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Short-term effects of air pollution and weather on physical activity in patients with chronic obstructive pulmonary disease (COPD)

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ABSTRACT

Introduction: Patients with chronic obstructive pulmonary disease (COPD) accumulate low levels of physical activity. How environmental factors affect their physical activity in the short-term is uncertain. Aim: to assess the short-term effects of air pollution and weather on physical activity levels in COPD patients.

Methods: This multi-center panel study assessed 408 COPD patients from Catalonia (Spain). Daily physical activity (i.e., steps, time in moderate-to-vigorous physical activity (MVPA), locomotion intensity, and sedentary time) was recorded in two 7-day periods, one year apart, using the Dynaport MoveMonitor. Air pollution (nitrogen dioxide (NO_2), particulate matter below 10 μm (PM_{10}) and a marker of black carbon (absorbance of $PM_{2.5}$: $PM_{2.5ABS}$), and weather (average and maximum temperature, and rainfall) were estimated the same day (lag zero) and up to 5 days prior to each assessment (lags 1–5). Mixed-effect distributed lag linear regression models were adjusted for age, sex, weekday, public holidays, greenness, season, and social class, with patient and city as random effects.

Results: Patients (85% male) were on average (mean ± SD) 68 ± 9 years old with a post-bronchodilator forced expiratory volume in 1 s (FEV_1) of 57 ± 18% predicted. Higher NO_2, PM_{10} and $PM_{2.5ABS}$ levels at lag four were associated with fewer steps, less time in MVPA, reduced locomotion intensity, and longer sedentary time (e.g., coefficient (95% CI) of −60 (−105, −15) steps per 10 $\mu g/m^3$ increase in NO_2). Higher average and maximum

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temperatures at lag zero were related to more steps and time in MVPA, and less sedentary time (e.g., +85 (15, 154) steps per degree Celsius). Higher rainfall at lag zero was related to fewer steps and more sedentary time.
Conclusion: Air pollution affects the amount and intensity of physical activity performed on the following days in COPD patients, whereas weather affects the amount of physical activity performed on the same day.

Abbreviations

COPD	Chronic obstructive pulmonary disease
DALYs	Disability adjusted life years
FEV_1	Forced expiratory volume in 1 s
FVC	Forced vital capacity
MVPA	Moderate-to-vigorous physical activity
NO_2	Nitrogen Dioxide.
PM_{10}	Particulate Matter <10 μm
$PM_{2.5}$	Particulate Matter <2.5 μm
$PM_{2.5ABS}$	Black Carbon
GIS	Geographic Information Systems
mMRC	Modified Medical Research Council dyspnea scale
C-PPAC	Clinical visit- PROactive Physical Activity in COPD
HADS	Hospital anxiety and depression scale
HADS-A	Hospital anxiety and depression scale – Anxiety
HADS-D	Hospital anxiety and depression scale – Depression
6MWT	6-min walking test
AR-1	Autoregressive term

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Ethics committee

The study was approved by the Ethics Committees of the participating institutions (Comitè Ètic d'Investigació Clínica de l'Hospital Universitari de Bellvitge (PR197/11), Comitè Ètic d'Investigació Clínica de l'IDIAP Jordi Gol i Gurina (P11/116), Comitè Ètic d'Investigació Clínica de l'Hospital Universitari Germans Trias i Pujol AC-12-004, Comitè Ètic d'Investigació Clínica Parc de Salut MAR (2011/4291/I), Comitè Ètic d'Investigació Clínica de l'Hospital de Mataró, Comitè Ètic d'Investigació Clínica de l'Hospital Clínic de Barcelona (2011/7061), November 23rd, 2011).

1. Introduction

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death and ranks fourth in terms of disability-adjusted life years (DALYs) worldwide (Institute for Health Metrics and Evaluation. Seattle, WA: IHME, U. of W, 2016). It is a preventable lung condition characterized by airflow limitation and persistent respiratory symptoms (Global Initiative for Chronic Obstructive Lung Disease, 2023). As COPD progresses, exacerbations, i.e., the worsening of symptoms, including acute decreases in lung function, become more frequent and severe, and can result in life-threatening situations that demand hospital admission. Among the factors that can improve the prognosis of patients with COPD, physical activity is a key element in the risk reduction of exacerbations and the attenuation of both clinical and functional decline (Demeyer et al., 2019; Garcia-Aymerich et al., 2006, 2009; Garcia-Rio et al., 2012; Pitta et al., 2006). Consequently, regular physical activity is a critical pillar in the treatment and rehabilitation of COPD (Global Initiative for Chronic Obstructive Lung Disease, 2023). The adoption or maintenance of daily routines, such as habitual physical activity bouts, rely on daily decisions. As a result, it is crucial to identify factors that modulate the decision of completing or rejecting an opportunity to engage in physical activity. Since most physical activity takes place outdoors, and because climate change and continued urbanization result in increased air pollution and extreme temperature exposures, it is important to understand how environmental threats affect physical activity levels in patients with COPD.

Within the general population and in the elderly, air pollution and extreme weather exposures (both hot and cold) have been shown to reduce physical activity levels (Chan et al., 2006; Sumukadas et al., 2009; Tainio et al., 2021). In contrast, the effect of air pollution exposure, ambient temperature, relative humidity and rainfall on physical activity levels in patients with COPD has been studied in only a handful of studies. A panel study from London (UK) was among the first to report that higher ozone (O_3) and particulate matter of <10 μm in aerodynamic diameter (PM_{10}) concentrations were associated with a decrease in step count of the same day (Alahmari et al., 2015). In addition, three studies from Europe and North America found that higher mean and maximum temperature, as well as lower rainfall, were associated with increased daily step count (Alahmari et al., 2015; Balish et al., 2017) and active time (Furlanetto et al., 2017). Above a temperature threshold of 22.5 °C a negative effect on daily step count was observed (Alahmari et al., 2015). However, there is reason to believe that the impact of air pollution and weather exposures on physical activity levels in patients with COPD has been underestimated. First, the role of traffic-related air pollutants such as nitrogen dioxide (NO_2) or black carbon (BC), which are of concern particularly in urban areas, has not been studied yet. Second, the effect of environmental exposures from previous days (i.e., lag effects), to study delayed impacts on physical activity levels, has been overlooked. Third, the assessments of air pollution and physical activity from fixed monitoring sites and pedometers, respectively, likely resulted in measurement errors (Martin et al., 2012) that can be overcome with wearable air pollution sensors and accelerometers. Finally, and particularly important in the context of climate change, previous research is limited by the lack of days with high temperatures (e.g., temperatures above 25 °C).

Consequently, the aim of this study was to determine the effect of air pollution and weather factors of the same and of previous days on objectively-measured physical activity amount, intensity, and sedentary time. We hypothesized that higher air pollution concentrations and higher rainfall and relative humidity would relate to lower physical activity amount and intensity and more sedentary time. In contrast, higher temperatures were hypothesized to relate to higher physical activity amount and intensity, and less sedentary time, up to a threshold beyond which physical activity would decrease.

2. Methods

2.1. Study design and patients

This is a panel study using daily measurements of air pollution concentrations, weather factors (i.e., temperature, humidity and rainfall), and physical activity amount, intensity, and sedentary time, collected during two periods of 7 days with one year in between. Patients with COPD ($n = 408$) were recruited between October 2013 and February 2015 from five tertiary hospitals and 33 primary care services of five Catalan seashore municipalities (Barcelona, Badalona, Mataró, Viladecans and Gavà) as part of the Urban Training Study, described elsewhere (Arbillaga-Etxarri et al., 2018). Recruitment and assessments took place in five centers classified as Barcelona-Clínic, Barcelona-Mar, Badalona, Mataró and Viladecans/Gavà (as these are adjacent municipalities). Of the 408 patients who completed the baseline visit, 286 participated in an identical follow-up visit 12-months after baseline (between October 2014 and March 2016). COPD was diagnosed based on the American Thoracic Society's/European Respiratory Society's recommendations (post-bronchodilation forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio inferior to 0.70) (Celli et al., 2004). Exclusion criteria were: less than 45 years old; more than three months/year spent away from their residence; any mental illness; and comorbidities limiting survival to one year or any other severe comorbidity. Having another concomitant chronic respiratory disease (e.g., severe asthma or bronchiectasis) was not an exclusion criterium.

The study was authorised by the Ethics Committees of the participating institutions (Comití Ètic d'Investigació Clínica de l'Hospital Universitari de Bellvitge (PR197/11), Comitè Ètic d'Investigació Clínica de l'IDIAP Jordi Gol i Gurina (P11/116), Comitè Ètic d'Investigació Clínica de l'Hospital Universitari Germans Trias i Pujol AC-12-004, Comitè Ètic d'Investigació Clínica Parc de Salut MAR (2011/4291/I), Comitè Ètic d'Investigació Clínica de l'Hospital de Mataró, Comitè Ètic d'Investigació Clínica de l'Hospital Clínic de Barcelona (2011/7061), November 23rd, 2011). All patients provided written informed consent prior to data collection.

2.2. Measures

2.2.1. Physical activity

Objective physical activity was measured with a triaxial accelerometer (Dynaport MoveMonitor, McRoberts BV, The Netherlands), which was previously validated for patients with COPD (Rabinovich et al., 2013; van Remoortel et al., 2012). Patients wore the MoveMonitor daily, both at baseline and at the follow-up visit, and were instructed to only remove it for personal hygiene (i.e., showering or taking baths) and other water-based activities, as the device was not water-resistant. Although the device and its continuous use did not allow us to differentiate between indoor and outdoor physical activity, cultural customs and small housing units in the study region result in the majority of physical activity to be performed outdoors.

A valid day of physical activity measurement was defined as at least eight wearing time hours within waking hours (i.e. 7:00 a.m. to 10:00 p.m.) (Demeyer et al., 2021). For the present study, we got information on daily step count, daily time in moderate-to-vigorous physical activity (MVPA, ≥ 3 metabolic equivalent for task (MET)), daily intensity of physical activity during locomotion (intensity while walking, stair climbing or cycling, in cm/s^2), and sedentary time (i.e., sum of lying down and daily sitting time) with the accelerometer's sampling frequency set to 100 Hz.

2.2.2. Air pollution and weather

Exposure to air pollution and weather factors was estimated at lags zero to five, meaning that we assessed the exposure to air pollution, ambient temperature, relative humidity, and rainfall on the same day and up to five days prior to physical activity measurements. A spatiotemporal approach was applied to estimate daily exposure to the following main pollutants: nitrogen dioxide (NO_2), particulate matter (PM) of <10 μm in aerodynamic diameter (PM_{10}), and the absorbance of PM of <2.5 μm in aerodynamic diameter ($PM_{2.5ABS}$), a marker of black carbon; and particulate matter of <2.5 μm in aerodynamic diameter ($PM_{2.5}$) as a secondary pollutant, for every patient and day of interest (in $\mu g/m^3$). Specifically, concentrations were estimated based on each patient's geocoded residential address using land-use regression (LUR) models as previously described (Beelen et al., 2013; Dadvand et al., 2013; Eeftens et al., 2012). Briefly, air pollution concentrations were measured by integrating information from passive air pollution samplers and potential predictor variables that were estimated using Geographic Information Systems (GIS). After a series of tests, only statistically significant variables were selected and kept for the final model (NO_2: surface area of high density residential land within a 300 m buffer, squared inverse distance to the nearest major road, total length of all roads within a 1000 m buffer, and product of the traffic intensity in the nearest road and the inverse distance to this road; PM_{10}: square root of altitude, total length of all roads within a 25 m buffer, and product of the traffic intensity in the nearest road and the inverse distance to this road; $PM_{2.5ABS}$: surface area of high density residential land within a 300 m buffer, traffic intensity in the nearest road within a 50 m buffer, and product of the traffic intensity in the nearest road and the inverse distance to this road; and $PM_{2.5}$: green area within a 1000 m buffer, traffic intensity in the nearest road within a 100 m buffer, and product of the traffic intensity in the nearest road and the squared inverse distance to this road). The estimated concentrations were further adjusted for the daily values measured by the monitoring station that was closest to each residential address. Since monitoring stations did not provide daily levels of $PM_{2.5ABS}$ and $PM_{2.5}$ during the study period, its models were adjusted for the daily average of nitrogen oxide (NO_x) and PM_{10} levels, respectively, as previously done (Kogevinas et al., 2021, 2023), considering that NO_x and $PM_{2.5ABS}$, and $PM_{2.5}$ and PM_{10}, respectively, are primary combustion traffic-related pollutants of very similar pollutant behavior.

Daily maximum and mean temperature (°C), relative humidity (%), and rainfall (mm) levels were obtained from the automated station closest to each patient's address of the Catalan Meteorology Service (Meteocat, http://www.meteo.cat/). The estimates of relative humidity were not of sufficient spatial resolution to accurately characterize the relative humidity across the area of the study because only a subset of automated stations measure humidity (i.e. two out of six stations). Consequently, we did not include humidity measures in the statistical analyses.

The mean distance from the residential address to the weather station was 192 m.

2.2.3. Other measurements

At baseline, an interviewer-administered questionnaire was used to assess patients' characteristics including age, sex, smoking history, and socioeconomic status (according to the UK National Statistics Socio-Economic Classification: I-professional, II-managerial and technical, IIIN-skilled non-manual, IIIM-skilled manual, IV-partly skilled, and V-unskilled occupations). Other clinical characteristics were measured using validated instruments: dyspnea level (through the modified Medical Research Council dyspnea scale, mMRC) (Bestall et al., 1999), physical activity experience (Clinical-PROactive Physical Activity in COPD (C-PPAC): total, amount and difficulty scores) (Garcia-Aymerich et al., 2021), self-reported regular physical activity (Yale Physical Activity Survey (YPAS)) (Donaire-Gonzalez et al., 2011) and anxiety and depression (hospital anxiety and depression scale (HADS)) (Snaith, 2003; Zigmond and Snalth, 1983). Lung function (FEV_1 and FVC) was measured by post bronchodilator spirometry (Miller et al., 2005), and exercise capacity through the 6-min walking test (6MWT) (American Thoracic Society, 2002). Comorbidities that may affect physical activity in patients with COPD (asthma (ICD-10 code J45), any cardiovascular disease (ICD-10 codes I00–I99), diabetes mellitus (International Classification of Diseases, 10th revision [ICD-10] code E10), and any musculoskeletal disease (ICD-10 codes M00-M99); pharmacological treatment (inhaled corticosteroids (ICS), long-acting 2-agonist (LABA) and long-acting muscarinic antagonist (LAMA)); and number of moderate-to-severe COPD exacerbations within the previous 12 months were obtained from medical records. COPD severity was classified using the GOLD classification grades (1-mild, 2-moderate, 3-severe, and 4-very severe) and retrofitted to the ABE group assessment taking into consideration symptoms and history of exacerbations (Global initiative for chronic obstructive pulmonary disease, 2022). Full details regarding study procedures have been reported elsewhere (Arbillaga-Etxarri et al., 2018). Finally, the geocoded residential address of each patient was used to obtain the average Normalized Difference Vegetation Index (NDVI) within a 300 m buffer from each residential address as a green vegetation density indicator.

2.3. Statistical analyses

The sample size for this study was calculated for the main objective of the original study (Arbillaga-Etxarri et al., 2018). Therefore, we calculated the statistical power of the sample ($n = 408$) to evaluate the association of environmental factors with physical activity. Considering the distributions of air pollution concentrations, and physical activity levels of patients with COPD from the same geographic areas and similar care settings in our own, unpublished data (Donaire-Gonzalez et al., 2013), we estimated that 408 patients would allow to detect the previously reported association of at least −5.4 steps/day for an increase in 1 μg/m^3 in particulate matter with a statistical power >99 % (Alahmari et al., 2015).

Continuous variables were shown as mean and standard deviation (SD), or as median and percentiles 25th –75th (P$_{25}$–P$_{75}$), depending on their distribution. Categorical variables were presented as absolute and relative frequencies.

Air pollution levels and weather exposure at each recruitment center were assessed using the day as unit of analysis. The distribution of all air pollution and weather factors were visualized through boxplots and compared between sites using two temporal periods: (1) the actual physical activity measurement days only and (2) the period of the entire Urban Training study (i.e., all calendar days from October 2013 to March 2016).

To study the associations of each main air pollutant (NO$_2$, PM$_{10}$ and PM$_{2.5ABS}$) and weather factor (mean and maximum temperature and rainfall) with physical activity parameters, the daily measurements of all patients, regardless of the measurement period (i.e., at baseline or follow-up) were analyzed together. We built constraint distributed lag mixed-effects models (one per each pair of environmental factor and physical activity parameter) with patient and center as random effects. A directed acyclic graph based on previous research and on subject matter knowledge was used to select the final co-variates to adjust our models, which were age (as a time-varying variable), sex, weekday, public holidays, greenness (NDVI), season and social class (Figure A1). After checking for linearity using non-linear distributed lag mixed effects models, we considered linear effects for air pollution and weather and explored delayed effects up to five lags. The lag effects were constrained to follow a natural cubic spline with two equally-spaced internal knots. A first order autoregressive term (AR-1) was included to account for serial correlation in the model residuals. As a *post-hoc* analysis to verify the robustness of the findings related to PM$_{10}$, we repeated the model using PM$_{2.5}$ as exposure, since PM$_{10}$ and PM$_{2.5}$ have been previously shown to highly correlate (Cyrys et al., 2003).

To assess potential effect modification of COPD severity, smoking, medication intake, and regular physical activity levels, on the observed associations, we stratified the final single-exposure models according to: (i) COPD severity stages (two categories: Mild-to-moderate/Severe-to-very severe); (ii) smoking status (Active smoker/Former or Never smoker); (iii) intake of inhaled corticosteroids (Yes/No) (since nearly all participants were on either a LABA or a LAMA medication (97.5 %), the models were not stratified by the intake of these medications); and (iv) regular physical activity levels (YPAS total score 0–50/>50), and tested for the presence of statistical interaction via the inclusion of interaction terms between significant air pollution and weather factors and each potential effect modifier. Furthermore, we evaluated the individual effect of each environmental factor through multi-exposure distributed-lag models including environmental factors that did not show collinearity among them in regression diagnostics.

Several analyses were performed to test the sensitivity of the estimates to various assumptions in terms of selection bias, information bias, confounding and model misspecification. First, patients with asthma and/or any cardiovascular disease were excluded because they might have been more affected by the effects of environmental variables than patients with COPD without these comorbidities. Second, extreme values (>percentile 95th) of physical activity, air pollution, and weather factors were separately excluded to ensure that results were not biased by outliers. Third, active workers were excluded to prevent potential exposure misclassification, as they are more likely to spend a significant proportion of time outside their residential address, for where air pollution exposure was estimated. Finally, to assess the robustness of findings to different statistical models, single-lag mixed effects models were built for each environmental variable and each of the lag days separately (e.g., focusing on only lag zero, or only on lag one as opposed to all lag days in one model).

All computations were performed using R (version 4.0.4., R Foundation for Statistical Computing, Vienna, Austria) and using a complete case approach.

3. Results

3.1. Patients' and environmental characteristics

At baseline, initially 412 patients together recorded a total of 2927 person-days of physical activity (e.g., ca. 7 days/patient). At the follow-up visit 12 months later, 286 patients together recorded 2014 person-days. After excluding days with less than 8 h of wearing time during waking hours, the study sample included 408 patients who provided jointly, when combining the person-days collected at baseline and follow-up visit, 4689 person-days (median (P$_{25}$–P$_{75}$) 14 (4–14) days/patient) (Figure A2), all of which had air pollution and weather data.

At baseline, patients' mean ± SD age was 69 ± 9 years, with most of them being men (85 %) (Table 1). Patients had a post-bronchodilator predicted FEV$_1$ of 57 % ± 18 and a 6MWT distance of 486 ± 95 m. In terms of COPD severity, 53% of patients had moderate COPD and 37% had severe-to-very severe COPD.

During the study visits, patients walked, on average, 7697 ± 5024 steps per day and spent 624 ± 120 min/day in sedentary activity (Table 2). Median (P$_{25}$–P$_{75}$) exposure concentrations of NO$_2$, PM$_{10}$, PM$_{2.5ABS}$ and PM$_{2.5}$ were 31.7 (20.9–46.4 μg/m^3), 18.3 (12.8–25.1) μg/m^3, 1.57 (1.05–2.37) μg/m^3 and 8.3 (6.3–11.6) μg/m^3, respectively. Mean ± SD average temperature was 15.1 ± 5.2 °C, and 73 % of the days were dry.

The 4689 person-days of physical activity corresponded to 691 calendar days that covered 87% of the period between October 2013 to March 2016. Figure 1 shows that the frequency of patients' physical activity collection was lower during summer months and some winter weeks in comparison to other periods. Also, the range of temperatures measured during the physical activity collection periods together was smaller than that observed during the whole study period (range of mean temperature: 4.6–28.7 °C *vs* 3.6–30.5 °C).

3.2. Associations between air pollution, weather, and physical activity

The association between each environmental factor and physical

Table 1
Baseline socio-demographic and clinical characteristics of the study sample.

All patients (n = 408)	
Age (years), mean ± SD	68.8 ± 8.5
Sex (Male), n (%)	346 (85)
Active worker (Yes), n (%)	48 (88)
Marital status (Married), n (%)	309 (76)
Low socio-economic status (IIIM + IV + V), n (%)	291 (72)
Current smoker, n (%)	98 (24)
Cumulative dose of smoking (pack-years) among ever smokers[a], median (25th-75th percentile)	50.0 (30.0–82.8)
Post-bronchodilator FEV_1 (% pred), mean ± SD	56.8 ± 17.5
History of moderate-to-severe COPD exacerbations in the last 12 months, n (%)	193 (47)
Dyspnoea (mMRC grade, 0–4), median (25th-75th percentile)	1 (1–2)
GOLD spirometric grades, n (%):	
Mild	39 (10)
Moderate	217 (53)
Severe	120 (29)
Very severe	31 (8)
GOLD ABE assessment, n (%):	
A	124 (31)
B	199 (50)
E	73 (19)
6-Minute walking distance (m), mean (SD)	486 ± 95
Anxiety (HAD-A score, 0–21), median (25th - 75th percentile)	4 (2–8)
Depression (HAD-D score, 0–21), median (25th -75th percentile)	2 (1–5)
Asthma[b], n (%)	15 (4)
Cardiovascular disease[b], n (%)	254 (64)
Diabetes, n (%)	114 (29)
Musculoskeletal disease[b], n (%)	154 (39)
Use of any ICS, alone or in combination, n (%)	222 (59)
Use of any LABA/LAMA, alone or in combination, n (%)	10 (3)
Physical activity experience (C-PPAC), median (25th-75th percentile):	
Total score (0, worst, to 100, best)	79 (69.8-86.0)
Amount (0, lowest, to100, highest)	77 (63.0–83.0)
Difficulty (0, top difficulty, to 100, least difficulty)	83 (72.5–94.0)
Regular physical activity levels (YPAS total score, 0, less activity, to 138, more activity)[b], median(25th-75th percentile)	51.0 (32.0–68.0)

Some variables had missing values: marital status (1), socioeconomic status (2), pack-years of smoking (2), history of COPD exacerbations (11), CCQ scale (2), CAT scale (2), HAD-D (4), HAD-A (2), C-PPAC (96), cardiovascular disease (7), diabetes (7), musculoskeletal disease (7), and treatment with LABA/LAMA (17). FEV_1: forced expiratory volume at 1 s mMRC: modified Medical Research Council Questionnaire. GOLD: Global Initiative for Chronic Obstructive Pulmonary Disease. HAD: Hospital Anxiety and Dyspnoea questionnaire. ICS: inhaled corticosteroids. LABA: long-acting β-agonist. LAMA: long-acting muscarinic antagonist.

[a] A pack-year is defined as twenty cigarettes smoked every day for one year.

[b] First visit.

Table 2
Physical activity and environmental data of the study sample.

All patient-days (PD = 4689)	mean ± SD/median (25th-75th percentile)
Daily physical activity	
Wearing time	15.0 (14.7–15.0)
Number of steps (steps/day)	7697 ± 5025
Time in moderate-to-vigorous activity (min/day)	108 ± 60
Locomotion movement intensity (cm/s^2)	187 ± 40
Time in sedentary activity (min/day)	624 ± 120
Air pollution and weather data (lag zero)	
NO_2 exposure (mg/m^3)	31.7 (20.9–46.4)
PM_{10} exposure (mg/m^3)	18.3 (12.8–25.1)
$PM_{2.5\text{-Absorbance}}$ exposure ($\mu g/m^3$)	1.57 (1.05–2.37)
$PM_{2.5}$ exposure (mg/m^3)	8.3 (6.3–11.6)
Average temperature (°C)	15.1 ± 5.2
Maximum temperature (°C)	15.5 ± 5.1
Rainfall (mm):	
0, n (%)	2376 (73.4)
<10, n (%)	690 (21.3)
10–45, n (%)	170 (5.3)

Some variables had missing values: exposure to NO_2 (2), exposure to PM_{10} (107), exposure to $PM_{2.5ABS}$ (2), average temperature (2), maximum temperature (1) and rainfall (1453).

NO_2: nitrogen dioxide. PM_{10}: particulate matter of ≤2.5 μm in diameter. $PM_{2.5ABS}$: absorbance of particulate matter ≤2.5 μm in diameter.

activity levels differed by physical activity parameter and lag. Exposure to NO_2 and $PM_{2.5ABS}$ four days prior to the physical activity assessment related to a reduction in daily steps with regression coefficients (95% CI) of −60 (−105, −15) steps per 10 $\mu g/m^3$ increase in NO_2 and of −88 (−156, −20) steps per 1 $\mu g/m^3$ increase in $PM_{2.5ABS}$. Similarly, increases in NO_2 and $PM_{2.5ABS}$ were associated with lower MVPA and locomotion movement intensity and with an increased sedentary time, as shown in Fig. 2 and Table A1. An increase in PM_{10} levels, three days prior to the physical activity assessment, was associated with more time spent in sedentary activity (3.7 (1.5, 5.8) minutes per 10 $\mu g/m^3$ increase in PM_{10}). Increases in NO_2 and $PM_{2.5ABS}$ exposures on the previous day (lag one) were associated with an increased time in MVPA (0.9 (0.4, 1.4) minutes per 10 $\mu g/m^3$ increase in NO_2 and 1.2 (0.5, 2.0) minutes per 1 $\mu g/m^3$ increase in $PM_{2.5ABS}$) and with a decrease in sedentary time (−1.8 (−2.8, −0.7) minutes per 10 $\mu g/m^3$ increase in NO_2 and -2.9 (−4.6, −1.3) minutes per 1 $\mu g/m^3$ increase in $PM_{2.5ABS}$. Finally, the *post-hoc* analysis, in which we assessed the effect of $PM_{2.5}$ on physical activity, confirmed our findings of the PM_{10} exposure (Figure A3).

With respect to weather factors, higher mean and maximum temperatures on the same day (lag zero) were associated with 85 (15, 154) and 84 (16, 153) more steps/day per degree Celcius, respectively, and with more time spent in MVPA (0.9 (0.1, 1.7) and 0.9 (0.2, 1.7) more minutes, respectively). Greater rainfall on the same day led to a change of −55 (−80, −30) daily steps, as well as to a reduced time spent in MVPA (−0.7, (−1.0, −0.4) minutes per 1 mm of rainfall) and increased time spent in sedentary activity (1.4 (0.8, 2.0) minutes). There was no evidence of an association between any weather factor and locomotion movement intensity.

Similar associations were obtained when stratifying by disease severity, smoking status, inhaled corticosteroids and self-reported regular physical activity levels (Figures A4-A7; Tables A2-A17). The negative effect of air pollutants at lags three and four on locomotion movement intensity was stronger in patients with severe-to-very severe COPD compared to those with mild-to moderate COPD, and patients with higher levels of regular physical activity compared to those with lower levels, but there was no evidence of a statistical interaction (p-interaction >0.3). The positive effect of NO_2 and $PM_{2.5ABS}$ on daily steps and time in MVPA at lag one remained only for mild-to-moderate patients with COPD and active smokers (p-interaction >0.1).

After checking for collinearity, two multi-exposure models were built: one including PM_{10}, NO_2, mean temperature and rainfall, and the other including PM_{10}, $PM_{2.5ABS}$, mean temperature and rainfall (Figures A8-A9; Tables A18-A21). In both models, the associations between increases in NO_2 and $PM_{2.5ABS}$ with a reduction in daily steps and with an increase in sedentary time four days later (lag four) remained stable. Additionally, an increase in PM_{10} concentrations at lag four was negatively associated with locomotion movement intensity. However, associations of air pollution concentrations and daily step count at lag one were no longer observed when using multi-exposure models. Regarding weather factors, mean temperature was no longer associated with any physical activity parameter, while results for rainfall were similar to those of the single-exposure models.

Various sensitivity analyses in which we excluded patients with asthma or any cardiovascular disease, extreme physical activity values, extreme environmental factors levels, or active workers, and used single lag models yielded similar results (Figures A6-A10).

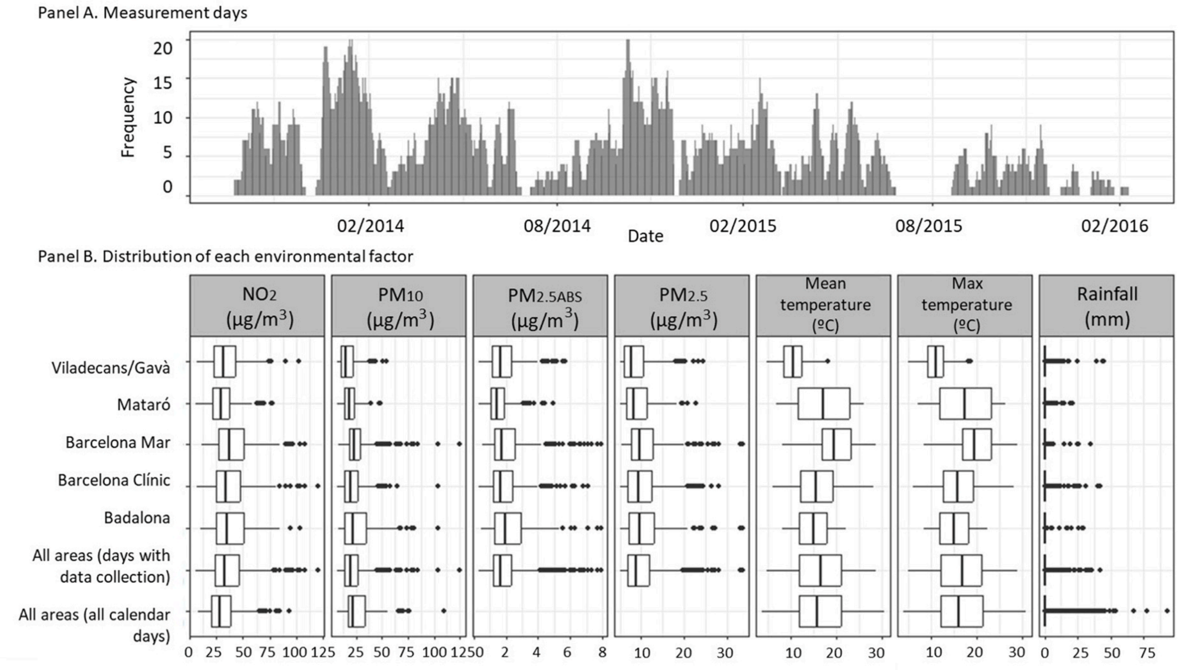

Fig. 1. Distribution of measurement days according to calendar (panel A) and air pollution and weather factors as measured for the study, by recruitment site, and at the Barcelona province during all calendar days (panel B).
The distribution of $PM_{2.5ABS}$ and $PM_{2.5}$ across study areas and for all calendar days is not shown since the available fixed monitoring stations did not provide daily $PM_{2.5ABS}$ and $PM_{2.5}$ concentrations during the period of the study.

4. Discussion

4.1. Summary and contextualization of results

The results of our panel study indicate that air pollution and weather factors impact daily physical activity amount and intensity, and sedentary time, in patients with COPD. Specifically, 1) higher NO_2, PM_{10}, $PM_{2.5ABS}$ and $PM_{2.5}$ concentrations were associated with lower daily step count, less time spent in MVPA, and a reduced locomotion movement intensity, as well as higher sedentary time, four days later (i.e., four days after the air pollution exposure), particularly in patients with higher levels of regular physical activity; and 2) higher average and maximal temperature as well as lower rainfall were associated with an increase in daily steps and more time spent in MVPA, and a decrease in sedentary time on the same day. These results were robust to several secondary and sensitivity analyses.

To our knowledge, this is the first study showing that exposure to air pollution concentrations, in the case of PM_{10} and $PM_{2.5}$ even below current WHO recommendations (World Health Organization, 2021), may lead to a delayed reduction in physical activity amount and intensity in patients with COPD. Our findings are consistent with research in the general population (An et al., 2019; Smith et al., 2019), and additionally support and go beyond a previous panel study conducted in London (N = 73), that tested the effects of O_3 and PM_{10} on daily step count on the same day (Alahmari et al., 2015). Our data also showed an increase in physical activity amount at higher air pollution concentrations one day after the exposure, particularly in patients with mild-to-moderate COPD and active smokers, although the findings at lag one were not replicated in secondary analyses (i.e., multi-exposure models).

In theory, both psychological and physiological mechanisms might have been responsible for the observed decreases in physical activity behavior when air pollution concentrations were higher (Bauman et al., 2012). Since variations in the concentrations of modelled daily air pollutants are generally not visible to the human eye, and air pollution advisories are typically only reported in mainstream weather forecasts when concentrations are high, it is unlikely that patients with COPD consciously modified their physical activity. Consequently, and in agreement with previous reports (Tainio et al., 2021), we assume that psychological mechanisms only played a minor role in the observed effects. In support of physiological mechanisms are the well-known short-term effects of air pollution exposure on pulmonary and systemic inflammation (Becker et al., 2003; MacNee and Donaldson, 2003), airway ciliary reactivity (Kakinoki et al., 1998), lung function (Bloemsma et al., 2016; Lagorio et al., 2006), and respiratory symptoms (Peacock et al., 2011a), all of which can develop gradually and become a measurable, yet by the patient still unnoticed or unconscious barrier for physical activity in the days after exposure to increased air pollution concentrations. This hypothesis is supported by previous studies in patients with COPD that reported a substantial negative impact on respiratory symptoms, lung function, episodes of exacerbations and hospitalization risk a few days after the exposure to several air pollutants (Bloemsma et al., 2016; Cortez-Lugo et al., 2015; Evangelopoulos et al., 2021; Gao et al., 2020; Karakatsani et al., 2012; Li et al., 2016; Peacock et al., 2011b; Sun et al., 2018). Further, it is possible that patients increased their medication use after the exposure to air pollution in response to subtle, acute air pollution-induced increases in symptoms, which might initially mask the negative effects of air pollution on respiratory health and could explain the apparently contradictory observation of increased physical activity amount one day after the exposure to higher air pollution concentrations. Further studies are needed to shed light onto the mechanisms explaining the effects of air pollution concentrations on physical activity in patients with COPD, and to replicate the abovementioned contradictory effects at lag one.

Regarding the weather factors, we observed that increased ambient temperature and lower rainfall were related with increased daily step count and time spent in MVPA, and with reduced sedentary time, which supports previous research (Alahmari et al., 2015; Balish et al., 2017; Furlanetto et al., 2017). Contrary to what we hypothesized, we did not notice a threshold for ambient temperature above which a negative

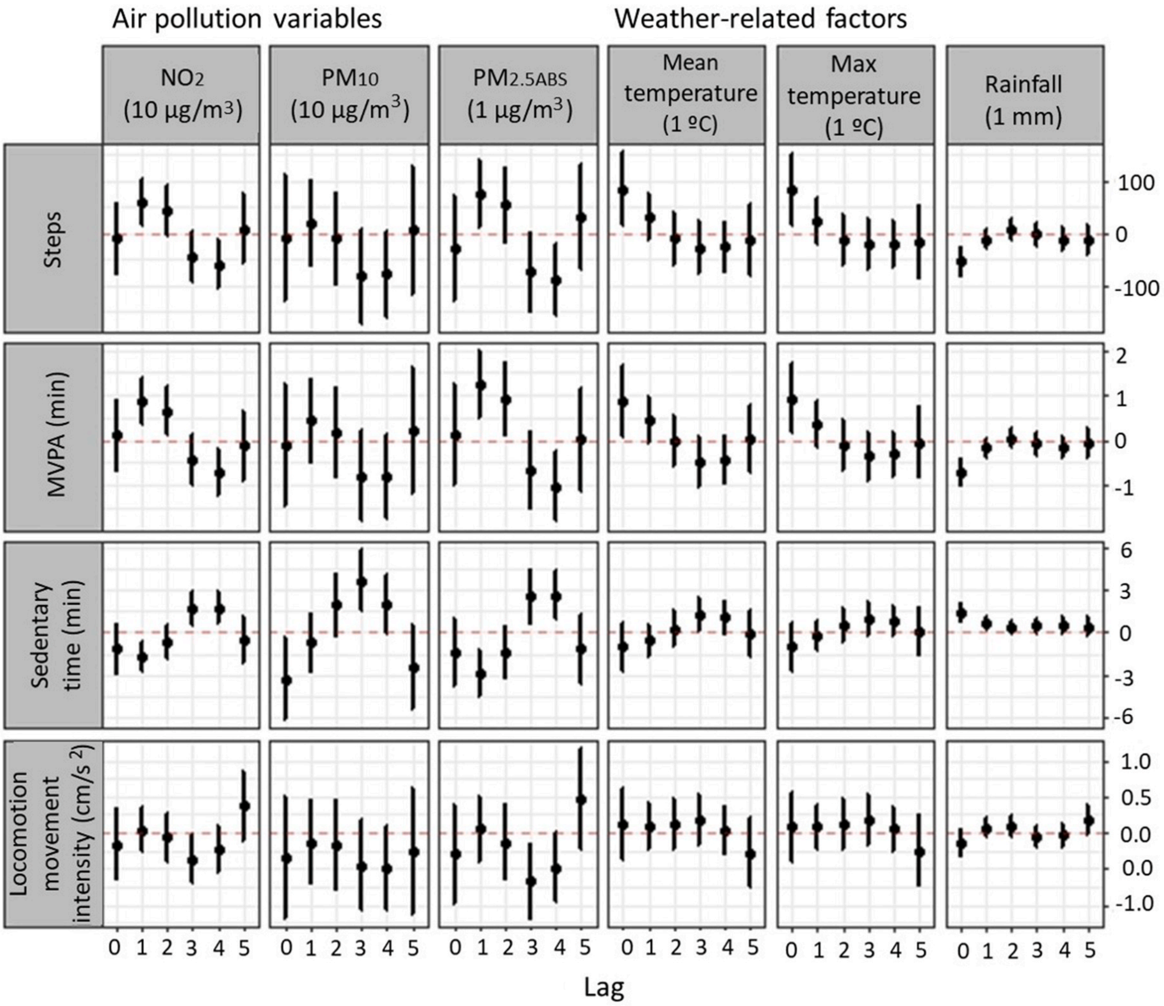

Fig. 2. Adjusted associations of air pollution and weather factors with physical activity parameters.
The effect is shown as an increase in 10 µg/m^3 for NO$_2$ and PM$_{10}$, 1 µg/m^3 for PM$_{2.5ABS}$, 1 °C for average and maximum temperature, and 1 mm for rainfall. Boxes and the error bars indicate the regression coefficients (β) and 95 % confidence intervals, respectively. Models were adjusted for the following covariates (number of patients with missing values): age (0), sex (0), weekday (0), public holidays (0), greenness (NDVI) (1), season (1), and social class (2).
MVPA: Moderate-to-vigorous physical activity.

impact on physical activity levels would be expected. This may be explained by two factors. First, we collected little physical activity recordings during the hottest months of the year. In fact, local health authorities recommend that patients do not practice physical activity outdoors during heat waves (Ministry of Home Affairs, G. de C, 2022). Thus, although our study's data collection was not stopped, patients did not wear the activity devices because they assumed those days would not be representative of their usual physical activity levels. Second, although our study included days with temperatures above the previously published threshold of 22.5 °C at which patients with COPD presented with reduced physical activity levels (Alahmari et al., 2015), the inflection point in our patient sample could be higher and therefore not observable with the available data, particularly given extensive research showing that the dose-response of temperature effects on health depends on patients' usually experienced temperatures (Guo et al., 2014). Future studies should consider physical activity measures also during the hottest period of the year to test whether a temperature threshold truly exists, particularly in the context of climate change and in anticipation of more frequent, longer lasting, and more extreme heat waves. Among the psychological mechanisms explaining the association between weather and physical activity, cold and precipitation, as well as unfavorable weather forecasts predictions may negatively impact patients' decisions on whether or not to engage in physical activity (O'Shea et al., 2007; Tucker and Gilliland, 2007). As for physiological mechanisms, low temperatures have been related to a rapid increase in respiratory symptoms and decrease in lung function, especially in patients with chronic respiratory diseases (Jenkins et al., 2012; Koskela, 2007; Mu et al., 2017) which could lead to (unconscious) changes in physical activity behavior on the same day.

4.2. Strengths and weaknesses

Strengths of the current study include both its design and statistical approach, e.g., the use of a distributed lag model, which allowed for the first ever assessment of lag effects of air pollution and weather effects on physical activity. Also, the objective measurement of physical activity prevented recall bias and enhanced the accuracy of the approach. The approach used to estimate air pollution levels and weather conditions reduced the risk of information bias compared to assigning the levels measured at a single fixed station or using questionnaires, which is particularly important in cities such as Barcelona, because it is characterised by significant differences in air pollution concentrations between streets. Finally, the wide distribution of participants across disease severity and socioeconomic status adds external validity to the findings.

The study has, however, some shortcomings. As previously discussed, we had access to only few measurements during the hottest summer periods. Second, despite our large sample size in terms of patient-days, the number of days per patient was relatively small (i.e., 14 days maximum) and all corresponded to the same season, which may have limited our capacity to account for intraindividual variability. Third, since this study took place in a coastal humid region with temperate temperatures, our findings may not be generalizable to other locations with different characteristics. Fourth, we could not disentangle the relative effect of each environmental factor on physical activity through a multi-exposure model, although we do not deem it relevant for the purpose of the study. Fifth, despite the advantages of advanced LUR air pollution modelling, there is a risk of exposure misclassification, as it estimates outdoor exposures based on patients' residential address without the ability to accounting for indoor exposure, exposure while commuting, or inhaled dose. Yet, because of building materials, mostly absent air filtration systems installed in residential housing, in addition to cultural customs related to room ventilation practises within the study area, outdoor and indoor air pollution concentrations have been found to be similar (Rivas et al., 2015). Also, excluding active workers, who likely spend less time indoors in their homes and more time commuting outdoors compared to retired study participants, yielded similar results. Finally, other air pollutants and weather factors previously related to physical activity levels in patients with COPD (e.g., O_3, relative humidity and solar radiation) have not been included in this study due to low variability in the studied area around Barcelona or insufficient spatial resolution of the obtained measurement.

4.3. Clinical, public health and research implications

Our study has important implications. From a clinical viewpoint, our findings suggest that physical activity recommendations and interventions should consider modifications to physical activity up to four days after increases in air pollution concentrations to account for lag effects. With respect to increases in temperature, modifications of physical activity levels should be considered for the same day. For example, patients should be advised to refrain from engaging in physical activity during air pollution peaks or on particularly cold days, and instead prioritize physical activity in low-pollution, cooler areas, either indoors in adequately climatized spaces or outdoors in green areas. These adaptations would help promote the adherence to habitual physical activity while also enhancing the safety of patients with COPD. Even though the effect of reduced physical activity levels in response to increases in air pollutant concentrations (even at PM_{10} levels below current WHO recommendations) and ambient temperature on downstream symptoms and COPD disease progression are still unknown, it is imperative to keep air pollution levels at an absolute minimum (Liu et al., 2021), for example through improved urban design and planning. Finally, our findings suggest that future studies investigating daily physical activity in patients with COPD should consider daily exposure to environmental factors, both on the same and previous days, as relevant covariates.

5. Conclusions

Our study suggests that NO_2, PM_{10}, $PM_{2.5ABS}$ and $PM_{2.5}$ concentrations are related to a reduction of the amount and intensity of physical activity three to four days after the exposure in patients with COPD, whereas higher temperature and lower rainfall relate to an increase in physical activity amount on the same day. These findings provide evidence that air pollution and weather factors must be considered when providing physical activity recommendations or assessing physical activity outcomes in patients with COPD, and that the effects of these factors on patients' health need to be known when planning and redesigning cities.

CRediT authorship contribution statement

Alícia Josa-Culleré: Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Xavier Basagaña:** Methodology, Writing – review & editing. **Sarah Koch:** Writing – review & editing. **Ane Arbillaga-Etxarri:** Writing – review & editing. **Eva Balcells:** Writing – review & editing. **Magda Bosch de Basea:** Writing – review & editing. **Nuria Celorrio:** Writing – review & editing. **Maria Foraster:** Writing – review & editing. **Robert Rodriguez-Roisin:** Writing – review & editing. **Alicia Marin:** Writing – review & editing. **Gabriela P. Peralta:** Writing – review & editing. **Diego A. Rodríguez-Chiaradia:** Writing – review & editing. **Pere Simonet:** Writing – review & editing. **Pere Torán-Monserrat:** Writing – review & editing. **Pere Vall-Casas:** Writing – review & editing. **Judith Garcia-Aymerich:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Robert Rodriguez-Roisin reports a relationship with Chiesi España SA that includes: consulting or advisory and speaking and lecture fees. Judith Garcia-Aymerich reports a relationship with Esteve that includes: speaking and lecture fees. Judith Garcia-Aymerich reports a relationship with Chiesi España SA that includes: speaking and lecture fees. Judith Garcia-Aymerich reports a relationship with AstraZeneca Pharmaceuticals LP that includes: speaking and lecture fees. Judith Garcia-Aymerich reports a relationship with Menarini Laboratories that includes: speaking and lecture fees. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2024.118195.

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