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Occupational exposure to aerosols in two French airports: Multi-year lung function changes

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Abstract

As differential exposure to airport-generated aerosols may affect employee lung function, the main objective of this study was to longitudinally evaluate spirometry measures among Air France employees. In addition, an exploratory exposure assessment to airport aerosol was performed in a small cohort of workers using personal monitoring devices. Change in lung function over a ~ 6.6 year period was documented for office workers (n=68) and mechanics (n=83) at Paris-Roissy airport, France and terminal (n=29) or apron (n=35) workers at Marseille airport, France. Overall, an excessive decline in lung-function was found for 24.75% of airport workers; excessive decline occurred more often for terminal workers (44.83%) as compared to mechanics (14.47%; P=0.0056), with a similar tendency for apron workers (35.29%) as compared to mechanics (P=0.0785). Statistically significant differences/tendencies were detected among the yearly rates of change for %-predicted values of forced expiratory volume in 1 second, forced vital capacity, peak expiratory flow and 25%-75% forced expiratory flow. For the latter variables, the terminal and/or apron workers at Marseille generally had significantly faster lung function decline as compared to office workers and/or mechanics at Paris, although the latter were exposed to a higher level of elemental carbon. No relation between lung function decline and exposure to airport tarmac environments was evidenced. Multivariate exploration of individual variables representing sex, smoking, atopy, respiratory disease, residential PM_{2.5} pollution, the peak size of particles in lung exhalates or exhaled CO at the time of follow-up failed to explain the observed differences. In conclusion, this study documents the first evidence of excessive lung function decline among certain airport workers in France, although the identification of emission sources (environmental factors, aircraft exhaust...) remain challenging.

Key words

aerosol exposure; carbon; Air France; airport worker; occupational health; pulmonary function; spirometry; personal monitoring;

What's Important About this Paper

This study documents lung function decline among certain airport employees and demonstrates that approximately 1/4 of the studied workers presented with excessive decrease in forced expiratory volume in 1 second (>15 point drop in % predicted values) over a ~6.6 year period.

Lung function decline was faster in apron and terminal workers in Marseille as compared to office workers and mechanics in Paris, but was not related to hours of exposure to a tarmac environment, which was also highlighted by the personal monitoring of aerosol exposure.

Determining the cause and means of preventing lung function decline among airport workers merits further research.

Abbreviations

- Al: aluminium
 BMI: body mass index
 Cd: cadmium
 Cr: chromium
 CO: carbon monoxide
 EBC: exhaled breath condensate
 EC: elemental carbon
 OC: organic carbon
 FEF: forced expiratory flow
 FEV1: forced expiratory volume in 1 second
 FVC: forced vital capacity
 PEF: peak expiratory flow
 PNC: particle number concentration
- SEG: similar exposure groups

Ti: titanium

TXRF: total reflection X-ray fluorescence

UFP: ultra-fine particle

Zn: zinc

Introduction

Airplane engine exhaust releases particulate matter into the air. The size distributions and number concentrations of such particles vary with engine type and thrust (Lobo *et al.* 2015). In combination with supporting activities associated with the airport apron (baggage and food carriers, tugs, refilling trucks, ground power units, etc) as well as transportation to and from the facilities (Masiol and Harrison 2014), airports are an important contributor to neighbouring urban pollution (Westerdahl *et al.* 2008; Hudda *et al.* 2014; Jones *et al.* 2020; Loehr and Turner 2022). High numbers of ultra-fine particles (UFPs, defined by aerodynamic diameters of <100 nm (Bendtsen *et al.* 2021)), especially the smallest fractions (~10 nm), are characteristic of airport-related pollution (Rahim, Pal and Ariya 2019a; Artous *et al.* 2024). Overall, background air particle number concentrations on airport aprons can reach ~ 2.5×10^6 /cm³ (Lobo *et al.* 2015; Rahim, Pal and Ariya 2019b; Artous *et al.* 2024), with local peaks around ~ 4.5×10^6 during aircraft landing and take-off (Westerdahl *et al.* 2008; Campagna *et al.* 2016).

For a given mass, aerosol particle lung toxicity tends to increase as particle size decreases (MacNee and Donaldson 2003); the small particle sizes associated with airport-derived air pollution are therefore of particular concern. The potential for UFP aerosol exposure to associate with adverse health effects is a source of ongoing debate and research (Ohlwein *et al.* 2019; Møller *et al.* 2020). It follows that respiratory complaints have been linked with airport vicinity (Bendtsen *et al.* 2021). Arter et al (2022) found that asthma exacerbations related to landing and take-off emissions in the United States increased from 100,000 to 170,000 over a span of six years (2011 to 2016).

Studies evaluating how airport UFP exposure affects lung function are few (Merzenich *et al.* 2021). One crosssectional study found no relationship between airport aerosol exposure levels and spirometric lung function findings, despite an excess of certain respiratory symptoms among male airport workers (Tunnicliffe *et al.* 1999). A second cross-sectional study similarly found no differences in lung function between 'exposed' and 'reference' groups of airport workers (Andersen *et al.* 2021). A review on the subject has underlined the absence of studies demonstrating any relationship between jet exhaust particles and respiratory symptoms (Touri *et al.* 2013). However, a recent short-term study demonstrated a significant decrease in forced vital capacity (FVC) associated with exposure to UFPs, with a tendency towards decreased forced expiratory volume in 1 second (FEV1) (Lammers *et al.* 2020). In the latter, additional sensitivity analyses demonstrated that the observed acute decreases in FVC and FEV1 were both significant for exposure to particles \leq 20 nm (Lammers *et al.* 2020). Interestingly, metals in airborne nanoparticle forms are also emerging as an important aspect of airport-related pollution (Rahim, Pal and Ariya 2019b). Despite the concern raised by these short-term results, no study documents long-term changes in the lung function of airport employees.

In this study, we assessed change in lung function over an approximately 6.6-year time span in airport workers representing four similar exposure groups (SEG) which exposure to airport aerosols was characterized concomitantly using personal samplings. Such exposure data on elemental carbon concentrations and metallic elements are intended to identify the future development of tracer profiles within personal exposure samples. SEG were chosen to differ in exposure to outdoor proximity to airplanes, and our aim was to determine correlation between such exposure and long-term decline in lung function. Simultaneously, we also assessed exhaled carbon monoxide, and heavy metal concentrations in exhaled breath condensates and urine from a subset of study participants.

Methods

Study design

This prospective, observational, follow-up study was proposed to adult Air France employees working at the Paris-Roissy Airport, Paris, France, or the Marseille-Provence Airport, Marseille, France, who had previously participated in a similar baseline cross-sectional initiative between October 2011 and June 2012 (NANERO1, NCT03098784). The current study (NANERO2) was proposed to all NANERO1 participants still working at their respective airports at the time of follow-up. Study size was determined by willingness to participate.

Inclusions started on November, 2017 and concluded on September, 2019, with laboratory assessments completed by January, 2020. Pregnant/lactating women or those with contraindications for study procedures were excluded. This study was performed in accordance with the Declaration of Helsinki. The study protocol was approved by an independent ethics committee (Committee for the Protection of Personnes Sud Mediterranée III, reference number 2015.12.02 bis), the study registered on clinicaltrials.gov (NCT02872727) and informed consent collected from all subjects prior to enrolment. Subjects were divided into four groups defined as similar exposed groups (SEG) according to professional roles: (i) office workers, (ii) terminal workers, (iii) apron workers, and (iv) mechanics. A description of the main tasks carried out by the workers within each SEG has been provided in the supplementary material.

Assessments

Following consent procedures, subjects underwent a physical exam during which demographic information (age, sex, body mass index (BMI), smoking (yes/no)) as well as information including the participants' duration of work experience at the airport and the average hours per day spent outside on the apron/tarmac was recorded, based on the participant's self-report. The time elapsed since the NANERO1 baseline study was calculated. Lung function was evaluated as previously performed in NANERO1 study. In the current study, we also included exhaled carbon monoxide measurement, and finally exhaled breath condensate and urine samples were collected.

Lung function

Spirometry was performed according to European Respiratory Society / American Thoracic Society recommendations at the time (Miller *et al.* 2005) using the CareFusion Spiro USB Desktop spirometer. The following pre-bronchodilator measures were recorded: forced expiratory volume in 1 second (FEV1_{%P}; % predicted values), forced vital capacity (FVC_{%P}; % predicted values), the ratio FEV1/FVC (%L/L), peak expiratory flow (PEF_{%P}; % predicted values); mean forced expiratory flow between 25% and 75% of the FVC (FEF-25-75_{%P}, % predicted values). Changes in each parameter compared to similar baseline measurements

(NANERO1 study) made approximately 6.6 years prior were calculated and used to determine the average annual change in lung function parameters. The rate of decline defined as normal corresponds to a decrease in % predicted values exceeding 15 (i.e. current study value - past study value <-15; Redlich et al., 2014; Townsend, 2020).

Exhaled CO

Exhaled carbon monoxide is measured in parts per million (ppm). Briefly, following a deep inhalation and 15s of breath holding (timed by the machine), the participant is required to exhale into a single-usage, disposable, cardboard mouthpiece adapted to a specific device. The result is immediately readable on the device, quantifies the level of CO intoxication, and is often used to objectify smoking levels, but also pollution effects (Shi *et al.* 2013; Gregorczyk-Maga *et al.* 2019).

Exhaled breath condensate (EBC)

EBC collection was performed using the RTubeTM device from Respiratory Research (USA) as previously described (Marie-Desvergne *et al.* 2016) and following the European Respiratory Society / American Thoracic Society recommendations (Horváth *et al.* 2005). Briefly, subjects were asked to perform tidal breathing into the device using a noseclip during 15 min. The resulting EBC was then immediately frozen at -20 °C in the collecting parts of the RTubes, and subsequently sent frozen to the laboratory where they were frozen at -80 °C prior to analysis for chromium (Cr; µg/L), cadmium (Cd; µg/L), aluminium (Al; µg/L) and 8-isoprostane (ng/L) content using inductively coupled plasma mass spectrometry (ICP-MS). The size distributions of particles in the individual EBCs was also characterised according to the presence/absence of particles "150-1000nm", the size of the first peak in the particle size distribution (nm), the presence/absence of a second peak, and the size of the second peak (nm). Detailed methods for these assessments and associated quality controls are provided in the Supplementary Material.

Urine analyses

Participants were asked to provide a urine sample, skipping the first flow. Analyses analogous to those performed on EBC are performed, including the same heavy metals. Cr was quantified using atomic absorption spectroscopy (AAS, Analyst 600 from Perkin Elmer), while Cd and Al were analysed using ICP-MS (Nexion 2000 for Cd and 300 for Al, Perkin Elmer). Levels of 8-isoprostane were evaluated using HPLC-MS/MS analysis using a SCIEX Exion LC system coupled to a AB Sciex 6500+ triple quadrupole (see supplementary material for further details). To adjust differences in urine concentration, urinary creatinine concentrations were quantified using COBAS INTEGRA 400 plus system (Roche), and weighted units used in statistical analyses: $\mu g/g$ of creatinine for metals, and ng/g of creatinine for 8-isoprostane.

The presence of allergic/atopic status, respiratory disease, or residential area air pollution

An extensive health questionnaire was administered to participants included in the current study and was used to determine atopic and respiratory disease status. The patient's zipcode was also used to determine significant residential pollution caused by particles with an aerodynamic diameter smaller than 2.5 μ m ((PM_{2.5}), see the Supplementary Material).

Personal exposure of workers to aerosols

Measurements were carried out following the OECD tiered approach (OECD 2015) and the NF EN 17058:2018 standard (CEN 2018). A cohort of sixteen workers representative of each SEG was equipped with personal compact sampling devices (i.e. the Sioutas® and Particlever®, see description below) in order to characterize their exposure to airport aerosols at both locations (Paris-Roissy Airport, or Marseille-Provence Airport) in addition to lung function evaluation. These measurements were carried out in June 2018 at Marseille airport and in July 2018, June and September 2019 at Paris-Roissy airport.

Background samples were collected simultaneously, using personal monitoring devices. In the present study, background level corresponds to ambient air present at a long distance from the runways and thus not directly influenced by emission sources relative to commercial flight operations. In both airports, background samples

were collected at Air France medical facilities (see Figure S1) with one or two workers carrying the personal samplers.

The Sioutas[®] is a personal cascade impactor with four impactor stages plus a final filter that allows the separation and collection of airborne particles in four size fractions, which have 50% cut-points at 2.5 µm (Stage A), 1.0 µm (Stage B), 0.50 µm (Stage C), and 0.25µm (Stage D) at a volume flow of 9 L/min.. Particles were collected on Whatman[®] Nuclepore[™] Track-Etched membranes (one per size range), which were later analysed for elemental content. The impactor was clipped onto clothing with Leland Legacy Sample Pump Cat. No. 100-3002 (9L/min) attached at the belt.

The Particlever® sampler was worn from a strap-necklace. This device was equipped with a size-selective impactor with a cut-off diameter of $4\mu m$ (respirable particle fraction) and was used with a microfiber quartz MK360 membrane from Fioroni in order to obtain the elemental carbon concentration by thermo-optical analysis.

Membrane analyses

The membranes corresponding to Sioutas® stages A, B, C and D were analysed using total reflection X-ray fluorescence (TXRF Nanohunter benchtop spectrometer (Rigaku®)), operating with Cu and Mo target X-ray tubes, with excitation settings of 50 kV and 1 mA, as previously described (Artous *et al.* 2024). The elemental detection from stages A-B were merged to provide a micrometric analysis, and C-D a submicronic analysis.

Elemental and organic carbon deposits on quartz membranes from the Particlever sampler® were analysed using a Sunset Laboratory thermo-optical analyser. The inorganic carbon was oxidised to carbon dioxide which was then reduced to methane over a catalyst and measured using a flame ionization detector (FID).

Avoiding bias and sample size

The current study was proposed to all NANERO1 (NCT03098784) participants still working at their respective airports at the time of follow-up. Study size was determined by willingness to participate. Missing data are indicated by variation in reported sample size; no imputation was performed.

Statistics

Statistical analyses were performed using the SAS statistical programming environment (SAS enterprise guide 9.4, SAS Institute, Carey NC,USA). Descriptive statistics are presented as percentages for qualitative variables, as mean \pm standard deviation for normally distributed quantitative variables, and otherwise as median (interquartile range).

As concerns quantitative outcomes, group effects were ascertained using linear models adjusted for sex, age and smoking status as appropriate (spirometry values as a percentage of theoretical values are already corrected for age and sex). When the presence of between-group differences were detected, the latter were pinpointed using Bonferroni- corrected tests with similar adjustments. For qualitative variables, the analogous tool used were multivariable logistic regression.

To further unravel group differences that were confounded by site/city, we sought data to test three additional potential covariates at the individual level: i) the presence/absence of respiratory illness, ii) the presence/absence of allergic/atopic status and iii) pollution levels more-specific to the participants' places of residence. Multivariable linear models were then used to explain the annual decline in lung function parameters as a function of sex, smoking, employment group, lung particle exposure as represented by the size of the first peak in the EBC particle size distribution (nm), lung inflammation as represented by exhaled CO (ppm), atopy, respiratory disease, and residential pollution. Variable effects were determined using standardised coefficients and their associated 95% confidence intervals and significance levels.

Results

Population characteristics

Among the 471 participants with a baseline assessment, 231 were included for the follow-up study (Figure 1). Of the latter, 218 consented for follow-up and with a final total of 215 participants with analysable data (Figure

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1). Table 1 presents descriptive statistics for the total population, and each of the four worker profiles (office workers (n=68), airport terminal workers (n=29), apron workers (n=35) and mechanics (n=83)). Follow-up took place at a median of 6.61 (6.35 to 7.21) years (Table 1). At the time of their inclusion in the current study, participants had a median age of 48 (42-55) years and 21.4% were women. The median BMI (24.7 (22.5 to 27.2)) was at the upper edge of the normal range (i.e. <25) and 23.72% were current smokers. The vast majority were long-term workers at their respective airports, with a median duration of work history of 21 (19-29) years, but with variable tarmac exposure at a median of 3 (0 to 6) hours per week.

There are strict differences in sex between groups, with all apron workers and mechanics being men (Table 1). The four groups are statistically similar in terms of BMI and years of work experience, but differences exist amongst them in terms of smoking, follow-up time, and daily hours of tarmac exposure (Table 1). Because we originally expected the latter to affect lung function, groups are presented in tables and figures ordered according to this variable, with the least exposed group on the left (office workers) and the most exposed group (mechanics) on the right. Further group comparisons are adjusted to take into account the previously mentioned potential confounding factors. Finally, the four groups also have strict differences in location, with participating administrative staff and mechanics hailing from Paris-Roissy, and the terminal and apron workers from Marseille. BMI and smoking status evolution since NANERO1 study was evaluated as it can influence lung function trajectories. While tobacco status remained stable since the first assessment (Table S1), the median BMI increased by 0.6 kg/m² (Table S2).

Lung function at baseline and follow-up

Baseline lung function assessed during the previous study (NANERO1) differed between groups. In general, the groups from Marseille (i.e. terminal and apron workers) had higher baseline FEV1, FEV1/FVC, PEF and FEF-25-75 as compared to the groups from Paris (office workers and mechanics) (Table 2). At follow-up, the differences in lung function apparent at baseline disappeared (Table 2). Lung obstruction (i.e. FEV1/FVC < 70%) was detected in 4.46% (9/202 individuals) of the overall population at baseline and 16.42% at follow up

(33/201 individuals). Concerning the latter, lung obstruction was observed for 24.59% of office workers (n=15), 24.14% of terminal workers (n=7), 8.57% of apron workers (n=3) and 10.53% of mechanics (n=8).

Annual change in lung function

The average yearly changes in lung function (with significance values adjusted for sex and smoking) are presented for each group in Figure 2. No differences between groups were detected for the yearly rate of change in FVC_{%P}. However, statistically significant differences (or tendencies) were detected between the four groups in terms of the yearly rates of change for FEV1_{%P}, FEV1/FVC_{%P}, PEF_{%P} and FEF-25-75_{%P}. For these variables, the terminal and/or apron workers at Marseille had significantly faster lung function decline as compared to the office workers and/or mechanics at Paris (Figure 3). Excessive decline is defined as an overall change <-15 in percent predicted values during follow-up (Redlich *et al.* 2014), and this was observed for 24.75% of the total population (Table S3). Between group comparisons demonstrate a significantly higher rate of excessive decline for terminal workers (44.83%) as compared to mechanics (14.47%), and a similar tendency for apron workers (35.29%) as compared to mechanics (Figure 3).

Exhaled carbon monoxide (CO) levels at follow-up

Exhaled CO values are presented in Figure S2. In general, overall results were similar to lung function in that the highest exhaled CO values were found for the terminal and apron workers. However, the only significant difference found among the four groups was a significantly higher CO value for terminal workers (a least squares means adjusted for age, sex and smoking [95% confidence interval] of 16.70 [13.31 to 20.09] ppm) versus office workers 10.67 [7.98 to 13.37] ppm; P=0.0411; Figure S2/Table S4). A similar tendency for higher exhaled CO in terminal workers as compared to mechanics (10.60 [7.67 to 13.53] ppm; P=0.0651) was also found.

Exhaled breath condensates

In all EBCs, estimates for particle size distributions presented a main peak centred at 427 nm. In more than 75% of subjects, a second peak of a median size of 118 nm was also observed (Table 3). The concentrations of Cr,

Cd, Al and 8-isoprostane were assessed in EBCs; however, the vast majority of samples had estimates below the lower levels of quantification and no significant differences were found amongst the four groups (Table 3).

Urine analyses

Except for Cd, the concentrations of metals in urine samples were for the vast majority of individuals below the limits of quantification (Table S5). Mechanics and apron workers had significantly higher urine Cd levels as compared to terminal workers (Figure 4), with a similar tendency found for office workers (Figure 4). All point assessments were within normal bounds (i.e. <0.8 or $<1 \mu g/g$ creatinine for non-smokers and smokers, respectively (Agence Nationale de Sécurité Sanitaire Alimentation, Environment, Travail (ANSES) 2018)). 8-Isoprostane was also quantifiable in almost all urine samples with an overall median concentration of 731 (571 to 861) ng/g creatinine, but no differences were found between groups (Table S5).

Determinants of lung function decline

Figure S3 presents the standardized coefficients and their 95% confidence intervals for variables used to explain the decline in lung function variables. Beyond group identity, none of the explored variables were significantly associated with lung function decline. Being a terminal or apron worker at Marseille was associated with stronger decline in FEV1_{%P}, PEF_{%P} and FEF-25-75_{%P}.

Aerosol exposure

Table 4 summarises the levels of exposure to both organic (OC) and elemental carbon (EC) measured at the level of the four groups, simultaneously with background samples collected in a remote area of the airport. Exposure to OC was below the limit of detection (LOD) for all the samples irrespective of the location and the group. However, a quantifiable and similar concentration of EC was measured in both personal and ambient air samples of mechanics and office workers from Paris-Roissy but not in those from Marseille (terminal and apron workers).

TXRF analysis demonstrated that elements were more abundant at the micron scale than at the submicron scale (Artous *et al.* 2024). Interestingly, elemental analysis of emission sources indicated that zinc (Zn) and, to a

lesser extent, titanium (Ti) were detected in aircraft engine aerosols and could therefore be identified as potential tracers of aircraft activities (Artous *et al.* 2024), in accordance with Rahim et al (Rahim, Pal and Ariya 2019b). Regarding the micron fraction of background samples at both airports, a greater number of metallic elements were observed at Paris-Roissy with a higher frequency compared to Marseille airport (Figure 5A). Figure 5B presents the metallic elements identified in the samples from each SEG at the Marseille and Paris-Roissy airports. For all SEG, classical background elements were found (e.g. Si, S, K, Ca, Mn and Fe). As for elements associated with aircraft activities in the present study (Ti and Zn, and to a lesser extent bromine), it was not possible to differentiate the two groups at the Paris-Roissy airport, probably due to higher background levels. By contrast, differences between the two groups at Marseille were obvious (Figure 5B), with Ti and Zn systematically found among apron workers, whereas Ti was found two out four times and Zn only once in the samples from terminal workers.

Discussion

The main results of this study demonstrate that, according to the American Thoracic Society technical standards for spirometry in occupational settings (Redlich *et al.* 2014), 24.75% of the studied French airport employee population had excessive decline in pulmonary function as represented by change in FEV1_{%P} < -15 over an approximately 6.6 year period (with a median change of -0.77 (-2.27 to 0.47) FEV1_{%P} points per year). Decline was not strong enough to result in a similar conversion rate to objective lung obstruction during the study, with only 16.42% of the population presenting with FEV1/FVC<70% at follow-up as compared to 4.45% at study initiation. A large majority of the study population therefore maintained normal lung function parameters throughout the study. Lung function decline was also not homogenously distributed among occupational subgroups; rather, it was significantly stronger among terminal and apron workers in Marseille as compared to office workers or mechanics in Paris, although the latter were exposed to a higher level of elemental carbon.

The latter pattern of decline was significant for $FEV1_{\text{%P}}$, $PEF_{\text{%P}}$ and $FEF-25-75_{\text{%P}}$, indicating that both the large and small airway components are likely involved. Group differences in lung function decline corresponded neither with group differences in average hours per week spent on the tarmac, as was initially expected, nor with the level of particles to which workers were exposed.

In non-smokers, the annual decline in FEV1 due to ageing is quite heterogeneous according to the studies, ranging from 9.9 to 56.0 mL/year (Thomas et al. 2019), while this decline is accelerated in smokers (Thomas et al. 2019; Oelsner et al. 2020). The overall annual decline in FEV1 estimated in the studied population (-0.77 FEV1_{%P} points per year, corresponding to a median decline (Q1-Q3) of -60.22 mL/year (-113.68 ; -19.11)) therefore falls within normal range. Excluding any pathology, several factors such as sex, tobacco or BMI index may impact lung function decline trajectories (Oostrom et al. 2018; Thomas et al. 2019). Here, while an expected but limited increase in the BMI (Yang et al. 2021) was observed in the total population, the percentage of smokers was stable since the previous NANERO1 assessment. In the current study, the groups at Marseille had the highest rates of smokers, though adjustments on this variable and also on sex were unable to completely explain group differences. Exhaled CO, a marker of individual lung inflammation, was highest in terminal workers as compared to office or mechanics, supporting the direction and differences in lung function decline among groups. However, none of these factors were able to explain (within multivariable models) the decline in lung function observed. However, although we adjusted data on tobacco consumption evaluated on a declarative basis using validated questionnaires, rather than exposure measurements using biomarkers, we cannot exclude residual confounding by smoking to account for some of the outcome observed in office workers. Similarly, it is difficult to establish a link between the decrease in lung function and carbon emission due to i) the limited number of aerosol samples; ii) the specificity of aircraft emissions, which comprise a high particle number concentration (PNCs) with a median particle size (d_{mn50}) below 20nm (Artous et al. 2024), representing low emitted masses (Marie-Desvergne et al. 2016); iii) the actual time spent on the tarmac, (around 4 hours per work day), which reduces the difference between exposed versus employment-type group. Nevertheless, both exposed and unexposed groups were distinguishable at the Marseille airport, implying that background levels may affect group monitoring. The personal carbon metrology showed that employees are subject to the influence of the geographical location of the airport, with higher elemental carbon (EC) levels recorded at the Paris-Roissy airport than in Marseille. In addition to the geographical location, season may also impact the composition of the aerosol. The current exposure measurement campaign was conducted during summertime, in order to target a peak period activity in airports. However, further measurements at different periods of time, to investigate the influence of parameters such as the weather and the seasons on the aerosol composition would greatly improve measurement representability.

Chronic exposure to $PM_{2.5}$ pollution has been previously associated with reduced and faster declines in lung function (Guo *et al.* 2018); however, we found no evidence of such an association between the presence of $PM_{2.5}$ at the participant's place of residence and the observed patterns of lung function decline in the present study. Multivariate exploration of individual variables representing sex, smoking, atopy, respiratory disease, residential $PM_{2.5}$ pollution, the peak size of particles in lung exhalates or exhaled CO at the time of follow-up failed to explain the observed group differences. Nevertheless, it is noteworthy that these patterns of lung function decline did not clinically affect the respiratory health of workers at the time of the study.

Previous studies have suggested that inhaled metals within nanoparticles may be an emerging facet of airportrelated pollution (Bendtsen *et al.* 2019; Rahim, Pal and Ariya 2019b). Furthermore, elemental analyses of the individual samples indicated that the markers of airport activity identified in the present study (Ti, Zn) were present at the micron scale in the majority of aerosols. We found little to no evidence of Cr, Cd, Al or even 8-isoprostane, a biomarker of oxidative stress (Cracowski, Durand and Bessard 2002; Shoman *et al.* 2020), in the exhaled breath condensates of airport workers, despite exhaled CO profiles consistent with inflammation in certain participants. However, urinary Cd levels under the 0.2 μ g/g creatinine reference value in non-exposed populations (Agence Nationale de Sécurité Sanitaire Alimentation, Environment, Travail (ANSES) 2018) was a common occurrence, with significantly higher levels for mechanics, apron workers and office workers as compared to terminal workers. Exhaled breath condensates may therefore not consistently reflect exposure, and the lack of metal containing particles therein may suggest lung deposition rather than exhalation. Group differences in urinary Cd may be explained by the presence of Cd-plated surfaces in aircraft. Unfortunately, this difference in urinary levels could not be correlated to any Cd exposure level, given that the concentrations measured in our aerosol samples were below detection limits using TXRF analysis. As Cd plating tends to be substituted for less toxic alternatives, it would be interesting to monitor the evolution of urinary Cd levels in these workers.

The observed patterns of lung function decline may be explained by variables not covered in this study. Socioeconomic status, for example, can associate with lung function (Rocha *et al.* 2020), as well as simple geographical gradients such as the use of air conditioning in the warmer climate of Marseille (Khaliq, Sharma and Tandon 2006; D'Amato *et al.* 2018). Exposure to chemicals used for cleaning is also associated with excess lung function decline (Vizcaya *et al.* 2015; Svanes *et al.* 2018). Heavy drinking has been demonstrated to have an independent negative effect on lung function decline among smokers (Frantz *et al.* 2014; Mehta and Guidot 2017). Interestingly, current alcohol consumers also have lower urine Cd levels (Sartor *et al.* 1992) and ethanol consumption may affect Cd turnover and body burden in complex ways (Brzóska *et al.* 2002; Brzóska, Galażyn-Sidorczuk and Dzwilewska 2013). As these hypotheses could broadly correlate with the patterns observed in the present study, future research on lung function decline among airport employees should include additional socioeconomic, occupational/indoor pollution and lifestyle factors.

A previous study examining controlled, acute (5h) exposure of young healthy subjects to ultrafine particulate matter (UFP) near airports estimated that a 5–95th percentile increase in UPF exposure (125,400 particles/cm³) was associated to a related decrease in lung function (–73.8 mL decrease in FVC) (Lammers *et al.* 2020), along with some changes in the urinary metabolome (Selley *et al.* 2021). Beyond this single experimental study, no observations linking variation in pulmonary function parameters to variation in airport aerosol exposure have resulted in clear correlation. Habre et al (2018) compared inflammatory markers and lung function in a 2-hr

walking exercise with a cross-over design (22 asthma participants) inside and outside high-UFP zones. An airport UFP factor was associated with increases in Interleukin 6 (IL-6), a circulating marker of inflammation, but not lung function. Tunnicliffe et al. (1999) found no differences in spirometric measures between low, medium and highly exposed airport workers, whose group averages were normal despite stratification by smoking. The results of the present study further support a lack of obvious association between measured near-field exposures to aircraft engine combustion and variation in spirometrically-determined lung function decline.

The results of the present study must be interpreted in the context of certain limitations. First, as with all observational studies, the assignment of causality would be premature. In particular, the number and volumes of aerosol samples were limited due to constraints linked to workplace conditions and schedules, which did not permit to establish a relationship between exposure to airport aerosol and the observed lung function decline. Secondly, there may be a healthy-worker bias in airports, as indicated by the high lung function levels among the terminal and apron works at baseline (Table 2). We must also recognize that acute, transient alterations in lung function are not captured by this study (Tunnicliffe *et al.* 1999; Lammers *et al.* 2020). Finally, the study was performed at only two airports and included only two time-points with a span time of 6.6 years during which we lack information on the workers' evolution. In particular, many workers were lost to follow-up. Further similar studies including a higher number of employees and a better stratification of groups will therefore be required to reinforce the generalizability of the observed patterns. Nevertheless, the primary strength of this study is its longitudinal nature, unique in this domain, associated to the characterization of occupational exposure to airport near-field aerosols.

In conclusion, we present the first observation of long-term lung function decline for airport workers in France, with excessive decline demonstrated for approximately one quarter of the study population, while maintaining normal lung function for a large majority. Contrary to initial expectations, lung function decline did not occur as a function of weekly hours of exposure to the outdoor tarmac environment. Individual participants considered as having excessive lung function decline were found in all employment-type groups (even in office workers), and

especially in terminal and apron workers at Marseille. Further research is required to determine factors affecting lung function decline among airport employees. Other sources of pollution surrounding the studied airports, or socioeconomic/lifestyle differences, may be more important in terms of impacts on lung function.

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Conflicts of interest / Competing interests

Carey M Suehs reports a previous grant and fees from Astra Zeneca, and a grant from GSK, outside the present work.

Nicolas Molinari reports personal fees from Astra Zeneca, grants from GSK, outside the submitted work.

Pascal Chanez is an advisor for Boehringer Ingelheim, Boston Scientific, GSK, AstraZeneca, Novartis, Chiesi, Sanofi and SNCF; he is on the advisory boards for Boehringer Ingelheim, GSK, AstraZeneca, Novartis, Chiesi, ALK, AB science, Argenx and Sanofi; he has received honorariums from Boehringer Ingelheim, GSK, AstraZeneca, Novartis, Chiesi, Boston Scientific and ALK; he has received grants from Boston Scientific, Boehringer Ingelheim, GSK, AstraZeneca, ALK, and Novartis; he was elected president of the scientific committee of the Fondation du Souffle (2020-2025).

The remaining authors have nothing to disclose.

Data Availability

The data that support the findings of this study are available upon reasonable request to the corresponding author, following approval by the research consortium members.

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Tables

Table 1. Descriptive statistics for the study population and subpopulations at the time of their inclusion in the current study, with P-values for tests detecting overall differences between groups, as well as Bonferroni-corrected P-values for statistical comparisons between subgroups.

	Total population	Office 1	Terminal 2	Apron 3	Mechanics 4	Overal I	1 vs 2	1 vs 3	1 vs 4	2 vs 3	2 vs 4	3 vs 4
		Sample size ^a Number(%) or median (IQR)					P-values					
Sex (female)	n=215 46 (21.40%)	n=68 27 (39.71%)	n=29 19 (65.52%)	n=35 0 (0%)	n=83 0 (0%)	χ2 <0.000 1	χ2 0.2971	χ2 <0.000 1	χ2 <0.000 1	χ2 <0.000 1	χ2 <0.000 1	
Age (years)	n=215 48.00 (42.00 to 55. 00)	n=68 55.00 (50.50 to 57. 00)	n=29 48.00 (42.00 to 55. 00)	n=35 47.00 (42.00 to 54. 00)	n=83 43.00 (40.00 to 48. 00)	KW <0.000 1	WMW 0.0006	WMW <0.000 1	WMW <0.000 1	WMW 0.9999	WMW 0.0594	WMW 0.254 2
BMI (kg/m²)	n=215 24.70 (22.50 to 27. 20)	n=68 24.90 (22.55 to 27. 75)	n=29 23.10 (21.00 to 28. 40)	n=35 24.90 (23.00 to 26. 70)	n=83 24.50 (22.70 to 26. 90)	KW 0.7939						
Smokin g (yes)	n=215 51 (23.72%)	n=68 6 (8.82%)	n=29 13 (44.83%)	n=35 13 (37.14%)	n=83 19 (22.89%)	χ2 0.0003	χ2 0.0221	χ2 0.0201	χ2 0.5346	χ2 0.9999	χ2 0.9999	χ2 0.513 9
Follow- up time (years)	n=204 6.61 (6.35 to 7.21)	n=61 7.07 (6.43 to 7.23)	n=29 6.09 (6.02 to 6.32)	n=35 6.49 (6.01 to 6.61)	n=79 6.69 (6.60 to 7.29)	KW <0.000 1	WMW <0.000 1	WMW 0.0001	WMW 0.9999	WMW 0.1407	WMW <0.000 1	WMW <0.00 01
Years working at airport	n=215 21.00 (19.00 to 29. 00)	n=68 20.00 (17.50 to 30. 00)	n=29 22.00 (20.00 to 30. 00)	n=35 20.00 (19.00 to 29. 00)	n=83 22.00 (19.00 to 28. 00)	KW 0.6957	WMW <0.000 1	WMW 0.0137	WMW <0.000 1	t 0.4409	t 0.9999	t 0.999 9
Tarmac exposur e (h/day)	n=214 3.00 (0.00 to 6.00)	n=68 0.00 (0.00 to 0.50)	n=29 1.00 (0.00 to 1.00)	n=35 5.00 (4.00 to 7.00)	n=82 6.00 (4.00 to 8.00)	KW <0.000 1	WMW 0.0017	WMW <0.000 1	WMW <0.000 1	WMW <0.000 1	WMW <0.000 1	WMW 0.571 2

^a Variation is due to missing data.

%P = percentage of theoretical values; $\chi 2$ = chi-squared test; AN = Analysis of variance (ANOVA) test; BMI = body mass index; IQR = interquartile range; KW = Kruskal-Wallis test; PEF = peak expiratory flow; t = t-test; WMW = Wilcoxon Mann Whitney U test.

Table 2. Lung function parameters measured at baseline (NANERO1) and at follow-up (NANERO2) for the total population and the four sub-groups

	Total	Office	Terminal	Apron	Mechanics	Overall	1 vs 2	1 vs 3	1 vs 4	2 vs 3	2 vs 4	3 vs 4
	population	1	2	3	4							
		Sample size ^a			P-values							
Baseline values												
	n=202	n=59	n=29	n=34	n=80							
FEV1%P	105.90 (97.00 to 115.00)	102.00 (95.00 to 112.00)	114.50 (108.10 to 123.60)	109.50 (99.10 to 120.50)	102.40 (94.00 to 110.00)	KW <0.0001	WMW <0.0001	t 0.0720	t 0.9999	WMW 0.2777	WMW <0.0001	t 0.0301
FVC _{%P}	106.00 (96.80 ; 115.20)	106.00 (95.00 ; 116.00)	111.60 (104.40 ; 116.50)	104.40 (94.50 ; 115.10)	106.00 (98.50 ; 114.50)	KW 0.0670						
FEV1/FVC(%L/L)	82.27 (± 6.61)	80.17 (± 7.02)	86.64 (± 4.38)	86.74 (± 5.58)	80.33 (± 5.70)	AN <0.0001	t <0.0001	t 0.0001	t 0.9999	t 0.9999	t <0.0001	t <0.0001
PEF _{%P}	109.75 (± 19.16)	108.23 (± 18.27)	123.86 (± 23.06)	115.87 (± 21.69)	103.14 (± 12.99)	AN <0.0001	t 0.0052	t 0.4388	t 0.4254	t 0.9737	t 0.0003	t 0.0160
FEF-25-75%P	99.57 (± 33.08)	86.96 (± 28.40)	128.15 (± 27.91)	125.94 (± 35.43)	87.31 (± 22.82)	AN <0.0001	t <0.0001	t <0.0001	t 0.9999	t 0.9999	t <0.0001	t <0.0001
Follow-up values (NANERO2)												
	n=201	n=61	n=29	n=35	n=76							
FEV1%P	100.05 (± 19.14)	101.84 (± 22.16)	100.93 (± 17.96)	97.97 (± 15.25)	99.25 (± 18.79)	AN 0.7706						
FVC _{%P}	100.00 (87.00 to 115.00)	101.00 (86.00 to 130.00)	104.00 (94.00 to 117.00)	98.00 (89.00 to 108.00)	96.50 (83.50 to 113.00)	KW 0.2773						
FEV1/FVC(%L/L)	81.92 (75.78 to 86.95)	81.67 (70.00 to 86.69)	80.28 (74.25 to 84.05)	80.00 (77.56 to 88.19)	83.15 (78.42 to 87.65)	KW 0.3850						
PEF _{%P}	87.73 (± 24.42)	90.87 (± 27.02)	81.93 (± 22.90)	84.89 (± 23.60)	88.74 (± 23.07)	KW 0.3125						
FEF-25-75%P	89.00 (69.00 to 108.00)	87.00 (58.00 to 107.00)	77.00 (63.00 to 105.00)	86.00 (71.00 to 112.00)	94.00 (77.50 to 111.50)	KW 0.2779						-

a Variation is due to missing data.

%P = percentage of theoretical values; AN = Analysis of variance (ANOVA) test; FEF-25-75 = forced expiratory flow between 25% and 75% of the FVC; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; KW = Kruskal-Wallis test; PEF = peak expiratory flow. Table 3. Current exhalate assessments for the total population and the four sub-groups. Group effects are provided as age, sex and smoking adjusted P-values.

	Total population	Office	Terminal	Apron	Mechanics	Overall
		1	2	3	4	
	Sample size ^a					P-values
	Number (%) or media	an (IQR)				
	Least squares means	adjusted for age, sex ar	nd smoking [95% confider	nce interval]		
Exhaled breath condens	ate metals and 8-lso	prostane at follow-up		•		-
Cr: % >LOQ	n=206	n=65	n=27	n=33	n=81	0.5847
	4 (1.94%)	1 (1.54%)	0 (0%)	0 (0%)	3 (3.70%)	
Cd: % >LOQ	n=206	n=65	n=27	n=33	n=81	0.7336
	6 (2.91%)	1 (1.54%)	1 (3.70%)	0 (0%)	4 (4.94%)	
AI: % >LOQ	n=206	n=65	n=27	n=33	n=81	0.6481
	10 (4.85%)	1 (1.54%)	2 (7.41%)	1 (3.03%)	6 (7.41%)	
8-Isoprostane: % >LOQ	n=204	n=64	n=26	n=33	n=81	0.1486
	16 (7.84%)	4 (6.25%)	1 (3.85%)	0 (0%)	11 (13.58%)	
Particle size distribution	S					
Particles 1-150nm	n=214	n=68	n=28	n=35	n=83	0.9384
present	112 (52.34%)	33 (48.53%)	15 (53.57%)	19 (54.29%)	45 (54.22%)	
Particles 150-1000nm	n=214	n=68	n=28	n=35	n=83	0.7619
present	201 (93.93%)	65 (95.59%)	25 (89.29%)	33 (94.29%)	78 (93.98%)	
Size of first peak (nm)	n=205	n=65	n=26	n=33	n=81	0.0721
	424 (367 to 549)	484 (390 to 600)	395 (335 to 481)	409 (352 to 442)	421 (367 to 587)	
	, ,	490.60[436.46 to	422.47[351.68 to	401.42[328.44 to	479.70[420.99 to	
		544.73]	493.26]	474.40]	538.41]	
% w/2 nd peak	n=214	n=68	n=28	n=35	n=83	0.3174
	165 (77.10%)	48 (70.59%)	23 (82.14%)	31 (88.57%)	63 (75.90)	
Size of second peak(nm)	n=165	n=48	n=23	n=31	n=63	0.8920
	118.0 (98.0 to 186.0)	119.5 (93.0 to 156.0)	125.0 (103.0 to 157.0)	121.0 (103.0 to 290)	113.0 (96.0 to216.0)	

^a Variation is due to missing data.

Al = aluminium; Cd = cadmium; Cr = chromium; LOQ = lower limit of quantification (Cr: 0.3 μ g/L; Cd: 0.1 μ g/L; Al: 3.9 μ g/L; 8-

isoprostane: 3.8 ng/L)

Table 4: Personal and background level of exposure to carbon particles in Marseille and Paris-Roissy airports

Airport	SEG	Mean Organic carbon level in Personal samples	Mean Organic carbon level in background samples	Mean Elemental carbon level in Personal samples	Mean Elemental carbon level in background samples	
		(µg/m³)	(µg/m³)	(µg/m³)	(µg/m³)	
Marseille Apron		< LOD	< LOD	< LOD	< LOD	
	Terminal	< LOD	< LOD	< LOD	< LOD	
Paris-Roissy Mechanics		< LOD	< LOD	10.1 ± 4.3	5.1 ± 0.7	
	Office	< LOD	< LOD	9.9 ± 3.9	7.8 ± 1.3	

LOD organic carbon = $10.24 \mu g/filter$

LOD elemental carbon = $0.35 \ \mu g/filter$

Figures Legends

Figure 1: The study flow chart.

Figure 2. Boxplots demonstrating annual change in pulmonary function parameters for the four study groups at Paris-Roissy (office workers and mechanics) and Marseille (terminal and apron workers) airports, France. Groups are presented from left to right in order of increasing exposure to airport pollution. Significance levels for group differences are given when P<0.1 and are from multivariate models adjusted for sex and smoking with Bonferroni corrections.

FEF = forced expiratory flow; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; PEF = peak expiratory flow.

Figure 3: Barchart demonstrating frequencies of subjects in each group with a decrease in FEV1 (% predicted) of at least 15 percent-predicted points at follow-up. Significance levels for group differences are given when P<0.1 and are from multivariate models adjusted for sex and smoking with Bonferroni corrections.

Figure 4 : Box plots demonstrating differences in urinary Cadmium levels for the four study groups at Paris-Roissy (office workers and mechanics) and Marseille (terminal and apron workers) airports, France. Groups are presented from left to right in order of increasing exposure to airport pollution. Significance levels for group differences are given when P<0.1 and are from multivariate models adjusted for age, sex and smoking with Bonferroni corrections

Figure 5: Micronic aerosol chemical elements identified by total reflection X-ray fluorescence (TXRF). Dots indicate when a given element was detected above the limit of quantification. Panel A represents background aerosols as represented by the analysis of membranes from devices located in the Air-France medical offices of either the Marseille or Paris-Roissy airports. Panel B represents membranes provided by workers (representing office, terminal and apron workers, as well as mechanics) at either the Marseille or Paris-Roissy airports.

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