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Association Between Initiation of Pulmonary Rehabilitation After Hospitalization for COPD and 1-Year Survival Among Medicare Beneficiaries

Peter K. Lindenauer, MD, MSc; Mihaela S. Stefan, MD, PhD; Penelope S. Pekow, PhD; Kathleen M. Mazor, EdD; Aruna Priya, MA, MSc; Kerry A. Spitzer, PhD, MPA; Tara C. Lagu, MD, MPH; Quinn R. Pack, MD, MSc; Victor M. Pinto-Plata, MD; Richard ZuWallack, MD

IMPORTANCE Meta-analyses have suggested that initiating pulmonary rehabilitation after an exacerbation of chronic obstructive pulmonary disease (COPD) was associated with improved survival, although the number of patients studied was small and heterogeneity was high. Current guidelines recommend that patients enroll in pulmonary rehabilitation after hospital discharge.

OBJECTIVE To determine the association between the initiation of pulmonary rehabilitation within 90 days of hospital discharge and 1-year survival.

DESIGN, SETTING, AND PATIENTS This retrospective, inception cohort study used claims data from fee-for-service Medicare beneficiaries hospitalized for COPD in 2014, at 4446 acute care hospitals in the US. The final date of follow-up was December 31, 2015.

EXPOSURES Initiation of pulmonary rehabilitation within 90 days of hospital discharge.

MAIN OUTCOMES AND MEASURES The primary outcome was all-cause mortality at 1 year. Time from discharge to death was modeled using Cox regression with time-varying exposure to pulmonary rehabilitation, adjusting for mortality and for unbalanced characteristics and propensity to initiate pulmonary rehabilitation. Additional analyses evaluated the association between timing of pulmonary rehabilitation and mortality and between number of sessions completed and mortality.

RESULTS Of 197 376 patients (mean age, 76.9 years; 115 690 [58.6%] women), 2721 (1.5%) initiated pulmonary rehabilitation within 90 days of discharge. A total of 38 302 (19.4%) died within 1 year of discharge, including 7.3% of patients who initiated pulmonary rehabilitation within 90 days and 19.6% of patients who initiated pulmonary rehabilitation after 90 days or not at all. Initiation within 90 days was significantly associated with lower risk of death over 1 year (absolute risk difference [ARD], −6.7% [95% CI, −7.9% to −5.6%]; hazard ratio [HR], 0.63 [95% CI, 0.57 to 0.69]; $P < .001$). Initiation of pulmonary rehabilitation was significantly associated with lower mortality across start dates ranging from 30 days or less (ARD, −4.6% [95% CI, −5.9% to −3.2%]; HR, 0.74 [95% CI, 0.67 to 0.82]; $P < .001$) to 61 to 90 days after discharge (ARD, −11.1% [95% CI, −13.2% to −8.4%]; HR, 0.40 [95% CI, 0.30 to 0.54]; $P < .001$). Every 3 additional sessions was significantly associated with lower risk of death (HR, 0.91 [95% CI, 0.85 to 0.98]; $P = .01$).

CONCLUSIONS AND RELEVANCE Among fee-for-service Medicare beneficiaries hospitalized for COPD, initiation of pulmonary rehabilitation within 3 months of discharge was significantly associated with lower risk of mortality at 1 year. These findings support current guideline recommendations for pulmonary rehabilitation after hospitalization for COPD, although the potential for residual confounding exists and further research is needed.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Peter K. Lindenauer, MD, MSc, Institute for Healthcare Delivery and Population Science, University of Massachusetts Medical School—Baystate, 3601 Main St, Springfield, MA 01199 (peter.lindenauer@baystatehealth.org).

Approximately 15.5 million individuals in the US reported having chronic obstructive pulmonary disease (COPD) in 2015, and exacerbations resulted in more than 1.5 million emergency department visits and nearly 700 000 hospitalizations annually between 2001 and 2012.[1,2] The period after hospital discharge is marked by high levels of health care utilization and elevated risk of mortality. In 2008-2014, among Medicare beneficiaries, mortality within 1 year of discharge was estimated to be 26%.[3]

Pulmonary rehabilitation involves exercise training and self-management education to improve physical and psychological well-being.[4] It is effective at relieving dyspnea, increasing exercise tolerance, and improving health-related quality of life for individuals with all stages of COPD, and may also reduce health care utilization.[4-6] Prior research has shown that few patients with COPD complete a course of pulmonary rehabilitation because of lack of physician referral, lack of access to facilities, and a variety of patient-related barriers.[7] While pulmonary rehabilitation has traditionally been viewed as beneficial for symptomatic, medically stable patients, recent attention has turned to its role after an exacerbation, when patients are at high risk of experiencing a self-reinforcing spiral of dyspnea-related deconditioning.[8,9] Although the mechanisms are uncertain, 2 recent meta-analyses of randomized trials found that initiation of pulmonary rehabilitation soon after COPD exacerbation was associated with reduced risk of readmission and death.[10,11] However, the total number of patients studied remains small. Current guidelines recommend that patients begin pulmonary rehabilitation within 3 to 4 weeks of a COPD exacerbation.[4,12,13]

Because results of randomized trials are not always generalizable to routine settings, this study investigated outcomes associated with pulmonary rehabilitation among a national sample of older adults hospitalized for COPD.[14-16] The primary objective was to determine the association between initiation of pulmonary rehabilitation within 90 days of discharge and 1-year survival.

Key Points

Question Is initiation of pulmonary rehabilitation after hospitalization for chronic obstructive pulmonary disease (COPD) associated with better survival?

Findings In this retrospective observational study that included 197 376 Medicare beneficiaries discharged after hospitalization for COPD, initiation of pulmonary rehabilitation within 3 months of discharge, compared with later or no initiation of pulmonary rehabilitation, was significantly associated with lower risk of mortality at 1 year (hazard ratio, 0.63).

Meaning These findings support current guideline recommendations for pulmonary rehabilitation after hospitalization for COPD, although the potential for residual confounding exists and further research is needed.

Methods

Design, Setting, Patients

This study was approved by the institutional review board of Baystate Health, which granted a waiver of informed consent. We conducted a retrospective cohort study of all fee-for-service Medicare beneficiaries older than 65 years who were hospitalized for COPD in 2014, with a final date of follow-up of December 31, 2015, the most recent year for which data were available. We defined the cohort using *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes in accordance with methods used by the Centers for Medicare & Medicaid Services (eTable in the Supplement). We identified the first hospitalization in the year as the index hospitalization. To create an inception, or new-user, cohort, we excluded beneficiaries who had received pulmonary rehabilitation during the previous year.[17,18] To emulate criteria used in previous trials we excluded patients with dementia, metastatic cancer, and acute myocardial infarction/acute coronary syndrome. We also excluded patients we thought would be unlikely to initiate pulmonary rehabilitation within 90 days of discharge and to have a high risk of mortality. These included patients with an index hospital stay longer than 31 days, those transferred to another acute care hospital, individuals discharged to skilled nursing facilities who remained in the facility for more than 30 days, and individuals who died within 30 days of discharge (**Figure 1**).

Participation in Pulmonary Rehabilitation

We used the Medicare outpatient and carrier files to identify patients who received pulmonary rehabilitation, using common procedure coding system codes G0424 (COPD-specific pulmonary rehabilitation) and G0237, G0238, and G0239 (nonspecific pulmonary rehabilitation). We counted the number of days from the index hospitalization discharge to the first session and the number of sessions completed within the year after discharge.

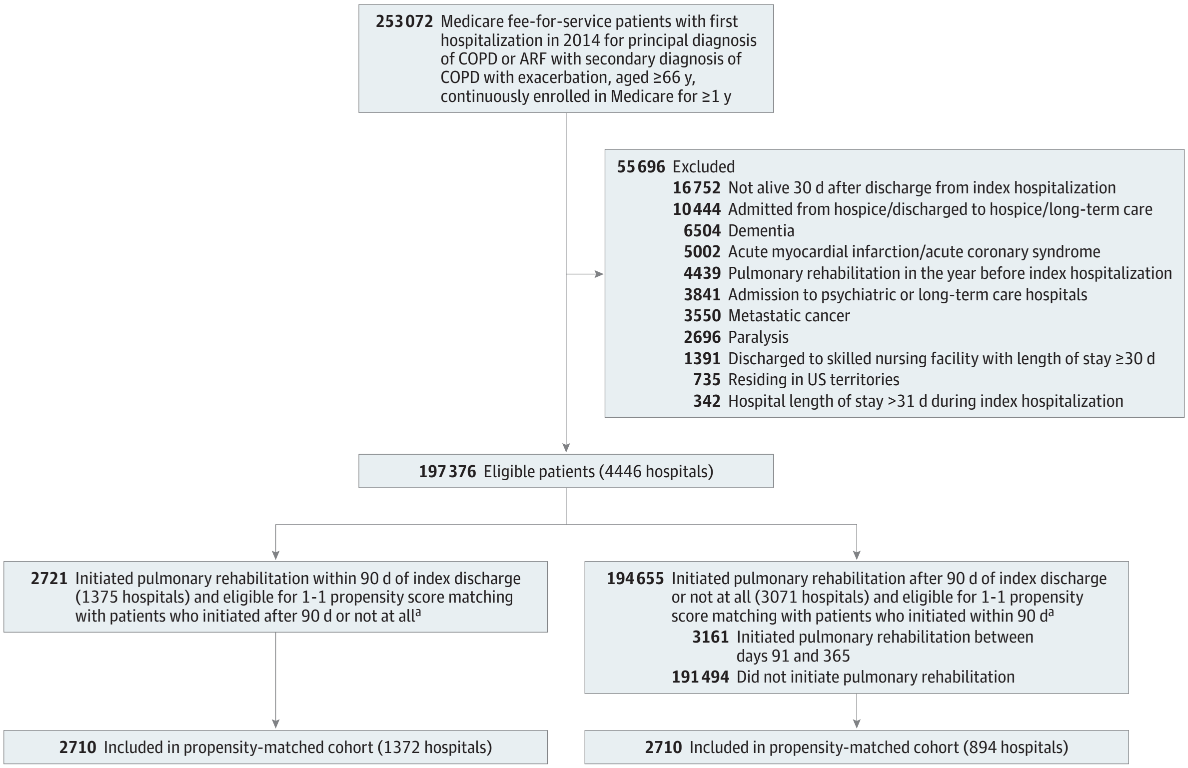
Primary Outcome

The primary outcome was death due to any cause within 1 year of discharge from the index hospitalization. Vital status was obtained from the Medicare Beneficiary Summary File, which includes a date of death for all beneficiaries but not cause of death.

Patient and Hospital Factors

Sociodemographic characteristics included age, sex, race/ethnicity, Medicaid dual eligibility (a proxy for lower socioeconomic status), current tobacco use, and distance to the nearest pulmonary rehabilitation facility.[19] Race/ethnicity was included as we have noted variation in access to and use of pulmonary rehabilitation associated with race in prior research.[20] Race/ethnicity was determined using an enhancement to the Social Security Administration categorical race variable, which uses an algorithm to assign beneficiaries to Hispanic or Asian based on last name when race was unknown. Asian/Pacific Islander and American Indian/Alaska Native were grouped into the "other" category because of

Figure 1. Patient Selection in a Study of Pulmonary Rehabilitation After Hospitalization for COPD



COPD indicates chronic obstructive pulmonary disease; ARF, acute respiratory failure.

[a] Propensity scores were calculated using a logistic regression model accounting for patient clustering within hospitals in the cohort. This was a nonparsimonious logistic (generalized estimating equations) model that included patient demographics, tobacco use, Medicaid dual-eligibility, comorbidities, claims-based frailty indicator, markers of disease severity, features of index admission, characteristics of hospitals to which patients were admitted (including size, rural/urban status, teaching status, and Census region), and selected interaction terms. Patients discharged from hospitals where pulmonary rehabilitation was not provided were excluded from model development because such patients had no possibility of receiving pulmonary rehabilitation. Parameter estimates were then applied to all patients at all hospitals to compute the propensity score. Based on this score and using a greedy match algorithm, patients who received pulmonary rehabilitation within 90 days of discharge were matched 1-to-1 with patients who never initiated or initiated within days 91 and 365. To avoid immortal time bias, the matched control was required to be alive on the day of the pulmonary rehabilitation participant's first session. In the matched cohort, distance to nearest pulmonary rehabilitation facility, hospital rural/urban status, and hospital size were imbalanced between the groups.

small numbers. We assessed individual comorbidities using Agency for Healthcare Research and Quality (AHRQ) comorbidity software and computed a longitudinal Charlson Comorbidity Index score.[21,22] We calculated each patient's risk of frailty using methods described by Segal et al.[23] Markers of COPD severity included a count of hospitalizations in the prior 12 months, receipt of home oxygen within 90 days before admission, and receipt of mechanical ventilation during the index hospitalization. Additionally, we assessed emergency department visits and readmissions after hospital discharge but before the initiation of pulmonary rehabilitation. Hospital characteristics included number of beds, Census region, teaching status, and rurality.

Statistical Analysis

Our primary analysis focused on the association between initiation of pulmonary rehabilitation within 90 days of an index hospital discharge and 1-year survival; additional analyses explored the relationships of timing of initiation and the number of sessions completed with survival. Given the large size of our sample, we calculated absolute standardized differences (ASDs) to compare patients who initiated pulmonary rehabilitation within 90 days of discharge with those who never initiated or who initiated between days 91 and 365 after discharge.[24] We developed a nonparsimonious propensity model to predict initiation of pulmonary rehabilitation within 90 days of discharge using generalized estimating equations (GEE) logistic regression, accounting for clustering of patients within hospitals. The model included all patient sociodemographic characteristics, Medicaid dual eligibility, tobacco use, comorbidities, frailty, markers of disease severity, features of the index admission, and selected interaction terms. In propensity model development, we excluded patients discharged from hospitals where pulmonary rehabilitation was not provided because such patients had no possibility of receiving it. We then applied model coefficients to estimate a propensity for treatment for patients at all hospitals.

Association Between Initiation of Pulmonary Rehabilitation and Survival

To assess the association between initiation of pulmonary rehabilitation and survival, we modeled time from hospital discharge to death, using Cox regression. We evaluated the proportionality assumption by adding an interaction term for pulmonary rehabilitation with time; the test for proportionality was not met. We then modeled survival with time-varying pulmonary rehabilitation exposure. This approach attributed days alive after discharge, but before pulmonary rehabilitation initiation, as "unexposed" or "untreated" time; it also addressed nonproportionality. Patients who initiated pulmonary rehabilitation after 90 days, but before 365 days, contributed time until initiation toward survival among those who never initiated and then were censored when they started pulmonary rehabilitation. We computed an E-value to quantify the minimum strength of association necessary for an unmeasured confounder to negate any significant association observed between pulmonary rehabilitation and survival.[25,26]

We performed additional analyses to evaluate whether our primary analytic strategy was robust to different methodologic approaches and to explore potential interactions associated with selected patient characteristics. First, rather than treating pulmonary rehabilitation as a time-varying exposure, we restricted the cohort to individuals who survived at least 90 days from discharge to eliminate overlap of exposure and outcome assessment periods. We fit GEE logistic regression models for mortality within the year after discharge, adjusting for unbalanced covariates and propensity to start pulmonary rehabilitation. Second, within this same cohort we fit models using stabilized inverse probability of treatment weighting (SIPTW), as well as standardized mortality rate weighting (SMR).[27,28]

Third, we repeated this analysis adding interaction terms with pulmonary rehabilitation initiation for age group, frailty, comorbid heart failure, tertiles of overall comorbidity burden, and receipt of home oxygen before the index admission. Fourth, we conducted a propensity-matched analysis, matching each individual who initiated pulmonary rehabilitation within 90 days of discharge to an individual with a similar propensity who had not initiated within 90 days using a greedy matching algorithm. To avoid immortal time bias, we required that the matched control be alive on the day of the pulmonary rehabilitation participant's first session.[29] Kaplan-Meier curves were then used to compare mortality of those who initiated pulmonary rehabilitation within 90 days of discharge with those matched who never initiated or did so after 90 days. Differences in mortality within 1 year of discharge among the matched pairs were assessed using the McNemar test. In addition, in the propensity-matched cohort, we used Cox regression to model time from pulmonary rehabilitation initiation to death, adding adjustment for hospital readmissions and emergency department visits that occurred after the index hospitalization but before initiation of pulmonary rehabilitation.

Timing of Pulmonary Rehabilitation Initiation

We carried out exploratory analyses to investigate whether the timing of pulmonary rehabilitation initiation in relation to hospital discharge moderates its association with survival. Recognizing that mortality risk is highest in the early days after discharge, and because it is common for patients to experience readmission after an index discharge, we computed the number of days between a patient's first pulmonary rehabilitation visit and the closest COPD discharge. Then, using our full study cohort, we developed a Cox model with time-varying exposure to pulmonary rehabilitation, adjusting for all patient factors including propensity to start within 90 days and adding interaction terms allowing for a change in hazard for initiation after 30 days and after 60 days.

Number of Pulmonary Rehabilitation Sessions Completed

In an additional exploratory analysis, to evaluate a potential dose-response relationship, we created a new cohort restricted to individuals who initiated pulmonary rehabilitation and survived at least 90 days after discharge. We defined the exposure period as the first 90 days after the most recent COPD discharge and assessed outcomes in the subsequent 9 months. We counted the number of sessions completed in the exposure period and then modeled survival from 91 days to death (or censoring at 1 year), evaluating the number of sessions completed as a continuous variable.

Missing Data

Files received from the CMS have minimal missing data. A few fields include an "unknown" category; however, use was rare, and cases categorized as unknown were excluded from analysis.

We present absolute risk differences from the adjusted models for all analyses. No adjustment for multiple comparisons was made; thus, the findings of the timing of initiation and number of sessions completed analyses should be interpreted as exploratory.

All statistical testing was 2-sided, using a .05 level of significance. All analyses were performed using SAS version 9.4 (SAS Institute Inc) and figures were created using Stata release 16 (StataCorp).

Results

Of 197 376 patients assessed from 4446 hospitals, 2721 (1.5%) initiated pulmonary rehabilitation within 90 days of discharge and 3161 (1.6%) initiated within days 91 and 365. Compared with those who never participated or who initiated pulmonary rehabilitation after 90 days of discharge, those who initiated within 90 days were younger (mean, 74.5 vs 77 years; ASD, 0.36), more often men (47.6% vs 41.3%; ASD, 0.13), more often non-Hispanic white (92.6% vs 85.1%; ASD, 0.24), and lived closer to a pulmonary rehabilitation facility (mean, 5.8 vs 9.8 miles; ASD, 0.35). Those who initiated pulmonary rehabilitation within 90 days of discharge had less comorbidity (mean, 3.5 vs 4.2; ASD, 0.25), a lower risk of frailty (mean, 13% vs 20%; ASD, 0.51), and were more likely to have no prior-year admissions (61.9% vs 52.4%; ASD, 0.24) but were more likely to receive home oxygen before hospitalization (39.4% vs 31.7%; ASD, 0.16) (**Table 1**). A total of 38 302 beneficiaries

Table 1. Patient Characteristics by Pulmonary Rehabilitation Status

Characteristic	Full cohort: Pulmonary rehabilitation, No. (%): Within 90 d of discharge (n = 2721)	Full cohort: Pulmonary rehabilitation, No. (%): 91-365 d after discharge or not at all (n = 194 655)	Full cohort: ASD[b]	Propensity-matched cohort[a]: Pulmonary rehabilitation, No. (%): Within 90 d of discharge (n = (2710)	Propensity-matched cohort[a]: Pulmonary rehabilitation, No. (%): 91-365 d after discharge or not at all (n = 2710)	Propensity-matched cohort[a]: ASD[b]
Demographics						
Age, mean (SD), y	74.5 (6.1)	77.0 (7.6)	0.359	74.5 (6.1)	74.6 (6.3)	0.018
Sex			0.126			0.034
Women	1427 (52.4)	114 263 (58.7)		1422 (52.5)	1376 (50.8)	
Men	1294 (47.6)	80 392 (41.3)		1288 (47.5)	1334 (49.2)	
Race/ethnicity[c]			0.244			0.031
Non-Hispanic white	2520 (92.6)	165 594 (85.1)		2510 (92.6)	2493 (92)	
Black or African American	126 (4.6)	16 759 (8.6)		125 (4.6)	138 (5.1)	
Hispanic	46 (1.7)	8038 (4.1)		46 (1.7)	44 (1.6)	
Other	29 (1.1)	4264 (2.2)		29 (1.1)	35 (1.3)	
Claims-based frailty indicator, %[d]			0.506			0.021
Mean (SD)	13 (10)	20 (16)		13 (10)	13 (10)	
Median (IQR)	9.9 (6.3-16.7)	14.7 (8.1-26.7)		9.9 (6.3-16.8)	9.8 (6.1-16.0)	
Distance to nearest pulmonary rehabilitation, mean (SD), mi[e]	5.8 (6.4)	9.8 (14.8)	0.350	5.8 (6.4)	8.9 (12.1)	0.319
Dual eligibility (Medicaid buy-in)	304 (11.2)	51980 (26.7)	0.404	304 (11.2)	313 (11.5)	0.011
Current tobacco user	595 (21.9)	45 922 (23.6)	0.041	591 (21.8)	634 (23.4)	0.038
Weighted Charlson Comorbidity Index, mean (SD)[f]	3.5 (2.9)	4.2 (3.2)	0.251	3.5 (2.9)	3.4 (2.9)	0.008
Comorbidities[g]						
Hypertension	1947 (71.6)	145 673 (74.8)	0.074	1942 (71.7)	1921 (70.9)	0.017
Fluid and electrolyte disorders	700 (25.7)	56 675 (29.1)	0.076	696 (25.7)	641 (23.7)	0.047
Diabetes	685 (25.2)	62 999 (32.4)	0.159	683 (25.2)	675 (24.9)	0.007
Congestive heart failure	556 (20.4)	61 874 (31.8)	0.261	556 (20.5)	508 (18.7)	0.045
Pneumonia	486 (17.9)	39 705 (20.4)	0.065	483 (17.8)	483 (17.8)	0.000
Obstructive sleep apnea	466 (17.1)	25 320 (13.0)	0.115	464 (17.1)	412 (15.2)	0.052
Hypothyroidism	432 (15.9)	34 724 (17.8)	0.074	415 (15.3)	387 (14.3)	0.029
Obesity	427 (15.7)	29 003 (14.9)	0.022	427 (15.8)	356 (13.1)	0.075
Depression	415 (15.3)	29 629 (15.2)	0.001	332 (12.3)	311 (11.5)	0.024
Deficiency anemias	337 (12.4)	36 071 (18.5)	0.171	337 (12.4)	331 (12.2)	0.007
Kidney failure	332 (12.2)	35 387 (18.2)	0.167	430 (15.9)	385 (14.2)	0.047
Peripheral vascular disease	271 (10)	20 784 (10.7)	0.024	269 (9.9)	257 (9.5)	0.015
Valvular disease	215 (7.9)	17 545 (9)	0.040	213 (7.9)	176 (6.5)	0.053
Other neurologic disorders	128 (4.7)	14 261 (7.3)	0.110	127 (4.7)	116 (4.3)	0.020
Hospital admissions in year before index admission			0.240			0.039
None	1684 (61.9)	101 992 (52.4)		1678 (61.9)	1634 (60.3)	
1	584 (21.5)	45 062 (23.1)		582 (21.5)	615 (22.7)	
2	266 (9.8)	22 452 (11.5)		263 (9.7)	259 (9.6)	
≥3	187 (6.9)	25 149 (12.9)		187 (6.9)	202 (7.5)	
Home oxygen use in 90 d before index hospitalization[h]	1073 (39.4)	61 761 (31.7)	0.162	1068 (39.4)	1079 (39.8)	0.008
Principal diagnosis			0.029			0.015
Acute respiratory failure	469 (17.2)	31 423 (16.1)		465 (17.2)	450 (16.6)	
COPD	2252 (82.8)	163 232 (83.9)		2245 (82.8)	2260 (83.4)	
Noninvasive ventilation during index admission	215 (7.9)	14 960 (7.7)	0.008	214 (7.9)	186 (6.9)	0.040
Invasive ventilation during index admission	84 (3.1)	6248 (3.2)	0.007	80 (3)	81 (3)	0.002
Admitted from skilled nursing facility	141 (5.2)	24 341 (12.5)	0.260	138 (5.1)	165 (6.1)	0.043

(continued)

Table 1. Patient Characteristics by Pulmonary Rehabilitation Status (continued)

Characteristic	Full cohort: Pulmonary rehabilitation, No. (%): Within 90 d of discharge (n = 2721)	Full cohort: Pulmonary rehabilitation, No. (%): 91-365 d after discharge or not at all (n = 194 655)	Full cohort: ASD[b]	Propensity-matched cohort[a]: Pulmonary rehabilitation, No. (%): Within 90 d of discharge (n = (2710)	Propensity-matched cohort[a]: Pulmonary rehabilitation, No. (%): 91-365 d after discharge or not at all (n = 2710)	Propensity-matched cohort[a]: ASD[b]
Discharged to skilled nursing facility	109 (4)	27 919 (14.3)	0.364	108 (4.0)	99 (3.7)	0.017
Readmission before pulmonary rehabilitation initiation or match date (in matched cohort)[i]	NA	NA	NA	461 (17.0)	505 (18.6)	0.042
Emergency department encounter before rehabilitation initiation or match date (in matched cohort)[i]	NA	NA	NA	323 (11.9)	357 (13.2)	0.038

Abbreviations: ASD, absolute standardized difference; COPD, chronic obstructive pulmonary disease; NA, not applicable.

[a] Propensity scores were calculated using a logistic regression model accounting for patient clustering within hospitals in the cohort. This was a nonparsimonious logistic (generalized estimating equations) model that included patient demographics, tobacco use, Medicaid dual-eligibility, comorbidities, claims-based frailty indicator, markers of disease severity, features of index admission, characteristics of hospitals where the patients were admitted (including size, rural/urban status, teaching status and Census region), and selected interaction terms. We excluded patients discharged from hospitals where pulmonary rehabilitation was not provided from model development because such patients had no possibility of receiving pulmonary rehabilitation. We then applied the parameter estimates to all patients at all hospitals to compute the propensity score. Based on this score and using a greedy match algorithm, patients who received pulmonary rehabilitation within 90 days of discharge were matched 1-to-1 with patients who never initiated or initiated within days 91 and 365. To avoid immortal time bias, we required that the matched control was alive on the day of the pulmonary rehabilitation participant's first session. In the matched cohort, distance to nearest pulmonary rehabilitation facility, hospital rural/urban status, and hospital size were imbalanced between the groups.

[b] For continuous variables: absolute standardized difference = 100*(x_bar_treatment − x_bar_control)/sqrt[(s^2_treatment + s^2_control)/2], where x_bar indicates sample mean in respective groups and s^2 indicates sample variance in respective groups. For binary variables: 100*(*P*_treatment − *P*_control)/sqrt{[*P*_treatment*(1 − *P*_treatment) + *P*_control*(1 − *P*_control)]/2}, where *P* indicates the prevalence of binary variable in treatment and control groups, respectively. For categorical variables, the standardized difference is computed using a multivariable Mahalanobis distance method. We used this method from a macro generated from Yang and Dalton.[30]

[c] Determined using an enhancement to the social security administration categorical race variable that uses an algorithm to assign beneficiaries to Hispanic or Asian based on last name when race was unknown. "Asian/Pacific Islander" and "American Indian/Alaska Native" were grouped into the "other" category because of small numbers.

[d] Claims-based frailty indicator for predicting the frailty phenotype; enables assessment of frailty using a combination of diagnoses. Probability score that ranges between 0% and 100%, with greater values meaning higher likelihood of frailty. The indicator was used as a continuous variable and patients were not categorized into frail vs not frail. In the Segal study, the threshold was set at 20%.

[e] From centroid of patient's home zip code. To convert miles to kilometers, multiply values by 1.6.

[f] Accounts for number and seriousness of comorbid conditions that might alter the risk of mortality among medical patients. The weights were assigned to the conditions based on adjusted relative risks from the model where conditions with relative risk 1.2 or greater and less than 1.5 were assigned a weight of 1; conditions with a risk 1.5 or greater and less than 2.5, a weight of 2; conditions with a relative risk of 2.5 or greater and less than 3.5, a weight of 3; and conditions with relative risk greater than 6, a weight of 6.

[g] Comorbidites are computed using Agency for Healthcare Research and Quality (AHRQ) comorbidity software based on patients' Medicare Severity-Diagnosis Related Group (MS DRG), principal diagnosis, and all secondary diagnoses. Patients are assigned indicators for 30 conditions as comorbidities.

[h] Indicates that Centers for Medicare & Medicaid Services (CMS) paid a claim for home oxygen use for eligible patients within 90 days of index admission.

[i] Hospital readmissions and emergency department visits occurring after index hospitalization but prior to the day of pulmonary rehabilitation initiation are computed in the propensity-matched cohort.

(19.4%) died within a year of hospital discharge, including 198 (7.3%) among those who initiated pulmonary rehabilitation within 90 days and 38 104 (19.6%) among those who initiated after 90 days or not at all. Eighteen hospitals (0.4%) with unknown region (with 25 patients total) were excluded from analyses (**Table 2**).

Association Between Initiation of Pulmonary Rehabilitation and Survival

In the full study cohort, attributing time before initiation of pulmonary rehabilitation as untreated time, and adjusting for unbalanced covariates and propensity to start pulmonary rehabilitation, participation was significantly associated with a lower risk of death within 1 year of discharge (absolute risk difference [ARD], −6.7% [95% CI, −7.9% to −5.6%]; hazard ratio [HR], 0.63 [95% CI, 0.57 to 0.69]; *P* < .001). The E-value for this model was 2.1 (eFigure in the Supplement). Multiple alternative analytic approaches restricted to survivors of the first 90 days yielded similar effect estimates (**Figure 2**). There was no statistically significant heterogeneity of association based on age (*P* = .85 for interaction), frailty (*P* = .13 for interaction), or comorbid heart failure (*P* = .50 for interaction), but there was a significant interaction of pulmonary rehabilitation with prior home oxygen use (among users: crude mortality rates, 8.8% vs 15.9%; ARD, −5.7% [95% CI, −7.4% to −3.5%]; odds ratio [OR], 0.60 [95% CI, 0.49 to 0.75]; *P* < .001; among nonusers: crude mortality rates, 4.5% vs 12.7%; ARD, −6.8% [95% CI, −8.0% to −5.4%]; OR, 0.43 [95% CI, 0.34 to 0.54]; *P* < .001) and comorbidity burden (low: crude mortality rates, 2.6% vs 10.7%; ARD, −7.6% [95% CI, −8.6% to −6.2%]; OR, 0.27 [95% CI, 0.19 to 0.39]; *P* < .001; medium: crude mortality rates, 6.1% vs 12.5%; ARD, −5.0% [95% CI, −6.7% to −2.8%]; OR, 0.57 [95% CI, 0.43 to 0.75]; *P* < .001; high: crude mortality rates, 13.8% vs 18.6%; ARD, −3.8% [95% CI, −6.7% to −0.5%]; OR, 0.76 [95% CI, 0.59 to 0.97]; *P* = .03).

In the sample matched on propensity and survival to pulmonary rehabilitation initiation, a high level of covariate balance was achieved, with the exceptions of distance to

Table 2. Hospital Characteristics by Patient Pulmonary Rehabilitation Status

	Full cohort					Propensity-matched cohort[a]				
	Pulmonary rehabilitation, No. (%)					Pulmonary rehabilitation, No. (%)				
	Within 90 d of discharge (n = 2721)		91-365 after discharge or not at all (n = 194 655)[b]			Within 90 d of discharge (n = (2710)		91-365 d after discharge or not at all (n = 2710)		
Characteristic	Patients	Hospitals	Patients	Hospitals	ASD[c]	Patients, No. (%)	Hospitals, No. (%)	Patients, No. (%)	Hospitals, No. (%)	ASD[c]
Region[d]					0.321[e] 0.295[f]					0.059[e] 0.152[f]
Northeast	442 (16.3)	234 (17.0)	35 050 (18)	330 (10.8)		440 (16.2)	234 (17.1)	387 (14.3)	113 (12.6)	
Midwest	1056 (38.8)	483 (35.1)	48 170 (24.7)	843 (27.5)		1048 (38.7)	481 (35.1)	1050 (38.7)	294 (32.9)	
South	891 (32.8)	456 (33.2)	86 687 (44.5)	1222 (39.8)		891 (32.9)	456 (33.2)	916 (33.8)	335 (37.5)	
West	331 (12.2)	201 (14.6)	24 724 (12.7)	659 (21.5)		331 (12.2)	201 (14.7)	357 (13.2)	152 (17.0)	
Urban/rural					0.011[e] 0.496[f]					0.163[e] 0.356[f]
Urban	2099 (77.1)	996 (72.4)	149 255 (76.7)	1502 (48.9)		2093 (77.2)	996 (72.6)	1899 (70.1)	499 (55.8)	
Rural	622 (22.9)	379 (27.6)	45 400 (23.3)	1569 (51.1)		617 (22.8)	376 (27.4)	811 (29.9)	395 (44.2)	
Teaching status					0.049[e] 0.377[f]					0.090[e] 0.221[f]
Nonteaching	1629 (59.9)	865 (62.9)	121 214 (62.3)	2447 (79.7)		1620 (59.8)	863 (62.9)	1738 (64.1)	654 (73.2))	
Teaching	1092 (40.1)	510 (37.1)	73 441 (37.7)	624 (20.3)		1090 (40.2)	509 (37.1)	972 (35.9)	240 (26.9)	
No. of beds					0.069[e] 0.685[f]					0.202[e] 0.418[f]
≤200	1004 (36.9)	629 (45.8)	72 280 (37.1)	2365 (77.0)		997 (36.8)	627 (45.7)	1265 (46.7)	583 (65.2)	
201-400	878 (32.3)	427 (31.1)	67 870 (34.9)	464 (15.1)		877 (32.4)	426 (31.1)	747 (27.6)	205 (22.9)	
≥401	839 (30.8)	319 (23.2)	54 505 (28.0)	242 (7.9)		836 (30.8)	319 (23.3)	698 (25.8)	106 (11.9)	

Abbreviations: ASD, absolute standardized difference; COPD, chronic obstructive pulmonary disease.

[a] Propensity scores were calculated using a logistic regression model accounting for patient clustering within hospitals in the cohort. This was a nonparsimonious logistic (generalized estimating equations) model that included patient demographics, tobacco use, Medicaid dual-eligibility, comorbidities, claims-based frailty indicator, markers of disease severity, features of index admission, characteristics of hospitals where the patients were admitted (including size, rural/urban status, teaching status and Census region), and selected interaction terms. We excluded patients discharged from hospitals where pulmonary rehabilitation was not provided from model development because such patients had no possibility of receiving pulmonary rehabilitation. We then applied the parameter estimates to all patients at all hospitals to compute the propensity score. Based on this score and using a greedy match algorithm, patients who received pulmonary rehabilitation within 90 days of discharge were matched 1-to-1 with patients who never initiated or initiated within days 91 and 365. To avoid immortal time bias, we required that the matched control was alive on the day of the pulmonary rehabilitation participant's first session. In the matched cohort, distance to nearest pulmonary rehabilitation facility, hospital rural/urban status, and hospital size were imbalanced between the groups.

[b] Pulmonary rehabilitation initiation between days 91 and 365 of index discharge

[c] For continuous variables: absolute standardized difference = 100*(x_bar_treatment − x_bar_control)/sqrt[(s^2_treatment + s^2_control)/2], where x_bar indicates sample mean in respective groups and s^2 indicates sample variance in respective groups. For binary variables: 100*(*P*_treatment − *P*_control)/sqrt{[*P*_treatment*(1 − *P*_treatment) + *P*_control*(1 − *P*_control)]/2}, where *P* indicates the prevalence of binary variable in treatment and control groups, respectively. For categorical variables, the standardized difference is computed using a multivariate Mahalanobis distance method. We used the method from a macro generated from Yang and Dalton.[30]

[d] Eighteen hospitals (0.4%) with unknown region (with 25 patients total) were excluded from analyses.

[e] Patient-level difference.

[f] Hospital-level difference.

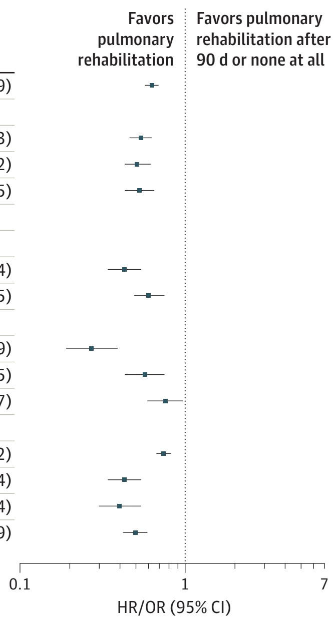
pulmonary rehabilitation facility, hospital size, and urban location (Table 1 and Table 2). Kaplan-Meier curves showed pulmonary rehabilitation initiation within 90 days was significantly associated with lower mortality compared with initiation after 90 days or not at all (*P* < .001), as did the McNemar test (*P* < .001) (**Figure 3**). Mortality within 1 year of pulmonary rehabilitation initiation was 7.3% among those who initiated pulmonary rehabilitation within 90 days and 14.1% among those matched who initiated after 90 days or not at all. Modeling the time from initiation of pulmonary rehabilitation in the propensity-matched cohort, pulmonary rehabilitation was significantly associated with lower risk of death (ARD, −6.8% [95% CI, −8.4% to −5.2%]; HR, 0.50 [95% CI, 0.42 to 0.59]; *P* < .001).

Timing of Initiation

Among individuals who initiated pulmonary rehabilitation within 90 days of discharge from their most recent COPD hospitalization, 1020 (37.5%) initiated rehabilitation within 30 days and 115 (11.3%) died within 1 year; 1075 (39.5%) between 31 and 60 days, with 59 (5.5%) deaths within 1 year, and 626 (23.0%) between 61 and 90 days, with 24 (3.8%) deaths within 1 year. In exploratory analysis, allowing a change in hazard at different start dates relative to discharge, initiation of pulmonary rehabilitation within 30 days (ARD, −4.6% [95% CI, −5.9% to −3.2%]; HR, 0.74 [95% CI, 0.67 to 0.82]; *P* < .001), 31 to 60 days (ARD, −10.6% [95% CI, −12.4% to −8.4%]; HR, 0.43 [95% CI, 0.34 to 0.54]; *P* < .001), and 61 to 90 days (ARD, −11.1% [95% CI, −13.2% to −8.4%]; HR, 0.40 [95% CI, 0.30 to 0.54]; *P* < .001)

Figure 2. Risk of Mortality Associated With Initiation of Pulmonary Rehabilitation After Hospital Discharge

	No./total (%)			
	Pulmonary rehabilitation within 90 d	Pulmonary rehabilitation after 90 d or none at all[a]	Absolute risk difference (95% CI)	HR/OR (95% CI)
Full cohort, adjusted[b,c]	198/2721 (7.3)	38 104/194 655 (19.6)	−6.7 (−7.9 to −5.6)	HR, 0.63 (0.57 to 0.69)
Among 90-d survivors[d]				
Adjusted	166/2689 (6.2)	24 826/181 377 (13.4)	−5.8 (−6.9 to −4.6)	OR, 0.54 (0.46 to 0.63)
SIPTW, adjusted[c,e]	166/2689 (6.2)	24 826/181 377 (13.4)	−6.2 (−7.3 to −4.8)	OR, 0.51 (0.43 to 0.62)
SMRW, adjusted[c,f]	166/2689 (6.2)	24 826/181 377 (13.4)	−5.9 (−7.3 to −4.4)	OR, 0.53 (0.43 to 0.65)
Subgroup analyses, adjusted[c]				
Home oxygen use[g,h]				
No	73/1629 (4.5)	15 720/124 155 (12.7)	−6.8 (−8.0 to −5.4)	OR, 0.43 (0.34 to 0.54)
Yes	93/1060 (8.8)	9106/57 222 (15.9)	−5.7 (−7.4 to −3.5)	OR, 0.60 (0.49 to 0.75)
Comorbidity burden[h,i]				
Low	32/1212 (2.6)	6825/63 589 (10.7)	−7.6 (−8.6 to −6.2)	OR, 0.27 (0.19 to 0.39)
Medium	56/912 (6.1)	7892/63 308 (12.5)	−5.0 (−6.7 to −2.8)	OR, 0.57 (0.43 to 0.75)
High	78/565 (13.8)	10 109/54 480 (18.6)	−3.8 (−6.7 to −0.5)	OR, 0.76 (0.59 to 0.97)
Timing of pulmonary rehabilitation initiation, days[j]				
≤30	115/1020 (11.3)	38 104/194 655 (19.6)	−4.6 (−5.9 to −3.2)	HR, 0.74 (0.67 to 0.82)
31-60	59/1075 (5.5)	38 104/194 655 (19.6)	−10.6 (−12.4 to −8.4)	HR, 0.43 (0.34 to 0.54)
61-90	24/626 (3.8)	38 104/194 655 (19.6)	−11.1 (−13.2 to −8.4)	HR, 0.40 (0.30 to 0.54)
Matched cohort[k,l]	198/2710 (7.3)	382/2710 (14.1)	−6.8 (−8.4 to −5.2)	HR, 0.50 (0.42 to 0.59)



Abbreviations: HR, hazard ratio; OR, odds ratio.

[a] Pulmonary rehabilitation initiation between days 91 and 365 of index discharge. This group combined with those who never initiated pulmonary rehabilitation is the referent group for all models.

[b] Survival (Cox regression) models; modeling time from index discharge, with time-varying exposure.

[c] All models adjusted for patient demographics, severity markers during hospitalization, prior admissions, prior 90-day home oxygen use, comorbidities, claims-based frailty indicator, and propensity score.

[d] Logistic (generalized estimating equations) model among 90-day survivor cohort.

[e] Stabilized inverse probability of treatment-weighted (SIPTW) logistic (generalized estimating equations) model.

[f] Standardized mortality ratio–weighted (SMRW) logistic (generalized estimating equations) model; odds ratio.

[g] Claim of home oxygen in 90 days before index admission.

[h] Logistic (generalized estimating equations) models.

[i] Comorbidity burden: weighted Charlson Comorbidity Index accounts for number and seriousness of comorbid conditions that might alter the risk of mortality among medical patients. The weights were assigned to the conditions based on adjusted relative risks from the model where conditions with relative risk 1.2 or greater and less than 1.5 were assigned a weight of 1; conditions with a risk 1.5 or greater and less than 2.5, a weight of 2; conditions with a relative risk of 2.5 or greater and less than 3.5, a weight of 3; and conditions with relative risk greater than 6, a weight of 6.

[j] In full cohort, in which timing of pulmonary rehabilitation start is counted from patients' most recent chronic obstructive pulmonary disease discharge; survival (Cox regression) models; hazard ratio.

[k] Propensity score–matched cohort. Propensity scores were calculated using a logistic regression model accounting for patient clustering within hospitals in the cohort. This was a nonparsimonious logistic (generalized estimating equations) model that included patient demographics, tobacco use, Medicaid dual-eligibility, comorbidities, claims-based frailty indicator, markers of disease severity, features of index admission, characteristics of hospitals to which the patients were admitted (including size, rural/urban status, teaching status, and Census region), and selected interaction terms. Patients discharged from hospitals where pulmonary rehabilitation was not provided were excluded from model development because such patients had no possibility of receiving pulmonary rehabilitation. Parameter estimates were then applied to all patients at all hospitals to compute the propensity score. Based on this score and using a greedy match algorithm, patients who received pulmonary rehabilitation within 90 days of discharge were matched 1-to-1 with patients who never initiated or initiated within days 91 and 365. To avoid immortal time bias, the matched control was required to be alive on the day of the pulmonary rehabilitation participant's first session. In the matched cohort, distance to nearest pulmonary rehabilitation facility, hospital rural/urban status, and hospital size were imbalanced between the groups.

[l] Survival (Cox regression models) modeling time from pulmonary rehabilitation initiation after adjusting for hospital readmissions and emergency department visits occurring after the index hospitalization, but prior to the day of pulmonary rehabilitation initiation.

were each significantly associated with lower mortality compared with initiation after 90 days or no initiation (Figure 2).

Number of Sessions Completed

Among the group of patients who initiated pulmonary rehabilitation within 90 days of the index hospitalization, 2689 (98.8%) survived at least 90 days from discharge and 166 (6.2%) died within 1 year. These patients completed a median of 9 sessions (interquartile range, 4-14) during the 90-day period from their most recent COPD discharge. In exploratory analysis evaluating the number of sessions as a continuous factor, after adjusting for age, comorbidity, prior home oxygen use, and frailty, every 3 additional sessions (a suggested weekly dose) in the first 90 days was significantly associated with lower mortality (HR, 0.91 [95% CI, 0.85 to 0.98]; P = .01).

Discussion

In this large, population-based cohort of more than 190 000 Medicare fee-for-service patients hospitalized for COPD in the US, initiation of pulmonary rehabilitation within 90 days of discharge, while rare, was significantly associated with better 1-year survival compared with initiation after 90 days or not at all. The strength of association was similar to estimates reported in recent meta-analyses of randomized trials. In exploratory analyses, initiation of pulmonary rehabilitation was significantly associated with lower mortality across a range of potential start times relative to discharge, and there was a statistically significant association between the number of sessions completed and survival. These observations corroborate the results of multiple small randomized trials within routine clinical settings and thus lend additional support to current guideline recommendations produced by professional societies in the US and Europe that recommend pulmonary rehabilitation after hospitalization for COPD.

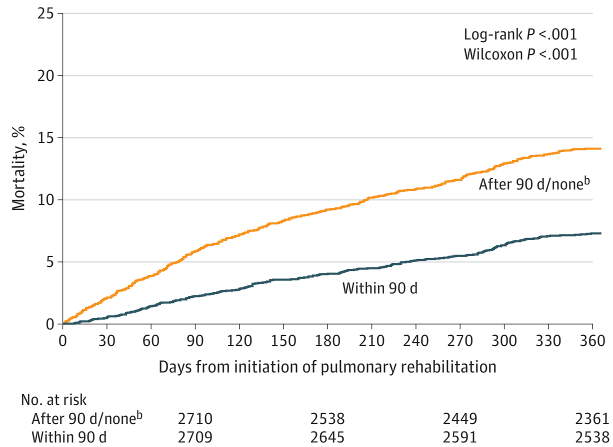
A 2016 Cochrane meta-analysis pooled the results of 6 trials, involving 670 patients, in which pulmonary rehabilitation after an exacerbation of COPD was compared with conventional care and in which mortality was reported. While early pulmonary rehabilitation had a pooled OR for mortality of 0.68 (95% CI, 0.28 to 1.67), the nature of the intervention varied between trials, and results demonstrated high levels of heterogeneity and study bias.[10] A more recent meta-analysis of 13 clinical trials, involving 801 participants, reported lower mortality associated with early pulmonary rehabilitation that reached statistical significance (relative risk, 0.58 [95% CI, 0.35 to 0.98]).[11] By contrast, this study included more than 2700 patients treated with pulmonary rehabilitation, allowing the production of more precise estimates, and the investigation of heterogeneity related to patient characteristics. Additionally, because of uncertainty surrounding the optimal timing of initiation,[31] and with current guidelines recommending initiation within 3 to 4 weeks of an exacerbation, this study explored the association between pulmonary rehabilitation start date relative to discharge date and mortality. In these analyses, estimates were fairly similar across a set of start dates ranging from less than 30 days to more than 60 days, allaying concern that delayed initiation may be ineffective. A unique finding from this analysis is the significant association between the number sessions completed within the first 90 days of discharge and 1-year survival.

Given the significant association of postexacerbation pulmonary rehabilitation with lower mortality suggested by this and prior studies, it is notable that less than than 2% of patients initiated treatment within 90 days of hospital discharge. To put this into broader context, noninvasive ventilation and long-term oxygen therapy are the only treatments shown to improve survival for patients requiring hospitalization for COPD. As such, the results of this study reinforce the importance of developing more effective strategies for increasing participation in rehabilitation.[32] Furthermore, earlier research has demonstrated that this is especially true for women, members of racial and ethnic minority groups, and individuals with lower socioeconomic status.[22]

Limitations

This study has several limitations. First, treatment assignment was not random. Although this study adjusted for numerous potential confounders, and while several alternative analytic approaches yielded similar results, there is likely residual bias due to unmeasured confounding. Individuals who initiated pulmonary rehabilitation were younger and less frail, and may have differed in other ways that contributed toward their better outcomes, a phenomenon known as healthy user bias.[33] Second, this study accounted for multiple factors that serve as proxies for disease severity (eg, use of home oxygen, receipt of mechanical ventilation); however, pulmonary function tests results or physiologic measures such as those used to compute the BODE (Body Mass Index, Airflow Obstruction, Dyspnea and Exercise Capacity) index, a tool for predicting the risk of mortality among patients with COPD, were not available.[34] Nevertheless, the E-value of 2.1 in the primary analysis, a measure of the minimum strength of association with both treatment and outcome for an unmeasured confounder to render the result nonsignificant, suggests that the observed association between pulmonary rehabilitation and 1-year survival was robust. To provide additional perspective, for an unmeasured confounder to negate the association observed between pulmonary rehabilitation and survival, it would need to have a stronger relationship to mortality

Figure 3. One-Year Mortality After Initiation of Pulmonary Rehabilitation in the Propensity-Matched Cohort[a]



[a] Propensity scores were calculated using a logistic regression model accounting for patient clustering within hospitals in the cohort. This was a nonparsimonious logistic (generalized estimating equations) model that included patient demographics, tobacco use, Medicaid dual-eligibility, comorbidities, claims based frailty indicator, markers of disease severity, features of index admission, characteristics of hospitals to which the patients were admitted (including size, rural/urban status, teaching status, and Census region), and selected interaction terms. Patients discharged from hospitals where pulmonary rehabilitation was not provided were excluded from model development because such patients had no possibility of receiving pulmonary rehabilitation. Parameter estimates were then applied to all patients at all hospitals to compute the propensity score. Based on this score and using a greedy match algorithm, patients who received pulmonary rehabilitation within 90 days of discharge were matched 1-to-1 with patients who never initiated or initiated within days 91 and 365. To avoid immortal time bias, the matched control was required to be alive on the day of the pulmonary rehabilitation participant's first session. In the matched cohort, distance to nearest pulmonary rehabilitation facility, hospital rural/urban status, and hospital size were imbalanced between the groups.

[b] Pulmonary rehabilitation initiation between days 91 and 365 of index discharge.

than receipt of home oxygen and also would need to be much more unevenly distributed across the treatment and control groups. Third, because this study relied on claims data, information about the individual components of pulmonary rehabilitation delivered during sessions, such as education, exercise training, nutrition counseling, or smoking cessation were not available. Therefore, it was not possible to determine whether and how these components contributed to the observed mortality association. Potential mechanisms through which pulmonary rehabilitation may improve survival include increased physical activity, medication adherence, and improved care coordination.[35] Because pulmonary rehabilitation programs are heterogeneous, these results should be interpreted as representing the association of treatment with survival across all US programs.[36]

Fourth, more patient-centered outcomes, such as exercise capacity or quality of life, were not available. Fifth, receipt of physical therapy or cardiac rehabilitation as an alternative to pulmonary rehabilitation was not assessed. To the extent that such interventions are beneficial and were disproportionately received by patients who did not initiate pulmonary rehabilitation, this would have biased the findings toward the null. Sixth, the study was restricted to the 70% of Medicare beneficiaries in the traditional fee-for-service program who were older than 65 years. Caution is thus warranted before extrapolating the findings to younger patients or those in Medicare Advantage Plans. Seventh, because of lack of availability of cause of death, it cannot be established whether pulmonary rehabilitation is associated with a lower risk of death because of COPD or because of other causes.

Conclusions

Among fee-for-service Medicare beneficiaries hospitalized for COPD, initiation of pulmonary rehabilitation within 3 months of discharge was significantly associated with lower risk of mortality at 1 year. These findings support current guideline recommendations for pulmonary rehabilitation after hospitalization for COPD, although the potential for residual confounding exists and further research is needed.

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Author Affiliations: Institute for Healthcare Delivery and Population Science, University of Massachusetts Medical School—Baystate, Springfield (Lindenauer, Stefan, Pekow, Priya, Spitzer, Lagu, Pack); Department of Medicine, University of Massachusetts Medical School—Baystate, Springfield (Lindenauer, Stefan, Lagu, Pack, Pinto-Plata); Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester (Lindenauer); University of Massachusetts School of Public Health and Health Sciences, Amherst (Pekow, Priya); The Meyers Primary Care Institute, University of Massachusetts Medical School, Worcester (Mazor); Division of Cardiovascular Medicine, University of Massachusetts Medical School—Baystate, Springfield (Pack); Divsion of Pulmonary and Critical Care Medicine, University of Massachusetts Medical School—Baystate, Springfield (Pinto-Plata); Pulmonary and Critical Care Division, Saint Francis Hospital and Medical Center, Hartford, Connecticut (ZuWallack).

Author Contributions: Drs Lindenauer and Pekow had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Lindenauer, Stefan, Pekow, Mazor, Lagu, ZuWallack.
Acquisition, analysis, or interpretation of data: Lindenauer, Stefan, Pekow, Priya, Spitzer, Pack, Pinto-Plata, ZuWallack.
Drafting of the manuscript: Lindenauer, Pekow, Priya.
Critical revision of the manuscript for important intellectual content: Stefan, Pekow, Mazor, Priya, Spitzer, Lagu, Pack, Pinto-Plata, ZuWallack.
Statistical analysis: Pekow, Priya.
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REFERENCES

1. Croft JB, Wheaton AG, Liu Y, et al. Urban-rural county and state differences in chronic obstructive pulmonary disease—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2018;67(7):205-211. doi:10.15585/mmwr.mm6707a1

2. Ford ES. Hospital discharges, readmissions, and ED visits for COPD or bronchiectasis among US adults: findings from the Nationwide Inpatient Sample 2001-2012 and Nationwide Emergency Department Sample 2006-2011. *Chest*. 2015;147(4):989-998. doi:10.1378/chest.14-2146

3. Lindenauer PK, Dharmarajan K, Qin L, Lin Z, Gershon AS, Krumholz HM. Risk trajectories of readmission and death in the first year after hospitalization for chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2018;197(8):1009-1017. doi:10.1164/rccm.201709-1852OC

4. Spruit MA, Singh SJ, Garvey C, et al; ATS/ERS Task Force on Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2013;188(8):e13-e64. doi:10.1164/rccm.201309-1634ST

5. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2015;2(2):CD003793. doi:10.1002/14651858.CD003793.pub3

6. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2020 Report. Published 2020. Accessed February 19, 2020. https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf

7. Cox NS, Oliveira CC, Lahham A, Holland AE. Pulmonary rehabilitation referral and participation are commonly influenced by environment, knowledge, and beliefs about consequences: a systematic review using the Theoretical Domains Framework. *J Physiother*. 2017;63(2):84-93. doi:10.1016/j.jphys.2017.02.002

8. Maddocks M, Kon SSC, Singh SJ, Man WD-C. Rehabilitation following hospitalization in patients with COPD: can it reduce readmissions? *Respirology*. 2015;20(3):395-404. doi:10.1111/resp.12454

9. Nici L, Raskin J, Rochester CL, et al. Pulmonary rehabilitation: what we know and what we need to know. *J Cardiopulm Rehabil Prev*. 2009;29(3):141-151. doi:10.1097/HCR.0b013e3181a3324a

10. Puhan MA, Gimeno-Santos E, Cates CJ, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2016;12:CD005305. doi:10.1002/14651858.CD005305.pub4

11. Ryrsø CK, Godtfredsen NS, Kofod LM, et al. Lower mortality after early supervised pulmonary rehabilitation following COPD-exacerbations: a systematic review and meta-analysis. *BMC Pulm Med*. 2018;18(1):154. doi:10.1186/s12890-018-0718-1

12. Criner GJ, Bourbeau J, Diekemper RL, et al. Prevention of acute exacerbations of COPD:

American College of Chest Physicians and Canadian Thoracic Society Guideline. *Chest*. 2015;147(4):894-942. doi:10.1378/chest.14-1676

13. Wedzicha JA, Miravitlles M, Hurst JR, et al. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. *Eur Respir J*. 2017;49(3):1600791. doi:10.1183/13993003.00791-2016

14. Newhouse JP, McClellan M. Econometrics in outcomes research: the use of instrumental variables. *Annu Rev Public Health*. 1998;19(1):17-34. doi:10.1146/annurev.publhealth.19.1.17

15. Concato J. Study design and "evidence" in patient-oriented research. *Am J Respir Crit Care Med*. 2013;187(11):1167-1172. doi:10.1164/rccm.201303-0521OE

16. Frieden TR. Evidence for health decision making—beyond randomized, controlled trials. *N Engl J Med*. 2017;377(5):465-475. doi:10.1056/NEJMra1614394

17. Ray WA. Evaluating medication effects outside of clinical trials: new-user designs. *Am J Epidemiol*. 2003;158(9):915-920. doi:10.1093/aje/kwg231

18. Cox E, Martin BC, Van Staa T, Garbe E, Siebert U, Johnson ML. Good research practices for comparative effectiveness research: approaches to mitigate bias and confounding in the design of nonrandomized studies of treatment effects using secondary data sources: the International Society for Pharmacoeconomics and Outcomes Research Good Research Practices for Retrospective Database Analysis Task Force Report—Part II. *Value Health*. 2009;12(8):1053-1061. doi:10.1111/j.1524-4733.2009.00601.x

19. National Academies of Sciences, Engineering, and Medicine. *Accounting for Social Risk Factors in Medicare Payment: Identifying Social Risk Factors*. National Academies Press; 2016.

20. Spitzer KA, Stefan MS, Priya A, et al. Participation in pulmonary rehabilitation after hospitalization for chronic obstructive pulmonary disease among Medicare beneficiaries. *Ann Am Thorac Soc*. 2019;16(1):99-106. doi:10.1513/AnnalsATS.201805-332OC

21. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36(1):8-27. doi:10.1097/00005650-199801000-00004

22. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in *ICD-9-CM* and *ICD-10* administrative data. *Med Care*. 2005;43(11):1130-1139. doi:10.1097/01.mlr.0000182534.19832.83

23. Segal JB, Chang H-Y, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a claims-based frailty indicator anchored to a well-established frailty phenotype. *Med Care*. 2017;55(7):716-722. doi:10.1097/MLR.0000000000000729

24. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28(25):3083-3107. doi:10.1002/sim.3697

25. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. *Ann Intern Med*. 2017;167(4):268-274. doi:10.7326/M16-2607

26. Haneuse S, VanderWeele TJ, Arterburn D. Using the E-value to assess the potential effect of unmeasured confounding in observational studies. *JAMA*. 2019;321(6):602-603. doi:10.1001/jama.2018.21554

27. Curtis LH, Hammill BG, Eisenstein EL, Kramer JM, Anstrom KJ. Using inverse probability-weighted estimators in comparative effectiveness analyses with observational databases. *Med Care*. 2007;45(10)(suppl 2):S103-S107. doi:10.1097/MLR.0b013e31806518ac

28. Kurth T, Walker AM, Glynn RJ, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. *Am J Epidemiol*. 2006;163(3):262-270. doi:10.1093/aje/kwj047

29. Suaya JA, Stason WB, Ades PA, Normand S-LT, Shepard DS. Cardiac rehabilitation and survival in older coronary patients. *J Am Coll Cardiol*. 2009;54(1):25-33. doi:10.1016/j.jacc.2009.01.078

30. Yang D, Dalton JE. Paper 335-2012: A Unified Approach to Measuring the Effect Size Between Two Groups Using SAS. Published 2012. Accessed April 8, 2020. https://www.lerner.ccf.org/qhs/software/lib/stddiff.pdf

31. Greening NJ, Williams JEA, Hussain SF, et al. An early rehabilitation intervention to enhance recovery during hospital admission for an exacerbation of chronic respiratory disease: randomised controlled trial. *BMJ*. 2014;349:g4315. doi:10.1136/bmj.g4315

32. Rochester CL, Vogiatzis I, Holland AE, et al; ATS/ERS Task Force on Policy in Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2015;192(11):1373-1386. doi:10.1164/rccm.201510-1966ST

33. Brookhart MA, Patrick AR, Dormuth C, et al. Adherence to lipid-lowering therapy and the use of preventive health services: an investigation of the healthy user effect. *Am J Epidemiol*. 2007;166(3):348-354. doi:10.1093/aje/kwm070

34. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350(10):1005-1012. doi:10.1056/NEJMoa021322

35. Casaburi R, ZuWallack R. Pulmonary rehabilitation for management of chronic obstructive pulmonary disease. *N Engl J Med*. 2009;360(13):1329-1335. doi:10.1056/NEJMct0804632

36. Spruit MA, Pitta F, Garvey C, et al; ERS Rehabilitation and Chronic Care, and Physiotherapists Scientific Groups; American Association of Cardiovascular and Pulmonary Rehabilitation; ATS Pulmonary Rehabilitation Assembly and the ERS COPD Audit team. Differences in content and organisational aspects of pulmonary rehabilitation programmes. *Eur Respir J*. 2014;43(5):1326-1337. doi:10.1183/09031936.00145613