Environmental Research 214 (2022) 113956

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Urban environment and physical activity and capacity in patients with chronic obstructive pulmonary disease

Maria Koreny[a,b,c], Ane Arbillaga-Etxarri[d], Magda Bosch de Basea[a,b,c], Maria Foraster[a,b,c,e], Anne-Elie Carsin[a,b,c,f], Marta Cirach[a,b,c], Elena Gimeno-Santos[a,b,c,g], Anael Barberan-Garcia[h], Mark Nieuwenhuijsen[a,b,c], Pere Vall-Casas[i], Robert Rodriguez-Roisín[h], Judith Garcia-Aymerich[a,b,c,*]

[a] *ISGlobal, Barcelona, Spain*
[b] *Pompeu Fabra University (UPF), Barcelona, Spain*
[c] *CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain*
[d] *Physiotherapy Department, Faculty of Health Sciences, University of Deusto, Donostia-San Sebastián, Spain*
[e] *PHAGEX Research Group, Blanquerna School of Health Science, Universitat Ramon Llull (URL), Barcelona, Spain*
[f] *IMIM (Hospital Del Mar Medical Research Institute), Spain*
[g] *Hospital Clínic de Barcelona, Universitat de Barcelona, Barcelona, Spain*
[h] *University of Barcelona, Institut D'Investigació Biomèdica August Pi I Sunyer (IDIBAPS), CIBER Enfermedades Respiratorias (CIBERES), Hospital Clínic, Barcelona, Spain*
[i] *Universitat Internacional de Catalunya (UIC), Barcelona, Spain*

A R T I C L E I N F O

Keywords:
Urban environment
Noise
Air pollution
Physical activity
Exercise capacity
Chronic obstructive pulmonary disease

A B S T R A C T

Background: Physical activity and exercise capacity are key prognostic factors in chronic obstructive pulmonary disease (COPD) but their environmental determinants are unknown.
Objectives: To test the association between urban environment and objective physical activity, physical activity experience and exercise capacity in COPD.
Methods: We studied 404 patients with mild-to-very severe COPD from a multi-city study in Catalonia, Spain. We measured objective physical activity (step count and sedentary time) by the Dynaport MoveMonitor, physical activity experience (difficulty with physical activity) by the Clinical visit-PROactive (C-PPAC) instrument, and exercise capacity by the 6-min walk distance (6MWD). We estimated individually (geocoded to the residential address) population density, pedestrian street length, slope of terrain, and long-term (i.e., annual) exposure to road traffic noise, nitrogen dioxide (NO_2) and particulate matter ($PM_{2.5}$). We built single- and multi-exposure mixed-effects linear regressions with a random intercept for city, adjusting for confounders.
Results: Patients were 85% male, had mean (SD) age 69 (9) years and walked 7524 (4045) steps/day. In multi-exposure models, higher population density was associated with fewer steps, more sedentary time and worse exercise capacity (−507 [95% CI: 1135, 121] steps, +0.2 [0.0, 0.4] h/day and −13 [-25, 0] m per IQR). Pedestrian street length related with more steps and less sedentary time (156 [9, 304] steps and −0.1 [-0.1, 0.0] h/day per IQR). Steeper slope was associated with better exercise capacity (15 [3, 27] m per IQR). Higher NO_2 levels related with more sedentary time and more difficulty in physical activity. $PM_{2.5}$ and noise were not associated with physical activity or exercise capacity.
Discussion: Population density, pedestrian street length, slope and NO_2 exposure relate to physical activity and capacity of COPD patients living in highly populated areas. These findings support the consideration of neighbourhood environmental factors during COPD management and the attention to patients with chronic diseases when developing urban and transport planning policies.

* Corresponding author. Barcelona Institute for Global Health (ISGlobal), C/ Doctor Aiguader 88, 08003, Barcelona, Spain.
E-mail addresses: maria.koreny@gmx.com (M. Koreny), ane.arbillaga@deusto.es (A. Arbillaga-Etxarri), magda.boschdebasea@isglobal.org (M. Bosch de Basea), maria.foraster@isglobal.org (M. Foraster), anneelie.carsin@isglobal.org (A.-E. Carsin), marta.cirach@isglobal.org (M. Cirach), elena.gimeno@isglobal.org (E. Gimeno-Santos), anaelbg@gmail.com (A. Barberan-Garcia), mark.nieuwenhuijsen@isglobal.org (M. Nieuwenhuijsen), perevall@uic.es (P. Vall-Casas), ROROR0@clinic.cat (R. Rodriguez-Roisín), judith.garcia@isglobal.org (J. Garcia-Aymerich).

https://doi.org/10.1016/j.envres.2022.113956
Received 9 March 2022; Received in revised form 9 July 2022; Accepted 19 July 2022
Available online 22 July 2022
0013-9351/© 2022 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Abbreviations

BMI	body mass index
CAT	COPD assessment test
CCQ	clinical COPD questionnaire
COPD	chronic obstructive pulmonary disease
C-PPAC	Clinical visit—PROactive Physical Activity in COPD
dB	decibels
FEV_1	forced expiratory volume in 1 s
FFMI	fat free mass index
FVC	forced vital capacity
GIS	Geographic Information Systems
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HADS-A:	hospital anxiety and depression scale – anxiety
HADS-D:	hospital anxiety and depression scale – depression
INE	Instituto Nacional de Estadística
ICGC	Institut Cartogràfic i Geològic de Catalunya
IQR	interquartile range
L_{den}	day evening night sound level
LUR	land-use regression
mMRC	modified Medical Research Council
6MWD	6-min walk distance
6MWT	6-min walk test
NO_2	nitrogen dioxide
PM	particulate matter
P25	25^{th} percentile
P75	75^{th} percentile
SD	standard deviation
VIF	variance inflation factor
$\dot{V}O_2$	oxygen uptake

1. Introduction

Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality worldwide (Soriano et al., 2017). The global burden of disease study estimated that COPD affected more than 174 million patients and caused 3.2 million deaths in 2015 (Soriano et al., 2017). COPD is characterised by a progressive airflow limitation leading to breathlessness that often limits the ability to carry out daily activities, including physical activities. Patients are typically less active than healthy controls from the early stages of the disease onwards (Pitta et al., 2005; Shrikrishna et al., 2012; Van Remoortel et al., 2013) and this inactivity affects COPD prognosis. Indeed, COPD patients who maintain regular levels of physical activity have lower risk of exacerbations of the disease, attenuated lung function decline and lower mortality (Demeyer et al., 2019; Gimeno-Santos et al., 2014). Thus, COPD guidelines such as those provided by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommend physical activity for all COPD patients (Vestbo et al., 2013). To provide adequate support to physical activity interventions, knowing and understanding which factors other than the disease itself may influence the physical activity behaviour is key.

The ecological model of the determinants of physical activity (Bauman et al., 2012) suggests a major role for factors in the 'environmental' domain. In line with this notion, a range of studies have reported that environmental factors such as residential density or land-use mix (Cerin et al., 2020; Ding et al., 2013; Frank et al., 2005; McCormack, 2017; Witten et al., 2012), noise or noise annoyance (Dzhambov et al., 2017; Foraster et al., 2016; Roswall et al., 2017) and air pollution (An et al., 2018) are associated with physical activity in the general population. Thus, it is likely that such environmental factors can influence the physical activity of COPD patients also. Nonetheless, the evidence for this assumption remains currently uncertain. One study found that high levels of ozone (O_3) and particulate matter (PM_{10}) were associated with a reduced step count in patients with COPD (Alahmari et al., 2015). However, another study based on the same cohort as the current manuscript observed that urban greenness was not related to physical activity in COPD patients, which lead to the hypothesis that the ability of environment to stimulate physical activity could be lower in these patients than in the general population due to their underlying chronic condition (Arbillaga-Etxarri et al., 2017). Unfortunately, the role of other environmental factors in the physical activity of COPD patients has not been tested so far.

At difference with previous research (mostly in the general population), where physical activity is assessed as an individual single characteristic, we postulate that understanding the determinants of 'physical activity behaviour' in subjects suffering from chronic conditions that limit their mobility in daily life requires a wider approach. Accordingly, we propose to include as outcomes of the environmental factors not only objective measures of physical activity as obtained by an activity monitor, but also the patient's experience of difficulty with physical activity (Gimeno-Santos et al., 2015), and the patient's functional exercise capacity which strongly determines how active a patient can be (Holland et al., 2015; Troosters et al., 2019).

With this background in mind, we aimed to estimate the association between environmental factors (population density, pedestrian street length, slope of terrain, road traffic noise, nitrogen dioxide (NO_2) and $PM_{2.5}$), and objective physical activity (daily step count, sedentary time), physical activity experience (difficulty with physical activity) and functional exercise capacity (6-min walk distance (6MWD)) in patients with mild-to-very severe COPD. We anticipate that our results will allow for developing strategies to effectively promote physical activity in COPD patients.

2. Methods

2.1. Study design and patient population

This is a cross-sectional analysis of baseline pre-randomisation data from the multi-centre Urban Training study (NCT01897298) (Arbillaga-Etxarri et al., 2018) that enrolled 407 patients from five Catalan seaside municipalities (Badalona, Barcelona [centre and shore areas], Mataró, Viladecans and Gavà) at 33 primary care centres and 5 tertiary hospitals between October 2013 and February 2015. All patients had a diagnosis of COPD, according to American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines (post--bronchodilator forced expiratory volume in 1 s [FEV_1] to forced vital capacity [FVC] ratio <0.70) (Celli et al., 2004). For the present analysis we used the data collected at baseline only and included patients if they had valid data on objective physical activity, physical activity experience, functional exercise capacity, and environmental variables (n = 404, 99% of the total).

The study was approved by all local institutional ethic boards and written informed consent was obtained from all patients.

2.2. Physical activity and capacity outcomes

Objective physical activity was recorded during 24 h of 7 consecutive days using the Dynaport MoveMonitor (McRoberts BV, The Hague, The Netherlands) (Rabinovich et al., 2013; Van Remoortel et al., 2012). Data during waking hours (from 07:00 h to 22:00 h) were retrieved. A valid physical activity measurement was defined as a minimum of three days with at least 8 h of wearing time within waking hours; details have been previously published (Arbillaga-Etxarri et al., 2018). For the present study, we obtained information on daily step count and sedentary time (sum of lying and sitting time, in hours/day).

Experience with physical activity was assessed by the Clinical visit version of the PROactive physical activity in COPD (C-PPAC) instrument. Briefly, the C-PPAC combines a short patient-reported outcome questionnaire with data from an activity monitor to assess the physical activity experience in three scores: amount of physical activity, difficulty with physical activity, and total physical activity experience, all ranging from 0 (worse physical activity experience, i.e., less amount, more difficulty) to 100 (better physical activity experience, i.e., more amount, less difficulty) (Garcia-Aymerich et al., 2021; Gimeno-Santos et al., 2015). For the present study, we used the difficulty score as an outcome, as the amount score was highly correlated with the objective physical activity variables in our sample (Spearman correlation coefficient [ρ] of amount score with step count $\rho = 0.75$, p-value <0.001, and with sedentary time $\rho = -0.62$, p-value <0.001).

Functional exercise capacity was assessed using the 6-min walk test (6MWT) following published recommendations (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories 2002; Manual de Procedimientos SEPAR, 4; Erratum in ATS statement: Guidelines for the six-minute walk test 2016), determining the 6MWD for each patient. Patients completed two 6MWTs with at least a 30-min rest between, and the longer of the two distances was used for analysis.

2.3. Urban environmental exposures

We estimated the exposure to urban environmental factors individually using Geographic Information Systems (GIS) for each patient at his/her geocoded residential address. We obtained population density (habitants per square kilometre within the census area) from the Spanish National Statistics Institute (Instituto Nacional de Estadística, INE) for the year 2016 (INE, 2016). We obtained pedestrian street length (sum of pedestrian street length [metres] within a 300-m buffer around the residence) from Navteq (licensed data under ArcGIS software, ESRI ArcMap ™ 10.0, ArcGIS Desktop 10 Service Pack 4) (ESRI, 2012). We obtained slope of terrain from now on 'slope' (average slope [degrees] within a 300-m buffer around the residence) from the topographic map of the Cartographic Institute of Catalonia (Institut Cartogràfic i Geològic de Catalunya, ICGC) (ICGC, 2012). We obtained road traffic noise from now on 'noise' (annual residential average levels of road traffic noise in the nearest street from the residence [24 h day-evening-night level (L_{den}) EU indicator in decibels (dB)]) from the official strategic noise maps for the year 2012, except for Mataró for which only the 2017 map was available, developed under the EU Directive 2002/49/EC as described previously (Dadvand et al., 2014b; Mapes estratègics del soroll, 2012). Finally, we estimated the annual residential averages of NO_2 and $PM_{2.5}$ (μg/m3) temporarily adjusted for each patient (i.e., 12 months prior to data collection). To do that we applied land-use regression (LUR) models from 2009 that were corrected to 2013 levels using daily time series from fixed air quality monitors as described previously (Beelen et al., 2013; Cyrys et al., 2012; Eeftens et al., 2012a, 2012b).

2.4. Other measurements

We obtained the following data (presented along the lines of the ecological model of the determinants of physical activity (Bauman et al., 2012)) from all patients using standardised procedures: (i) sociodemographic: age, sex, smoking history, education and individual socioeconomic status (based on the employment characteristics and categorised according to the National Statistics Socio-economic Classification); (ii) interpersonal: marital status and working status; (iii) environmental: season of recruitment, land-surface yearly average temperature (average temperature within a 50-m buffer around the residence, derived from three land-surface temperature maps from the Landsat 5 Thematic Mapper data as described previously (Dadvand et al., 2014b)) and urban vulnerability index (a measure of socioeconomic status at the census tract level) (Atlas of Urban Vulnerability in Spain); (iv) clinical: FEV_1 and FVC by forced spirometry post bronchodilator, the COPD assessment test (CAT) and the clinical COPD questionnaire (CCQ; total score and the three subdomains: symptom, functional and mental state) to measure quality of life, the modified Medical Research Council dyspnoea scale (mMRC), the number of acute COPD exacerbations requiring a hospital admission in the previous 12 months, body mass index (BMI) and fat free mass index (FFMI) by physical examination and bioelectrical impedance; and (v) psychological: the hospital anxiety and depression scale (HADS), providing a score for anxiety (HADS-A) and a score for depression (HADS-D) (Snaith, 2003; Zigmond and Snaith, 1983). Full details on study procedures and quality control have been reported previously (Arbillaga-Etxarri et al., 2017, 2018).

2.5. Statistical analysis

Since the sample size was fixed by the main objective of the Urban Training study (Arbillaga-Etxarri et al., 2018), we calculated the statistical power of the available sample ($n = 404$) to test the association between environmental factors and physical activity in COPD patients. Based on own unpublished data about distribution of population density and air pollution levels in the same geographic areas, and physical activity levels of COPD patients from the same geographic areas and similar care settings (Donaire-Gonzalez et al., 2013), 404 patients allow to detect an association of −493 steps/day or higher per a change of ≈20,000 inhabitants/km^2 in population density as previously reported (Annegarn et al., 2012; McCormack, 2017), and an association of −5.4 steps/day or higher per increase in 1 μg/m^3 in particulate matter as previously reported (Alahmari et al., 2015) with a statistical power of >99%. Due to the small proportion of missing data (<2% of total data), we used a complete case strategy and reported missing data in the table footnotes.

We estimated the Spearman's rank correlation between the environmental exposures (population density, pedestrian street length, slope, noise, NO_2 and $PM_{2.5}$). To test the association between each of the environmental factors and objective physical activity, physical activity experience and functional exercise capacity variables, we used mixed-effects linear regression models reported per change of an interquartile range (IQR) in exposure. We first built unadjusted single-exposure models with a random intercept for city. We then built single-exposure multivariable models, adjusting for age, sex, socioeconomic status, urban vulnerability index, FEV_1, CCQ mental score, exacerbation with hospital admission in previous 12 months and anxiety (HADS-A score) which we defined a priori as the most compelling confounders based on available literature or those variables which differed across cities and were a source of heterogeneity (see directed acyclic graphs in Appendix, Figures A1 and A2) (Arbillaga-Etxarri et al., 2017). Other relevant factors which had been used as covariates in the literature previously (e.g., depression or dyspnoea) were considered as potential effect modifiers or mediators in our analysis and so not included as covariates in the main models. Finally, we built a multi-exposure model additionally adjusting for all environmental factors simultaneously to control for mutual residual confounding, after checking for possible collinearity (average variance inflation factor (VIF) < 3). We tested goodness of fit of the final models.

Based on observed results and to help interpretation, we conducted two *post-hoc* analyses: (1) we stratified the association between population density and step count, sedentary time and exercise capacity for depression symptoms level (HAD-D score $</\geq 11$ based on previous research) (Snaith, 2003) to test its role as potential effect modifier of the observed associations; and (2) we included the mMRC dyspnoea score in the single-exposure multivariable model for NO_2, to indirectly test its role as potential mediator for the effect of NO_2 on sedentary time and C-PPAC difficulty score (see a priori built directed acyclic graph in Appendix, Figure A1).

Finally, as sensitivity analyses, (1) we restricted the final models to patients not working actively to test for potential miss-classification in the exposures (i.e., assuming that patients who work away from home spend an important part of their time not exposed to residential environmental factors), and (2) we repeated the final models after excluding patients with extreme values (<5th and >95th percentile) in the environmental exposures to omit the influence of extreme observations.

All analyses were performed using Stata/SE 14.2 (StataCorp, College Station, TX, USA).

3. Results

Of 404 patients included in the present analysis 85% were male, age was mean (standard deviation [SD]) 69 ± 9 years, FEV_1 was 57 (18) % predicted and mMRC dyspnoea score was 1.2 (0.9) (Table 1).

Compliance with the activity monitor was excellent with median (P25–P75) 7 (3–7) valid days and m (SD) 14.6 (0.7) wearing hours. The patients walked on average 7524 (4045) steps/day and the 6MWD was 486 (95) metres (Table 2). There were no differences in physical activity, physical activity experience or functional exercise capacity variables according to the season of recruitment. Median population density was 31,284 (14,020–45344) habitants/km^2 within the census area, pedestrian street length was 245.1 (50.5–517.5) metres within a 300-m buffer around the residence, slope was 2.0 (1.2–3.5) degrees within a 300-m buffer around the residence, noise was 63 (59–67) dB in the nearest street from the residence, annual NO_2 was 43.5 (35.0–48.7) μg/m^3 and annual $PM_{2.5}$ was 12.6 (10.7–13.8) μg/m^3 (Table 2).

We found weak to moderate (positive and negative) correlations between all environmental factors (population density, pedestrian street length, slope, noise, NO_2 and $PM_{2.5}$), except for population density with pedestrian street length and slope, and for noise with NO_2 and $PM_{2.5}$ which were not correlated (Fig. 1). Due to the lack of strong correlations and no evidence of strong collinearity according to the VIF levels we subsequently built multi-exposure models including all exposures simultaneously.

Higher population density was associated with a lower step count, more sedentary time and reduced functional exercise capacity, in unadjusted, single- and multi-exposure adjusted models, although in some models the association did not reach statistical significance (Fig. 2, Appendix Table A1). After stratification by depression symptoms level, the results were stronger and statistically significant among COPD patients with depression symptoms, while they were reduced and lost precision in the COPD patients without depression symptoms (see Appendix, Table A2).

Pedestrian street length was associated with more steps and less sedentary time in single- and multi-exposure adjusted models. Steeper slope was consistently associated with an increased functional exercise capacity in unadjusted, single- and multi-exposure adjusted models but not with the rest of physical activity parameters.

Higher levels of NO_2 were associated with more sedentary time and worse physical activity experience (i.e. more experienced difficulty with physical activity). The latter association was attenuated and lost precision when the mMRC dyspnoea score was included as a covariate (see Appendix, Table A3).

$PM_{2.5}$ and noise were not associated with any physical activity or exercise capacity parameter in this cohort of COPD patients.

When restricting the adjusted models to patients not working actively, all associations persisted except for the associations of pedestrian street length with daily step count and sedentary time (see Appendix, Table A4). When we excluded extreme values in exposure variables, the associations were attenuated (see Appendix, Table A5).

Table 1
Characteristics of 404 patients with mild-to-very severe COPD.

	All patients n = 404[a]
Sociodemographic characteristics	
Age (years), m (SD)	68.8 (8.5)
Sex: men, n (%)	343 (85)
Current smoker, n (%)	97 (24)
Cumulative smoking (pack-years), m (SD)	59.3 (41.4)
Education: high school or higher[b], n (%)	123 (31)
Socioeconomic status: non-manual skilled or higher[c], n (%)	114 (28)
Interpersonal characteristics	
Living with a partner[d], n (%)	306 (76)
Active worker[e], n (%)	48 (12)
Environmental characteristics	
Recruitment season	
Spring, n (%)	101 (25)
Summer, n (%)	44 (11)
Fall, n (%)	143 (35)
Winter, n (%)	116 (29)
Land surface temperature (°C)[f], median (P25–P75)	24.4 (24.1–24.7)
Urban vulnerability index (from 0-lowest to 1-highest)[g], m (SD)	0.64 (0.17)
Clinical characteristics	
FEV_1 (% predicted), m (SD)	56.8 (17.5)
FEV_1/FVC ratio, m (SD)	0.54 (0.12)
Airflow limitation severity:	
Mild ($FEV_1 \geq 80\%$), n (%)	38 (9)
Moderate (FEV_1 50–79%), n (%)	215 (53)
Severe (FEV_1 30–49%), n (%)	120 (30)
Very severe ($FEV_1 < 30\%$), n (%)	31 (8)
CAT score (from 0-better to 40-worse), m (SD)	12.3 (7.2)
CCQ-total score (from 0-better to 6-worse), m (SD)	1.4 (1.0)
CCQ-symptom score (from 0-better to 6-worse), m (SD)	1.6 (1.1)
CCQ-functional score (from 0-better to 6-worse), m (SD)	1.3 (1.2)
CCQ-mental score (from 0-better to 6-worse), m (SD)	1.3 (1.5)
mMRC dyspnoea score (from 0-better to 4-worse), m (SD)	1.2 (0.9)
Any COPD exacerbation with hospital admission in previous 12 months, n (%)	23 (6)
BMI (kg/m^2), m (SD)	28.4 (5.0)
FFMI (kg/m^2), m (SD)	19.5 (3.2)
Psychological characteristics	
Anxiety (HADS-A score, 0–21), m (SD)	5.2 (4.0)
Depression (HADS-D score, 0–21), m (SD)	3.5 (3.4)

BMI: body mass index; CAT: COPD assessment test; CCQ: clinical COPD questionnaire; FEV1: forced expiratory volume in 1 s; FFMI: fat free mass index; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HADS-A: hospital anxiety and depression scale – anxiety; HADS-D: hospital anxiety and depression scale – depression; mMRC: modified Medical Research Council; P25: 25th percentile; P75: 75th percentile; SD: standard deviation.

[a] Some variables have missing values, as follows: 2 in pack-years, 1 in education, 2 in socioeconomic status, 1 in living with a partner, 2 in CCQ scores, 11 in any COPD exacerbation with hospital admission in previous 12 months, 39 in FFMI, 2 in anxiety, 4 in depression.

[b] Education: high school or higher vs maximum compulsory school.

[c] Socioeconomic status: non-manual skilled or higher vs manual skilled, partly skilled of unskilled occupations (IIIN, II and I vs IIIM, IV and V according to the National Statistics Socio-economic Classification).

[d] Marital status: living with a partner vs single, widowed or divorced.

[e] Working status: active worker (working full-time or part-time) vs unemployed, housework or retired.

[f] Average land-surface temperature within a 50-m buffer around the residence, derived from three land-surface temperature maps.

[g] The urban vulnerability index is a measure of socioeconomic status at the census tract level that combines demographic, economic, residential and subjective indicators, and ranges from lowest [0] to highest [1] level of neighbourhood vulnerability.

4. Discussion

This study observed that some urban environmental factors were associated with objective physical activity, physical activity experience and functional exercise capacity in COPD patients, specifically: (1) a higher population density was associated with fewer steps, more sedentary time and worse functional exercise capacity, and this association was stronger in COPD patients with symptoms of depression; (2) more pedestrian street length was associated with more steps and less sedentary time; (3) a steeper slope was associated with better functional

Table 2

Objective physical activity, physical activity experience and functional exercise capacity and environmental factors in 404 patients with mild-to-very severe COPD.

	All patients n = 404[a]
Physical activity and exercise capacity	
Step count (steps/day), m (SD)	7524 (4045)
Sedentary time (h/day), m (SD)	10.4 (1.6)
Physical activity experience (C-PPAC difficulty score, 0-more to 100-less difficulty), m (SD)	81.9 (14.6)
6MWD (metres), m (SD)	486 (95)
Environmental exposures	
Population density (habitants/km^2)[b], median (P25–P75)	31,284 (14,020–45344)
Pedestrian street length (metres)[c], median (P25–P75)	245.1 (50.5–517.5)
Slope (degrees)[d], median (P25–P75)	2.0 (1.2–3.5)
Noise (L_{den}, dB)[e], median (P25–P75)	63 (59–67)
NO_2 (µg/m^3)[f], median (P25–P75)	43.5 (35.0–48.7)
$PM_{2.5}$ (µg/m^3)[f], median (P25–P75)	12.6 (10.7–13.8)

C-PPAC: Clinical visit—PROactive Physical Activity in COPD (higher numbers indicate a better physical activity experience); L_{den}: day evening night sound level; 6MWD: 6-min walk distance; NO_2: nitrogen dioxide; PM: particulate matter; P25: 25th percentile; P75: 75th percentile; SD: standard deviation.

[a] Some variables have missing values, as follows: 93 in C-PPAC difficulty score, 1 in noise.

[b] Habitants per square kilometre within the census area.

[c] Sum of pedestrian street length within a 300-m buffer around the residence.

[d] Average slope of terrain within a 300-m buffer around the residence.

[e] Annual average levels of road traffic noise in the nearest street from the residence.

[f] Annual residential averages of NO_2 and $PM_{2.5}$.

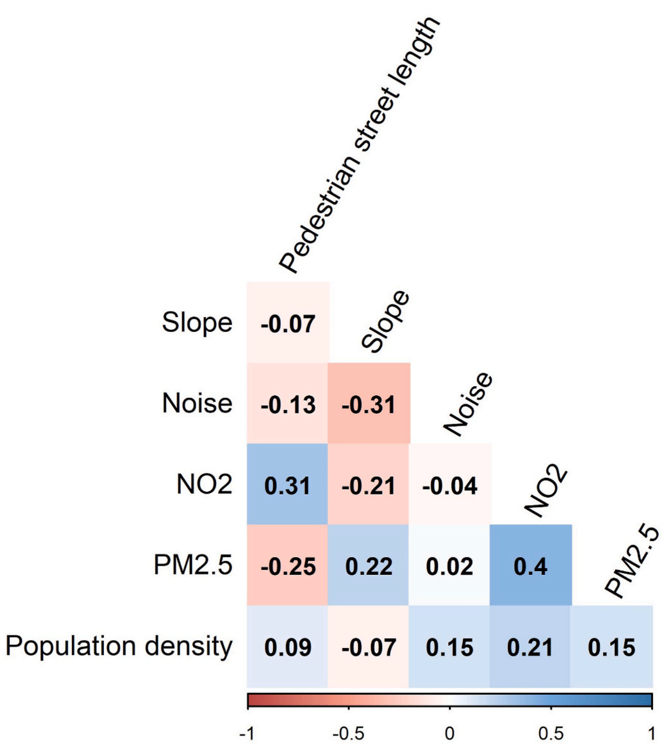

Fig. 1. Correlations between the environmental factors (Spearman correlation coefficients).

NO_2: nitrogen dioxide; PM: particulate matter.

exercise capacity but not with physical activity parameters; (4) higher long-term NO_2 exposure was associated with more sedentary time and more difficulty with physical activity, and this association could be partly mediated by dyspnoea; and (5) $PM_{2.5}$ and noise exposure were not associated with physical activity or exercise capacity.

A first striking result is that higher population density was associated with worse physical activity and capacity outcomes in COPD patients. This is in contrast with several previous studies that reported a positive association between population density and physical activity of older adults (Corseuil et al., 2016; Hino et al., 2020; Portegijs et al., 2017) and attributed this to a stimulating effect of a more liveable neighbourhood (i.e., more shops and services, better public transport) (Udell et al., 2014). However, we need to consider that those studies refer to cities with a lower population density. Barcelona (where 46% of our patients were recruited) is among one of the most densely populated cities of Europe (Population Stat, 2020; World population review, Barcelona. 2020). Indeed, the median population density for our study population was very high, above 30,000 habitants/km^2. In agreement with our results, other studies have found higher population density associated with lower physical activity (McCormack, 2017; Cerin et al., 2020) and hypothesised that extreme density may have negative effects on physical activity due to increased traffic hazards, fumes and noise. Indeed, our results support the latter thesis. We additionally speculate that the negative effect of high population density might be stronger in our patients due to their COPD. These patients report the need to take breaks or slow down during walking (Dobbels et al., 2014), which could deter them from walking in crowded environments. Additionally, the underlying chronic lung disease can impact negatively on the mood when practicing physical activity. We observed that the negative effect of high population density was much stronger in COPD patients with symptoms of depression. Although these findings are derived from *post hoc* analyses and are based on small numbers, they are in line with previous qualitative research reporting that the embarrassment caused by symptoms such as breathlessness and immobility in public was a personal barrier for physical activity in COPD patients (Kosteli et al., 2017).

Secondly, and in line with previous literature in the general older population (Cerin et al., 2017), we found pedestrian street length associated with higher physical activity (more steps and less sedentary time). Of note, the magnitude of the association in our study was small (around 150 steps and 3 min sedentary time/day per IQR change, i.e., 467 m within a 300-m buffer) but similar as the one observed for other built environment factors such as shop and service density, or sidewalk length in the general population (McCormack, 2017). There is debate on whether pedestrian street length is directly promoting more walking or whether this association could be explained by the fact that more pedestrian walkways reflect less air pollution. The fact that the association persisted in the multi-exposure models and that pedestrian street length and NO_2 exposure were positively correlated (Fig. 1) does not support this latter hypothesis. Unfortunately, we did not have any information on complementary features of pedestrian streets (e.g., benches, trees, or shadow/sun) which could have provided further insights (Cerin et al., 2017; Steinmetz-Wood et al., 2020). Finally, it has been reported that good pedestrian infrastructure may promote active commuting in the general population (Mäki-Opas et al., 2016) which in turn would increase physical activity levels (Rissel et al., 2012). Our sample was composed of a mostly retired population and our sensitivity analysis excluding active workers resulted in the loss of an association between pedestrian street length and physical activity (Appendix, Table A4), thus supporting that the observed association between pedestrian street length and physical activity could have been indeed driven by patients who were still working, and actively commuted to work.

Another novel finding was the association between steeper slope and better exercise capacity, which had not been tested before despite the clinical relevance of understanding determinants of exercise capacity. Hills are mostly perceived as a barrier to physical activity (Barnett et al., 2017). However, the very fact that walking on a slope is more strenuous than walking at an even level could actually help to protect the patients' functional exercise capacity. Actually, a validation study of urban trails for COPD patients (Arbillaga-Etxarri et al., 2016) showed that urban

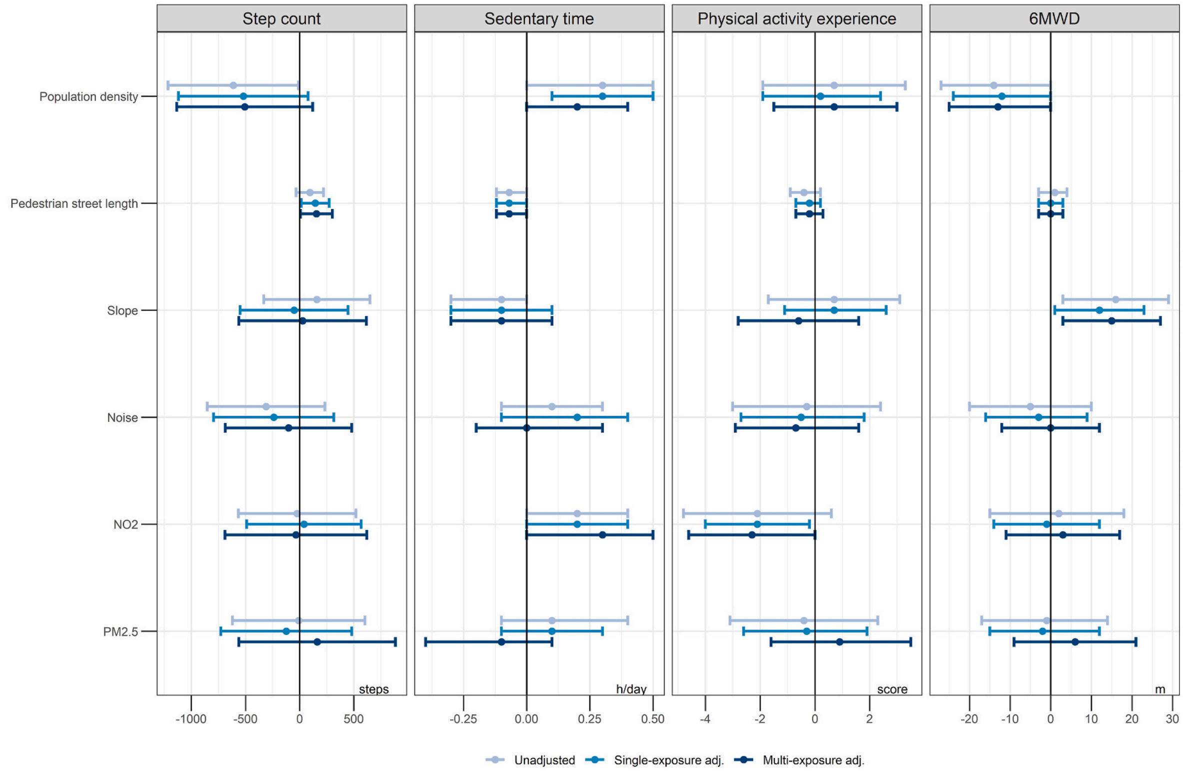

Fig. 2. Associations between the urban environmental factors, and objective physical activity, physical activity experience and functional exercise capacity in 387 patients with mild-to-very severe COPD.
See values in Appendix, Table A1.
Unadjusted models are mixed-effects linear regression models with a random intercept for city. Single-exposure models were adjusted for age, sex, socioeconomic status, urban vulnerability index, %predicted of FEV_1, CCQ mental score, exacerbation with hospital admission in previous 12 months and anxiety. Multi-exposure models were additionally adjusted for all other environmental exposures simultaneously.
6MWD: 6-min walk distance; NO_2: nitrogen dioxide; PM: particulate matter.

elements such as stairs and ramps indeed increased the exercise intensity in COPD patients as reflected by oxygen uptake (i.e., $\dot{V}O_2$), supporting the hypothesis that walking on hills can have a training effect. Evidence from the rehabilitation field shows that downhill walking training can positively affect leg strength in healthy participants (Rodio and Fattorini, 2014) and speed the response to rehabilitation in COPD patients (Camillo et al., 2020), attributable to the increased eccentric activity in the quadriceps femoris muscle (Camillo et al., 2015). Of note, the observed association in our study could be translated into an increase of 12.3 m in the 6MWD per an increase of 2.3° (which corresponds to a very gentle slope (Slope Steepness Index)). This effect appears relevant, given that a change of more than 30 m in the 6MWD is considered as clinically meaningful (Polkey et al., 2013). We therefore argue that COPD patients who live in a hilly neighbourhood may benefit from a "continuous training effect" and that slope has the potential to increase functional exercise capacity in these patients, which would impact in their regular physical activity (Troosters et al., 2019).

Our results showed that higher NO_2 was associated with more sedentary time and the experience of more difficulty with physical activity. These effects were consistent across different complementary and sensitivity analyses, which reinforces their plausibility, and is in line with the established harmful effects of NO_2 as an irritant to the human airways (Federal Register, 2018). However, when we excluded subjects with extreme values, the associations were attenuated suggesting that extremely high NO_2 levels may be especially harmful and drive the observed association. Several mechanisms are conceivable to explain how long-term air pollution in general could influence physical activity and capacity in COPD patients: First, higher levels of air pollution could increase dyspnoea in COPD patients (Schraufnagel et al., 2019). To avoid the feeling of breathlessness, COPD patients often reduce exertion which leads to deconditioning with a decline in functional exercise capacity and further dyspnoea (Ramon et al., 2018; Reardon et al., 2006); increased pollution could thus trigger the 'vicious circle of dyspnoea and inactivity' (Ramon et al., 2018; Reardon et al., 2006). While the sample size and lack of repeated measurements precluded a formal mediation analysis, we found that the effect of NO_2 on sedentary time and C-PPAC difficulty score was attenuated when we added dyspnoea to the analysis, which indirectly supports this hypothesis. Second, patients may be aware of the potential harms associated with air pollution and may therefore avoid to walk in neighbourhoods with more intense traffic (Exercise and air quality: 10 top tips - European Lung Foundation). Finally, exacerbations and hospital admissions due to air pollution could lead to a decrease in physical activity and functional exercise capacity (Alahmari et al., 2014; Demeyer et al., 2018). However, the fact that the association persisted in our models which adjusted for acute COPD exacerbations with hospital admission in the previous twelve months, suggests that the latter mechanism is only of secondary importance.

Of interest, only NO_2 (an indicator of traffic related air pollution) was associated with physical activity in our study while $PM_{2.5}$ (indicator of pollution more generally) was not. Whether this was due to the fact that NO_2 levels deviated more than $PM_{2.5}$ levels from the WHO and EU recommendations, that NO_2 could be a surrogate for pollution with other traffic related constituents such as NO_x, O_3 and ammonium nitrate aerosols thereby reflecting a higher true burden (Johannson et al., 2015; Schraufnagel et al., 2019), or that NO_2 could exert a specific (and more harmful) effect in COPD patients (Dadvand et al., 2014a; Lepeule et al., 2014; Morrow et al., 1992) remains speculative.

We found no association between noise and any of the physical activity or capacity variables. To our knowledge no study has assessed this association in COPD patients so far. A few studies have previously explored this association in the general population and observed that noise and noise annoyance (Dzhambov et al., 2017; Foraster et al., 2016; Roswall et al., 2017) were negatively associated with physical activity, particularly among patients with a chronic disease. Unfortunately, we do not have any information on noise annoyance for the present study. Whether noise levels alone are not sensitive enough to determine an effect on physical activity in COPD patients or whether noise has less impact on COPD patients due to their underlying disease, will need to be addressed in future studies. The low correlation between noise and air pollutants may seem surprising and could raise doubts on the validity of noise measures. However, it is not unexpected based on the existing literature. Although engine combustion of vehicles is a common source for both noise and air pollution, factors such as road layout and urban planning and a different propagation mode have been shown to impact their exposure levels (Stansfeld, 2015).

Our findings have implications for research, clinical management and urban health policy. First, previous research on the environment was mostly focusing on the general population whilst often ignoring patients with a chronic condition who represent around 35% of the current city population in Europe (Eurostat), something to address in future studies. Second, research on physical activity interventions needs to consider the importance of calibrating the specific role of the environment in the physical activity with the needs of COPD patients and eventually of subjects with other chronic conditions. Specifically, it will be interesting to explore further the likely ‘utilitarian’ role of pedestrian streets (i.e., higher density of stores, shops and services) (Sugiyama et al., 2012) as well as features of the micro-scale environment (e.g., the availability and condition of benches) (Steinmetz-Wood et al., 2020)) and how these can be integrated into interventions to promote physical activity. Third, the patients’ feelings of vulnerability associated with the chronic disease (such as breathlessness or shame to be seen with limited mobility in COPD) may counteract the positive effects of environmental factors (e.g., liveable streets) observed in the general population. The clinical management of COPD patients will need to address such potential barriers to physical activity (especially in those with mental health issues), and advise patients to consider walking in hilly neighbourhoods (to improve functional exercise capacity) and in less polluted areas or hours (to increase the physical activity and mitigate the negative effects of traffic related air pollution) (Carlsten et al., 2020). Finally, urban health policy must aim for an environment which is adequate (e.g., walkable yet not too crowded) for the specific needs of patients with a chronic disease such as COPD and for rigorous control of air pollution. The chronic disease certainly entails a particular lens through which the environment is perceived and which influences patients’ behaviour. The understanding of this lens should be at the forefront of future research, COPD management and policy measures.

One of the strengths of our study is the novelty of our research question in COPD patients. We recruited patients with a broad range of COPD severities from several primary care and hospital centres which increases the external validity of our findings. We included a range of objectively measured variables to characterise both the exposures and the outcomes thereby reducing information bias. The use of LUR models for air pollution and geocoding of the home address allowed us to assess individual-level exposure and gain further insight into the distinct roles of NO_2 and $PM_{2.5}$. The multi-exposure models allowed us to control for residual confounding by the other environmental factors and to assess the specific effect of the factors within the overall neighbourhood context.

A limitation of the present study is that some features of the environment which may also influence physical activity behaviour (neighbourhood safety, design, street connectivity, land use mix, facility or residential density) (Cerin et al., 2018; Frank et al., 2005; Salvo et al., 2018; Udell et al., 2014) were not available in our dataset. [Of note, we did not include greenspace variables in our analyses because these had been assessed and reported for this patient cohort previously (Arbillaga-Etxarri et al., 2017).] Moreover, we do not report other common pollutants such as PM_{10} or O_3. Indeed, we decided a priori to focus on NO_2 and $PM_{2.5}$ under the hypothesis that they capture well traffic related air pollution and urban pollution more generally. Secondly, the exposure variables data was not directly measured in our study, but obtained from external sources, and there may be some misclassification due to temporal variations. Specifically, population density, pedestrian street length, slope and annual average noise levels referred to a fixed time point ranging from 1 year before to 1 year after data collection. We consider improbable this has biased our estimates as these variables are stable over time in the absence of major urban changes or migration waves and unlikely to change during such short study period. Therefore, these exposure estimates are probably representative of exposure prior to the study. Thirdly, the use of annual residential averages does not allow us to accurately estimate the real exposure to e.g., air pollutants or noise during physical activity. Particularly, if patients living in more polluted/noisy areas used to practice physical activity in the evenings when pollution and noise are lower, our estimates of exposure would be higher than the real, and this would be underestimating the real association between exposures and physical activity. Fourthly, it could be speculated that some of the environmental factors assessed could act more as a mediator than as an independent risk factor themselves (e.g., higher population density may lead to more air pollution and noise). However, the associations of the individual factors were similar in the single-exposure and multi-exposure models. Finally, our design limits conclusions on directionality of the associations and also makes it difficult to rule out self-selection bias concerning the choice of the residential neighbourhood. However, the relatively low socioeconomic status of our sample makes it unlikely that our patients moved due to their COPD.

5. Conclusion

In conclusion, population density, pedestrian street length, slope and NO_2 exposure relate to physical activity and exercise capacity of COPD patients living in highly populated areas. These neighbourhood environmental factors should be considered in clinical contacts with patients and when developing urban and transport planning policies that aim to promote physical activity in patients with chronic diseases.

Author contributions (credit roles)

Maria Koreny: Conceptualisation; Data curation; Formal analysis; Methodology; Visualisation; Writing – original draft; Writing - review editing; **Ane Arbillaga-Etxarri**: Conceptualisation; Data curation; Funding acquisition; Investigation; Writing - review editing; **Magda Bosch de Basea**: Methodology; Writing - review editing; **Maria Foraster**: Conceptualisation; Data curation; Formal analysis; Funding acquisition; Methodology; Supervision; Visualisation; Writing - review editing; **Anne-Elie Carsin**: Data curation; Formal analysis; Methodology; Supervision; Validation; Visualisation; Writing - review editing; **Marta Cirach**: Data curation; Investigation; Writing - review editing; **Elena Gimeno-Santos**: Conceptualisation; Funding acquisition; Investigation; Writing - review editing; **Anael Barberan-Garcia**: Conceptualisation; Funding acquisition; Investigation; Writing - review editing; **Mark Nieuwenhuijsen**: Resources; Writing - review editing; **Pere Vall-Casas**: Conceptualisation; Funding acquisition; Writing - review editing; **Robert Rodriguez-Roisín**: Conceptualisation; Funding acquisition; Resources; Writing - review editing; **Judith Garcia-Aymerich**: Conceptualisation; Formal analysis; Funding acquisition; Methodology; Project administration; Resources; Supervision; Visualisation; Roles/Writing - original draft; Writing - review editing.

Funding

The Urban Training study was funded by grants from Fondo de Investigación Sanitaria, Instituto de Salud Carlos III (ISCIII, PI11/01283 and PI14/0419), integrated into Plan Estatal I + D + I 2013–2016 and co-funded by ISCIII-Subdirección General de Evaluación y Fomento de la Investigación and Fondo Europeo de Desarrollo Regional (FEDER); Sociedad Española de Neumología y Cirugía Torácica (SEPAR, 147/2011 and 201/2011), Societat Catalana de Pneumologia (Ajuts al millor projecte en fisioteràpia respiratòria 2013). We acknowledge support from the Spanish Ministry of Science and Innovation through the "Centro de Excelencia Severo Ochoa 2019–2023" Program (CEX 2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Program. MF is beneficiary of an AXA Research Fund grant.

The funders had no role in study design, data collection, analysis or interpretation, writing of the report, nor in the decision to submit the article for publication.

Acknowledgements

The Urban Training study group

ISGlobal, Barcelona: Ane Arbillaga-Etxarri, Marta Benet, Anna Delgado, Judith Garcia-Aymerich, Elena Gimeno-Santos, Jaume Torrent-Pallicer; FCS Blanquerna, Universitat Ramon Llull, Barcelona: Jordi Vilaró; Servei de Pneumologia, Hospital Clínic de Barcelona, Barcelona: Anael Barberan-Garcia, Robert Rodriguez-Roisín; Hospital del Mar, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Barcelona: Eva Balcells, Diego A Rodríguez Chiaradía; Hospital Universitari Germans Trias i Pujol, Badalona: Alicia Marín; Hospital de Mataró, Consorci Sanitari del Maresme, Mataró: Pilar Ortega; Hospital de Viladecans, Viladecans: Nuria Celorrio; Institut Universitari d'Investigació en Atenció Primària Jordi Gol (IDIAP Jordi Gol): Mónica Monteagudo, Nuria Montellà, Laura Muñoz, Pere Toran; Centre d'Atenció Primària Viladecans 2, Institut Català de la Salut, Viladecans: Pere Simonet; Centre d'Atenció Primària Passeig de Sant Joan, Institut Català de la Salut, Barcelona: Carme Jané, Carlos Martín-Cantera; Centre d'Atenció Primària Sant Roc, Institut Català de la Salut, Badalona: Eulàlia Borrell; Universitat Internacional de Catalunya (UIC), Barcelona: Pere Vall-Casas.

Data statement

Data contain potentially identifying variables. For example, built environment variables together with sociodemographics and clinical conditions could allow identification of patients in some geographic areas. Therefore, data cannot be made publicly available according to the Regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data. The corresponding author and the Coordination and Research Management Office of the Projects Unit (research.management@isglobal.org) could provide, upon request, individual participant data that underlie some of the results reported in this article (except variables that may allow identification of patients), after applying necessary measures to guarantee that no individual is identified or identifiable.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Elena Gimeno-Santos reports a relationship with Chiesi and Boehringer Ingelheim that includes: speaking and lecture fees. Judith Garcia-Aymerich reports a relationship with AstraZeneca that includes: consulting or advisory and speaking and lecture fees. Judith Garcia-Aymerich reports a relationship with Esteve and Chiesi that includes: speaking and lecture fees. Robert Rodriguez-Roisin reports a relationship with Chiesi that includes: consulting or advisory and speaking and lecture fees. Maria Foraster is beneficiary of an AXA Research Fund grant.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.113956.

References

Alahmari, A.D., Patel, A.R., Kowlessar, B.S., Mackay, A.J., Singh, R., Wedzicha, J.A., et al., 2014. Daily activity during stability and exacerbation of chronic obstructive pulmonary disease. BMC Pulm. Med. 14 (98), 1–8. https://doi.org/10.1186/1471-2466-14-98.

Alahmari, A.D., Mackay, A.J., Patel, A.R.C., Kowlessar, B.S., Singh, R., Brill, S.E., et al., 2015. Influence of weather and atmospheric pollution on physical activity in patients with COPD. Respir. Res. 16, 71. https://doi.org/10.1186/s12931-015-0229-z.

An, R., Zhang, S., Ji, M., Guan, C., 2018. Impact of ambient air pollution on physical activity among adults: a systematic review and meta-analysis. Perspect Public Health 138, 111–121. https://doi.org/10.1177/1757913917726567.

Annegarn, J., Spruit, M.A., Savelberg, H.H.C.M., Willems, P.J.B., van de Bool, C., Schols, A.M.W.J., et al., 2012. Differences in walking pattern during 6-min walk test between patients with COPD and healthy subjects. PLoS One 7, e37329. https://doi.org/10.1371/journal.pone.0037329.

Arbillaga-Etxarri, A., Torrent-Pallicer, J., Gimeno-Santos, E., Barberan-Garcia, A., Delgado, A., Balcells, E., et al., 2016. Validation of walking trails for the urban TrainingTM of chronic obstructive pulmonary disease patients. PLoS One 11, e0146705. https://doi.org/10.1371/journal.pone.0146705.

Arbillaga-Etxarri, A., Gimeno-Santos, E., Barberan-Garcia, A., Benet, M., Borrell, E., Dadvand, P., et al., 2017. Socio-environmental correlates of physical activity in patients with chronic obstructive pulmonary disease (COPD). Thorax 72, 796–802. https://doi.org/10.1136/thoraxjnl-2016-209209.

Arbillaga-Etxarri, A., Gimeno-Santos, E., Barberan-Garcia, A., Balcells, E., Benet, M., Borrell, E., et al., 2018. Long-term efficacy and effectiveness of a behavioural and community-based exercise intervention (Urban Training) to increase physical activity in patients with COPD: a randomised controlled trial. Eur. Respir. J. 52, 1800063 https://doi.org/10.1183/13993003.00063-2018.

Atlas of Urban Vulnerability in Spain. Available: https://atlasvulnerabilidadurbana.mitma.es/#c=home [accessed 20 October 2018].

ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002. ATS statement: guidelines for the six-minute walk test. Am. J. Respir. Crit. Care Med. 166, 111–117. https://doi.org/10.1164/ajrccm.166.1.at1102.

Barnett, D.W., Barnett, A., Nathan, A., Van Cauwenberg, J., Cerin, E., 2017. Built environmental correlates of older adults' total physical activity and walking: a systematic review and meta-analysis. Int. J. Behav. Nutr. Phys. Activ. 14, 103. https://doi.org/10.1186/s12966-017-0558-z.

Bauman, A.E., Reis, R.S., Sallis, J.F., Wells, J.C., F Loos, R.J., Martin, B.W., et al., 2012. Correlates of physical activity: why are some people physically active and others not? Lancet 380, 258–271. https://doi.org/10.1016/S0140-6736(12)60735-1.

Beelen, R., Hoek, G., Vienneau, D., Eeftens, M., Dimakopoulou, K., Pedeli, X., et al., 2013. Development of NO2 and NOx land use regression models for estimating air pollution exposure in 36 study areas in Europe - the ESCAPE project. Atmos. Environ. 72, 10–23. https://doi.org/10.1016/j.atmosenv.2013.02.037.

Camillo, C.A., Burtin, C., Hornikx, M., Demeyer, H., De Bent, K., Van Remoortel, H., et al., 2015. Physiological responses during downhill walking: a new exercise modality for subjects with chronic obstructive pulmonary disease. Chron. Respir. Dis. 12, 155–164. https://doi.org/10.1177/1479972315575717.

Camillo, C.A., Osadnik, C.R., Burtin, C., Everaerts, S., Hornikx, M., Demeyer, H., et al., 2020. Effects of downhill walking in pulmonary rehabilitation for patients with COPD: a randomised controlled trial. Eur. Respir. J. 56, 2000639 https://doi.org/10.1183/13993003.00639-2020.

Carlsten, C., Salvi, S., Wong, G.W.K., Chung, K.F., 2020. Personal strategies to minimise effects of air pollution on respiratory health: advice for providers, patients and the public. Eur. Respir. J. 55, 1902056 https://doi.org/10.1183/13993003.02056-2019.

Celli, B.R., Macnee, W., Agusti, A., Anzueto, A., Berg, B., Buist, A.S., et al., 2004. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur. Respir. J. 23, 932–946. https://doi.org/10.1183/09031936.04.00014304.

Cerin, E., Nathan, A., van Cauwenberg, J., Barnett, D.W., Barnett, A., 2017. The neighbourhood physical environment and active travel in older adults: a systematic review and meta-analysis. Int. J. Behav. Nutr. Phys. Activ. 14, 15. https://doi.org/10.1186/s12966-017-0471-5.

Cerin, E., Conway, T.L., Adams, M.A., Barnett, A., Cain, K.L., Owen, N., et al., 2018. Objectively-assessed neighbourhood destination accessibility and physical activity in adults from 10 countries: an analysis of moderators and perceptions as mediators. Soc. Sci. Med. 211, 282–293. https://doi.org/10.1016/j.socscimed.2018.06.034.

Cerin, E., Barnett, A., Zhang, C.J.P., Lai, P.C., Sit, C.H.P., Lee, R.S.Y., 2020. How urban densification shapes walking behaviours in older community dwellers: a cross-sectional analysis of potential pathways of influence. Int. J. Health Geogr. 19, 14. https://doi.org/10.1186/s12942-020-00210-8.

Corseuil, W., Schneider, G., Weber, M., Giehl, C., Hallal, P.C., Corseuil, C.W., et al., 2016. Built environment and walking behavior among Brazilian older adults: a population-based study. J. Phys. Activ. Health 13, 617–624. https://doi.org/10.1123/jpah.2015-0355.
Cyrys, J., Eeftens, M., Heinrich, J., Ampe, C., Armengaud, A., Beelen, R., et al., 2012. Variation of NO2 and NOx concentrations between and within 36 European study areas: results from the ESCAPE study. Atmos. Environ. 62, 374–390. https://doi.org/10.1016/j.atmosenv.2012.07.080.
Dadvand, P., Nieuwenhuijsen, M.J., Agustí, À., De Batlle, J., Benet, M., Beelen, R., et al., 2014a. Air pollution and biomarkers of systemic inflammation and tissue repair in COPD patients. Eur. Respir. J. 44, 603–613. https://doi.org/10.1183/09031936.00168813.
Dadvand, P., Ostro, B., Figueras, F., Foraster, M., Basagaña, X., Valentín, A., et al., 2014b. Residential proximity to major roads and term low birth weight: the roles of air pollution, heat, noise, and road-adjacent trees. Epidemiology 25, 518–525. https://doi.org/10.1097/EDE.0000000000000107.
Demeyer, H., Costilla-frias, M., Louvaris, Z., Gimeno-Santos, E., Tabberer, M., Rabinovich, R.A., et al., 2018. Both moderate and severe exacerbations accelerate physical activity decline in COPD patients. Eur. Respir. J. 51, 1702110 https://doi.org/10.1183/13993003.02110-2017.
Demeyer, H., Donaire-Gonzalez, D., Gimeno-Santos, E., Ramon, M.A., De Battle, J., Benet, M., et al., 2019. Physical activity is associated with attenuated disease progression in chronic obstructive pulmonary disease. Med. Sci. Sports Exerc. 51, 833–840. https://doi.org/10.1249/MSS.0000000000001859.
Ding, D., Adams, M.A., Sallis, J.F., Norman, G.J., Hovell, M.F., Chambers, C.D., et al., 2013. Perceived neighborhood environment and physical activity in 11 countries: do associations differ by country? Int. J. Behav. Nutr. Phys. Activ. 10, 1–11. https://doi.org/10.1186/1479-5868-10-57.
Dobbels, F., de Jong, C., Drost, E., Elberse, J., Feridou, C., Jacobs, L., et al., 2014. The PROactive innovative conceptual framework on physical activity. Eur. Respir. J. 44, 1223–1233. https://doi.org/10.1183/09031936.00004814.
Donaire-Gonzalez, D., Gimeno-Santos, E., Balcells, E., Rodríguez, D.A., Farrero, E., De Batlle, J., et al., 2013. Physical activity in COPD patients: patterns and bouts. Eur. Respir. J. 42, 993–1002. https://doi.org/10.1183/09031936.00101512.
Dzhambov, A., Tilov, B., Markevych, I., Dimitrova, D., 2017. Residential road traffic noise and general mental health in youth: the role of noise annoyance, neighborhood restorative quality, physical activity, and social cohesion as potential mediators. Environ. Int. 109, 1–9. https://doi.org/10.1016/j.envint.2017.09.009.
Eeftens, M., Beelen, R., De Hoogh, K., Bellander, T., Cesaroni, G., Cirach, M., et al., 2012a. Development of land use regression models for PM2.5, PM 2.5 absorbance, PM10 and PMcoarse in 20 European study areas; Results of the ESCAPE project. Environ. Sci. Technol. 46, 11195–11205. https://doi.org/10.1021/es301948k.
Eeftens, M., Tsai, M.Y., Ampe, C., Anwander, B., Beelen, R., Bellander, T., et al., 2012b. Spatial variation of PM2.5, PM10, PM2.5 absorbance and PMcoarse concentrations between and within 20 European study areas and the relationship with NO2 - results of the ESCAPE project. Atmos. Environ. 62, 303–317. https://doi.org/10.1016/j.atmosenv.2012.08.038.
Erratum in ATS statement: guidelines for the six-minute walk test. Am. J. Respir. Crit. Care Med. 193, 2016, 1185. https://doi.org/10.1164/rccm.19310erratum.
ESRI, 2012. ArcGIS 10 (Desktop, engine, server) service pack 4 - English. Available: https://support.esri.com/es/download/1843. (Accessed 17 June 2021).
Eurostat. Available: https://ec.europa.eu/eurostat [accessed 19 June 2021].
Exercise and air quality: 10 top tips - European Lung Foundation. Available: https://europeanlung.org/en/information-hub/factsheets/exercise-and-air-quality-10-top-tips/[accessed 1 June 2021].
Federal Register, 2018. Environmental protection agency (EPA). Review of the primary national ambient air quality standards for oxides of nitrogen. Available: https://www.federalregister.gov/documents/2018/04/18/2018-07741/review-of-the-primary-national-ambient-air-quality-standards-for-oxides-of-nitrogen. (Accessed 2 June 2021).
Foraster, M., Eze, I.C., Vienneau, D., Brink, M., Cajochen, C., Caviezel, S., et al., 2016. Long-term transportation noise annoyance is associated with subsequent lower levels of physical activity. Environ. Int. 91, 341–349. https://doi.org/10.1016/j.envint.2016.03.011.
Frank, L.D., Schmid, T.L., Sallis, J.F., Chapman, J., Saelens, B.E., 2005. Linking objectively measured physical activity with objectively measured urban form: findings from SMARTRAQ. Am. J. Prev. Med. 28, 117–125. https://doi.org/10.1016/j.amepre.2004.11.001.
Garcia-Aymerich, J., Puhan, M.A., Corriol-Rohou, S., De Jong, C., Demeyer, H., Dobbels, F., et al., 2021. Validity and responsiveness of the daily- and clinical visit-PROactive physical activity in COPD (D-PPAC and C-ppac) instruments. Thorax 0, 1–11. https://doi.org/10.1136/thoraxjnl-2020-214554.
Gimeno-Santos, E., Frei, A., Steurer-Stey, C., De Batlle, J., Rabinovich, R.A., Raste, Y., et al., 2014. Determinants and outcomes of physical activity in patients with COPD: a systematic review on behalf of PROactive consortium. Thorax 69, 731–739. https://doi.org/10.1136/thoraxjnl-2013-204763.
Gimeno-Santos, E., Raste, Y., Demeyer, H., Louvaris, Z., De Jong, C., Rabinovich, R.A., et al., 2015. The PROactive instruments to measure physical activity in patients with chronic obstructive pulmonary disease. Eur. Respir. J. 46, 988–1000. https://doi.org/10.1183/09031936.00183014.
Hino, K., Usui, H., Hanazato, M., 2020. Three-year longitudinal association between built environmental factors and decline in older adults' step count: gaining insights for age-friendly urban planning and design. Int. J. Environ. Res. Publ. Health 17, 1–11. https://doi.org/10.3390/ijerph17124247.
Holland, A.E., Spruit, M.A., Singh, S.J., 2015. How to carry out a field walking test in chronic respiratory disease. Breathe 11, 129–139. https://doi.org/10.1183/20734735.021314.
ICGC, 2012. Topographic base of Catalonia. Available: https://www.icgc.cat/en/Public-Administration-and-Enterprises/Downloads/Topographic-cartography/Topographic-base-of-Catalonia-1-5-000. (Accessed 4 June 2020).
INE, 2016. Instituto nacional de Estadística/national Statistics Institute. Available: https://www.ine.es/dynt3/inebase/es/index.htm?type=pcaxis&file=pcaxis&path=%2Ft20%2Fe245%2Fp07%2F%2Fa2016. (Accessed 4 June 2020).
Johannson, K.A., Balmes, J.R., Collard, H.R., 2015. Air pollution exposure: a novel environmental risk factor for interstitial lung disease? Chest 147, 1161–1167. https://doi.org/10.1378/chest.14-1299.
Kosteli, M.-C., Heneghan, N.R., Roskell, C., Williams, S.E., Adab, P., Dickens, A.P., et al., 2017. Barriers and enablers of physical activity engagement for patients with COPD in primary care. Int. J. Chronic Obstr. Pulm. Dis. 12, 1019–1031. https://doi.org/10.2147/COPD.S119806.
Lepeule, J., Bind, M.A.C., Baccarelli, A.A., Koutrakis, P., Tarantini, L., Litonjua, A., et al., 2014. Epigenetic influences on associations between air pollutants and lung function in elderly men: the normative aging study. Environ. Health Perspect. 122, 566–572. https://doi.org/10.1289/ehp.1206458.
Mäki-Opas, T.E., Borodulin, K., Valkeinen, H., Stenholm, S., Kunst, A.E., Abel, T., et al., 2016. The contribution of travel-related urban zones, cycling and pedestrian networks and green space to commuting physical activity among adults - a cross-sectional population-based study using geographical information systems. BMC Publ. Health 16, 760. https://doi.org/10.1186/s12889-016-3264-x.
Manual de Procedimientos SEPAR, 4. Available: https://issuu.com/separ/docs/procedimientos4. (Accessed 18 November 2020).
Mapes estrategics del soroll, 2012. Dir gen qual ambient dep territ i sostenibilitat general Catalunya. Available: https://www.diba.cat/web/carreteres-locals-i-mobilitat/mapes-estrategics-del-soroll. (Accessed 1 October 2020).
McCormack, G.R., 2017. Neighbourhood built environment characteristics associated with different types of physical activity in Canadian adults. Heal Promot Chronic Dis Prev Canada 37, 175–185. https://doi.org/10.24095/hpcdp.37.6.01.
Morrow, P.E., Utell, M.J., Bauer, M.A., Smeglin, A.M., Frampton, M.W., Cox, C., et al., 1992. Pulmonary performance of elderly normal subjects and subjects with chronic obstructive pulmonary disease exposed to 0.3 ppm nitrogen dioxide. Am. Rev. Respir. Dis. 145, 291–300. https://doi.org/10.1164/ajrccm/145.2_pt_1.291.
Pitta, F., Troosters, T., Spruit, M.A., Probst, V.S., Decramer, M., Gosselink, R., 2005. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. 171, 972–977. https://doi.org/10.1164/rccm.200407-855OC.
Polkey, M.I., Spruit, M.A., Edwards, L.D., Watkins, M.L., Pinto-Plata, V., Vestbo, J., et al., 2013. Six-minute-walk test in chronic obstructive pulmonary disease: minimal clinically important difference for death or hospitalization. Am. J. Respir. Crit. Care Med. 187, 382–386. https://doi.org/10.1164/rccm.201209-1596OC.
Population Stat, Barcelona, Spain, 2020. Available: https://populationstat.com/spain/barcelona. (Accessed 4 August 2020).
Portegijs, E., Keskinen, K.E., Tsai, L.T., Rantanen, T., Rantakokko, M., 2017. Physical limitations, walkability, perceived environmental facilitators and physical activity of older adults in Finland. Int. J. Environ. Res. Publ. Health 14, 333. https://doi.org/10.3390/ijerph14030333.
Rabinovich, R.A., Louvaris, Z., Raste, Y., Langer, D., Van Remoortel, H., Giavedoni, S., et al., 2013. Validity of physical activity monitors during daily life in patients with COPD. Eur. Respir. J. 42, 1205–1215. https://doi.org/10.1183/09031936.00134312.
Ramon, M.A., Riet, G Ter, Carsin, A.E., Gimeno-Santos, E., Agustí, A., Antó, J.M., et al., 2018. The dyspnoea–inactivity vicious circle in COPD: development and external validation of a conceptual model. Eur. Respir. J. 52, 1800079 https://doi.org/10.1183/13993003.00079-2018.
Reardon, J.Z., Lareau, S.C., ZuWallack, R., 2006. Functional status and quality of life in chronic obstructive pulmonary disease. Am. J. Med. 119, 32–37. https://doi.org/10.1016/j.amjmed.2006.08.005.
Rissel, C., Curac, N., Greenaway, M., Bauman, A., 2012. Physical activity associated with public transport use-a review and modelling of potential benefits. Int. J. Environ. Res. Publ. Health 9, 2454–2478. https://doi.org/10.3390/ijerph9072454.
Rodio, A., Fattorini, L., 2014. Downhill walking to improve lower limb strength in healthy young adults. Eur. J. Sport Sci. 14, 806–812. https://doi.org/10.1080/17461391.2014.908958.
Roswall, N., Ammitzbøll, G., Christensen, J.S., Raaschou-Nielsen, O., Jensen, S.S., Tjønneland, A., et al., 2017. Residential exposure to traffic noise and leisure-time sports – a population-based study. Int. J Hyg Environ. Health 220, 1006–1013. https://doi.org/10.1016/j.ijheh.2017.05.010.
Salvo, G., Lashewicz, B.M., Doyle-Baker, P.K., McCormack, G.R., 2018. Neighbourhood built environment influences on physical activity among adults: a systematized review of qualitative evidence. Int. J. Environ. Res. Publ. Health 15, 897. https://doi.org/10.3390/ijerph15050897.
Schraufnagel, D.E., Balmes, J.R., Cowl, C.T., De Matteis, S., Jung, S.-H., Mortimer, K., et al., 2019. Air pollution and noncommunicable diseases A review by the forum of international respiratory societies' environmental committee, Part 2: air pollution and organ systems. Chest 155, 417–426. https://doi.org/10.1016/j.chest.2018.10.041.
Shrikrishna, D., Patel, M., Tanner, R.J., Seymour, J.M., Connolly, B.A., Puthucheary, Z. A., et al., 2012. Quadriceps wasting and physical inactivity in patients with COPD. Eur. Respir. J. 40, 1115–1122. https://doi.org/10.1183/09031936.00170111.
Slope steepness index. Available: https://geographyfieldwork.com/SlopeSteepnessIndex.htm. (Accessed 4 August 2020).

Snaith, R.P., 2003. The hospital anxiety and depression scale. Health Qual. Life Outcome 1, 29. https://doi.org/10.1186/1477-7525-1-29.

Soriano, J.B., Abajobir, A.A., Abate, K.H., Abera, S.F., Agrawal, A., Ahmed, M.B., et al., 2017. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir. Med. 5, 691–706. https://doi.org/10.1016/S2213-2600(17)30293-X.

Stansfeld, S.A., 2015. Noise effects on health in the context of air pollution exposure. Int. J. Environ. Res. Publ. Health 12, 12735–12760. https://doi.org/10.3390/ijerph121012735.

Steinmetz-Wood, M., El-Geneidy, A., Ross, N.A., 2020. Moving to policy-amenable options for built environment research: the role of micro-scale neighborhood environment in promoting walking. Health Place 66, 102462. https://doi.org/10.1016/j.healthplace.2020.102462.

Sugiyama, T., Neuhaus, M., Cole, R., Giles-Corti, B., Owen, N., 2012. Destination and route attributes associated with adults' walking: a review. Med. Sci. Sports Exerc. 44, 1275–1286. https://doi.org/10.1249/MSS.0b013e318247d286.

Troosters, T., Blondeel, A., Rodrigues, F.M., Janssens, W., Demeyer, H., 2019. Strategies to increase physical activity in chronic respiratory diseases. Clin. Chest Med. 40, 397–404. https://doi.org/10.1016/j.ccm.2019.02.017.

Udell, T., Daley, M., Johnson, B., Tolley, D.R., 2014. Does Density Matter? the Role of Density in Creating Walkable Neighbourhoods. National Heart Foundation of Australia, Melbourne, Australia.

Van Remoortel, H., Raste, Y., Louvaris, Z., Giavedoni, S., Burtin, C., Langer, D., et al., 2012. Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. PLoS One 7, e39198. https://doi.org/10.1371/journal.pone.0039198.

Van Remoortel, H., Hornikx, M., Demeyer, H., Langer, D., Burtin, C., Decramer, M., et al., 2013. Daily physical activity in subjects with newly diagnosed COPD. Thorax 68, 962–963. https://doi.org/10.1136/thoraxjnl-2013-203534.

Vestbo, J., Hurd, S.S., Agustí, A.G., Jones, P.W., Vogelmeier, C., Anzueto, A., et al., 2013. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am. J. Respir. Crit. Care Med. 187, 347–365. https://doi.org/10.1164/rccm.201204-0596PP.

Witten, K., Blakely, T., Bagheri, N., Badland, H., Ivory, V., Pearce, J., et al., 2012. Neighborhood built environment and transport and leisure physical activity: findings using objective exposure and outcome measures in New Zealand. Environ. Health Perspect. 120, 971–977. https://doi.org/10.1289/ehp.1104584.

World population review, Barcelona, 2020. Available: https://worldpopulationreview.com/world-cities/barcelona-population. (Accessed 31 August 2020).

Zigmond, A.S., Snaith, R.P., 1983. The Hospital Anxiety and Depression Scale. Acta Psychiatr. Scand. 67, 361–370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x.