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Long-term exposure to PM_{10} and respiratory health among Parisian subway workers

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ABSTRACT

Exposure to ambient PM10 may increase the risk of chronic obstructive pulmonary disease (COPD) and lung function decline. We evaluated the long-term exposure to PM10 and its relationship with COPD prevalence and lung function in Parisian subway workers.

Participants were randomly selected from a 15,000-subway worker cohort. Individual annual external exposure to PM10 (ePM10) was estimated using a company-specific job-exposure-matrix based on PM10 measurements conducted between 2004 and 2019 in the Parisian subway network. Mean annual inhaled PM10 exposure (iPM10) was modeled as function of ePM10 exposure, inhalation rate, and filtration efficiency of the respiratory protection used. COPD diagnosis was performed in March–May 2021 based on post-bronchodilator spirometry. The relationship between iPM10 and outcomes was assessed using logistic and linear regression models, adjusted for exposure duration and potential confounders.

Amongst 254 participants with complete data, 17 were diagnosed as COPD. The mean employment duration was 23.2 ± 7.3years, with annual mean ePM10 of 71.8 ± 33.7 μg/m^3 and iPM10 of 0.59 ± 0.27 μg/shift, respectively. A positive but statistically non-significant association was found for COPD prevalence with iPM10 (OR = 1.034, 95%-CI = 0.781; 1.369, per 100 ng/shift) and ePM10 (OR = 1.029, 95%-CI = 0.879; 1.207, per 10 μg/m^3). No decline in lung function was associated with PM10 exposure. However, forced expiratory volume during the first second and forced vital capacity lower than normal were positively associated with exposure duration (OR = 1.125, 95%-CI = 1.004; 1.260 and OR = 1.171, 95%-CI = 0.989; 1.386 per year, respectively). Current smoking was strongly associated with COPD prevalence (OR = 6.85, 95%-CI = 1.87; 25.10) and most lung function parameters.

This is the first study assessing the relationship between long-term exposure to subway PM10 and respiratory health in subway workers. The risk estimates related with subway PM10 exposure are compatible with those related to outdoor PM10 exposure in the large recent studies. Large cohorts of subway workers are necessary to confirm these findings.

1. Introduction

According to the latest estimates, the ambient (outdoor) air pollution have caused 4.2 million premature deaths worldwide in 2019 (WHO, 2022). Eighteen percent of these deaths were due to cancer within the respiratory tract, 23% to the acute lower respiratory infections and 18% to the exacerbation of the chronic obstructive pulmonary disease (COPD) (WHO, 2022). On average, an increase of 10 μg/m^3 in the 2-day moving average of particulate matter (PM10) concentration was associated with increases of 0.47% (95%-CI = 0.35; 0.58) in daily

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respiratory mortality (Liu et al., 2019). Notewithstanding, the evidence for impacts on lung function and COPD development is still limited. A causal role of ambient air pollution in the development of COPD is considered biologically plausible, identifying oxidative stress and inflammation as adverse outcome pathways of exposure to several air pollutants (Celli et al., 2022; Eisner et al., 2010). The last and the largest study using UK-biobank data found that ambient PM10 was significantly associated with lower lung function and increased COPD prevalence (OR 1.08, 95%-CI = 1.00; 1.16, per 10 μg/m^3 of PM10) (Dany et al., 2019). However, in the analysis of four cohort studies participating in ESCAPE project, COPD was not associated with PM10 in any individual cohort (Schikowski et al., 2014). In the meta-analyses of COPD prevalence, a positive but not statistically significant association was observed for ambient PM10 (OR 1.04, 95%-CI = 0.71; 1.53, per 10 μg/m^3) (Schikowski et al., 2014).

In all cohort studies, pre-bronchodilator spirometry measurements were used conversely to guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnosis, which advocates for post-bronchodilator spirometry (Agustí et al., 2023). Moreover, outdoor PM10 exposure was assessed based on the participants' home address, without controlling for exposure duration. Yet, the latter is determinant for assessing the effect of cumulative long-term exposure and its variation, especially in the context of occupational exposure to airborne pollutants, including particles and dusts. Indeed, at some workplaces, such as subway transport network, particle concentration can be much higher than the PM concentration measured outdoor (Guseva Canu et al., 2021a; Pétremand et al., 2021, 2022). Air quality measurements in the subway networks in different countries and cities have revealed mass concentrations of PM10 by a factor of 3 on average higher than those measured outdoors in the urban background, and in the vicinity of road traffic (Otuyo et al., 2023; ANSES, 2022; Wen et al., 2020).

The physical-chemical composition of subway aerosols also differs from that of urban outdoor air, with a high content of metallic elements, mostly iron (ANSES, 2022; Loxham et al., 2013). Subway aerosols are also composed of larger, denser particles and more variable in shape (flaky, ellipsoidal, semi-spherical or spherical) compared with outside air. The toxicity of subway particles remains poorly documented and existing studies focus solely on short-term effects. The review of available *in vitro* and *in vivo* studies of subway PM suggests that subway PM have a high intrinsic oxidizing potential greater than or equal to that of urban particles in cell-free conditions; a capacity to induce oxidative stress that is sometimes higher in exposed cells than that induced by urban particles; greater cytotoxicity than urban particles or particles from abrasive processes; greater genotoxicity than particles from combustion or tire wear processes; lower *in vitro* pro-inflammatory effect than urban particles; a capacity to induce transient lung inflammation in mice, observed to a lesser extent for reference diesel particles; and persistent inflammation at very high doses not associated with fibrosis (ANSES, 2022; Wen et al., 2020; Cooper and Loxham, 2019; Loxham and Nieuwenhuijsen, 2019).

Human studies focused on the effect of subway PM have not reveal any adverse effect on respiratory health (including lung function), either in subway workers (Bigert et al., 2011; Gustavsson et al., 2008; Heo et al., 2010), or in volunteers (Klepczyńska-Nyström et al., 2012; Klepczyńska Nyström et al., 2010; Strak et al., 2012). None of these studies assessed long-term exposure to PM, and all studies have been conducted on samples including less than 100 workers, except one registry-based study with qualitative exposure assessment (Gustavsson et al., 2008).

The aim of this study was twofold. First, we aimed to evaluate the long-term exposure to subway PM10 in a sample of randomly selected Parisian subway workers older than 40. Secondly, we aimed to assess its association with COPD prevalence and lung function, considering both the exposure duration and an exposure metric approximating internal exposure.

Paris and its suburbs constitute France's largest transport network (624 stations and 331 km of train lines) and one of the busiest network in the world, with more than 5 million passengers a day) (OMNIL, 2023). While the duration of subway journeys on this subway network is estimated at 36 min per day on average and can reach over 1 h and 40 min per day (ANSES, 2022), subway workers spend an average of 6 h per day there, over a career span of approximately 25 years. Consequently, if the air quality in subway amenities is damaging to health, it is the health of subway workers that is most at stake, explaining the choice of this study population.

2. Material and methods

2.1. Study design

This was a cross-sectional analytical study with an etiological focus, where we combined a retrospective exposure assessment and contemporary outcome measurements to meet the temporality condition.

2.2. Study sample

The study sample was constructed by applying a stratified random sampling procedure to the company employee roster comprising 15,000 subway workers. The strata were defined by sex, 10-year age classes, smoking status, and job (restricted to the three main jobs: station agents, locomotive operators, and security guards). The company occupational physician coordinating the study in the field contacted one by one the randomly selected workers in each stratum and included those who accepted participation (Fig. 1). During the inclusion call, the physician verified the inclusion criteria (i.e., being employed at the company for at least one year and older than 40 years). The age restriction aimed at maximizing the number of COPD cases; given the rarity of COPD among young adults in France (Fuhrman and Delmas, 2010). The detailed description of the sample size estimation and participant recruitment are provided in the published study protocol (Guseva Canu et al., 2021b). In case of refusal, retirement, or employment in another company, the physician called the next worker listed in the same strata, and so on, until recruiting at least 300 participants, as required by the study protocol (Guseva Canu et al., 2021b).

2.3. Data collection

All data were collected from March through May 2021. Data collection procedures were previously described in the study protocol (Guseva Canu et al., 2021b). Briefly, we used three main sources of individual and health data: the epidemiological questionnaire completed by study participants; the biomedical tests and corresponding forms completed by the research team in the field (*i.e.,* 3 company occupational physicians, 2 nurses, 1 pharmacologist, and 1 pulmonologist); individual occupational medicine records. The latter were used for cross-checking information for epidemiological questionnaire.

2.4. Exposure assessment

2.4.1. External exposure to subway PM10

We obtained annual average PM10 estimates (in μg/m^3) from the company-specific job exposure matrix (JEM) (Ben Rayana et al., 2023). This JEM was constructed based on PM10 measurements conducted in Parisian subway network between 2004 and 2019 (Ben Rayana et al., 2022). The JEM distinguishes three types of subway jobs, defined by the worker's professional position and tasks assigned to this position (*i.e.*, station agents, locomotive operators, and security guards). Each job is further specified by the workplace location within the subway network, defined by a metro or suburb train (RER) line (for locomotive drivers and station agents who are appointed to a specific line) and a sector (for station agents and security guards, whose daily activity includes travels and interventions within a network sector). It worth mentioning that the

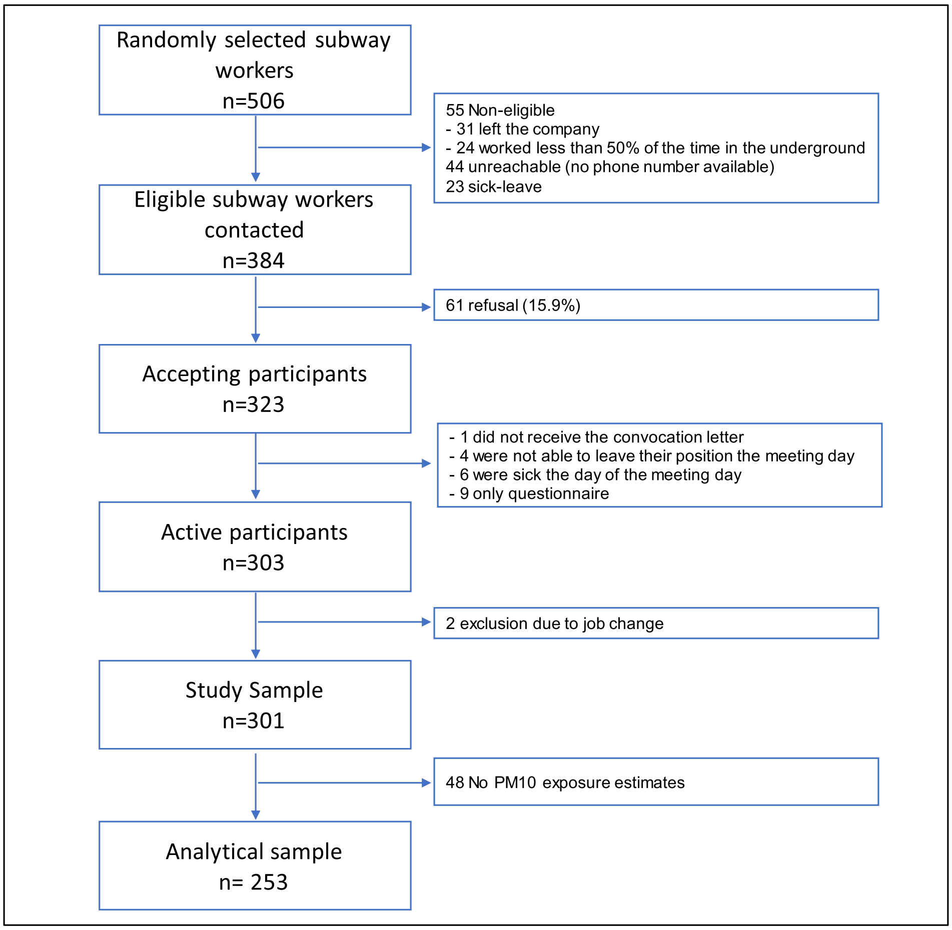

Fig. 1. Flowchart of participant selection.

exposure estimates for security guards were insufficiently valid, being based on a small number of measurement data leading to an unrealistically high value of estimated PM10 concentrations (Ben Rayana et al., 2023). Consequently, we did not use them in this study to avoid biased results, and limited the analytical sample to station agents and locomotive operators (Fig. 1). We linked their individual work histories with the JEM estimates to assign PM10 exposure to each study participant in each year (ePM10). The work histories were completed by study participants as part of the interactive questionnaire managed via RedCAP software (Guseva Canu et al., 2021b). The completion was done after inclusion into the study and before the biomedical test session, to enable the study coordinator to check the completeness when starting the session. For calendar years prior to 2004 and posterior to 2019 we extrapolated the temporal trend assessed in the JEM to estimate the annual PM10 levels and, thus, to enable cumulating occupational exposure for workers who started their employment as subway worker before 2004.

2.4.2. Modelling of inhaled PM10 exposure

We estimated the average annual inhaled PM10 exposure (iPM10, in μg/shift) as a product of the annual mean subway PM10 external exposure (in μg/m^3), the inhalation rate of study participants (in L/min) during the work shift (6 hours/day), and the filtration efficiency of personal respiratory protection (*i.e.*, masks) used at the company (in %). The inhalation rates per physical activity level (sedentary, light, moderate, vigorous), age, sex, BMI, and region were defined by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) using the energy-based approach and reported as the reference values of inhalation rate for the French population (Guseva Canu et al., 2021c). We assigned the inhalation rate to each study participant, in accordance with his/her age, sex, BMI, and the physical activity level in his/her job (*i.e.*, sedentary for locomotive drivers, light for station agents, and moderate for security guards).

As the study was partially conducted during the COVID-19 pandemic (2020–2021), when all French subway workers had to wear a respiratory protection equipment (*i.e.*, face mask), we corrected the annual internal exposure estimates for the mask filtration efficiency (FE). The latter was determined using the Aerosol penetration test of the experimental protocol adapted from EN 13274–7 (Respiratory protective devices – Methods of test-Part 7: Determination of particle filter penetration) applied to 28 types of masks used at the company. A sodium chloride aerosol (0.6%), continuously generated by nebulization (Collison-type; flow rate 1.0 L/min) was mixed with dry air (1.5 L/min) to reach a final relative humidity of 40–50%. The resulting NaCl aerosol was characterized in terms of mass concentration (mg/m^3) using a direct reading light scattering particle counter number DUSTTRAK II Model 8530/31 Desktop. Prior particle size distribution of the aerosol was carried out using Scanning Mobility Particle Sizer (model SMPS+C model 5400, Grimm Aerosol Technik Ainring GmbH und Co. KG, Germany) that confirmed the presence of ultrafine particles (size distribution<300 nm). The penetration rate was determined using differential measurements in which the aerosol air stream was sequentially forced to pass through a sealed filter housing containing a sample of the filtering media of the mask to be analyzed (circular punches 37 mm diameter; about 10 cm^2) and the bypass path, driving the aerosol generated directly to the particle measurement system. At least three samples of each mask type were tested. Three consecutive measurements were systematically averaged to calculate the FE, defined as follows:

$$Filtration = 100 \times \left(1 - \frac{[particle]_{mask}}{[particle]_{background}}\right)$$

The determination of the FE for the tested masks showed high reproducibility as indicated by the calculated standard deviation lower than 1%. However, the filtration rates distribution provided clear evidence of the heterogeneity in the filtering capacity for the series of mask analyzed (Supplementary Material Fig. S1). Although 17 out of 28 masks (60%) exhibited a high filtration rate (>80%), about 10% (3/28) showed low FE (<50%) in the ultrafine particle domain (<300 nm). The overall geometric mean and median values were about 76% and 90%, respectively. Since we could neither trace which type of mask has been used, for how long time, and by which subway worker, nor perform any fit test in the field, we applied a PM10 exposure reduction coefficient of 0.05 as a central estimate, 0.001 as a best-case estimate, and 0.1, as a worth-case estimate (Fig. S1).

The resulting estimate of inhaled PM10 exposure (iPM10) was expressed in the mass unit (μg or ng) of subway particles inhaled per work shift assigned for each exposure year (i.e., each year of employment as subway worker). Based on this estimate we defined our primary predictor variable as the mean annual inhaled PM10 exposure over the worker's career in the subway (iPM10, in ng/shift). We also estimated the cumulative iPM10 (in ng/shift-years) as a sum of the annual inhaled PM10 concentrations over the duration (in years) of the employment at the company for the sensitivity analysis.

2.5. Outcome definition and measurement

As a primary outcome we considered the COPD defined based on post-bronchodilator spirometry results validated by the study pulmonologist (Guseva Canu et al., 2021b). Spirometry was performed by the trained nurses using an electronic spirometer according to the American Thoracic Society/European Respiratory Society guidelines (Pellegrino et al., 2005). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines spirometrically confirmed COPD based on a forced expiratory volume during the first second (FEV1) to a forced vital capacity (FVC) ratio smaller than 0.7 (Agustí et al., 2023; Vogelmeier et al., 2017). Participants having a FEV1/FVC ratio > 0.7 were classified as non-COPD. The severity stages of COPD defined by GOLD are as follows: Stage 0: FEV1/FVC ≥ 0.7 and FEV1 ≥ 80% of predicted value and respiratory symptoms (cough, phlegm); Stage 1 (mild): FEV1/FVC < 0.7 and FEV1 ≥ 80% of predicted value; Stage 2 (moderate): FEV1/FVC < 0.7 and FEV1 < 80% but ≥ 50% of predicted value; Stage 3 (severe): FEV1/FVC < 0.7 and FEV1 < 50% but ≥ 30% of predicted value; and Stage 4 (very severe): FEV1/FVC < 0.7 and FEV1 < 30% of predicted value (Vogelmeier et al., 2017). Preserved ratio impaired spirometry (PRISm) is defined as FEV1 < 80% of predicted value and FEV1/FVC ratio ≥ 0.70 (Wijnant et al., 2020). FEF 25–75% was defined as forced expiratory flow during the middle half of the FVC.

Lung function parameters, either defined as z-scores of FEV1, FVC, FEF 25–75, or FEV1/FVC ratio or as dichotomized according to the lower limit of normal (LNN) defined by GLI were our secondary outcome.

2.6. Statistical analysis

The research hypothesis tested in this study was as follows: the association between iPM10 and outcome is positive for the dichotomized outcomes (*i.e.*, COPD diagnosis and spirometry parameters below LNN, with an odds ratio (OR) > 1) and negative for the continuous outcome variables (i.e., z-scores of spirometry values, with a regression coefficient β < 0).

For each dichotomized outcome we constructed a logistic regression model, while quantitative outcomes were analyzed using linear regression models. We first examined the crude association of the primary outcome with the annual iPM10 averaged over the workers' career. Then we examined the association adjusted for the duration of employment (as metric of subway PM10 exposure duration), and finally, the association additionally controlled for an interaction between iPM10 and exposure duration. According to the Akaike information criterion and Bayesian information criterion, the model adjusted for exposure duration, without interaction had the best performance. Consequently, we considered this model for all other outcomes. Furthermore, we constructed a multivariate model, adjusted for smoking status, home-work commuting using metro or RER, and physical activity. We decided against the inclusion of sex, age, and BMI in the model to avoid an overadjustment, as these variables were accounted for in the

Table 1
Sociodemographic, lifestyle, medical and occupational characteristic of participants.

Characteristics	Study sample (N = 301)		Analytical sample (N = 253)	
Sex	n	%	n	%
Female	153	50.8	147	58.1
Male	148	49.2	106	41.9
Age in years (Mean (SD))	52.3 (5.3)		52.6 (5.4)	
Smoking status				
Non-smoker	156	51.8	127	50.2
Smoker	107	35.5	92	36.4
Ex-smoker	38	12.6	34	13.4
Tobacco use in pack-years (Mean (SD))	15.5 (14.9)		16.6 (15.3)	
Alcohol consumption				
Never	119	39.5	102	40.3
Occasional	117	38.9	102	40.3
Regular	65	21.6	49	19.4
Pysical activity (>10 h/week)	74	24.6	56	22.1
Body Mass Index (Mean (SD))	25.9 (4.3)		26.0 (4.6)	
Global health score ([0; 100])	67.3 (18.0)		66.0 (17.8)	
Self-reported health problems				
Chronic bronchitis	8	2.7	8	3.2
COPD and emphysema	6	2.0	5	2.0
Asthma	30	10.0	26	10.3
Coronaropathy	4	1.3	4	1.6
Blood pressure disorder	30	10.0	27	10.7
Other cardiovasular disease	1	0.3	1	0.4
High cholesterol	11	3.7	7	2.8
Diabetes	16	5.3	14	5.5
Thyroid disease	12	4.0	11	4.3
Gastroesophageal reflux	8	2.7	8	3.2
Depression	5	1.7	4	1.6
Use of medication	126	41.9	112	44.3
Use of vitamins	77	25.6	64	25.3
Post-bronchodilator spirometry results				
Stage 0: At-risk	62	20.6	56	22.1
Stage 1: Mild	12	4.0	9	3.6
Stage 2: Moderate	8	2.7	7	2.8
Stage 3: Severe	1	0.3	1	0.4
COPD (GOLD)	21	7.0	17	6.7
PRISm	18	6.0	16	6.3
FEV1<LNN (GLI)	14	4.7	13	5.1
FVC<LNN (GLI)	7	2.3	7	2.8
FEV1/FEV1<LNN (GLI)	17	5.6	14	5.5
FEF25-75<LNN (GLI)	16	5.3	15	5.9
Missing	3	1.0	3	1.2
Occupation				
Station agent	132	43.9	132	52.2
Locomotive operator	122	40.5	121	47.8
Security guard	47	15.6		
Employement duration in years (Mean (SD))	24.1 (6.3)		24.5 (6.4)	
Exposure duration in years (Mean (SD))	23.0 (7.0)		23.2 (7.3)	
Home-work commuting in minutes (Mean (SD))	41.2 (24.1)		41.4 (24.2)	
Commuting by foot (n, %)	12	4.0	11	4.3
Commuting by subway or RER (n, %)	111	36.9	104	41.1

GOLD Global initiative for obstructive lung disease, PRISm preserved ratio abnormal spirometry, SD standard deviation. For definitions of GOLD stage and PRISm refer to the methods section.

Table 2
Summary of the exposure metrics considered and corresponding estimates to subway PM10 exposure in the analytical sample.

Exposure metrics considered in main and sensitivity analyses	Mean (SD)
Mean external PM10 exposure during the last year[a] (μg/m^3)	59.5 (31.0)
Mean annual external PM10 exposure during the last 5 years (μg/m^3)	60.9 (31.4)
Mean annual external PM10 exposure during the last 10 years (μg/m^3)	66.0 (33.3)
Mean annual external PM10 exposure during employment at subway (μg/m^3)	71.8 (33.7)
Mean inhaled PM10 exposure during the last year (μg/shift)	0.024 (0.009)
Mean annual inhaled PM10 exposure during the last 5 years (μg/shift)	0.374 (0.135)
Mean annual inhaled PM10 exposure during the last 10 years (μg/shift)	0.471 (0.161)
Mean annual inhaled PM10 exposure during employment at subway (μg/shift)	0.586 (0.268)
Cumulative inhaled PM10 exposure (μg/shift-years)	13.912 (7.974)

[a] From 13.05.2020 through 13.05.2021.

exposure metric and in the computation of the z-scores. The results from linear regression models were presented as β regression coefficients and those from logistic regression models as OR, both with their associated 95% confidence intervals (95%-CI).

2.7. Sensitivity analysis

To assess the sensitivity of the central estimate of particle filtration efficiency by the masks used in 2020–2021, we run the same models considering the best and the worse-case estimates. Furthermore, to test the sensitivity of the study results to the uncertainty in the annual exposure estimates (which might be more robust in the most recent years, where more measurements data were available), we considered as predictor the annual internal exposure averaged over the 1, 5, and 10 years before the outcome measurement. We then run the same models using the annual external exposure to subway PM10 as predictor to compare the results using this exposure metric. Finally, we applied the models with exposure duration to the study sample including security guards (excluded from the main analysis) to check the association estimate sensitivity to the sample size and composition.

3. Results and discussion

3.1. Sample description

We included 301 participants of whom 47 were security guards and were discarded from the analytical sample (Table 1). The participants' characteristics were similar in both samples, but security guards tended to be healthier, reporting less health problems and scoring their general health better on the 100-point scale: 74.1 ± 18.0 *versus* 70.2 ± 18.5 in locomotive operators and 62.2 ± 16.3 in station agents. They were also more often non-smokers and those who were current or ex-smokers smoked less. The employment and exposure duration were slightly lower in security guards: 22.1 and 21.8 years *versus* 25.9 and 23.8 years in locomotive operators and 23.2 et 22.7 in station agents. Two participants were not anymore employed as subway workers and three participants could not perform spirometry test. For those with available and validated spirometry results, the diagnosis of COPD was positive in 21 participants. As only two participants reported having COPD diagnosed by a physician, all but these two cases were newly diagnosed cases. Most were graded as GOLD 1 COPD stage (Table 1).

Table 3
Results of the multivariable logistic regression of the COPD.

Variables	OR	95%-CI	*p*
iPM10 (per 100 ng/shift)	1.034	(0.781; 1.369)	0.815
Exposure duration (y)	1.012	(0.936; 1.095)	0.758
Current smoking	6.851	(1.870; 25.095)	**0.004**
Former smoking	1.341	(0.133; 13.567)	0.804
Physical activity >10 h/week	1.532	(0.493; 4.760)	0.461
Commuting by metro/RER	1.174	(0.422; 3.272)	0.758

The one way home to work commuting time was about 40 min in average, and about 40% of participants commuted by subway or RER.

The occupational exposure to subway PM10 is summarized in Table 2. As expected, the iPM10 during the last year was an order of magnitude lower than in the previous five and more years, due to the use of respiratory protection during the pandemic (2020–2021), which strongly reduced the inhalation of particles in subway workers. The comparison of annual means of external exposure estimated over different calendar periods (Table 2) shows that estimates of annual concentrations of PM10 averaged over the entire career of workers in the analytical sample are higher than the estimates over the last ten and five years (71.8, 66.0, and 60.9 μg/m^3, respectively).

3.2. Dose-response relationship between inhaled PM10 concentration and outcomes

The association between COPD prevalence and iPM10 was positive but statistically non-significant (Table 3). The observed OR was 1.034 (95%-CI = 0.781; 1.369), per 100 ng/shift of inhaled PM10 exposure) corresponding to 3%-increase in COPD prevalence per every 100 ng/shift of PM10 inhaled. The relationship with exposure duration was also positive and statistically non-significant, suggesting a 2%-increase in risk per year of employment as subway worker. The analysis revealed the expected strong positive association with current smoking (OR = 6.851, 95%-CI = 1.870; 25.095 (Table 3).

We found no association between iPM10 and any of lung function parameters, either modeled as dichotomized variables (Table 4) or as z-scores (Table 5). However, FEV1 and FVC lower than the low limit of normal were positively associated with exposure duration with corresponding OR of 1.125 (95%-CI = 1.004; 1.260) and 1.171 (95%-CI = 0.989; 1.386) per year, respectively (Table 4). A strong positive association with current smoking was observed for all lung function parameters, especially when modeled as z-scores (Table 5).

3.3. Choice of exposure metric and impact on the study results

The sensitivity analysis results showed that the choice of exposure metric did not affect the results of the dose-response relationship between exposure to subway PM10 and COPD diagnosis. When using the cumulative iPM10, the estimated adjusted OR was 1.003 (95%-CI = 0.996; 1.009) per 100 ng/shift-year of inhaled subway PM10. When considering the exposure duration solely, the adjusted OR was 1.016 (95%-CI = 0.945; 1.092, p = 0.667) per year in the analytical sample, and 1.024 (95%-CI = 0.956; 1.097, p = 0.494) per year in the study sample including security guards (Table S1). This indicates that the exclusion of the latter from the main analysis did not yield a selection bias towards null in the study result. Finally, the use of external exposure to PM10 as exposure metric neither changed the study findings. Converted into an OR per 10 μg/m^3 of subway PM10 and additionally

Table 4
Results of the multivariable logistic regression of the lung function parameters.

Variables	FEV1<LNN (GLI)			FVC<LNN (GLI)			FEV1/FVC<LNN (GLI)			FEF25-75<LNN (GLI)		
	OR	95%-CI	*p*	OR	95%-CI	*p*	OR	95%-CI	*p*	OR	95%-CI	*p*
iPM10 (per 10 ng/shift)	0.977	(0.941; 1.015)	0.233	0.946	(0.888; 1.007)	0.082	0.996	(0.965; 1.029)	0.824	0.999	(0.969; 1.030)	0.954
Exposure duration (y)	1.125	(1.004; 1.260)	**0.043**	1.171	(0.989; 1.386)	0.067	1.019	(0.936; 1.111)	0.661	1.049	(0.960; 1.147)	0.289
Current smoking	3.359	(0.981; 11.503)	0.054	3.422	(0.628; 18.645)	0.155	4.929	(1.309; 18.566)	**0.018**	3.824	(1.147; 12.745)	**0.029**
Former smoking							1.208	(0.121; 12.009)	0.872	0.894	(0.096; 8.305)	0.922

Table 5
Results of the multivariable linear regression of the lung function parameters.

Variables	Z-score FEV1			Z-score FVC			Z-score FEV1/FVC			Z-score FEF25-75		
	β	95%-CI	*p*	β	95%-CI	*p*	β	95%-CI	*p*	β	95%-CI	*p*
iPM10 (per 10 ng/shift)	0.002	(-0.005; 0.009)	0.500	0.003	(-0.003; 0.010)	0.340	−0.002	(-0.007; 0.004)	0.604	0.000	(-0.006; 0.007)	0.955
Exposure duration (y)	−0.009	(-0.027; 0.010)	0.345	−0.012	(-0.030; 0.006)	0.179	0.003	(-0.013; 0.018)	0.717	0.002	(-0.015; 0.020)	0.801
Current smoking	−0.586	(-0.857; −0.315)	**<.001**	−0.335	(-0.593; −0.077)	**0.011**	−0.420	(-0.645; −0.195)	**<.001**	−0.624	(-0.879; −0.369)	**<.001**
Former smoking	−0.026	(-0.406; 0.354)	0.892	0.049	(-0.312; 0.411)	0.788	−0.137	(-0.452; 0.178)	0.391	−0.149	(-0.506; 0.209)	0.413

adjusted for the same variables as in UK-biobank and ESCAPE studies (i.e., age, sex, BMI), the observed risk estimate (OR = 1.030, 95%-CI = 0.879; 1.207, per 10 μg/m^3, Table S2) was comparable to the latter (Schikowski et al., 2014).

3.4. *Impact of uncertainty in the exposure assessment on the dose-response results*

The results of sensitivity analysis, testing the association between health outcomes and annual mean inhaled concentration of subway PM10 estimated over different calendar periods are shown in Table S3. These results show that none of iPM10 estimates is associated in a statistically significant manner with any of the health outcomes, whatever the calendar period over which the annual iPM10 was averaged. The OR and β estimated during the last 5 or 10 years and over the total worker's career are very similar for each outcome of interest. However, as expected, the average annual iPM10 during the last year, being an order of magnitude lower than in previous years due to the mask usage during COVID-19 pandemic, was associated with higher risk estimates. This result is however, not relevant per se, as this study is focused on the long-term exposure effect on health. As the estimated means over the last 5 years have similar association results as the means estimated over a longer period, the uncertainty regarding the temporal exposure trend in the JEM on the exposure-effect results had no obvious impact on the exposure estimate used in the main analyses (annual mean estimated over the workers' entire career).

Another uncertainty was related to the true value of mask filtration efficiency on iPM10 reduction. Table S4 summarizes the results obtained when applying the best and the worth case scenarios, compared with the central value (used in the main analysis). For the sake of precision, we focused on the iPM10 estimate during the last year only. As mentioned above, this estimate per se is of limited interest when assessing long-term effect of exposure on workers' health. However, assuming the potential continuation of the mask usage in the future, the comparison of the FE assumed in the model is relevant to assess its impact on the results. As expected, the best-case scenario (FE = 0.001, i.e., with less than 0.1% particles available for inhalation) was associated with the lowest OR, while in two other scenarios the OR was close to 1. Thus, the uncertainty on this parameter, and particularly the underestimation of FE does not change the study conclusions, as none of the risk estimate in the adjusted models reached statistical significance.

3.5. *Study limitations and strengths*

The most important limitation is the study sample size, too small for precisely quantifying the dose-response relationship with iPM10 and respiratory health outcomes. Indeed, we reused the sample initially set up for assessing the COPD and its association with biomarkers of oxidative and metabolic changes in exhaled breath condensate (Guseva Canu et al., 2021b). In contrast to the relationship with current smoking, the relationship between iPM10 and respiratory health outcomes was weak and statically non-significant, indicating an insufficient statistical power to detect a weak effect. Therefore, this study should be considered as a proof-of-concept demonstration, where, for the first time a JEM was applied for assessing occupational exposure to subway PM10 and its effect at a long-term.

Another limitation is the absence of exposure estimates for particles smaller than PM10, namely fine (PM2.5) and ultrafine particles. The risk of adverse respiratory health outcomes associated with concentration of these particles in the ambient air is stronger than that related to PM10 (WHO, 2022; Liu et al., 2019; Amaral et al., 2021; Bourbeau et al., 2022; Doiron et al., 2021; Adamkiewicz et al., 2020) and several studies reported higher concentration of fine and ultrafine particles in the subway environment compared to the outdoor (Pétremand et al., 2021, 2022; Byeon et al., 2015; Choi et al., 2019; Luglio et al., 2021; Smith et al., 2020; Strasser et al., 2018). Since the data on PM2.5 concentrations available in the database are less numerous than data on PM10 (Ben Rayana et al., 2022), we focused on PM10 exposure when developing the JEM (Ben Rayana et al., 2023). However, further efforts are needed to complete the database and to build a JEM for PM2.5 and ultrafine particles and assess their respective effects on the subway workers' health.

The application of JEM is known to lead to the Berkson error and reducing the contrast in the exposure estimates (Heid et al., 2004). However, given that the JEM used had additional dimensions (e.g., metro or RER line and geographic sector) and accounted for the temporal changes in PM10 concentration) (Ben Rayana et al., 2023) we believe to have minimized the bias resulting from Berkson error for independent variables.

The healthy worker effect, especially its healthy worker survivor effect (HWSE) component, might be a concern in this study. The HWSE results from a continuing selection process where workers who remain employed tend to be healthier than those who leave employment

(Arrighi and Hertz-Picciotto, 1994). The HWSE generally attenuates an adverse effect of exposure and can be problematic when evaluating subtle associations (Guseva Canu et al., 2020, 2022). Given an exploratory nature of this study, its limited sample size and cross-sectional design it was not possible to assess the HWSE. However, this should be considered in a future larger cohort study of subway workers.

Exposure estimates were refined to approximate the internal exposure by considering individual parameters such as sex, age, BMI, and physical activity, when applying the inhalation rates. As far as we know, this is the first time when such an approach is used for modelling PM10 exposure, and especially the long-term exposure to PM10 in subway workers.

The consistency of the results from different sensitivity analyses confirms the method relevance and encourages its replication in a large cohort of subway workers for a precise quantification of the dose-response relationship. This seems feasible, as Parisian transport company employes about 45000 workers and conducts epidemiological studies (Campagna et al., 2008). However, the feasibility of the outcome assessment as precise as in this study can be a challenge. Indeed, in most studies COPD status is assessed without a post-bronchodilatation spirometry, which is against the current diagnostic guidelines (Agustí et al., 2023). Having COPD diagnosis according to these guidelines is therefore an important strength of the present study but results in a high burden on researchers and study participants, with a high corresponding cost.

4. Conclusion

This is the first study assessing the relationship between long-term exposure to subway PM10 and a series of respiratory health outcomes in subway workers. The outcomes were measured according to the latest GOLD standard. Annual means of inhaled PM10 concentration were estimated to approximate internal exposure to subway PM10. Several sensitivity analyses, testing other exposure metrics and estimations completed this study. All these analyses consistently showed that the annual mean PM10 exposure levels estimated in subway station agents and locomotive drivers are associated with a statistically non-significant increase in COPD prevalence but not with decline in lung function. However, FEV1 and FVC lower than LLN were positively associated with exposure duration. Since the direction of regression results were in line with the hypothesis tested, although not statistically significantly, we cannot exclude a risk of adverse effect of subway PM10 exposure on respiratory health of subway workers, especially after long exposure duration. Notwithstanding, this effect, if further confirmed, seems rather weak, in contrast to the strong negative effect of smoking on lung function. Indeed, the study has an insufficient statistical power and could only identify factors with a strong effect on outcomes. The study does, however, demonstrate the feasibility and relevance of using JEM to model occupational exposure to particulate matter, and should be replicated on a large cohort of subway workers.

Ethics approval and consent to participate

The study was approved by the French Personal Protection Committee South-Est IV (N°2020-A03103–36), Declaration of conformity to the French National Commission for Computing and Freedoms (CNIL) N° 2220108. Written informed consent was requested from all study participants.

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Conflicts of interest

The authors declare no conflict of interest.

CRediT authorship contribution statement

Irina Guseva Canu: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Validation, Writing – original draft. **Pascal Wild:** Formal analysis, Methodology, Validation, Writing – review & editing. **Thomas Charreau:** Data curation, Formal analysis, Visualization, Writing – review & editing. **Romain Freund:** Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – review & editing. **Antonio Toto:** Conceptualization, Data curation, Formal analysis, Methodology, Resources, Writing – review & editing. **Jacques Pralong:** Conceptualization, Investigation, Software, Validation, Writing – review & editing. **Kirushanthi Sakthithasan:** Data curation, Investigation, Resources, Supervision, Validation, Writing – review & editing. **Valérie Jouannique:** Conceptualization, Funding acquisition, Investigation, Resources, Validation, Writing – review & editing. **Amélie Debatisse:** Conceptualization, Investigation, Project administration, Resources, Supervision, Validation, Writing – review & editing. **Guillaume Suarez:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2023.114316.

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