**ABSTRACT**

**Objective:** To investigate the long-term effectiveness of a general practice monitoring system with respiratory expert recommendations for general practitioners’ management of patients with chronic obstructive pulmonary disease (COPD), compared with usual care.

**Design, settings and participants:** A multicentre randomised controlled trial of patients with COPD, clustered by general practices; 200 participants were recruited to maintain at least 75 participants per group for analysis. The trial took place from July 2005 to February 2008 in the south-western region of the Netherlands.

**Intervention:** Ongoing half-yearly monitoring of COPD patients with respiratory expert recommendations for the GP was compared with usual care.

**Main outcome measures:** Primary outcome — Chronic Respiratory Questionnaire (CRQ) score; secondary outcomes — CRQ domain scores, generic health-related quality of life (Short-Form 12 and EuroQol-5D), breathlessness (Modified Medical Research Council score), exacerbations, and decline in forced expiratory volume in 1 second. A detailed process evaluation was performed along with the trial.

**Results:** Data from 170 participants were analysed. Based on repeated measurement analyses, the additional gain in CRQ score during follow-up was 0.004 points for monitoring compared with usual care (95% CI, 0.172 to 0.180). Also, no important differences between monitoring and the usual care group were found for secondary outcomes. Half the monitoring visits resulted in disease management recommendations by a respiratory expert, and 46% of these recommendations were implemented by the GPs. Patient adherence to lifestyle recommendations was low.

**Conclusion:** An expert-supported monitoring system for patients with COPD was not clinically effective. As patients had a pre-existing entry in the monitoring system, the population may be well regulated, with reduced room for improvement.

**Trial registration:** www.clinicaltrials.gov NCT00542061.


**METHODS**

**Study design**

We conducted a multicentre parallel group study with a 24-month patient follow-up (www.clinicaltrials.gov NCT00542061). The trial took place from July 2005 to February 2008. We allocated general practices to intervention (ie, respiratory expert-supported COPD monitoring system) or usual care. All participants at each general practice were allocated to the same treatment group (cluster randomised design).

We hypothesised that ongoing half-yearly monitoring with respiratory expert recommendations of patients with COPD would result in a clinically relevant gain in quality of life compared with usual care.

The study protocol was approved by the medical ethics committee of the Arnhem Nijmegen region in the Netherlands. All patients gave written informed consent.

**Participants and sample size calculation**

We selected and invited study participants based on patient records already available at a regional diagnostic centre (RDC) in the south-western region of the Netherlands.

Inclusion criteria were:
- patient diagnosed with COPD or asthma with persistent airflow obstruction, as confirmed with the patient’s most recent spirometry (forced expiratory volume in 1 second [FEV₁]/forced vital capacity [FVC] <70%, or postbronchodilator FEV₁ <80% predicted and ≥9% reversibility),
- the patient's lung function data from the previous year were available at the general practice diagnostic centre; and
- patient aged at least 25 years.

Exclusion criteria were:
- patient treated by a chest physician;
- patient participating in another respiratory intervention study;
- GP considered it detrimental to the patient to participate in the study;
- patient had any serious other non-pulmonary diseases (or disease stages) or pulmonary diseases (eg, sarcoidosis, lung cancer, lung fibrosis); or
- patient could not read.
GPs at practices who had referred more than six patients to the RDC were contacted and asked to participate. We used computerised minimisation to allocate practices to the monitoring and usual care groups\textsuperscript{13,14} while stratifying for:
- group versus solo practice;
- practice nurse employed versus no practice nurse employed; and
- \( \leq 10 \) versus \( > 10 \) patients fulfilling the study inclusion criteria.

A multilevel power calculation (ie, correction for clustering of subjects within general practices) was based on the mean difference in change in Chronic Respiratory Questionnaire (CRQ) score between monitoring and usual care. A difference of 0.5 points is generally accepted as a minimum important clinical difference for the CRQ score.\textsuperscript{15} We initially aimed to recruit 100 participants per group based on the following assumptions: an intracluster correlation coefficient of 0.04, \( \alpha = 0.05 \); 1 – \( \beta \) = 0.80; and a dropout rate of 25%.

**Blinding**

In their study information letters, GPs and patients were informed that patients were invited for an unspecified number of visits to the RDC. GPs were informed that participation could imply that the outcome of their patients’ visits would not be forwarded to them during the study as it had been previously. After minimisation, GPs received specific research information for their practice. The respiratory experts involved and the lung function technicians who performed the spirometric tests and collected medical information were not aware of patients’ participation and allocation.

**Intervention**

The expert-supported COPD monitoring system had been in use in the RDC since 1995, and comprised several steps.

**Step A.** Patients with COPD were invited to the RDC for monitoring visits every 6 months. Pre- and post- (after inhaling 400 µg salbutamol) bronchodilator FEV\textsubscript{1} and FVC were measured at each visit with a SpiroPerfect spirometer (WelchAllyn, Delft, The Netherlands) by certified lung function technicians. Body mass index was assessed, and information on respiratory symptoms, exacerbations, smoking and medication use in the previous 6 months was collected in a standardised way.

**Step B.** Information from the monitoring visit and previous visits was sent to a respiratory expert (chest physician or GP with special respiratory interest). The respiratory experts gave recommendations regarding treatment, additional diagnostic tests and referrals to other disciplines, based on national clinical practice guidelines for COPD and asthma\textsuperscript{11,12} Experts’ interpretation based on spirometry results and written information has been shown to be valid.\textsuperscript{16}

**Step C.** Written feedback was sent to the patient’s GP. The patient was instructed to visit the GP 2 weeks after the monitoring visit to discuss the outcome. During these visits, the expert recommendations could be implemented by the GP (eg, checking inhalation technique) or recommended to the patient. Half-yearly visits from a nurse consultant to the practice to support GPs in implementing the recommendations were an integral part of the expert-supported monitoring system.

**Step D.** Ultimately, the patient should implement the recommendations made (eg, quit smoking, increase exercise).

**Usual care**

We invited participants from the usual care group for spirometry at the beginning and at the end of the trial. No recommendations or feedback were given, and no nurse consultant practice visits were scheduled during the study period.

**Outcomes and process evaluation**

Participants completed questionnaires at baseline, at 1 year, and at the end of the
study. The primary study outcome was the CRQ score.\textsuperscript{17} Secondary outcomes were: CRQ domain scores; generic health-related quality of life (physical and mental domains of the Short-Form 12 [SF-12] and the EuroQol-5D); respiratory symptoms (breathlessness according to the Short-Form 12 [SF-12] and the EuroQol-5D); disease severity (Modified Medical Research Council [MMRC] score, dichotomised as 0–1 and 2–4); occurrence rate of self-reported exacerbations; and annual FEV\textsubscript{1} decline.

For the process evaluation, the respiratory experts’ database was examined to collect data on their recommendations. The nurse consultant collected data on GPs’ implementation of recommendations. Patient questionnaires comprised questions about disease management. At the end of the study, the nurse consultant collected information on disease management from GPs in the usual care group.

**Statistical analysis**

Baseline characteristics for the participants in each group were compared using unpaired \( t \) tests, \( \chi^2 \) tests, and Mann–Whitney \( U \) tests, depending on the type of variable and normality of distribution.

Multilevel repeated measurement regression analysis was used to model the effect of monitoring on CRQ overall score, CRQ domain scores, SF-12 scores, EuroQol-5D scores, FEV\textsubscript{1} decline, and dichotomised MMRC scores. We used a PROC MIXED procedure in SAS statistical software (SAS Institute, Cary, NC, USA), with general practice as the random coefficient and compound symmetry correlation structure. Multilevel logistic regression analysis was used to analyse effects on exacerbations. All models were corrected for sex, age, socioeconomic status, baseline cigarette smoking status, reversibility, exacerbations at baseline, use of inhaled corticosteroids, use of long-acting bronchodilators, and post-bronchodilator FEV\textsubscript{1} % of the predicted value. Participants were included in the analysis if they participated in the study (intention-to-treat analysis).

**RESULTS**

**Study population**

Box 1 shows the process of practice and patient recruitment and follow-up. Thirty-four general practices participated. From these, 261 of 286 eligible patients (91%) responded to the invitation, and 213 (74%) were willing to participate. No significant differences between participants and non-participants with regard to sociodemographic characteristics, medication use, and spirometric indices were found. Twenty-four patients did not enter the study, and 19 patients were excluded from analyses. Data from 170 participants were used for the analyses. Box 2 shows the baseline characteristics of both groups.

The study was originally designed to evaluate monitoring of patients with COPD and asthma with a chronic airflow obstruction. However, after the recruitment phase we found that almost all of the patients fulfilled the criteria for COPD (ie, FEV\textsubscript{1}/FVC < 70% postbronchodilator); therefore, we decided to focus on COPD.

**Clinical effectiveness of the expert-supported monitoring system**

Box 3 shows the mean overall CRQ scores in the monitoring and usual care groups. Based on repeated measurement analyses, the additional gain in CRQ score during follow-up was 0.004 points for monitoring compared with usual care (95% CI, −0.172 to 0.180). Box 4 summarises the results for the secondary outcomes. No significant differences between the monitoring and usual care groups were observed other than CRQ domain mastery.

**Process evaluation**

A total of 292 visits took place among the monitoring group participants. Fifty-eight participants attended all four planned monitoring visits at the RDC (71%). Fifteen patients (18%) attended three, six patients attended two, and three patients attended one planned visit.

In total, respiratory experts gave 290 recommendations (Box 5). Smoking cessation was the most frequent recommendation (28% of all recommendations), and inhaler technique training and assessment of compliance with medical treatment were also recommended regularly. In 146 monitoring visits (50%), the respiratory experts did not consider any modification in disease management necessary. For 73 patients (89%), the GPs received at least one recommendation to change disease management.

Information about 274 of the 290 recommendations could be collected (Box 5). According to GPs, they attempted to implement 125 (46%) of the 274 recommenda-
4 Effects of expert-supported chronic obstructive pulmonary disease monitoring compared with usual care on outcomes of respiratory health and quality of life

A. Mean (95% CI) at baseline, change (95% CI) at follow-up, and difference between groups (95% CI) for continuous variables

<table>
<thead>
<tr>
<th></th>
<th>Monitoring group (n = 82)</th>
<th>Usual care group (n = 88)</th>
<th>Adjusted incremental 2-year change* MICD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall CRQ score</td>
<td>5.1 (4.9 to 5.3)</td>
<td>5.3 (5.2 to 5.5)</td>
<td>0.12 (0.00 to 0.24)</td>
</tr>
<tr>
<td>CRQ domain dyspnoea</td>
<td>4.9 (4.6 to 5.3)</td>
<td>5.4 (5.1 to 5.7)</td>
<td>0.29 (0.07 to 0.50)</td>
</tr>
<tr>
<td>CRQ domain fatigue</td>
<td>4.9 (4.7 to 5.2)</td>
<td>5.1 (4.9 to 5.3)</td>
<td>0.13 (-0.09 to 0.34)</td>
</tr>
<tr>
<td>CRQ domain emotions</td>
<td>5.4 (5.2 to 5.6)</td>
<td>5.5 (5.3 to 5.7)</td>
<td>0.09 (-0.06 to 0.24)</td>
</tr>
<tr>
<td>CRQ domain mastery</td>
<td>4.8 (4.7 to 5.0)</td>
<td>5.1 (4.9 to 5.3)</td>
<td>-0.03 (-0.16 to 0.11)</td>
</tr>
<tr>
<td>SF-12 physical scale</td>
<td>44.5 (43.0 to 46.1)</td>
<td>43.8 (42.3 to 45.4)</td>
<td>-0.16 (-1.73 to 1.42)</td>
</tr>
<tr>
<td>SF-12 mental scale</td>
<td>52.2 (50.2 to 54.1)</td>
<td>52.7 (51.1 to 54.2)</td>
<td>-0.23 (-1.94 to 1.49)</td>
</tr>
<tr>
<td>EuroQol-5D score</td>
<td>0.89 (0.86 to 0.92)</td>
<td>0.87 (0.84 to 0.89)</td>
<td>0.00 (-0.03 to 0.03)</td>
</tr>
</tbody>
</table>

B. Frequency (no. [%]) of categorical variables at baseline and follow-up, and odds ratios

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Monitoring group (n = 82)</th>
<th>Usual care group (n = 88)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMRC score ≥ 2</td>
<td>8 (9.9%)</td>
<td>12 (15.8%)</td>
<td>1.05 (0.34–3.24)</td>
</tr>
<tr>
<td>≥ 1 exacerbations in previous year</td>
<td>16 (20.0%)</td>
<td>12 (15.8%)</td>
<td>0.87† (0.38–2.11)</td>
</tr>
</tbody>
</table>

CRQ = Chronic Respiratory Questionnaire. SF-12 = Short-Form 12. MICD = minimum important clinical difference. MMRC = Modified Medical Research Council.

* Monitoring versus usual care based on multilevel repeated measurement analysis corrected for sex, age, socioeconomic status, smoking status at baseline, reversibility, exacerbations at baseline, use of inhaled corticosteroids, use of long-acting bronchodilators, and postbronchodilator forced expiratory volume in 1 second % of predicted value.

† Difference between monitoring and usual care is significant; P<0.05. ‡ Two missing values. § Difference between monitoring and usual care is significant; P<0.01.

5 Number of times a respiratory expert recommended each disease management change, and general practitioner adherence to recommendations overall and in practices with and without a practice nurse

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Expert recommendations</th>
<th>Recommendations evaluated*</th>
<th>Overall</th>
<th>Practices with nurse†</th>
<th>Practices without nurse†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cease smoking</td>
<td>82</td>
<td>78</td>
<td>44</td>
<td>25/47</td>
<td>19/31</td>
</tr>
<tr>
<td>Optimise physical condition</td>
<td>21</td>
<td>20</td>
<td>6</td>
<td>2/5</td>
<td>4/15</td>
</tr>
<tr>
<td>Avoid allergens and triggers</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>1/2</td>
<td>2/3</td>
</tr>
<tr>
<td>Check inhaler technique</td>
<td>47</td>
<td>45</td>
<td>21</td>
<td>15/23</td>
<td>6/22</td>
</tr>
<tr>
<td>Check treatment compliance</td>
<td>49</td>
<td>46</td>
<td>29</td>
<td>18/25</td>
<td>11/21</td>
</tr>
<tr>
<td>Reduce bodyweight</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>1/2</td>
<td>0/1</td>
</tr>
<tr>
<td>Introduce ICS</td>
<td>15</td>
<td>14</td>
<td>5</td>
<td>2/7</td>
<td>3/7</td>
</tr>
<tr>
<td>Increase ICS dosage</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>1/2</td>
<td>2/4</td>
</tr>
<tr>
<td>Reduce dosage or cease ICS</td>
<td>10</td>
<td>10</td>
<td>6</td>
<td>6/10</td>
<td>0/0</td>
</tr>
<tr>
<td>Introduce short-acting BD</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1/1</td>
<td>0/0</td>
</tr>
<tr>
<td>Introduce long-acting BD</td>
<td>10</td>
<td>8</td>
<td>0</td>
<td>0/4</td>
<td>0/4</td>
</tr>
<tr>
<td>Additional diagnostic procedures</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0/2</td>
<td>0/1</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>14</td>
<td>13</td>
<td>3</td>
<td>1/8</td>
<td>2/5</td>
</tr>
<tr>
<td>Refer to chest physician</td>
<td>24</td>
<td>23</td>
<td>3</td>
<td>1/9</td>
<td>2/14</td>
</tr>
<tr>
<td>Total</td>
<td>290</td>
<td>274</td>
<td>125</td>
<td>74/146‡</td>
<td>51/128‡</td>
</tr>
</tbody>
</table>

Adherence = GP attempted to implement recommendation. BD = bronchodilator. ICS = inhaled corticosteroids. * Eleven recommendations were not discussed by GPs and three GPs’ responses were missing. † No. of GPs adhering to recommendation/no. of recommendations evaluated in each type of practice. ‡ Difference between practices with and without practice nurses is significant; P < 0.05 (χ² test).
The question remains whether the lack of effect was due to implementation failure — and therefore the system has the potential to be effective if implementation could be improved — or was a result of an ineffective intervention. Many participants failed to visit the GP, although the adherence rate to GP visits was significantly higher in general practices that invited patients for regular visits. Moreover, the presence of a practice nurse resulted in higher implementation levels. Therefore, implementation can be improved, but it is not possible to fully prevent dilution of effects in the process of monitoring and feedback. Options to reduce disease progression are limited in COPD. Moreover, little evidence exists that chronic disease management in primary care patients with COPD is effective. Potential effects are further diminished by the low adherence of the participants to health behaviour recommendations, which is in concordance with other studies. In conclusion, an ongoing respiratory expert-supported monitoring system for patients with COPD was not effective in terms of clinical outcomes. The lack of effectiveness may have been the result of a combination of limited options to intervene, the diluting effect on the intervention caused by the many steps in this complex process, and the low adherence of patients to crucial recommendations such as smoking cessation.

ACKNOWLEDGEMENTS
We thank the employees of the Stichting Huisartsen Laboratorium (SHL, diagnostic centre, Breda) who were involved in the lung function service of the SHL and therefore responsible for the collection of the data presented in the article. Moreover, we are very grateful to all the participants and GPs. Special thanks go to Reinier Akkermans (statistician). Finally, we would like to thank "Partners in Care Solutions for COPD" (PICASSO) for their financial support, which enabled us to conduct this study.

COMPETING INTERESTS
None identified.
REFERENCES


23 Jacobs JE. Patient-tailored monitoring of patients with asthma and COPD [thesis]. Nijmegen, The Netherlands: Radboud University Medical Centre, 2006.


(Received 13 Apr 2009, accepted 19 Jun 2009)