EARLY ASSISTED DISCHARGE WITH COMMUNITY NURSING FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS: RESULTS OF A RANDOMISED CONTROLLED TRIAL

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Title:

Early assisted discharge with generic community nursing for Chronic Obstructive Pulmonary Disease exacerbations: results of a randomised controlled trial

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Abstract

Objectives: To determine effectiveness of early assisted discharge with home care provided by generic community nurses, compared to usual hospital care.

Design: Prospective, randomised controlled, multi-centre trial with 3 months follow-up.

Setting: Five hospitals and 3 home care organisations in the Netherlands.

Participants: Patients admitted to the hospital with an exacerbation of Chronic Obstructive Pulmonary Disease. Patients with no or limited improvement of respiratory symptoms and patients with severe unstable comorbidities, social problems or those unable to visit the toilet independently were excluded and not randomised.

Intervention: Early discharge from hospital after 3 days inpatient treatment. Home visits by generic community nurses. Primary outcome measure was change in health status measured by the Clinical COPD Questionnaire (CCQ). Treatment failures, readmissions, mortality and change in generic health-related quality of life (HRQL) were secondary outcome measures.

Results: 139 patients were randomised. No difference between groups was found in change in CCQ score at day 7 (difference in mean change -0.29 (95% CI -0.61 to 0.03)) or at 3 months

(difference in mean change -0.04 (95% CI -0.49 to 0.41)). No difference was found in secondary outcomes. At day 7 there was a significant difference in change in generic HRQL, favouring usual hospital care.

Conclusion: While patients' disease-specific health status after seven days treatment tended to be somewhat better in the usual hospital care group, the difference was small and not clinically relevant or statistically significant. After three months, the difference had disappeared. A significant difference in generic health-related quality of life at the end of the treatment had disappeared after 3 months and there was no difference in treatment failures, readmissions or mortality. Early assisted discharge with community nursing is feasible and an alternative to usual hospital care for selected patients with an acute COPD exacerbation COPD.

Trial registration: NetherlandsTrialRegister NTR 1129

Article summary

Article focus:

- What is the effectiveness of early assisted discharge with community nursing for COPD exacerbations in comparison to usual hospital care as measured by the Clinical COPD Questionnaire.

Key Messages:

- There is no short term or long term difference in change in health status as measured by the Clinical COPD Questionnaire.

- A significant difference in generic health-related quality of life at the end of the treatment disappeared after 3 months.

- Early assisted discharge with home visits by community nurses is a feasible and an alternative to usual hospital care for selected patients with an acute exacerbation of their COPD.

Strength and limitations:

- 139 patients were randomised where 165 was calculated to be the required sample size. However, because the difference between the groups was only 0.29 instead of 0.4 it is unlikely that this difference would have increased to the clinically relevant difference of 0.4 with an additional 26 patients.
- This study is the first larger randomised controlled trial on early assisted discharge in the Dutch health care system

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic disease with high prevalence [1], mortality and morbidity [2,3]. Exacerbations of the disease have negative effects on patient outcomes [4-6] and are the main cause for hospitalisation [7]. Hospitalisations are not only the main cost driver in COPD, they also put pressure on scarce hospital beds, especially during winters [8]. Several studies have shown that some patients with an exacerbation, who would otherwise be admitted to the hospital, can be treated at home safely after examination in the emergency department or a short hospital admission [9-16]. This is called hospital-at-home. Hospital-at-home aims to avoid admission, or reduce length of stay (early assisted discharge schemes). Previous studies found no differences in readmissions, mortality and disease-specific quality of life between hospital-at-home and usual hospital care [9-11,15,16]. Most published hospital-at-home studies originate from the United Kingdom and Spain, where this service is mainly provided by hospital-based respiratory nurses who visit patients at home. Davison et al. [17] and Nicholson et al. [18] suggested the use of non-specialised

'generic' community nursing teams for home supervision to increase the capacity of hospital-at-home schemes.

The Netherlands has a nation-wide, good infrastructure for community nursing, which could be used for hospital-at-home. Therefore we designed an early assisted discharge hospital-at-home scheme for COPD exacerbations, mainly operated by generic community nurses who performed the home visits [19]. Main objective of the GO AHEAD study (GO AHEAD is the acronym for Assessment Of Going Home under Early Assisted Discharge) was to determine the effectiveness and cost-effectiveness of early assisted discharge followed by community-based nursing care at home. In addition, evaluation of patient satisfaction and preferences, carer strain and preferences and an evaluation among professional care providers was performed. The focus of this paper is on the effectiveness of early assisted discharge, with the Clinical COPD Questionnaire (CCQ) as the primary outcome measure. In addition, treatment failures, readmissions, mortality and generic quality of life were assessed as secondary outcomes.

Methods

GO AHEAD was a randomised controlled trial comparing usual hospital care with early assisted discharge for COPD exacerbations. Five hospitals and three home care organisations participated. Treatment consisted of seven days in-hospital care as usual or three days in-hospital treatment followed by four days care at home. Patients were followed until three months after randomisation.

All patients admitted to one of the participating hospitals with a COPD exacerbation were screened for potential eligibility on their first day of admission according to the inclusion and

exclusion criteria (table 1). On day 3 of admission, clinical stability was assessed in patients who gave written informed consent (see randomisation criteria in table 1). For each hospital separately, participating patients were randomised on day 3 of admission, in a 1:1 ratio using a block-size of 6. Randomisation was performed by the study nurses. The randomisation sequence was computer-generated a priori by an independent researcher. Allocation sequence was placed in sealed envelopes. The study was approved by the Ethics Committee of the Catharina Hospital, the Netherlands, approval number M07-1755.

Table 1 Inclusion and exclusion criteria (applied at admission) and randomisation criteria (applied at day 3 of admission)

Inclusion criteria (checked on day 1)	**Exclusion criteria (checked on day 1)**
Age ≥40 years	Major uncontrolled co morbidity
Competent to give informed consent	Mental disability
Diagnosed with COPD at least GOLD stage I and 10pack years of smoking	Living outside care region of the home care organisation
Hospitalisation for COPD exacerbation	Inability to understand the program
	Indication for admission to intensive care unit or for non invasive ventilation
	Active alcohol and/or drug abuse
	Insufficient availability of informal care at home
Randomisation criteria (checked on day 3)	
Completed Informed Consent on day three of admission	
Acceptable general health: - Decrease physical complaints	

- Non dependency of therapies that cannot be given at home - Being able to visit toilet independently
Normal or moderately increased blood sugar levels, defined as ≤15 mmol/L or ≥15 mmol/L but patient is capable to regulate blood sugar levels independently
Respiratory complaints of dyspnoea, wheezing and rhonchi must have decreased in comparison with day of admission.

During the first three days of the admission all patients were treated in the hospital according to the study protocol [19]. Treatment consisted of systemic corticosteroids, nebulised bronchodilators and antibiotics and oxygen upon indication. Exacerbation symptoms were scored each day. Physiotherapists visited all patients for instruction of breathing and coughing techniques. On the fourth day of admission all randomised patients switched to oral medication and metered dosed inhalations. Patients randomised to early assisted discharge were discharged home on the fourth day of admission and further treated at home. Community nurses visited or contacted the patient at least once daily on the day of discharge and the three consecutive days. They continued to score exacerbation symptoms and provided reassurance and counselling. Furthermore, medication compliance and inhalation techniques were addressed. Community nurses had the highest levels of generic nursing training in the Netherlands. No additional training was provided for the trial. The nurses could contact the hospital to discuss the patient's condition. If necessary, patients were readmitted to the hospital. For patients a 24-hour telephone access to the hospital respiratory ward was installed for emergencies.

Patients in the usual hospital care group received care as usual at the discretion of the hospital staff. General practitioners were informed about the patient's participation in the trial and the

discharge date. Clinical responsibility during home care remained with the respiratory physician. A detailed description of the research protocol and the early assisted discharge intervention has been published previously [19].

Primary outcome was the change in CCQ scores between baseline (T0= day 3 of admission) and the end of the supervised treatment (T+4 days). The CCQ is a disease-specific questionnaire measuring health status [20]. It consists of 10 questions in three domains: symptoms, functional state and mental state, resulting in a overall score varying from 6 (worst score) to 0 (best score) [20]. The CCQ has proved to be responsive to change. The minimal clinical important difference is 0.4 [21]. To detect a difference of 0.4 in CCQ change scores between the two groups, in favour of the early discharge group, with a power of 0.80 and alpha of 0.05, the required sample size was 165 [19]. Secondary outcomes were: 1) change in CCQ scores between baseline and three months after randomisation (T+90 days); 2) number of treatment failures (i.e. either death or clinical deterioration leading to prolonged hospital stay beyond the standardised seven days (usual hospital care) or death or readmission during the four days treatment at home (early discharge)); 3) mortality and 4) readmissions during the three month follow-up; and 5) generic health-related quality of life measured by the EuroQol-5D (EQ-5D)[22] at baseline, T+4 days and T+90 days. Utilities were calculated using the Dutch value set [22]. Higher scores represent better generic quality of life.

Statistical analysis

Change in CCQ scores and EQ-5D scores was analysed using a repeated measures model with an unstructured covariance matrix. Backward selection of covariates was applied. In addition to time (i.e. measurement at T+4 days, end of treatment, and T+90 days, end of follow-up), the interaction of time and treatment, the following variables were tested: baseline CCQ or

EQ-5D score, treatment centre, age, gender, comorbidity, smoking status, living situation, availability informal caregiver, presence of home care prior to admission, course of oral corticosteroids and/or antibiotics prior to admission. Variables were retained in the model if their exclusion led to a 10% change in the estimated treatment effect [23]. For the analysis of CCQ scores, only baseline score was included in the final model. For the analysis of EQ-5D scores, baseline score, comorbidity and gender were included. Results are presented as mean differences in change and 95% confidence intervals (95% CI). Numbers of patients with treatment failures, readmissions and mortality were analysed using multiple logistic regression analysis. Numbers of readmissions per patient in each group were analysed in a Poisson regression. Time to readmission was analysed with a Cox proportional hazards model. Results are presented as odds ratios (OR) or hazard ratios (HR) with 95% CI. Again, backward selection was used to select covariates. Only baseline CCQ score was retained in the models. The significance level for a difference between treatment groups was set at $p \leq 0.05$.

Results

In total, 1371 patients were screened for eligibility between November 2007 and March 2011, of whom 508 met the criteria for eligibility on day 1. Figure 1 shows an overview of the patient flow during the trial from hospital admission to the end of the follow-up. Three patients in the early assisted discharge group and 7 in the usual hospital care group were not satisfied with the allocated place of treatment and withdrew consent immediately after randomisation. The total dropout over the study period was 16%, 25% in the usual hospital care group and 10% in the early assisted discharge group. Baseline CCQ scores of patients dropping out were not different from those who completed the study, but they did have more comorbidities. Table 2 shows the baseline characteristics of randomised patients by treatment

group. These were comparable across the groups. At end of the follow-up period lung function testing was performed by which classification of disease severity according to the GOLD criteria [2] could be made (supplementary data file 1).

Figure 1 Patient flow through study.

Table 2 Baseline characteristics and treatment at admission. Values represent mean (SD), unless stated otherwise.

Characteristic	Usual hospital care (N=69)	Early assisted discharge (N=70)
Age (years)	67.8 (11.3)	68.3 (10.3)
Men (%)	38 (55.1)	48 (68.6)
Smoking history:		
Current smokers (%)	27 (39.1)	23 (32.9)
Pack years, median inter quartile range	37 36.9	44 26.7
Body Mass Index (kg/m^2)	25.6 (4.3)	25.0 (5.1)
Charlson comorbidity score[24]†	1.68 (1.1)	1.74 (1.1)
Comorbidity score of 1 (%)	42 (60.0)	38 (54.0)
Comorbidity score > 1 (%)	27 (39.0)	32 (46.0)
Living situation:		
Living alone (%)	21 (30.4)	22 (31.4)
Receiving care at home before admission (%)	16 (23.2)	17 (24.3)
Treatment at admission:		
Long term oxygen treatment (%)	4 (5.8)	5 (7.1)

Oral steroids (%)	5 (7.2)	10 (14.3)
Course of oral steroids prior to admission (%)	34 (50.0)	35 (50.7)
Course antibiotics prior to admission (%)	31 (45.6)	32 (46.4)
Inhaled β2-agonist (LABA) (%)	9 (13.0)	7 (10.0)
Inhaled corticosteroid (%)	3 (12.0)	3 (15.0)
Inhaled corticosteroid/LABA combination (%)	44 (63.7)	50 (71.4)
Inhaled anticholinergic (%)		
Tiotropium	31 (44.9)	36 (51.4)
Ipratropium	12 (17.4)	13 (18.6)
Followed rehabilitation program in year prior to admission (%)	10 (14.9)	12 (17.4)
Heart Rate (beats/minute)	91.0 (14.2)	95.6 (18.4)
Arterial blood gas[#]*:*	N=37	N=42
pH	7.44 (0.05)	7.43 (0.04)
pO_2 (mmHg)	70.7 (13.2)	67.3 (8.1)
pCO_2 (mmHg)	37.2 (6.2)	39.1 (5.3)
Saturation	94 (2.5)	94 (3.6)

† Charlson Comorbidity Index, 1= only COPD, higher score means more comorbidities; # only data of blood gas measurements in patients without oxygen supplement;
LABA: long acting beta2 agonist

Supplementary file 2 shows the unadjusted CCQ scores at the different measuring points. At T0 CCQ scores were 2.22 (0.97) for the usual hospital care group and 2.63 (1.06) for the early discharge group. Figure 2 shows the change in CCQ scores from T0, adjusted for baseline score. CCQ scores improved between T0 and T+4 days for the usual hospital care group, and were almost stable for the early assisted discharge group, but there was no significant

difference between the groups at T+4 days (difference in mean change from T0 -0.29, 95% CI -0.61 to 0.03, p=0.078). At T+90 days, CCQ scores of both groups scores were slightly higher in comparison to T0. There was no difference between the groups at three months (difference in mean change from T0 -0.04, 95% CI -0.48 to 0.41, p=0.858).

Figure 2 CCQ total score, differences in mean change from baseline

Treatment failed in five patients. One patient in the early discharge group needed readmission to the hospital before the end of the home treatment and 4 patients in the usual hospital care group required hospital admission beyond the 7 days that were stated in the protocol. This difference was not significant (OR early discharge group 0.27, 95% CI 0.026 – 2.70, p=0.263). Table 3 shows the number of readmissions during follow-up. Seventeen patients in each group had 1 or more readmission to the hospital of which 14 first readmissions were due to an exacerbation or other pulmonary indication (OR early discharge group 0.80, 95% CI 0.36 – 1.79, p=0.592). There was no difference in the number of readmissions per patient between the groups, or in the total number of readmissions in each group. There was no difference in time to first readmission between the two groups (HR early discharge group 0.77, 95% CI 0.39 to 1.53, p=0.461).

Table 3 Readmissions during follow-up. Values are numbers of patients (%).

	Usual hospital care	Early assisted discharge
Patients with readmission	17 (25)	17 (24)
Patients with 1, 2 or ≥ 3 readmissions		
1 readmission	11	12

2 readmissions	4	3
3 or more readmissions	2	2

No patient died during the hospital or home treatment, but 1 patient from each group died during follow-up. Cause of death was unknown in one case (patient died during sleep at home) and an acute abdomen in the other. Both were not related to the trial.

EQ-5D utility scores (SD) at T0 were 0.713 (0.22) for the usual hospital care group and 0.664 (0.26) for the early assisted discharge group. Table 4 shows the mean changes and mean difference in change from baseline of EQ-5D utility. In the usual hospital care group, mean utility scores improved from T0 to T+4 days and decreased to baseline at T+90 days. In the early assisted discharge group mean utility scores remained close to baseline. The mean change in utility scores on T+4 days was significant greater in the usual hospital care group. At T+90 days this difference between treatment groups had disappeared.

Table 4 Mean changes and mean differences in change for EQ-5D.

		Mean change from baseline (SE)		Adjusted mean (95% CI) difference in change from baseline*	p value
Utility		Usual hospital care	Early assisted discharge	Usual care - early discharge	
	T+ 4 days†	0.051 (0.0261)	-0.005 (0.029)	0.0746 (0.010 to 0.139)	0.024
	T+ 90 days‡	-0.036 (0.0447)	0.008 (0.039)	-0.022 (-0.116 to 0.072)	0.639

*Results from repeated measures analysis, adjusted for baseline value † hospital care N=57, early discharge N=61; ‡ hospital care N=47, early discharge N=54
SE: Standard Error; 95% CI: 95% Confidence Interval

Discussion

This is the first randomised controlled trial that investigated the effectiveness of early assisted discharge for COPD exacerbations with supervision at home by community nurses. In addition, this is the first evaluation of early discharge for this disease in the Dutch health care system. While patients' disease-specific health status as expressed in the mean CCQ score after seven days treatment tended to be somewhat better in the usual hospital care group, the difference was small, not clinically relevant and not statistically significant. After three months, the difference had disappeared. The same pattern was found in generic health-related quality of life measured with the EQ-5D, although this difference was statistically significant at the end of the supervised treatment. The difference had disappeared at the end of the 3-month follow up period. There was no difference in treatment failures, readmissions or mortality.

These study results confirm previously published positive results by Davison et al. [17] and Nicholson et al. [18], but these two studies were either not randomised [17] or included a small number of patients [18]. We found no significant difference in CCQ scores, which corresponds with the findings of Davies et al. [9] and Hernandez et al. [16], who found no differences in disease-specific quality of life measured with the St George's Respiratory Questionnaire. Furthermore, our results are in line with those of earlier studies involving specialised hospital-based nurses [9-12,15,16,24,25]. The readmission rate in our study was 25%, which is comparable to the 30% in previously published studies [9-11]. Characteristics like age, smoking history and living situation of patients in our study were similar to those in studies from the United Kingdom [9-12] and to that of a survey on hospital-at-home services in British hospitals by Quantrill et al. [26].

Earlier studies did not measure the impact of hospital-at-home on generic health-related quality of life. We found a significant difference between the two groups, in favour of usual hospital care, at the end of the hospital and home treatment. This difference had disappeared after three months. The utility scores are in line with O'Reilly et al. [27], but they found much worse scores at admission than in our study, probably because we did not include patients with more severe exacerbations. Utility and CCQ scores in both groups follow the same pattern. The greater improvement in CCQ and EQ-5D scores of the usual hospital care group at the end of the hospital treatment in comparison to the early discharge group may reflect a true difference in recovery, in which case usual hospital care is the preferred treatment. However, an alternative explanation could be that patients who were discharged early were confronted with their symptoms and limitations earlier and more intensely when they tried to pick up normal life at home. Furthermore, some patients have difficulties viewing hospital care followed by early discharge as one treatment period [28]. Expecting to be in a certain state at discharge, and experiencing this is not the case, might be expressed in worse scores on the CCQ and the EQ-5D.

In our trial multiple hospitals participated with different socioeconomic and geographic characteristics, which makes it likely that our sample is representative of eligible patients. The percentage of admissions initially considered to be eligible for early discharge at admission was similar to that of previous studies (±37%). Early discharge is possible when the exacerbation is the main problem and comorbidities are (relatively) stable. The percentage of patients living alone suggests that this is not an absolute reason for exclusion, provided that patients have a sufficiently functioning social support system. Still, 25% of screened patients were considered ineligible, because of living in a nursing home, overburden of informal caregiver(s) or living alone with insufficient social support. This suggests that social

environment is an important factor when deciding for admission and (early) discharge. Finally, 37% of screened patients was ineligible because of comorbidities.

Considering the very low number of treatment failures in the early discharge group it might be possible to relax the inclusion criteria and randomisation criteria. In our trial, criteria were applied very strictly for safety reasons, but more patients with comorbidities might be eligible in daily practice. Furthermore, the strict review and exclusion of patients at day 1 of admission (e.g. those treated with NIV), precluded patients from early discharge even if they had become eligible at day 3 of admission. Therefore, review of eligibility for early discharge should be performed after a few days of hospital treatment. Thirty percent of patients who consented to participate were not randomised because they showed insufficient recovery and/or were depending on oxygen supply. Unlike in the British hospital-at-home schemes, patients were not sent home with nebulisers or oxygen cylinders, unless these were already part of their treatment. Extension of the treatment possibilities at home may enable early discharge of patient with more severe disease. However, it would also require more expertise of the nursing staff supervising patients at home, which might currently not be present in community-based home care organisations. Future research should focus on determining which treatments can be safely provided at home, which treatments require the supervision of generic or specialised nurses and which criteria should be applied for selecting eligible patients. In addition, a direct comparison between early discharge with generic and early discharge with specialised nursing care would provide more information on which scheme is most safe and effective.

Our study has some limitations. Firstly, in total 139 patients were randomised, where a number of 165 was calculated to be needed to detect a difference of 0.4 in CCQ change scores

between the two groups. A post-hoc power analysis with these 139 patients and the actual variances in CCQ scores showed that the power to detect a difference in change from baseline of 0.4 between the groups was 73% instead of 80%, which was aimed for. We believe that this slight reduction in power does not have a substantial influence on our final results, because the difference between the groups was only 0.29. It is highly unlikely that this difference would have increased to the clinically relevant difference of 0.4 with an additional 26 patients. In previous randomised studies of early discharge in patients diagnosed with COPD numbers varied between 25 and 222, and only 15 to 35% of admitted patients was randomised [9-12,16,29]. Secondly, our study was not an equivalence trial, which would determine best whether hospital care and early discharge care are equally effective. However, in order to demonstrate equal effectiveness with CCQ score, over 500 patients would have been needed, which is beyond what is attainable in this population. Thirdly, 16% of patients dropped out after randomisation. However, comparison of patients who dropped out with patients who completed the study only revealed more comorbidities for those who dropped out. CCQ scores were not different. Finally, due to the nature of the intervention, patients and health care staff could not be blinded to the allocated group.

In conclusion, we found no significant short-term or long-term differences in outcomes between early discharge and usual hospital care, except for generic health-related quality of life at the end of treatment (T+4 days). Early assisted discharge with home visits by community nurses can reduce length of hospital stay for a selected group of patients admitted with a COPD exacerbation and is an alternative to usual hospital care. The decision to implement early assisted discharge with community nursing does not only depend on the results of the effectiveness analysis. Costs and cost-effectiveness evaluations are of high

importance as well. An economic evaluation is currently being performed and results will be published separately.

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Competing interests

"All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) LG, MR, OvS have had support from ZonMw for the submitted work; (2) CU,

FS, MvV, MB, LvE have no relationships with companies that might have an interest in the submitted work in the previous 3 years; LG and MR haves relationships (received grants to perform cost- and cost-effectiveness studies) from multiple pharmaceutical companies, OvS has relationships (consultancy) with Pfizer, Boehringer Ingelheim and Astra Zeneca that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) CU, LG, FS, MR, MvV, MB, LvE and OvS have no non-financial interests that may be relevant to the submitted work."

Contributors

CU was involved in patient recruitment, database management, administration of questionnaires, data analysis, data interpretation and wrote the manuscript. LG was involved in data analysis and data interpretation and preparation of the manuscript. FS was local coordinating physician and involved in data interpretation and preparation of the manuscript. MR designed the study and involved in data interpretation and preparation of the manuscript. MvV was local coordinating physician in the Atrium Medical Centre and involved in the preparation of the manuscript. MB and LvE were coordinators of the home care organisations and involved in the preparation of the manuscript. OvS designed the study and was involved in data interpretation and writing the manuscript. OvS is guarantor for the study. All researchers had access to all data.

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Data sharing

No additional data available

References

1. Buist AS, McBurnie MA, Vollmer WM et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet 2007;370:741-750.
2. Rabe KF, Hurd S, Anzueto A et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532-555.
3. Lopez AD, Shibuya K, Rao C et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J 2006;27:397-412.
4. Seemungal TA, Donaldson GC, Paul EA et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998;157:1418-1422.
5. Donaldson GC, Seemungal TA, Bhowmik A et al. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. Thorax 2002;57:847-852.
6. Esteban C, Quintana JM, Moraza J et al. Impact of hospitalisations for exacerbations of COPD on health-related quality of life. Respir Med 2009;103:1201-1208.
7. Toy EL, Gallagher KF, Stanley EL et al. The economic impact of exacerbations of chronic obstructive pulmonary disease and exacerbation definition: a review. COPD 2010;7:214-228.
8. Jordan RE, Hawker JI, Ayres JG et al. Effect of social factors on winter hospital admission for respiratory disease: a case-control study of older people in the UK. Br J Gen Pract 2008;58:400-402.

9. Davies L, Wilkinson M, Bonner S et al. "Hospital at home" versus hospital care in patients with exacerbations of chronic obstructive pulmonary disease: prospective randomised controlled trial. BMJ 2000;321:1265-1268.

10. Cotton MM, Bucknall CE, Dagg KD et al. Early discharge for patients with exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Thorax 2000;55:902-906.

11. Skwarska E, Cohen G, Skwarski KM et al. Randomized controlled trial of supported discharge in patients with exacerbations of chronic obstructive pulmonary disease. Thorax 2000;55:907-912.

12. Ojoo JC, Moon T, McGlone S et al. Patients' and carers' preferences in two models of care for acute exacerbations of COPD: results of a randomised controlled trial. Thorax 2002;57:167-169.

13. British Thoracic Society. Intermediate care--Hospital-at-Home in chronic obstructive pulmonary disease: British Thoracic Society guideline. Thorax 2007;62:200-210.

14. Diaz LS, Gonzalez LF, Gomez Mendieta MA et al. [Evaluation of a home hospitalization program in patients with exacerbations of chronic obstructive pulmonary disease]. Arch Bronconeumol 2005;41:5-10.

15. Gravil JH, Al-Rawas OA, Cotton MM et al. Home treatment of exacerbations of chronic obstructive pulmonary disease by an acute respiratory assessment service. Lancet 1998;351:1853-1855.

16. Hernandez C, Casas A, Escarrabill J et al. Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients. Eur Respir J 2003;21:58-67.

17. Davison AG, Monaghan M, Brown D et al. Hospital at home for chronic obstructive pulmonary disease: an integrated hospital and community based generic intermediate care service for prevention and early discharge. Chron Respir Dis 2006;3:181-185.

18. Nicholson C, Bowler S, Jackson C et al. Cost comparison of hospital- and home-based treatment models for acute chronic obstructive pulmonary disease. Aust Health Rev 2001;24:181-187.

19. Utens CM, Goossens LM, Smeenk FW et al. Effectiveness and cost-effectiveness of early assisted discharge for Chronic Obstructive Pulmonary Disease exacerbations: the design of a randomised controlled trial. BMC Public Health 2010;10:618

20. van der Molen T, Willemse BW, Schokker S et al. Development, validity and responsiveness of the Clinical COPD Questionnaire. Health Qual Life Outcomes 2003;1:13

21. Kocks JW, Tuinenga MG, Uil SM et al. Health status measurement in COPD: the minimal clinically important difference of the clinical COPD questionnaire. Respir Res 2006;7:62

22. Lamers LM, McDonnell J, Stalmeier PF et al. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. Health Econ 2006;15:1121-1132.

23. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology (3rd edition). Philidelphia: Lippincott Williams & Wilkins 2008.

24. Ansari K, Shamssain M, Farrow M et al. Hospital-at-home care for exacerbations of chronic obstructive pulmonary disease: an observational cohort study of patients managed in hospital or by nurse practitioners in the community. Chron Respir Dis 2009;6:69-74.

25. Sala E, Alegre L, Carrera M et al. Supported discharge shortens hospital stay in patients hospitalized because of an exacerbation of COPD. Eur Respir J 2001;17:1138-1142.

26. Quantrill SJ, Lowe D, Hosker HS et al. Survey of early discharge schemes from the 2003 UK National COPD Audit. Respir Med 2007;101:1026-1031.

27. O'Reilly JF, Williams AE, Rice L. Health status impairment and costs associated with COPD exacerbation managed in hospital. Int J Clin Pract 2007;61:1112-1120.

28. Clarke A, Sohanpal R, Wilson G et al. Patients' perceptions of early supported discharge for chronic obstructive pulmonary disease: a qualitative study. Qual Saf Health Care 2010;19:95-98.

29. Aimonino RN, Tibaldi V, Leff B et al. Substitutive "hospital at home" versus inpatient care for elderly patients with exacerbations of chronic obstructive pulmonary disease: a prospective randomized, controlled trial. J Am Geriatr Soc 2008;56:493-500.

30. Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383

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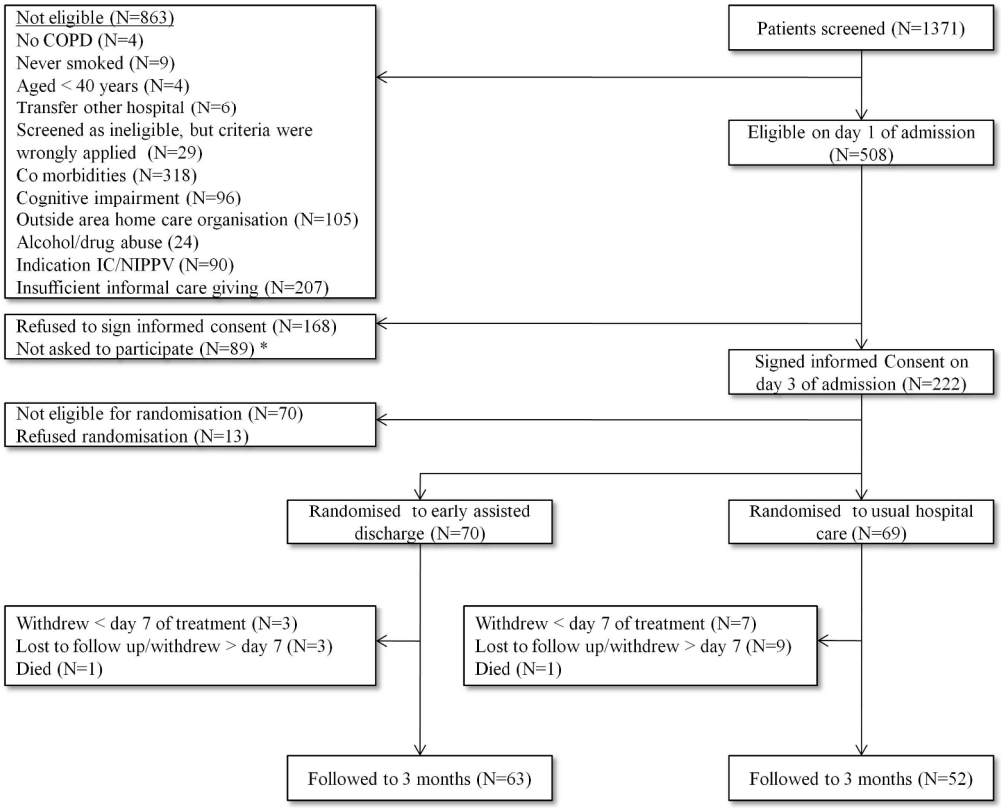
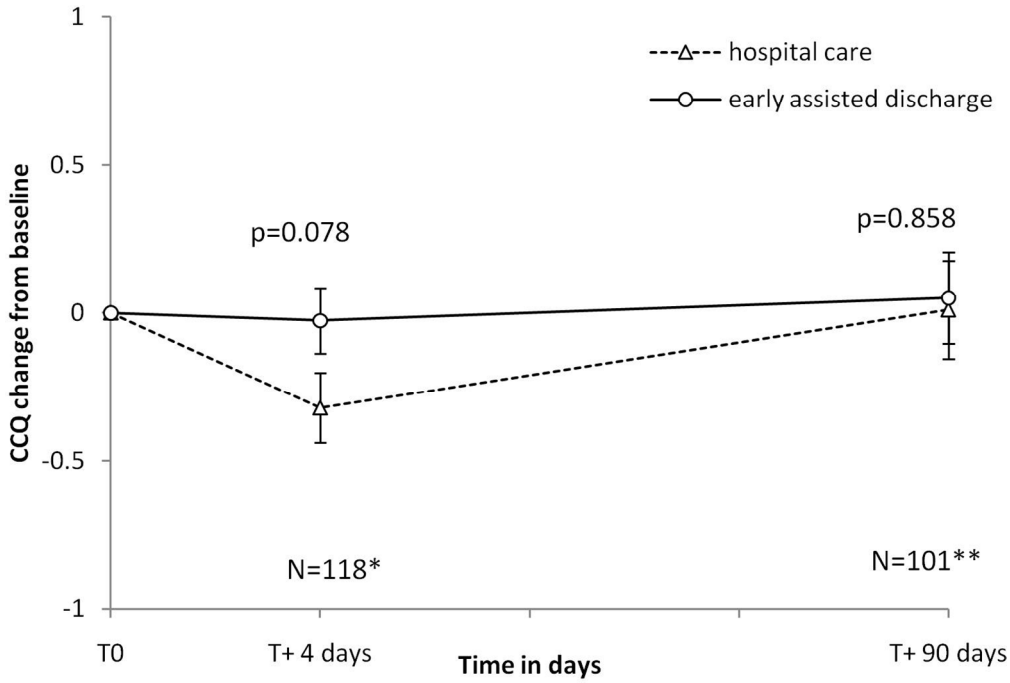


*Not asked to participate because of logistical reasons (e.g. no study staff available or patient not admitted to respiratory ward)
226x182mm (300 x 300 DPI)



Error bars represent standard errors. P values are based on repeated measures analysis, adjusted for baseline value.
*Number of patients at T+4 days that completed questionnaire that produced valid total score; **number of patients at T+90 days that completed questionnaire that produced valid total score.

128x86mm (300 x 300 DPI)

Supplemental file 1

Lung function testing at end of 3 month follow-up. Values represent mean (SD)

	Usual hospital care	Early assisted discharge
Postbronchodilator FEV_1 (litres)	1.25 (0.07)	1.21 (0.07)
% of predicted postbronchodilator FEV_1	50.29 (2.71)	45.20 (2.13)
% GOLD stage I	10.3	2.9
% GOLD stage II	32.4	32.9
% GOLD stage III	41.2	44.3
% GOLD stage IV	16.2	20.0

Supplementary file 2

Unadjusted CCQ total scores (SD) at each time of measurement by treatment group.

Time of measurement	Usual hospital care	Early assisted discharge
T- 2 days	3.21 (1.07)	3.49 (1.07)
T0	2.22 (0.97)	2.63 (1.06)
T+ 4 days	2.00 (1.09)	2.55 (1.21)
T+ 90 days	2.41 (1.14)	2.70 (1.32)

CCQ total score range is 0-6;

0 represents best possible score and 6 represents worst possible score

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5-6
	2b	Specific objectives or hypotheses	5-6
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	6-7 & table 1
	4b	Settings and locations where the data were collected	6-7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9 & reference 19
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	18
	11b	If relevant, description of the similarity of interventions	8-9
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n/a
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10 & fig 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	10 & fig 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6 & 10
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	All tables and figures with results
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	13-14 Tables & figures
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n/a
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	18
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15 to 18
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15 to 18
Other information			
Registration	23	Registration number and name of trial registry	abstract
Protocol	24	Where the full trial protocol can be accessed, if available	Reference 19
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

EARLY ASSISTED DISCHARGE WITH COMMUNITY NURSING FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS: RESULTS OF A RANDOMISED CONTROLLED TRIAL

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Title:

Early assisted discharge with generic community nursing for Chronic Obstructive Pulmonary Disease exacerbations: results of a randomised controlled trial

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Keywords: Hospital at home; Early assisted discharge from hospital; Chronic Obstructive Pulmonary Disease; Community nursing, Randomised controlled trial

Abstract

Objectives: To determine effectiveness of early assisted discharge for COPD exacerbations, with home care provided by generic community nurses, compared to usual hospital care.

Design: Prospective, randomised controlled, multi-centre trial with 3 months follow-up.

Setting: Five hospitals and 3 home care organisations in the Netherlands.

Participants: Patients admitted to the hospital with an exacerbation of Chronic Obstructive Pulmonary Disease. Patients with no or limited improvement of respiratory symptoms and patients with severe unstable comorbidities, social problems or those unable to visit the toilet independently were excluded.

Intervention: Early discharge from hospital after 3 days inpatient treatment. Home visits by generic community nurses. Primary outcome measure was change in health status measured by the Clinical COPD Questionnaire (CCQ). Treatment failures, readmissions, mortality and change in generic health-related quality of life (HRQL) were secondary outcome measures.

Results: 139 patients were randomised. No difference between groups was found in change in CCQ score at day 7 (difference in mean change 0.29 (95% CI -0.03 to 0.61)) or at 3 months

(difference in mean change 0.04 (95% CI –0.40 to 0.49)). No difference was found in secondary outcomes. At day 7 there was a significant difference in change in generic HRQL, favouring usual hospital care.

Conclusion: While patients' disease-specific health status after seven days treatment tended to be somewhat better in the usual hospital care group, the difference was small and not clinically relevant or statistically significant. After three months, the difference had disappeared. A significant difference in generic health-related quality of life at the end of the treatment had disappeared after 3 months and there was no difference in treatment failures, readmissions or mortality. Early assisted discharge with community nursing is feasible and an alternative to usual hospital care for selected patients with an acute COPD exacerbation.

Trial registration: NetherlandsTrialRegister NTR 1129

Article summary

Article focus:

- What is the effectiveness of early assisted discharge with community nursing for COPD exacerbations in comparison to usual hospital care as measured by the Clinical COPD Questionnaire.

Key Messages:

- There is no short term or long term difference in change in health status as measured by the Clinical COPD Questionnaire.
- A significant difference in generic health-related quality of life at the end of the treatment disappeared after 3 months.
- Early assisted discharge with home visits by community nurses is a feasible and an alternative to usual hospital care for selected patients with an acute exacerbation of their COPD.

Strength and limitations:

- 139 patients were randomised where 165 was calculated to be the required sample size. However, because the difference between the groups was only 0.29 instead of 0.4 it is unlikely that this difference would have increased to the clinically relevant difference of 0.4 with an additional 26 patients.
- This study is the first larger randomised controlled trial on early assisted discharge in the Dutch health care system

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic disease with high prevalence [1], mortality and morbidity [2,3]. Exacerbations of the disease have negative effects on patient outcomes [4-6] and are the main cause for hospitalisation [7]. Hospitalisations are not only the main cost driver in COPD, they also put pressure on scarce hospital beds, especially during winters [8]. Several studies have shown that some patients with an exacerbation, who would otherwise be admitted to the hospital, can be treated at home safely after examination in the emergency department or a short hospital admission [9-16]. This is called hospital-at-home. Hospital-at-home aims to avoid admission, or reduce length of stay (early assisted discharge schemes). Previous studies found no differences in readmissions, mortality and disease-specific quality of life between hospital-at-home and usual hospital care [9-11,15,16]. Most published hospital-at-home studies originate from the United Kingdom and Spain, where this service is mainly provided by hospital-based respiratory nurses who visit patients at home. Davison et al. [17] and Nicholson et al. [18] suggested the use of non-specialised 'generic' community nursing teams for home supervision to increase the capacity of hospital-at-home schemes.

The Netherlands has a nation-wide, good infrastructure for community nursing, which could be used for hospital-at-home. Therefore we designed an early assisted discharge hospital-at-home scheme for COPD exacerbations, mainly operated by generic community nurses who performed the home visits [19]. Main objective of the GO AHEAD study (GO AHEAD is the acronym for Assessment Of Going Home under Early Assisted Discharge) was to determine the effectiveness and cost-effectiveness of early assisted discharge followed by community-based nursing care at home. In addition, evaluation of patient satisfaction and preferences, carer strain and preferences and an evaluation among professional care providers was performed. The focus of this paper is on the effectiveness of early assisted discharge, with the Clinical COPD Questionnaire (CCQ) as the primary outcome measure. In addition, treatment failures, readmissions, mortality and generic quality of life were assessed as secondary outcomes.

Methods

GO AHEAD was a randomised controlled trial comparing usual hospital care with early assisted discharge for COPD exacerbations. Five hospitals and three home care organisations participated. Treatment consisted of seven days in-hospital care as usual or three days in-hospital treatment followed by four days care at home. Patients were followed until three months after randomisation.

All patients admitted to one of the participating hospitals with a COPD exacerbation, as diagnosed by the reviewing physician, were screened for potential eligibility on their first day of admission according to the inclusion and exclusion criteria (table 1). On day 3 of admission, clinical stability was assessed in patients who gave written informed consent (see randomisation criteria in table 1). For each hospital separately, participating patients were

randomised on day 3 of admission, in a 1:1 ratio using a block-size of 6. Randomisation was performed by the study nurses. The randomisation sequence was computer-generated a priori by an independent researcher. Allocation sequence was placed in sealed envelopes. The study was approved by the Ethics Committee of the Catharina Hospital, the Netherlands, approval number M07-1755.

Table 1 Inclusion and exclusion criteria (applied at admission) and randomisation criteria (applied at day 3 of admission)

Inclusion criteria (checked on day 1)	**Exclusion criteria (checked on day 1)**
Age ≥40 years	Major uncontrolled comorbidity, including pneumonia that is prominent, heart failure that is prominent or acute changes on electro cardiogram and (suspected) underlying malignancy.
Competent to give informed consent	Mental disability, including dementia, impaired level of consciousness and acute confusion.
Diagnosed with COPD. COPD was defined as at least GOLD stage I and 10 pack years of smoking	Living outside care region of the home care organisation
Hospitalisation for COPD exacerbation	Inability to understand the program
	Indication for admission to intensive care unit or for non invasive ventilation
	Active alcohol and/or drug abuse
	Insufficient availability of informal care at

	home
Randomisation criteria (checked on day 3)	
Completed Informed Consent on day three of admission	
Acceptable general health: - Decrease physical complaints - Non dependency of therapies that cannot be given at home (intravenous therapy and newly prescribed oxygen supply). - Being able to visit toilet independently	
Normal or moderately increased blood sugar levels, defined as ≤15 mmol/L or ≥15 mmol/L but patient is capable to regulate blood sugar levels independently	
Respiratory complaints of dyspnoea, wheezing and rhonchi must have decreased in comparison with day of admission.	

During the first three days of the admission all patients were treated in the hospital according to the study protocol [19]. Treatment consisted of systemic corticosteroids, nebulised bronchodilators and antibiotics and oxygen upon indication. Exacerbation symptoms were scored each day. Physiotherapists visited all patients for instruction of breathing and coughing techniques. On the fourth day of admission all randomised patients switched to oral medication and metered dosed inhalations. Patients randomised to early assisted discharge were discharged home on the fourth day of admission and further treated at home. Community nurses visited or contacted the patient at least once daily on the day of discharge and the three consecutive days. They continued to score exacerbation symptoms and provided reassurance and counselling. Furthermore, medication compliance and inhalation techniques were addressed. Community nurses had the highest levels of generic nursing training in the Netherlands. No additional training was provided for the trial. The nurses could contact the

hospital to discuss the patient's condition. If necessary, patients were readmitted to the hospital. For patients a 24-hour telephone access to the hospital respiratory ward was installed for emergencies.

Patients in the usual hospital care group received care as usual at the discretion of the hospital staff. General practitioners were informed about the patient's participation in the trial and the discharge date. Clinical responsibility during home care remained with the respiratory physician. A detailed description of the research protocol and the early assisted discharge intervention has been published previously [19].

Primary outcome was the change in CCQ scores between baseline (T0= day 3 of admission) and the end of the supervised treatment (T+4 days). The CCQ is a disease-specific questionnaire measuring health status [20]. It consists of 10 questions in three domains: symptoms, functional state and mental state, resulting in a overall, continuous score varying from 6 (worst score) to 0 (best score) [20]. In order to produce a valid overall score, 3, 3 and 2 questions on the symptoms domain, functional state and mental state domain, respectively need to be answered. The CCQ has proved to be responsive to change. The minimal clinical important difference is 0.4 [21]. Secondary outcomes were: 1) change in CCQ scores between baseline and three months after randomisation (T+90 days); 2) number of treatment failures (i.e. either death or clinical deterioration leading to prolonged hospital stay beyond the standardised seven days (usual hospital care) or death or readmission during the four days treatment at home (early discharge)); 3) mortality and 4) readmissions during the three month follow-up; and 5) generic health-related quality of life measured by the EuroQol-5D (EQ-5D)[22] at baseline, T+4 days and T+90 days. Utilities were calculated using the Dutch value set [22]. Higher scores represent better generic quality of life.

Statistical analysis

To detect a difference of 0.4 in CCQ change scores between the two groups, in favour of the early discharge group, with a power of 0.80 and alpha of 0.05, with standard deviation in the usual hospital care group of 0.922 and 0.988 in the early discharge group, the required sample size was 165 [19]. Change in CCQ scores and EQ-5D scores was analysed using a linear repeated measures model with correlated errors. An unstructured covariance matrix for the residuals of the different measurements was used. Backward selection of covariates was applied. In addition to time (i.e. measurement at T+4 days, end of treatment, and T+90 days, end of follow-up), the interaction of time and treatment, the following variables were tested: baseline CCQ or EQ-5D score, treatment centre, age, gender, comorbidity, smoking status, living situation, availability informal caregiver, presence of home care prior to admission, course of oral corticosteroids and/or antibiotics prior to admission. Variables were retained in the model if their exclusion led to a 10% change in the estimated treatment effect [23]. For the analysis of CCQ scores, only baseline score was included in the final model. For the analysis of EQ-5D scores, baseline score, comorbidity and gender were included. Results are presented as mean differences in change and 95% confidence intervals (95% CI). Numbers of patients with treatment failures, readmissions and mortality were analysed using multiple logistic regression analysis. Numbers of readmissions per patient in each group were analysed in a Poisson regression. Time to readmission was analysed with a Cox proportional hazards model. Results are presented as odds ratios (OR) or hazard ratios (HR) with 95% CI. Again, backward selection was used to select covariates. Only baseline CCQ score was retained in the models. The significance level for a difference between treatment groups was set at $p \leq 0.05$. All analyses were performed using the Statistical Package for Social Sciences (SPSS), version 17.0, IBM.

Results

In total, 1371 patients were screened for eligibility between November 2007 and March 2011, of whom 508 met the criteria for eligibility on day 1. Figure 1 shows an overview of the patient flow during the trial from hospital admission to the end of the follow-up. Three patients in the early assisted discharge group and 7 in the usual hospital care group were not satisfied with the allocated place of treatment and withdrew consent immediately after randomisation. The total dropout over the study period was 16%, 25% in the usual hospital care group and 10% in the early assisted discharge group. Baseline CCQ scores of patients dropping out were not different from those who completed the study, but they did have more comorbidities. At T+4 days 118 of 129 still participating patients produced a valid overall score on the CCQ and were included in the analysis. The other patients did not withdraw consent and continued to participate in the study in order to contribute to the other analyses and to produce a valid score at other measuring points. This approach fits with the intention-to-treat principle and the repeated measures analysis. At T+90 days, 101 of 115 patients produced a valid overall CCQ score.

Table 2 shows the baseline characteristics of randomised patients by treatment group. These were comparable across the groups. At end of the follow-up period lung function testing was performed by which classification of disease severity according to the GOLD criteria [2] could be made (see table 3).

Figure 1 Patient flow through study.

Table 2 Baseline characteristics and treatment at admission. Values represent mean (SD), unless stated otherwise.

Characteristic	Usual hospital care (N=69)	Early assisted discharge (N=70)
Age (years)	67.8 (11.3)	68.3 (10.3)
Men n (%)	38 (55.1)	48 (68.6)
Smoking history:		
Current smokers n (%)	27 (39.1)	23 (32.9)
Pack years, median inter quartile range	37 36.9	44 26.7
Body Mass Index (kg/m^2)	25.6 (4.3)	25.0 (5.1)
Charlson comorbidity score[24]†	1.68 (1.1)	1.74 (1.1)
Comorbidity score of 1 n (%)	42 (60.0)	38 (54.0)
Comorbidity score > 1 n (%)	27 (39.0)	32 (46.0)
Living situation:		
Living alone n (%)	21 (30.4)	22 (31.4)
Receiving care at home before admission n (%)	16 (23.2)	17 (24.3)
Treatment at admission:		
Long term oxygen treatment n (%)	4 (5.8)	5 (7.1)
Oral steroids n (%)	5 (7.2)	10 (14.3)
Course of oral steroids prior to admission n (%)	34 (50.0)	35 (50.7)
Course antibiotics prior to admission n (%)	31 (45.6)	32 (46.4)
Inhaled β2-agonist (LABA) n (%)	9 (13.0)	7 (10.0)
Inhaled corticosteroid n (%)	3 (12.0)	3 (15.0)

Inhaled corticosteroid/LABA combination n (%)	44 (63.7)	50 (71.4)
Inhaled anticholinergic n (%)		
Tiotropium	31 (44.9)	36 (51.4)
Ipratropium	12 (17.4)	13 (18.6)
Followed rehabilitation program in year prior to admission n (%)	10 (14.9)	12 (17.4)
Heart Rate (beats/minute)	91.0 (14.2)	95.6 (18.4)
Arterial blood gas[#]*:*	N=37	N=42
pH	7.44 (0.05)	7.43 (0.04)
pO_2 (mmHg)	70.7 (13.2)	67.3 (8.1)
pCO_2 (mmHg)	37.2 (6.2)	39.1 (5.3)
Saturation	94 (2.5)	94 (3.6)

† Charlson Comorbidity Index, 1= only COPD, higher score means more comorbidities; # only data of blood gas measurements in patients without oxygen supplement;
LABA: long acting beta2 agonist

Table 3

Lung function testing at end of 3 month follow-up. Values represent mean (SD), unless stated otherwise.

	Usual hospital care	Early assisted discharge
Postbronchodilator FEV_1 (litres)	1.25 (0.07)	1.21 (0.07)
% of predicted postbronchodilator FEV_1	50.29 (2.71)	45.20 (2.13)
GOLD stage I, n (%)	7 (10.3)	2 (2.9)
GOLD stage II, n (%)	22 (32.4)	23 (32.9)
GOLD stage III, n (%)	28 (41.2)	31 (44.3)
GOLD stage IV, n (%)	11 (16.2)	14 (20.0)

Table 4 shows the unadjusted CCQ scores at the different measuring points. At T0 CCQ scores were 2.22 (0.97) for the usual hospital care group and 2.63 (1.06) for the early discharge group. Figure 2 shows the change in CCQ scores from T0, adjusted for baseline score. CCQ scores improved between T0 and T+4 days for the usual hospital care group, and were almost stable for the early assisted discharge group, but there was no significant difference between the groups at T+4 days (difference in mean change from T0 0.29, 95% CI -0.03 to 0.61, p=0.078). At T+90 days, CCQ scores of both groups were slightly higher in comparison to T0. There was no difference between the groups at three months (difference in mean change from T0 0.04, 95% CI -0.40 to 0.49, p=0.858).

Table 4

Unadjusted mean (SD) CCQ total scores at each time of measurement by treatment group.

Time of measurement	Usual hospital care	Early assisted discharge
T- 2 days	3.21 (1.07)	3.49 (1.07)
T0	2.22 (0.97)	2.63 (1.06)
T+ 4 days	2.00 (1.09)	2.55 (1.21)

T+ 90 days	2.41 (1.14)	2.70 (1.32)

CCQ total score range is 0-6; 0 represents best possible score and 6 represents worst possible score

Figure 2 CCQ total score, differences in mean change from baseline

Treatment failed in five patients. One patient in the early discharge group needed readmission to the hospital because of deterioration of respiratory symptoms, before the end of the home treatment and 4 patients in the usual hospital care group required hospital admission beyond the 7 days that were stated in the protocol (2 because of deterioration of respiratory symptoms, 2 patients because of deterioration of general condition due to gastroenteritis caused by norovirus). This difference was not significant (OR early discharge group 0.27, 95% CI 0.026 – 2.70, p=0.263). Table 5 shows the number of readmissions during follow-up. Seventeen patients in each group had 1 or more readmission to the hospital of which 14 first readmissions were due to an exacerbation or other pulmonary indication (OR early discharge group 0.80, 95% CI 0.36 – 1.79, p=0.592). There was no difference in the number of readmissions per patient between the groups, or in the total number of readmissions in each group. There was no difference in time to first readmission between the two groups (HR early discharge group 0.77, 95% CI 0.39 to 1.53, p=0.461).

Table 5 Readmissions during follow-up. Values are numbers of patients (%).

	Usual hospital care	Early assisted discharge
Patients with readmission	17 (25)	17 (24)
Patients with 1, 2 or ≥ 3 readmissions		
1 readmission	11	12

2 readmissions	4	3
3 or more readmissions	2	2
Average (SD) time to first readmission in days	61 (36.5)	69 (33.8)

No patient died during the hospital or home treatment, but 1 patient from each group died during follow-up. Cause of death was unknown in one case (patient died during sleep at home) and an acute abdomen in the other. Both were not related to the trial.

EQ-5D utility scores (SD) at T0 were 0.713 (0.22) for the usual hospital care group and 0.664 (0.26) for the early assisted discharge group. Table 6 shows the mean changes and mean difference in change from baseline of EQ-5D utility. In the usual hospital care group, mean utility scores improved from T0 to T+4 days and decreased to baseline at T+90 days. In the early assisted discharge group mean utility scores remained close to baseline. The mean change in utility scores on T+4 days was significant greater in the usual hospital care group. At T+90 days this difference between treatment groups had disappeared.

Table 6 Mean changes and mean differences in change for EQ-5D.

		Mean change from baseline (SE)		Adjusted mean (95% CI) difference in change from baseline*	p value
Utility		Usual hospital care	Early assisted discharge	Usual care - early discharge	
	T+ 4 days†	0.051 (0.0261)	-0.005 (0.029)	0.0746 (0.010 to 0.139)	0.024
	T+ 90 days‡	-0.036 (0.0447)	0.008 (0.039)	-0.022 (-0.116 to 0.072)	0.639

*Results from repeated measures analysis, adjusted for baseline value † hospital care N=57, early discharge N=61; ‡ hospital care N=47, early discharge N=54
SE: Standard Error; 95% CI: 95% Confidence Interval

Discussion

This is the first randomised controlled trial that investigated the effectiveness of early assisted discharge for COPD exacerbations with supervision at home by community nurses. In addition, this is the first evaluation of early discharge for this disease in the Dutch health care system. While patients' disease-specific health status as expressed in the mean CCQ score after seven days treatment tended to be somewhat better in the usual hospital care group, the difference was small, not clinically relevant and not statistically significant. After three months, the difference had disappeared. The same pattern was found in generic health-related quality of life measured with the EQ-5D, although this difference was statistically significant at the end of the supervised treatment. The difference had disappeared at the end of the 3-month follow up period. There was no difference in treatment failures, readmissions or mortality.

These study results confirm previously published positive results by Davison et al. [17] and Nicholson et al. [18], but these two studies were either not randomised [17] or included a small number of patients [18]. We found no significant difference in CCQ scores, which corresponds with the findings of Davies et al. [9] and Hernandez et al. [16], who found no differences in disease-specific quality of life measured with the St George's Respiratory Questionnaire. Furthermore, our results are in line with those of earlier studies involving specialised hospital-based nurses [9-12,15,16,24,25]. The readmission rate in our study was 25%, which is comparable to the 30% in previously published studies [9-11]. Characteristics like age, smoking history and living situation of patients in our study were similar to those in studies from the United Kingdom [9-12] and to that of a survey on hospital-at-home services in British hospitals by Quantrill et al. [26].

Earlier studies did not measure the impact of hospital-at-home on generic health-related quality of life. We found a significant difference between the two groups, in favour of usual hospital care, at the end of the hospital and home treatment. This difference had disappeared after three months. The utility scores are in line with O'Reilly et al. [27], but they found much worse scores at admission than in our study, probably because we did not include patients with more severe exacerbations. Utility and CCQ scores in both groups follow the same pattern. The greater improvement in CCQ and EQ-5D scores of the usual hospital care group at the end of the hospital treatment in comparison to the early discharge group may reflect a true difference in recovery, in which case usual hospital care is the preferred treatment. However, an alternative explanation could be that patients who were discharged early were confronted with their symptoms and limitations earlier and more intensely when they tried to pick up normal life at home. Furthermore, some patients have difficulties viewing hospital care followed by early discharge as one treatment period [28]. Expecting to

be in a certain state at discharge, and experiencing this is not the case, might be expressed in worse scores on the CCQ and the EQ-5D.

In our trial multiple hospitals participated with different socioeconomic and geographic characteristics, which makes it likely that our sample is representative of eligible patients. The percentage of admissions initially considered to be eligible for early discharge at admission was similar to that of previous studies (±37%). Early discharge is possible when the exacerbation is the main problem and comorbidities are (relatively) stable. The percentage of patients living alone suggests that this is not an absolute reason for exclusion, provided that patients have a sufficiently functioning social support system. Still, 25% of screened patients were considered ineligible, because of living in a nursing home, overburden of informal caregiver(s) or living alone with insufficient social support. This suggests that social environment is an important factor when deciding for admission and (early) discharge. Finally, 37% of screened patients was ineligible because of comorbidities.

Considering the very low number of treatment failures in the early discharge group it might be possible to relax the inclusion criteria and randomisation criteria. In our trial, criteria were applied very strictly for safety reasons, but more patients with comorbidities might be eligible in daily practice. Furthermore, the strict review and exclusion of patients at day 1 of admission (e.g. those treated with NIV), precluded patients from early discharge even if they had become eligible at day 3 of admission. Therefore, review of eligibility for early discharge should be performed after a few days of hospital treatment. Thirty percent of patients who consented to participate were not randomised because they showed insufficient recovery and/or were depending on oxygen supply. Unlike in the British hospital-at-home schemes, patients were not sent home with nebulisers or oxygen cylinders, unless these were already

part of their treatment. Extension of the treatment possibilities at home may enable early discharge of patient with more severe disease. However, it would also require more expertise of the nursing staff supervising patients at home, which might currently not be present in community-based home care organisations. Future research should focus on determining which treatments can be safely provided at home, which treatments require the supervision of generic or specialised nurses and which criteria should be applied for selecting eligible patients. In addition, a direct comparison between early discharge with generic and early discharge with specialised nursing care would provide more information on which scheme is most safe and effective.

Our study has some limitations. Firstly, in total 139 patients were randomised, where a number of 165 was calculated to be needed to detect a difference of 0.4 in CCQ change scores between the two groups. A post-hoc power analysis with these 139 patients and the actual variances in CCQ scores showed that the power to detect a difference in change from baseline of 0.4 between the groups was 73% instead of 80%, which was aimed for. We believe that this slight reduction in power does not have a substantial influence on our final results, because the difference between the groups was only 0.29. It is highly unlikely that this difference would have increased to the clinically relevant difference of 0.4 with an additional 26 patients. In previous randomised studies of early discharge in patients diagnosed with COPD numbers varied between 25 and 222, and only 15 to 35% of admitted patients was randomised [9-12,16,29]. Secondly, our study was not an equivalence trial, which would determine best whether hospital care and early discharge care are equally effective. However, in order to demonstrate equal effectiveness with CCQ score, over 500 patients would have been needed, which is beyond what is attainable in this population. Thirdly, 16% of patients dropped out after randomisation. However, comparison of patients who dropped out with

patients who completed the study only revealed more comorbidities for those who dropped out. CCQ scores were not different. Fourthly, although our variable selection for the analyses is justifiable, treatment centre could also be considered as an important covariate in the analyses, based on the randomisation design of the study. However, adding treatment centre as additional fixed factor to the analyses did not result in different outcomes in any of the analyses. It was therefore omitted and the analyses remained unchanged. Finally, due to the nature of the intervention, patients and health care staff could not be blinded to the allocated group.

In conclusion, we found no significant short-term or long-term differences in outcomes between early discharge and usual hospital care, except for generic health-related quality of life at the end of treatment (T+4 days). Early assisted discharge with home visits by community nurses can reduce length of hospital stay for a selected group of patients admitted with a COPD exacerbation and is an alternative to usual hospital care. The decision to implement early assisted discharge with community nursing does not only depend on the results of the effectiveness analysis. Costs and cost-effectiveness evaluations are of high importance as well. An economic evaluation is currently being performed and results will be published separately.

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Competing interests

"All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) LG, MR, OvS have had support from ZonMw for the submitted work; (2) CU, FS, MvV, MB, LvE have no relationships with companies that might have an interest in the submitted work in the previous 3 years; LG and MR haves relationships (received grants to perform cost- and cost-effectiveness studies) from multiple pharmaceutical companies, OvS has relationships (consultancy) with Pfizer, Boehringer Ingelheim and Astra Zeneca that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) CU, LG, FS, MR, MvV, MB, LvE and OvS have no non-financial interests that may be relevant to the submitted work."

Contributors

CU was involved in patient recruitment, database management, administration of questionnaires, data analysis, data interpretation and wrote the manuscript. LG was involved in data analysis and data interpretation and preparation of the manuscript. FS was local coordinating physician and involved in data interpretation and preparation of the manuscript. MR designed the study and involved in data interpretation and preparation of the manuscript. MvV was local coordinating physician in the Atrium Medical Centre and involved in the preparation of the manuscript. MB and LvE were coordinators of the home care organisations and involved in the preparation of the manuscript. OvS designed the study and was involved in data interpretation and writing the manuscript. OvS is guarantor for the study. All researchers had access to all data.

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Data sharing

No additional data available

References

1. Buist AS, McBurnie MA, Vollmer WM et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet 2007;370:741-750.
2. Rabe KF, Hurd S, Anzueto A et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532-555.
3. Lopez AD, Shibuya K, Rao C et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J 2006;27:397-412.
4. Seemungal TA, Donaldson GC, Paul EA et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998;157:1418-1422.
5. Donaldson GC, Seemungal TA, Bhowmik A et al. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. Thorax 2002;57:847-852.
6. Esteban C, Quintana JM, Moraza J et al. Impact of hospitalisations for exacerbations of COPD on health-related quality of life. Respir Med 2009;103:1201-1208.
7. Toy EL, Gallagher KF, Stanley EL et al. The economic impact of exacerbations of chronic obstructive pulmonary disease and exacerbation definition: a review. COPD 2010;7:214-228.
8. Jordan RE, Hawker JI, Ayres JG et al. Effect of social factors on winter hospital admission for respiratory disease: a case-control study of older people in the UK. Br J Gen Pract 2008;58:400-402.

9. Davies L, Wilkinson M, Bonner S et al. "Hospital at home" versus hospital care in patients with exacerbations of chronic obstructive pulmonary disease: prospective randomised controlled trial. BMJ 2000;321:1265-1268.

10. Cotton MM, Bucknall CE, Dagg KD et al. Early discharge for patients with exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Thorax 2000;55:902-906.

11. Skwarska E, Cohen G, Skwarski KM et al. Randomized controlled trial of supported discharge in patients with exacerbations of chronic obstructive pulmonary disease. Thorax 2000;55:907-912.

12. Ojoo JC, Moon T, McGlone S et al. Patients' and carers' preferences in two models of care for acute exacerbations of COPD: results of a randomised controlled trial. Thorax 2002;57:167-169.

13. British Thoracic Society. Intermediate care--Hospital-at-Home in chronic obstructive pulmonary disease: British Thoracic Society guideline. Thorax 2007;62:200-210.

14. Diaz LS, Gonzalez LF, Gomez Mendieta MA et al. [Evaluation of a home hospitalization program in patients with exacerbations of chronic obstructive pulmonary disease]. Arch Bronconeumol 2005;41:5-10.

15. Gravil JH, Al-Rawas OA, Cotton MM et al. Home treatment of exacerbations of chronic obstructive pulmonary disease by an acute respiratory assessment service. Lancet 1998;351:1853-1855.

16. Hernandez C, Casas A, Escarrabill J et al. Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients. Eur Respir J 2003;21:58-67.

17. Davison AG, Monaghan M, Brown D et al. Hospital at home for chronic obstructive pulmonary disease: an integrated hospital and community based generic intermediate care service for prevention and early discharge. Chron Respir Dis 2006;3:181-185.

18. Nicholson C, Bowler S, Jackson C et al. Cost comparison of hospital- and home-based treatment models for acute chronic obstructive pulmonary disease. Aust Health Rev 2001;24:181-187.

19. Utens CM, Goossens LM, Smeenk FW et al. Effectiveness and cost-effectiveness of early assisted discharge for Chronic Obstructive Pulmonary Disease exacerbations: the design of a randomised controlled trial. BMC Public Health 2010;10:618

20. van der Molen T, Willemse BW, Schokker S et al. Development, validity and responsiveness of the Clinical COPD Questionnaire. Health Qual Life Outcomes 2003;1:13

21. Kocks JW, Tuinenga MG, Uil SM et al. Health status measurement in COPD: the minimal clinically important difference of the clinical COPD questionnaire. Respir Res 2006;7:62

22. Lamers LM, McDonnell J, Stalmeier PF et al. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. Health Econ 2006;15:1121-1132.

23. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology (3rd edition). Philidelphia: Lippincott Williams & Wilkins 2008.

24. Ansari K, Shamssain M, Farrow M et al. Hospital-at-home care for exacerbations of chronic obstructive pulmonary disease: an observational cohort study of patients managed in hospital or by nurse practitioners in the community. Chron Respir Dis 2009;6:69-74.

25. Sala E, Alegre L, Carrera M et al. Supported discharge shortens hospital stay in patients hospitalized because of an exacerbation of COPD. Eur Respir J 2001;17:1138-1142.

26. Quantrill SJ, Lowe D, Hosker HS et al. Survey of early discharge schemes from the 2003 UK National COPD Audit. Respir Med 2007;101:1026-1031.

27. O'Reilly JF, Williams AE, Rice L. Health status impairment and costs associated with COPD exacerbation managed in hospital. Int J Clin Pract 2007;61:1112-1120.

28. Clarke A, Sohanpal R, Wilson G et al. Patients' perceptions of early supported discharge for chronic obstructive pulmonary disease: a qualitative study. Qual Saf Health Care 2010;19:95-98.

29. Aimonino RN, Tibaldi V, Leff B et al. Substitutive "hospital at home" versus inpatient care for elderly patients with exacerbations of chronic obstructive pulmonary disease: a prospective randomized, controlled trial. J Am Geriatr Soc 2008;56:493-500.

30. Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383

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Title:

Early assisted discharge with generic community nursing for Chronic Obstructive Pulmonary Disease exacerbations: results of a randomised controlled trial

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Keywords: Hospital at home; Early assisted discharge from hospital; Chronic Obstructive Pulmonary Disease; Community nursing, Randomised controlled trial

Abstract

Objectives: To determine effectiveness of early assisted discharge for COPD exacerbations, with home care provided by generic community nurses, compared to usual hospital care.

Design: Prospective, randomised controlled, multi-centre trial with 3 months follow-up.

Setting: Five hospitals and 3 home care organisations in the Netherlands.

Participants: Patients admitted to the hospital with an exacerbation of Chronic Obstructive Pulmonary Disease. Patients with no or limited improvement of respiratory symptoms and patients with severe unstable comorbidities, social problems or those unable to visit the toilet independently were excluded.

Intervention: Early discharge from hospital after 3 days inpatient treatment. Home visits by generic community nurses. Primary outcome measure was change in health status measured by the Clinical COPD Questionnaire (CCQ). Treatment failures, readmissions, mortality and change in generic health-related quality of life (HRQL) were secondary outcome measures.

Results: 139 patients were randomised. No difference between groups was found in change in CCQ score at day 7 (difference in mean change 0.29 (95% CI -0.03 to 0.61)) or at 3 months

(difference in mean change 0.04 (95% CI –0.40 to 0.49)). No difference was found in secondary outcomes. At day 7 there was a significant difference in change in generic HRQL, favouring usual hospital care.

Conclusion: While patients' disease-specific health status after seven days treatment tended to be somewhat better in the usual hospital care group, the difference was small and not clinically relevant or statistically significant. After three months, the difference had disappeared. A significant difference in generic health-related quality of life at the end of the treatment had disappeared after 3 months and there was no difference in treatment failures, readmissions or mortality. Early assisted discharge with community nursing is feasible and an alternative to usual hospital care for selected patients with an acute COPD exacerbation ~~COPD~~.

Trial registration: NetherlandsTrialRegister NTR 1129

Article summary

Article focus:

- What is the effectiveness of early assisted discharge with community nursing for COPD exacerbations in comparison to usual hospital care as measured by the Clinical COPD Questionnaire.

Key Messages:

- There is no short term or long term difference in change in health status as measured by the Clinical COPD Questionnaire.

- A significant difference in generic health-related quality of life at the end of the treatment disappeared after 3 months.

- Early assisted discharge with home visits by community nurses is a feasible and an alternative to usual hospital care for selected patients with an acute exacerbation of their COPD.

Strength and limitations:

- 139 patients were randomised where 165 was calculated to be the required sample size. However, because the difference between the groups was only 0.29 instead of 0.4 it is unlikely that this difference would have increased to the clinically relevant difference of 0.4 with an additional 26 patients.
- This study is the first larger randomised controlled trial on early assisted discharge in the Dutch health care system

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic disease with high prevalence [1], mortality and morbidity [2,3]. Exacerbations of the disease have negative effects on patient outcomes [4-6] and are the main cause for hospitalisation [7]. Hospitalisations are not only the main cost driver in COPD, they also put pressure on scarce hospital beds, especially during winters [8]. Several studies have shown that some patients with an exacerbation, who would otherwise be admitted to the hospital, can be treated at home safely after examination in the emergency department or a short hospital admission [9-16]. This is called hospital-at-home. Hospital-at-home aims to avoid admission, or reduce length of stay (early assisted discharge schemes). Previous studies found no differences in readmissions, mortality and disease-specific quality of life between hospital-at-home and usual hospital care [9-11,15,16]. Most published hospital-at-home studies originate from the United Kingdom and Spain, where this service is mainly provided by hospital-based respiratory nurses who visit patients at home. Davison et al. [17] and Nicholson et al. [18] suggested the use of non-specialised

'generic' community nursing teams for home supervision to increase the capacity of hospital-at-home schemes.

The Netherlands has a nation-wide, good infrastructure for community nursing, which could be used for hospital-at-home. Therefore we designed an early assisted discharge hospital-at-home scheme for COPD exacerbations, mainly operated by generic community nurses who performed the home visits [19]. Main objective of the GO AHEAD study (GO AHEAD is the acronym for Assessment Of Going Home under Early Assisted Discharge) was to determine the effectiveness and cost-effectiveness of early assisted discharge followed by community-based nursing care at home. In addition, evaluation of patient satisfaction and preferences, carer strain and preferences and an evaluation among professional care providers was performed. The focus of this paper is on the effectiveness of early assisted discharge, with the Clinical COPD Questionnaire (CCQ) as the primary outcome measure. In addition, treatment failures, readmissions, mortality and generic quality of life were assessed as secondary outcomes.

Methods

GO AHEAD was a randomised controlled trial comparing usual hospital care with early assisted discharge for COPD exacerbations. Five hospitals and three home care organisations participated. Treatment consisted of seven days in-hospital care as usual or three days in-hospital treatment followed by four days care at home. Patients were followed until three months after randomisation.

All patients admitted to one of the participating hospitals with a COPD exacerbation, as diagnosed by the reviewing physician, were screened for potential eligibility on their first day

of admission according to the inclusion and exclusion criteria (table 1). On day 3 of admission, clinical stability was assessed in patients who gave written informed consent (see randomisation criteria in table 1). For each hospital separately, participating patients were randomised on day 3 of admission, in a 1:1 ratio using a block-size of 6. Randomisation was performed by the study nurses. The randomisation sequence was computer-generated a priori by an independent researcher. Allocation sequence was placed in sealed envelopes. The study was approved by the Ethics Committee of the Catharina Hospital, the Netherlands, approval number M07-1755.

Table 1 Inclusion and exclusion criteria (applied at admission) and randomisation criteria (applied at day 3 of admission)

Inclusion criteria (checked on day 1)	**Exclusion criteria (checked on day 1)**
Age ≥40 years	Major uncontrolled comorbidity, including pneumonia that is prominent, heart failure that is prominent or acute changes on electro cardiogram and (suspected) underlying malignancy.
Competent to give informed consent	Mental disability, including dementia, impaired level of consciousness and acute confusion.
Diagnosed with COPD. COPD was defined as at least GOLD stage I and 10 pack years of smoking	Living outside care region of the home care organisation
Hospitalisation for COPD exacerbation	Inability to understand the program

	Indication for admission to intensive care unit or for non invasive ventilation
	Active alcohol and/or drug abuse
	Insufficient availability of informal care at home
Randomisation criteria (checked on day 3)	
Completed Informed Consent on day three of admission	
Acceptable general health: - Decrease physical complaints - Non dependency of therapies that cannot be given at home (intravenous therapy and newly prescribed oxygen supply). - Being able to visit toilet independently	
Normal or moderately increased blood sugar levels, defined as ≤15 mmol/L or ≥15 mmol/L but patient is capable to regulate blood sugar levels independently	
Respiratory complaints of dyspnoea, wheezing and rhonchi must have decreased in comparison with day of admission.	

During the first three days of the admission all patients were treated in the hospital according to the study protocol [19]. Treatment consisted of systemic corticosteroids, nebulised bronchodilators and antibiotics and oxygen upon indication. Exacerbation symptoms were scored each day. Physiotherapists visited all patients for instruction of breathing and coughing techniques. On the fourth day of admission all randomised patients switched to oral medication and metered dosed inhalations. Patients randomised to early assisted discharge were discharged home on the fourth day of admission and further treated at home. Community nurses visited or contacted the patient at least once daily on the day of discharge

and the three consecutive days. They continued to score exacerbation symptoms and provided reassurance and counselling. Furthermore, medication compliance and inhalation techniques were addressed. Community nurses had the highest levels of generic nursing training in the Netherlands. No additional training was provided for the trial. The nurses could contact the hospital to discuss the patient's condition. If necessary, patients were readmitted to the hospital. For patients a 24-hour telephone access to the hospital respiratory ward was installed for emergencies.

Patients in the usual hospital care group received care as usual at the discretion of the hospital staff. General practitioners were informed about the patient's participation in the trial and the discharge date. Clinical responsibility during home care remained with the respiratory physician. A detailed description of the research protocol and the early assisted discharge intervention has been published previously [19].

Primary outcome was the change in CCQ scores between baseline (T0= day 3 of admission) and the end of the supervised treatment (T+4 days). The CCQ is a disease-specific questionnaire measuring health status [20]. It consists of 10 questions in three domains: symptoms, functional state and mental state, resulting in a overall, continuous score varying from 6 (worst score) to 0 (best score) [20]. In order to produce a valid overall score, 3, 3 and 2 questions on the symptoms domain, functional state and mental state domain, respectively need to be answered. The CCQ has proved to be responsive to change. The minimal clinical important difference is 0.4 [21]. ~~To detect a difference of 0.4 in CCQ change scores between the two groups, in favour of the early discharge group, with a power of 0.80 and alpha of 0.05, the required sample size was 165 [19].~~ Secondary outcomes were: 1) change in CCQ scores between baseline and three months after randomisation (T+90 days); 2) number of treatment

failures (i.e. either death or clinical deterioration leading to prolonged hospital stay beyond the standardised seven days (usual hospital care) or death or readmission during the four days treatment at home (early discharge)); 3) mortality and 4) readmissions during the three month follow-up; and 5) generic health-related quality of life measured by the EuroQol-5D (EQ-5D)[22] at baseline, T+4 days and T+90 days. Utilities were calculated using the Dutch value set [22]. Higher scores represent better generic quality of life.

Statistical analysis

To detect a difference of 0.4 in CCQ change scores between the two groups, in favour of the early discharge group, with a power of 0.80 and alpha of 0.05, with standard deviation in the usual hospital care group of 0.922 and 0.988 in the early discharge group, the required sample size was 165 [19]. Change in CCQ scores and EQ-5D scores was analysed using a linear repeated measures model with correlated errors. A~~a~~n unstructured covariance matrix for the residuals of the different measurements was used. Backward selection of covariates was applied. In addition to time (i.e. measurement at T+4 days, end of treatment, and T+90 days, end of follow-up), the interaction of time and treatment, the following variables were tested: baseline CCQ or EQ-5D score, treatment centre, age, gender, comorbidity, smoking status, living situation, availability informal caregiver, presence of home care prior to admission, course of oral corticosteroids and/or antibiotics prior to admission. Variables were retained in the model if their exclusion led to a 10% change in the estimated treatment effect [23]. For the analysis of CCQ scores, only baseline score was included in the final model. For the analysis of EQ-5D scores, baseline score, comorbidity and gender were included. Results are presented as mean differences in change and 95% confidence intervals (95% CI). Numbers of patients with treatment failures, readmissions and mortality were analysed using multiple logistic regression analysis. Numbers of readmissions per patient in each group were analysed in a

Poisson regression. Time to readmission was analysed with a Cox proportional hazards model. Results are presented as odds ratios (OR) or hazard ratios (HR) with 95% CI. Again, backward selection was used to select covariates. Only baseline CCQ score was retained in the models. The significance level for a difference between treatment groups was set at $p \leq 0.05$. All analyses were performed using the Statistical Package for Social Sciences (SPSS), version 17.0, IBM.

Results

In total, 1371 patients were screened for eligibility between November 2007 and March 2011, of whom 508 met the criteria for eligibility on day 1. Figure 1 shows an overview of the patient flow during the trial from hospital admission to the end of the follow-up. Three patients in the early assisted discharge group and 7 in the usual hospital care group were not satisfied with the allocated place of treatment and withdrew consent immediately after randomisation. The total dropout over the study period was 16%, 25% in the usual hospital care group and 10% in the early assisted discharge group. Baseline CCQ scores of patients dropping out were not different from those who completed the study, but they did have more comorbidities. At T+4 days 118 of 129 still participating patients produced a valid overall score on the CCQ and were included in the analysis. The other patients did not withdraw consent and continued to participate in the study in order to contribute to the other analyses and to produce a valid score at other measuring points. This approach fits with the intention-to-treat principle and the repeated measures analysis. At T+90 days, 101 of 115 patients produced a valid overall CCQ score.

Table 2 shows the baseline characteristics of randomised patients by treatment group. These were comparable across the groups. At end of the follow-up period lung function testing was performed by which classification of disease severity according to the GOLD criteria [2] could be made (see table 3)~~supplementary data file 1)~~.

Figure 1 Patient flow through study.

Table 2 Baseline characteristics and treatment at admission. Values represent mean (SD), unless stated otherwise.

Characteristic	Usual hospital care (N=69)	Early assisted discharge (N=70)
Age (years)	67.8 (11.3)	68.3 (10.3)
Men n (%)	38 (55.1)	48 (68.6)
Smoking history:		
Current smokers n (%)	27 (39.1)	23 (32.9)
Pack years, median inter quartile range	37 36.9	44 26.7
Body Mass Index (kg/m^2)	25.6 (4.3)	25.0 (5.1)
Charlson comorbidity score[24]†	1.68 (1.1)	1.74 (1.1)
Comorbidity score of 1 n (%)	42 (60.0)	38 (54.0)
Comorbidity score > 1 n (%)	27 (39.0)	32 (46.0)
Living situation:		
Living alone n (%)	21 (30.4)	22 (31.4)
Receiving care at home before admission n (%)	16 (23.2)	17 (24.3)
Treatment at admission:		

Long term oxygen treatment n (%)	4 (5.8)	5 (7.1)
Oral steroids n (%)	5 (7.2)	10 (14.3)
Course of oral steroids prior to admission n (%)	34 (50.0)	35 (50.7)
Course antibiotics prior to admission n (%)	31 (45.6)	32 (46.4)
Inhaled β2-agonist (LABA) n (%)	9 (13.0)	7 (10.0)
Inhaled corticosteroid n (%)	3 (12.0)	3 (15.0)
Inhaled corticosteroid/LABA combination n (%)	44 (63.7)	50 (71.4)
Inhaled anticholinergic n (%)		
Tiotropium	31 (44.9)	36 (51.4)
Ipratropium	12 (17.4)	13 (18.6)
Followed rehabilitation program in year prior to admission n (%)	10 (14.9)	12 (17.4)
Heart Rate (beats/minute)	91.0 (14.2)	95.6 (18.4)
Arterial blood gas[#]*:*	N=37	N=42
pH	7.44 (0.05)	7.43 (0.04)
pO_2 (mmHg)	70.7 (13.2)	67.3 (8.1)
pCO_2 (mmHg)	37.2 (6.2)	39.1 (5.3)
Saturation	94 (2.5)	94 (3.6)

† Charlson Comorbidity Index, 1= only COPD, higher score means more comorbidities; # only data of blood gas measurements in patients without oxygen supplement;
LABA: long acting beta2 agonist

Table 3

Lung function testing at end of 3 month follow-up. Values represent mean (SD), unless stated otherwise.

	Usual hospital care	Early assisted discharge
Postbronchodilator FEV_1 (litres)	1.25 (0.07)	1.21 (0.07)
% of predicted postbronchodilator FEV_1	50.29 (2.71)	45.20 (2.13)
GOLD stage I, n (%)	7 (10.3)	2 (2.9)
GOLD stage II, n (%)	22 (32.4)	23 (32.9)
GOLD stage III, n (%)	28 (41.2)	31 (44.3)
GOLD stage IV, n (%)	11 (16.2)	14 (20.0)

Table 4~~Supplementary file 2~~ shows the unadjusted CCQ scores at the different measuring points. At T0 CCQ scores were 2.22 (0.97) for the usual hospital care group and 2.63 (1.06) for the early discharge group. Figure 2 shows the change in CCQ scores from T0, adjusted for baseline score. CCQ scores improved between T0 and T+4 days for the usual hospital care group, and were almost stable for the early assisted discharge group, but there was no significant difference between the groups at T+4 days (difference in mean change from T0 -0.29, 95% CI -0.03~~-0.61~~ to 0.61~~0.03~~, p=0.078). At T+90 days, CCQ scores of both groups ~~scores~~ were slightly higher in comparison to T0. There was no difference between the groups at three months (difference in mean change from T0 -0.04, 95% CI -0.40~~-0.48~~ to 0.49~~0.41~~, p=0.858).

Table 4

Unadjusted mean (SD) CCQ total scores at each time of measurement by treatment group.

Time of measurement	Usual hospital care	Early assisted discharge
T- 2 days	3.21 (1.07)	3.49 (1.07)
T0	2.22 (0.97)	2.63 (1.06)

T+ 4 days	2.00 (1.09)	2.55 (1.21)
T+ 90 days	2.41 (1.14)	2.70 (1.32)

CCQ total score range is 0-6; 0 represents best possible score and 6 represents worst possible score

Figure 2 CCQ total score, differences in mean change from baseline

Treatment failed in five patients. One patient in the early discharge group needed readmission to the hospital because of deterioration of respiratory symptoms, before the end of the home treatment and 4 patients in the usual hospital care group required hospital admission beyond the 7 days that were stated in the protocol (2 because of deterioration of respiratory symptoms, 2 patients because of deterioration of general condition due to gastroenteritis caused by norovirus). This difference was not significant (OR early discharge group 0.27, 95% CI 0.026 – 2.70, p=0.263). Table ~~3~~5 shows the number of readmissions during follow-up. Seventeen patients in each group had 1 or more readmission to the hospital of which 14 first readmissions were due to an exacerbation or other pulmonary indication (OR early discharge group 0.80, 95% CI 0.36 – 1.79, p=0.592). There was no difference in the number of readmissions per patient between the groups, or in the total number of readmissions in each group. There was no difference in time to first readmission between the two groups (HR early discharge group 0.77, 95% CI 0.39 to 1.53, p=0.461).

Table ~~3~~5 Readmissions during follow-up. Values are numbers of patients (%).

	Usual hospital care	Early assisted discharge
Patients with readmission	17 (25)	17 (24)
Patients with 1, 2 or ≥ 3 readmissions		

1 readmission	11	12
2 readmissions	4	3
3 or more readmissions	2	2
Average (SD) time to first readmission in days	61 (36.5)	69 (33.8)

No patient died during the hospital or home treatment, but 1 patient from each group died during follow-up. Cause of death was unknown in one case (patient died during sleep at home) and an acute abdomen in the other. Both were not related to the trial.

EQ-5D utility scores (SD) at T0 were 0.713 (0.22) for the usual hospital care group and 0.664 (0.26) for the early assisted discharge group. Table ~~4~~6 shows the mean changes and mean difference in change from baseline of EQ-5D utility. In the usual hospital care group, mean utility scores improved from T0 to T+4 days and decreased to baseline at T+90 days. In the early assisted discharge group mean utility scores remained close to baseline. The mean change in utility scores on T+4 days was significant greater in the usual hospital care group. At T+90 days this difference between treatment groups had disappeared.

Table 46 Mean changes and mean differences in change for EQ-5D.

		Mean change from baseline (SE)		Adjusted mean (95% CI) difference in change from baseline*	p value
Utility		Usual hospital care	Early assisted discharge	Usual care - early discharge	
	T+ 4 days†	0.051 (0.0261)	-0.005 (0.029)	0.0746 (0.010 to 0.139)	0.024
	T+ 90 days‡	-0.036 (0.0447)	0.008 (0.039)	-0.022 (-0.116 to 0.072)	0.639

*Results from repeated measures analysis, adjusted for baseline value † hospital care N=57, early discharge N=61; ‡ hospital care N=47, early discharge N=54
SE: Standard Error; 95% CI: 95% Confidence Interval

Discussion

This is the first randomised controlled trial that investigated the effectiveness of early assisted discharge for COPD exacerbations with supervision at home by community nurses. In addition, this is the first evaluation of early discharge for this disease in the Dutch health care system. While patients' disease-specific health status as expressed in the mean CCQ score after seven days treatment tended to be somewhat better in the usual hospital care group, the difference was small, not clinically relevant and not statistically significant. After three months, the difference had disappeared. The same pattern was found in generic health-related quality of life measured with the EQ-5D, although this difference was statistically significant at the end of the supervised treatment. The difference had disappeared at the end of the 3-month follow up period. There was no difference in treatment failures, readmissions or mortality.

These study results confirm previously published positive results by Davison et al. [17] and Nicholson et al. [18], but these two studies were either not randomised [17] or included a small number of patients [18]. We found no significant difference in CCQ scores, which corresponds with the findings of Davies et al. [9] and Hernandez et al. [16], who found no differences in disease-specific quality of life measured with the St George's Respiratory Questionnaire. Furthermore, our results are in line with those of earlier studies involving specialised hospital-based nurses [9-12,15,16,24,25]. The readmission rate in our study was 25%, which is comparable to the 30% in previously published studies [9-11]. Characteristics like age, smoking history and living situation of patients in our study were similar to those in studies from the United Kingdom [9-12] and to that of a survey on hospital-at-home services in British hospitals by Quantrill et al. [26].

Earlier studies did not measure the impact of hospital-at-home on generic health-related quality of life. We found a significant difference between the two groups, in favour of usual hospital care, at the end of the hospital and home treatment. This difference had disappeared after three months. The utility scores are in line with O'Reilly et al. [27], but they found much worse scores at admission than in our study, probably because we did not include patients with more severe exacerbations. Utility and CCQ scores in both groups follow the same pattern. The greater improvement in CCQ and EQ-5D scores of the usual hospital care group at the end of the hospital treatment in comparison to the early discharge group may reflect a true difference in recovery, in which case usual hospital care is the preferred treatment. However, an alternative explanation could be that patients who were discharged early were confronted with their symptoms and limitations earlier and more intensely when they tried to pick up normal life at home. Furthermore, some patients have difficulties viewing hospital care followed by early discharge as one treatment period [28]. Expecting to

be in a certain state at discharge, and experiencing this is not the case, might be expressed in worse scores on the CCQ and the EQ-5D.

In our trial multiple hospitals participated with different socioeconomic and geographic characteristics, which makes it likely that our sample is representative of eligible patients. The percentage of admissions initially considered to be eligible for early discharge at admission was similar to that of previous studies (±37%). Early discharge is possible when the exacerbation is the main problem and comorbidities are (relatively) stable. The percentage of patients living alone suggests that this is not an absolute reason for exclusion, provided that patients have a sufficiently functioning social support system. Still, 25% of screened patients were considered ineligible, because of living in a nursing home, overburden of informal caregiver(s) or living alone with insufficient social support. This suggests that social environment is an important factor when deciding for admission and (early) discharge. Finally, 37% of screened patients was ineligible because of comorbidities.

Considering the very low number of treatment failures in the early discharge group it might be possible to relax the inclusion criteria and randomisation criteria. In our trial, criteria were applied very strictly for safety reasons, but more patients with comorbidities might be eligible in daily practice. Furthermore, the strict review and exclusion of patients at day 1 of admission (e.g. those treated with NIV), precluded patients from early discharge even if they had become eligible at day 3 of admission. Therefore, review of eligibility for early discharge should be performed after a few days of hospital treatment. Thirty percent of patients who consented to participate were not randomised because they showed insufficient recovery and/or were depending on oxygen supply. Unlike in the British hospital-at-home schemes, patients were not sent home with nebulisers or oxygen cylinders, unless these were already

part of their treatment. Extension of the treatment possibilities at home may enable early discharge of patient with more severe disease. However, it would also require more expertise of the nursing staff supervising patients at home, which might currently not be present in community-based home care organisations. Future research should focus on determining which treatments can be safely provided at home, which treatments require the supervision of generic or specialised nurses and which criteria should be applied for selecting eligible patients. In addition, a direct comparison between early discharge with generic and early discharge with specialised nursing care would provide more information on which scheme is most safe and effective.

Our study has some limitations. Firstly, in total 139 patients were randomised, where a number of 165 was calculated to be needed to detect a difference of 0.4 in CCQ change scores between the two groups. A post-hoc power analysis with these 139 patients and the actual variances in CCQ scores showed that the power to detect a difference in change from baseline of 0.4 between the groups was 73% instead of 80%, which was aimed for. We believe that this slight reduction in power does not have a substantial influence on our final results, because the difference between the groups was only 0.29. It is highly unlikely that this difference would have increased to the clinically relevant difference of 0.4 with an additional 26 patients. In previous randomised studies of early discharge in patients diagnosed with COPD numbers varied between 25 and 222, and only 15 to 35% of admitted patients was randomised [9-12,16,29]. Secondly, our study was not an equivalence trial, which would determine best whether hospital care and early discharge care are equally effective. However, in order to demonstrate equal effectiveness with CCQ score, over 500 patients would have been needed, which is beyond what is attainable in this population. Thirdly, 16% of patients dropped out after randomisation. However, comparison of patients who dropped out with

patients who completed the study only revealed more comorbidities for those who dropped out. CCQ scores were not different. Fourthly, although our variable selection for the analyses is justifiable, treatment centre could also be considered as an important covariate in the analyses, based on the randomisation design of the study. However, adding treatment centre as additional fixed factor to the analyses did not result in different outcomes in any of the analyses. It was therefore omitted and the analyses remained unchanged. Finally, due to the nature of the intervention, patients and health care staff could not be blinded to the allocated group.

In conclusion, we found no significant short-term or long-term differences in outcomes between early discharge and usual hospital care, except for generic health-related quality of life at the end of treatment (T+4 days). Early assisted discharge with home visits by community nurses can reduce length of hospital stay for a selected group of patients admitted with a COPD exacerbation and is an alternative to usual hospital care. The decision to implement early assisted discharge with community nursing does not only depend on the results of the effectiveness analysis. Costs and cost-effectiveness evaluations are of high importance as well. An economic evaluation is currently being performed and results will be published separately.

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Competing interests

"All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) LG, MR, OvS have had support from ZonMw for the submitted work; (2) CU, FS, MvV, MB, LvE have no relationships with companies that might have an interest in the submitted work in the previous 3 years; LG and MR haves relationships (received grants to perform cost- and cost-effectiveness studies) from multiple pharmaceutical companies, OvS has relationships (consultancy) with Pfizer, Boehringer Ingelheim and Astra Zeneca that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) CU, LG, FS, MR, MvV, MB, LvE and OvS have no non-financial interests that may be relevant to the submitted work."

Contributors

CU was involved in patient recruitment, database management, administration of questionnaires, data analysis, data interpretation and wrote the manuscript. LG was involved in data analysis and data interpretation and preparation of the manuscript. FS was local coordinating physician and involved in data interpretation and preparation of the manuscript. MR designed the study and involved in data interpretation and preparation of the manuscript. MvV was local coordinating physician in the Atrium Medical Centre and involved in the preparation of the manuscript. MB and LvE were coordinators of the home care organisations and involved in the preparation of the manuscript. OvS designed the study and was involved in data interpretation and writing the manuscript. OvS is guarantor for the study. All researchers had access to all data.

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Data sharing

No additional data available

References

1. Buist AS, McBurnie MA, Vollmer WM et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet 2007;370:741-750.
2. Rabe KF, Hurd S, Anzueto A et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532-555.
3. Lopez AD, Shibuya K, Rao C et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J 2006;27:397-412.
4. Seemungal TA, Donaldson GC, Paul EA et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998;157:1418-1422.
5. Donaldson GC, Seemungal TA, Bhowmik A et al. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. Thorax 2002;57:847-852.
6. Esteban C, Quintana JM, Moraza J et al. Impact of hospitalisations for exacerbations of COPD on health-related quality of life. Respir Med 2009;103:1201-1208.
7. Toy EL, Gallagher KF, Stanley EL et al. The economic impact of exacerbations of chronic obstructive pulmonary disease and exacerbation definition: a review. COPD 2010;7:214-228.
8. Jordan RE, Hawker JI, Ayres JG et al. Effect of social factors on winter hospital admission for respiratory disease: a case-control study of older people in the UK. Br J Gen Pract 2008;58:400-402.

9. Davies L, Wilkinson M, Bonner S et al. "Hospital at home" versus hospital care in patients with exacerbations of chronic obstructive pulmonary disease: prospective randomised controlled trial. BMJ 2000;321:1265-1268.

10. Cotton MM, Bucknall CE, Dagg KD et al. Early discharge for patients with exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Thorax 2000;55:902-906.

11. Skwarska E, Cohen G, Skwarski KM et al. Randomized controlled trial of supported discharge in patients with exacerbations of chronic obstructive pulmonary disease. Thorax 2000;55:907-912.

12. Ojoo JC, Moon T, McGlone S et al. Patients' and carers' preferences in two models of care for acute exacerbations of COPD: results of a randomised controlled trial. Thorax 2002;57:167-169.

13. British Thoracic Society. Intermediate care--Hospital-at-Home in chronic obstructive pulmonary disease: British Thoracic Society guideline. Thorax 2007;62:200-210.

14. Diaz LS, Gonzalez LF, Gomez Mendieta MA et al. [Evaluation of a home hospitalization program in patients with exacerbations of chronic obstructive pulmonary disease]. Arch Bronconeumol 2005;41:5-10.

15. Gravil JH, Al-Rawas OA, Cotton MM et al. Home treatment of exacerbations of chronic obstructive pulmonary disease by an acute respiratory assessment service. Lancet 1998;351:1853-1855.

16. Hernandez C, Casas A, Escarrabill J et al. Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients. Eur Respir J 2003;21:58-67.

17. Davison AG, Monaghan M, Brown D et al. Hospital at home for chronic obstructive pulmonary disease: an integrated hospital and community based generic intermediate care service for prevention and early discharge. Chron Respir Dis 2006;3:181-185.

18. Nicholson C, Bowler S, Jackson C et al. Cost comparison of hospital- and home-based treatment models for acute chronic obstructive pulmonary disease. Aust Health Rev 2001;24:181-187.

19. Utens CM, Goossens LM, Smeenk FW et al. Effectiveness and cost-effectiveness of early assisted discharge for Chronic Obstructive Pulmonary Disease exacerbations: the design of a randomised controlled trial. BMC Public Health 2010;10:618

20. van der Molen T, Willemse BW, Schokker S et al. Development, validity and responsiveness of the Clinical COPD Questionnaire. Health Qual Life Outcomes 2003;1:13

21. Kocks JW, Tuinenga MG, Uil SM et al. Health status measurement in COPD: the minimal clinically important difference of the clinical COPD questionnaire. Respir Res 2006;7:62

22. Lamers LM, McDonnell J, Stalmeier PF et al. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. Health Econ 2006;15:1121-1132.

23. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology (3rd edition). Philidelphia: Lippincott Williams & Wilkins 2008.

24. Ansari K, Shamssain M, Farrow M et al. Hospital-at-home care for exacerbations of chronic obstructive pulmonary disease: an observational cohort study of patients managed in hospital or by nurse practitioners in the community. Chron Respir Dis 2009;6:69-74.

25. Sala E, Alegre L, Carrera M et al. Supported discharge shortens hospital stay in patients hospitalized because of an exacerbation of COPD. Eur Respir J 2001;17:1138-1142.

26. Quantrill SJ, Lowe D, Hosker HS et al. Survey of early discharge schemes from the 2003 UK National COPD Audit. Respir Med 2007;101:1026-1031.

27. O'Reilly JF, Williams AE, Rice L. Health status impairment and costs associated with COPD exacerbation managed in hospital. Int J Clin Pract 2007;61:1112-1120.

28. Clarke A, Sohanpal R, Wilson G et al. Patients' perceptions of early supported discharge for chronic obstructive pulmonary disease: a qualitative study. Qual Saf Health Care 2010;19:95-98.

29. Aimonino RN, Tibaldi V, Leff B et al. Substitutive "hospital at home" versus inpatient care for elderly patients with exacerbations of chronic obstructive pulmonary disease: a prospective randomized, controlled trial. J Am Geriatr Soc 2008;56:493-500.

30. Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383

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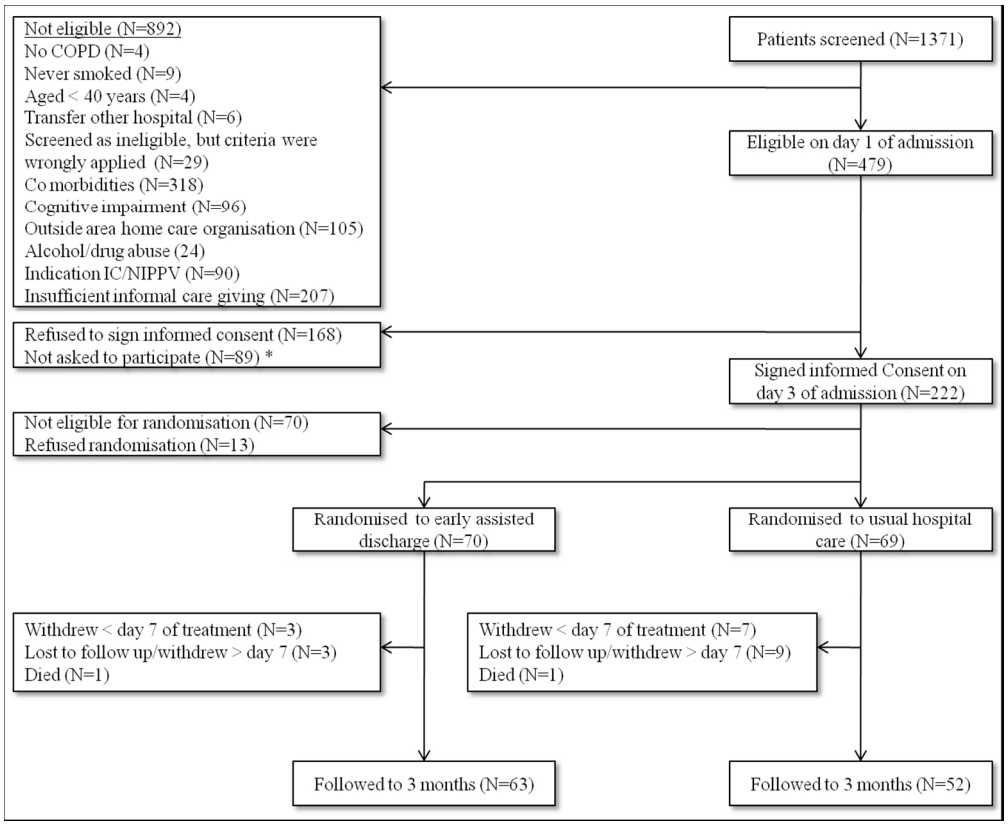

*Not asked to participate because of logistical reasons (e.g. no study staff available or patient not admitted ot respiratory ward)
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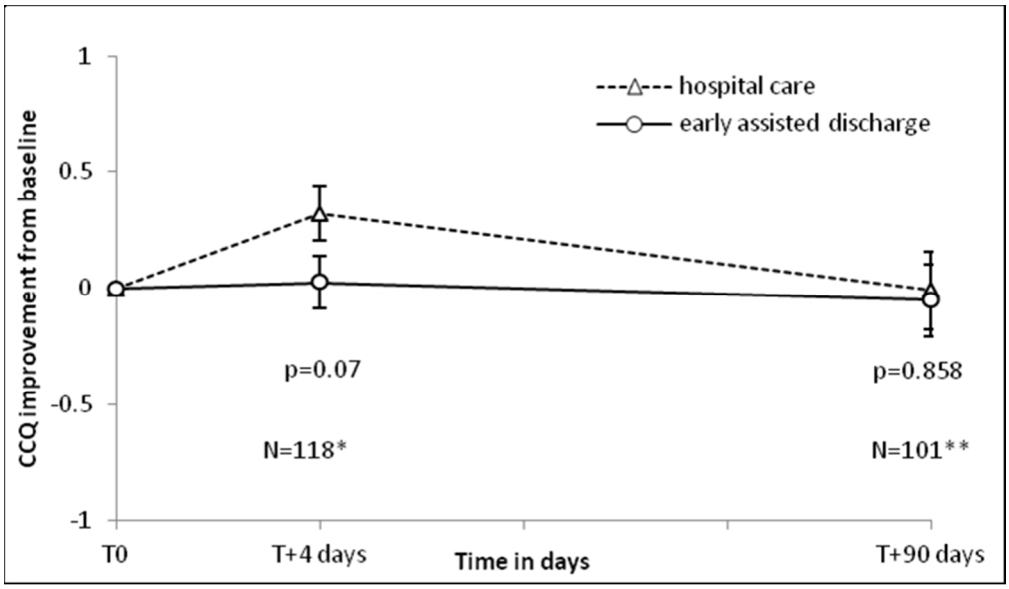

Error bars represent standard errors. P values are based on repeated measures analysis, adjusted for baseline value.
*Number of patients at T+4 days that completed questionnaire that produced valid total CCQ; **number of patients at T+90 days that completed questionnaire that produced valid total CCQ score.
NOTE: for interpretation reasons the sign of the CCQ has been reversed. Positive change in CCQ scores represents improvement of patients condition, which is a decrease in CCQ scores.

60x34mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5-6
	2b	Specific objectives or hypotheses	5-6
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	6-7 & table 1
	4b	Settings and locations where the data were collected	6-7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	8-9 & reference 19
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	18
	11b	If relevant, description of the similarity of interventions	8-9
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n/a
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10 & fig 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	10 & fig 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6 & 10
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	All tables and figures with results
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	13-14 Tables & figures
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n/a
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	18
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15 to 18
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15 to 18
Other information			
Registration	23	Registration number and name of trial registry	abstract
Protocol	24	Where the full trial protocol can be accessed, if available	Reference 19
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.