cost-effective	
						€20,000 per QALY	€50,000 per QALY
Base case							
Imputation method							
SA1: completers	2751 (631–6372)	0.30 (0.03–0.56)	9078	0.08 (–0.01–0.18)	32425	0.33	0.67
Time horizon							
SA2: 4 months	1024 (534–1,525)	0.34 (0.11–0.57)	2976	0.01 (0–0.03)	90990	0.01	0.19
SA3: 12 months	1042 (–730–2895)	0.11 (–0.14–0.36)	9303	0.04 (0–0.09)	23894	0.44	0.74
SA4: excluding patients referred to in-patient pulmonary rehabilitation	909 (–1665–3519)	0.36 (0.09–0.62)	2641	0.11 (0.01–0.20)	8421	0.74	0.92

Data presented as mean or proportion (95% confidence interval), unless otherwise stated. SGRQ: St George's Respiratory Questionnaire; QALY: quality-adjusted life years; INTERCOM: INTERdisciplinary COMMunity-based chronic obstructive pulmonary disease management programme. [#]: ≥4 units improvement in SGRQ total score.

In both the base case analysis and sensitivity analysis, the ICERs for exacerbations avoided were negative, because the number of COPD exacerbations was slightly higher in the INTERCOM group. The definition of an exacerbation in this study was based on resource use reported by the patient (moderate exacerbations) and obtained from hospital records (severe exacerbations). The frequently scheduled caregiver contacts might have increased the opportunity to detect an exacerbation. In addition, improved self-management skills in the INTERCOM group might have enhanced the ability to recognise and report exacerbations sooner as has also been seen in other studies [37, 38].

Only two comprehensive economic evaluations on pulmonary rehabilitation have been published previously [11, 12]. The study of GOLDSTEIN *et al.* [11] reported the cost-effectiveness of a 2-month inpatient rehabilitation programme followed by 4 months of outpatient training in patients with severe stable COPD. The cost required for a single patient to achieve a clinically important improvement in different components of the health-related quality of life questionnaire ranged from \$28,993 for mastery to \$51,027 for fatigue (Canadian dollars). The second study is a 1-yr study by GRIFFITHS *et al.* [12] that reported the cost-utility of a 6-week multidisciplinary outpatient rehabilitation programme. Compared to standard care the incremental costs of the programme were -£152 (95% CI -£881–£577) per patient, while the incremental utility per patient was 0.030 (95% CI 0.002–0.058), suggesting that the health improvements were accompanied by net savings. Comparison of the studies of GOLDSTEIN *et al.* [11] and GRIFFITHS *et al.* [12] with our study is complicated by differences in the type of intervention, outcome measures and patient population. Both the studies of GOLDSTEIN *et al.* [11] and GRIFFITHS *et al.* [12] included patients with severe COPD/lung disease reflected by a mean FEV₁ of 35% pred and 40% pred respectively, whereas in our study this was 60% pred. We have not found a full economic evaluation on outpatient or home-based pulmonary rehabilitation in less severe patients.

Whether an interdisciplinary programme, such as INTERCOM, can be implemented in other countries than the Netherlands depends, among other things, on the organisational structure of the healthcare system, the reimbursement system, the costs of health services for COPD and the geographical circumstances. Furthermore, it is important that COPD is acknowledged as a systemic disease requiring regular assessments other than lung function, and a collaborative network of the different healthcare providers in the local community is needed.

From the combined results of the clinical analyses published elsewhere [13–15] and the cost-effectiveness analyses presented here, we conclude that compared to usual care, the INTERCOM programme resulted in significant improvements in SGRQ total score and several exercise performance and dyspnoea measures at a cost increase of €2,751 per patient. In terms of costs per QALY, the programme is moderately cost-effective.

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CLINICAL TRIALS

The trial started before January 2006 and was registered retrospectively at www.clinicaltrials.gov (NCT00840892).

STATEMENT OF INTEREST

Statements of interest for C.R. van Wetering, M.P.M.H. Rutten-van Mölken and for the study itself can be found at www.erj.ersjournals.com/misc/statements.dtl

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