

BMJ Open Home oxygen therapy reduces risk of hospitalisation in patients with chronic obstructive pulmonary disease: a population-based retrospective cohort study, 2005–2012

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ABSTRACT

Objective: This study evaluated the effect of home oxygen therapy (HOT) on hospital admissions in chronic obstructive pulmonary disease (COPD) patients.

Design and setting: Using nationwide health insurance claims from 2002–2012, we conducted a longitudinal population-based retrospective cohort study.

Participants: Individuals who were aged 40 years or above and newly diagnosed with COPD in 2005.

Outcome measures: The primary outcome was total number of hospitalisations during the study period. Participants were matched using HOT propensity scores and were stratified by respiratory impairment (grade 1: FEV₁ ≤25% or PaO₂ ≤55 mm Hg; grade 2: FEV₁ ≤30% or PaO₂ 56–60 mm Hg; grade 3: FEV₁ ≤40% or PaO₂ 61–65 mm Hg; 'no grade': FEV₁ or PaO₂ unknown), then a negative binomial regression analysis was performed for each group.

Results: Of the 36 761 COPD patients included in our study, 1330 (3.6%) received HOT. In a multivariate analysis of grade 1 patients performed before propensity score matching, the adjusted relative risk of hospitalisation for patients who did not receive HOT was 1.27 (95% CI 1.01 to 1.60). In a multivariate analysis of grade 1 patients performed after matching, the adjusted relative risk for patients who did not receive HOT was 1.65 (95% CI 1.25 to 2.18). In grade 2 or grade 3 patients, no statistical difference in hospital admission risk was detected. In the 'no grade' group of patients, HOT was associated with an increased risk of hospitalisation.

Conclusions: HOT reduces the risk of hospital admission in COPD patients with severe hypoxaemia. However, apart from these patients, HOT use is not associated with hospital admissions.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common frequently undiagnosed disease characterised by progressive airflow limitation that is not fully reversible, causing disability.¹ COPD is a major cause of

Strengths and limitations of this study

- We analysed the association between home oxygen therapy and hospitalisation for chronic obstructive pulmonary disease patients using nationwide claims data and conducted a longitudinal population-based prospective analysis based on claims from 2005 to 2012.
- We were able to increase the homogeneity of our study sample by identifying patients who were newly diagnosed in 2005.
- We made an effort to accurately determine the net effect of home oxygen therapy via propensity score matching.
- Our findings may have potential unmeasured variable bias because we used data based on claims.

morbidity and mortality, responsible for an increasing and substantial societal burden,² and hence is viewed as a serious public health problem in many countries. According to WHO estimates, 80 million people have moderate to severe COPD, and 3 million people died of COPD in 2005. The same estimates also predicted that it will become the fourth leading cause of death by 2030.³

In an effort to combat COPD-related hospitalisation, researchers have studied the effects of oxygen therapy. Long-term oxygen therapy (LTOT) has been shown to improve survival and quality of life as well as to stabilise pulmonary hypertension in COPD patients.^{4–9} In Korea, clinical practitioners and policy-makers have begun to recognise the benefits of LTOT. Social welfare services are offered home oxygen therapy to those with respiratory related disabilities for free.¹⁰ Home oxygen therapy (HOT) is the administration at home of oxygen at concentrations

greater than the ambient air concentration and has been covered by the Korean national health insurance system since 2006. However, ambulatory oxygen delivery systems and home ventilator services are not currently covered by the health insurance system. As the burden of COPD continues to increase, analysing the status of healthcare utilisation in patients with COPD is important for establishing healthcare plans that encourage proper management of COPD. These issues have been raised in Korea as well as in many other countries where the burden of COPD is increasing, so guidelines for the provision of HOT are needed.

However, findings concerning the effect of HOT on hospitalisation have varied. Although several studies have indicated that LTOT decreases hospital admissions,^{11–14} one study found no effect.¹⁵ Most studies that found LTOT had an effect on hospital admission detected the greatest association among severely hypoxemic COPD patients ($\text{PaO}_2 \leq 60$ mm Hg at rest on room air).^{11–14} However, in moderately hypoxemic COPD patients (PaO_2 55–70 mm Hg at rest on room air: 7.3–9.5 kPa), HOT may not reduce hospitalisations.¹⁵ Also, regarding oxygen prescription, hospital admission is more likely in LTOT users and medical costs are increasing due to the inappropriate use of oxygen.¹⁶

The aim of this study was to assess the effect of HOT on hospital admissions in COPD patients stratified according to forced expiratory volume 1 s or arterial oxygen tension values, and to provide evidence on appropriate indications for HOT.

METHODS

Data and study design

This study used 2002–2012 claims from the Korean National Health Insurance Service (KNHIS) claims database. We conducted a longitudinal population-based retrospective cohort study of newly diagnosed adult COPD patients to investigate the association between HOT and hospital admissions over a 7-year follow-up period. Participants were 40 years of age or older with newly diagnosed COPD (International Classification of Disease, 10th edition (ICD-10) codes J43.x (emphysema) (except for J43.0, McLeod's syndrome) and J44.x (COPD)). A new diagnosis was confirmed by a lack of COPD-related claims in 2002–2004 and the first COPD-related claim in 2005. The presence or absence of HOT was analysed from 2006 onwards, and hospital admissions were analysed from 2007 to 2012. If a patient died during the study period, we observed hospital admissions until the time of death. Ethics approval for this study was granted by the institutional review board of the Graduate School of Public Health, Yonsei University, Seoul, Korea.

Study population

We identified 1 538 711 individuals in 2002–2012 who were aged 40 years or older and had COPD. Of these patients, 138 680 received their diagnosis in 2005 and

were still alive in 2006. We modified the criteria used by Kim *et al*¹⁷ to define COPD patients using claims data. Hence COPD was defined in this study by the following criteria: (1) age ≥ 40 years; (2) ICD-10 codes for COPD (J43.x (emphysema) (except for J43.0) and J44.x (COPD)); and (3) use of one or more COPD medications at least twice per year. Unfortunately, we could not review all prescriptions and thus replaced the third criterion with having over four outpatient visits per year due to COPD as the primary diagnosis. Since we inferred COPD diagnoses from information contained in the KNHIS claims database, we developed a process to help identify participants who actually had COPD. We excluded 101 919 patients consisting of 9566 who had died by 2005 and 92 353 who had fewer than four outpatient visits with COPD as the primary complaint, did not receive HOT, and did not experience a hospital admission due to COPD during 2006. The exclusion criterion of less than four outpatient visits was based on a previous study where COPD patients in 2009 had a mean number of outpatient visits of 7.4; the mean number of outpatient visits in 2005 was 3.2 in our sample. Our final study sample included 36 761 patients, 1330 who received HOT and 35 431 who did not.

Variables

The dependent variable in this study was the total number of hospital admissions due to COPD during the study period. We defined hospital admission due to COPD as the use of inpatient medical services for more than 1 day and primary emphysema or COPD according to ICD-10 codes J43.x (except for J43.0) or J44.x.

Covariates considered included age, sex, health insurance status (national health insurance or medical aid), the Charlson Comorbidity Index (0, 1 or 2+),¹⁸ HOT (yes, no), use of the intensive care unit (ICU) (yes, no), number of hospital admissions (0, 1 or 2+), and respiratory impairment (1, 2, 3 or 'no grade'). In Korea, the Ministry of Health and Welfare provides social welfare services to disabled people through the Welfare of Disabled Persons Act, but employs strict criteria due to a lack of finances for disabled people. According to the Welfare of Disabled Persons Act, the severity of respiratory impairment is determined according to dyspnoea, predicted FEV_1 and PaO_2 . The criteria for grade 1 were chronic respiratory failure requiring oxygen therapy and a predicted FEV_1 of $\leq 25\%$ or a resting PaO_2 of ≤ 55 mm Hg (room air); grade 2 criteria were dyspnoea when walking at home and a predicted FEV_1 of $\leq 30\%$ or PaO_2 of 56–60 mm Hg (room air); and grade 3 criteria were with dyspnoea when walking at one's own pace on level ground and a predicted predicted FEV_1 of $\leq 40\%$ or PaO_2 of 61–65 mm Hg (room air). We defined the 'no grade' group as patients with unknown predicted FEV_1 or PaO_2 . Only the comorbidity component of the Charlson Comorbidity Index was calculated. All variables were measured at the 2006 baseline.

Statistical analysis

First, the demographic characteristics of patients who received HOT and those who did not were compared; the χ^2 test was used to assess categorical variables, and t tests were used to assess continuous variables. Next, a non-parsimonious multivariable logistic regression model was used to estimate propensity scores for HOT. Propensity score matching (PSM) is a statistical matching technique that attempts to estimate the effect of a treatment, policy or other intervention by accounting for the covariates that predict treatment reception. The PSM allows one to design and analyse an observational study so that it mimics certain characteristics of a randomised controlled trial.¹⁹ We included the following in our propensity model: age, sex, health insurance type, Charlson Comorbidity Index, ICU use, number of hospital admissions in 2006, and respiratory disability grade. The c-statistic for our propensity model was 0.784. Subjects who received HOT were matched on a one-to-one basis with those who did not. We then stratified participants according to their respiratory disability grade, based on hypoxemic status, and evaluated the relationship between HOT and hospital admissions in each group using a negative binomial regression analysis, which was chosen due to over-dispersion. All analyses were performed using SAS V.9.3.

RESULTS

Of the 36 761 patients in our study, 1330 (3.6%) received HOT. Before PSM, baseline characteristics differed significantly between patients who received HOT and those who did not (table 1). However, after PSM only the number of hospital admissions and respiratory disability grade differed between the two groups.

Table 2 presents incidence (ID) rates for hospital admission according to HOT usage. Before PSM, the ID rate for grade 1 (predicted FEV₁ ≤25% or PaO₂ ≤55 mm Hg) patients who received HOT was 0.60 versus 1.01 for those who did not. However, for grade 2 and grade 3 patients (predicted FEV₁ ≤30% or PaO₂ 56–60 mm Hg and predicted FEV₁ ≤40% or PaO₂ 61–65 mm Hg) or those categorised as ‘no grade’ (predicted FEV₁ or PaO₂ unknown), the ID rate was higher for those who received HOT than for those who did not (0.61 vs 0.63; 0.47 vs 0.46; and 0.34 vs 0.05, respectively). Similar results were obtained after PSM. For grade 1 patients, the ID rate was lower for patients who received HOT than for those who did not (0.62 vs 0.79), while for grades 2 and 3 or ‘no grade’, the ID rate was higher for patients who received HOT (0.59 vs 0.37; 0.47 vs 0.23; and 0.34 vs 0.07, respectively).

Table 1 Baseline characteristics of the study sample, stratified according to use of home oxygen therapy

Characteristics	Before matching (N=36 761)				p Value	After matching (1:1; N=2478)				
	Yes, n (%)		No, n (%)			Yes, n (%)		No, n (%)		
	1330	(3.6)	35 431	(96.4)		1239	(50.0)	1239	(50.0)	
Age (years), mean (SD)	67.1	(9.6)	63.8	(12.0)	<0.0001	67.4	(9.7)	68.0	(9.9)	0.14
Sex										
Male	964	(4.7)	19 353	(95.3)	<0.0001	884	(49.2)	912	(50.8)	0.21
Female	367	(2.2)	16 078	(97.8)		355	(52.0)	327	(48.0)	
Health insurance type										
National health insurance	1279	(3.8)	32 645	(96.2)	<0.0001	1188	(50.5)	1163	(49.5)	0.02
Medical aid	51	(1.8)	2786	(98.2)		51	(40.2)	76	(59.8)	
Charlson Comorbidity Index*										
0	692	(6.5)	9983	(93.5)	<0.0001	628	(48.4)	670	(51.6)	0.13
1	62	(5.7)	1021	(94.3)		57	(47.1)	64	(52.9)	
≥2	576	(2.3)	24 427	(97.7)		554	(52.3)	505	(47.7)	
ICU use										
Yes	11	(6.9)	148	(93.1)	<0.0001	9	(39.1)	12	(60.9)	0.30
No	1319	(3.6)	35 283	(96.4)		1230	(50.1)	1225	(49.9)	
Number of hospital admissions										
0	1147	(3.5)	31 923	(96.5)	<0.0001	1067	(51.5)	1004	(48.5)	0.002
1	127	(4.9)	2486	(95.1)		119	(40.6)	174	(59.4)	
≥2	56	(5.2)	1022	(94.8)		53	(46.5)	61	(53.5)	
Respiratory impairment rating										
Grade 1 (predicted FEV ₁ ≤25% or PaO ₂ ≤55 mm Hg)	163	(43.2)	214	(56.8)	<0.0001	91	(43.1)	120	(56.9)	0.001
Grade 2 (predicted FEV ₁ ≤30% or PaO ₂ ≤60 mm Hg)	121	(35.6)	219	(64.4)		102	(55.7)	81	(44.3)	
Grade 3 (predicted FEV ₁ ≤40% or PaO ₂ ≤65 mm Hg)	110	(26.6)	304	(73.4)		110	(61.1)	70	(38.9)	
No grade	936	(2.6)	34 694	(97.4)		936	(49.2)	968	(50.8)	

*Calculated comorbidity component; subtracted age scores.
ICU, intensive care unit.

Table 2 Incidence rate for hospital admission according to use of home oxygen therapy

Respiratory impairment rating*	Before matching				After matching (1:1)			
	Yes N=1330	No N=35 431	Yes ID†	No ID†	Yes N=1239	No N=1239	Yes ID†	No ID†
Grade 1								
Total number of hospital admissions	416	748	0.60	1.01	244	319	0.62	0.79
Person-years	694.1	743.3			390.8	406.0		
Grade 2								
Total number of hospital admissions	358	601	0.61	0.63	291	128	0.59	0.37
Person-years	585.6	953.4			495.9	341.4		
Grade 3								
Total number of hospital admissions	245	672	0.47	0.46	245	81	0.47	0.23
Person-years	517.8	1455.4			517.8	348.3		
No grade								
Total number of hospital admissions	1409	9286	0.34	0.05	1409	322	0.34	0.07
Person-years	4123.0	184 555.3			4123.0	4837.3		

*Grade 1 patients were defined as having chronic respiratory failure requiring oxygen therapy and an FEV₁ ≤25% predicted or resting PaO₂ ≤55 mm Hg (room air); grade 2 patients were defined as having dyspnoea when walking at home and an FEV₁ ≤30% predicted or PaO₂ 56–60 mm Hg (room air); grade 3 patients were defined as having dyspnoea when walking at their own pace on level ground and FEV₁ ≤40% predicted or PaO₂ 61–65 mm Hg (room air); 'no grade' was defined as predicted FEV₁ or PaO₂ unknown.

†Calculated total number of hospital admissions divided into sum of person-years.

ID, incidence rate.

Table 3 presents the adjusted relative risk (RR) for hospital admission before PSM. After controlling for all covariates, the adjusted RR for grade 1 patients who did not receive HOT compared to the reference group (those who did receive HOT) was 1.12 (95% CI 1.01 to 1.60). The RR for grade 2 patients was 0.96, but this difference was not statistically significant. In the grade 3 and 'no grade' groups, the adjusted RRs for patients who did not receive HOT were less than 1 (RR, 0.74, 95% CI 0.58 to 0.93; and RR, 0.65, 95% CI 0.60 to 0.70, respectively).

After PSM, the adjusted RR for grade 1 patients who did not receive HOT was 1.65 (95% CI 1.25 to 2.18); in grade 2 patients, the adjusted RR was 1.07 (95% CI, 0.80 to 1.43); in grade 3 patients, the adjusted RR was 0.72 (95% CI 0.51 to 1.02); and in patients without a grade, the adjusted RR was 0.73 (95% CI 0.62 to 0.86) (table 4).

DISCUSSION

We found that HOT was associated with a 27% decreased risk of hospitalisation in grade 1 COPD patients (predicted FEV₁ ≤25% or PaO₂ ≤55 mm Hg) before PSM and a 65% decreased risk after matching. However, apart from grade 1 patients, the use of HOT did not show a statistically significant association with hospital admission before or after matching in grade 2 patients. Also, in grade 3 and 'no grade' COPD patients (predicted FEV₁ ≤40% or PaO₂ ≤65 mm Hg, and predicted FEV₁ or PaO₂ unknown), HOT was associated with an increased risk of hospital admission before PSM.

In Korea, HOT can be prescribed by pulmonologists as well as internists and thoracic surgery specialists based on the results of a single arterial blood gas analysis. Similar to the criteria used in most other countries, the

indications for reimbursement for HOT are PaO₂ ≤55 mm Hg or SpO₂ ≤88%. Patients with PaO₂ 56–60 mm Hg or SpO₂ <89%, must also have congestive heart failure, polycythaemia (haematocrit >55%) or pulmonary hypertension to qualify during the stable period following 3 months of conservative therapy such as medication. Physicians can prescribe for patients with grade 1 or grade 2 respiratory impairment without conducting any other tests. If patients without a grade receives a HOT prescription, then that patient was seen by a physician under the COPD code but did not fill out the necessary form to receive an assigned grade. Hence the patient's clinical status fulfils the indications for HOT prescription and so may in fact belong to any of the grades described above, including grade 1. Therefore, in patients without a grade, the use of HOT means that they may have conditions that are clinically more severe than those who do not use HOT.

Our results are comparable to the findings of previous studies. We could not distinguish between PaO₂ and predicted FEV₁ predicted. We could only infer patients' PaO₂, FEV₁ or shortness of breath according to respiratory impairment grade. However, for grade 1 patients with PaO₂ ≤55 mm Hg or predicted FEV₁ ≤25%, use of HOT was associated with a reduced risk of hospital admission. Most previous studies have shown a consistent tendency in patients with severe hypoxaemia (PaO₂ <8.0 kPa) in whom HOT was associated with decreased hospital admissions. However, Ringbaek *et al*¹⁵ found that HOT did not reduce hospitalisation in patients with moderate hypoxaemia (PaO₂ >8.0 kPa). In addition, many previous studies have found that FEV₁% predicted could be a predictor of acute exacerbation hospitalisation.^{20–22} One recent paper suggested that oxygen use outside the National Institute for Health and Care

Table 3 Relative risk for hospital admission stratified according to respiratory disability grade calculated using a negative binomial regression model

Characteristics	Relative risk (95% CI)							
	Grade 1		Grade 2		Grade 3		No grade	
Age (years)	1.002	(0.993 to 1.010)	0.992	(0.983 to 1.001)	1.010	(0.993 to 1.021)	1.006	(1.004 to 1.009)***
Sex								
Male	1.06	(0.87 to 1.29)	1.25	(0.96 to 1.62)	0.94	(0.75 to 1.18)	1.16	(1.10 to 1.23)***
Female	1.00		1.00		1.00		1.00	
Health insurance type								
National health insurance	1.00	(0.80 to 1.25)	0.94	(0.75 to 1.17)	0.60	(0.49 to 0.75)***	0.69	(0.65 to 0.73)***
Medical aid	1.00		1.00		1.00		1.00	
Home oxygen therapy								
Yes	1.00		1.00		1.00		1.00	
No	1.27	(1.01 to 1.60)*	0.96	(0.75 to 1.22)	0.74	(0.58 to 0.93)*	0.65	(0.60 to 0.70)***
Charlson Comorbidity Index†								
0	1.00		1.00		1.00		1.00	
1	0.86	(0.66 to 1.13)	1.00	(0.72 to 1.39)	0.82	(0.57 to 1.17)	1.00	(0.93 to 1.07)
≥2	1.12	(0.84 to 1.49)	1.11	(0.81 to 1.53)	0.90	(0.67 to 1.21)	1.11	(1.02 to 1.21)*
ICU use								
Yes	1.13	(0.74 to 1.70)	1.05	(0.42 to 2.59)	0.31	(0.09 to 1.09)	1.02	(0.82 to 1.27)
No	1.00		1.00		1.00		1.00	
Number of hospital admissions								
0	1.00		1.00		1.00		1.00	
1	1.65	(1.29 to 2.11)***	1.45	(1.12 to 1.88)**	1.24	(0.98 to 1.57)	1.69	(1.58 to 1.81)***
≥2	1.73	(1.34 to 2.24)***	1.48	(1.11 to 1.96)**	1.65	(1.28 to 2.12)***	2.04	(1.88 to 2.21)***

Grade 1 patients were defined as having chronic respiratory failure requiring oxygen therapy and an FEV₁ ≤25% predicted or resting PaO₂ ≤55 mm Hg (room air); grade 2 patients were defined as having dyspnoea when walking at home and an FEV₁ ≤30% predicted or PaO₂ 56–60 mm Hg (room air); grade 3 patients were defined as having dyspnoea when walking at their own pace on level ground and FEV₁ ≤40% predicted or PaO₂ 61–65 mm Hg (room air); 'no grade' was defined as predicted FEV₁ or PaO₂ unknown.

*p<0.05; **p<0.01; ***p<0.001.

†Calculated comorbidity component; subtracted age scores.

ICU, intensive care unit.

Excellence (NICE) guidance did not appear to prevent admissions²³ and predicted FEV₁ was the only significant predictor of readmission.¹⁶ In South Korea, although HOT is used according to NICE guidelines, HOT was not associated with decreased risk of hospital admission even in grade 2 patients (PaO₂ 56–60 mm Hg or predicted FEV₁ ≤30%). In grade 3 or 'no grade' patients, admission to hospital was more likely in HOT users before matching, while after matching, there was no statistically significant difference in grade 3 patients. There

are two possible explanations for this result. One is that because admission for exacerbation is more common in severe COPD²⁴ patients and in oxygen users,²⁵ hospital admissions are more frequently expected in HOT users as they have more severe lung disease. The second possibility may be explained through residual confounding. Garcia-Aymerich *et al*²⁶ showed that the risk of readmission was high in LTOT users after adjustment for severity variables such as predicted FEV₁ or PaO₂. The authors explained these results using residual confounding, in

Table 4 Relative risk for hospital admission after propensity score matching calculated using a negative binomial regression model

Characteristics	Relative risk (95% CI)							
	Grade 1		Grade 2		Grade 3		No grade	
Home oxygen therapy								
Yes	1.00		1.00		1.00		1.00	
No	1.65	(1.25 to 2.18)***	1.07	(0.80 to 1.43)	0.72	(0.5 to –1.02)	0.73	(0.62 to 0.86)***

Grade 1 patients were defined as having chronic respiratory failure requiring oxygen therapy and an FEV₁ ≤25% predicted or resting PaO₂ ≤55 mm Hg (room air); grade 2 patients were defined as having dyspnoea when walking at home and an FEV₁ ≤30% predicted or PaO₂ 56–60 mm Hg (room air); grade 3 patients were defined as having dyspnoea when walking at their own pace on level ground and FEV₁ ≤40% predicted or PaO₂ 61–65 mm Hg (room air); 'no grade' was defined as FEV₁ or PaO₂ unknown.

*p<0.05; **p<0.01; ***p<0.001.

that the excess risk of COPD re-admission associated with medical care related factors might be partially due to confounding by indication. Our findings suggest that HOT use reduces hospitalisation in COPD patients with severe hypoxaemia ($\text{PaO}_2 \leq 55$ mm Hg) and a predicted FEV_1 of $\leq 25\%$. However, although HOT may improve quality of life and help breathing during activities in COPD patients without severe hypoxaemia, use of HOT should be considered to prevent hospital admissions in COPD patients with $\text{PaO}_2 > 55$ mm Hg or a predicted $\text{FEV}_1 > 25\%$. Further research on the cost-effectiveness for HOT use in these patients is required and the criteria for HOT prescription may need to be modified.

This study has several limitations. First, because we used claims data, which are based on information in the KNHIS claims database, we were not able to assess some factors that could potentially influence hospital admissions. For example, we had no data on smoking history, body mass index, health behaviours, use of systemic corticosteroids, laboratory results, etc. Second, we categorised respiratory impairment into four respiratory disability grades, as determined by predicted FEV_1 , PaO_2 and dyspnoea. Therefore, we did not use quantitative predicted FEV_1 or PaO_2 values, instead estimating a patient's hypoxemic status. Especially in the 'no grade' group, it is possible that patients with different severity were grouped together. The third limitation is the accuracy of our COPD diagnosis. The accuracy of diagnoses in KNHIS claims data is roughly 70%.²⁷ To increase accuracy, a review of all prescriptions would be required. Unfortunately, we could not perform such a review here. However, the accuracy of COPD diagnoses in this study may have been compromised. The fourth limitation involves the definition of newly diagnosed patients. In this study, newly diagnosed patients were defined as those who did not have COPD claims in 2002–2004 but did have a COPD claim in 2005. Thus, patients diagnosed before 2002 who did not utilise COPD-related medical services in 2002–2004 may have been included in the sample. The final limitation is related to patterns of HOT use. Although all our study subjects used HOT in or after 2006 and we adjusted for the number of hospital admission at baseline, because previous studies hypothesized that an effect of oxygen therapy in patients who start HOT as outpatients is less likely to be derived from a 'regression to the mean phenomenon',¹² we did not know the duration of usage per day, whether use was continuous or non-continuous, or whether patient compliance was good.

Despite these limitations, our study has several strengths. First, we analysed COPD patients using nationwide claims data and conducted a longitudinal population-based prospective analysis based on claims from 2005 to 2012. Our study population was relatively large and our follow-up period was relatively long compared to previous studies evaluating the association between oxygen therapy and hospitalisation.^{12–28} Second, we were able to increase the homogeneity of

our study sample by identifying patients who were newly diagnosed in 2005. We could observe the progression of their disease over time via hospital admissions. Finally, we made an effort to accurately determine the net effect of HOT via PSM.

In conclusion, HOT reduces hospital admission risk in COPD patients with severe hypoxaemia or a predicted FEV_1 of $\leq 25\%$. However, except for these patients, HOT use is not associated with hospital admissions, or an increase in the likelihood of hospital admission. Further research on the cost-effectiveness of HOT in patients who do not meet the indications for HOT is needed.

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Contributors KHC and E-CP designed the study; E-CP guided and directed the study; SJK and K-TH were clinical investigators; KHC and CMN analysed data; KHC, E-CP, and YSK interpreted the results; YSK was scientific advisor; and KHC and THK wrote the manuscript.

Competing interests None declared.

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