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Association between self-reported moderate to vigorous physical activity and the rate of outpatient treated COPD exacerbations: retrospective cohort study

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ABSTRACT

Introduction Little has been published regarding the relationship between physical activity (PA) and outpatient treated, mild to moderate acute exacerbation of chronic obstructive pulmonary disease exacerbations (AECOPD). The purpose of this study was to determine the association between self-reported PA and outpatient treated AECOPD over 2 years using real-world data obtained from existing electronic medical records (EMRs).

Methods We included 44 896 patients with a chronic obstructive pulmonary disease diagnosis from the EMR in this retrospective cohort study. Moderate to vigorous PA was measured via patient self-report, obtained during routine clinical care; patients were classified as inactive (0 min/week), insufficiently active (1–149 min/week) or active (≥150 min/week). AECOPDs were measured using both encounter and prescription fill (antibiotics and/or oral steroids) data. We used Poisson regression models to compare the unadjusted and adjusted rates of outpatient treated AECOPD over 2 years across the PA categories.

Results In adjusted models, the 2-year AECOPD incidence rate ratio (IRR) was not different between the inactive and insufficiently inactive groups (IRR 0.98, 95% CI 0.96 to 1.01) and only marginally meaningful lower for the active group (IRR 0.97, 95% CI 0.95 to 0.98). Sensitivity analyses of patients meeting or not meeting obstructive criteria produced similar results with generally weak or non-significant associations.

Conclusion The lack of an association between PA and AECOPD contrasts with previous published findings of a strong relationship between moderate to vigorous PA and hospitalisations for severe AECOPD. This difference could partially be attributed to the imprecision of our measurements for both the exposure and outcome.

Key message

- What is the association between self-reported physical activity (PA) and the rate of outpatient treated acute exacerbations of chronic obstructive pulmonary disease (AECOPD) ?
- The association between self-reported moderate to vigorous PA and the rate of mild to moderate outpatient treated AECOPD over 2 years of follow-up was generally weak or not significant.
- This is the largest cohort study using real-world data on patient self-reported PA and mild to moderate COPD exacerbations obtained from electronic medical records.

BACKGROUND

Observational studies consistently show that physical inactivity is associated with increased hospitalisations and mortality.[1–5] We previously showed that hospitalised patients with chronic obstructive pulmonary disease (COPD) who were physically active in the year prior to the index admission had a 34% lower risk of 30-day readmission[6] and up to 47% lower risk of mortality in the 12 months following hospital discharge[7] compared with inactive patients. Very little has been published regarding the relationship between physical activity (PA) and outpatient treated, mild to moderate acute exacerbations of chronic obstructive pulmonary disease (AECOPD) that do not result in hospitalisations. The purpose of this study was to determine the association between self-reported moderate to vigorous PA, captured as part of routine care in a large integrated healthcare system, and the rate of outpatient treated AECOPD over 2 years.

METHODS

Study design and setting

We performed a retrospective cohort study using longitudinal electronic medical record (EMR) data from Kaiser Permanente Southern California (KPSC) and Kaiser Permanente Pacific Northwest (KPNW) healthcare systems. We identified all patients

aged >40 years old with diagnosed COPD between January 2011 and September 2015 based on having ≥1 encounter with an International Classification of Diseases, Ninth Revision, code for COPD (491 .XX, 492 .XX, 493.2X and 496) and ≥1 dispensed inhaler. Baseline sociodemographic and clinical characteristics, Charlson Comorbidity Index,[8] spirometry, lifestyle behaviours, inhaler use and healthcare use were obtained in the year prior to exacerbation ascertainment (October 2014–September 2015).

SELF-REPORTED PA

Every patient, regardless of their condition or presenting problem in the health system, is asked two questions that capture their regular PA during the intake process for all outpatient visits.[9] This is called the exercise vital sign (EVS) and is presented as (1) 'On average, how many days per week do you engage in moderate to strenuous (vigorous) exercise (like a brisk walk)?' and (2) 'On average, how many minutes do you engage in exercise at this level?' These questions are typically asked by front office medical staff, and patients' responses are entered into the EMR. Response choices for days are categorical (0–7). Minutes are recorded as 0, 10, 20, 30, 40, 50, 60, 90, 120 and 150 min or greater. The EMR then multiplies the responses to display total minutes per week of moderate or vigorous PA. Patients can be categorised into three cohorts as used by the National Health and Examination Survey: inactive (0 min/week), insufficiently active (1–149 min/week) or active, meeting PA recommendations (≥150 min/week). We used all available EVS data in the year prior to ascertainment of COPD exacerbations to classify patients into their usual pattern of PA based on both the modal/median EVS values. The EVS has evidence of construct and predictive validity.[6 7 10]

COPD EXACERBATIONS

Two years of follow-up data for outpatient treated AECOPD were obtained from October 2015 to September 2017 via pharmacy and use data. AECOPD have been identified by changes in the current therapy to include increased use of bronchodilators and a short course of prednisone and/or antibiotics.[11] For this study, an outpatient AECOPD was defined as (1) encounters with a documented COPD diagnosis followed by a prescription fill of antibiotics, steroids, or antibiotics and steroids and (2) encounters with no documented COPD diagnosis but followed by a prescription fill of antibiotics and steroids, both within 2 days of the encounter; this definition yielded a sensitivity of 67% and a specificity of 84% based on a review of 185 charts.[12]

STATISTICAL ANALYSES

We used Poisson regression models to compare crude and adjusted rates of outpatient AECOPD per member-year; the log of the latter was included as an offset term. Covariates in adjusted models included age, gender, marital status, race/ethnicity, smoking status, use of inhaled steroids and oxygen, Charlson index, depression, anxiety, chronic pain, all-cause acute care use (hospitalisation, observation stay and ED visits) and number of outpatient treated AECOPD in the previous 12 months. Models were stratified by availability of spirometry and by Global initiative for chronic obstructive lung disease (GOLD) class. We also used negative binomial models to assess the sensitivity of our findings to possible overdispersion in AECOPD counts. Analyses were conducted using SAS V.9.4. A two-sided p value of <0.05 was considered statistically significant.

PATIENT AND PUBLIC INVOLVEMENT

Since this study strictly relied on existing data via an approved waiver of written consent, we did not engage with patient stakeholders in the design or conduct of the analyses nor interpretation of the findings.

RESULTS

Baseline characteristics

Among 44 896 eligible adults with COPD, 56% were physically inactive; 23% were insufficiently active; and 21% were active. There were clinically and statistically meaningful differences in the gender distribution, smoking status, body mass index, GOLD class, oxygen use, comorbidities, and baseline all-cause and COPD-specific healthcare use across the PA categories (tables 1 and 2). Approximately a quarter of the patients did not have spirometry data (25%) or had an forced expiratory volume in one second (FEV_1):forced vital capacity (FVC) ratio of ≥0.70 (26%). Patients who were inactive experienced more outpatient treated AECOPD at baseline compared with other patients.

Association between PA and rate of outpatient treated COPD exacerbations over 2 years

For the overall cohort, the unadjusted model showed a lower rate of AECOPD in the insufficiently active and active groups compared with the inactive group, but this was no longer significant in the adjusted model for the insufficiently inactive group (incidence rate ratio (adjusted IRR) 0.98, 95% CI 0.96 to 1.01) and only marginally meaningful for the active group (adjusted IRR 0.97, 95% CI 0.95 to 0.98) (table 3). There were no significant associations between PA and AECOPD for patients in GOLD classes I and II. For GOLD III/IV patients, there appears to be some marginal though non-significant association between any PA and AECOPD (adjusted IRR 0.95, 95% CI 0.90 to 1.00) compared with inactive patients. For patients with FEV_1:FVC of ≥0.70, the adjusted model showed that insufficiently active patients had lower AECOPD risk compared with inactive patients (IRR 0.90, 95% CI 0.85 to 0.95). No significant associations were noted for patients who did not have

Table 1 Baseline sociodemographic and clinical characteristics by self-reported moderate to vigorous physical activity (exercise vital sign)

	Inactive (n=25 117)	Insufficiently active (n=10 221)	Active (n=9558)	P value
Age (years)	71.6 (10.53)	70.5 (10.37)	69.5 (9.97)	<0.01
40–49	573 (2%)	293 (3%)	311 (3%)	<0.01
50–59	2894 (12%)	1231 (12%)	1217 (13%)	
60–69	6647 (26%)	3038 (30%)	3026 (32%)	
70–79	8923 (36%)	3590 (35%)	3491 (37%)	
80+	6080 (24%)	2069 (20%)	1513 (16%)	
Female	14 129 (56%)	5545 (54%)	4307 (45%)	<0.01
Marital status: partnered	12 988 (52%)	5502 (54%)	5486 (57%)	<0.01
Education: college+	6238 (25%)	2795 (28%)	2910 (31%)	<0.01
Median household income: ≥$50 000	14 156 (57%)	5884 (58%)	5684 (60%)	<0.01
Race/ethnicity: white	19 637 (78%)	7374 (72%)	7273 (76%)	<0.01
Insurance status: public	18 142 (72%)	6959 (68%)	6543 (68%)	<0.01
Smoking status				<0.01
Never	4248 (17%)	2126 (21%)	2027 (21%)	
Former	15 615 (62%)	6326 (62%)	6016 (63%)	
Current	5037 (20%)	1687 (17%)	1431 (15%)	
Missing	217 (1%)	82 (1%)	84 (1%)	
Body mass index	30.2 (27.81)	28.9 (6.97)	27.7 (6.77)	<0.01
Underweight (<18.5)	775 (3%)	240 (2%)	246 (3%)	<0.01
Normal weight (18.5–24.9)	5868 (23%)	2774 (27%)	3149 (33%)	
Overweight (25.0–29.9)	7407 (29%)	3446 (34%)	3315 (35%)	
Obese (>30)	10 860 (43%)	3693 (36%)	2779 (29%)	
Missing	207 (1%)	68 (1%)	69 (1%)	
Spirometry	18 479 (74%)	7768 (76%)	7261 (76%)	
FEV_1/FVC<0.70	11 802 (47%)	5035 (49%)	4910 (51%)	<0.01
FEV_1/FVC	63.8 (13.39)	63.5 (13.29)	63.2 (12.63)	<0.01
FEV_1% predicted	72.6 (21.68)	74.4 (22.16)	77.3 (33.83)	<0.01
GOLD I (≥80%)	2795 (11%)	1322 (13%)	1616 (17%)	<0.01
GOLD II (50%≤FEV_1<80%)	6401 (26%)	2695 (26%)	2517 (26%)	
GOLD III/IV (FEV_1<50%)	2605 (10%)	1018 (10%)	777 (8%)	
FEV_1/FVC≥0.7	6677 (27%)	2733 (27%)	2351 (25%)	
No spirometry	6639 (26%)	2453 (24%)	2297 (24%)	
Medications (use in 2015)				
LABAs	8628 (34%)	3452 (34%)	3112 (33%)	<0.01
LAMA	7332 (29%)	2797 (27%)	2361 (25%)	<0.01
ICS	8804 (35%)	3512 (34%)	3195 (33%)	0.02
LAMA and ICS	3850 (15%)	1448 (14%)	1131 (12%)	<0.01
LABA and ICS	8367 (33%)	3335 (33%)	3018 (32%)	<0.01
Long-term systemic corticosteroids	311 (1%)	107 (1%)	82 (1%)	<0.01
Oxygen use	4310 (17%)	1154 (11%)	656 (7%)	<0.01
Comorbidities (all available data, 2011–2015)				
Charlson Comorbidity Index	3.5 (2.41)	3.0 (2.15)	2.6 (1.99)	<0.01
Quartile 1 (0–1)	5538 (22%)	2847 (28%)	3289 (34%)	<0.01
Quartile 2 (2)	5144 (20%)	2491 (24%)	2344 (25%)	
Quartile 3 (3-4)	7334 (29%)	2811 (28%)	2451 (26%)	
Quartile 4 (>4)	7099 (28%)	2072 (20%)	1474 (15%)	

Continued

Table 1 Continued

	Inactive (n=25 117)	Insufficiently active (n=10 221)	Active (n=9558)	P value
Myocardial infarction	3028 (12%)	947 (9%)	836 (9%)	<0.01
Congestive heart failure	4480 (18%)	1168 (11%)	820 (9%)	<0.01
Peripheral vascular disease	13 958 (56%)	5034 (49%)	4233 (44%)	<0.01
Cerebrovascular disease	2548 (10%)	755 (7%)	557 (6%)	<0.01
Dementia	361 (1%)	72 (1%)	27 (0%)	<0.01
Connective tissue disease–rheumatic disease	1319 (5%)	424 (4%)	336 (4%)	<0.01
Peptic ulcer disease	356 (1%)	95 (1%)	76 (1%)	<0.01
Mild liver disease	1551 (6%)	514 (5%)	506 (5%)	<0.01
Diabetes without complications	2967 (12%)	1289 (13%)	1013 (11%)	<0.01
Diabetes with complications	5424 (22%)	1636 (16%)	1121 (12%)	<0.01
Paraplegia and hemiplegia	308 (1%)	63 (1%)	47 (0%)	<0.01
Renal disease	7463 (30%)	2459 (24%)	1863 (19%)	<0.01
Cancer	1879 (7%)	612 (6%)	596 (6%)	<0.01
Moderate or severe liver disease	142 (1%)	41 (0%)	41 (0%)	0.06
Metastatic carcinoma	419 (2%)	140 (1%)	93 (1%)	<0.01
Other non-Charlson morbidities				
Depression	7197 (29%)	2365 (23%)	1763 (18%)	<0.01
Anxiety	5441 (22%)	1805 (18%)	1489 (16%)	<0.01
Chronic pain	5502 (22%)	1531 (15%)	1265 (13%)	<0.01

FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global initiative for chronic obstructive lung disease; ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting anticholinergic.

Table 2 Baseline healthcare use by self-reported moderate to vigorous physical activity (exercise vital sign)

	Inactive (n=25 117)	Insufficiently active (n=10 221)	Active (n=9558)	P value
Baseline healthcare use (Oct 2014–Sept 2015)				
All cause				
Hospitalisations	5869 (23%)	1461 (14%)	1036 (11%)	<0.01
	0.4 (0.93)	0.2 (0.64)	0.2 (0.58)	<0.01
Observational stays	1830 (7%)	485 (5%)	338 (4%)	<0.01
	0.1 (0.34)	0.1 (0.25)	0.0 (0.26)	<0.01
Emergency department visits	9258 (37%)	2829 (28%)	2369 (25%)	<0.01
	0.8 (1.74)	0.5 (1.26)	0.4 (1.33)	<0.01
Primary care visits	4.9 (4.75)	4.2 (3.92)	4.1 (4.27)	<0.01
Specialty care visits	9.7 (12.48)	8.2 (10.82)	8.4 (12.51)	<0.01
COPD-related acute care encounters				
Hospitalisations	1045 (4%)	258 (3%)	141 (1%)	<0.01
	0.2 (0.47)	0.1 (0.33)	0.1 (0.26)	<0.01
Observational stays	244 (1%)	73 (1%)	35 (0%)	<0.01
	0.0 (0.18)	0.0 (0.16)	0.0 (0.12)	<0.01
Emergency department visits	1208 (5%)	359 (4%)	226 (2%)	<0.01
	0.2 (0.56)	0.1 (0.44)	0.1 (0.37)	<0.01
Outpatient treated exacerbations	9550 (38%)	3340 (33%)	2992 (31%)	<0.01
	0.7 (1.16)	0.5 (1.00)	0.5 (1.00)	<0.01

COPD, chronic obstructive pulmonary disease.

Table 3 Association between self-reported moderate to vigorous physical activity and rate of outpatient treated COPD exacerbations over 2 years of follow-up

	Outpatient treated COPD exacerbations n (%), mean (SD)	Crude IRR	Unadjusted IRR (95% CI)	Adjusted IRR* (95% CI)
All patients (N=44 896)				
Inactive (25 117)	12 483 (50%), 1.24 (2.04)	Ref	Ref	Ref
Insufficiently active (10 221)	4882 (48%), 1.14 (1.90)	0.92	0.93 (0.91 to 0.95)	0.98 (0.96 to 1.01)
Active (9558)	4440 (46%), 1.07 (1.84)	0.86	0.86 (0.84 to 0.88)	0.97 (0.95 to 0.98)
FEV_1/FVC<0.7 (n=21 746)				
GOLD I (n=5733)				
Inactive (2795)	1330 (48%), 1.09 (1.87)	Ref	Ref	Ref
Insufficiently active (1322)	581 (44%), 0.95 (1.64)	0.87	0.89 (0.84 to 0.95)	1.03 (0.97 to 1.11)
Active (1616)	722 (45%), 0.95 (1.62)	0.87	0.88 (0.83 to 0.93)	1.0 (0.94 to 1.07)
GOLD II (n=11 613)				
Inactive (6401)	3570 (56%), 1.47 (2.20)	Ref	Ref	Ref
Insufficiently active (2695)	1461 (54%), 1.37 (2.16)	0.93	0.94 (0.91 to 0.98)	0.99 (0.95 to 1.04)
Active (2517)	1355 (54%), 1.29 (2.01)	0.88	0.88 (0.85 to 0.92)	1.02 (0.98 to 1.06)
GOLD III/IV (n=4400)				
Inactive (2605)	1737 (67%), 2.22 (2.85)	Ref	Ref	Ref
Insufficiently active (1018)	648 (64%), 1.97 (2.66)	0.89	0.90 (0.85 to 0.94)	0.95 (0.9 to 1.0)
Active (777)	517 (67%), 2.04 (2.69)	0.92	0.93 (0.88 to 0.98)	0.95 (0.9 to 1.0)
FEV_1/FVC≥0.7 (n=11 761)				
Inactive (6677)	2843 (43%), 0.91 (1.61)	Ref	Ref	Ref
Insufficiently active (2733)	1097 (40%), 0.84 (1.5)	0.92	0.93 (0.89 to 0.98)	0.9 (0.85 to 0.95)
Active (2351)	876 (37%), 0.72 (1.39)	0.79	0.79 (0.75 to 0.83)	1.05 (0.98 to 1.12)
No spirometry (n=11 389)				
Inactive (6639)	3003 (45%), 1.03 (1.78)	Ref	Ref	Ref
Insufficiently active (2453)	1095 (45%), 0.97 (1.57)	0.94	0.95 (0.90 to 0.99)	0.97 (0.92 to 1.03)
Active (2297)	970 (42%), 0.93 (1.69)	0.90	0.91 (0.86 to 0.95)	1.03 (0.98 to 1.08)

*Adjusted models accounted for age, gender, marital status, race/ethnicity, smoking status, use of inhaled steroids and oxygen, comorbidity, depression, anxiety, chronic pain, all-cause acute care use (hospitalisation, observation stay and emergency department visits),and baseline outpatient treated COPD exacerbations in the previous 12 months. Sample sizes for unadjusted and adjusted models may vary by ~100 to 345 fewer than the listed n for each subgroup primarily due to missing body mass index (n=344).
COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global initiative for chronic obstructive lung disease; IRR, incidence rate ratio; Ref, reference.

spirometry data. The negative binomial models provided similar point estimates but with wider CIs.

DISCUSSION

We found that the association between baseline moderate to vigorous PA captured as part of routine care and the rate of mild to moderate outpatient treated AECOPD over 2 years of follow-up was generally weak or non-significant, which is in contrast to the strong relationship observed between PA and hospitalisations for severe exacerbations, despite differences in how PA was measured and classified across these prior studies.[1–7] To the best of our knowledge, this is the first 'real-world' large-scale study to examine the association between self-reported PA, captured during routine care, with AECOPD in an entire clinical population of patients diagnosed with COPD from an integrated healthcare system.

The weak to null findings in this study could partly be attributed to the difficulty of capturing AECOPD in the EMR and incomplete ascertainment of these events in contrast to near complete capture of severe AECOPD that result in hospitalisations, in combination with the imprecision and errors associated with self-reported PA.[13] Given the need for any behavioural assessment to be streamlined for use in routine care across broad populations and for different clinical and population surveillance purposes,[14] the self-reported measure of PA used in this study only provides an overall assessment of 'regular' PA in the previous year and did not distinguish between light, moderate and vigorous activities.[9] A recent study of 177 patients with stable COPD that measured PA with an accelerometer over an 8-day period found that for every increase of 1000 daily steps at low average intensity, the risk of COPD hospitalisation was reduced by 20% over a

2-year period; high-intensity PA was not associated with any risk reduction.[5] In our previous paper, using the same self-reported moderate to vigorous PA measure as the current study, we also found a significant risk reduction (34%) in 30-day readmissions for 4596 patients with COPD who reported engaging in any amount of PA.[6] It is possible that, although the PA questions asked about moderate to vigorous exercise, patients may have actually reported on what would be perceived as lower intensity activities in normal adults without airflow obstruction and that the challenge we faced in this study had more to do with difficulties capturing the AECOPD events using data that were intended for clinical care, not research purposes. Interestingly, a recent meta-analysis of 39 studies reported that higher levels of total PA, *at any intensity*, was associated with lower risk of mortality.[15]

Another limitation of the study was that our models did not include other intervening events and changes in PA patterns over the 2 years of follow-up. With broader use of biometric sensors, future studies could improve on these methods by using objective PA data combined with electronic logs of symptoms, sensors to detect changes in breathing patterns and treatments to explore the real-time, dynamic relationships between different PA intensities and AECOPD across a broad, representative population of patients with COPD.[16 17]

In conclusion, although our findings show little to no association between PA and the rate of AECOPD based on data obtained as part of routine clinical care, the positive health effects of PA is indisputable based on the existing high-quality evidence base regarding the survival benefits of PA in COPD[1–4 7 18 19] and healthy adults and older adults.[15 20 21]

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Kaiser Permanente Southern California and Kaiser Permanente Pacific Northwest institutional review boards approved this study.

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement Data are available upon reasonable request. Due to the significant time and costs associated with the removal of all identifiers to protect the identities of participants, the requester will be asked to incur these costs.

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