Roles of the physical environment in health-related quality of life in patients with chronic obstructive pulmonary disease

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ABSTRACT

Rationale: Many clinical and psychological factors are known to influence the health-related quality of life (HRQL) in chronic obstructive pulmonary disease (COPD). However, research on whether environmental factors, such as air pollution, noise, temperature, and blue/green spaces also influence HRQL in COPD has not been systematically investigated.

Objective: To assess the relationship between air pollution, road traffic noise, temperature, and distance to blue/green spaces and respiratory-specific HRQL in COPD.

Methods: We used cross-sectional data from a multicenter study in 407 stable mild-to-very severe COPD patients from Barcelona (Catalonia). Patients answered the COPD Assessment Test (CAT) and Clinical COPD Questionnaire (CCQ). Individual residential exposure to air pollutants (nitrogen dioxide [NO_2] and particulate matters of varying aerodynamic diameters [$PM_{2.5}$, PM_{10}, and $PM_{2.5absorbance}$]), road traffic noise (L_{den}), and land surface temperature were estimated using long-term averages from land-use regression models, 24-h noise maps, and land surface temperature maps, respectively. We measured residential distances to blue/green spaces from the Urban Atlas. We used mixed-effect negative binomial (for CAT) and linear (for CCQ) regression models, adjusted for potential confounders, with a random effect by center.

Results: Of those patients, 85% were male and had a mean (SD) age of 69 (9) years, CAT score of 12 (7), CCQ-total score of 1.4 (1.0), and post-bronchodilator forced expiratory volume in 1 second (FEV_1) of 57 (18) %predicted. We found that NO_2 and $PM_{2.5absorbance}$ were associated with worsened CAT and CCQ-mental scores, e.g., 0.15-unit change in CAT score [regression coefficient (β) = 0.15; 95% confidence interval (CI) = 0.03, 0.26] per interquartile range in NO_2 [13.7 $\mu g/m^3$]. Greater distances to blue/green spaces were associated with worsened CCQ-mental scores [0.08; 0.002, 0.15].

Conclusions: Our study showed that increased air pollution, particularly NO_2 and $PM_{2.5absorbance}$ and greater distances to blue/green spaces negatively influence HRQL in COPD patients. These findings have important implications for the WHO promotion to develop healthy cities for our future.

Keywords: Air pollution; Environment; Airflow limitation; COPD; Quality of life

1. Introduction

In chronic obstructive pulmonary disease (COPD), health-related quality of life (HRQL) has become one of the most important health outcome tools to assess disease outcome and progression through patients' personal experience (Curtis and Patrick 2003; Wijnhoven et al. 2001). Respiratory-specific HRQL instruments provide a comprehensive subjective overview regarding symptoms and functional status associated with the disease. Along with exacerbations, symptoms such as chronic cough, dyspnea, and phlegm and several comorbidities contribute to poorer HRQL in patients with COPD (Burgel et al. 2013; Koskela et al. 2014). Although studies have confirmed the potential influence of age, socioeconomic, and psychological conditions on HRQL in COPD (Ketelaars et al. 1996), much less attention has been paid to environmental factors which could have a major influence on HRQL in COPD.

Among the environmental factors with a potential influence on HRQL in chronic obstructive airway diseases, air pollution plays a major role in aggravating the course of disease (Szyszkowicz et al. 2018). It is well known that air pollution increases the risk of exacerbations and hospitalization among patients suffering from asthma, COPD, and many other chronic respiratory diseases (Cao et al. 2017; DeVries et al. 2016; Nakao et al. 2018; Song et al. 2014). Moreover, some reports demonstrated that the perceived experience of transportation noise was negatively associated with HRQL (Heritier et al. 2014; Shepherd et al. 2010), and that neighbouring proximity to green spaces minimized wheezing, hospitalization due to asthma attacks, and risk of asthma development among children living in highly polluted areas (Feng and Astell-Burt 2017; Tischer et al. 2017). Although a recent report stated that airborne particulate matters <10 µm in diameter (PM_{10}) was associated with poor HRQL in COPD (Pothirat et al. 2019), much is still unknown about this association with other air pollutants. On the other hand, research on relationships between environmental factors and respiratory-specific HRQL has so far mainly centered on individual factors, thus lacking a comprehensive understanding of the role of the whole physical environment in COPD patients' quality of life. To overcome this limitation, it is important to include, together with air pollution, other potentially relevant factors, such as road-traffic noise, temperature, and residential distance to blue or green spaces.

We aimed to assess the individual relationship between the components of the physical environment, such as exposure to air pollutants, road traffic noise, temperature, and residential distances to blue (near the lake, river, or ocean) or green (near parks or forests) spaces, and HRQL among stable mild-to-very severe patients with COPD.

2. Methodology

2.1. Study design and participants

This cross-sectional study analyses the baseline pre-randomization data of the COPD patients who took part in a non-pharmacological clinical trial, "Effectiveness of an intervention of urban training in patients with COPD: a randomized controlled trial" (NCT01897298) (Arbillaga-Etxarri et al. 2018). Patients approaching any of the 33 primary care centers and five tertiary hospitals of five major seaside Catalan municipalities: Barcelona, Badalona, Mataró, Viladecans and Gavà between October 2013 and February 2015, and diagnosed with COPD (according to American Thoracic Society and European Respiratory Society [ATS/ERS] criteria) (Celli et al. 2004) were recruited. After excluding those who, at recruitment, had, i) resided away from home for more than 3 months; ii) mental disability including severe psychiatric disease; and iii) any severe comorbidity including those with the potential to restrain survival up to <1 year, a total of 407 clinically stable (defined as at least 4 weeks without antibiotics and/or systemic glucocorticosteroids) COPD patients were enrolled. The study was conducted in accordance with the amended Declaration of Helsinki and the Urban Training trial was approved by the Ethics Committees of all participating institutions (Comitè Ètic d'Investigació Clínica Parc de Salut MAR 2011/4291/I, Comitè Ètic d'Investigació Clínica de l'IDIAP Jordi Gol i Gurina P11/116, Comitè Ètic d'Investigació Clínica de l'Hospital Universitari de Bellvitge PR197/11, Comitè Ètic d'Investigació Clínica de l'Hospital Universitari Germans Trias i Pujol AC-12-004, Comitè Ètic d'Investigació Clínica de l'Hospital Clínic de Barcelona 2011/7061, Comitè Ètic d'Investigació Clínica de l'Hospital de Mataró November 23rd, 2011). All participants provided signed informed consent.

2.2. Procedures and Measures

The HRQL of the participants was measured using the COPD assessment test (CAT) questionnaire (Jones et al. 2009), and the clinical COPD questionnaire (CCQ) (van der Molen et al. 2003). CAT score ranges between 0–40. Higher scores (>10) denote a more severe impact of COPD on a patient's life with a difference of 2 points is considered as the minimum clinically important difference (MCID) (Kon et al. 2014). The CCQ is scored in three subdomains (symptoms, functional state, and mental state) and a total score (average of subdomains). CCQ scores range between 0-6, higher scores denote a worse health status and the MCID of the CCQ-total score is 0.4 (Kocks et al. 2006).

Exposure to environmental factors was estimated individually for each participant at their geocoded residential address. Annual average levels of the air pollutants nitrogen dioxide (NO_2), particulate matter with a varied aerodynamic diameter (≤2.5 µm ($PM_{2.5}$) and ≤10 µm (PM_{10})), and $PM_{2.5}$ absorbance ($PM_{2.5absorbance}$) were estimated using temporally adjusted land-use regression (LUR) models as described previously (Beelen et al. 2013; Dadvand et al. 2013; Eeftens et al. 2012). Annual average levels of road traffic noise (24h EU indicator L_{den}, in dB[A]), from now onwards "noise", were estimated using Barcelona's strategic noise map (2012) derived under EU Directive 2002/49/EC and as described previously (2007; Dadvand et al. 2014). The land surface temperature within a 50m buffer space around the residence, from now onwards "temperature," was derived from 3 land surface temperature satellite-based maps obtained from the Landsat 5 Thematic Mapper data, as described previously (Dadvand et al. 2014). We calculated residential distance to blue/green spaces within a buffer range of 500m as the network distance from the home to the nearest blue (i.e., inland and non-inland water bodies) or green space (i.e., green urban areas, agricultural land, and pastures, and forests or country parks) using Urban Atlas 2007 .

We also collected information on: (i) education (>primary and ≤primary), marital status (unmarried/widowed/divorced and married/living with a partner), working status (actively working or not), socioeconomic status (SES) (I-professional, II-managerial and technical, IIIN-skilled nonmanual, IIIM-skilled manual, IV-partly skilled, and V-unskilled occupations) and smoking history (active smokers, age of starting smoking, the total duration of smoking, severity of smoking and cumulative dose), from an interviewer-administered questionnaire; (ii) dyspnea, using the modified Medical Research Council scale (mMRC); (iii) anxiety and depression symptoms using the Hospital Anxiety and Depression scale (HAD); (iv) post-bronchodilator forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) and distance walked in the 6-minute walk test (6MWD) using standardized methods (Celli et al. 2004); (v) height, weight, body mass index (BMI), and fat-free mass index (FFMI) by physical examination and bioelectric impedance; (vi) previous COPD exacerbations and the Charlson comorbidity index from medical records; (vii) physical activity by the Dynaport accelerometer (McRoberts BV, The Hague, The Netherlands) validated for COPD (Rabinovich et al. 2013), as previously described (Arbillaga-Etxarri et al. 2018); and (viii) physical activity experience (total, amount, and difficulty scores) by the Clinical-PROactive Physical Activity (C-PPAC) questionnaire (Gimeno-Santos et al. 2015).

2.3. Statistical analyses

Sample size was fixed by the main objective of the Urban Training study (Arbillaga-Etxarri et al. 2018). We calculated that, based on previous data about air pollution levels and HRQL of COPD patients from the same geographic areas, the available sample size (n=407) allowed us to detect an association similar to that previously observed between air pollutants and HRQL in COPD (Pothirat et al. 2019), with a statistical power of 86%. No clustering by site was considered as the study was planned as multicenter.

The patients' characteristics were described as frequencies and percentages for qualitative variables, mean and SD for normal distributed quantitative variables and median and 25th-75th percentiles for non-normal distributed quantitative variables. We determined the relationships between the environmental factors (NO_2, PM_{10}, $PM_{2.5}$, $PM_{2.5absorbance}$, noise, temperature, and residential distance to blue/green spaces) using Spearman's rank-order correlation.

To assess the relationship between the environmental factors (NO_2, PM_{10}, $PM_{2.5}$, $PM_{2.5absorbance}$, noise, temperature, and residential distance to blue/green spaces) and HRQL (CAT, CCQ-total, CCQ-symptom, CCQ-mental, and CCQ-functional scores), we first assessed the bivariate associations between quartiles of exposure variables (i.e., environmental factors) and outcomes (i.e., HRQL variables) using Kruskal-Wallis test. Secondly, we constructed univariable (unadjusted) and multivariable (adjusted) regression models. Specifically, we applied mixed-effect negative binomial regression for the CAT score (count variable), and a mixed-effect linear regression for each of the CCQ scores (normally distributed continuous variables), with a random effect by center. Age, sex, education, marital, socio-economic, and working status, smoking history (status, age of onset, duration, intensity, and cumulative dose), FEV_1, FVC, FEV_1/FVC ratio, previous

COPD exacerbations, BMI, dyspnea, anxiety, depression, 6MWD, steps per day, and Charlson comorbidity index were tested as potential confounders. The model building included step-forward and backward algorithms, and covariates were included in the final model if (i) they were associated with the exposure and the outcome in bivariate analysis, (ii) modified the estimates of the remaining variables in the multivariable models by >10%, or (iii) there was consistent evidence in the literature of their association with HRQL. Regression diagnostics suggested good model performance except for two influential points that were consequently excluded from models (Cook's distance for influence reached 0.09, rule of thumb cut-off >0.01 for n=407). We also created multi-exposure models, i.e., including in the same model all environmental factors that did not exhibit collinearity among them in regression diagnostics (variance inflation factor <3). Finally, as secondary analyses, we repeated final models excluding subjects with extreme values (<5th and >95th percentile) in the environmental factors. The analysis was conducted using a complete case approach in Stata V.14.0 (StataCorp, College Station, Texas, USA).

3. Results

Patients were mostly male (85%) and had a mean (standard deviation: SD) age of 69 (9) years and a post-bronchodilator FEV_1 of 56.8 (17.5) % predicted (**Table 1**). Low socioeconomic status was present in 72% of the sample. Median (25th – 75th percentile) exposure concentrations to NO_2, $PM_{2.5,}$ PM_{10}, and $PM_{2.5absorbance}$ were 43.5 (35.0 – 48.7), 12.6 (10.7 – 13.8), 24.9 (22.3 – 27.7), and 2.2 (1.9 – 2.5) $\mu g/m^3$, respectively. Median (25th – 75th percentile) exposure level to noise was 63 (59 – 67) dB. These levels are above the WHO recommended annual average levels to protect health, both for air pollution (recommendations: $NO_2 < 40\ \mu g/m^3$, $PM_{2.5} < 10\ \mu g/m^3$, $PM_{10} < 20\ \mu g/m^3$, $PM_{2.5absorbance}$: not available) and road traffic noise ($L_{den} < 53$ dB). Mean (SD) exposure level to temperature was 24 (1) °C. Mean (SD) distance to blue/green space was 299 (178) m. In regard to HRQL, patients had a mean (SD) CAT score of 12 (7) and a CCQ-total score of 1.4 (1.0). We observed a moderate-high correlation (ρ values ranged between 0.37 and 0.89; all values were significant at $p<0.001$) between the pollution indices (NO_2, PM_{10}, $PM_{2.5}$, and $PM_{2.5absorbance}$) (**Figure 1**). Higher land surface temperature was significantly associated with higher air pollution indices, except PM_{10}. Distance to blue/green space was significantly associated with higher NO_2, and PM_{10}. A higher distance to blue/green space was also associated with higher land surface temperature.

In single-exposure multivariable models (**Figure 2 and Tables S1-S5**), NO_2, $PM_{2.5absorbance}$, and distance to blue/green space were associated with worsened CAT and CCQ-mental scores. Specifically, an IQR increment in NO_2 was associated with 0.13 (95%CI = 0.04 to 0.22) points worse CAT score and 0.17 (0.001 to 0.34) points worse CCQ-mental scores. An IQR increment in $PM_{2.5absorbance}$ was associated with 0.10 (0.001 to 0.20) points worse CAT and 0.21 (0.03 to 0.39) points worse CCQ-mental scores. These associations remained consistent in the multi-exposure models. While distance to blue/green spaces was associated with worse CAT score (0.03; 0.002 to 0.06, per 100-meter increment of distance) and marginally associated with CCQ-mental scores (0.07; -0.003 to 0.14) in single-exposure models, in multi-exposure models it was associated with CCQ-mental scores (0.08; 0.002 to 0.15) and it lost statistical significance with CAT score (0.02; -0.007 to 0.05). Although higher temperature was marginally associated with worsened CAT score in single-exposure models, the association lost statistical significance in multi-exposure models and was slightly smaller in magnitude. Noise tended to be associated with worse CCQ-functional scores in both in single and multi-exposure models, but it did not reach statistical significance. No association was found between any of the environmental factors and CCQ-total or symptom scores.

After excluding extreme values of environmental factors (**Supplementary Tables S6-S10**), the magnitude of the observed associations of NO_2 increased, those of $PM_{2.5absorbance}$ remained unvaried, and the association between $PM_{2.5absorbance}$ with worse CAT scores was marginally attenuated based on the estimate of effect (0.11; -0.05 to 0.26). There was also a marginally significant association between PM_{10} and worse CCQ-mental scores. As for temperature, the association with worse CAT scores became stronger in magnitude and statistically significant. Associations with distance to blue/green spaces were inconsistent across the outcomes and tended to the null.

4. Discussion

4.1. Summary of Results in Contextual References

To our knowledge, this is the first study to assess the relationship between major environmental factors and respiratory-specific HRQL among clinically stable mild-to-very severe COPD patients. We observed that exposure to main traffic-related air pollutants (NO_2 and $PM_{2.5absorbance}$) and residential distances to blue/green spaces were associated with worse respiratory-specific HRQL. Although exposure to higher temperatures was found to be associated with poor HRQL in COPD patients, the association could not be confirmed in the multi-exposure model. No association was observed between residential exposure to road traffic noise and the HRQL of COPD patients.

The association between NO_2, a major traffic-related gaseous air pollutant, and worsened HRQL, particularly with CAT and the CCQ-mental scores, is plausible given the previously described effects and mechanisms of action for this pollutant. NO_2 acts primarily through oxidative stress and has been well studied as a risk factor for COPD (Morrow et al. 1992). It has also been reported to be associated with impaired lung function (Lamichhane et al. 2018), increased risk of pneumonia (Ho et al. 2019), and greater risk of exacerbation and hospitalization in patients with COPD (Liang et al. 2019; Moore et al. 2016), all of which could be potential mediating factors in NO_2-associated poor HRQL.

In our study, $PM_{2.5absorbance}$ was also associated with worsened HRQL whereas associations for the other particulate matter pollutants ($PM_{2.5}$ or PM_{10}) were null or inconsistent. $PM_{2.5absorbance}$ is the fraction of $PM_{2.5}$ related to localized soot emanating from traffic-related combustion (Beelen et al. 2013), and has been reported to be associated with asthma incidence (Jacquemin et al. 2015). Likewise, PM_{10} has been associated with HRQL in COPD in a study that did not evaluate other PMs (Pothirat et al. 2019). The fact that we observed findings with $PM_{2.5absorbance}$, but not $PM_{2.5}$ or PM_{10}, suggests that different components of air pollution may have different effects on health, and may highlight the relevance of the indicators of traffic-related combustion. Finally, short-term exposure to $PM_{2.5}$ has been associated with a higher rate of hospitalization in COPD patients (Li et al. 2016; Zhao et al. 2019), which could be mediated through air pollution-quality of life association as far as NO_2 is concerned.

Our study could not disentangle the relative contribution of each of the two traffic-related air pollutants (NO_2 or $PM_{2.5absorbance}$) to poor HRQL, because of their high correlation and collinearity (VIF around 5) when included in the same models. Accordingly, we hypothesize that the observed isolated association between PM_{10} and better CAT score in the multi-exposure model, after adjusting for $PM_{2.5absorbance}$ and $PM_{2.5}$, could also be an artefact due to residual collinearity (VIF=1.21), a contention that cannot be overlooked. More epidemiological studies, especially in countries with higher air pollution, are warranted to understand the independent relationship between air pollutants and HRQL in COPD.

In our study, we found that increased residential distances to blue/green spaces may negatively affect respiratory-specific HRQL in patients with COPD. This observation was more consistent for the CCQ-mental score and independent of other environmental factors. One explanation could be that the perception of residing close to blue/green spaces reduces stress, hence contributing to cognitive and physiological restoration, a pathway consistently supported by previous evidence (Nieuwenhuijsen et al. 2017). Another hypothesis could be related to the mediating role of physical activity (Klompmaker et al. 2018), although our group previously reported no significant association between residential distance from blue/green spaces and physical activity in terms of steps/day in COPD patients (Arbillaga-Etxarri et al. 2017). Finally, the fact that we recruited only patients who lived within 500m of the nearest urban trail (usually located in blue/green spaces) may have affected the association between this factor and HRQL. Further studies with a broader range of distances to these blue/green spaces are needed.

The association between higher temperature and worsened CAT scores, became statistically non-significant and slightly smaller in magnitude after adjustment for other environmental factors, which could suggest potential confounding by such factors. In contrast with our results, a recent panel study in Korea reported that higher temperature was associated with worse physical functioning and general health perception, increased risk of exacerbation, and an increased risk of outpatient visits in patients with COPD (Nakao et al. 2018) . Nevertheless, the study in Korea used 4-weeks average temperature, ranging from -11.8 to 29.9ºC, while the temperature range of our study was small (our yearly average only ranged from 22 to 27ºC), which could also explain differences in findings. Future research on this topic should approach wider temperature ranges and evaluate which time lags influence HRQL.

We also did not observe any association between road traffic noise and respiratory-specific HRQL. The few existing studies on the influence of transportation noise on HRQL assessed healthy populations and observed more consistent associations with noise annoyance (perception of noise) than with the noise level by itself (Heritier et al. 2014; Shepherd et al. 2010). In the current study, we did not have information about noise annoyance. Evaluating both the perception and objective noise level may be necessary to understand the global effects of noise on HRQL in chronic diseases.

4.2. Clinical and Public Health Implications

Our findings support the relevance to foresee HRQL as a health outcome in COPD to capture the impact of the environment on the progression of the disease. These findings might help clinicians to provide recommendations to patients with COPD with the aim to improve HRQL, such as avoiding traffic-related sources and being close to blue/green spaces. On the other hand, our findings also strongly endorse the urge for minimizing traffic-related environmental perturbations, more specifically the reduction of traffic as a general policy measure to minimize the health burden of air and noise pollution, and increasing temperature, particularly for those with respiratory disorders. Lastly, our findings also accentuate the necessity for eco-friendlier urban planning, i.e., increasing green spaces, which is a cornerstone of mitigating increasing urban temperature and could also facilitate more space for physical activity and is the focus of the World Health Organization (WHO) in the promotion for healthy cities (WHO 2018).

4.3. Strengths and Limitations

The strength of our study lies in its novel approach of characterizing a wide range of environmental factors that could improve the information of the complex exposure scenario of everyone. Moreover, it includes patients who are well distributed across disease severity, which adds external validity to our study findings. In clinical terms, it also assesses a large sample of 407 COPD patients while assessing a Mediterranean population for the first time. The one previous study in this domain was performed on 59 patients from South-Asia and evaluated PM_{10} only (Pothirat et al. 2019).

The study has however some limitations. This study has a cross-sectional design so that we cannot determine causality. Nevertheless, results are supported by the biological plausibility and previous epidemiological evidence on the effects of environmental factors, particularly air pollution, on COPD. Despite exploring several relevant environmental factors, other important pollutants (i.e., ultrafine particles, ozone, sulfur oxides, carbon monoxide, among others), other factors such as the quality of and accessibility to green spaces or noise annoyance, time spent in the outdoor environment, and indoor quality of the households (dampness, light, ventilation in the houses, and insulation to noise) were not available and need to be addressed in future studies. Although this initial study assessed a sufficiently large clinical sample and the findings are in line with previous direct and indirect evidence, a greater sample size would be further warranted in future studies to increase the statistical power to detect effects of multiple environmental factors. It might be of argument that we have not shown the overall effects of environmental exposures using mixture models or similar. However, this is another research question that goes beyond the objectives of the current manuscript. Moreover, this study was conducted on a specific Mediterranean (Spanish) population, therefore more studies are needed in different COPD populations across the globe to obtain a more comprehensive picture of the role of environmental factors that are often related to local geography, culture, and policies.

5. Conclusion

In conclusion, higher residential exposure to traffic-related air pollutants, particularly NO_2 and $PM_{2.5absorbance}$ are associated with poorer HRQL in patients with stable COPD with a wide range of airflow limitation. Other physical environmental factors such as greater residential distances to blue/green spaces are also associated with poor HRQL. Our findings strongly advocate the urgency to curb air pollution and redefining urban policies for the betterment of humankind, particularly for the overwhelming number of patients with respiratory diseases across the world. Tackling these environmental factors may be important for the daily management and quality of life of these patients.

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Data sharing policy: Data contain potentially identifying variables. For example, built environment variables together with socio-demographics 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 27 April 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.

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TABLE 1: Socio-demographic and clinical characteristics, environmental factors, and health-related quality of life in 407 COPD patients

	All (n = 407)
Demographics, clinical features and physical activity measures	
Age (years), mean (SD)	69 (9)
Sex: male, n (%)	346 (85)
Education: >primary, n (%)	123 (30)
Marital status: married/living with partner, n (%)	309 (76)
Current smoker, n (%)	98 (24)
Cumulative dose of smoking (pack-year) among ever smokers, mean (SD)	60 (41)
Low socioeconomic status: IIIM + IV + V, n (%)	291 (72)
Post-bronchodilator FEV_1 (% predicted), mean (SD)	56.8 (17.5)
History of COPD exacerbation in the last 12 months, n (%)	178 (45)
GOLD spirometric grades	
1 - Mild	39 (10)
2 - Moderate	217 (53)
3 - Severe	120 (29)
4 - Very severe	31 (8)
BMI (kg/m^2), mean (SD)	28.5 (4.9)
Dyspnea (mMRC grade, 0-4), median (25th – 75th percentile)	1 (1-2)
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)
Charlson comorbidity index, median (25th – 75th percentile)	2 (1-3)
6-min walking distance (m), mean (SD)	486 (95)
Steps (number/day), mean (SD)	7547 (4044)
Physical activity experience (C-PPAC)	
C-PPAC amount [0 (worse-less amount) to 100 (better-more amount)], median (25th – 75th percentile)	77 (63-83)
C-PPAC difficulty [0 (worse-more difficulty) to 100 (better- less difficulty)], median (25th – 75th percentile)	83 (72-94)
C-PPAC Total [0 (worse) to 100 (better)], median (25th – 75th percentile)	79 (70-86)
Environmental factors	
Air pollutants	
NO_2 ($\mu g/m^3$), median (25th – 75th percentile)	43.5 (35.0-48.7)
$PM_{2.5}$ ($\mu g/m^3$), median (25th – 75th percentile)	12.6 (10.7-13.8)
PM_{10} ($\mu g/m^3$), median (25th – 75th percentile)	24.9 (22.3-27.7)

$PM_{2.5\text{-absorbance}}$ (μg/m^3), median (25th – 75th percentile)	2.2 (1.9-2.5)
Noise (L_{den}, dB), median (25th – 75th percentile)	63 (59-67)
Temperature (°C), mean (SD)	24 (1)
Distance to blue/green space (m), mean (SD)	299 (178)
Outcomes (HRQL)	
CAT score (0 better - 40 worse), mean (SD)	12 (7)
CCQ scores (0 better – 6 worse), mean (SD)	
CCQ-total	1.4 (1.0)
CCQ-symptom	1.6 (1.1)
CCQ-mental	1.3 (1.5)
CCQ-functional	1.3 (1.2)

Data presented as frequency (%), mean (SD: standard deviation) or median (25th – 75th percentile). BMI: body mass index. CAT: COPD assessment test. CCQ: clinical COPD questionnaire. C-PPAC: Clinical visit version of the PROactive Physical Activity in COPD (PPAC), FEV_1: forced expiratory volume at 1 second, FVC: forced vital capacity, GOLD: Global Initiative for Chronic Obstructive Lung Disease, HAD: hospital anxiety and dyspnea, HRQL: health-related quality of life, mMRC: modified Medical Research Council Questionnaire, NO_2: nitrogen dioxide, $PM_{2.5}$: particulate matter of ≤2.5 μm in diameter, PM_{10}: particulate matter of ≤10 μm in diameter. Missing values for: education (1); low socioeconomic status (2); history of COPD exacerbations in the last 12 months (11); C-PPAC scores (96); all air pollution parameters (3); noise (4); temperature (3); and distance to blue/green space (3).

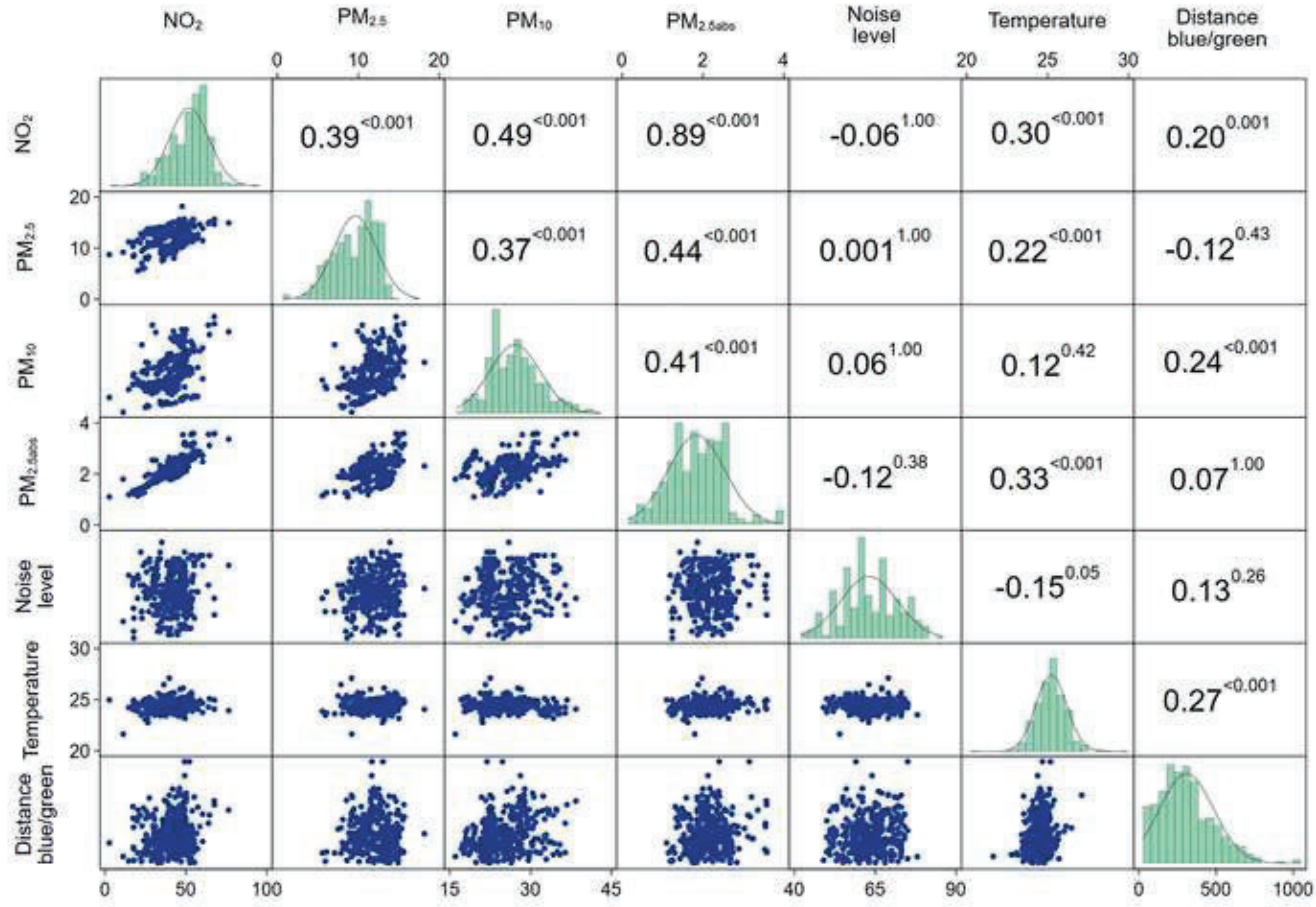
Figure Legend

Figure 1: Scatterplot matrix, distribution (histograms), and correlation of the exposure variables.

Bivariate scatterplots of continuous variables are presented below the diagonal; (distribution) histograms of each variable on the diagonal; Spearman's correlation coefficient (ρ) above the diagonal. Superscript numbers are the corrected (Bonferroni) p-values for each of the correlation coefficients. For abbreviations and units, please see the text.

Figure 2: Adjusted associations between environmental factors and HRQL scores in COPD patients. Boxes and the error bars indicate the regression coefficients (β) and 95% confidence intervals (95%CI), respectively.

Multivariable models were adjusted for age, education (categorized as >primary and ≤primary), %predicted of FEV_1, modified Medical Research Council (mMRC) score (categorical: <2 and ≥2), anxiety (HAD-A score), body mass index (BMI) and mean steps/day, and centers as random factor variable. Multi-exposure 1: all exposures, except $PM_{2.5absorbance}$, Multi-exposure 2: all exposures, except NO_2. For abbreviations, see Table 1.


NO₂
PM₂.₅
PM₁₀
PM₂.₅abs
Noise level
Temperature
Distance blue/green
0.39 <0.001
0.49 <0.001
0.89 <0.001
-0.06 1.00
0.30 <0.001
0.20 0.001
0.37 <0.001
0.44 <0.001
0.001 1.00
0.22 <0.001
-0.12 0.43
0.41 <0.001
0.06 1.00
0.12 0.42
0.24 <0.001
-0.12 0.38
0.33 <0.001
0.07 1.00
-0.15 0.05
0.13 0.26
0.27 <0.001
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10
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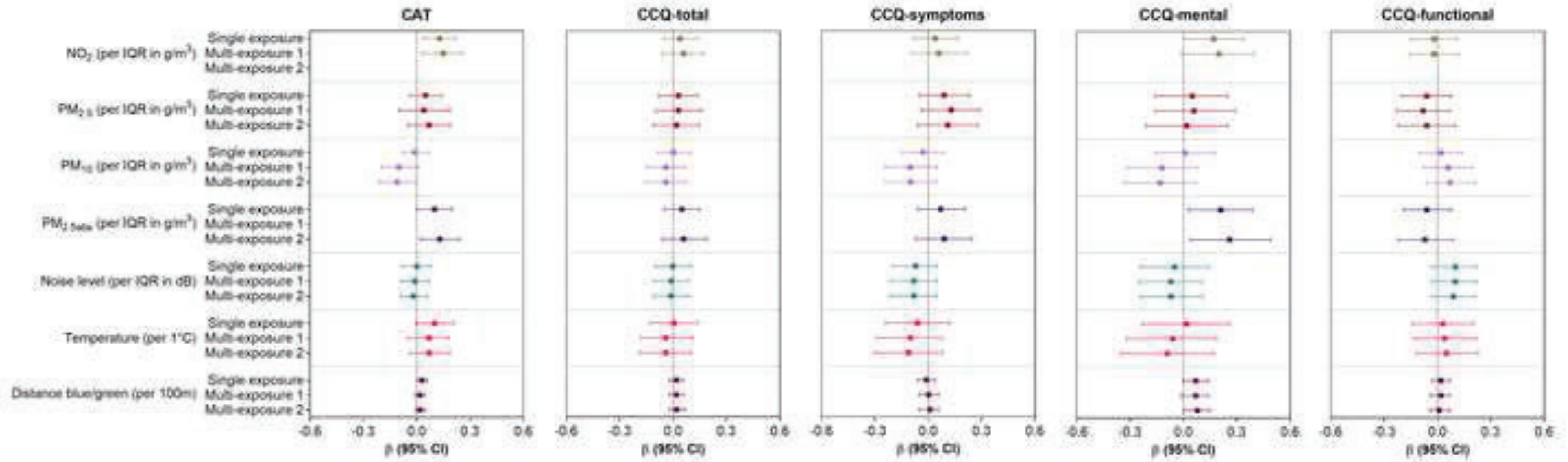
CAT
CCQ-total
CCQ-symptoms
CCQ-mental
CCQ-functional
NO_2 (per IQR in g/m^3)
$PM_{2.5}$ (per IQR in g/m^3)
PM_{10} (per IQR in g/m^3)
$PM_{2.5abs}$ (per IQR in g/m^3)
Noise level (per IQR in dB)
Temperature (per 1°C)
Distance blue/green (per 100m)
Single exposure
Multi-exposure 1
Multi-exposure 2
-0.6
-0.3
0.0
0.3
0.6
β (95% CI)