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Assessment of the Occupational Exposures to Fine and Ultrafine Particles in Several Industrial Settings and Exploration of its Respiratory Health Effects

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Assessment of the Occupational Exposures to Fine and Ultrafine Particles in Several Industrial Settings and Exploration of its Respiratory Health Effects

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Abstract

Respiratory effects, such as lung function, of short-term exposures to fine and ultrafine particles are not well documented for occupational exposures, even though many workers are exposed daily to levels considerably higher than in the general environment. This limited understanding can be attributed to the lack of exposure data. Currently, studies assessing occupational exposures to fine particles and ultrafine fraction are few and lack standardized methods to allow a general conclusion about workers' exposures. The steps for improving exposure assessment include the harmonization of sampling strategies and the assessment of additional information related to the size distribution (e.g. particles of median diameter of 2.5 and 4 µm, and ultrafine particles), chemical composition, and the oxidative potential of these particles. Thus, in a context of uncertainty about the acute respiratory risks, with many potentially exposed workers and in the absence of comparable exposure data, the needs for developing knowledge in this field are enormous.

Hence, the main objective of this thesis was to estimate the risk of daily exposures to fine and ultrafine particles in various workplaces with three specific objectives: (1) to quantify and characterize exposures to fine and ultrafine particles in different workplaces in Québec by an innovative multi-metric approach; (2) to estimate the oxidative potential and oxidative burden of particles in two occupational settings from a construction trades school; (3) to separately estimate, by a systematic review and meta-analysis, the associations between short-term (i.e. daily and sub-daily) occupational and environmental exposures to fine particles and its acute respiratory effects on lung function in healthy adults.

For the first objective, measurements were performed in an underground mine, a subway tunnel, a truck repair workshop, and a smelting industry for at least 12 sampling days each. Direct-reading instruments and filter-based methods were used and included measurements of the number concentration, mass concentration, size distribution, transmission electron microscopy and composition (e.g. Total carbon (TC) and elemental carbon (EC)) of particles. For the second objective, the oxidative potential (OP^{AA}) and oxidative burden (OB^{AA}) were assessed by the ascorbate assay with a synthetic respiratory tract lining fluid. Personal PM_4 ($N_{welding}$ = 53; $N_{construction}$ = 54) samples were collected from the breathing zone, while area samples of both PM_4

($N_{welding}$ = 54; $N_{construction}$ = 33) and $PM_{2.5}$ fractions ($N_{welding}$ = 53; $N_{construction}$ = 34) were collected at distances of around 1.5 meter from the apprentices. For the third objective, we searched bibliographic databases to identify studies investigating associations between daily and sub-daily exposures to fine particles (i.e. $PM_{2.5}$ and PM_4) and lung function parameters (e.g. Forced Expiratory Volume in 1 sec, FEV_1) in healthy adults. Separately for environmental and occupational studies, we summarized findings using random-effects meta-analyses when five or more independent estimates of association were available.

The highest particle number concentrations were observed in the underground mine, welding shop and smelting industry. For the workplaces with diesel exposure, the underground mine had the highest geometric mean of particle number concentration (134,000 particles/cm^3) compared to the subway tunnel (32,800 particles/cm^3) and the truck repair workshop (22,700 particles/cm^3). This same pattern of exposure in these workplaces were also observed for the mass concentration of fine particles, TC and EC. The TC/EC ratio was 1.4 in the mine, 2.5 in the tunnel and 8.7 in the workshop, indicating significant organic carbon interference in the non-mining workplaces that can affect exposure estimation when TC is used as an indicator of diesel exposure. Measurements of the size distribution and images captured by transmission electron microscopy indicated that the particles found in all workplaces were mainly in the ultrafine size fraction.

Particles collected in the welding shop and construction site were associated with important levels of redox activity. Welding particles had higher OP^{AA} (3.3 pmol/min/µg) and OB^{AA} (1,750 pmol/min/m^3) compared to the construction site (OP^{AA} = 1.4 pmol/min/µg; OB^{AA} = 486 pmol/min/m^3). These levels of OB^{AA} largely exceeded the levels found in environmental settings. In both workplaces, OP^{AA} levels were not influenced by the different sampling strategies (i.e. area versus personal measurements) or size fractions (i.e. $PM_{2.5}$ and PM_4). However, driven by the higher particulate matter concentrations, the OB^{AA} from personal samples was higher compared to area samples in the welding shop.

The systematic review and meta-analysis showed that associations between daily exposures to fine particles and lung function in environmental settings were more pronounced than in occupational settings for a same exposure increment. An increase of 10 µg/m^3 in the daily

and sub-daily exposures to respirable fine particles were associated with FEV_1 reductions of 0.87 mL (95% CI: -1.36 to -0.37 mL; I^2= 54%) in occupational studies, and a similar increase in fine particles was associated with a reduction of 7.63 mL (95% CI: -10.62 to -4.63 mL; I^2= 0%) in environmental studies. Similar results were observed for associations with the forced vital capacity.

In summary, this thesis's results showed that workers are exposed to important levels of particles expressed in terms of mass and number concentrations, and these particles are mainly in the ultrafine size range. The high particulate matter concentrations combined with an elevated oxidative potential resulted in significant levels of oxidative burden that largely exceeded those from environmental settings. Also, occupational exposures during a work shift may result in respiratory health effects described in terms of reduction in workers' lung function. Based on our results, improvements in industrial hygiene practices and the surveillance of exposure to fine and ultrafine particles in the workplace are needed to control and limit potential health risks of daily exposure to these pollutants.

Keywords : fine particles, ultrafine particles, occupational exposures, oxidative potential, oxidative burden, lung function.

Résumé

Les effets respiratoires aigus des expositions journalières à des particules fines et ultrafines ne sont pas pleinement documentés pour les expositions professionnelles, même si de nombreux travailleurs sont exposés à des niveaux de particules considérablement plus élevés que dans l'environnement. Cela est en partie attribuable au manque de données sur l'exposition. Actuellement, les études évaluant les expositions professionnelles aux particules fines et ultrafines sont peu nombreuses et manquent de méthodes standardisées pour permettre une conclusion générale sur l'exposition des travailleurs. Les paramètres pour améliorer l'évaluation de l'exposition incluent l'harmonisation des stratégies d'échantillonnage et l'évaluation de la distribution des tailles (e.g. particules de diamètres médians de 2.5 et 4 µm et particules ultrafines), de la composition chimique et du potentiel oxydatif de ces particules. Ainsi, dans un contexte d'incertitude sur les risques respiratoires aigus, et considérant le grand nombre de travailleurs potentiellement exposés en l'absence de données d'exposition comparables entre les milieux de travail, les besoins de produire des nouvelles connaissances dans ce domaine sont énormes.

Ainsi, l'objectif principal de cette thèse était d'estimer les risques associés à l'exposition journalière aux particules fines et ultrafines dans divers milieux de travail avec les trois sous-objectifs suivant: (1) estimer des niveaux de particules fines et ultrafines dans différents milieux de travail; (2) évaluer le potentiel oxydatif et le fardeau du potentiel oxydatif des expositions professionnelles aux particules fines dans deux milieux d'une école des métiers de la construction; (3) estimer, par une revue systématique et une méta-analyse, la relation entre les expositions professionnelles et environnementales à court terme (c.-à-d. journalière) aux particules fines et leurs effets respiratoires aigus sur la fonction pulmonaire.

Pour le premier objectif, des mesures ont été effectuées pendant 12 jours d'échantillonnage dans une mine souterraine, un tunnel de métro, un atelier de réparation de camions et une fonderie. Des instruments à lecture directe et des mesures intégrées ont été utilisés et comprenaient des mesures de la concentration numérique, la concentration massique, la distribution granulométrique, la microscopie électronique à transmission et la composition (par exemple, le carbone total (CT) et le carbone élémentaire (CE)) des particules. Pour le

deuxième objectif, le potentiel oxydatif (OP^{AA}) et le fardeau oxydatif (OB^{AA}) ont été évalués par le test d'ascorbate en utilisant un fluide de revêtement des voies respiratoires synthétique. Des échantillons personnels de PM_4 ($N_{soudage}$ = 53; $N_{construction}$ = 54) ont été prélevés dans la zone respiratoire, tandis que des mesures en postes fixes de PM_4 ($N_{soudage}$ = 54; $N_{construction}$ = 33) et de $PM_{2.5}$ ($N_{soudage}$ = 53; $N_{construction}$ = 34) ont été collectées à une distance d'environ 1,5 mètre des apprentis. Pour le troisième objectif, nous avons recherché des bases de données bibliographiques pour identifier les études portant sur les associations entre les expositions journalières aux particules fines (c.-à-d. $PM_{2.5}$ et PM_4) et les paramètres de la fonction pulmonaire (e.g. volume expiratoire forcé en 1 sec, FEV_1) chez les adultes en bonne santé. Séparément pour les études environnementales et professionnelles, nous avons résumé les résultats à l'aide de méta-analyses à effets aléatoires lorsque cinq estimés d'association ou plus étaient disponibles.

Les concentrations en nombre de particules les plus élevées ont été observées dans la mine souterraine, l'atelier de soudage et la fonderie. Pour les milieux de travail avec une exposition au diesel, la mine souterraine présentait la concentration numérique la plus élevée (134 000 particules/cm^3) par rapport au tunnel de métro (32 800 particules/cm^3) et à l'atelier de réparation de camions (22 700 particules/cm^3). De plus, les concentrations massiques des particules fines, du CT et du CE étaient également plus élevées dans la mine souterraine par rapport aux autres milieux. Le ratio CT/CE était de 1,4 dans la mine, 2,5 dans le tunnel et 8,7 dans l'atelier, indiquant la présence d'une importante source de carbone organique non associée aux émanations de moteur diesel dans les milieux de travail non miniers. Cette source de carbone organique peut affecter l'estimation de l'exposition lorsque le CT est utilisé comme indicateur d'exposition au diesel. Les mesures de la distribution de la taille et les images capturées par microscopie à transmission électronique ont indiqué que les particules trouvées dans tous les milieux de travail étaient majoritairement dans la fraction ultrafine.

Les particules collectées dans les milieux de travail ont été associés à différents niveaux de potentiel oxydatif. Les particules de soudage présentaient des niveaux plus élevés de OP^{AA} (3,3 ρmol /min/µg) et OB^{AA} (1750 ρmol/min/m^3) que le site de construction (OP^{AA} = 1,4 ρmol/min/µg; OB^{AA} = 486 ρmol/min/m^3). Ces niveaux d'OB^{AA} dépassaient largement les niveaux trouvés dans l'environnement général. Dans les deux milieux de travail, les niveaux d'OP^{AA} n'ont

pas été influencés par les différentes stratégies d'échantillonnage (c.-à-d. mesures personnelles et en postes fixes) ou par la taille des particules (c.-à-d. $PM_{2.5}$ et PM_4). Cependant, en raison des concentrations de particules plus élevées, l'OB^{AA} des échantillons personnels était significativement plus grand que celui des mesures d'ambiance dans l'atelier de soudage.

La revue systématique et méta-analyse a montré que les associations entre les expositions journalières aux particules fines dans l'environnement général étaient plus prononcées qu'en milieu de travail pour un même incrément d'exposition. Une qu'une augmentation de 10 ug/m^3 des expositions journalières aux particules fines respirables était associée à des réductions du FEV_1 de 0,87 ml (IC à 95%: -1,36 à -0,37 ml; I^2 = 54 %) dans les études professionnelles, et une augmentation similaire des particules fines était associée à une réduction de 7,62 mL (IC à 95%: -10,62 à -4,63 mL; I^2 = 0%) dans les études environnementales. Des résultats similaires ont été observés pour les associations avec la capacité vitale forcée.

En résumé, les résultats de cette thèse montrent que les travailleurs sont exposés à des niveaux importants de particules exprimées en termes de concentrations massiques et numériques, et que ces particules se trouvent principalement dans la fraction ultrafine. Les concentrations élevées de ces particules combinées à un potentiel oxydatif important entrainent un fardeau oxydatif qui dépasse largement celui d'études environnementales. De plus, les expositions professionnelles pendant un quart de travail entraineraient des effets sur la santé respiratoire décrits en termes de réduction de la fonction pulmonaire des travailleurs. À la lumière de ces résultats, des améliorations des pratiques d'hygiène industrielle et de la surveillance de l'exposition aux particules fines et ultrafines dans les milieux de travail sont nécessaires pour contrôler et limiter les risques sanitaires potentiels des expositions journalières à ces polluants.

Mots-clés : particules fines, particules ultrafines, expositions professionnelles, potentiel oxydatif, fonction pulmonaire.

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List of Abbreviations

COPD: Chronic obstructive pulmonary disease
CPC: Condensation particle counter
DEE: Diesel engine exhaust
DPM: Diesel particulate matter
DRI: Direct-reading instruments
EC: Elemental carbon
$EC_{1:}$ Submicron fraction of elemental carbon
EC_R: Respirable fraction of elemental carbon
EEPS: Engine exhaust particle sizer spectrometer
ELPI: Electrical low-pressure impactor
FCAW: Flux-cored arc welding
FeNO: Fractional exhaled nitric oxide
FEV_1: Forced expiratory volume in 1 second
FVC: Forced vital capacity
FMPS: Fast mobility particle sizer spectrometer
GM: Geometric mean
GMAW: Gas metal arc welding
GSD: Geometric standard deviation
GTAW: Gas tungsten arc welding
IARC: International Agency for Research on Cancer
ICP-MS: Inductively coupled plasma mass spectrometry
JEM: Job Exposure Matrix
OB: Oxidative burden
OB^{AA}: Ascorbate oxidative burden
OC: Organic carbon
OEL: Occupational exposure limits
OP^{AA}: Ascorbate assay for oxidative potential
OP^{DTT}: Dithiothreitol assay for oxidative potential
OP^{GSH}: Glutathione assay for oxidative potential
OP^{ESR}: Electron spin resonance assay for oxidative potential
PM: Particulate matter
$PM_{2.5}$: Particulate matter with median aerodynamic diameter of 2.5µm
PM_4: Particulate matter with median aerodynamic diameter of 4µm
PNC: Particle number concentration
QFF: Quartz fiber filters

ROS: Reactive oxygen species
RTLF: Respiratory tract lining fluid
SMAW: Shielded metal arc welding
SMPS: Scanning mobility particle sizer
TC: Total carbon
$TC_{1:}$ Submicron fraction of total carbon
TC_R: Respirable fraction of total carbon
UFP: Ultrafine particles

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Chapter 1 – Introduction

1.1 Introduction

The particulate air pollution is known to cause cardiorespiratory health effects in humans (1, 2). According to the Global Burden of Disease Group, exposure to ambient fine particles (i.e. particles with an aerodynamic diameter of less than 2.5 µm) was the fifth-ranking mortality risk factor in 2015; it caused 1.8 million deaths and 51.4 million disability-adjusted life-years (DALYs) due to respiratory diseases (3). Regarding respiratory effects, in the general environment, both short-term and long-term exposures to fine particles have been related to respiratory mortality, morbidity, symptoms and lung function decrease (4-7). In occupational settings, exposures to particulate matter of varying sizes are also known to contribute to mortality by respiratory outcomes (8, 9). However, effects of short-term exposures, such as on lung function, are not well documented for occupational exposures, although exposure levels are considerably higher than in the general environment. In addition, repeated daily exposures at high concentrations (e.g. during work-shifts) may contribute to the development of long-term respiratory effects.

This lack of understanding of the respiratory risks associated with short-term (i.e. during a work shift) occupational exposures is concerning because millions of workers worldwide are exposed to tasks associated with the emission of particles – including the fine and ultrafine fractions (i.e. smaller than 0.1 µm) – at concentrations higher than the typical urban background. For instance, in Canada, it is estimated that almost 900,000 workers are exposed to diesel particulate matter from diesel engine exhaust, 381,000 workers are exposed to fine crystalline silica particles, and around 146,000 welders and foundry workers are exposed to fine particles rich in metals such as lead, nickel and chromium (10). Most of these emissions also include ultrafine particles (UFP), that are believed to be more toxic because of their small size, which causes them to penetrate and deposit deeply in the lungs, and also to translocate from the alveolar space into the bloodstream. This can lead to health effects outside of the respiratory system including in the brain, and in the cardiovascular system such as on morbidity (i.e. ischemic heart disease and heart failure-related hospital admissions and emergency department visits) and mortality (1, 2, 11-14).

This limited understanding regarding the short-term respiratory health risks despite the significant number of workers exposed can be attributed to the lack of exposure data. Currently, studies assessing occupational exposures to fine particles, and especially the ultrafine fraction, are few and lack standardized methods to allow a general conclusion about workers' exposure. Thus, there is a need for the harmonization of sampling strategies and the assessment of additional information related to the size distribution (i.e. fine and ultrafine fractions), metrics of exposure (i.e. mass and number concentration) and the composition of particles in different workplaces to generate more reliable and comparable data on exposure.

Occupational exposure assessment to particles is usually performed by identifying surrogates of exposures. In most cases, the mass concentration of particles or individual components, such as elemental carbon for diesel engine exhaust and different metals such as nickel, iron, manganese and chromium for welding fumes are measured. Although this approach has been historically important to link the effects of individual elements to health outcomes, it does not provide an integrative measurement of multiple components or information regarding the synergistic interactions between chemical species. In this context, the measurement of the oxidative potential and oxidative burden – a technique used to assess the potential of multiple components of particulate matter in generating oxidative stress – has been widely applied in environmental studies (15). However, it has not been extensively studied in occupational contexts. Therefore, a comprehensive investigation of the oxidative potential and oxidative burden of particles collected in the context of different workplaces, activities, size fractions and sampling strategies would contribute to the exposure assessment to occupational particles.

Thus, in a context of uncertainty about the short-term respiratory risks, with many of potentially exposed workers and in the absence of comparable exposure data, the needs for developing knowledge in this field are enormous.

1.2 Thesis Outline

This thesis focuses on the assessment of the occupational exposure to fine particles – including the ultrafine fraction - in several industrial settings and on the exploration of the short-term respiratory health effects (i.e. lung function decrease) associated with the daily and sub-

daily exposures to these particles. **Chapter 2** continues with a background section and gaps in the literature on these topics, while **Chapter 3** introduces the general and specific objectives of the thesis and **Chapter 4** describes the methods used throughout this thesis. **Chapter 5** focusses on assessing occupational exposures to particles, including the fine and ultrafine fractions in workplaces with powered diesel equipment, which is a main source of particulate matter. The first article of this chapter, published in the *Journal of Occupational and Environmental Hygiene,* describes an innovative sampling strategy to estimate DPM in underground mines that integrates different sampling methods (i.e. direct reading instruments and filter-based methods), size fractions (i.e. fine and ultrafine), metrics (i.e. mass and number concentration) and surrogates of exposure to particles. The second article, published in the *Annals of Work Exposures and Health,* expands this sampling strategy to compare exposure to DPM in different workplaces, namely an underground mine, a subway tunnel, and a truck repair workshop. **Chapter 6** presents a scientific article submitted to the *Annals of Work Exposures and Health*; this manuscript aims to estimate the oxidative potential and oxidative burden in the context of occupational exposures to fine particles. This characterization includes the comparison in different workplaces, activities, sampling strategies and size fractions of particles. **Chapter 7** explores the relationship between short-term exposures to fine particles and its acute lung function effects in a systematic review and meta-analysis, where estimates for occupational and environmental exposures were separately calculated. **Chapter 8** presents a general discussion and conclusion of the thesis. Finally, the **Appendix** presents information that is complementary to the sampling strategy presented in Chapter 5. Appendix 1 is an article published in the *Journal of Environmental and Occupational Hygiene* that compares two different methodologies for measuring DPM in mines. Appendix 2, published in the *International Journal of Mining Science and Technology*, validates the use of a dual-port system for simultaneous sampling of DPM and crystalline silica, pollutants that are common in workplaces like underground mines and construction sites. Finally, Appendix 3 presents the results of measurements of fine and ultrafine metallic particles in two sectors of a stainless-steel smelting industry: a foundry and a machining shop.

Chapter 2 - Background

2.1 Description and Sources of Fine and Ultrafine Particles

The determination of the aerodynamic size fraction of particulate matter (PM) is essential because particles with varying aerodynamic dimensions can penetrate and deposit in different regions of the human respiratory tract. Fine particles - or $PM_{2.5}$ - are of particular toxicological interest because of their capacity to reach the gas-exchange region (alveoli) when inhaled (1). Although $PM_{2.5}$ is also measured in some occupational studies, this fraction is not present in regulations of the industrial hygiene field. Instead, the definition of respirable particles - or PM_4 (particulate matter with a median aerodynamic diameter of 4 μm) - is used in the occupational hygiene field to represent particles with the capacity of reaching the deepest parts of the lung (16). By this definition, $PM_{2.5}$ is included in PM_4.

Ultrafine particles (UFP) are found as individual, aggregated, or agglomerated forms. The term "*nanoparticles*" has, in many cases, been used as a synonym for UFP. However, nanoparticles can also refer to engineered nanomaterials that are intentionally manufactured for consumer products and industrial applications, such as titanium dioxide, aluminum oxide, and zinc oxide (17). For this reason, in the present thesis, the term UFP is used to refer to unintentionally released nanometric particles.

Airborne particles contain both primary (i.e. emitted directly from the source) and secondary (i.e. formed in the atmosphere by gaseous precursors) compounds, and the processes involved in their formation differ according to the aerodynamic size of the particles. Contrary to coarse particles - that are generated by mechanical activities (e.g. construction, resuspension by traffic or friction) - fine particles, including the ultrafine fraction, can be emitted directly as primary particles or produced by the condensation of gases in pre-existing particles or by the nucleation of organic compounds, H_2SO_4, H_2O or NH_3 (1). Sources of these particles in the general environment can be natural - such as forest fires and volcanism - or anthropogenic - such as traffic, industry, biomass burning and coal and oil combustion (18). Furthermore, different industrial processes were identified as suitable for occupational emissions of fine and ultrafine particles and they were classified in the following categories: fragmentation of the material (e.g.

crushing, earthworks), thermal degradation by combustion (e.g. melting, food cooking), shaping (e.g. moulding, extrusion), machining (e.g. grinding, sanding), surface treatment and coating (e.g. quenching), assembly (e.g. welding, thermal cutting) as well as activities related to emissions from diesel engines (19).

2.2 Toxicity of Particulate Matter

2.2.1 Deposition, Clearance and Distribution

The transport and deposition of particles in the respiratory system depends primarily on the size distribution, breathing route (i.e. nasal or mouth), tidal volume, breathing frequency and respiratory tract morphology (12). Inhalable (i.e. 100 μm) and thoracic particles (i.e. 10 μm) will preferentially deposit in the extra-thoracic and thoracic regions. In contrast, fine and ultrafine particles are predicted to deposit more efficiently in the bronchiole and alveolar region, with peak deposition in the alveoli at 20-30 nm (14).

The mechanisms of deposition also differ according to the diameter of the particle. For particles between 1 and 10 μm, the main deposition mechanisms are interception, impaction, and sedimentation, while Brownian diffusion is the primary mechanism of deposition of particles having a diameter less than 0.1 μm. In addition to these mechanisms, the electrical charge on some particles may result in enhanced deposition compared to the uncharged ones. The efficiency of deposition is reduced for particles between 0.1 and 1 μm. In this size range, they are small enough to have minimal sedimentation or impaction and sufficiently large to have a minimal diffusive deposition. Furthermore, biological factors can modulate deposition rates, such as physical activity, age, sex, anatomical variability, respiratory tract disease and hygroscopicity of aerosols (1).

Clearance of inhaled PM also varies according to the deposited region. Particles deposited in the extra-thoracic and the tracheobronchial regions are moved by mucociliary transport and removed by swallowing, sneezing, or weeping. This is considered a rapid process (i.e. 24-48h). In the bronchioles and alveoli, however, inhaled particles are cleared by phagocytosis by the alveolar macrophages, a slower process than the clearance in the upper regions of the lung (20).

The inefficiency of this process may lead to prolonged interaction of the particles with lung cells and translocation to other regions.

Translocation across the airway epithelium into the bronchial circulation or across the alveolar epithelium into the systemic circulation is described for soluble components from all PM size fractions. However, due to their reduced size, fine and ultrafine particles have a more significant potential for translocation into the blood via the lung, with subsequent transport to other organs, including the heart and the brain (14). It is suggested that transportation may occur by endocytotic and exocytotic mechanisms or diffusion across membranes (21).

2.2.2 Mechanisms of Pulmonary Toxicity

Following short-term exposure, fine and ultrafine particles are deposited and retained. Insoluble and soluble components may interact with cells in the respiratory tract, such as epithelial cells, inflammatory cells, and sensory nerve cells. Acute respiratory effects may then occur by two main proposed pathways. The first one involves the activation of sensory nerves in the respiratory system, potentially triggering local reflex responses and transmitting signals to regions of the central nervous system that regulate autonomic outflow. The second pathway, further described in the sections below, involves production of reactive oxygen species (ROS) and inflammation (12).

2.2.2.1 Reactive Oxygen Species

The main ROS involved in oxidative stress are the superoxide anion (O2•-), the hydroxyl radical (OH•), hydrogen peroxide (H_2O_2) and singlet oxygen ($^1O_2$). ROS may be directly generated from the action PM's surface components, such as metals and organic species. The main mechanisms in which organic species generate oxidative stress are through redox cycling of quinone-based radicals, by complexing of metal resulting in electron transport, and by depleting antioxidants by reactions between quinones and thiol-containing compounds. Furthermore, metals can generate ROS by directly supporting the electron transport to generate oxidants and by diminishing antioxidants' levels (22). In addition to the direct production of oxidant species, PM can also be an indirect source of ROS in the respiratory system. For example, exposure to PM may increase intracellular ROS production by stimulating the NADPH oxidase in macrophages and

epithelial cells, disruption of intracellular iron homeostasis, absorption of soluble components and the induction of nitric oxide synthase to produce reactive nitrogen species (1).

The human body has a complex set of exogenous and endogenous antioxidant defences responsible for protecting against the deleterious effects of ROS. Exogenous antioxidants are provided by the diet rich in ascorbic acid, vitamin E, carotenoids, ubiquinone, flavonoids or lipoic acid, while endogenous antioxidants consist of enzymes (e.g., superoxide dismutase, glutathione peroxidase and catalase), proteins (e.g. ferritin, transferrin, ceruloplasmin and albumin) and systems for repairing oxidative damage (e.g. endonucleases). Also, some trace elements such as selenium, copper and zinc are cofactors of antioxidant enzymes (23, 24). The unstable characteristics of the ROS make them very reactive with biological targets. When their concentration exceeds the defence capacity of antioxidants, the excessive amount of these substances results in deleterious oxidative modifications associated with the appearance of pathologies. This process is also known as oxidative stress, and the main biological targets are: 1) the DNA, resulting in genotoxicity; 2) amino acids, resulting in protein damage; and 3) membrane lipids, resulting in an alteration of the membrane fluidity (23, 24). In this context, oxidative stress is proposed as one of the mechanisms involved in respiratory effects such as altered lung function, hospitalizations or deaths for asthma, pneumonia, COPD and lung cancer (25).

Although all size fractions of PM may generate ROS and cause oxidative stress, fine and ultrafine particles may have a higher oxidative potential due to their large surface/volume ratio and the enrichment of redox-active surface components, such as metals and organics compounds. Consequently, these particles could interact more with the cell surface and potentially deliver relatively more adsorbed soluble components to cells compared to larger particles (1, 23).

2.2.2.2 Inflammation

In addition to oxidative stress, an inflammation process may also be initiated after short-term exposure to particles, and it is composed of two major events: increased vascular permeability, and local recruitment and activation of cells. After exposure, the activation of transcription factors in macrophages and epithelial cells stimulates the synthesis and release of ROS, nitrogen species and specific cytokines, such as tumour necrosis factor alpha and interleukin

1 (26). These cytokines play a role in recruiting inflammatory cells such as neutrophils to the lung. Besides, interactions between macrophages and epithelial cells enhance these particle-mediated cytokine responses (27).

The neutrophils recruited become hyperresponsive to activating signals, resulting in neutrophil degranulation, respiratory burst response, and soluble mediators release such as interleukin 6, platelet-derived growth factor and interleukin 8 (1, 28).

During lung inflammation, elevated levels of nitric oxide are released from epithelial cells of the bronchial walls. Thus, the measurement of the fractional concentration of the exhaled nitric oxide (FeNO) constitutes a non-invasive method to monitor airway inflammation (29). An increased level of nitric oxide may also act as an oxidative stressor which will further contribute to an inflammatory response, resulting in adverse effects such as lung function reduction. This scenario has been demonstrated by several studies in the general environment that described an increase in the FeNO and a reduction in lung function for several hours and days after short-term exposure to $PM_{2.5}$ (30-34).

2.3 Lung Function and Short-Term Exposures

Oxidative stress and inflammation are the main mechanisms involved in lung function decreases. Short-term PM exposure may lead to an increased tonus of airway smooth muscles that is rapidly antagonized by an increased cellular level of nitric oxide (NO). This increased NO level may also act as an oxidative stressor and contribute to an inflammatory response, resulting in reductions in lung function (1, 33). The assessment of changes in lung function parameters has frequently been used in epidemiological studies investigating the respiratory effects of short-term exposures to ambient particles in the general environment. Lung function is also used to diagnose chronic respiratory diseases like asthma and COPD. Changes in lung function parameters can be assessed by spirometry. The main parameters investigated in epidemiological studies are the forced vital capacity (FVC), which is the volume that is forcefully and completely delivered during expiration, and the forced expiratory volume in one second (FEV_1), which is the volume of air blown in the first second of an FVC maneuver. Other important parameters are the

forced expiratory flow (FEF), FEF_{25-75}, the peak expiratory flow (PEF) and maximum mid-expiratory flow (MMEF) (35).

Short-term exposures to particles have been associated with decreased lung function in vulnerable individuals, including children, elders, and adults with pre-existing respiratory diseases (36-39). For instance, Bloemsma et al. (2016) performed a systematic review and meta-analysis of panel studies on acute effects of air pollution among patients with COPD. Results showed that a 10 $\mu g/m^3$ increase in ambient PM was associated with a 3.4 mL decrease in FEV_1 (95% CI: -6.39 mL to -0.37 mL) (36). Also, McCreanor et al. (2007) evaluated the acute effects of air pollution in asthmatic pedestrians walking for 2 hours in Oxford Street, London. The authors found reduced lung function and increased lung inflammation after exposure to UFP, $PM_{2.5}$ and elemental carbon (37). However, this relationship is less established for healthy adults when compared to vulnerable individuals; there is also almost no study on the association between the short-term exposure of workers to particles and lung function. The current evidence on this association in healthy adults from the general population and in workers is reviewed in Chapter 7.

2.4 Exposure Assessment

The estimation of the associations between exposure to particles and respiratory effects, like lung function, relies on exposure assessment strategies that provide accurate and comparable results. Some factors to be considered for the exposure assessment of fine and ultrafine particles include the size fraction, metrics of exposure (i.e. mass, number, or surface concentration) and measurement methods (i.e. filter-based sampling or direct-reading instruments). These concepts, along with an overview of exposure levels in different workplaces, are presented in the sections below.

2.4.1 Metrics of Exposure

The concentrations of airborne particles are usually quantified in mass, number, or surface-area concentration, being the first two metrics the most commonly reported. Size fractions in the micrometric range, including $PM_{2.5}$ and PM_4, are typically reported as mass

concentration (e.g. $\mu g/m^3$), and it is used by environmental and occupational regulatory agencies. However, the measurement of the mass concentration of UFP is challenging due to the very low contribution of these particles to the total mass of the aerosols. Thus, based on toxicological studies, the number concentration (e.g. particles/cm^3) has been suggested as a more suitable metric of UFP exposure (14). However, UFP - expressed as particle number concentration - is currently not regulated as a distinct part of current occupational exposure limits, nor is it regulated in the general environment.

2.4.2 Methods of Measurement of Occupational PM

The capacity to collect representative samples for analysis is an essential element in studying occupational aerosol exposures. These samples must accurately characterize the features, such as concentration and size distribution, of the airborne particles. In this context, the measurements can be performed by filter-based sampling or by using direct-reading instruments.

Filter-based sampling requires the collection of the particles for subsequent laboratory analyses. These measurements are primarily used to assess compliance with industrial hygiene recommendations and regulatory standards. Examples of these analyses include gravimetric measurements, inductively coupled plasma mass spectrometry (ICP-MS) for metal fumes, and specific thermo-optical analysis of elemental carbon (EC) and total carbon (TC) for diesel particulate matter (DPM). In addition, filter-based sampling requires the use of particle size selectors - such as cyclones and impactors - for the measurements of PM_4, $PM_{2.5}$ and PM_1 fractions. For example, methods for assessing DPM exposures include measurements of PM_4 or PM_1 fractions of EC and TC (40).

The exposure assessment by direct-reading instruments (DRI) in occupational settings relies on measuring properties that are indirectly related to the particles, such as light scattering (41). Besides, sampling of specific size fractions, such as respirable particles, can be performed by attaching a pre-collector (i.e. cyclones and impactors) to the instrument. Laser photometers based on light-scattering, such as the DustTrak™ (TSI Inc.), are used to estimate mass concentrations of different aerosol size fractions. Furthermore, number concentration can be measured by different classes of instruments, namely condensation particle counters (CPC),

scanning mobility particle sizers (SMPS) or fast mobility particle sizer spectrometers (FMPS), and electrical low pressure impactors (ELPI) (42). A CPC (e.g. P-Trak, TSI inc) is used to measure the number concentration of particles between 20 and 1000 nm by increasing the particles' size by vapour supersaturation and subsequent detection by laser. A SMPS/FMPS is composed by a differential mobility analyzer and a condensation particle counter, and allows real-time detection based on electrical mobility diameter (between 10 to 800 nm) and number concentration. Finally, the ELPI uses diffusion charging and impaction to measure particle number concentration for each size channel of particles between 30 nm to 10,000 nm (42).

There are many challenges related to the measurement of particles by DRI. For example, the many types of equipment available may make a choice difficult. Also, particles' measurements can show significant variations, even for emissions from the same source/material and location. This variation can be attributed to the instrument used for measuring particles (43). For instance, some studies have suggested a loss of precision of the P-Trak in situations of very high concentrations (44, 45). Finally, the methodology of operation differs between equipment, even for the same parameter. For example, UFP can be quantified by light scattering using a CPC or electrical mobility diameter by a SMPS/FMPS. However, positive characteristics of DRI include a short reading time, which allows the identification of peaks of exposure and the acquisition of data in real-time without the necessity for additional laboratory analysis (46).

2.4.3 Levels of Occupational Exposures

As previously mentioned, many workers are exposed to fine and ultrafine particles in different workplaces at concentrations potentially higher than in the general environment. The use of diesel-powered equipment such as heavy machinery and vehicles are known to contribute to fine and ultrafine particulate levels in the workplaces. Exposure to the solid phase of these particles from diesel engines are usually expressed in terms of elemental carbon (i.e. the solid carbon core of the particles) or total carbon (i.e. the sum of elemental carbon and organic carbon). Also, a significant portion of these particles are in the ultrafine range (47). Below, an overview of the concentrations of fine and ultrafine particles found in some of these workplaces

is presented. After, the limitations on the current knowledge of exposure assessment are presented.

Exposures expressed in terms of mass concentration have been reported for different workplaces (Table 1). In a review by the International Agency for Research on Cancer (IARC), levels of exposure to EC from diesel particulate matter were assessed from several workplaces. These environments include the mining industry, where concentrations ranging from 148 to 637 μg/m³ were reported for underground work and from 3.5 to 23 μg/m³ for surface work (48). More recently, Debia et al. (2016) reported mean daily concentrations of 40.4 μg/m³ of PM_4 with a laser photometer and 19.5 μg/m³ of total carbon by filter measurements in a port facility with DPM emissions (49). In welding, Hoffmeyer et al. (2014) found that workers using FCAW were exposed to median concentrations of PM_4 up to 7.14 mg/m³ (50) and Kim et al. (2004) reported $PM_{2.5}$ geometric mean concentration of 300 μg/m^3 with a laser photometer and 310 μg/m^3 by gravimetry in a welding training school and power plant (51).

The number concentration of UFP in different workplaces was reported in a review by Viitanen et al. (2017) (52). These articles covered 314 occupational exposure situations, including asphalt/bitumen, machining, metalworking, paint and coating, power plants, diesel engine transport, welding, office work, catering and cooking fumes. 76% of the reported mean concentrations were above a typical urban background of 10,760 particles/cm^3, while the highest mean concentrations were reported for diesel, welding, and basic metal industry (52). Levels of UFP from studies performed in these workplaces are presented in Table 1. For diesel exposures, Debia et al. (2016) reported a mean concentration of 32,000 particles/cm^3 and a peak concentration of up to 64,000 particles/cm^3 emitted from trucks in Montreal's port (49). Jeong et al. (2017) assessed exposure from diesel-powered commuter trains. The authors reported mean concentration of 126,000 particles/cm^3 and peak concentration of 693,000 particles/cm^3 (53). In addition, the mean concentration of 699,000 particles/cm^3 was measured during highway maintenance work (54). For other workplaces, Debia et al. (2014) evaluated concentrations associated with various welding activities and reported average daily concentrations of 50,000 to 150,000 particles/cm^3, with peak concentrations of up to 500,000 particles/cm^3, corresponding to the maximum value of the instrument (55). Jarvela et al. (2016) measured

number concentrations during the production of stainless steel and ferrochromium. The authors reported UFP daily concentrations between 58,000 and 662,000 particles/cm^3 (56). Freund et al. measured average concentrations between 19,000 and 111,000 particles/cm^3 during road paving and related road construction operations, with peak concentrations of 467,000 particles/cm^3 (57).

Table 1: Levels of fine and ultrafine particles in some occupational settings.

Study	Method of Measurement	Context of Exposure	Levels of Exposure
Mass Concentration			
Debia et al. (2016) (49)	PM_4 by DRI (i.e. Laser Photometer) and TC by filter	DPM in a port facility	Geometric mean: PM_4 = 40.4 µg/m^3; TC = 19.5 µg/m^3;
Hoffmeyer et al. (2014) (50)	PM_4 by filter	Welding (FCAW)	Median: 7.14 mg/m^3
IARC (2014) (48)	EC by filter	DPM in underground mines	Average: 148 to 637 µg/m^3
IARC (2014) (48)	EC by filter	DPM in surface mines	Average: 3.5 to 23 µg/m^3
Kim et al. (2004) (51)	$PM_{2.5}$ by DRI (i.e. Laser Photomoter) and filter	Welding training school and power plant	Geometric Mean: DRI = 300 µg/m^3; filter = 310 µg/m^3
Number Concentration			
Debia et al. (2014) (55)	UFP by DRI (i.e. CPC)	Welding	Geometric means: 50,000 to 150,000 particles/cm^3
Debia et al. (2016) (49)	UFP by DRI (i.e. CPC)	DPM in a port facility	Geometric mean: 32,000 particles/cm^3
Freund et al. (2012) (57)	UFP by DRI (i.e. Modified Electrical Aerosol Detector)	Road paving and related road construction operations	Average: 19,000 to 111,000 particles/cm^3
Jarvela et al. (2016) (56)	UFP by DRI (i.e. SMPS)	Production of stainless steel and ferrochromium	Average: 58,000 to 662,000 particles/cm^3

Jeong et al. (2017) (53)	UFP by DRI (i.e. Diffusion Charger)	DPM from diesel-powered commuter trains	Geometric mean: 126,000 particles/cm^3
Meier et al. (2014) (54)	UFP by DRI (i.e. Diffusion Charger)	Diesel/traffic emissions during highway maintenance work	Average: 699,000 particles/cm^3

However, despite these exposure estimations, there is still a lack of UFP measurements in many workplaces and tasks to allow a general conclusion about workers' exposure. For instance, which work activities are worse and to which levels of UFP and PM are workers usually exposed to remain unclear. In addition, as reported in the review and also observed in Table 1, exposures levels are estimated by different instruments (e.g. CPC, SMPS, Diffusion Charger) that have distinct principles of operations and do not report comparable concentrations, even for the same type of exposure. Thus, there is a need for more measurements across different exposure situations and parallel measurements using different techniques in order to improve the understanding of UFP assessments and increase comparability with previous studies.

These limitations are also discussed in a study that developed a Job Exposure Matrix (JEM) for UFP exposures (i.e. MatPUF JEM) (58). Although UFP exposures were documented through the parameters of probability and frequency of exposure, this JEM did not include a parameter for the estimated intensity of exposure. The authors attributed this fact to the lack of measurement data and the heterogeneity of these data in terms of the measurement methods used (i.e. sampling strategy and type of instruments) (58).

As observed in the information presented in this section, processes from several workplaces emit particles in the fine and ultrafine ranges. However, the research in this thesis regarding the exposure assessment (Chapter 5) is focused on workplaces with diesel particulate matter. The reasons for this choice include the probability of finding high levels of particles in both fine and ultrafine ranges, and the high number workers exposed to diesel in Canada (10); thus, providing the opportunity to estimate exposure levels and test sampling strategies in workplaces that are relevant to public health.

2.5 Oxidative Potential and Oxidative Burden

As shown in the previous section, the exposure assessment to particles is usually performed by measuring their concentrations in the air. In this context, mass concentration is currently the most reported metric. However, particles' toxicity is also dependent on different factors other than mass concentration alone, as the composition. In this context, measurements of oxidative potential (OP) and oxidative burden (OB) could be used to complement the information regarding occupational exposures to particles.

OP is defined as the capacity of PM – and its components – to cause oxidation of target molecules per unit of mass, and it is a measure of the hazard associated with PM (59). This is a promising technique due to the integration of different biologically relevant properties such as size fraction, mass concentration and chemical composition. This analysis, therefore, could generate more relevant information than PM mass or individual components alone (60). The oxidative burden (OB) is a per-volume measure and refers to the product of OP with the mass concentration of PM, therefore representing a risk metric that combines both exposure (i.e. PM mass) and hazard (i.e. OP) (61).

Several cellular and acellular assays have been developed to estimate the OP of PM. In this regard, although cellular assays have the advantage of accounting for some oxidative pathways resulting from particle-biological system interactions (62), these methods may be time-consuming and require highly trained personnel and specialized equipment. Acellular assays, however, allow for high-throughput and straightforward analysis and have been extensively used to characterize environmental exposures. Common acellular assays include the measurement of the generation of hydroxyl radical by electron spin resonance (OP^{ESR}) and the quantification of the depletion of chemical proxies for cellular reductants (such as dithiothreitol; OP^{DTT}) or antioxidants (such as ascorbic acid and glutathione; OP^{AA} and OP^{GSH}, respectively), which are proportional to the generation of ROS (15). Also, OP^{AA} and OP^{GST} assays can be performed using a synthetic respiratory tract lining fluid (RTLF) that works as a surrogate for the composition of the antioxidants found in the lining fluid of the lungs.

One of the differences between these assays relates to the responsiveness to different PM components. Although all assays are in some extent reactive to metals, OP^{AA}, for example have shown to be sensitive to copper, iron, manganese, lead and zinc (60, 63-65), while OP^{GSH} is described to be responsive to iron, lead and aluminum (63, 65). OP^{DTT}, on the other hand, is also sensitive to organic components (66, 67). In addition, other factors that may affect OP are photochemical ageing, pH and volatility (15).

Many environmental studies have characterized the OP of particles from urban sources like traffic, biomass burning and road dust (60, 68, 69). Also, the OB of particles from environmental settings was associated with cardiorespiratory health effects (70, 71). However, despite the increasing number of research in the last years focused on OP and OB's characterization from urban and other environmental sources, very few studies have investigated the oxidative potential of particles emitted in occupational settings (62).

2.6 Conclusion of the Chapter and Gaps in the Literature

In summary, many workers are daily exposed to tasks and processes capable of emitting fine and ultrafine particles at concentrations higher than a typical urban background. However, there are still many uncertainties surrounding exposure data, especially regarding the ultrafine fraction since studies in occupational settings are few and lack standardized methods to allow a general conclusion about workers' exposure. Thus, the harmonization of sampling strategies and the assessment of additional information related to the size distribution (i.e. fine and ultrafine fractions), metrics of exposure (i.e. mass and number concentration) and the composition of particles in different workplaces is essential to generate more reliable and comparable data on exposure.

In addition, the measure of oxidative potential has been established as a promising technique that integrates the composition and mass concentration of airborne particles. Although it has been extensively explored as a metric for the characterization of environmental particles, this is still an underexplored application in the occupational field. The use of this technique in industrial settings would expand the collection of exposure information beyond

mass concentration alone and, therefore, be an important tool of exposure assessment to be integrated into the industrial hygiene and industrial toxicology practice.

Finally, long-term exposures to particles have been associated with respiratory health effects, while daily and sub-daily exposures were found to reduce the lung function of vulnerable individuals. However, the relationship between short-term exposures to particles and respiratory effects is less established for healthy adults, especially for workers in the context of occupational exposures. Knowledge gaps also include how daily occupational exposures to fine particles compare with associations from environmental exposures.

By addressing these questions, the present thesis can provide a better and broader understanding of workers' exposure to fine and ultrafine particles, help to develop recommendations of good practices and prevention to minimize the risk of exposure to particles in the workplace and, ultimately, to protect workers' health.

Chapter 3 - Objectives

3.1 General Objective

The general objective of this thesis was to estimate the risk of daily exposures to fine and ultrafine particles in various workplaces.

3.2 Specific Objectives

Three specific objectives were identified to answer the general question of this thesis:

i. To quantify and characterize exposures to fine and ultrafine particles in different workplaces in Québec by an innovative multi-metric approach by:
   a. assessing diesel particulate matter exposure in two underground mines by filter-based methods and direct-reading instruments, as well as the relationship between these metrics.
   b. quantifying and characterizing diesel particulate matter exposures in three workplaces with different exposure levels: an underground mine, a subway tunnel, and a truck repair workshop.

ii. To estimate the oxidative potential and oxidative burden of particles in two occupational settings from a construction trades school.

iii. To separately estimate, by a systematic review and meta-analysis, the associations between occupational and environmental short-term exposures (i.e. daily and sub-daily) to fine particles and lung function in healthy adults.

Chapter 4 – Research Methodology

This chapter summarizes the research methodology used throughout the thesis. First, we present a description of the workplaces, instruments and analyses performed in Chapters 5 and 6. After, the methods of the systematic review and meta-analysis of the association between daily exposure to particles and short-term respiratory effects in healthy adults are presented. A detailed description of the instruments and all analyses carried out can be found in the articles of Chapters 5, 6 and 7.

4.1 Description of the Workplaces

Workplaces were selected based on the high probability of finding substantial levels of exposure to fine and ultrafine particles. In Chapter 5, three workplaces located in the province of Quebec and affected by the presence of diesel-powered equipment and exposure to diesel particulate matter at different levels were selected. The first workplace, underground mine, was characterized as an enclosed environment with intense activities of on-road and off-road vehicles. A mechanical ventilation system provided fresh air in the different sections of the mine. The second workplace was a subway tunnel in Montreal where, during the night shift, workers performed repairs and cleaning tasks on the rails and tunnels with the aid of locomotives and auxiliary engines powered by diesel. This workplace was also characterized as an underground environment with limited ventilation. The third workplace was a truck repair workshop where DPM exposures were caused by the frequent transit of on-road trucks. The workshop was equipped with a general ventilation system and, although this workplace is classified as an indoor setting, the doors of the workshop were frequently opened, resulting in a greater air exchange than the two other workplaces.

In Chapter 6, two workplaces from a trade school in Montreal were selected: a welding shop with exposure to metallic particles and a construction site with bricklaying activities and exposure to brick/concrete dust. Activities in the welding shop included different welding processes (i.e. SMAW, FCAW, GMAW and GTAW) and oxyfuel cutting and grinding of the metallic pieces. Tasks were performed by the apprentices inside individual welding booths equipped with a local exhaust system (i.e. movable hoods), and the shops also had a general ventilation system.

During the construction activities, the tasks included corner assembly, stone cutting and laying, and laying to a line. The bricklayer apprentices worked in a room equipped with a general ventilation system and fans installed in the walls' upper portion.

4.2 Description of the Sampling Strategy

A harmonized sampling strategy, consisting of a combination of real-time ambient measurements and filter-based mass measurements, was developed to assess the fine and ultrafine particles across all workplaces with DPM exposure, and an example of the setup is presented in Figure 1. We used these different methods to have a complete overview of exposures from different metrics of exposure and types of particles in the workplaces. For instance, the filter measurements of carbon species provided information on mass concentration that is specific for diesel particulate matter, while most direct-reading instruments measured the mass or number concentrations of particles that are not specific to diesel particulate matter but can also be found in these workplaces.

For the development of the sampling strategy described in Chapter 5, all devices were installed in portable suitcases and consisted of a combination of a set of DRI for recording a wide range of parameters in real-time, and sampling trains for filter-based measurements of the aerosol mass concentrations in different fractions and subsequent analyses. An in-depth description the direct-reading instruments and filter-based measurements is described below.

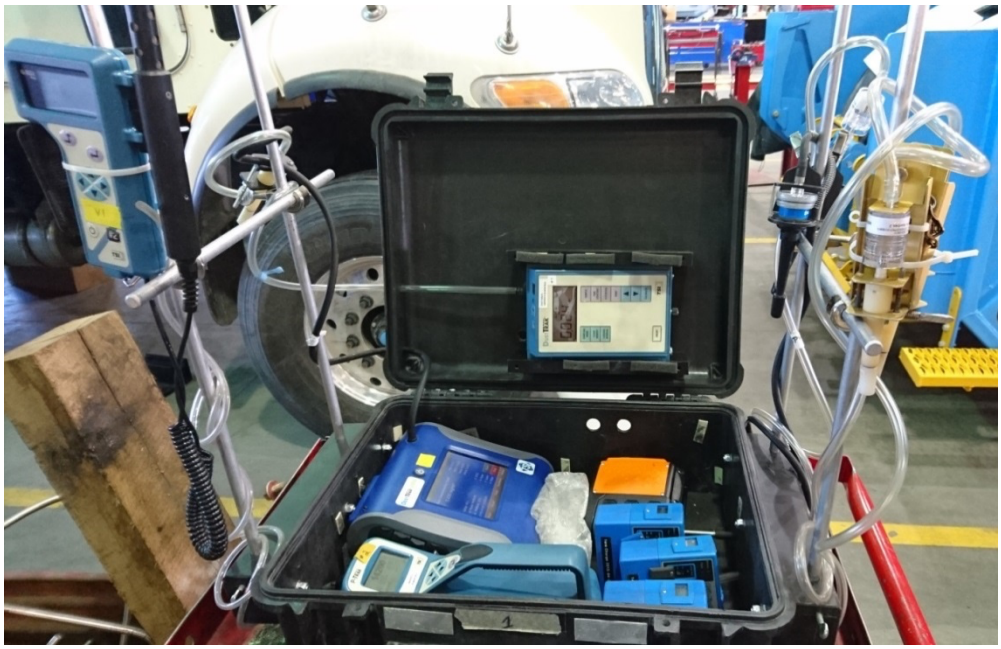

Figure 1: Example of the assembly of the instruments in the suitcase.

4.2.1 Direct-Reading Instruments

Table 2 lists the DRI, as well as its characteristics and the parameters measured. Except for the engine exhaust particle sizer (EEPS), shown in Figure 2, the instruments were arranged in the above-described suitcases and the sampling inlets/tubing were positioned vertically outside the case with aluminum rods. This allowed for the measurement of the mass and number concentration of particles at the same location and time, which was essential for the comparison of the different metrics of exposure.

The Airtec (FLIR Systems, Albuquerque, NM, USA) recorded a specific real-time estimate of the submicron fraction of elemental carbon (EC_1) by optical transmittance. Contrary to the other direct-reading instruments presented here, this equipment is specific to DPM measurements (i.e. EC), which gives the advantage of being directly comparable to the filter-based method that is classically used for the exposure assessment of DPM (i.e. NIOSH 5040 method) (72). Laser photometers were used to measure the mass concentrations of particles larger than 100 nm. A DustTrak 8520 (TSI Inc., Shoreview, MN, USA) was equipped with a nylon cyclone and had its flow rate set to 1.7 L/min to select the respirable fraction of the particles, while the DustTrak DRX (TSI Inc., Shoreview, MN, USA) concomitantly estimated the mass

concentrations of five size fractions of particulate matter (i.e. PM_1, $PM_{2.5}$, PM_4, PM_{10} and PM_{TOTAL}). These instruments measure the mass concentration of PM independently of the source; thus, being non-specific to DPM measurements. Particle number concentration was measured by the P-Trak 8525 (TSI Inc., Shoreview, MN, USA). This instrument was chosen because it is the most used in occupational measurements of UFP (57). The size range of the particles measured by this instrument is between 20 and 1000 nm; it also has an upper limit of the numerical concentration at 500,000 particles/cm^3. Finally, the EEPS was used to also estimate particle number concentration and size distribution data. This equipment has 32 size channels between 5.6 and 560 nm, which gives it an advantage over the P-Trak by measuring particles of smaller aerodynamic diameter. It is a fast response, high-resolution instrument that uses sensitive electrometers.

The instrumentation was regularly maintained and calibrated following good industrial hygiene practices. The zero calibration was performed before each sampling day. All instruments were equipped with Tygon tubing, and air samples were taken at the height of about 1.5 m, corresponding to the shared breathing zone. The devices were configured to record measurements every 10 seconds during operation.

The complete setup of the DRI was used for the development of the sampling strategy described in Chapter 5. For Chapter 6, the P-Trak was the only DRI used since the sampling strategy in this chapter focused collecting particles in filters for subsequent analysis of the oxidative potential.

Table 2: Description of DRI used in the workplaces.

Model	Parameter measured (unit of concentration)	Type of instrument	Measured particle size (in nm)
Airtec (FLIR)	EC mass concentration ($\mu g\ m^{-3}$)	Light transmission	< 1,000
DustTrak™ DRX 8533 (TSI Inc.)	Mass concentration ($\mu g/m^3$) for 4 particle size fractions (PM_1, $PM_{2.5}$, PM_4, and PM_{10})	Laser photometer	100 – 15,000
DustTrak™ 8520 (TSI Inc.)	Mass concentration ($\mu g/m^3$)	Laser photometer	100 – 15,000
P-Trak® 8525 (TSI Inc.)	Number concentration ($particles/cm^3$)	Condensation nucleus counter (CNC)	20 – 1,000
EEPS 3090 (TSI Inc.)	Number concentrations ($particles/cm^3$) for 32 size fractions	Engine exhaust particle sizer	5.6 – 560

Figure 2: Engine exhaust particle sizer 3090 (EEPS 3090).

4.2.2 Filter-Based Measurements

Table 3 shows the parameters and the sampling devices used for the filter-based measurements. For the measurements in Chapter 5, area samples were collected for the analyses of elemental carbon (EC), total carbon (TC) and organic carbon (OC) by the NIOSH 5040 method (40). These parameters were chosen because DPM, the solid phase of diesel engine exhaust, is composed of a solid elemental carbon core onto which organic carbon compounds are adsorbed, and the sum of elemental carbon and organic carbon is called the total carbon. The ratio TC/EC was calculated and compared across workplaces to estimate the influence of non-diesel OC to the TC measurements. In this context, a ratio of 1.3 is expected for DPM particles, with higher ratios being indicative of interference from other sources such as oil mist, cigarette smoke, or environmental sources of organic carbon (73). Finally, respirable combustible dust (RCD) was measured in the first article of Chapter 5. RCD, which is defined as the portion of a respirable dust sample that can be burned off a filter when exposed to a temperature of 400°C for two hours, used to be the indicator of DPM exposures in Quebec until 2016.

DPM was collected on quartz fiber filters (QFF) and cassettes attached to Dorr-Oliver nylon cyclones to select particles with a 4 µm median aerodynamic diameter cut-point. For the submicron fraction, in addition to the cyclone, QFF and cassettes were also attached to jewelled impactors (SKC Inc., Eighty Four, PA, USA) to collect particles with a 0.8 µm median aerodynamic diameter cut-point.

For the collection of particles in Chapter 6, area samplers of PM_4 and $PM_{2.5}$ were installed at a distance of 1 meter from the workers/apprentices, while personal PM_4 samples were collected from the breathing zone (i.e. around 30 cm from the mouth and nose of the worker). Samples were collected in 37 mm cassettes equipped with pre-weighed Polytetrafluoroethylene (PTFE) filters (Mitex Membrane Filter with 5.0 µm and support pads, Sigma-Aldrich; St. Louis, MO/USA). The $PM_{2.5}$ fraction was selected using a cyclone at a flow rate of 1.5 L/min (BGI; Butler, NJ/USA), while the PM_4 fraction was selected using a Dorr-Oliver nylon cyclone at a flow rate of 1.7 L/min.

For all these filter-based measurements, GilAir pumps (Sensidyne, LP, St. Petersburg, FL), set at a flow rate of 1.7 L/min, were used. Flow rates of the pumps were measured before and

after the work shifts using a mass flow meter (TSI Inc.; Shoreview, MN/USA). A difference of 5% was considered acceptable, as recommended by the good practices in industrial hygiene. Field blanks were collected for each day of field sampling. All reported results are corrected for blank values.

Table 3: Parameters and sampling devices of the filter-based measurements.

	Parameters measured	**Sampling devices**
Chapter 5	Respirable fractions of elemental carbon (EC_R), organic carbon (OC_R) and total carbon (TC_R)	Gilair pump (1.7 L/min) with a 37-mm closed cartridge and quartz fibre filter, equipped with a Dorr-Oliver cyclone
	PM_1 fractions of elemental carbon (EC_1), organic carbon (OC_1) and total carbon (TC_1)	Same setup as EC_R, OC_R and TC_R with the addition of an impactor
	Respirable fractions of dust (D_R) and combustible dust (RCD)	Gilair pump (1.7 L/min) with a 37-mm closed cartridge and quartz fibre filter, equipped with a Dorr-Oliver cyclone
Chapter 6	Personal and area samples of PM_4	Gilair pump (1.7 L/min), with a 37-mm closed cartridge and Polytetrafluoroethylene (PTFE) filter, equipped with a Dorr-Oliver cyclone
	Personal samples of $PM_{2.5}$	Gilair pump (1.5 L/min), with a 37-mm closed cartridge and and Polytetrafluoroethylene (PTFE) filter, equipped with a BGI cyclone

4.3 Characterization

4.3.1 Carbon Species

Samples collected in the three workplaces with DPM exposures were analyzed for carbon species at the laboratories of the *Institut de recherche Robert-Sauvé en santé et en sécurité du travail* (IRSST) and Galson (Ontario, Canada). EC and OC levels were measured using the IRSST

388 method and the NIOSH 5040 method (40). TC levels were calculated by summing the EC and OC values (TC = EC + OC). Measurements of EC and TC by the NIOSH 5040 methods are considered the surrogates of DPM and are used in regulations to set Occupational Exposure Limits to diesel emissions. Respirable combustible dust was analyzed gravimetrically, using the method IRSST 384.

4.3.2 Transmission Electron Microscopy

Aerosol sampling was performed directly on 3 mm TEM grids using the Mini Particle Sampler (MPS; ECOMESURE, Janvry, France). Using a GilAir pump at a flow rate of 0.3 L/min for 1 min sampling, particles were deposited onto 400 mesh copper grids covered by a carbon film with a hole diameter of 1.2 µm and a spacing of 1.3 µm between the holes (Quantifoil; Großlöbichau, Germany).

Microscopy analyses of the particles were performed by bright field imaging on a JEOL 2100F TEM at the *Centre de Caractérisation Microscopique des Matériaux* of the *École Polytechnique de Montréal*. The qualitative elemental characterization was performed by energy dispersive X-ray spectroscopy (EDS) using an Oxford INCA x-sight EDS detector (Model 6498). Three different square-shaped openings were randomly selected from the grid. A general observation of the openings was made to visualize the distribution of particles and agglomerates at a magnification of 50X.

The analyses of individual particles and agglomerates were then performed at a magnification of 5,000X to 25,000X. A total of 100 primary particles were analyzed per grid. For each one of these agglomerates, an image was acquired, and an EDS analysis was performed. The particles were randomly selected but with the aim of ensuring a good representation of the diversity found on the grid during the initial scan. For each particle or group of particles, the stereological parameters evaluated were the diameter of primary particles (dp), the maximum projected length of the agglomerate (L_A), the maximum projected width of the agglomerate (W_A), the average between L_A and W_A, and the ratio L_A/W_A (i.e. an indicator of the shape of the agglomerate).

4.3.3 Oxidative Potential

Samples collected from the welding shop and construction site (Chapter 6) were analyzed for the oxidative potential and oxidative burden using the ascorbic acid assay (OP^{AA} and OB^{AA}, respectively) (63). Although other methods are also available (i.e. OP^{DTT} and OP^{GSH}, OP^{ESR}), the OP^{AA} is a suitable assay to estimate the oxidative potential in the exposure situations investigated, namely from welding and bricklaying emissions. For instance, this assay is performed using a synthetic respiratory tract lining fluid that simulates the composition and concentration of the antioxidants found in lining fluid of the lungs, contrary to OP^{DTT} and OP^{ESR}. Although not used in this thesis, the OP^{GSH} is also present in the synthetic lining fluid and this assay can complement the information given by the OP^{AA}. In addition, the OP^{AA} is sensitive to metals such as copper, iron, manganese, lead and zinc, which makes it a suitable method for the assessment of the oxidative potential of particles from occupational settings with high emissions of metals, such as in welding facilities that we studied. Because welding and bricklaying activities are not associated with emissions to organic components, OP^{DTT} was not measured.

After the collection of the particles, filters were stored at −20 °C until extraction. For the extraction, filters were placed in Falcon tubes, immersed in 10mL of Optima grade methanol (Thermo Fisher Scientific; Waltham, MA/USA), vortexed for 2 minutes and sonicated for 60 minutes. The extracts were then dried for 4h under a constant flow of nitrogen. Dry extracts were stored at −20 °C until OP^{AA} analyses. Filters were weighed in triplicate before and after extraction using a microbalance (Model XPR2U, Mettler Toledo; Columbus, OH/USA).

Extracted samples were resuspended in Chelex-resin treated MeOH/H_2O 5% to concentrations of 25 µg/mL. This concentration was determined after observing no effects of the sample concentration in preliminary tests performed between 50 µg/mL and 5 µg/mL. Resuspended samples were separated in triplicates and incubated in a microplate spectrophotometer (Model Epoch 2, BioTek; Winooski, VT/USA) for 10 minutes at 37°C alongside positive controls (1.0 µM $Cu(NO_3)_2$) and experimental blanks (MeOH/H_2O 5%). After adding RTLF containing 200 µM of physiologically relevant antioxidants including ascorbate, urate, and glutathione adjusted to pH 7.4, the absorption at 265 nm was measured every 2 min for 4 h.

The OP^{AA} was calculated from the linear section of the curve by plotting the absorbance against time and normalizing by PM mass based on the quantity used in each assay (i.e. ρmol/min/μg). These values were corrected relative to the particle-free field blanks. Values were also converted to units of OB^{AA} (i.e. ρmol/min/m^3) by multiplying the OP^{AA} values with the PM mass concentration of each filter.

4.4 Systematic Review and Meta-Analysis

This section presents the systematic review and meta-analysis methods for the association between daily exposure to particles and acute effects on lung function in healthy adults (Chapter 7). This includes the description of the search strategy, inclusion and exclusion criteria, study selection, data extraction and quality assessment. The statistical analyses are presented in section 4.5, along with the statistical methods of the other data chapters.

4.4.1 Search Strategy

The literature search included studies published in English between 1964 and 2020. The following electronic bibliographic databases were searched: Web of Science (Web of Science Core Collection and MEDLINE) and PubMed. The search included terms for the exposure to fine particles (i.e. respirable dust and $PM_{2.5}$) and the selected outcomes lung function parameters: FEV_1 and FVC. These two indices were chosen given they are the most investigated in studies associating air pollution exposures and lung function effects. We also added terms to exclude studies on animal models, children, *in vitro* models and long-term exposure studies. The complete list of keywords can be found in Chapter 7.

4.4.2 Inclusion and Exclusion Criteria

Studies were included if they repeatedly investigated acute respiratory effects (within 24h after exposure) of short-term exposures (i.e. duration between 1h and 24h) to fine particles in healthy adults of working age (i.e. between 18 and 60 years old). In terms of the study population, we restricted the review to healthy adults of working age to compare occupational and environmental health studies associations. Studies with both healthy and non-healthy subjects were included if the authors mentioned that they controlled for health status or if results were

reported separately by health status. We restricted this review's scope to exposure to the mass concentration of $PM_{2.5}$ and respirable dust (i.e.PM_4), which are common classifications from the environmental and occupational studies, respectively. Regarding study design, we restricted the review to studies with repeated measurements of the outcomes because such design allowed us to separate effects of daily exposures from cumulative (long-term) exposures; therefore, cross-sectional studies were excluded. The selected study designs included panel and crossover environmental studies, as well as cross-shift occupational studies. Panel studies involve repeated measurements on each subject at specified short time intervals (i.e. daily); thus each subject acts as his/her own control (36). Crossover studies also involve repeated measurements, but the exposure situations are controlled by the researchers (e.g. cycling on high- and low- traffic routes) (74). Occupational cross-shift studies involve the measurements of the outcome before and after the work-shift, when exposure is assessed.

Studies were excluded if: (1) they were based on reviews, they were experimental studies, case reports, letters, posters and conference abstracts; (2) the study population was formed exclusively by children, elders or subjects with a pre-existing chronic respiratory disease such as asthma and Chronic Obstructive Pulmonary Disease (COPD); (3) the respiratory outcomes of interest were not measured within 24 hours after exposure; (4) exposure duration was not within 24 hours; (5) the studies reported only one measurement of the outcome per subject (i.e. no repeated measurements); (6) size fractions other than $PM_{2.5}$ and PM_4 were measured; and (7) the exposure was focused on the measurement of environmental tobacco smoke.

4.4.3 Studies Selection and Data Extraction

All titles and abstracts retrieved from the search strategy were screened during the first round of study selection. All potentially relevant studies were identified, and, in the second round, the full texts were reviewed considering the inclusion and exclusion criteria. Data from each study using a pre-designed data extraction form. The following information was manually extracted: (1) authors and year; (2) study location; (3) study design (i.e. panel, crossover and occupational cross-shift studies); (4) population (N, sex, % of smokers and mean age); (5) exposure information such as type of measurement (i.e. personal/quasi-personal and central/near station), exposure duration, exposure context and type of particles; (6) physiological

outcomes; (7) confounders and effect modifiers; and (8) results (mean concentration of particles and respiratory outcome results (e.g. estimate ± 95% CI or T-test result).

4.4.4 Quality Assessment

The assessment of the risk of bias was performed according to the Office of Health Assessment and Translation (OHAT) tool developed by the National Institutes of Environmental Health Sciences-National Toxicology Program (75). Within each study, we evaluated the risk of bias across seven parameters divided as key criteria (i.e. exposure assessment, outcome assessment, and confounding and modifiers) and other criteria (i.e. selection bias, selective reporting, incomplete outcome data and conflict of interest). The risk of bias for each parameter was evaluated as “low”, “medium”, “high”, or “not applicable”. The OHAT guideline recommends the exclusion of studies for which all the key criteria and most of the other criteria are characterized as “high”.

4.5 Statistical Analyses

Statistical analyses for Specific Objective 1

For the measurements of diesel exposures in the different workplaces, the geometric mean (GM), geometric standard deviation (GSD), median and range of the daily concentrations were used to describe the distributions of exposure levels. The undetected values were processed by dividing the quantification limit by the square root of 2. The association between the different carbon species was assessed by linear regression, and the slopes were compared between each workplace. Correlation coefficients were calculated to assess the linear relationship between the different exposure parameters, such as between carbon species and the different DRI.

Statistical analyses for Specific Objective 2

For the oxidative potential analyses, values were expressed in terms of mean and standard deviation, median and percentiles, and ranges. Results were presented separately according to the workplace, weeks of activities, size fraction and sampling strategies. The Mann-Whitney test and the Kruskal-Wallis followed by Dunn’s *posthoc* test were used to compare OP^{AA}

and OB^{AA} levels between workplaces and weeks of activities, respectively; while the Wilcoxon signed-rank test was used to compare paired samples according to the sampling strategy (i.e. personal versus area sampling) and size fraction (i.e. PM_4 versus $PM_{2.5}$).

Statistical analyses for Specific Objective 3

For the meta-analysis, we pooled studies separately according to the type of study (i.e. environmental and occupational) and outcome. We computed meta-estimates when a minimum of five independent risk estimates were available. A random-effect meta-analysis was performed due to the expected heterogeneity caused by the different study designs, populations, and exposure characteristics. Meta-estimates, 95% confidence intervals and 95% prediction intervals were calculated for a 10 $\mu g/m^3$ of particulate concentration; we used a similar increment given that we aimed at contrasting the effect across these two different areas. We assessed heterogeneity using the I^2 statistics, whereas publication bias was examined using funnel plots (76).

In the sensitivity analysis, we performed a leave-one-out test to explore each study's influence on the meta-estimate and the I^2 statistic. Sensitivity analyses were also performed to explore the influence of the studies that had a small percentage of non-healthy subjects in its population. In addition, subgroup analyses were performed to explore the influence of key study criteria such as the type of measurement, duration of exposure and study design. However, because of the small number of studies per subgroup, only a descriptive analysis was performed. The heterogeneity variance was assessed by the DerSimonian and Laird method. Statistical analyses were all performed using Review Manager 5.3 and the *metaphor* package for R (version 3.4.1). (77).

Chapter 5 – Estimation of Occupational Levels of Fine and Ultrafine Particles by a Multi-Metric Sampling Strategy

The knowledge regarding worker's exposure to fine, and especially, ultrafine particles is currently limited by the lack of exposure data and standardized methods. This results in limited comparability of exposure levels between the already few studies assessing concentrations of fine and ultrafine particles in various workplaces. Thus, this data chapter addresses the first specific objective of this thesis, that is to quantify and characterize exposures to fine and ultrafine particles in different workplaces in Québec by an innovative multi-metric approach; thus, addressing the gaps regarding the lack of standardized methods and, consequently, of exposure data in occupational settings.

This chapter is presented in the form of two research articles, where the first one assessed the number concentration, mass concentration and carbonaceous components of diesel particulate matter in two underground mines and the relationship between the surrogates of exposures. The second article extended the scope of these analyses by performing additional measurements in another mine, by including analyses such as the size distribution and transmission electron microscopy, and by expanding this sampling strategy to other workplaces with intermediate and low levels of exposure to diesel particulate.

5.1: Diesel engine exhaust exposure in underground mines: Comparison between different surrogates of particulate exposure

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5.1.1 Abstract

Exposure to diesel particulate matter (DPM) is frequently assessed by measuring indicators of carbon speciation, but these measurements may be affected by organic carbon (OC) interference. Furthermore, there are still questions regarding the reliability of direct-reading instruments (DRI) for measuring DPM, since these instruments are not specific and may be interfered by other aerosol sources. This study aimed to assess DPM exposure in two underground mines by filter-based methods and DRI; and to assess the relationship between the measures of elemental carbon (EC) and the DRI to verify the association of these instruments to DPM. Filter-based methods of respirable combustible dust (RCD), EC and total carbon (TC) were used to measure levels of personal and ambient DPM. The relationship between these indicators was evaluated to assess OC contamination. Ambient measurements of particle number concentration (P-Trak), particle mass concentration (DustTrak DRX and DustTrak 8520) and the submicron fraction of EC ($EC_{1;}$Airtec) were measured by DRI. The association between ambient EC and the DRI was assessed by Spearman correlation. Geometric mean concentrations of RCD, respirable TC (TC_R) and respirable elemental EC (EC_R) were 170 µg/m^3, 148 µg/m^3 and 83 µg/m^3 for personal samples, and 197 µg/m^3, 151 µg/m^3 and 100 µg/m^3 for ambient samples. Personal samples had higher $TC_{R:}EC_R$ ratios compared to ambient samples (1.8 vs 1.50) and weaker association between EC_R and TC_R. Among the DRI, the measures of EC_1 by the Airtec (ρ=0.86; P<0.001) and the respirable particles by the DustTrak 8520 (ρ=0.74; P<0.001) showed the strongest association with EC, while particle number concentration showed a weak and non-significant association with EC. In conclusion, this study provided information about the concentrations of DPM in underground mines by measuring several indicators using filter-based methods and DRI. Among the DRI, the Airtec proved to be a good tool for estimating EC concentrations and, although the DustTrak showed good association with EC, interferences from other aerosol sources should be considered when using this instrument to assess DPM.

Keywords: Diesel Exposure, Elemental Carbon, Ultrafine Particles, Direct-reading Instrument, DPM, Respirable Dust.

5.1.2 Introduction

The use of diesel-powered equipment is frequent in the mining industry. These machines are energetically more efficient and emit lower quantities of carbon monoxide and dioxide than their gasoline counterpart (1). However, diesel-powered engines emit more particles than gasoline equipment during the combustion process. This is an important issue in enclosed spaces, such as underground mines, where miners can be overexposed (2).

Diesel exhaust (DE) exposure has been linked to harmful health effects in humans. Short-term exposure to DE has been associated with pulmonary inflammatory response, eye irritation, nasal irritation and cardiovascular effects (2-5). In addition, epidemiological studies have shown association between long-term exposure to DE and increased lung cancer risk. Vermeulen et al. reported that 6% of deaths from lung cancers could be linked to occupational exposures to DE (6). Peters et al. estimated a lifetime career (45 years) excess lung cancer deaths per 1000 males of 5.5 and 38 for miners experiencing exposure levels of 14 and 44 $\mu g/m^3$ of elemental carbon (EC), respectively (7). Furthermore, DE has been classified as a human carcinogen (group 1) by the International Agency for Research on Cancer and has become a contaminant of primary interest at the international level (8).

DE refers to the complex mixture of chemical substances in solid, liquid or gaseous states resulting from the incomplete combustion of diesel fuel. The type of engine, fuel, oil, and operations are some of the factors that can affect the composition of DE. Carbon oxides (CO and CO_2), nitric oxides (NO and NO_2), sulfur dioxide (SO_2), water vapor, sulfur compounds, low molecular weight hydrocarbons (e.g. benzene, 1,3-butadiene), and oxygenated compounds (e.g. aldehydes) can be found in the mixture (9). Diesel particulate matter (DPM) is composed of EC onto which organic carbon (OC) compounds and other particles (unburnt fuel, lubricant droplets, metallic additives, etc.) are adsorbed. The majority of the particles are within the respirable fraction (particles with aerodynamic diameter lower than 10 µm, with 50% efficiency cut-off at 4 µm) and most are ultrafine particles (UFP; 100 nm in diameter or lower) (10).

Occupational exposure limits (OEL) for DE vary between and within countries. In the province of Quebec, Canada, a limit of 600 $\mu g/m^3$ of respirable combustible dust (RCD) was implemented in the mining industry until 2016. In 2016, it was changed to 400 $\mu g/m^3$ of total

carbon (TC) (11). The Canadian province of Ontario has a regulatory time-weighted limit value of 400 µg/m^3 of TC transposable to EC via a conversion factor of 1.3 (i.e. about 310 µg/m^3 for EC) for the mining industry (12). Both monitoring strategies imply a size-selective sampler to collect the respirable fraction. In addition, the U.S. Mine Safety and Health Administration has prescribed an 8-h OEL of 160 µg/m^3 of TC based on recommendations and methods of the National Institute for Occupational Safety and Health (NIOSH) (13). In this case, the monitoring strategy requires a size-selective sampler to collect the submicron range. This size fraction is selected to avoid interference from aerosol with larger size. There is currently no time-weighted average threshold limit value for DE proposed by the American Conference of Governmental Industrial Hygienists (ACGIH).

Due to the complex nature of DE, a surrogate of exposure must be used. Examples of indicators include the gas fraction or the DPM fraction. For DPM, the measurement of different surrogates is described, such as the carbonaceous fraction (EC and TC), RCD, particulate matter (PM_1 and $PM_{2.5}$) and UFP (8, 14-20). In addition, portable monitors have been developed and tested for the real-time evaluation of EC (21, 22).

Despite the frequent use of TC as an indicator to DPM exposure, OC from other sources such as cigarette smoke, oil mist and other fuels may interfere with these analyses (since TC= OC+EC) (23, 24). Thus, measurements of EC have been proposed to reduce the influence of OC contamination in DPM assessment (17, 23). Furthermore, there are still questions regarding the reliability of direct-reading instruments (DRI) for measuring DPM, since these instruments are not specific and may be interfered by other aerosol sources.

The aim of this study was to assess DPM exposure in two underground mines by filter-based methods and DRI, as well as to assess the relationship between the measures of elemental carbon (EC) and the DRI in order to verify the association of these instruments to DPM.

5.1.3 Methods

Mines Description and Sampling Design

The present study was performed in two underground gold mines located in Quebec, Canada. The two mines operate at a maximum depth of around 3,000 meters below the surface

and the presence of off-road, diesel-powered mobile machinery contributes to workers' diesel exposure. Sampling was carried out over three separate campaigns (Spring 2016, Summer 2016 and Winter 2017) of two weeks each.

Two strategies were used to assess DPM: personal sampling using filter-based methods; and ambient sampling using DRI and filter-based methods.

This project was approved by the Ethics Committee for Health Research of the University of Montreal (Project Number: 16-057-CERES-D).

Personal Measurements

For personal measurements, two filter-based methods for assessing DPM were used: the NIOSH 5040 method used for sampling the respirable fraction of EC and TC (EC_R, TC_R), and the RCD method (25, 26). For the NIOSH 5040 method, nylon cyclones were used with 25 mm quartz filter cassettes and GilAir pumps (Sensidyne, LP, St. Petersburg, FL, USA) set at a flow rate of 1.7 L/min. For the RCD method, nylon cyclones were used with 25-mm silver membrane cassettes and GilAir pumps (Sensidyne, LP, St. Petersburg, FL, USA) set at a flow rate of 1.7 L/min. The RCD method was developed by Natural Resources Canada, CANMET, and is based on gravimetric principle. The silver membrane is put into a furnace at 400°C for 2 hours and the mass loss of the membrane is measured by a micro-balance. The mass loss is assumed to be a good estimate of the DPM (26). The RCD is therefore less specific than the NIOSH 5040 method, the latter relying on specific measurements of carbon performed with an instrument using a temperature and atmosphere-controlled program.

Side-by-side personal RCD, EC_R and TC_R samples (one filter for RCD, and one filter for both TC and EC) were taken in the workers' breathing zone during their full shift (between 10 and 12 hours). For all measurements, pumps were calibrated before and after every sampling period using a DryCal volumetric flow meter (Mesa Labs Inc., Lakewood, CO, USA). Samples were analyzed by the laboratories of the *Institut de Recherche Robert-Sauvé en Santé et en Sécurité du Travail* (IRSST) (Montreal, Canada). Field blank samples of RCD, EC_R and TC_R were collected each day.

Personal exposure was stratified by mine as well as according to workers' job title. The description of the activities related to each job title is presented in Table S1 of the supporting information.

Ambient Measurements

For ambient measurements, instruments (DRI and filter-based methods) were installed in two identical suitcases that were placed near the main circulation routes (i.e. bypasses and ramps) and next to vehicles on each day and over periods ranging from 4 to 6 hours. All instruments were equipped with Tygon® tubing and air was sampled at a height of about 1–1.5 meters, corresponding to the shared breathing zone of workers.

DRI were used to monitor PM mass concentrations (DustTrak DRX 8533 and DustTrak 8520, TSI Inc., Shoreview, USA), particle number concentration, (P-Trak 8525, TSI Inc., Shoreview, USA) and submicron fraction of EC (EC_1) (Airtec, FLIR Systems, Albuquerque, USA) (Table 1). The Airtec is an instrument that uses light-transmission to provide a real-time estimate of EC, and so unlike the other DRI's that cannot distinguish between particle types based on their composition. The dust monitors were calibrated prior to the sampling period according to the manufacturer's requirements, and zeroing was performed each day before the monitoring when applicable. The DustTrak 8520 was equipped with a nylon cyclone and had its flow rate set to 1.7 L/min to select the respirable fraction of the particles. A user calibration of the DustTrak DRX 8533 was performed on-site prior to the sampling period using a 2.5 µm inlet impactor to improve the relative accuracy between the five mass channels. In addition, a photometric calibration factor of 1.00 (Factory factor) was used for the DustTrak 8520 and the DustTrak DRX 8533.

Ambient EC_R and TC_R samples were taken using the same methods described for the personal sampling. This ambient samples were taken to provide mean of comparing the DRI with the filter-based methods, which would not be possible via personal sampling. In addition to the respirable fraction of EC, TC and RCD, a submicron fraction (less than 1 µm) of EC and TC (EC_1 and TC_1) was selected using a pre-filter which consists of a cassette with a submicron impactor (Airtec, FLIR System Inc., Albuquerque USA). For sampling this submicron aerosol fraction, GilAir pumps (Sensidyne, LP, St. Petersburg, USA), set at a flow rate of 1.7 L/min, were used. EC_1 and TC_1 were sampled only during the second and third campaigns. For this reason, the comparison between

the EC:TC ratios of the respirable and submicron fractions are performed only for the days that both fractions were measured side by side (i.e. common shifts).

Statistical Analysis

The geometric mean, geometric standard deviation, as well as the maximum and minimum values of the geometric means were used for describing the exposure profiles. Non-detected values were treated by dividing the limit of quantification by the square root of 2. Since there were very few non-detected values, the impact of this approach in the results was negligible.

A linear regression analysis was used to evaluate the relationship between TC_R and RCD, as well as TC_R and EC_R for both personal and ambient samples. The coefficient of determination was computed for each regression analysis.

Spearman correlation coefficients (ρ) were calculated for the comparison of EC concentrations and the DRI values. For this, the geometric means of EC (EC_1 and EC_R) were individually paired with the geometric means of each indicator measured by the DRI that were taken in the same day and in the same suitcase to certify that the values used for the correlation were matched.

New calibration factors for the direct-reading instruments were estimated by calculating mean ratios between the respirable and submicron fractions of the filter measurements and the direct-reading instruments. The distribution of ratios was summarized by its arithmetic mean, standard deviation, geometric mean, geometric standard deviation, minimum and maximum. Ratios were computed only for ambient measurements.

The level of significance for these analyses was set at 5%. Analyses were performed using the R software (version 3.4.2, R Development Core Team, Vienna, Austria).

5.1.4 Results

Personal Measurements

216 personal samples were taken in the two mines over a period of 23 days, with 122 samples (56% of total) in Mine 1 and 94 (44%) in Mine 2. 212 samples were retained for RCD with

3 flagged as non-detects, 213 samples for EC_R and 214 TC_R (1 non-detect each for EC_R and TC_R). The median sampling duration for RCD was 586 minutes (range 122-684 minutes, interquartile interval 494-603 minutes) and 583 minutes for EC_R and TC_R (range 120-684 minutes, interquartile interval 474-600 minutes). Altogether the samples covered 18 job titles, the most frequently monitored being Truck operators (n=30), Load haul dump (LHD) operators (n=30) and Boom truck operators (n=15).

Table 2 presents the descriptive statistics of RCD, EC_R and TC_R concentration over all samples and stratified by mine and job title.

The geometric means of RCD, EC_R and TC_R were 170 µg/m^3, 83 µg/m^3, 148 µg/m^3, respectively, for both mines combined. The average ratio between TC and EC was 1.8 in the overall analysis or stratified by mine. However, this ratio varied according to job title (from 1.4 to 3.0).

Ambient Measurements

A total of 45 daily area samples were collected for the respirable fraction, involving both integrated sampling and direct-reading instruments in parallel. Compared to personal samples, the sampling duration was shorter with a median of 308 minutes for RCD and 315 minutes for respirable carbon. For the EC_1 and TC_1 samples (n=30), the median sampling duration was 279 minutes. Overall, there were 28 work shifts for which carbon concentrations were available for both fractions concurrently.

Table 3 presents the descriptive statistics for overall ambient results and stratified by mine. The ratio between TC and EC was lower for ambient measurements compared to the ratios presented in Table 2 for the personal measurements. The ratio between respirable and submicron fractions of EC and TC in the common shifts shows that 90% of the EC and 88% of the TC measured in the mines have aerodynamic diameters lower than 1µm. In addition, there was no significant difference between the mean values of ratios TC_R:EC_R and TC_1:EC_1 (1.42 and 1.38 respectively; p=0.51), suggesting that both fractions contain the same amount of organic carbon.

Association Between Filter-Based Samples in Personal and Ambient Samples

Figure 1 presents the relationship between the RCD and TC_R, as well as TC_R and EC_R concentrations observed among ambient and personal samples, with the corresponding equation and coefficient of determination of the linear model. Overall, the associations between the contaminants were stronger among area samples relative to personal samples.

Direct-Reading Instruments and Association with Elemental Carbon

Table 4 presents the descriptive concentrations measured by the DRI. For each instrument, the statistics were based on the geometric mean of the concentrations measured in 1-minute intervals of a given sampling day/shift.

Spearman rank correlations were computed in order to evaluate the associations between the EC_R and EC_1 concentration in ambient measurements and the geometric mean of the exposure profile measured by direct-reading instruments (Table 5). The strongest association was reported between the EC_1 measured by the Airtec and the ambient EC_1 measured with filters (ρ=0.86; p <0.001). This strong positive association is corroborated by the similar concentration of EC_1 measured by the two methods and reported in Tables 3 and 4 (110 µg/m^3 and 121 µg/m^3 for ambient EC_1 measured with filters and the Airtec, respectively). For dust measurements, the strongest correlation was found for the respirable fraction of the DustTrak 8520 (ρ=0.74; p<0.001). On the other hand, a weak and non-significant correlation was found between EC and particle number concentration.

Arithmetic and geometric mean ratios between the respirable and submicron fractions of the filter measurements (TC_R, TC_1, EC_R and EC_1) and the direct-reading instruments (DustTrak 8520, DustTrak DRX 8533 and Airtec) are presented in Table 6. Mean ratios between filter-based methods and both DustTrak instruments ranged from 0.29 to 0.44, showing that these instruments may overestimate the concentrations of particles reported by a factor of 3.4. In addition, a good correspondence between the Airtec and EC_1 measured by the NIOSH 5040 method was found (arithmetic mean ratio of 0.97; Geometric mean ratio of 0.91).

5.1.5 Discussion

In this study, we assessed DPM exposure of workers in two underground gold mine using personal (i.e. filter-based) and ambient monitoring (i.e. filter-based and direct-reading instruments) methods. For personal measurements, exposures reported in this study are higher than concentrations reported in recent studies regarding diesel exposure in mines and other environments (7, 19, 27). For instance, in an Australian study conducted by Peters et al covering 146 different jobs at 124 mine sites, personal EC concentrations of underground mine workers ranged from 18 to 44 $\mu g/m^3$ (7). Comparatively, mean exposure ranging from 40 to 157 $\mu g/m^3$ and a maximum individual EC concentration of 540 $\mu g/m^3$ is reported in our study. The ultradeep mining environment, where the mines exceed 1,500 m of depth underground, could explain these differences due to challenges related to exposure control at this depth (28). However, Peters et al. also indicated that the concentrations reported in Australia were at the lower end of the exposure concentrations reported internationally because of the implemented efforts for controlling DE in the Australian mines (7). In this regard, several efforts for reducing mine workers' exposure to DE has been proposed, such the use of alternative fuels in order to reduce the respirable diesel particulate matter released by engines (e.g. low-sulfur diesel, 75% biodiesel/25% diesel blend (B75) and natural gas/diesel blend) (29), the use of high-efficiency particulate filters (30), and the importance of the type of ventilation and its rate (31).

We found a TC:EC ratio of 1.8 for personal samples. This value is close to the ones found by Roberge et al. (2006) but higher than the conversion factor of 1.27 suggested by Noll et al. (2015) to predict TC from EC values, and the factor of 1.3 used in the US and Ontario regulations (32, 33). However, Noll et al. (2015) collected the samples in areas of minimal interference and corrected these samples for vapor-phase OC interference by using a tandem filter correction procedure (33). These differences may explain the variability of TC:EC ratio between the two studies. The TC:EC ratio of personal samples shows an important variability, and it is indicative of interference from non-diesel related organic carbon. This interference can skew the interpretation of results when relying solely on TC data. When comparing the TC:EC ratios among the different job titles, the conventional and buggy operators presented higher values, indicating larger interference from non-diesel related organic carbon. For instance, the conventional

workers had the highest mean for TC_R (406 µg/m^3), above Quebec's OEL of 400 µg/m^3 of TC. However, this group also had the largest TC_R:EC_R ratio (ratio: 3.0), suggesting that most part of this value is due to organic carbon interference, which can lead to a misinterpretation of risk assessment. The drilling activities and the related tools that characterize the tasks performed by the conventional and buggy operators are recognized to be related to oil mist exposure, and such interferences could be explained by the oil mist produced during these activities (24).

In addition, ambient measurements showed lower TC:EC ratios (Table 3) and better correlation between TC and EC (Figure 1) when compared to personal measurements, suggesting that ambient measurements are less affected by organic carbon interference than personal measurements in this study context. Other authors also reported variability in TC:EC ratios and interferences after using the NIOSH 5040 method. Birch and Cary suggest that the method 5040 should not be applied for monitoring DPM when other sources of EC are present (e.g. black carbon) (34). Noll et al. indicated that cigarette smoke and oil mist cannot always be avoided when taking personal samples even when sampling the submicron fraction with a size selective sampler (33). According to Liu et al. (2005), the distribution of EC and organic carbon may vary depending on several factors, such as the fuel and engine type, the load, duty cycle, engine maintenance, composition of lubricant oil and sampling conditions (35). Thus, in order to avoid interference from organic carbon not related to diesel exposure, EC should be used as a surrogate of DPM instead of TC.

The mean particle number concentration measured in the underground mines was 10 times higher than the typical urban background concentration (10,800 particles/cm^3) (36) and significantly higher than the mean exposure concentrations reported in other occupational contexts using condensation particle counters (CPC), such as in a port (mean concentration: 32,000 particles/cm^3), an underground station platform (mean concentration: 24,000 particles/cm^3), a bus platform (mean concentration: 78,000 particles/cm^3) and an underground tunnel (mean concentration: 47,900 particles/cm^3) (19, 37-39). On the other hand, higher concentrations were reported in other studies, such as in a distribution depot (mean concentration: 218,000 particles/cm^3) (16). However, the weak correlation between particle number concentration and EC suggests that this measure is not a good surrogate of diesel

exposure in an underground mine. This result is in disagreement with other studies which reported particle number concentration as a good proxy for DE in other exposure contexts. For example, Debia et al. showed that the particle number concentration measured by a CPC can be considered as a good surrogate to estimate workers' exposure to diesel exhaust at EC concentrations lower than 20 µg/m^3 (19, 27). However, this conclusion does not seem to apply in environments of higher DE levels such as an underground mine. Two factors may explain this result: the superior limit of detection of 500,000 particles/cm^3 of the P-Trak was occasionally reached during this study, which may underestimate the results; also, the loss of precision of this equipment in situations of elevated concentrations might negatively impact the correlation. In this regard, Zhu et al. (2006) showed that the P-Trak is generally effective to compare UFP exposure in relation to other more sensitive but non portable instruments, except in occasions of very high concentrations (40).

The strongest correlations between EC and the direct-reading instruments were found for the Airtec and the DustTrak 8520, which measure EC_1 and the mass concentration of the respirable fraction, respectively. The Airtec is a personal instrument developed specifically for the mining environment as an alternative to the NIOSH 5040 method for estimating the concentration of the submicron fraction of EC. Thus, the results from this instrument can be compared to EC concentrations. In fact, the average ratio of 0.97 between the EC_1 measured by the NIOSH 5040 method and Airtec (Table 6) confirms the good relationship between the concentrations reported by these two different methods. Indeed, the specificity of the Airtec was ratified during our study when the dust suppressor system was not efficient and produced a large quantity of aerosols in the air. During this day, the ratio EC_R:Airtec was 1.21 (322 µg/m^3 versus 264 µg/m^3) while the ratio EC_R: DustTrak 8520 was 0.11 (322 µg/m^3 versus 2511 µg/m^3) (Data not shown), suggesting that the Airtec is not largely influenced by aerosol contamination from other sources, contrary to dust monitors such as the DustTrak. In this context, the effectiveness of the Airtec was also evaluated in other studies where the instrument showed good agreement with the NIOSH method 5040 and it was not significantly affected by interferences, such as temperature, relative humidity and dust (21, 22).

The main advantages for the use of the DustTrak 8520 are the ease in handling the instrument and interpreting the data, the identification of peak concentrations due to the fast response time of the instrument, and the possibility of using a cyclone to select different particle size fractions. Miller et al. (2007) evaluated the efficacy of a photometer to directly measure the DPM concentration emitted from vehicles. The authors found strong correlation between the photometer and the method NIOSH 5040 for EC (R^2=0.97) in laboratory conditions, suggesting that the photometer is an inexpensive and reliable method to estimate DPM exposure in real-time (41). However, a disadvantage for the use of a laser photometer as a surrogate of DPM exposure is that this type of instrument is not specific and will measure aerosol from other sources (i.e. oil mist, cigarette smoke or silica). As another disadvantage, the DustTrak is calibrated according to a reference aerosol that, in some cases, may not reflect the characteristics of aerosols from different sources. This may overestimate the concentrations measured, and a calibration factor may be used in these cases. For instance, Stephenson et al. (2006) calculated the ratio between TC and the DustTrak, suggesting a calibration factor of 0.33 (arithmetic mean value) when measuring DPM (42). In the present study, mean ratios between the concentrations measured by the reference method and the laser photometers were between 0.29 and 0.44 (arithmetic mean). These values are close to the one reported by Stephenson et al. (2006), but the fluctuation of these values may be influenced by the contaminant (EC or TC) or the fraction (respirable and submicron) that is being used for the calculation.

5.1.6 Conclusion

This study provided information about the concentrations of DPM in underground mines by measuring several indicators using filter-based methods and DRI. Regarding the association between DRI and EC measured by the NIOSH 5040 method, the measurement of particle number concentration by the CPC showed a weak and non-significant correlation with EC, contrary to results previously reported in the literature for conditions of low diesel exposure. The measurements of EC_1 by the Airtec showed the strongest associations with EC and, although the DustTrak was also associated with EC, interferences from other aerosol sources should be considered when using this instrument to assess DPM.

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G.L and H.C work at the moment of the project for Agnico Eagle Mines and IAMGold, respectively, companies that were investigated in the study. The authors declare no other conflict of interest relating to the material presented in this article.

5.1.8 Contributions

ASF contributed to the study design, measurements, data analysis and manuscript preparation. CC, PEM and ENG contributed to the measurements in the mines. JFS contributed to the data analysis. HC, SH and JL contributed to the study design and implementation. SA performed the analyses of carbon species. MD contributed to the study design and preparation of the manuscript.

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5.1.10 Tables and Figures

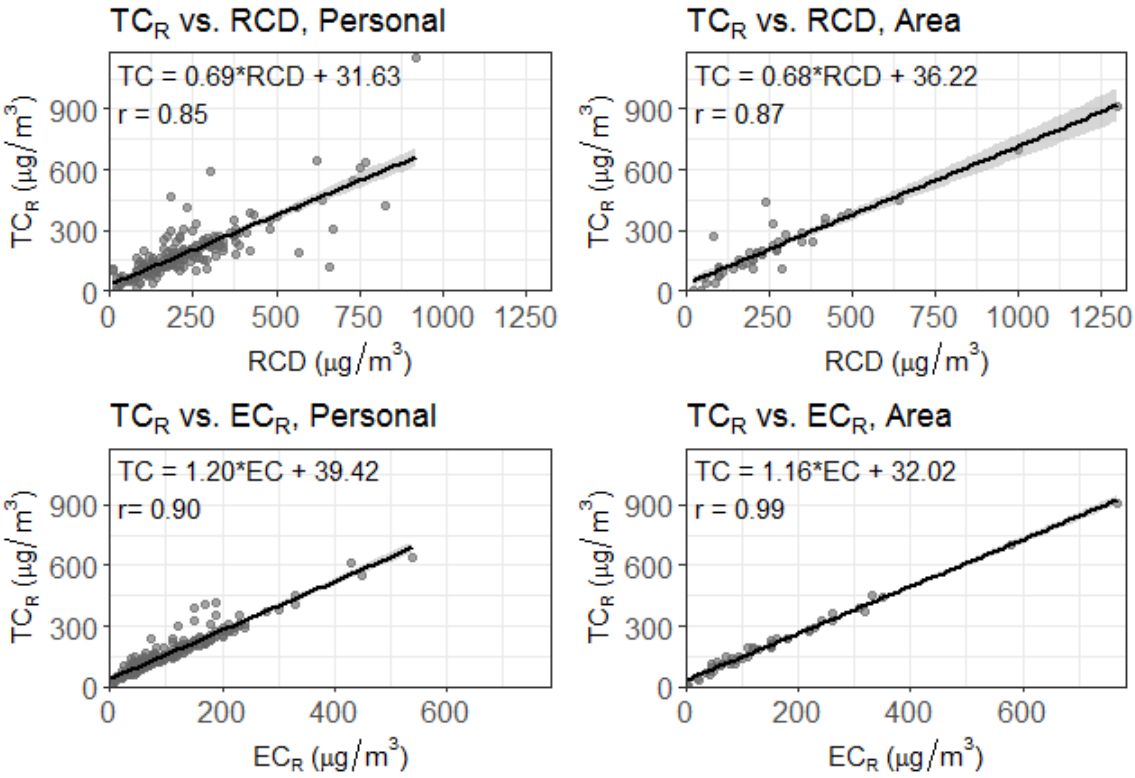

Figure 1: Linear regression analysis between TC_R and RCD, as well as TC_R and EC_R, for personal and ambient measurements.

TC_R: Respirable total carbon; **EC_R:** Respirable elemental carbon; **RCD:** Respirable combustible dust. **R^2:** coefficient of determination of the linear model.

Table 1. Direct-reading instruments used in the ambient measurements.

Model	Type of Instrument	Parameters Measured (unit of concentration)	Particle Size (nm)
P-Trak 8525 (TSI Inc.)	Condensation particle counter (CPC)	Particle number concentration (#/cm^3)	20 – 1 000
DustTrak DRX 8533 (TSI Inc.)	Laser Photometer	Particle mass concentration (µg/m^3) for 5 size fractions (PM_1, $PM_{2.5}$, $PM_{respirable}$, PM_{10} and PM_{TOTAL})	100 – 15 000
DustTrak 8520 (TSI Inc.)	Laser Photometer	Respirable particles; mass concentration (µg/m^3)	4000 (50% cut-off)
Airtec (Flir)	Optical Transmittance	Submicron fraction of EC (µg/m^3)	<1000

PM: Particulate matter; **EC**: Elemental carbon; **NA**: Not applicable

Table 2: Descriptive statistics of the personal RCD, EC_R and TC_R concentrations by mine, job title and exposure group

	N	RCD (µg/m³)	EC_R (µg/m³)	TC_R (µg/m³)	TC_R:EC_R ratio[1]
Overall	216	170 (2.1)	83 (2.3)	148 (1.9)	1.8
Mine					
Mine 1	122	141 (2.1)	68 (2.2)	124 (1.9)	1.8
Mine 2	94	216 (2.0)	103 (2.4)	184 (1.9)	1.8
Job title					
Truck operator	30	228 (1.6)	139 (1.6)	201 (1.5)	1.4
Diamond driller operator	4	140 (1.6)	91 (1.5)	132 (1.4)	1.4
Chisel operator	4	216 (1.7)	119 (1.3)	171 (1.3)	1.4
LHD operator	30	259 (1.8)	146 (2.1)	222 (1.8)	1.5
Foreman	14	146 (2.6)	86 (1.4)	136 (1.2)	1.6
Boom truck operator	15	173 (1.6)	97 (1.7)	154 (1.6)	1.6
Cement truck operator	6	218 (1.4)	88 (1.5)	151 (1.4)	1.7
Hammer operator	6	79 (2.1)	57 (3.0)	96 (2.2)	1.7
OHS advisor	10	125 (2.3)	54 (3.8)	94 (3.4)	1.8
Jumbo operator	9	231 (1.8)	108 (1.7)	199 (1.4)	1.8
Mechanic	14	128 (1.7)	60 (1.6)	111 (1.4)	1.9
Miner	10	185 (1.8)	75 (2.7)	143 (1.7)	1.9
Electrician	6	104 (1.7)	46 (2.1)	93 (1.5)	2.0
Cableman	6	129 (1.9)	58 (1.7)	122 (1.8)	2.1
Rock bolter operator	8	96 (2.2)	40 (2.7)	89 (2.3)	2.2
Shotcrete operator	5	225 (1.3)	66 (1.9)	154 (1.3)	2.4
Buggy operator	14	120 (2.8)	41 (1.8)	105 (2.2)	2.6
Conventional	7	504 (1.7)	137 (2.1)	406 (1.9)	3.0

N: Total number of work shifts sampled**; RCD:** Respirable combustible dust; **EC_R:** Respirable elemental carbon; **TC_R:** Respirable total carbon. Data expressed as geometric mean and geometric standard deviation.

[1] Ratio between the GMs of total carbon and elemental carbon concentrations.

Table 3: Descriptive statistics of RCD, EC and TC concentrations for ambient samples.

	Respirable fraction					PM_1 fraction			
	N	**RCD ($\mu g/m^3$)**	**EC_R ($\mu g/m^3$)[3]**	**TC_R ($\mu g/m^3$)**	**TC_R:EC_R ratio[1]**	**N**	**EC_1**	**TC_1**	**TC_1:EC_1 ratio[2]**
Overall	45	197 (2.2)	100 (3.3)	151 (3.0)	1.50	29	110 (3.3)	151 (2.9)	1.37
Common shifts[3]	28	208 (2.2)	118 (3.4)	167 (3.0)	1.42	28	106 (3.3)	146 (2.9)	1.38
Mine									
Mine 1	23	176 (2.2)	94 (3.1)	143 (2.7)	1.52	16	133 (2.1)	176 (1.9)	1.32
Mine 2	22	220 (2.3)	107 (3.7)	159 (3.3)	1.48	13	87 (5.0)	125 (4.2)	1.43

RCD: Respirable combustible dust; **EC_R:** Respirable elemental carbon; **EC_1:** submicron fraction of elemental carbon; **TC_R:** Respirable total carbon; **TC_1:** Submicron fraction of total carbon; **N:** Number of samples. Data are expressed as geometric mean and geometric standard deviation.

[1] Ratio between respirable total carbon and elemental carbon concentrations.

[2] Ratio between the submicron fraction of total carbon and elemental carbon concentrations.

[3] Restricted to work shifts for which results for the respirable and submicron fractions were concurrently available.

Table 4: Descriptive statistics of ambient EC_R and particles as numerical and mass concentrations measured by the direct-reading instruments.

Instrument	Indicator	N	GM (GSD)	Min-Max
Airtec	Average EC_1 (µg/m^3)	45	121 (2.2)	19–870
DustTrak 8520	Respirable dust (µg/m^3)	39	424 (2.1)	86–2220
DustTrak DRX 8533	PM_1 (µg/m^3)	40	338 (2.5)	8–1781
	$PM_{2.5}$ (µg/m^3)	40	367 (2.5)	9–1970
	Respirable dust (µg/m^3)	40	392 (2.5)	9–2187
	PM_{10} (µg/m^3)	40	462 (2.5)	13–3217
	Total dust (µg/m^3)	40	501 (2.4)	20–3475
P-Trak	Particles/cm^3	38	93,176 (1.9)	23,861–239,598

GM: Geometric mean; **GSD:** Geometric standard deviation; **N:** Number of samples.

Table 5: Correlation coefficients for ambient EC (respirable and submicron fractions) and daily geometric means from direct-reading instruments.

Instrument	**Indicator**	**N**	**EC_R**	**N**	**EC_1**
Airtec	EC_1	40	0.80**	25	0.86**
DustTrak 8520	Respirable dust	36	0.71**	25	0.74**
DustTrak DRX 8533	PM_1	35	0.61**	21	0.69**
	$PM_{2.5}$	35	0.59**	21	0.64**
	Respirable dust	35	0.56**	21	0.60**
	PM_{10}	35	0.51**	21	0.58**
	Total dust	35	0.45**	21	0.53*
P-Trak	Particles/cm^3	30	0.30	23	0.32

EC_1: Submicron fraction of elemental carbon; EC_R: Respirable fraction of elemental carbon**; PM:** particulate matter. **N**: Number of samples.

*p<0.01, ** p <0.001. Test: Spearman rank correlation.

Table 6: Average ratios between filter-based methods and direct-reading instruments.

Indicators	N	GM(GSD)	AM (SD)	Min-Max
TC_R: DustTrak 8520	39	0.39 (1.5)	0.44 (0.28)	0.17-1.97
EC_R: DustTrak 8520	39	0.26 (1.6)	0.31 (0.25)	0.11-1.70
TC_R: DustTrak DRX 8533 (PM_4)	38	0.38 (1.6)	0.42 (0.24)	0.01-1.50
EC_R: DustTrak DRX 8533 (PM_4)	38	0.25 (1.7)	0.29 (0.16)	0.01-0.89
TC_1: DustTrak DRX 8533 (PM_1)	24	0.36(1.5)	0.39 (0.15)	0.15-0.61
EC_1: DustTrak DRX 8533 (PM_1)	24	0.26 (1.6)	0.30 (0.12)	0.12-0.49
Airtec: DustTrak DRX 8533 (PM_1)	39	0.29 (1.7)	0.34 (0.16)	0.09-0.84
EC_1:Airtec	28	0.91 (1.4)	0.97 (0.39)	0.35-2.41

N: Number of samples; **GM**: Geometric mean; **GSD**: Geometric standard deviation; **AM:** Arithmetic mean; **SD**: Arithmetic standard deviation; **Min-Max:** Minimum and maximum values of the averages.

5.1.11 Supplementary Material

Table S1: Description of job titles in the underground mines.

Job title	Description
Truck operator	Displacement of ore or waste rocks
Diamond driller operator	Exploratory drilling (core sampling)
Chisel operator	Installation of services (ventilation, electrical grid, compressed air, water and embankment pipes) and safety of working zones
LHD operator	Racking waste rocks or ores in a stack to transfer to the truck
Foreman	Inspection of construction sites
Boom truck operator	Displacement of material in the mine
Cement truck operator	Reception and distribution of concrete
Hammer operator	Ore reception and crushing
OHS advisor	Verification of sampling equipment, observation of workers' tasks and identification of associated risks
Jumbo operator	Horizontal drilling of the loading holes of explosives
Mechanic	Repaired of fixed and mobile equipment
Miner	Installation of ducts and explosives, regular use of rock drills, transport of people and materials
Electrician	Electrical installation and repair
Cableman	Anchoring cables installation
Rock bolter operator	Walls and ceiling reparation with welded mesh panels and bolts
Shotcrete operator	Projection of concrete on the walls of the gallery
Buggy operator	Vertical drilling of small blasting holes
Conventional	Manual work (i.e. jackleg), transport of the material

5.2: Characterisation and quantification of ultrafine particles and carbonaceous components from occupational exposures to diesel particulate matter in selected workplaces

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5.2.1 Abstract

Questions still exist regarding which indicator better estimates worker's exposure to diesel particulate matter (DPM) and, especially for ultrafine particles (UFP), how exposure levels and the characteristics of the particles vary in workplaces with different exposure conditions. This study aimed to quantify and characterize DPM exposures in three workplaces with different exposure levels: an underground mine, a subway tunnel and a truck repair workshop. The same sampling strategy was used and included measurements of the particle number concentration (PNC), mass concentration, size distribution, transmission electron microscopy (TEM) and the characterization of carbonaceous fractions. The highest geometric means of PNC and elemental carbon (EC) were measured in the mine (134,000 [GSD=1.5] particles/cm^3 and 125 [GSD=2.1] $\mu g/m^3$), followed by the tunnel (32,800 [GSD=1.7] particles/cm^3 and 24.7 [GSD=2.4] $\mu g/m^3$) and the truck workshop (22,700 [GSD=1.3] particles/cm^3 and 2.7 [GSD=2.4] $\mu g/m^3$). This gradient of exposure was also observed for total carbon (TC) and particulate matter. The TC/EC ratio was 1.4 in the mine, 2.5 in the tunnel and 8.7 in the workshop, indicating important organic carbon interference in the non-mining workplaces. EC and PNC were strongly correlated in the tunnel (r=0.85; $p<0.01$) and the workshop (r=0.91; $p<0.001$), but a moderate correlation was observed in the mine (r=0.57; $p<0.05$). Results from TEM showed individual carbon spheres between 10 nm and 56.5 nm organized in agglomerates, while results from the size distribution profiles showed bimodal distributions with a larger accumulation mode in the mine (93 nm) compared to the tunnel (39 nm) and the truck workshop (34 nm). In conclusion, the composition of the carbonaceous fraction varies according to the workplace and can interfere with DPM estimation when TC is used as indicator. Also, the dominance of particles <100 nm in all workplaces, the high levels of PNC measured and the good correlation with EC suggest that UFP exposures should receive more attention on occupational routine measurements and regulations.

Keywords: diesel particulate matter, ultrafine particles, elemental carbon, occupational exposures, TEM

5.2.2 Introduction

Millions of workers worldwide are exposed to diesel engine exhaust (DEE) as a result of the frequent use of diesel-powered equipment in light and heavy-duty vehicles, electric generators and heavy machinery in the transportation, manufacturing, wholesale and retail trade, and mining industries (1). In Canada, it is estimated that approximately 897,000 workers are exposed to DEE, contributing to 2.4% of the lung cancer cases diagnosed annually (2, 3). In addition to being classified as a human carcinogen (Group 1) by the International Agency for Research on Cancer (IARC), DEE exposure has also been associated with cardiorespiratory effects (4-8).

DEE consists of a complex mixture of substances in solid, liquid and gaseous states. The type of engine, fuel characteristics, combustion temperature and load of operations are parameters that influence composition and levels of exposure (9, 10). Diesel particulate matter (DPM), the solid phase of DEE, is composed of elemental carbon (EC) onto which organic carbon (OC) compounds and other substances (e.g. water-soluble ions, metallic compounds, lubricant droplets, and unburned fuel) are adsorbed (6). The sum of the EC and OC fractions of DPM is called the total carbon (TC) fraction. The size of the particles is mainly in the respirable fraction (i.e. the mass fraction of particles that can reach the alveoli, the median value of the size distribution of particles in this category is 4.25 μm with a GSD of 1.5), including a high number of ultrafine particles (UFP; particles with an aerodynamic diameter <100 nm) (11).

Occupational exposure limits (OEL) for DPM are expressed in mass concentration and they vary between and within countries. In Quebec (Canada), an OEL of 400 $\mu g/m^3$ of respirable TC is implemented in the mining industry (12), while the Canadian province of Ontario also has a regulatory time-weighted limit value of 400 $\mu g/m^3$ of respirable TC for the mining industry, transposable to EC via a conversion factor of 1.3 (13). In the USA, the U.S Mine Safety and Health Administration has prescribed an 8-hr OEL of 160 $\mu g/m^3$ of submicron TC (14). In the European Union, a recent regulation was approved and the OEL will be set at 50 $\mu g/m^3$ of EC for all diesel emissions, without distinguishing between sources or workplaces. In Canada and USA, however, no OEL for DPM exposure exists outside the mining industry. In consequence, very little information is available outside this workplace regarding occupational DPM exposures.

Because of their small size, UFP contained in DPM can translocate from the alveolar space and spread systematically through the bloodstream, reaching other targets such as the cardiovascular system, liver and central nervous system (15, 16). In addition, for the same mass, the surface area of UFP can be larger than the surface area of micrometric particles, which may result in more harmful substances adsorbed (e.g. heavy metals and volatile organic compounds). These toxicological evidences suggest that the particle number concentration (PNC) could be explored as a potential indicator of DPM exposure.

However, studies measuring specifically the UFP levels in occupational settings are insufficient to allow a general conclusion about workers' exposure (17). As a consequence, occupational exposures are currently not regulated in terms of particle number concentration. Thus, the harmonization of sampling strategies along with the assessment of additional information such as the correlation between different indicators, the size distribution and the physicochemical characteristics of particles in different workplaces are essential to generate more reliable and comparable data on exposure and to provide a more comprehensive overview.

The aims of this study are: i) to assess DPM exposure in terms of carbonaceous components (i.e. TC and EC) mass concentration, particle number concentration, size distribution as well as the physicochemical characteristics determined by transmission electron microscopy in three selected workplaces with distinct exposure levels; and ii) to estimate the relationship between the different surrogates of DPM exposure across the selected workplaces.

5.2.3 Methods

This project was approved by the Ethics Committee for Health Research of the University of Montreal (Project Number: 16-056-CERES-D).

Description of the workplaces and sampling design

This study was conducted in three workplaces selected based on the potential for finding different levels of DPM, from intense to intermediate and low concentrations. This classification was determined *a priori,* based on the expected concentrations, after considering data from the literature for similar settings, the characteristics of the workplaces and the intensity of activities.

The first workplace was an underground gold mine. The mine, located in the province of Quebec (Canada), operates at a maximum depth of around 3,000 m. The workplace is characterized by an enclosed environment with intense activities of on-road and off-road vehicles. A mechanical ventilation system provides fresh air in the different sections of the mine. The second workplace was a subway tunnel in Montreal (Canada) where, during the night shift, workers perform repairs and cleaning tasks on the rails and tunnels with the aid of locomotives and auxiliary engines powered by diesel. In the present study, one locomotive was followed for each work shift. This workplace is also characterized as an enclosed (underground) environment with limited general ventilation. The third workplace was a truck repair workshop located in Laval (Canada) where DPM exposures are caused by the frequent transit of on-road trucks. The workshop was equipped with a general ventilation system and, although this workplace is classified as an indoor setting, the doors of the workshop were frequently opened resulting in a greater air exchange compared to the two other workplaces.

Ambient measurements of DPM were performed with instruments installed in two suitcases specifically designed for this study. In the underground mine, measurements were performed in the main circulation routes (e.g. bypasses and ramps) where the intense transit of vehicles loading and transporting the ore was observed. In the subway tunnel, the suitcases were placed in the tunnels or on the platforms close to the diesel-powered locomotive and the workers performing repairs and cleaning tasks. In the truck workshop, the suitcases were installed at different working stations next to the mechanics repairing the trucks. Because measurements were performed in fixed stations, the distance between the instruments and the sources of DPM (e.g. the vehicles) varied during a working day.

Sampling campaigns were carried out between Fall 2016 and Spring 2018. Sixteen measurements were performed in the underground mine and 12 measurements were performed in the subway tunnel and truck workshop. Measurements were performed in different locations to map the exposure of the entire settings and to ensure the presence of significant work activity during the sampling period. The duration of each measurement ranged between 5 and 8 hours.

As shown in Supplementary Figure 1, both suitcases were equipped with:

a) A set of filters and pumps for the integrated measurements of TC and EC following the NIOSH 5040 method.

b) A set of direct-reading instruments for concomitant real-time measurements of aerosol mass concentration, number concentration and the submicron fraction of elemental carbon.

Details of the instruments and analytical methods are presented in the next sections.

TC and EC analyses by the NIOSH 5040 method

The respirable and submicron fractions of total carbon (TC_R and TC_1, respectively) and elemental carbon (EC_R and EC_1, respectively) were sampled in parallel in all workplaces. For the respirable fraction, 25-mm quartz fiber filters (QFF) and cassettes were attached to Dorr-Oliver nylon cyclones to collect particles with a 4 µm aerodynamic diameter cut-point. For the submicron fraction, 37-mm QFF and cassettes equipped with jeweled impactors (SKC Inc. Eighty Four, PA, USA) were used in addition to cyclones to collect particles with a 0.8 µm aerodynamic diameter cut-point. For both fractions, GilAir pumps (Sensidyne, LP, St. Petersburg, FL, USA) set at a flow rate of 1.7 L/min were used. The pumps were calibrated before and after each sampling using a DryCal volumetric flow meter (Mesa Labs Inc., Lakewood, CO, USA). Field blank samples were collected each day. Samples were analyzed by the laboratories of the *Institut de Recherche Robert-Sauvé en Santé et en Sécurité du Travail* (IRSST; Montreal, Canada) following the NIOSH 5040 method.

Direct reading instruments (DRI)

Table 1 presents the DRI used to monitor aerosol mass concentration, PNC and EC_1 concentration.

The Airtec (FLIR Systems, Albuquerque, NM, USA) is an instrument that uses optical transmittance to provide a specific real-time estimate of EC_1. This is an advantage compared to the other DRIs used in this study that are not specific for the type of particle being measured.

Laser photometers were used to measure the mass concentrations of particles larger than 100 nm. A DustTrak 8520 (TSI Inc., Shoreview, MN, USA) was equipped with a nylon cyclone and had its flow rate set to 1.7 L/min to select the respirable fraction of the particles. The

concentrations reported in this study for the laser photometers were estimated using a photometric calibration factor of 1.00 (Factory factor). However, DPM has different light scattering properties than the calibrated test aerosol (i.e. Arizona Road Dust). For this reason, photometric calibration factors specific for DPM were also calculated daily for each workplace. This was done by dividing the values of the reference method (i.e. TC_R or EC_R measured by the NIOSH 5040 method) by the geometric mean concentrations of $PM_{RESPIRABLE}$ measured in parallel with the DustTrak 8520. In addition, a size calibration for the DustTrak DRX 8533 (TSI Inc., Shoreview, MN, USA) was performed prior to each sampling period to improve the relative accuracy between the five mass channels of this instrument in relation to the size distribution of the aerosols of interest. The instrument calculates this size correction by measuring the aerosol size distribution with and without a $PM_{2.5}$ impactor, and then calculating the ratio of these two size distributions.

The P-Trak 8525 (TSI Inc., Shoreview, MN, USA) is a condensation particle counter (CPC) that measures PNC between 20 nm and 1000 nm, with an upper limit of 500,000 particles/cm^3. In addition, parallel measurements with the Engine Exhaust Particle Sizer (EEPS 3090; TSI Inc., Shoreview, MN, USA) were performed during one working day in each workplace to determine the size distribution of the particles and the comparison of the PNC between this instrument and the CPC. The EEPS spectrometer is a fast response, high-resolution instrument that uses sensitive electrometers to provide particle size and number concentration data in 32 size channels. For this study, the default inversion matrix was used.

All instruments were equipped with Tygon tubing and air samples were taken at a height of about 1.5 m, corresponding to the shared breathing zone. All devices were calibrated prior to the sampling period according to the manufacturer's requirements, and zeroing was performed each day before the monitoring when applicable.

Transmission electron microscopy (TEM)

Aerosol sampling on 3 mm TEM grids was performed using the Mini Particle Sampler (MPS; ECOMESURE, Janvry, France). This sampler allows the collection of particles directly on the TEM grids (18). Particles were deposited onto 400 Mesh copper grids covered by a carbon film

with a hole diameter of 1.2 µm and a spacing of 1.3 µm between the holes (Quantifoil; Großlöbichau, Germany). A Gilair pump was used with a flow rate of 0.3 L/min during 1 minute. In order to perform a semi-quantitative characterization of the collected agglomerates, one microscopic grid was collected at each workplace near diesel sources (i.e. around 1 meter) during periods of activity.

Microscopic analyses of the particles were performed by bright field imaging on a JEOL 2100F FEG-TEM at an operation voltage of 200 kV. The qualitative elemental characterization was performed by Energy-Dispersive X-ray Spectroscopy (EDS) using an Oxford INCA x-sight EDS detector (Model 6498) and an acquisition time of 60s of live time. Three different square-shaped openings were randomly selected. A general observation of the openings was made to visualize the distribution of particles and agglomerates on the grid. The analyses of individual particles and agglomerates were then performed. Seven agglomerates were measured per opening for three openings, for a total of 21 agglomerates. On these 21 agglomerates, a total of 100 primary particles were then analyzed per grid. For each one of these agglomerates, an image was acquired, and an EDS analysis was performed. The particles were randomly selected, but with the aim of ensuring a good representation of the diversity found on the grid during the initial scan. For each particle or group of particles, the following stereological parameters were evaluated: the diameter of primary particles (d_p), the maximum projected length of the agglomerate (L_A), the maximum projected width of the agglomerate (W_A), the average between L_A and W_A, and the ratio L_A/W_A (i.e. an indicator of the form of the agglomerate). These measurements were performed with the aid of the image analysis software Digital Micrograph, version 3.11.0 (Gatan Inc., Pleasanton, CA, USA).

Statistical analysis

Although each workplace was assessed at least 12 times, the sections/locations where these measurements were performed were not repeated. For this reason, each full work shift measurement was treated as an independent sample. For each measurement, daily geometric means (GM) and geometric standard deviations (GSD) were calculated. The mass of 6 EC and 4 TC samples of the truck repair workshop were below the quantification limit (QL) and they were treated by dividing the QL by the square root of 2. The association between EC concentrations

measured by the Airtec and the NIOSH 5040 method was estimated by linear regression, and the slopes were compared between each workplace. Pearson correlation coefficients (*r*) were calculated to evaluate the associations between the EC concentrations measured by the NIOSH 5040 method and the concentration of the different indicators measured by the DRI (i.e. EC_1, mass concentration and PNC).

A P-value <0.05 was defined as the level of statistical significance. Statistical analyses were performed with SPSS, version 24.0 (IBM Inc. Chicago, IL, USA).

5.2.4 Results

TC and EC concentrations

Concentrations of the respirable and submicron fractions of TC and EC measured by the NIOSH 5040 method—as well as direct reading EC_1 measured by the Airtec—are presented in Table 2. For both sampling methods, the underground mine presented the highest concentrations in both size fractions, followed by the subway tunnel and the truck workshop. The percentage of TC and EC in the submicron fraction in relation to the respirable fraction was 93.1% and 97.6% in the underground mine, 61% and 63.5% in the subway tunnel, and 61.8% and 74% in the truck workshop, respectively (results not tabulated).

The mean ratio between TC_R and EC_R estimated by the NIOSH 5040 method was 1.4 in the underground mine; however, higher TC_R/EC_R ratios were observed in the subway tunnel (2.5) and in the truck repair workshop (8.7), where DPM concentrations were significantly lower. The TC_1/EC_1 ratios confirm these results.

Aerosol mass concentration

The mass concentrations measured by the DRIs for the different aerosol fractions are presented in Table 3. Overall, results followed the same pattern observed for carbon measurements reported by the NIOSH 5040 method and the Airtec, with the underground mine presenting the highest mass concentration for all aerosol fractions, followed by the subway tunnel and the truck repair workshop.

The photometric calibration factors for DPM are also presented in Table 3. Average ratios ranged from 0.41 to 1.4 when TC_R was used as a reference indicator and from 0.20 to 0.52 when EC_R was used as a reference indicator.

Workplace particle number concentration and size distribution

Table 3 presents the PNC measured by the CPC. The underground mine presented the highest concentration (GM = 134,000 particles/cm^3; GSD = 1.5) compared to the subway tunnel (GM = 32,800 particles/cm^3; GSD = 1.7) and the truck repair workshop (GM = 22,700 particles/cm^3; GSD = 1.3).

Side by side measurements show a larger ratio between the geometric mean of PNC measured by the EEPS and the geometric mean of PNC measured by the P-Trak in the underground mine (1.94) compared to the subway tunnel (1.24) and the truck repair workshop (1.24). This suggests a larger divergence between the two instruments in the environment where the highest levels of ultrafine particles were measured (Table 3). This difference is also illustrated in the Supplementary Figure 2, where the distribution profile comparing the real-time measurements of the two instruments shows significantly higher peak concentrations measured by the EEPS when compared to the peak levels measured by the CPC. The maximum peak concentration measured by the EEPS in the underground mine was 2,650,000 particles/cm^3 while the maximum peak concentration measured by the CPC reached the limit of the instrument (500,000 particles/cm^3), suggesting a limitation of the CPC in accurately estimating peak exposures in this workplace.

Figure 1 shows the size distribution of the ultrafine particles measured by the EEPS during a work shift in each workplace. In each case, a bimodal distribution is observed with a small nucleation mode with the mean diameter of 10.8 nm. Larger accumulation modes with mean diameters of 93 nm were observed in the underground mine, where concentrations were higher, compared to 39 nm for the subway tunnel and 34 nm for the truck repair workshop. In addition, Supplementary Figure 3 shows the size distribution of the ultrafine particles measured by the EEPS during individual emission peaks, representing measurements during intense activity and closer to the source. Results show an increased emission of primary particles (between 10 nm and 20 nm) in the underground mine. For the subway tunnel and the truck workshop, however,

the size distribution of the ultrafine particles during peak activities was closer to the size distribution measured for the complete work shift, with mean diameters between 34 nm and 52 nm.

Associations between elemental carbon, mass and number concentrations of aerosols

Table 4 presents the Pearson correlation coefficients (r) for the associations between elemental carbon (measured by the NIOSH 5040 method) and the indicators measured by the direct reading instruments.

We found strong and positive correlations between EC concentrations measured by the Airtec and the NIOSH 5040 method across all workplaces (Underground mine: $r = 0.98$; $p<0.001$, Subway tunnel: $r = 0.88$; $p<0.001$, Truck repair workshop: $r = 0.98$; $p<0.001$). In addition, Supplementary Figure 4 presents the results of the linear regression between EC concentrations measured by the Airtec and the NIOSH 5040 method. A slope of 1.01 was found in the underground mine, indicating a strong comparability between both methods. However, in the subway tunnel and truck workshop, the slopes of 0.57 and 0.46, respectively, suggest an overestimation of the Airtec data compared to the NIOSH 5040 data. The exclusion of the non-detected values slightly increased the linear regression parameters of the truck workshop.

Table 4 also shows the association between EC and the mass concentrations of respirable particles measured with the laser photometers. Strong and positive correlations ($r > 0.8$ and $p<0.001$) were observed for both instruments across all workplaces. Moreover, minimal variations between the correlation coefficients of the DustTrak DRX and the DustTrak 8525 were observed.

Strong and positive correlations were also observed for the association between EC and the PNC in the subway tunnel ($r = 0.85$; $p<0.01$) and the truck repair workshop ($r = 0.91$; $p<0.001$). However, a moderate and positive correlation coefficient ($r = 0.57$; $p<0.05$) was observed in the underground mine, where UFP levels are higher. This lower correlation coefficient value can be explained by the limitation of the CPC in measuring peak concentrations higher than 500,000 particles/cm^3, possibly resulting in an underestimation of the particle number concentration in the underground mine.

Transmission electron microscopy

Supplementary Figure 5 shows a general overview of the particles deposited on the TEM grids (400X magnification). The underground mine presented the larger density of particles (A), followed by the subway tunnel (B) and the truck repair workshop (C). DPM agglomerates (the smallest particles observed in the figure) were the most frequent type of particles collected.

Figure 2 shows a representative TEM image of the diesel particles collected by the MPS as well as the EDS spectrum of the elemental composition. The primary particles collected and analyzed in this study were spherical carbon particles with diameter ranging between 10 nm and 56.5 nm. The average diameter of the primary particles was 23.7 ± 9.1 nm in the underground mine, 25.1 ± 8.5 nm in the subway tunnel and 25 ± 7.1 nm in the truck workshop (Table 5). These particles were organized in agglomerates of varying sizes, with length (L_A) ranging between 84.9 nm and 2300 nm and width (W_A) between 59.7 nm and 1260 nm. The ratio L_A/W_A varied from 1.1 (i.e. nearly spherical) to about 3 (i.e. elongated agglomerates).

The presence of non-diesel particles has also been observed. Supplementary Figure 6a shows an irregular particle rich in or consisted of silicon, calcium and oxygen, attributed to the presence of silica dust in the underground mine. In addition, agglomerates of spherical nanometric particles composed of manganese, silicon, magnesium, titanium and especially iron has also been observed in this workplace (Supplementary Figure 6b). Finally, in the truck workshop, liquid droplets rich in carbon were collected in the grids, suggesting the presence of oil mist in this workplace.

5.2.5 Discussion

This study presented the results of the quantification and characterization of particle number concentration, size distribution, mass concentration, and carbonaceous components associated with occupational diesel particulate matter exposures, as well as their stereological parameters and elemental composition as determined by TEM bright field imaging and EDS. To our knowledge, this is the first time a study provides such an extensive assessment of

occupational exposures to DPM, using a comprehensive sampling strategy in different workplaces.

The highest, intermediate and lowest EC concentrations were found in the underground mine, in the subway tunnel and in the truck shop, respectively. The high concentrations in the underground mine are in the range reported in a literature review of 18 studies (between 27 and 658 $\mu g/m^3$) (19). This workplace is historically recognized as an environment with high occupational exposures to DPM. However, recent studies measured EC concentrations of 18–44 $\mu g/m^3$ and 18.9 $\mu g/m^3$ in Australian and Norwegian, respectively (9, 20). This difference could be the result of the lower OEL in these countries (e.g. 100 $\mu g/m^3$ of EC in Australian mines) and the successful implementation of measures for better controlling DEE exposure, such as newer and more efficient diesel engine technology. Two studies assessed EC exposure during tunnel finishing, construction and repairs. The authors reported EC concentrations between 11 $\mu g/m^3$ and 37.8 $\mu g/m^3$, a concentration range comparable to the one reported the subway tunnel in our study (9, 21). Finally, Smith et al. (2006) measured DPM exposure in different sectors and job titles of the US trucking industry. The authors reported EC levels between 0.3 $\mu g/m^3$ (office) and 1.54 $\mu g/m^3$ (shop area), with a mean exposure of 2 $\mu g/m^3$ for mechanics (22).

Although no personal measurement was conducted, comparing our results of full-shift measurements to OELs is still of interest in an occupational hygiene standpoint. In this context, when compared to Quebec's OEL of 400 $\mu g/m^3$ of TC_R, 2 out of 16 shift samples of TC_R exceeded this concentration. The concentrations in the subway tunnel and truck repair workshop, however, cannot be compared to local regulations since there is no OEL for DPM in non-mining workplaces in Quebec. Nonetheless, if our results are compared with the OEL of 50 $\mu g/m^3$ of EC recently approved in the European Union, 14 of the 16 EC samples would exceed the limit concentration in the underground mine, compared to 4 out 12 samples in the subway tunnel and none in the truck repair workshop. In addition, CAREX Canada recently recommended that Canadian jurisdictions move towards an OEL based on EC of 20 $\mu g/m^3$ for the mining industry and 5 $\mu g/m^3$ for other workplaces (23). When compared to these values, all EC concentrations measured in the underground mine and the subway tunnel—as well as 4 out 12 measurements in the truck workshop—were above these recommendations.

The TC/EC ratios of 1.4 in the underground mine are similar to the value reported in the literature for this workplace (24, 25). However, the ratios of 2.5 found in the subway tunnel and of 8.7 in the truck workshop indicate an important presence of OC in the mass of TC. It is recognized that when using TC as a surrogate of DPM exposure, OC from other sources such as cigarette smoke, oil mist, and environmental emissions (e.g. gasoline vehicles, forest fires) may interfere with these analyses (26, 27). According to Hao et al. (2019), emissions from gasoline vehicles show a higher content of OC compared to diesel emissions (28). Thus, the combination of low levels of diesel emissions, the presence of oil mist and the proximity to a highway may explain the larger OC fraction in the truck repair workshop. Other studies have also reported important OC content from sampling performed in different workplaces. For instance, Debia et al. (2016) reported a TC/EC ratio of 12 in port workers; Smith et al. (2006) found that EC contributed only 3% to 14% of the mass of TC in the trucking industry; and according to Hedmer et al. (2017), 25% of TC mass was composed of EC when assessing DPM exposure among tunnel construction workers (21, 22, 29).

We found strong and positive correlations between the mass concentration of aerosol measured by the laser photometers and EC concentrations measured by the NIOSH 5040 method. Miller et al. (2007) previously evaluated the efficiency of a photometer for the measurement of DPM associated with vehicle emissions. The authors found a strong correlation between the photometer and the NIOSH 5040 method for EC in laboratory conditions ($R^2 = 0.97$), suggesting that the photometer can be an inexpensive and reliable method to estimate real-time DPM exposure (30). However, the disadvantages and limitations for using these instruments should be considered. For instance, this type of instrument is not specific and measurements can be affected by aerosols from other sources. In this context, the presence of silica dust and metallic particles (observed by TEM bright field imaging in the underground mine samples) can overestimate the mass of DPM in this workplace. In addition, the DustTrak is calibrated using a reference aerosol that may not reflect the characteristics of aerosols from different sources in all cases. This may also result in overestimation of the concentrations measured. As a consequence, a reference method (e.g. NIOSH 5040) should be used for the calculation of a calibration factor for DPM. In this regard, we have observed important variations in the photometric calibration

factors between the workplaces when TC was used as the reference indicator (0.41, 1.1, and 1.4 for the underground mine, subway tunnel and truck workshop, respectively). These results suggest that the calculation of specific calibration factors for each workplace is preferred when using these instruments; and the use of a pre-defined calibration factor to be applied in different workplaces is not recommended.

The PNC measured in the underground mine (GM = 134,000 particles/cm^3) was among the highest reported in the literature for occupational DPM exposure (17). Our results can be compared to the number concentrations measured in a few other occupational contexts, such as in bus/tram drivers (GM: between 10,000 and 24,000 particles/cm^3) (31), at a bus platform/terminal (GM: between 64,000 and 113,000 particles/cm^3), a port terminal (GM: 32,700 particles/cm^3) (29), during a tunnel construction (GM: 97,600 particles/cm^3)(21), at a distribution depot (Arithmetic mean [AM]: between 50,000 and 218,000 particles/cm^3) (32), at a highway toll collection booth (AM: 65,000 particles/cm^3) (33), and during highway maintenance (AM: between 7,959 and 74,145 particles/cm^3) (34). However, exposure levels for many workplaces, tasks and job titles are still unknown, and the number of studies is insufficient to generate a complete portrait of occupational exposures to UFP. Some challenges regarding occupational measurements of UFP include the lack of OEL specific to particle number concentrations and the lack of instruments adapted to the occupational context, such as to routinely measure personal UFP exposures during a full work shift and the capability of accurately estimating extreme exposure concentrations.

Results from the TEM analyses showed agglomerates of nanometric spherical carbon particles. In addition, the analysis of the size distribution of these particles by the EEPS 3090 described a bimodal distribution with a small nucleation mode with a mean diameter of 10.8 nm and an accumulation mode where the agglomerates were concentrated. The higher mean mode of the particle size distribution found in the underground mine by the EEPS may be explained by the highest concentrations and the challenges related to the ventilation and dispersion of the particles in this workplace. Our results are in line with a review about the physical characterization of particulate emissions from diesel engines, where it is shown that typical diesel particulates are formed mainly by agglomerates of spherical primary particles between 15 nm

and 40 nm, and that the accumulation mode could be accompanied by a nucleation mode consisting of smaller particles (35).

The presence of a nucleation mode with very small particles is one of the factors that explain the divergences in the PNC reported by the CPC and the EEPS 3090, since the CPC model used in this study cannot detect particles smaller than 20 nm. In addition, the different limits of reading of the two instruments have also influenced the EEPS/CPC ratio. As reported in Supplementary Figure 2, intense peak concentrations up to 2,650,000 particles/cm^3 were detected by the EEPS 3090 in the underground mine. These high concentrations, however, could not be adequately measured by the CPC, which has an upper limit of reading of 500,000 particles/cm^3. This limitation of the CPC had a direct impact on the higher ratio between the two instruments and the weaker correlation between EC and PNC found in the underground mine compared to the other workplaces.

This study presents some limitations. Firstly, we have only performed ambient measurements of DPM. Although this study design is adequate for the comparison of several surrogates measured with different instruments, these concentrations may not be representative of the personal exposure of workers. Secondly, the influence of several determinants of exposure (i.e. ventilation systems, vehicles and fuel types) could not be estimated. Finally, we did not use a dynamic blank for the correction of the vapour phase OC, which may overestimate TC concentrations. Although the correction for the vapor phase OC by the dynamic blank was comparable to the field blank corrections in a previous study in an underground mine (36), the interference of vapour phase OC in the mass of TC is unknown for the two non-mining workplaces assessed in our study.

Despite these limitations, the findings derived from this study have important implications for future studies and recommendations for work exposure professionals and researchers:

- The Airtec provided results comparable to the NIOSH 5040 method for the estimation of EC_1 concentrations in the underground mine. However, the overestimation of EC values in non-mining workplaces indicates limitations for the use of this instrument in non-mining environments, and it should be further investigated.

- The results strongly support the idea that, due to interference related to non-diesel OC sources, EC is a more reliable surrogate than TC to estimate diesel exposure in non-mining workplaces.
- Direct-reading instruments are interesting devices for ranking exposures and making an initial and immediate estimation of the exposures. However, due to the presence of different non-carbonaceous particles which contribute to the mass concentration, the calibration of laser photometers against a reference method should be performed for each workplace, and the use of a standard calibration factor is not recommended.
- Particle counters with the capacity of measuring particles smaller than 20 nm are suggested. In addition, in the mining industry, instruments should be able to quantify concentrations higher than 500,000 particles/cm^3 for the accurate estimation of peak exposures.
- Ultrafine particles, which have a high capacity of deposition in the alveolar region of the lung, make up a major fraction of DPM emissions. Thus, future studies should focus on the relationship between particle number concentration and cardiorespiratory health outcomes in workers occupationally exposed to diesel engine exhaust. In addition, routine measurements of UFP in different workplaces are highly recommended, but they are challenged by the lack of OEL specific to particle number concentration, limited instruments suitable for occupational hygiene measurements and lack of sampling standards (17).

5.2.6 Conclusion

This study quantified and characterized DPM exposure in three different workplaces using an extensive strategy combining the assessment of PNC, size distribution, TEM analyses and the NIOSH 5040 method. It showed exposures mainly to agglomerated nanometric particles (<100 nm) composed by EC and OC, with higher concentrations for all indicators in the underground mine, followed by the subway tunnel and the truck workshop. Composition of the carbonaceous fraction varied according to the workplace. Due to the interference related to non-diesel OC, overestimation of TC may occur in non-mining workplaces and EC should be considered as a more reliable surrogate for exposure assessment. The dominance of particles <100 nm in all

workplaces, the high PNC measured and the good correlation with EC—the indicator classically used as a surrogate for DPM exposure—suggest that DPM-related UFP exposures should receive more attention in terms of occupational routine measurements and regulations.

5.2.7 Acknowledgements

The authors would like to thank Caroline Couture, Patrick Eddy Ryan, Ross Thuot and Simon Aubin for their expertise and assistance during this study. AF received a scholarship from the *Fonds de Recherche du Québec Nature et Technologies* (FRQNT).

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5.2.9 Conflicts of interest

The authors declare no conflict of interest related to the material presented in this article.

5.2.10 Contributions

ASF contributed to the study design, measurements in all workplaces, TEM analyses, data analysis and manuscript preparation. CC contributed to the measurements in all workplaces. GL and JPM contributed to the TEM analyses. BR contributed to the study design and implementation. MD contributed to the study design and preparation of the manuscript.

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5.2.12 Tables and Figures

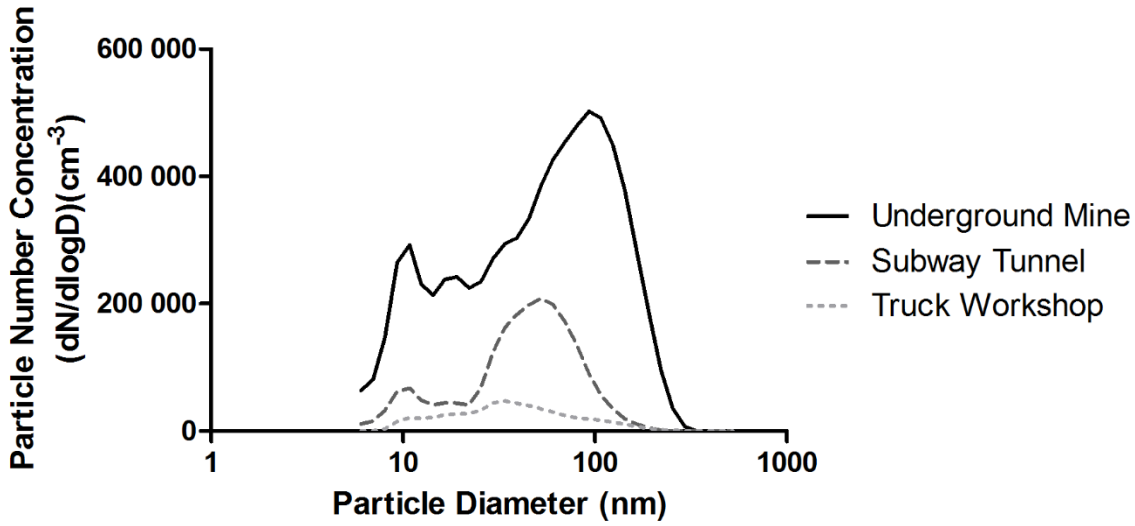


Figure 1: Size distribution of the ultrafine particles measured by the EEPS 3090 at each workplace.

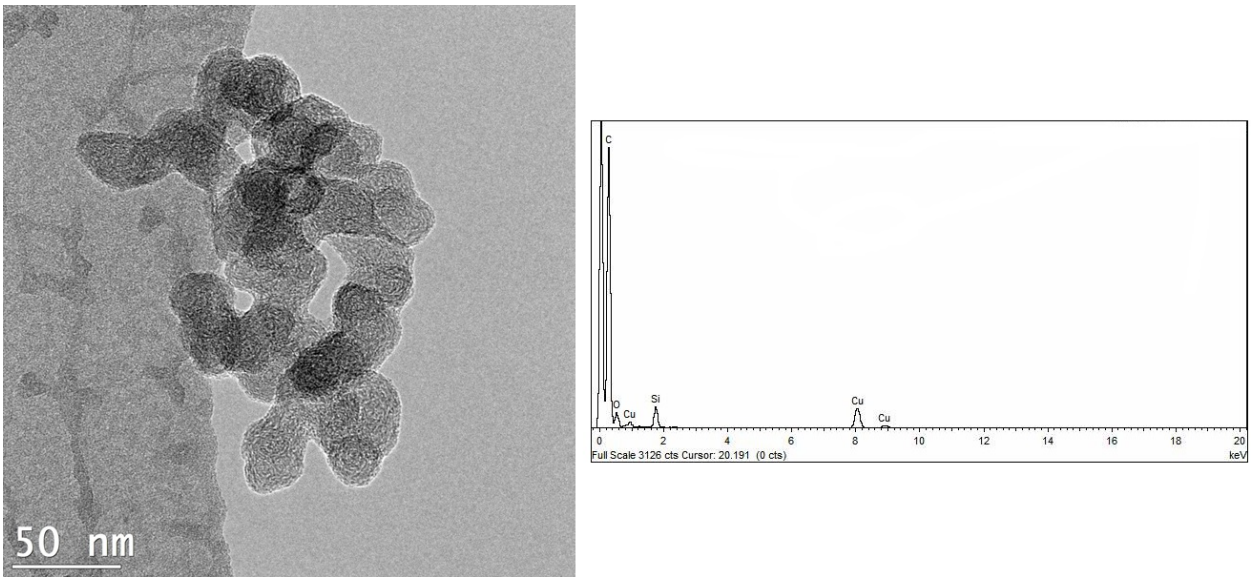


Figure 2: TEM bright field image and EDS spectrum of the diesel particles.

* Si and Cu signals are contributions from the film and grid.

Table 1: Direct-reading instruments used for ambient measurements in the workplaces.

Model	Type of Instrument	Parameters Measured (unit of concentration)	Particle Size (nm)[a]
Airtec (Flir)	Optical transmittance monitor	Submicron fraction of EC ($\mu g / m^3$)	<1000
P-Trak 8525 (TSI Inc.)	Condensation particle counter (CPC)	Particle number concentration (particles$/ cm^3$)	20 – 1000
Engine Exhaust Particle Sizer (EEPS) 3090 (TSI Inc.)	Fast-sizing spectrometer. Electrical mobility	Particle number concentration (particles$/cm^3$) in 32 channels	5.6 – 560
DustTrak DRX 8533 (TSI Inc.)	Laser photometer	Particle mass concentration ($\mu g/m^3$) for 5 size fractions (PM_1, $PM_{2.5}$, $PM_{RESPIRABLE}$, PM_{10} and PM_{TOTAL})	100 – 15,000
DustTrak 8520 (TSI Inc.)	Laser photometer	$PM_{RESPIRABLE}$; mass concentration ($\mu g/m^3$)	100 – 10,000

PM: Particulate matter; **EC**: Elemental carbon. [a] Particle size range of the instruments.

Table 2: Ambient concentrations (μg/m^3) of EC and TC, and TC/EC ratios in the three workplaces.

	Underground Mine			Subway Tunnel			Truck Workshop		
	N	**GM (GSD)**	**Min–Max**	**N**	**GM (GSD)**	**Min–Max**	**N**	**GM (GSD)**	**Min–Max**
TC_R	15	174 (1.9)	62–700	12	59.1 (2.3)	20 – 220	12	16 (3.5)	2.1–54
EC_R	15	125 (2.1)	37– 580	12	24.7 (2.4)	7.9–72	12	2.7 (2.4)	1.06–9.3
TC_1	16	162 (2.0)	51 – 600	12	36 (2.1)	16–110	12	9.9 (3.0)	2.1–39
EC_1	16	122 (2.2)	33 – 510	12	15.7 (2.2)	8.4–55	12	2 (2.0)	1.06–5.4
Airtec (EC_1)	16	141 (1.9)	44.2–503	12	25 (2.8)	2.7–120	12	4.1 (2.0)	1.7–10.6
Ratios									
	Underground Mine			**Subway Tunnel**			**Truck Workshop**		
TC_R/EC_R	1.4 ± 0.18			2.5 ± 0.9			8.7 ± 3.7[a]		
TC_1/EC_1	1.3 ± 0.15			2.4 ± 0.7			8.1 ± 2.2 [a]		

N: Number of measurements; **GM:** Geometric mean; **GSD:** Geometric standard deviation; **Min–Max:** Minimum and maximum daily values; **TC_R:** Respirable fraction of total carbon; **EC_R**: Respirable fraction of elemental carbon; **TC_1:** Submicron fraction of total carbon; **EC_1:** Submicron fraction of elemental carbon.

[a] All ratios for the truck workshop were calculated excluding the non-detected values.

Table 3: Ambient mass and number concentrations of aerosols measured by direct reading instruments.

Instrument	Indicator	Underground Mine			Subway Tunnel			Truck Workshop		
		N	GM (GSD)	Min–Max	N	GM (GSD)	Min–Max	N	GM (GSD)	Min–Max
DustTrak DRX	**PM_1 (µg/m³)**	14	442 (2.0)	195 – 1780	8[a]	62 (1.8)	26 – 127	12	21 (1.8)	9 – 48
	$PM_{2.5}$ (µg/m³)	14	486 (2.0)	203 – 1970	8	70 (1.8)	28 – 150	12	23 (1.7)	11 – 54
	$PM_{RESPIRABLE}$ (µg/m³)	14	521 (2.1)	210 – 2190	8	75 (1.8)	29 – 166	12	26 (1.7)	13 – 57
	PM_{10} (µg/m³)	14	599 (2.3)	219 – 3220	8	83 (1.9)	30 – 190	12	30 (1.7)	10 – 60
	PM_{TOTAL} (µg/m³)	14	628 (2.3)	219 – 3480	8	89 (1.9)	30 – 190	12	31 (1.8)	10 – 70
DustTrak 8520	**$PM_{RESPIRABLE}$ (µg/m³)**	14	487 (2.3)	182 – 2220	12	52 (1.9)	18.3 – 151	12	23 (1.7)	12 – 69
P–Trak 8525	**Particles/cm³**	14	134,000 (1.5)	51,200–229,000	10	32,800 (1.7)	12,900–58,600	12	22,700 (1.3)	14,700–33,800
EEPS 3090	**Particles/cm³**	1	378,000 (1.9)	86,700 – 2,650,000	1	83,000 (1.3)	51,800–216,000	1	29,400 (1.7)	11,400–184,000

Ratios

	Underground Mine	Subway Tunnel	Truck Workshop
TC_R/DustTrak 8520	0.41 ± 0.13	1.1 ± 0.33	1.4 ± 0.97[b]
EC_R/DustTrak 8520	0.30 ± 0.11	0.52 ± 0.22	0.20 ± 0.14[b]
EEPS 3090/P-Trak 8525[c]	1.96	1.24	1.24

N: Number of measurements; **GM:** Geometric mean; **GSD:** Geometric standard deviation; **Min–Max:** Minimum and maximum daily values; **TC_R:** Respirable fraction of total carbon; **EC_R**: Respirable fraction of elemental carbon.

[a] DustTrak DRX was not available for the first two days of measurement in the subway tunnel.

[b] Ratios for the truck workshop were calculated excluding the non–detected values of TC_R and EC_R.

[c] Ratios calculated from one day of simultaneous measurement.

Table 4: Pearson correlation coefficients between EC and the indicators measured by the direct reading instruments.

Instrument	Indicator	Underground mine		Subway Tunnel		Truck Workshop		All workplaces	
		N	r^a	N	*r*	N	*r*	N	*r*
Airtec	**EC_1 (µg/m³)**	16	0.98***	11	0.88***	11	0.98***	38	0.98***
DustTrak DRX[b, c]	**PM_R (µg/m³)**	14	0.87***	8	0.95***	12	0.82***	34	0.88***
DustTrak 8520[c]	**PM_R (µg/m³)**	15	0.86***	12	0.95***	11	0.83**	38	0.90***
P–Trak 8525	**10^3 particles/cm³**	15	0.57*	10	0.85**	12	0.91***	37	0.80**

N: Number of measurements; * P<0.05; **P<0.01; *** P<0.001

[a] Pearson correlation coefficient

[b] Only association with PM_R are presented due to the strong intercorrelation between the other size fractions of the DustTrak DRX.

[c] Mass concentrations measured by the DustTrak DRX and the DustTrak 8525 are corrected with a calibration factor calculated from TC values.

Table 5: Stereological parameters of DPM particles and agglomerates evaluated by TEM.

	Underground Mine		Subway Tunnel		Truck Workshop		All Workplaces	
	AM ± SD	**Min - Max**	**AM ± SD**	**Min - Max**	**AM ± SD**	**Min - Max**	**AM ± SD**	**Min - Max**
d_p (nm)[a]	23.8 ± 6.46	10 - 39.4	25.1 ± 8.47	10.6 - 54.3	25 ± 7.07	13.3 - 43.5	24.6 ± 8.2	10 - 56.5
L_A (nm)[b]	444 ± 287	149 - 1190	600 ± 424	177 - 1690	334 ± 159	142 - 597	487 ± 453	84.9 - 2300
W_A (nm)	247 ± 163	61.7 - 610	350 ± 287	87.2 - 1260	222 ± 118	89.2 - 427	290 ± 257	59.7 - 1260
L_A:W_A (nm)	346 ± 221	105 - 900	475 ± 348	132 - 1480	278 ± 137	116 - 484	388 ± 350	76.2 - 1700
L_A/W_A	1.95 ± 0.63	1.13 - 3.52	1.82 ± 0.48	1.28 - 3.04	1.56 ± 0.26	1.22 - 2.16	1.72 ± 0.45	1.08 - 3.04

d_p: Diameter of primary particles; **L_A**: Maximum projected length of the agglomerate; **W_A**: Maximum projected width of the agglomerate;

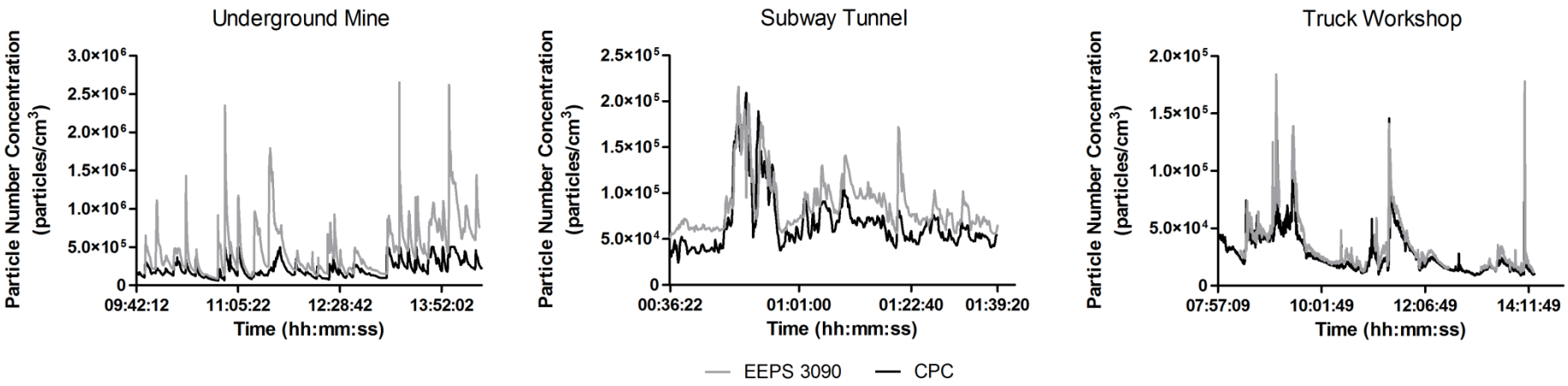
L_A:W_A: Average between L_A and W_A; **L_A/W_A:** Ratio between L_A and W_A; **AM ± SD:** Arithmetic mean and standard deviation; **Min- Max**: Minimum and maximum values; **nm:** Nanometers.

[a] 100 primary particles were evaluated per workplace.[b] 21 agglomerates were evaluated per workplace.

5.2.13 Supplementary Material

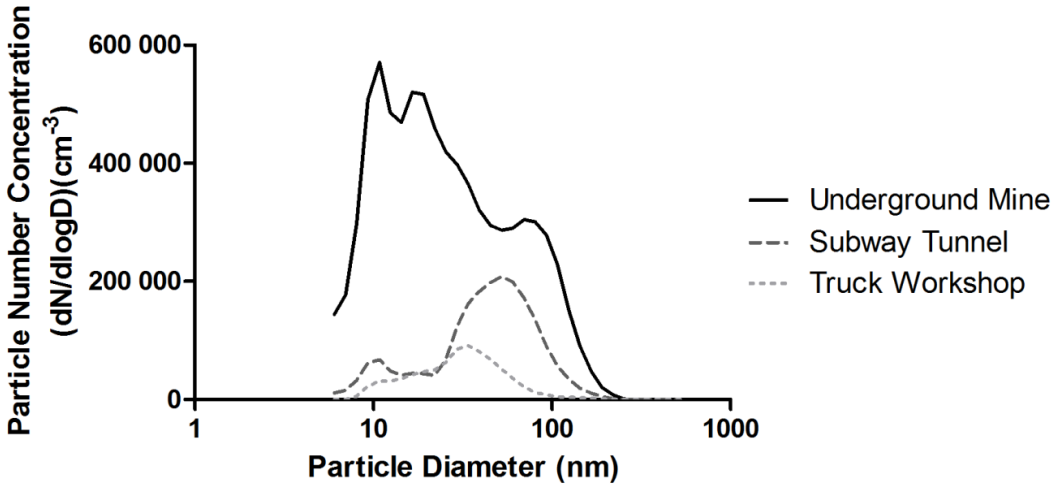
Supplementary Figure 1: Example of the assembly of the sampling devices in the suitcase.

FP: Fine particles; UFP: Ultrafine particles; EC: Elemental carbon; TC: Total carbon.

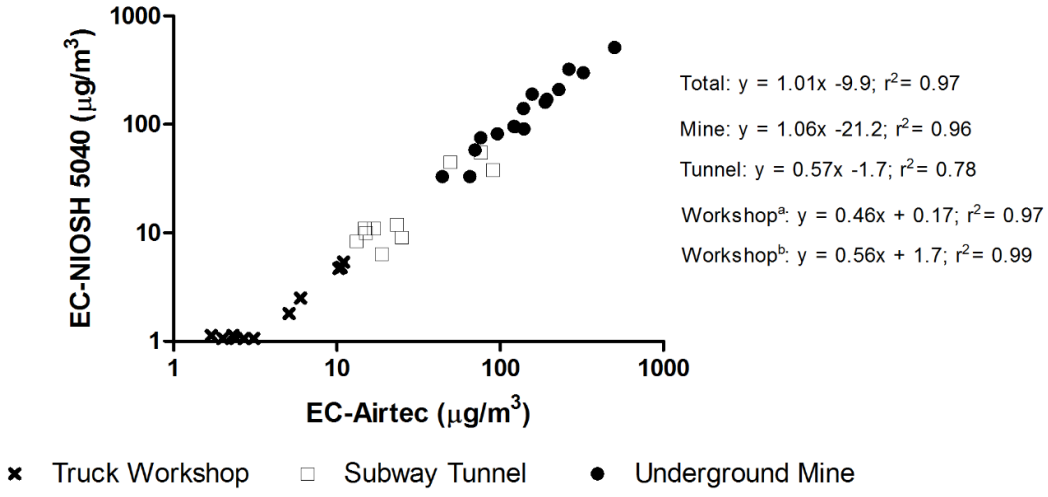


Supplementary Figure 2: Distribution profiles comparing the real-time measurements of the CPC and the EEPS 3090 in the three workplaces.

* Concentration range varied per workplace. The scale in y-axis was not fixed in order to optimize the visualization of the distribution profiles in each workplace.



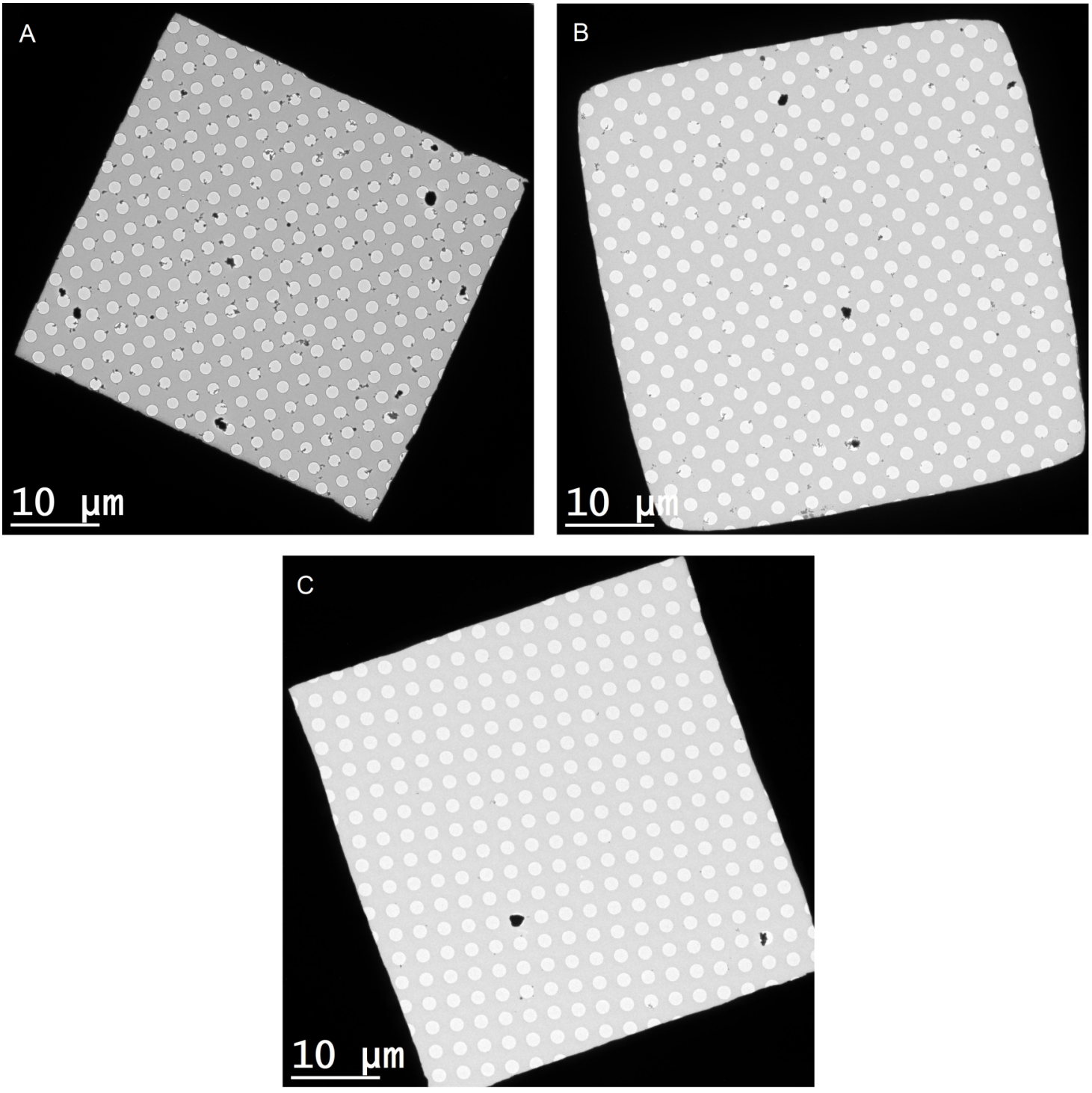
Supplementary Figure 3: Size distribution of the ultrafine particles measured by the EEPS 3090 at each workplace during individual emission peaks.



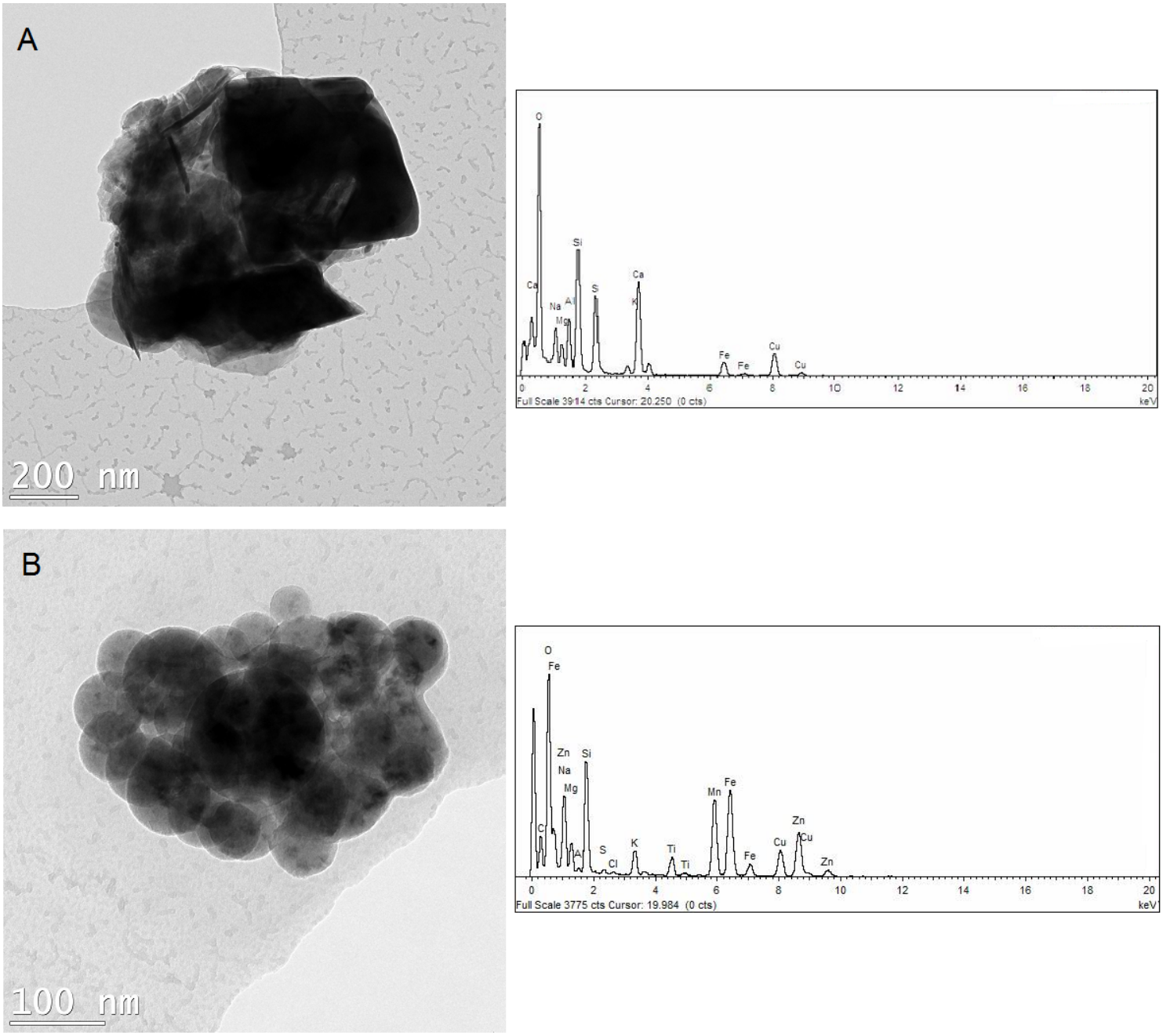
Supplementary Figure 4: Linear regression of EC concentrations measured by the Airtec and the NIOSH 5040 method in each workplace.

[a] With NIOSH 5040 non-detected values

[b] Without NIOSH 5040 non-detected values



Supplementary Figure 5: TEM bright field images showing a general overview of particles deposited on the TEM grids (magnification of 400X) in the underground mine (A), subway tunnel (B), and truck repair workshop (C).



Supplementary Figure 6: TEM bright field images and EDS spectra of non-diesel particles collected in the underground mine.

Chapter 6 - Assessment of the Oxidative Potential and Oxidative Burden from Occupational Exposures to Particulate Matter

Occupational exposures to particles are usually assessed by estimating the mass concentration. This approach, however, gives very limited information regarding the toxic potential of particles from different compositions. For instance, particles with elevated potential of generating reactive oxygen species can, even at low levels of exposure, represent a higher risk compared to particles at higher concentrations but with lower toxicity. This limitation can be addressed by the measurements of oxidative potential and oxidative burden, which integrates the assessment of the hazard and exposure to particles in a single metric. Thus, this data chapter addressed the second specific objective of this thesis that is to estimate the oxidative potential and oxidative burden of particles in two occupational settings from a construction trades school.

The measurements of oxidative potential and oxidative burden are still an underexplored application in the occupational field. The use of these assays in industrial settings is an important opportunity to improve the identification of occupational exposure situations to particles that may lead to a cascade of inflammatory processes and oxidative stress. Overall, the assessment of the oxidative potential and oxidative burden from occupational exposures to particles could lead to a better prevention of occupational diseases.

Assessment of the Oxidative Potential and Oxidative Burden from Occupational Exposures to Particulate Matter*

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* This article was accepted for publication with minor revisions

6.1 Abstract

Oxidative potential (OP) is a toxicologically relevant metric that integrates features like mass concentration and chemical composition of particulate matter (PM). Although it has been extensively explored as a metric for the characterization of environmental particles, this is still an underexplored application in the occupational field. This study aimed to estimate the OP of particles in two occupational settings from a construction trades school. This characterization also includes the comparison between activities, sampling strategies and size fractions.

Particulate mass concentrations ($PM_{4\text{-Personal}}$, $PM_{4\text{-Area}}$ and $PM_{2.5\text{-Area}}$) and number concentrations were measured during three weeks of welding and construction/bricklaying activities. The OP was assessed by the ascorbate assay (OP^{AA}) using a synthetic respiratory tract lining fluid (RTLF), while the oxidative burden (OB^{AA}) was determined by multiplying the OP^{AA} values with PM concentrations.

Median (25^{th}-75^{th} percentiles) of PM mass and number concentrations were 900 (672 – 1,730) $\mu g.m^{-3}$ and 128,000 (78,000 –169,000) $particles.cm^{-3}$ for welding, and 432 (345 – 530) $\mu g.m^{-3}$ and 2,800 (1,700 – 4,400) $particles.cm^{-3}$ for construction. Welding particles, especially from the first week of activities, were also associated with higher redox activity (OP^{AA}: 3.3 (2.3 – 4.6) $pmol.min^{-1}.\mu g^{-1}$; OB^{AA}: 1,750 (893 – 4,560) $pmol.min^{-1}.m^{-3}$) compared to the construction site (OP^{AA}: 1.4 (1.0 – 1.8) $pmol.min^{-1}.\mu g^{-1}$; OB^{AA}: 486 (341 – 695) $pmol.min^{-1}.m^{-3}$). The OP^{AA} was independent of the sampling strategy or size fraction. However, driven by the higher PM concentrations, the OB^{AA} from personal samples was higher compared to area samples in the welding shop, suggesting an influence of the sampling strategy on PM concentrations and OB^{AA}.

These results demonstrate that important levels of OP^{AA} can be found in occupational settings, especially during welding activities. Furthermore, the OB^{AA} found in both workplaces largely exceeded the levels found in environmental studies. Therefore, measures of OP and OB could be further explored as metrics for exposure assessment to occupational PM, as well as for associations with cardiorespiratory outcomes in future occupational epidemiological studies.

Keywords: oxidative potential, oxidative burden, particulate matter, occupational exposures, welding, construction.

6.2 Introduction

Short-term (i.e. daily and weekly) and long-term occupational and environmental exposures to particulate matter (PM) have been associated with cardiorespiratory health effects (1-5). Usually, the exposure assessment is performed by measuring the mass concentration of particles from different size fractions or by assessing the concentration of individual components. Although this approach has been historically important to link exposures to PM mass or individual elements with health outcomes, it does not provide an integrative measurement of multiple components or information regarding the synergistic interactions between chemical species (6, 7).

Oxidative stress is an important mechanism of PM toxicity (8-10). It occurs when the concentration of reactive oxygen species (ROS) - generated from the action of surface components of PM, such as metals and organic species - exceeds the body's antioxidant capacity, which can lead to a cascade of inflammatory processes and damage to the cell's DNA, proteins and lipids (6). In addition, the speed of ROS formation has also been correlated with oxidative damage in humans (11). The assessment of the oxidative potential (OP) of particles has been established as a promising exposure metric due to the integration of different biologically relevant proprieties such as size fraction, mass concentration and chemical composition. Thus, it could generate more relevant information than PM mass or individual components alone (7, 12). In this context, the oxidative potential (OP), measured in units of $pmol.min^{-1}.\mu g^{-1}$, reflects the per mass ability of particles to deplete antioxidants in a synthetic respiratory tract lining fluid (RTLF), while the oxidative burden (OB), measured in units of $pmol.min^{-1}.m^{-3}$, refers to the product of OP with the mass concentration of PM, therefore representing a marker for exposure levels (13).

Common acellular assays - each one sensitive to different metals and organic compounds - include the electron spin resonance (OP^{ESR}), dithiothreitol assay (OP^{DTT}), glutathione assay (OP^{GSH}) and ascorbate assay (OP^{AA}) (6, 14-16). In this context, OP measurements are dependent on factors like the pH, volatility, photochemical aging, and source composition (6). The OP^{AA}, which measures the depletion of the antioxidant ascorbate in RTLF exposed to PM, has been

shown to be sensitive to the presence of metals such as copper, iron, manganese, lead and zinc (12, 17-20). Therefore, the OP^{AA} could be a suitable method for the assessment of the oxidative potential of particles from occupational settings with high emissions of metals, such as in welding facilities and other construction sites.

Many environmental studies have characterized the oxidative potential of particles from urban sources like vehicular emissions, biomass burning and road dust (7, 12, 21, 22), as well as explored the association with cardiorespiratory health effects (13, 23-27). However, the oxidative potential and oxidative burden of particulate matter from different occupational activities have rarely been described (28, 29). This is, however, a topic of interest considering that many workplaces are associated with emissions of high levels of metals (e.g., welding) that are known to contribute to the generation of ROS and, therefore, may result in a high oxidative potential. In addition, the elevated mass concentration of particles in some workplaces, which are much higher than a typical urban background, may also contribute to important levels of oxidative burden. Furthermore, the use of these assays in industrial settings would expand the exposure information that is currently given by mass concentration alone and, therefore, be an important tool for exposure assessment to be integrated into the industrial hygiene and industrial toxicology practice.

6.3 Methods

This project was approved by the Ethics Committee for Clinical Research of the University of Montreal (project number CERC-19-050-P). An Informed Consent Form was signed by all workers who participated in this study.

Description of the workplaces

A welding shop and a construction site - both located in a Construction Trades School in Montreal, Canada - were selected for this study and were investigated for three weeks each.

Table 1 describes the activities and materials used during the sampling campaigns for each workplace. The techniques performed by the welder apprentices during the sampling campaign were Shielded metal arc welding (SMAW), Flux-cored arc welding (FCAW), Gas metal arc welding

(GMAW) and Gas Tungsten Arc Welding (GTAW). Most of the techniques used mild steel as base metal and filler material, with the exception of GTAW of Welding Week 3 that was performed with aluminum pieces. Tasks were performed inside individual welding booths equipped with a local exhaust ventilation system (i.e. movable hoods) and the shops also had a general ventilation system. Additional activities in this workplace also included oxy-fuel cutting and machining (i.e. grinding) of the metal pieces, which were equally performed by all apprentices.

The tasks performed during the construction activities included corner assembly (Construction Week 1), stone cutting and laying (Construction Week 2), and laying to a line (Construction Week 3). Bricks, stones and concrete blocks were used as materials. The bricklayer apprentices worked in a room equipped with a general ventilation system and three fans installed in the upper portion of the walls. There were no physical barriers between the apprentices.

Elemental characterization was performed by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) in one sample per activity to have a general overview of the composition of the particles in the workplaces. In addition, concentrations of crystalline silica (quartz) in the construction site were determined by X-ray diffraction (XRD). These analyses were performed at the *Institut de recherche Robert-Sauvé en santé et en sécurité du travail* (IRSST).

Field sampling

13 apprentices participated in the welding weeks and 15 in the construction weeks; each participated for 2 to 5 days. Only 5 out of the 13 apprentices used respiratory protection during welding activities and none during the construction/bricklaying activities. The sampling strategy included filter measurements of PM_4 and $PM_{2.5}$ (PM with median aerodynamic diameter of 4 µm (i.e. respirable fraction) and 2.5 µm, respectively). Personal PM_4 samples ($N_{welding}$ = 53; $N_{construction}$ = 54) were collected from the breathing zone (i.e. the zone within a 30 cm radius of a worker's nose and mouth), while area samples of both PM_4 ($N_{welding}$ = 54; $N_{construction}$ = 33) and $PM_{2.5}$ fractions ($N_{welding}$ = 53; $N_{construction}$ = 34) were collected at distances of around 1.5 meter from the apprentices. In the welding shop, the area samplers were installed inside each individual welding booth, while in the construction site, each area sampler represented measurements for 1 to 3

apprentices working in proximity. The median duration of activities in both workplaces was 6.5 hours with a range between 2 hours and 9 hours.

Samples were collected with 37 mm cassettes equipped with pre-weighed Polytetrafluoroethylene (i.e. PTFE or Teflon) filters (Mitex Membrane Filter with 5.0 µm and support pads, Sigma-Aldrich; St. Louis, MO/USA). The $PM_{2.5}$ fraction was selected using a cyclone at a flowrate of 1.5 L/min (BGI; Butler, NJ/USA), while the PM_4 fraction was selected using a Dorr-Oliver nylon cyclone at a flowrate of 1.7 L/min. Flow rates of the GilAir-5 pumps (Sensidyne; St. Petersburg, FL/USA) were measured before and after the work shifts using a mass flow meter (TSI Inc.; Shoreview, MN/USA). A difference of 5% in the flow rate was considered acceptable (30). Field blanks were collected for each day of sampling. Samples were stored at −18 °C until extraction.

Real-time particle number concentrations were measured by condensation particulate counters (CPC) (P-Trak 8525, TSI Inc.; Shoreview, MN/USA) positioned next to the area samplers. This instrument measures the number concentration of particles between 20 nm and 1,000 nm to a maximum of 500,000 particles/cm^3. In addition, the background concentration was measured once at the study location before the start of the activities. The background level of particulate number concentration was measured with a CPC, while the background mass concentrations were measured with a Dust-Trak equipped with a $PM_{2.5}$ impactor (TSI Inc.; Shoreview, MN/USA).

Oxidative Potential Analyses

Extraction

All glassware was decontaminated with nitric acid 10% overnight and washed using milli-Q water. Filters were placed in Falcon tubes, immersed in 10mL of Optima grade methanol (Thermo Fisher Scientific; Waltham, MA/USA), vortexed for 2 minutes and sonicated for 60 minutes. The extracts were then dried for 4h under a constant flow of nitrogen. Dry extracts were stored at −18 °C until OP^{AA} analyses. Filters were weighed in triplicate before and after extraction using a microbalance (Model XPR2U, Mettler Toledo; Columbus, OH/USA) at stable ambient conditions (Temperature = 21 ± 1 °C, Relative Humidity = 33 ± 3%).

Sample concentrations

OP^{AA} and OB^{AA} were measured in samples of re-suspended particles. Preliminary tests for the determination of the sample concentrations of particles for resuspension were performed and the results are described in the supplementary materials. Briefly, 10 PM_4 samples from welding fumes were collected in parallel. The first half of these samples were extracted in methanol, re-suspended in ultrapure water containing 5% HPLC methanol ($MeOH/H_2O$ 5%) to concentrations of 50 µg/mL and 25 µg/mL and measured for OP^{AA} (see below a detailed description of the method). The second half of the samples were sent to the Department of Chemical Engineering & Applied Chemistry of the University of Toronto for validation of the protocol at the same concentrations. Results of these tests showed that sample concentration generally had negligible effect on the depletion rate (Supplementary Figure 1). Thus, the concentration of 25 µg/mL was chosen for the analyses in this study. Further analyses at concentrations of 10 µg/mL and 5 µg/mL confirmed this same pattern of degradation.

OP^{AA} and OB^{AA}

Extracted samples were re-suspended in Chelex-resin treated $MeOH/H_2O$ 5% to concentrations of 25 µg/mL, separated in triplicates and incubated in a microplate spectrophotometer (Model Epoch 2, BioTek; Winooski, VT/USA) for 10 minutes at 37°C alongside positive controls (1.0 µM $Cu(NO_3)_2$) and experimental blanks ($MeOH/H_2O$ 5%). After adding a synthetic human respiratory tract lining fluid (RTLF) containing 200 µM of physiologically relevant antioxidants including ascorbate, urate, and glutathione adjusted to pH 7.4 (17), the absorption at 265 nm was measured every 2 min for 4 h.

The OP^{AA} was calculated from the linear section of the curve by plotting absorbance against time and normalizing by PM mass based on the quantity used in each assay (i.e. $pmol.min^{-1}.\mu g^{-1}$). These values were corrected relative to the particle-free field blanks. Values were also converted to units of OB^{AA} (i.e. $pmol.min^{-1}.m^{-3}$) by multiplying the OP^{AA} values with the PM mass concentration of each filter.

Statistical Analyses

The descriptive statistics for the mass and number concentrations, OP^{AA} and OB^{AA} were expressed in terms of mean and standard deviation, median and percentiles (i.e. 25^{th} and 75^{th} percentiles), and ranges (i.e. minimum and maximum values). Results are presented separately according to the workplace, weeks of activities, size fraction and sampling strategies. The distribution of the samples was asymmetrical. For this reason, the Mann-Whitney test and the Kruskal-Wallis followed by Dunn's *posthoc* test were used to compare levels between workplaces and weeks of activities, respectively; while the Wilcoxon signed-rank test was used to compare paired samples according to the sampling strategy (i.e. personal versus area sampling) and size fraction (i.e. PM_4 versus $PM_{2.5}$). For these later analyses, each area sample was paired with only one personal sample. A P-value less than 0.05 was considered to be as statistically significant for all cases.

6.4 Results

Concentration of Particles

Table 2 presents the descriptive statistics of the mass and number concentration of the particles collected during welding and construction activities. The highest concentrations of $PM_{2.5}$ and PM_4 were measured in the welding shop. The first week of welding activities showed the highest levels of particulate matter compared to the other weeks, with median (25^{th} and 75^{th} percentiles) of personal PM_4 of 1,790 (1,490 – 2,680) $\mu g.m^{-3}$ and the maximum concentration of 5,160 $\mu g.m^{-3}$ in a work-shift. In the construction site, the largest levels of particles were found in the second week - sourced by the stone cutting activity – with median of PM_4 concentration of 442 $\mu g.m^{-3}$ (25^{th} and 75^{th} percentiles: 394 – 490). This difference in concentrations across weeks, however, was less expressive in this workplace compared to the welding shop.

When comparing sampling strategies ($PM_{4\text{-Personal}}$ versus $PM_{4\text{-Area}}$), results showed a statistically significant difference in the levels of particles collected from personal samplers in the welding shop (median: 900 (25^{th}: 672 – 75^{th}: 1,730) $\mu g.m^{-3}$) compared to area samplers (median: 517 (25^{th}: 295 – 75^{th}:1,085) $\mu g.m^{-3}$) (Mean Difference (95% CI) = 697 (404 to 990)). In the construction site, a difference between personal samples (median: 432 (25^{th}: 345 – 75^{th}: 530) $\mu g.m^{-3}$) and area samples was also observed (Mean Difference (95% CI) = 66.1 (16.4 to 115.7)).

Table 2 also shows PM levels for the two size fractions collected in parallel ($PM_{4\text{-}Area}$ versus $PM_{2.5\text{-}Area}$). Higher levels of $PM_{4\text{-}Area}$ compared to $PM_{2.5\text{-}Area}$ were found in the welding school (Mean Difference (95% CI) = 68.5 (36.9 to 100.2)). A similar trend was found in the construction site, where $PM_{4\text{-}Area}$ levels were significantly higher compared to $PM_{2.5\text{-}Area}$ (Mean Difference (95% CI) = 93.3 (61.8 to 124.9)), suggesting the presence of particles in the $PM_{4\text{-}2.5}$ fraction in both workplaces.

The median of the particulate number concentration was 116,000 particles.cm^{-3} in the welding shop, with a maximum daily concentration of 248,000 particles.cm^{-3} (Table 2). These levels are up to 140x higher than the background of 1,760 particles.cm^{-3}, which showed an important presence of ultrafine particles in this workplace. In the construction site, however, the median number concentration of 2,800 particles.cm^{-3} was close to background levels, indicating that most of the particles emitted in this workplace were in the micrometric size range.

Composition of the Particles

Results of ICP-MS analyses from particles collected during the welding activities are presented in the Supplementary Table 1. Up to 40.6% of the mass of the particles collected during welding was composed of Fe. Other detected elements included Mn (up to 6.1%), Cu (up to 1.9%), Zn (0.4%), Pb (up to 0.4%) and Co (0.01%).

Supplementary Table 1 also shows that particles collected in the construction site were mainly composed of Mg, (22.3% of the mass) and traces of Cu (0.4%). In addition, crystalline silica (quartz) contributed to 3.1% of the average concentration of the particles in this workplace (Supplementary Table 2).

Oxidative Potential and Oxidative Burden of Workplace Particles

Comparison Between Workplaces and Activities

Results of OP^{AA} and OB^{AA} of the particles are summarized below, while the detailed descriptive results including averages, medians and ranges according to the workplace, week of activity, size fraction and sampling strategy can be found in the Supplementary Table 3. In total, 155 samples were analysed for OP^{AA} from welding while 101 samples were analysed from the construction activities. Only seven filter were not valid for analyses due to problems in the

extraction (N = 5) and insufficient mass of particles collected (n = 2). Figure 1A presents the OP^{AA} of the particles corrected for the blanks. OP^{AA} of the welding samples was statistically higher compared to the construction samples: Welding = median: 3.3 (25^{th}: 2.3 - 75^{th}: 4.6) pmol.min^{-1}.μg^{-1}; Construction = median: 1.4 (25^{th}: 1.0 - 75^{th}: 1.8) pmol.min^{-1}.μg^{-1}). Fig 1B gives the results of the oxidative burden of these particles, which represents the exposure levels of the workers, and it is calculated by multiplying the values of OP^{AA} by the corresponding concentration of particles. While the PM exposure of the welders was on average roughly double that of the bricklayers, once combined with the difference in the OP^{AA}, this yielded a factor of 3.6 difference in OB^{AA} (Welding = median: 1,750 (25^{th}: 893 - 75^{th}: 4,560) pmol.min^{-1}.m^{-3}; Construction = median: 486 (25^{th}: 341 - 75^{th}: 695) pmol.min^{-1}.m^{-3}).

When comparing OP^{AA} between the different weeks of activities, particles from the first week of welding showed a more intense redox activity compared to Welding Week 2 and Welding Week 3. No difference, however, was found between the OP^{AA} of the three weeks of construction activities (Figure 2A). As observed in Figure 2B, Welding Week 1 presented the highest OB^{AA} compared to the other welding activities, driven by the elevated mass concentration of particles during the SMAW and FCAW activities. Similar results were observed for Construction Week 2 compared to Construction Weeks 1 and 3, sourced by the higher PM concentrations from stone cutting activities.

Comparison Between Size Fractions and Sampling Strategies

Figure 3 presents OP^{AA} and OB^{AA} results according to the size fraction ($PM_{4\text{-}Area}$ versus $PM_{2.5\text{-}Area}$). There was no observed difference in the OP^{AA} of particles from different size fractions in the welding shop or in the construction site (Mean Difference (95% CI) = -0.15 (-0.5 to 0.2)). Similarly, the size fraction also had no effect on the OB^{AA} of particles from welding (Mean Difference (95% CI) = 259 (-267 to 785)) or from construction (Mean Difference (95% CI) = 47.5 (-82.5 to 177.5)).

Figures 4A shows that the sampling strategy ($PM_{4\text{-}Personal}$ versus $PM_{4\text{-}Area}$) also had no influence on the OP^{AA} of the particles in the welding shop (Mean Difference (95% CI) = 0.19 (-0.3 to 0.7)) or in the construction site (Mean Difference (95% CI) = -0.16 (-0.37 to 0.03)). However,

Figure 4B shows that welding particles collected by the personal samplers had higher levels of OB^{AA} compared to particles collected by area samplers (median: 2,970 (25^{th}: 1,370 - 75^{th}: 6,730) versus 1,500 (25^{th}: 685 – 75^{th}: 3,870) pmol.min^{-1}.m^{-3}; Mean Difference (95% CI) = 2,763 (1,348 to 4,178)). In the construction site, there was no influence of the sampling strategy on OB^{AA} levels.

6.5 Discussion

The present study evaluated the OP^{AA} and OB^{AA} of PM emitted from different occupational contexts. Important levels of OP^{AA} and OB^{AA} were observed, especially in the welding shop where particulate numbers and mass concentrations also exceeded those from the construction site. Analyses also included the comparison of oxidative potential between weeks of activities, size fractions and sampling strategies. To date, very few studies have described the oxidative potential of particles emitted in an occupational context. For instance, Graczyk et al. (2015) reported the ROS production potential of PM_4 particles collected from the breathing zone of apprentice welders using the DCFH assay (28), while Sauvain et al. (2016) reported OP^{DTT} levels from the respirable particles emitted from tunnels mechanical yards (29). However, the quantitative comparison between these occupational studies remains a challenge because of the differences between the several measurement assays reported in the literature about this subject.

Despite these challenges, our results can be compared with environmental studies that measured the oxidative potential of PM using similar techniques (i.e. acellular OP^{AA} assay in synthetic RTLF). As comparable examples, two studies reported the OP^{AA} and OB^{AA} from $PM_{2.5}$ collected within the city of Toronto, Canada. Jeong et al. (2020) reported levels of OP^{AA} ranging from 0.3 to 2.1 pmol.min^{-1}.µg^{-1} (average of 1.0 pmol.min^{-1}.µg^{-1}) and OB^{AA} of 6.4 ± 3.6 pmol.min^{-1}.m^{-3}, while Weichenthal et al. (2019) found an OP^{AA} ranging from 2.2 to 5.8 pmol.min^{-1}.µg^{-1} and OB^{AA} of 16.8 pmol.min^{-1}.m^{-3} (31, 32). Furthermore, values ranging between 0.2 and 3.3 pmol.min^{-1}.µg^{-1} were reported in London, UK (33). These OP^{AA} values are within the same range reported in our study for the construction activities. Interestingly, levels of OB^{AA} from both workplaces – driven by the higher PM concentrations, especially in the welding shop – considerably exceeded those from environmental studies. Having in mind the median

concentrations of 900 $\mu g.m^{-3}$ (25^{th} - 75^{th} percentiles: 672 - 1,730) of PM_4 in the welding shop, these levels are within the limit of 3 $mg.m^{-3}$ recommended by the ACGIH for respirable particles not otherwise specified (PNOS), and are also comparable to the ones reported by Graczyk et al. (2015) where the authors measured median concentration of 716 $\mu g.m^{-3}$ (25^{th} - 75^{th} percentiles: 300 - 1,300) of respirable particles at the breathing zone of apprentice welders exposed to GTAW fumes (28). It is important to notice, however, that average mass concentrations up to 10 times these are reported in the literature, indicating that the levels of fine particle - and consequently OB^{AA} – found in our study may not be considered the worst-case scenario (34, 35).

The highest levels of mass concentration, number concentration, OP^{AA} and OB^{AA} were observed during the first week of welding activities, when the apprentices performed FCAW and SMAW tasks. It has been suggested that FCAW have the capacity to generate higher concentrations of metallic particles compared to other processes (34-38). Although FCAW was also present in the second week of activities, the tasks in this period were performed in a different room with fewer apprentices working simultaneously (23 ± 2 apprentices/day in Week 1 versus 11 ± 2 apprentices/day in Week 2), which may explain the lower mass concentrations and OB^{AA} from Welding Week 2 compared to the other weeks. Furthermore, the skill of the welders may also be considered a determinant of exposure. Although the information about the apprentices' experience was not collected in our study, it has been suggested that ROS production potential is significantly higher for less experienced welders due to the burn of the metal during the welding task (28).

We have found no difference in OP^{AA} when comparing $PM_{2.5}$ and PM_4 size fractions in both workplaces, suggesting that choosing between $PM_{2.5}$ or PM_4 size fractions should not affect the oxidative potential of particles from workplaces comparable to the ones evaluated in our study. This result is in line with Sauvain et al. (2016) where the authors reported that 97% of the oxidative potential of PM_4 was already present in the $PM_{2.5}$ fraction (29). However, this lack of size dependency observed may just be a consequence of the narrow size fraction range measured. In this regard, Chang et al. (2013) evaluated the size dependency of welding particles in relation to ROS production and found higher ROS activity in the ultrafine ($PM_{0.1}$) and fine ($PM_{0.1-2.5}$) ranges compared to coarse particles ($PM_{2.5-10}$), suggesting the highest potential of ROS

generation present in the smaller size fractions for this workplace (39). Although we did not directly measure the size distribution of the welding particles, this information can be retrieved from Debia et al. (2014), where the authors reported the size distribution of particles during welding activities in the same school as the one investigated in our study. Using an Electrical Low-Pressure Impactor (ELPI), the authors found that the main modes of the number-based size distributions during the whole welding period were 30 nm for GMAW, FCAW, and SMAW and 98 nm for GTAW. When restricting the analysis during welding activities only, the main modes of the number-based size distributions were 214 nm, 98 nm, 50 nm, and 50 nm for GMAW, GTAW, FCAW, and SMAW, respectively. Therefore, knowing that an important portion of welding particles are found in the ultrafine size range (40), and considering the narrow size fraction range evaluated in our study (i.e. PM_4 and $PM_{2.5}$), the extrapolation of these results should be treated with caution.

Other studies also investigated the size distribution of welding particles during different activities and conditions. For instance, Hewett showed that the estimated main mode of the mass distribution was between 0.25 μm and 0.59 μm for GMAW and SMAW (41), while Cena et al. (2014) demonstrated that the mass of metals such as total Cr, Mn, Ni and Cr(VI) emitted in mild and stainless steel welding consisted of particles between 0.04 μm and 0.6 μm. In addition, particle size distribution of welding fumes has shown to be depend on welding parameters such as the arc resistance, the wire feed rate, the electrode sectional area and the shielding gas temperature (42-44).

In addition to the size fraction, the sampling strategy (i.e. personal versus area) also had no influence in the values of OP^{AA}. For the construction activities, this may be explained by the fact that tasks were performed in fixed working stations and with the same material for all workers within the same week. For the welding shop - although grinding and oxy-cutting tasks were also performed - these tasks were executed in the same metal pieces as the welding activities. Nonetheless, we found greater levels of OB^{AA} from personal samples – driven by the higher mass concentration - compared to area samples in the welding shop. This may be explained by two factors. First, particles from grinding and oxy-cutting tasks - which were performed outside the welding booths - could have been captured at a higher proportion by the

personal samplers and contributed to the highest mass concentration compared to the area samplers installed inside the welding booths. In addition, another explanation for the highest levels of personal OB^{AA} may be related to the fact that the mass concentration of particles tends to significantly decrease as the distance from the welding source increases (45). This could be caused by the dispersion of particles when the distance from the source increases.

This study also presented some limitations. First, we were unable to determine the elemental composition of all individual samples, which precluded us to correlate the OP^{AA} with individual chemical species. Nonetheless, a general characterization of the metals from a few samples was performed at each workplace for orientation purpose. This descriptive characterization from the welding shop showed that the most prevalent metals were Fe, Mn and Cu, with Zn, Pb and Co also present. In this context, Godri et al. (2010) showed positive correlation between total Fe and Pb with OP^{AA}, while Visentin et al. (2016) also demonstrated associations between Cu and Mn with the depletion of ascorbate (18, 19). Thus, the presence of high quantities of Fe, Cu and Mn in the welding shop may explain the highest levels of OP^{AA} in this workplace compared to the construction site. In addition to an in-depth elemental characterization, future studies would also benefit from the evaluation of additional acellular tests, especially when comparing different settings or with multiple sources of exposure. For instance, the OP^{GSH} assay - also demonstrated to be reactive to metals such as Fe, Pb and Al (6) - could complement the information given by the OP^{AA} assay. The link with metals was also demonstrated for the OP^{ESR} assay, as well as its association with *in vitro* and *in vivo* toxicological endpoints (16, 27). Furthermore, since the OP^{DTT} assay is also sensitive to organic components like quinones, PAHs and organic carbon (6), it could be explored as a measure for occupational exposures to diesel particulate matter - such as in underground mines and tunnels - and biomass burning, such as in forest fires.

In addition to the comparison between different OP assays, future studies could also explore the use of OB for the risk assessment of occupational exposures to particles. One of the key characteristics of this technique is the integration of measures of hazard (i.e. OP) and exposure (i.e. PM mass concentration). Thus, of particular interest would be the use of OB for the risk assessment in different occupational exposure situations. For instance, this technique

could be used to group and compare exposures according to the composition, such as processes with high metal content, like welding and smelting, and from emissions with carbon-rich particles like diesel. In addition, as previously mentioned, although measures of OP and OB have been explored for associations with adverse health effects in environmental studies, these relationships have not been yet extensively described in the context of occupational exposures. Therefore, the measurement of the OP and OB in different occupational exposure contexts, allied with the exploration of complementary OP assays and an in-depth elemental characterization of particles, could be used in future occupational epidemiological studies exploring associations with cardiorespiratory outcomes.

Finally, our study investigated the oxidative potential of particles using a per-mass based assay. However, several studies have shown that the surface area of metal nanoparticles (i.e. ZnO and TiO_2) and ultrafine particles are also associated with increased ROS production, oxidative stress and inflammation (46-49). Ultrafine particles, such as the ones emitted during welding activities, have a high cumulative particle surface per unit mass compared with larger particles which, in turn, results in larger reactivity. Thus, the association between surface area and oxidative potential assays could also be explored in future occupational studies.

6.6 Conclusion

The oxidative potential and oxidative burden of particulate matter was quantitatively determined for two occupational settings. Higher levels of OP^{AA} were observed for the welding shop compared to the construction site, which supports the argument that PM mass alone may not be enough to reflect exposure. This redox activity was independent of sampling strategy or size fraction evaluated. In addition, the elevated mass concentration of particles, especially for personal samples of welding fumes, resulted in levels of oxidative burden that largely exceeded the levels found in environmental studies measured with comparable methodologies. Therefore, given the characteristics of these techniques in integrating features of mass concentration and particle's composition, acellular assays of oxidative potential could be further explored as metrics for the exposure assessment of particulate matter in the workplace, as well as for associations with cardiorespiratory health effects in future occupational epidemiological studies.

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6.9 Conflicts of Interests

The authors declare that they have no competing interests.

6.10 Contributions

ASF contributed to the study design, measurements in the workplaces, OP analysis, data analysis and manuscript preparation. PER, AT and GE contributed to the OP analysis. CC contributed to the measurements in the workplaces. AS, MD and ES contributed to the study design and manuscript preparation.

6.11 References

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6.12 Tables and Figures

Table 1: Description of activities and material from each workplace.

Workplace	Week	Activities	Material
Welding	1	Welding (SMAW/FCAW), oxy-fuel cutting, grinding	Base metal: Mild steel Electrode/wire: Mild steel
	2	Welding (GMAW/FCAW), oxy-fuel cutting, grinding	Base metal: Mild steel Wire: Mild steel
	3	Welding (GMAW/GTAW), oxy-fuel cutting, grinding	Base Metal: Mild steel (GMAW), aluminum (GTAW) Electrode/wire: Mild steel (GMAW)
Construction	1	Corner assembly	Concrete blocks and bricks
	2	Stone cutting and laying	Stones
	3	Lay to a line	Concrete blocks

SMAW: Shielded metal arc welding; FCAW: Flux-cored arc welding; GMAW: Gas metal arc welding; GTAW: Gas Tungsten Arc Welding.

Table 2: Mass and number concentration of particulate matter for each workplace, size fraction and sampling strategy.

Workplace	$PM_{4-Personal}$ (µg.m^{-3})				PM_{4-Area} (µg.m^{-3})				$PM_{2.5-Area}$ (µg.m^{-3})				Number (1000 particles.cm^{-3})			
	N	GM (GSD)	Median (25^{th} – 75^{th} percentiles)	Min – Max	N	GM (GSD)	Median (25^{th} – 75^{th} percentiles)	Min – Max	N	GM (GSD)	Median (25^{th} – 75^{th} percentiles)	Min – Max	N	GM (GSD)	Median (25^{th} – 75^{th} percentiles)	Min– Max
All Welding	53	1,040 (2.1)	900 (672 – 1,730)	329 – 6,030	54	509 (2.1)	517 (295 – 1,085)	183 – 2,517	53	468 (2.0)	433 (256 – 1,022)	176 – 1,940	45	116 (1.6)	128 (78 – 169)	42– 248
Welding Week 1	19	1,980 (1.6)	1,790 (1,490 – 2,680)	916 – 5,160	19	1,200 (1.4)	1,210 (1,050 – 1,330)	549 – 2,520	19	1,060 (1.6)	1,060 (997 – 1,200)	244 – 1,940	18	170 (1.2)	168 (159 – 202)	106 – 248
Welding Week 2	16	684 (1.7)	680 (375 – 860)	375– 2,720	19	246 (1.3)	219 (206 – 272)	177 – 466	20	252 (1.4)	230 (197 – 312)	176 – 514	16	87 (1.3)	76 (72 – 96)	64– 124
Welding Week 3	18	769 (2.0)	710 (552 – 832)	329 – 6,030	16	439 (1.4)	468 (376 – 538)	201 – 900	16	386 (1.4)	404 (336 – 460)	181 – 755	11	72 (1.4)	67 (57 – 88)	42 – 135
All Bricklaying	54	430 (1.4)	432 (345 – 530)	264 – 832	33	344 (1.4)	353 (260 – 452)	129 – 676	34	241 (1.4)	227 (183 – 320)	125 – 522	22	3 (1.7)	2.8 (1.7 – 4.4)	1.4 – 8.5
Bricklaying Week 1	15	342 (1.3)	346 (276 – 395)	242 – 587	14	328 (1.4)	320 (277 – 355)	129 – 481	14	199 (1.4)	184 (171 – 218)	125 – 522	10	2.7 (1.6)	2.7 (1.7 – 3.6)	1.5 – 6.2
Bricklaying Week 2	20	497 (1.3)	480 (426 – 597)	242 – 1,060	12	439 (1.2)	442 (394 – 490)	198 – 676	12	310 (1.2)	322 (266 – 332)	240 – 429	6	2.3 (1.5)	2.1 (1.7 – 3.2)	1.4 – 3.9
Bricklaying Week 3	19	441 (1.4)	483 (344 – 548)	308 – 1,060	7	249 (1.5)	234 (220 – 296)	329 – 645	8	233 (1.2)	227 (218 – 252)	175 – 310	6	5.8 (1.5)	6.1 (4.6 – 8.5)	3.7 – 8.5

GM: Geometric Mean; GSD: Geometric standard deviation; N: Number of total samples; Min– Max: Minimum and maximum concentrations; IQR: Interquartile range; $PM_{4-Personal}$: Personal samples of PM_4; PM_{4-Area}: Area samples of PM_4; $PM_{2.5-Area}$: Area samples of $PM_{2.5}$.Background concentrations: $PM_{2.5}$ = 3.41 µg.m^{-3}; Number concentration = 1,760 particles.cm^{-3}. Note: In the construction site, each area sampler represented measurements for 1 to 3 apprentices, but it was paired with only one personal sample for statistical analyses.

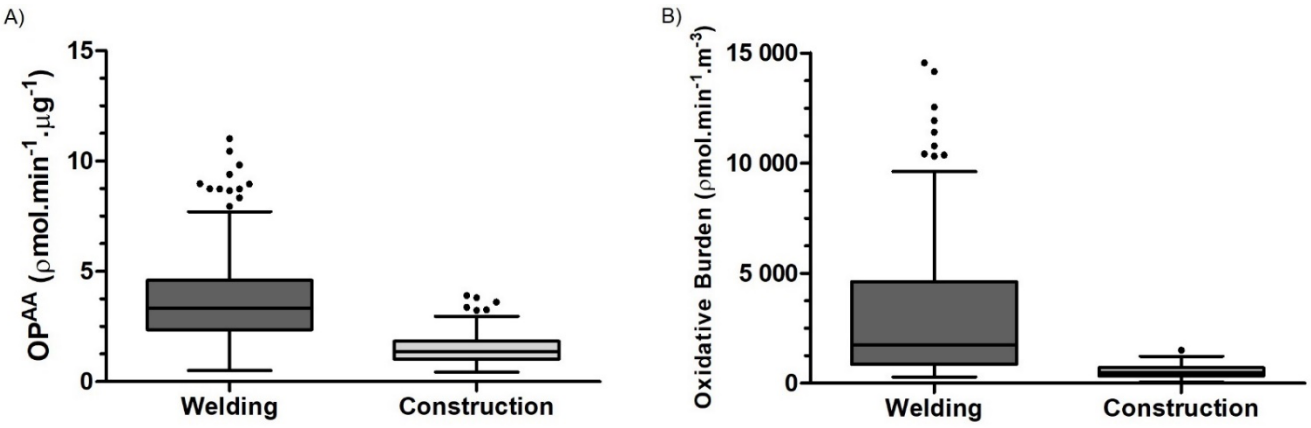

Figure 1: OP^{AA} (A) and oxidative burden (B) of particulate matter from welding and construction. Median concentration is represented by the solid line inside each box. The top and bottom of each box, whisker and dots represent the 25^{th}/75^{th} percentiles, the 10^{th}/90^{th} percentiles, and the outliers, respectively.

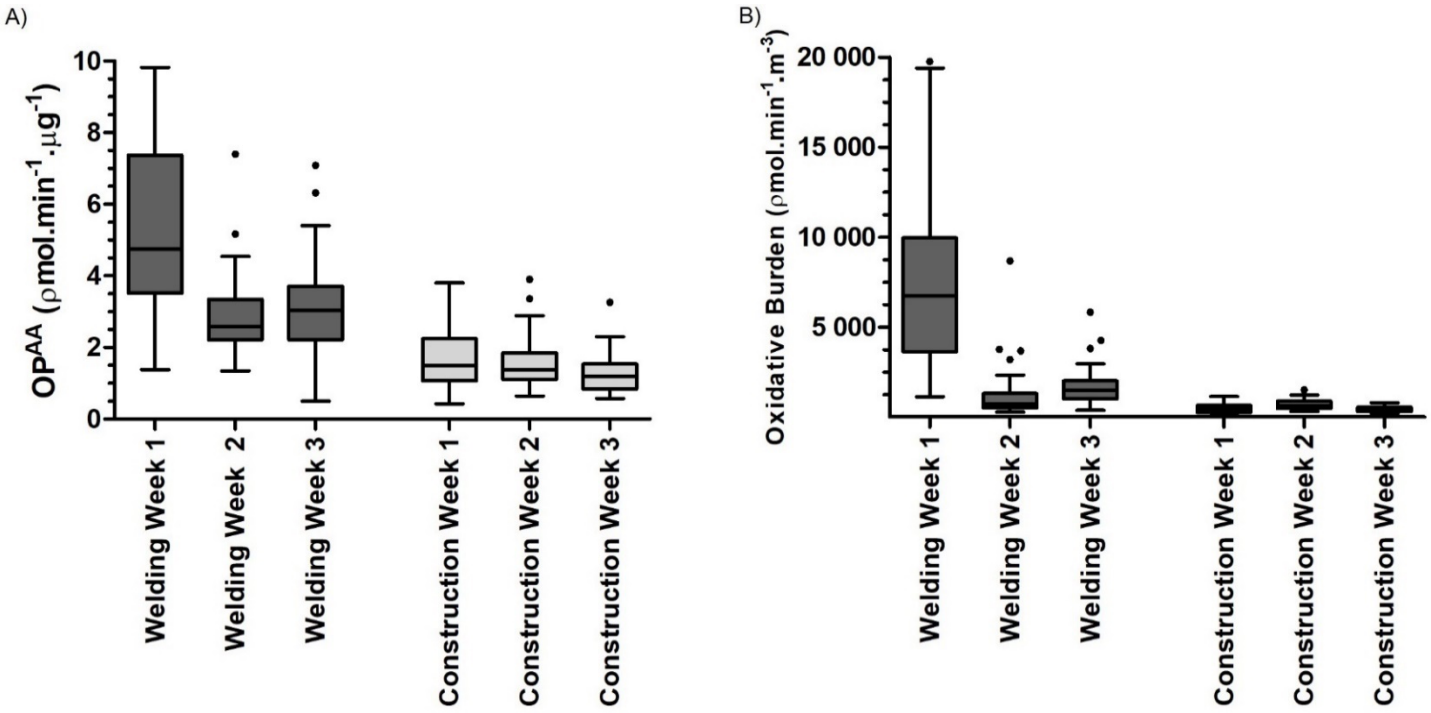

Figure 2: OP^{AA} (A) and oxidative burden (B) of particulate matter particles according to the week of activity in each workplace. Median concentration is represented by the solid line inside each box. The top and bottom of each box, whisker and dots represent the $25^{th}/75^{th}$ percentiles, the $10^{th}/90^{th}$ percentiles, and the outliers, respectively.

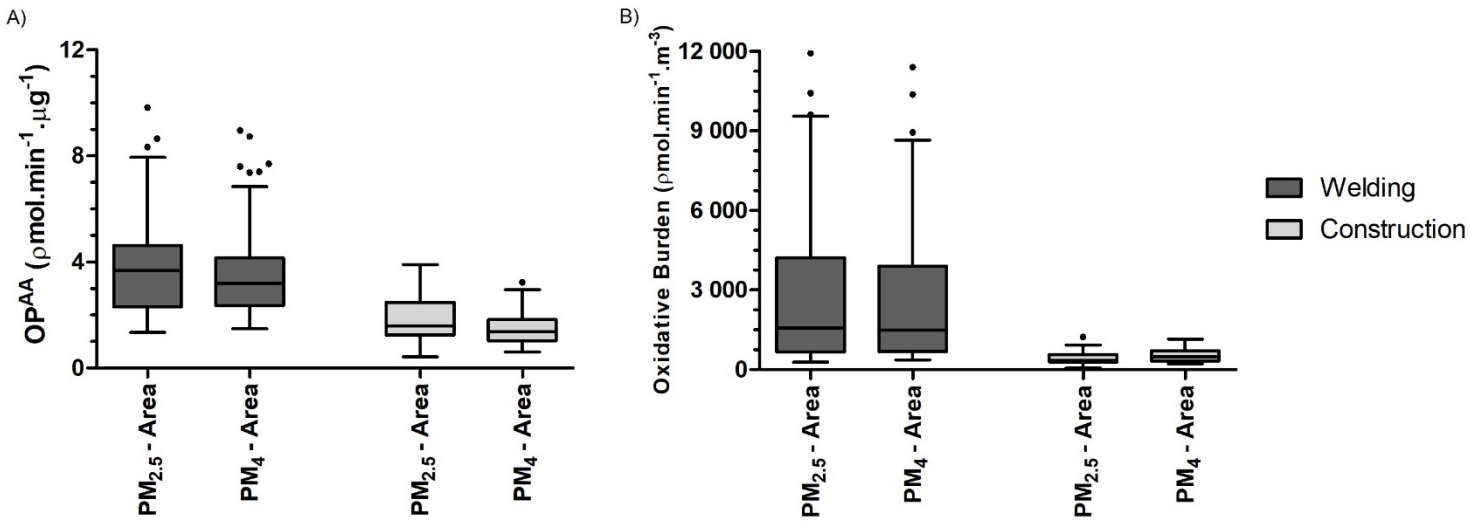

Figure 3: OP^{AA} (A) and oxidative burden (B) of particulate matter according to the size fraction ($PM_{2.5\text{-}Area}$ versus $PM_{4\text{-}Area}$). Median concentration is represented by the solid line inside each box. The top and bottom of each box, whisker and dots represent the $25^{th}/75^{th}$ percentiles, the $10^{th}/90^{th}$ percentiles, and the outliers, respectively.

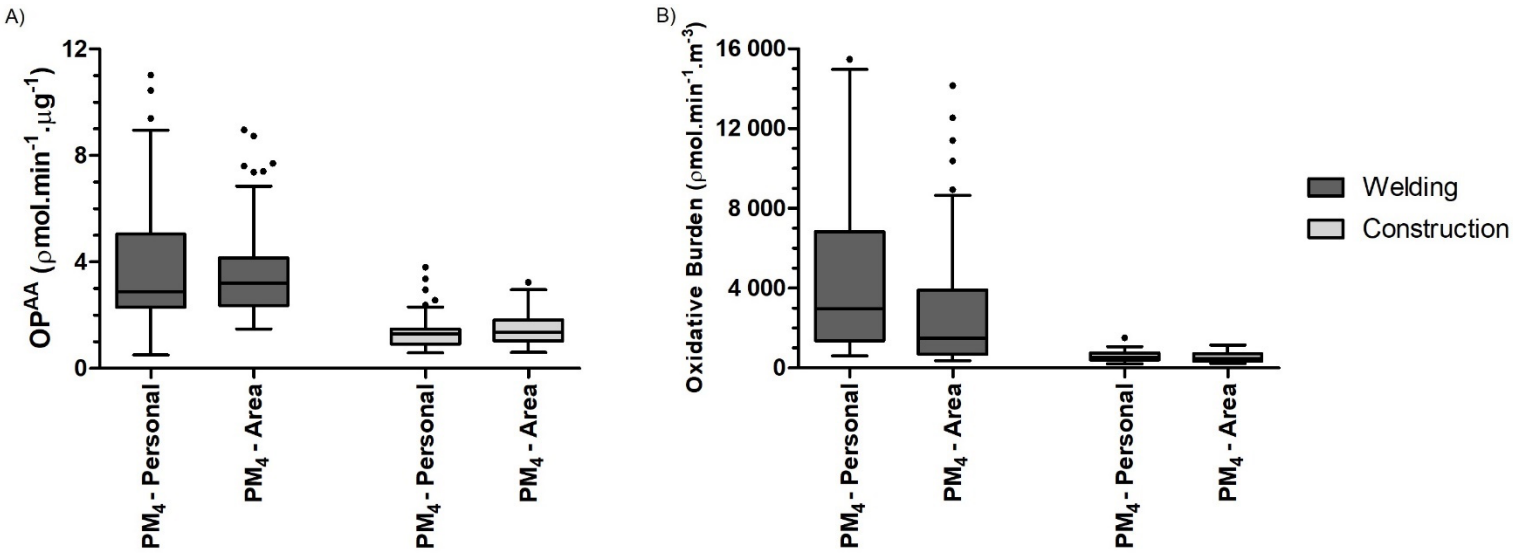

Figure 4: OP^{AA} (A) and oxidative burden (B) of particulate matter according to the sampling strategy ($PM_{4\text{-Personal}}$ versus $PM_{4\text{-Area}}$). Median concentration is represented by the solid line inside each box. The top and bottom of each box, whisker and dots represent the $25^{th}/75^{th}$ percentiles, the $10^{th}/90^{th}$ percentiles, and the outliers, respectively. Note: In the construction site, each area sampler represented measurements for 1 to 3 apprentices, but it was paired with only one personal sample for statistical analyses.

6.13 Supplementary Material

Sample concentration and interlaboratory validation

Preliminary OP^{AA} tests with concentrations ranging from 50 µg/mL to 5 µg/mL were performed in order to estimate the effect of the concentration of the particles in solution on OP^{AA}. Supplementary Figure 1 shows that all samples exhibited similar depletion rates, all of which were significantly higher than the depletion rate of the blank (One-Way ANOVA followed by Dunnet's *posthoc* test; $P < 0.001$). Further, the analysis concentration generally had a negligible effect on the depletion rate (One-Way ANOVA followed by Tukey *posthoc* test; $P = 0.14$).

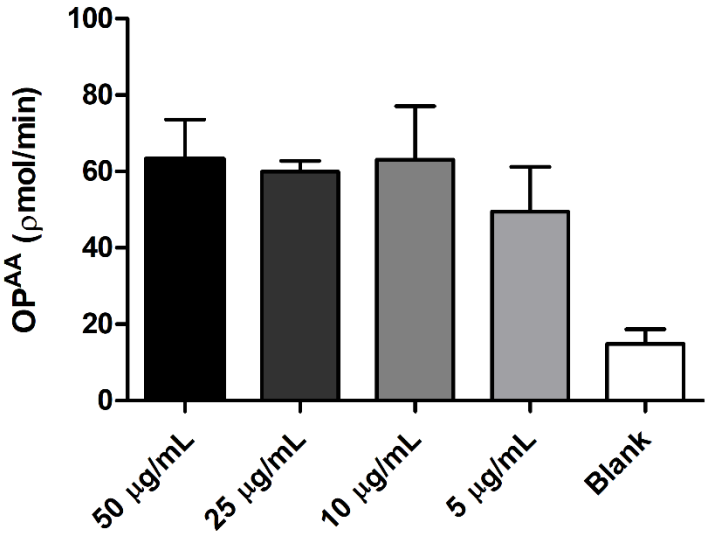

Figure S1: OP^{AA} according to the concentration of particles in solution.

Table S1: Elemental composition of PM_4 samples collected during welding and construction activities.

Element	Welding Week 1		Welding Week 2		Welding Week 3		Construction	
	Mass (μg)	%	Mass (μg)	%	Mass (μg)	%	Mass (μg)	%
Fe	314	35.2	23.7	35.9	240	40.6	<MRV	-
Mn	53.9	6.1	3.1	4.7	34.4	5.8	<MRV	-
Mg	<MRV	-	<MRV	-	<MRV	-	24.6	22.3
Al	<MRV	-	<MRV	-	<MRV	-	<MRV	-
V	<MRV	-	<MRV	-	<MRV	-	<MRV	-
Cr	<MRV	-	<MRV	-	<MRV	-	<MRV	-
Co	0.083	0.01	<MRV	-	<MRV	-	<MRV	-
Ni	<MRV	-	<MRV	-	<MRV	-	<MRV	-
Cu	16.9	1.9	0.53	0.8	2.3	0.4	0.45	0.41
Zn	3.5	0.4	<MRV	-	<MRV	-	<MRV	-
Cd	<MRV	-	<MRV	-	<MRV	-	<MRV	-
Pb	0.33	0.4	<MRV	-	0.11	0.2	<MRV	-
PM_4	**890**	**100**	**66**	**100**	**590**	**100**	**110**	**100**

Minimum Reported Value (MRV): Fe = 10 μg; Mn = 1 μg; Mg = 20 μg; Al = 10 μg; V = 0.1 μg; Cr = 1 μg; Co = 0.04 μg; Ni = 2 μg; Cu = 0.4 μg; Zn = 1 μg; Cd = 0.05 μg; Pb = 0.1 μg.

Table S2: Concentration of crystalline silica (quartz) in PM_4 samples collected during the construction activities.

	PM_4 ($\mu g/m^3$)	**Crystalline Silica ($\mu g/m^3$)**	**Crystalline Silica (%)**
Sample 1	740	25	3.3
Sample 2	830	26	3.1
Sample 3	770	22	2.8
Sample 4	730	25	3.4
Sample 5	750	23	3.0
AM (SD)	764 (39.7)	24.2 (1.6)	3.1 (0.2)

Table S3: OP^{AA} and oxidative burden of particles for each workplace, size fraction and sampling strategy.

Workplace	All Samples				$PM_{4\text{ - Personal}}$				$PM_{4\text{ – Area}}$				$PM_{2.5\text{ - Area}}$			
	N	**AM (SD)**	**Median (25^{th} - 75^{th} percentiles)**	**Min - Max**	**N**	**AM (SD)**	**Median (25^{th} - 75^{th} percentiles)**	**Min - Max**	**N**	**AM (SD)**	**Median (25^{th} - 75^{th} percentiles)**	**Min – Max**	**N**	**AM (SD)**	**Median (25^{th} - 75^{th} percentiles)**	**Min-Max**
OP^{AA} (pmol/min/ug)																
Welding	155	3.9 (2.1)	3.3 (2.3 - 4.6)	0.5 - 11	53	3.9 (2.4)	2.9 (2.3 – 5.0)	0.5 - 11	53	3.8 (1.9)	3.2 (2.4 - 4.1)	1.5 - 8.9	49	4.0 (2.0)	3.7 (2.3 - 4.6)	1.3 - 9.8
Construction	101	1.5 (0.7)	1.4 (1.0 - 1.8)	0.4 - 3.9	50	1.4 (0.7)	1.3 (0.9 - 1.5)	0.6 - 3.8	27	1.5 (0.7)	1.4 (1.0 - 1.8)	0.6 - 3.2	24	1.9 (0.8)	1.6 (1.2 - 2.2)	0.4 - 3.9
*Oxidative Burden (*pmol/min*/m^3)*																
Welding	153	3,900 (4,880)	1,750 (893 - 4,560)	290 - 29,960	50	5,070 (5,040)	2,970 (1,370 - 6,730)	607 - 29,960	52	3,290 (4,120)	1,500 (685 – 3,870)	372 - 19,400	49	3,160 (3,610)	1,570 (713 - 3,950)	290 - 14,600
Construction	101	554 (257)	486 (341 - 695)	66 - 1,510	50	588 (253)	541 (413 - 744)	201 - 1,510	27	530 (267)	486 (334 - 688)	221 - 1,150	24	453 (261)	359 (303 - 520)	66 - 1,230

AM(SD): Arithmetic mean and standard deviation; N: Number of samples; Min – Max: Minimum and maximum concentrations. $PM_{4–Personal}$: Personal samples of PM_4; $PM_{4–Area}$: Area samples of PM_4; $PM_{2.5–Area}$: Area samples of $PM_{2.5}$. Note: In the construction site, each area sampler represented measurements for 1 to 3 apprentices, but it was paired with only one personal sample for statistical analyses.

Chapter 7 – Environmental and occupational short-term exposures to airborne particles and lung function in healthy adults: a systematic review and meta-analysis

This chapter addresses the third specific objective of this thesis that is to separately estimate, by a systematic review and meta-analysis, the associations between occupational and environmental short-term (i.e. daily and sub-daily) exposures to fine particles and lung function in healthy adults.

It is well documented in the literature that short and long-term exposures to particles from ambient air in the general environment are associated with respiratory health effects. While daily and sub-daily exposures have been found to reduce the lung function of vulnerable individuals, this relationship is less established for healthy adults, especially for workers in the context of occupational exposures. The relevance of exploring short-term exposures and effects relies on the fact that exposure levels are much higher in occupational settings, yet effects of short-term exposures remain undocumented. Knowledge gaps addressed here also include how the estimations of effects when considering the distinct compositions, sources and concentrations of particles across environmental and occupation settings.

Environmental and occupational short-term exposures to airborne particles and lung function in healthy adults: a systematic review and meta-analysis

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7.1 Abstract

The relationship between short-term particulate exposures and lung function is not well established for healthy adults. Furthermore, no previous study has compared the effects of particulate exposure from environmental and occupational settings, despite potentially different levels, sources, and composition of particles. We aimed to separately estimate, by a systematic review and meta-analysis, the associations between occupational and environmental short-term (i.e. daily and sub-daily) exposures to fine particles and lung function in healthy adults. We systematically reviewed studies investigating associations between daily and sub-daily exposures to fine particles (i.e., $PM_{2.5}$ and PM_4) and the following lung function parameters in healthy adults: FEV_1 and FVC. Separately for environmental and occupational studies, we summarized findings using random-effects meta-analyses when five or more independent risk estimates were available. 33 studies were included in the qualitative synthesis, and a total of 14 studies were included in the meta-analyses of environmental and occupational exposures. In environmental studies, where exposure levels ranged between 2 $\mu g/m^3$ and 146.5 $\mu g/m^3$, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ exposure was associated with a FEV_1 reduction of 7.63 mL (95% CI: -10.62 to -4.63 mL; I^2= 0%). In occupational studies, where exposure levels ranged between 270 $\mu g/m^3$ and 2,390 $\mu g/m^3$, an increase of 10 $\mu g/m^3$ in PM_4 exposure was associated with a FEV_1 reduction of 0.87 mL (95% CI: -1.36 to -0.37 mL; I^2= 54%). Similar results were observed for associations with FVC. Both occupational and environmental short-term exposures to fine particles were associated with reductions in lung function in healthy adults. Associations in occupational studies are an order of magnitude lower than associations from the general environment for a similar exposure increment, suggesting a potentially nonlinear relationship linking PM exposure to lung function, with a steeper slope at lower concentrations.

Keywords: particulate matter, lung function, healthy adults, short-term, occupational exposures, environmental exposures

7.2 Introduction

Throughout the world, the burden of respiratory diseases related to short-term exposures to fine particles is substantial. Exposures to particulate matter have been linked to increased mortality, emergency room visits and hospitalizations due to the exacerbation of respiratory diseases in children, elders, and adults (1-4). In addition, short-term exposures have been associated with respiratory symptoms (5) and decreased lung function in individuals with pre-existing respiratory diseases (6, 7). However, the relationship between daily exposures to particles and lung function reductions is not established for healthy adults of the general and workers populations.

Episodes of high environmental exposures to particles during short periods are ubiquitous and strongly related to society's current urban organization model. Such exposures can occur while commuting (8), performing physical activity near a high traffic route (9-11), during episodes of high daily average concentrations of fine and ultrafine particles (12, 13), and at microenvironments as near transport hubs, roadways, underground train stations and industrial sites (14-17). In addition, millions of workers worldwide are daily exposed to processes and tasks associated with the emission of particles at concentrations higher than the typical urban background, such as welding fumes, forest fires, wood dust and diesel engine exhaust (18-21).

To our knowledge, no study has yet reviewed the short-term effects of occupational exposures to airborne particles on lung function. Furthermore, there has been no attempt to compare lung function effects from environmental and occupational exposures to airborne particles, even though daily and sub-daily exposures in these two contexts are shared by healthy adults. Such comparison may provide valuable insights into the relationship between short-term exposures to particles and lung function across different exposure ranges. In addition, of particular interest is how different the effects can be when considering the distinct sources, concentrations, and composition of particles across environmental and occupation settings.

The objective of this study was to perform a systematic review and meta-analysis to estimate the associations between occupational and environmental short-term exposures to fine

particles and changes in lung function parameters - specifically forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) - among healthy adults.

7.3 Methods

The protocol of this systematic review and meta-analysis was registered in PROSPERO (Registration Number: CRD42017078435). Also, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (22) was completed.

Search strategy

The literature search included studies published in English between 1964 and 2020. The following electronic bibliographic databases were searched: Web of Science (Web of Science Core Collection and MEDLINE) and PubMed. Searches were last updated on May 14, 2020. In addition, we examined the reference lists of all included studies.

The search included terms for the exposure to fine particles (i.e. respirable dust and $PM_{2.5}$) and the selected outcomes lung function parameters: FEV_1 and FVC. FEV_1 refers to the quantity of air a person can exhale during the first second of a forced breath, while the FVC refers to the total amount of air exhaled during the spirometry test. These two indices were chosen given they are the most commonly investigated in studies associating air pollution exposures and lung function effects.

We also added terms to exclude studies on animal models, children, *in vitro* models and long-term exposure studies. The complete search strategy and the keywords are presented in the supplementary material.

Inclusion and exclusion criteria

Studies were included if they repeatedly investigated acute respiratory effects (within 24h after exposure) of short-term exposures (i.e. duration between 1h and 24h) to fine particles in healthy adults of working age (i.e. between 18 and 60 years old). In terms of the study population, we restricted the review to healthy adults of working age to compare associations between occupational and environmental health studies. Studies with both healthy and non-healthy subjects were included if the authors mentioned that they controlled for health status or if results

were reported by health status. We also considered in this review a few studies that included a small percentage of non-healthy subjects; these studies are well-identified in the paper and were considered in the sensitivity analysis.

In terms of study design, we restricted the review to studies with repeated measurements of the outcomes because such design allowed to separate effects of daily exposures from those of cumulative (long-term) exposures; therefore, cross-sectional studies were excluded.

We restricted the scope of this review to exposure to the mass concentration of $PM_{2.5}$ (i.e. particles with a median aerodynamic diameter of 2.5 μm) and of respirable dust (i.e.PM_4; particles with a median aerodynamic diameter of 4 μm), which are common classifications from the environmental and occupational studies, respectively. Although the size range of $PM_{2.5}$ and PM_4 is not exactly the same, both particulate matter fractions have a high capacity to penetrate deep into the alveolar region (23). Furthermore, these different size fractions may not necessarily result significantly in different mass concentrations if the mean size distribution of the particles is smaller than 2.5 μm.

Studies were excluded if: (1) they were based on reviews, they were experimental studies, case reports, letters, posters and conference abstracts; (2) the study population was formed exclusively by children, elders or subjects with a pre-existing chronic respiratory disease such as asthma and Chronic Obstructive Pulmonary Disease (COPD); (3) the respiratory outcomes of interest were not measured within 24 hours after exposure; (4) exposure duration was not within 24 hours; (5) the studies reported only one measurement of the outcome per subject (i.e. no repeated measurements); (6) size fractions other than $PM_{2.5}$ and PM_4 were measured; and (7) the exposure was focused on the measurement of environmental tobacco smoke.

Studies selection and data extraction

The selection of the articles was performed in two rounds by two investigators (AF and MS). The first round consisted of a screening of all titles and abstracts. In the second round, the full texts of all potentially relevant studies were reviewed considering the inclusion and exclusion criteria. Potential divergences in the selection of the study were discussed and ultimately resolved by a third investigator (AS).

Data extraction was performed by one investigator (AF) and reviewed by a second one (MS). The following information was manually extracted: (1) authors and year; (2) study location; (3) study design (i.e. panel, crossover and occupational cross-shift studies); (4) population (N, sex, % of smokers and mean age); (5) exposure information such as type of measurement (i.e. personal/quasi-personal and central/near station), exposure duration, exposure context and type of particles; (6) physiological outcomes; (7) confounders and effect modifiers; and (8) results (mean concentration of particles and respiratory outcome results (e.g. estimate ± 95% CI or T-test result).

Quality Assessment

The assessment of the risk of bias was performed by two investigators (AF and MS) according to the Office of Health Assessment and Translation (OHAT) tool developed by the National Institutes of Environmental Health Sciences-National Toxicology Program (24). Within each study, we evaluated the risk of bias across seven parameters divided as key criteria (i.e. exposure assessment, outcome assessment, and confounding bias, which is an item of the OHAT that includes the lack of consideration of important modifiers) and other criteria (i.e. selection bias, selective reporting, incomplete outcome data and conflict of interest). The risk of bias for each parameter was evaluated as “low”, “medium”, “high”, or “not applicable”. The OHAT guideline recommends the exclusion of studies for which all the key criteria and most of the other criteria are characterized as “high”.

Meta-analyses

Our initial goal was to perform a meta-analysis of results, notably to investigate whether associations between short-term exposure to fine particles and FEV_1 and FVC differ between environmental and occupational settings. We thus considered separately environmental and occupational studies. However, the pooling of selected studies was limited by the different metrics used for the outcomes. Specifically, lung function parameters were expressed as: a) absolute change (mL change); b) percent change from a baseline or mean value (% change); c) percent change of a log-transformed outcome (log % change); d) percent change from a predicted value (%PV); e) percent change from a log-transformed predicted value (log %PV).

Table S1, in the supplementary material, presents the description of these five different outcome metrics identified in the studies. Pooling results of studies in a meta-analysis requires the measure of association to be expressed uniformly across studies (25); therefore, these different metrics used for the lung function parameters could not be combined into a single meta-analysis of results.

We thus pooled studies separately according to the outcome metric. We computed meta-estimates when a minimum of five independent risk estimates was available. Due to the expected heterogeneity caused by the different study designs, populations and exposure characteristics, a random-effect meta-analysis was performed, thus assuming that the true effect size varies across studies. Meta-estimates, 95% confidence intervals and 95% prediction intervals were calculated for a 10 $\mu g/m^3$ of particulate concentration; we used a similar increment given that we aimed at contrasting the effect across these two different settings. We assessed heterogeneity using the I^2 statistic (26), whereas publication bias was examined using funnel plots (27).

In some occupational cross-shift studies, an estimate of association from a regression model was not reported (19, 28-32). Instead, the authors reported the difference between the mean outcome response post-exposure and pre-exposure (with a t-test comparing both measurements). For these cases, we used the reported mean response and level of exposure to calculate the effect for a 10 $\mu g/m^3$ increase in the pollutant concentration.

In some studies, measurement of the outcome was made at several time points after the exposure ended (10, 11, 15, 16, 33-35). In this review, the main series of meta-analyses included estimates for the time point immediately after exposure ended, as this time point was the most frequently measured across studies. Results of other time periods, when available, are presented in the supplementary material (Table S2).

In the sensitivity analyses, we performed a leave-one-out test to explore the influence of each study included on the meta-estimate, and on the I^2 statistic. Sensitivity analyses were also performed to explore the influence of the studies that had a small percentage of non-healthy subjects in its population. In addition, subgroup analyses were performed to explore the influence of key study criteria such as the type of measurement, duration of exposure and study

design. The heterogeneity variance was assessed by the DerSimonian and Laird method. Statistical analyses were all performed using Review Manager 5.3 and the *metaphor* package for R (version 3.4.1) (36). Results of studies that could not be included in the meta-analysis are described in the supplementary material (Table S2).

7.4 Results

Figure 1 shows the flow diagram for the selection of the studies. The primary search on the databases returned 4,244 studies from which 2,938 abstracts were screened, and 294 full texts were assessed for eligibility. After considering the inclusion and exclusion criteria, 33 articles were included in the qualitative synthesis.

Characteristics of the selected studies

Table 1 describes the main characteristics the selected studies according to the type of exposure (i.e., environmental or occupational).

Environmental studies

Twenty environmental studies evaluated the association between $PM_{2.5}$ short-term exposure and changes in lung function. Nineteen of these studies measured FEV_1 while fifteen measured FVC. Most of these studies were performed in North America (n = 10), followed by East Asia (n = 7) and Europe (n = 3). The different contexts of exposure identified were: hourly exposure to particles while commuting (34, 35), performing physical exercise (9, 11, 37-39) and associated with different microenvironments (15, 16); daily average exposures varying according to different periods or areas (13, 14, 33, 40-44) and workers' exposure to ambient particles (45, 46). Although these latter studies were performed in a workers' population, we have considered that the type of exposure – including levels, composition and sources – was similar to the exposure experienced by individuals from the general environment. Environmental studies were designed predominantly as crossover (n=11) and panel (n=9) studies. Eleven studies estimated exposure by personal/quasi-personal measurements while nine used near/central station measurements. Mean levels of $PM_{2.5}$ exposure ranged between 2 $\mu g/m^3$ and 162 $\mu g/m^3$, while exposure duration ranged between 1 h and 24 h. The mean age of the subjects was 31.2 years

old and they were predominantly men (61.4%). Only 2 from the 20 studies included current smokers in the population.

Occupational studies

Thirteen occupational studies investigating associations between exposures to particles during a full work shift and lung function changes were included (19, 28-32, 47-53). All thirteen studies measured FEV_1, while eight also assessed FVC. Most of these occupational studies were carried out in North America (n = 4) and Middle East (n = 4), followed by Europe (n = 2), Oceania (n = 2) and East Asia (n = 1). In terms of study design, one was a panel study (n=1), whereas the remaining 12 studies were cross-shift studies (i.e., the health outcome is measured before and after the working shift). Exposure contexts included diesel exhaust; different types of dust such as cotton, wood and cement; and exposure to particles experienced by dairy workers, firefighters and dental laboratory technicians. All occupational studies assessed exposure by personal or quasi-personal measurements (i.e. measurements were performed close to the worker but not in the breathing zone). Mean levels of exposure to fine particles ranged between 35 $\mu g/m^3$ and 6,760 $\mu g/m^3$, while exposure duration ranged between 6h and 12h. The mean age of the subjects was 34.9 years old, and male workers comprised most of the population (86%). The mean percentage of current smokers was 33.8%.

Quality assessment

The quality assessment of the studies included in the meta-analyses is described in the supplementary material (Table S3). Overall, we have considered that all selected studies had enough quality to be included in the meta-analyses. Specifically, we considered occupational studies to have a higher quality in the exposure assessment criteria because most of them used personal measurements of exposure, compared to many environmental studies that assessed exposure by central stations. On the other hand, environmental studies were qualified as higher quality in the confounding bias criteria (that includes the lack of consideration of important modifiers). The crossover and panel designs of these studies, combined with the inclusion of co-variables in the regression models, allowed the control of important confounders. In occupational studies, however, the influence of important confounders, such as co-exposures,

and effect modifiers, such as smoking status, were not considered in some cross-shift studies. No clear differences between environmental and occupational studies were observed for the outcome assessment criteria in relation to the performance of the spirometry maneuvers by a trained technician and according to an official guideline.

Forest Plots and Meta-Analyses

The comparison of environmental and occupational studies was only possible for lung function parameters expressed as absolute changes (mL changes). 14 studies were included in this main set of meta-analyses. Figures 2 and 3 present forest plots showing separate estimates for FEV_1 (mL change) of environmental and occupational studies, respectively, whereas Figures 4 and 5 present forest plots for FVC (mL change). Other meta- estimates of associations between lung functions and environmental exposures to $PM_{2.5}$ that could not be compared with occupational studies are presented in the supplementary material (Figures S1-S2).

FEV_1 (mL change)

FEV_1 and $PM_{2.5}$ in environmental studies

Figure 2 shows the forest plot for the six environmental studies that reported associations between $PM_{2.5}$ short-term exposure, with duration between 1h and 24h, and FEV_1 in mL change. Across these studies, the exposure levels varied from 2 $\mu g/m^3$ (cycling indoors; Weichenthal et al. (2011)) and 146.5 $\mu g/m^3$ (average of daily concentrations in 2 cities of China; Hao et al. 2017)). A 10 $\mu g/m^3$ increase in exposure levels was associated with a reduction of 7.63 mL (95% CI: -10.62 to -4.63 mL) in FEV_1, with no heterogeneity across results given the substantial overlap of confidence intervals (I^2 = 0%). The 95% prediction interval indicates that estimates of similar future studies would be expected to be between -10.62 mL and -4.63 mL. In the leave-one-out test, the exclusion of Vilcassim et al. (2019), the study carrying the higher weight (56%), did not meaningfully affect the meta-estimate: -8.43 mL (95% CI: -12.96 to -3.89; I^2 = 0%). The exclusion of Hao et al. (2017), the study with the highest $PM_{2.5}$ concentration, also did not affect the interpretation of the model: -7.01 mL (95% CI: -10.62 to -3.41; I^2 = 0%). In addition, Weichenthal et al. (2011) reported 33% of asthmatics in the studied population; and the exclusion of this study did not affect the meta-estimate: -7.61mL (95% CI: -10.61 to -4.61; I^2 = 0%). Forest plots grouped

by exposure duration, study design and type of measurement are presented in the Figure S3 of the supplementary material; estimates based on central sites and daily exposures (24h) had much smaller confidence intervals.

FEV_1 and PM_4 in occupational studies

Figure 3 shows the forest plot for eight occupational studies that reported associations between short-term exposure to PM_4 and FEV_1 in mL change. Across these studies, the exposure levels varied from 270 μg/m^3 (wood dust exposure; Herbert et al. (1994)) and 2,390 μg/m^3 (cotton dust exposure; Bakirci et al. (2007)). A negative association was observed, but the meta-estimate was lower compared to environmental studies; a 10 μg/m^3 increase in PM_4 concentration was associated with a reduction of 0.87 mL (95% CI: -1.36 to -0.37 mL) in FEV_1 after a work shift. Heterogeneity across results was moderate (I^2= 54%). The 95% prediction interval indicates that the estimate of similar future studies would be expected to be between -1.85 mL and 0.11 mL. The removal of Bakirci et al. (2007), the study with the highest average dust concentration, reduced the heterogeneity of the model but did not affect the interpretation of the estimate: -1.14 mL (95% CI: -1.83 to -0.45; I^2 = 45%). Barkirci et al. (2007), Bakirci et al. (2006) and Altin et al. (2002) reported a percentage of non-healthy workers of 20%, 14% and 11.5%, respectively. The exclusion of these studies reduced the heterogeneity of the model but did not affect the interpretation of the estimate: -0.76 mL (95% CI: -1.34 to -0.18; I^2 = 18%).

FVC (mL changes)

FVC and $PM_{2.5}$ in environmental studies

Figure 4 shows for FVC, expressed as mL changes, five environmental studies that could be pooled. For an increment of 10 μg/m^3 in $PM_{2.5}$ exposure, the random-effect meta-estimate showed a reduction of 10.0 mL (95% CI: -18.62 to -1.37 mL) in FVC. Although there were substantial differences across primary mean effect estimates, statistical heterogeneity was low (I^2= 27%) given the wide confidence intervals, particularly for three studies. The 95% prediction interval indicates that the estimate of similar future studies would be expected to be between -22.9 mL and 2.9 mL. The exclusion of Weichenthal et al. (2011), which included non-healthy individuals, increased the heterogeneity and caused the confidence interval to include the zero

value: -9.59 mL (95% CI: -19.81 to 0.63; I^2= 45%). Forest plots grouped by exposure duration, study design and type of measurement are presented in the Figure S4 of the supplementary material; no clear trend was seen from this grouping.

FVC and PM_4 in occupational studies

Figure 5 presents the forest plot of the occupational studies associating exposures to PM_4 and mL changes in FVC. Since only three studies were included, pooled estimates were not calculated and only results of the individual studies are presented. All studies reported a reduction in FVC levels after a work shift. Estimates ranged from -12.3 mL to -1.37 mL for a 10 $\mu g/m^3$ increase in PM_4.

Publication bias

Funnel plots are presented in the supplementary material (Figure S5). In general, there are not enough studies to comprehensively examine publication bias, but visual inspections of the funnel plots revealed no strong indication of publication bias.

7.5 Discussion

This review is the first to compare associations from occupational and environmental health studies investigating short-term exposure to fine particles and lung functions in healthy adults. Our analysis shows that exposure to fine particles is associated with reductions in FEV_1 and FVC among healthy adults in both occupational and environmental exposure settings. For a similar exposure increment (10 $\mu g/m^3$), the associations with fine particles in healthy adults are an order of magnitude greater in environmental studies as compared to occupational studies. Even if PM exposure in occupational settings were from very diverse settings, the estimate for FEV_1 was relatively consistent considering the varied exposure contexts.

Two hypotheses may explain the 10-fold difference in the magnitude of the occupational and environmental meta-estimates of FEV_1 for the same exposure increment. Firstly, this difference may reflect the distinct characteristics between occupational and environmental studies, notably in the composition of particles due to the varied sources of ambient versus workplace exposures, size fraction (i.e. $PM_{2.5}$ versus PM_4), sampling strategy (i.e. personal

monitoring versus central station), study design (i.e. cross-shift versus panel studies), exposure duration (i.e. daily versus hourly), study population (i.e. sex and smoking status), and the healthy worker effect (54). In this regard, almost all environmental studies excluded smokers from the population, while occupational studies included smokers. Given that the association between PM and lung function can differ according to smoking status (55), this factor may also partially explain the difference observed between environmental and occupational studies. In addition, the assessment of co-exposures that are also relevant to lung function effects was not explored by many occupational studies.

However, although these factors may explain a portion of the observed difference, they may not fully explain the almost 10-fold difference between both meta-estimates. In this regard, another hypothesis may be related to differences in effects according to the range of PM concentrations in occupational (i.e. between 270 $\mu g/m^3$ and 2,390 $\mu g/m^3$) and environmental (i.e. between 2 $\mu g/m^3$ and 146.5 $\mu g/m^3$) studies. Indeed, there may be a nonlinear relationship linking PM exposure to lung function, with a steeper slope at lower concentrations (i.e., environmental exposure) that may flatten in the higher ranges, as observed in some mortality studies with ambient fine particles (56, 57). Biologically, this could indicate that high short-term exposure levels – such as observed in occupational studies – could lead to the saturation of cellular and biochemical mechanisms involved in acute lung inflammation and oxidative stress, resulting in a plateau in the exposure-response relationship at these concentrations (2, 57).

This study is the first to review the effect of short-term exposure to fine particles on lung function from occupational studies. Findings from our meta-analysis of environmental studies are in accordance with a recent meta-analysis published that showed a reduction of 7.02 mL (95% CI: -11.75 mL to -2.29 mL) in FEV_1 after short-term environmental exposures to $PM_{2.5}$ in healthy adults (58); while we observed a reduction in FEV_1 of 7.62 mL (95% CI: -10.62 to -4.73 mL) in environmental studies. In contrast to this other review of environmental studies, our analysis benefits, in terms of causal inference, of being restricted to studies involving repeated measurements (i.e. panel, crossover and occupational cross-shift but excluding cross-sectional). Studies with repeated measurements allow to adequately assess the variation in lung function that is attributed to short-term variations in air pollution by accounting for the baseline lung

function and controlling for the possible long-term effect of air pollution on lung function. We further improved over this previous review by including studies on FVC, by considering all outcome units (e.g. % change) and reviewing occupational studies, which reinforce the findings that short-term exposure to fine particles leads to decrement in lung function in healthy adults.

Future studies are needed to improve our understanding of the impacts of daily particulate exposure in both occupational and general environments. Notably, the clinical relevance of small daily changes in FEV_1 in healthy adults remains unclear, although reductions in lung function parameters are suggested as a predictor for cardiopulmonary mortality and morbidity (59). Furthermore, the minimal clinical important difference (MCID) for clinical trials in patients with COPD is 5% or 100 ml (60), which is a decrease observed in some occupational studies reported here (28-30, 32). Other research questions that need to be addressed include how high daily exposure levels may influence the duration and transience of respiratory effects and whether the short-term effects from repeated daily exposures are also linked to the longitudinal decline in lung function and the development of cardiopulmonary morbidities. In this regard, it is suggested that short-term PM exposure may lead to an increased tonus of airway smooth muscles that is typically rapidly antagonized by an increased cellular level of nitric oxide (NO), resulting in transitory airway resistance (61). This may explain why, for some studies, short-term exposures to particles did not result in significant reductions in lung function.

The impact of PM composition from different sources on lung function may be addressed in future studies by oxidative potential assays and compared across occupational and environmental contexts. Furthermore, panel studies with repeated measurements across different days could also be developed for occupational settings. This type of study design would be fundamental to understand how occupational exposures across different days (i.e. with different lags for effects) impact the duration and transience of lung function reductions in workers.

7.6 Conclusions

This systematic review and meta-analysis shows that environmental and occupational short-term exposures to fine particles are associated with reduced lung function in healthy adults. A lower meta-estimate was found in occupational studies than environmental studies for a similar exposure increment; however, exposure levels were substantially greater in occupational studies. This may reflect a potentially nonlinear relationship linking PM exposure to lung functions, with a steeper slope at lower concentrations. Differences in meta-estimates may also be, in part, due to differences across occupational and environmental study design and methods. Future meta-analyses would benefit from greater standardization of study design and methods, notably in terms of the metric used to express the lung function parameters and the fraction of particles measured.

7.7 Contributions

ASF contributed to the project design, literature search, data collection, data analysis and manuscript preparation. MS participated in the literature search, data collection and data analysis. SB and AS contributed to the project design, manuscript preparation and review. ES and MD contributed to manuscript preparation and review.

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7.9 Competing Interests

The authors declare that they have no competing interests.

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7.11 Tables and Figures

Table 1: Characteristics of the studies included in the systematic review and meta-analyses.

Author and Year	Location	Design	N	Men, %	Age, years	Smokers, %	Exposure Context	Measurement and Exposure Duration	Pollutants and Mean Concentration
Environmental Studies									
Baccarelli et al. (2014)	China	Panel	120	66%	33	39.1	Traffic-related PM2.5 exposure in truck drivers and office workers	Personal: 8h	$PM_{2.5}$: 127 μg/m^3 (drivers) and 94 μg/m^3 (office workers)
Cakmak et al. (2014)	Canada	Crossover	61	46%	24	0	Near steel plant and college campus	Near Station; 24h	$PM_{2.5}$: 12.8 μg/m^3 (plant) and 11.5 μg/m^3 (campus)
* Cole et al. (2018)	Canada	Crossover	38	74%	29	0	Cycling in downtown (D) and residential (R) areas	Quasi-personal: 1h	$PM_{2.5}$: 6 μg/m^3 (D) and 4.7 μg/m^3 (R)
Dales et al. (2013)	Canada	Crossover	61	75%	24	0	Exposure near steel plant and college campus	Near Station; 24h	$PM_{2.5}$: 12.8 μg/m^3 (plant) and 11.5 μg/m^3 (campus)
† Girardot et al. (2006)	USA	Panel	354	43%	43	0	Exposure while hiking in a mountain	Near Station; 5h	$PM_{2.5}$: 15 μg/m^3
* Hao et al. (2017)	China	Panel	42	62%	55	0	Daily exposures to particles	Personal; 24h	$PM_{2.5}$: 146.5μg/m^3
* Hu et al. (2018)	China	Panel	28	43%	20.6	0	Same day exposure to particles	Personal; 8h	$PM_{2.5}$: 65.1 μg/m^3
† Huang et al. (2016)	China	Crossover	40	42%	24	0	Exposure in a transport hub and park	Personal; 2h	$PM_{2.5}$: 162 μg/m^3 (transport hub) and 53 μg/m^3 (park)
Jarjour et al. (2013)	USA	Crossover	73	73%	32	0	Cycling on low traffic (LT) and high traffic (HT) routes	Personal; 2h	$PM_{2.5}$: 45 μg/m^3 (LT) and 44 μg/m^3 (HT)
Kubesch et al. (2015)	Spain	Crossover	28	46%	34	0	Exposure to high and low TRAP in combination with physical exercise	Quasi-Personal; 2h	$PM_{2.5}$: 30 μg/m^3 (LT) and 80.1 μg/m^3 (HT)

Liu et al. (2018)	Taiwan	Panel	100	50%	46	0	Daily exposure to particles	Central Station; 24h	$PM_{2.5}$: 25.6 μg/m^3
* Matt et al. (2016)	Spain	Crossover	30	50%	36	0	Exposure in high traffic (HT) and low traffic (LT) roads while performing physical activity	Near Station; 2h	$PM_{2.5}$: 39 μg/m^3 (LT) and 82 μg/m^3 (HT)
Mirabelli et al. (2015)	USA	Crossover	21	62%	35	0	Exposure while commuting	Quasi-Personal; 2h	$PM_{2.5}$: 28.8 μg/m^3
† Mirowsky et al. (2015)	USA	Crossover	23	48%	25	0	Walking near traffic routes	Quasi-Personal; 2h	$PM_{2.5}$: 20 μg/m^3; PM_{10}: 26 μg/m3
† Thaller et al. (2008)	USA	Panel	142	79%	19	27	Beach guards exposed to ambient $PM_{2.5}$	Central Station; 8h	$PM_{2.5}$: 10.7 μg/m^3
* Vilcassim et al. (2019)	USA	Panel	34	32%	27	0	Exposure in different cities while travelling by plane	Central Station; 24h	$PM_{2.5}$: From 8.7 μg/m^3 (New York) to 105 μg/m^3 (East Asia)
* Weichenthal et al. (2011)	Canada	Crossover	42	67%	35	0	Cycling indoors, low traffic (LT) and high traffic routes (HT)	Quasi-Personal; 1h	$PM_{2.5}$: 2 μg/m^3 (Indoor), 8.1 μg/m^3 (LT) and 44 μg/m^3 (HT)
† Wu et al. (2013a)	China	Panel	40	100%	20	0	Exposure in suburban and urban areas	Central Station; 24h	$PM_{2.5}$: 75.2 μg/m^3 (Suburban), 56.6 μg/m^3 (Urban 1) and 48.8 μg/m^3 (Urban 2)
† Wu et al. (2013b)	China	Panel	21	100%	20	0	Exposure in suburban and urban areas	Central Station; 24h	$PM_{2.5}$: 75.2 μg/m^3 (Suburban), 56.6 μg/m^3 (Urban 1) and 48.8 μg/m^3 (Urban 2)
† Zuurbier et al. (2011)	Netherlands	Crossover	34	70%	42	0	Commuting by bus, car and by bike	Quasi-Personal; 2h	$PM_{2.5}$: 58 μg/m^3 (vehicles) and 65.2 μg/m^3 (bike)
Occupational Studies									
* Altin et al. (2002)	Turkey	Cross-shift	223	78%	27	67	Occupational exposure to cotton dust	Personal; 8h	PM_4: 413 μg/m^3
* Bakirci et al. (2006)	Turkey	Cross-shift	66	100%	NA	79	Occupational exposure to cotton dust	Quasi-Personal; 8h	PM_4: 1,050 μg/m^3 (delinting), 1,870 μg/m^3 (hulling) and 610 μg/m^3 (baling)

* Bakirci et al. (2007)	Turkey	Cross-shift	157	20%	52	31.2	Occupational exposure to cotton dust	Personal; 8h	PM_4: 2,390 µg/m^3
* Fell et al. (2011)	Norway	Cross-shift	70	92%	41	41	Occupational exposure to cement dust	Personal; 8h	PM_4: 300 µg/m^3
* Gaughan et al. (2014)	USA	Cross-shift	17	94%	26	0	Firefighters exposed to particles	Personal; 12h	PM_4: 490 µg/m^3
* Herbert et al. (1994)	Canada	Cross-shift	99	NA	35	27.9	Occupational exposure to wood dust	Quasi-Personal; 6h	PM_4: 270 µg/m^3
Hu et al. (2006)	Taiwan	Panel	45	66%	30	31.3	Exposure in dental laboratories	Personal; 8h	$PM_{2.5}$: 107 µg/m^3
Mandryk et al. (1999)	Australia	Cross-shift	198	100%	37	33	Occupational exposure to wood dust	Personal; 8h	PM_4: 2,170 µg/m^3 (sawmill) and 1,700 µg/m^3 (joinery)
Mandryk et al. (2000)	Australia	Cross-shift	127	100%	36	47.1	Occupational exposure to wood dust	Personal; 8h	PM_4: 2,260 µg/m^3 (green mill) and 1,460 µg/m^3 (dry mill)
Mitchell et al. (2015)	USA	Cross-shift	205	100%	34	24.4	Dairy workers exposed to particles	Personal; 9.2h	$PM_{2.5}$: 35 µg/m^3 (Workers) and 19.6 µg/m^3 (Controls)
Neghab et al. (2018)	Iran	Cross-shift	200	100%	37	41	Occupational exposure to wood dust	Personal; 8h	PM_4: 6,760 µg/m^3
* Slaughter et al. (2004)	USA	Cross-shift	65	80%	29	16.9	Firefighters exposed to particles	Personal; 8h	PM_4: 880 µg/m^3
* Ulfvarson and Alexandersson (1990)	Sweden	Cross-shift	24	100%	35	0	Exposure to diesel exhaust	Quasi-Personal; 8h	PM_4: 240 µg/m^3

Abbreviations: N: number of subjects; h: hours; NA: Not available; $PM_{2.5}$: Particulate matter with median diameter of less than 2.5 µm; PM_4: Particulate matter with median diameter of 4 µm.

***** Studies included in the main set of meta-analyses. † Studies included in the meta-analyses of the supplementary material. Results of the studies wit no symbols are presented in Table S2.

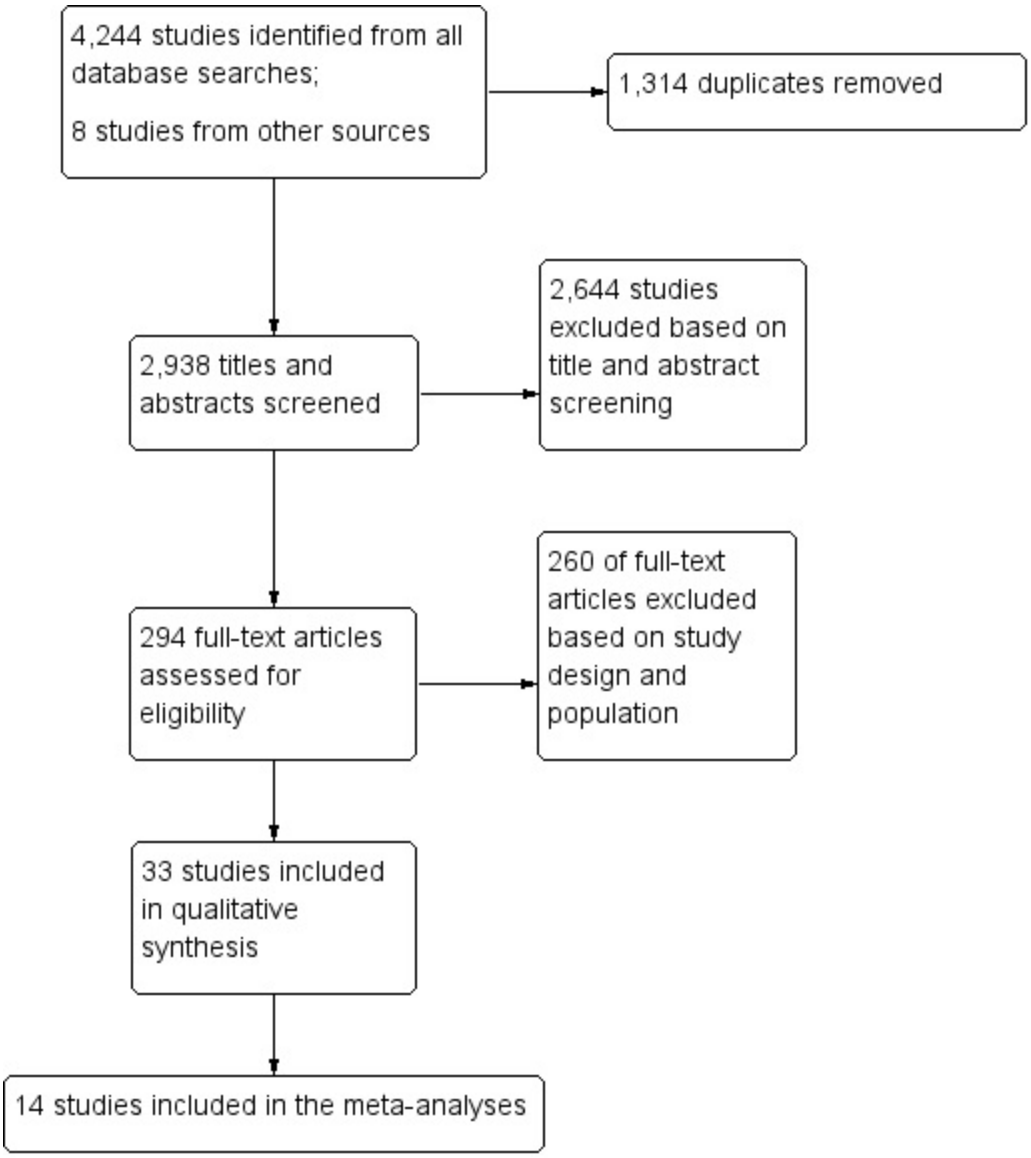

Figure 1: Flow diagram for the selection of studies.

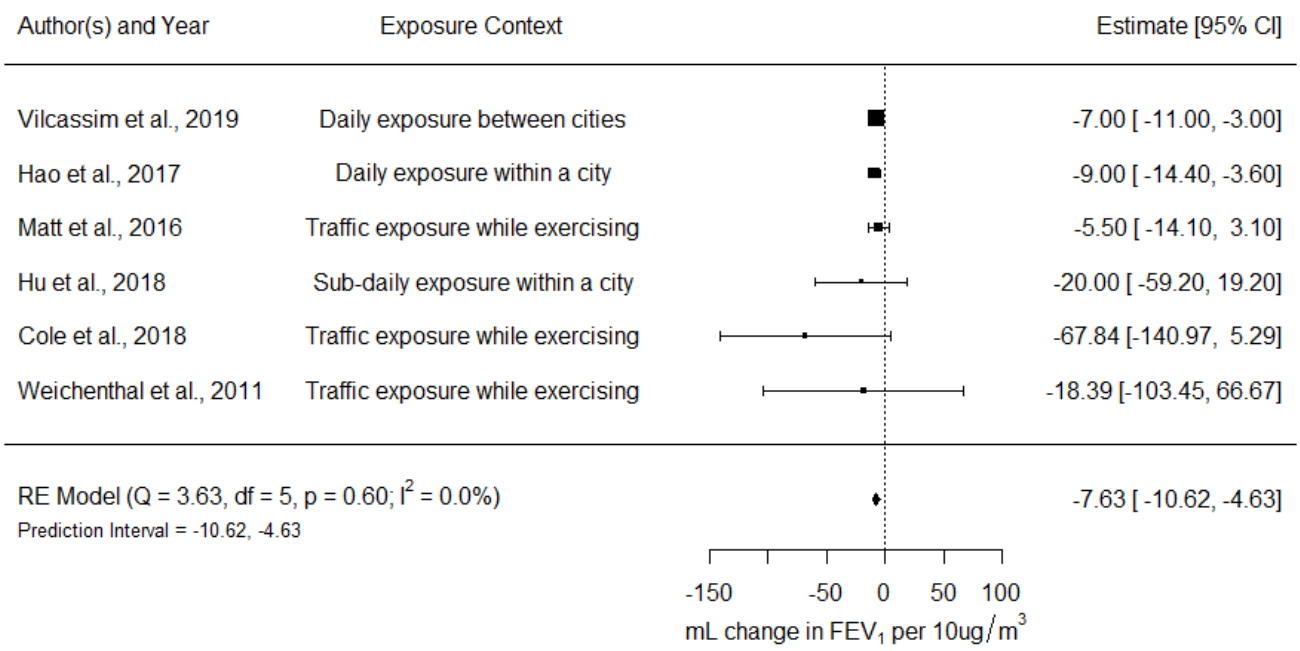

Figure 2: Meta-analysis of the association between environmental $PM_{2.5}$ and FEV_1 (mL changes). Random-effect meta-estimate of association is indicated by vertical point of diamond and 95% CI is represented by horizontal point. Squares represent individual effect size of primary studies and the bars the 95% CI; size of squares is proportional to weight in calculating random-effect summary estimates. A pooled effect size was estimated per 10 µg/m^3 increase in $PM_{2.5.}$ Daily exposure is defined as a 24h exposure duration, while sub-daily is defined as an exposure duration <24h.

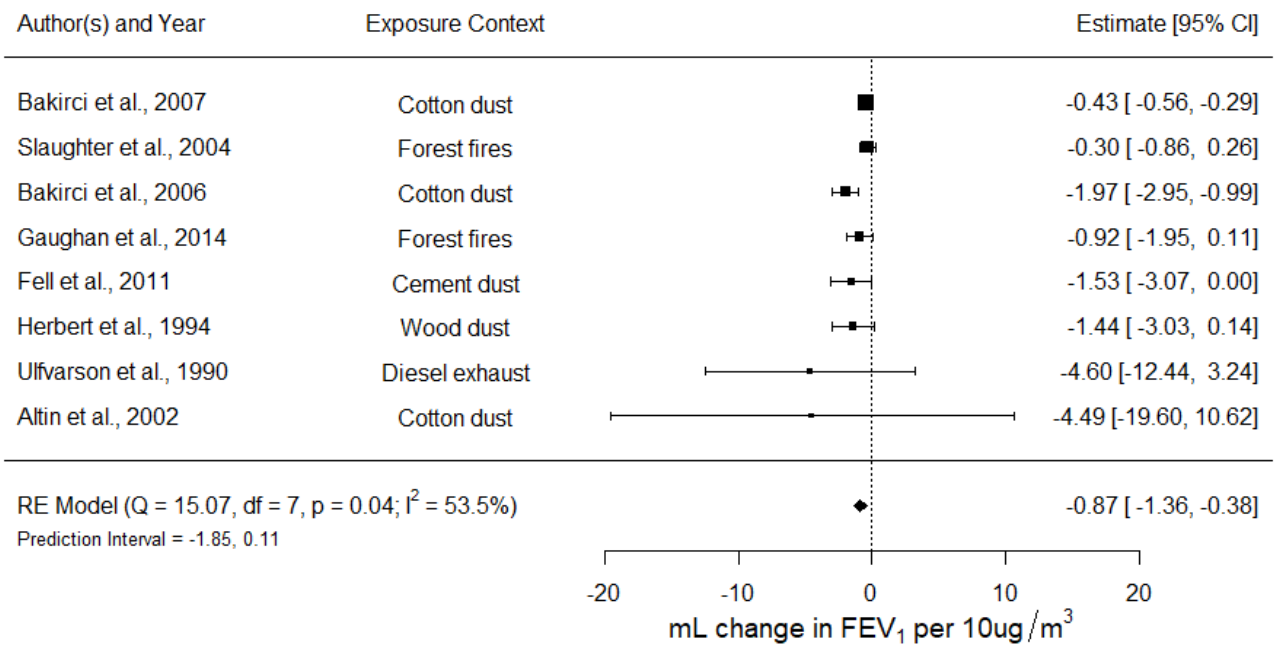

Figure 3: Meta-analysis of the association between occupational PM_4 and FEV_1 (mL changes). Random-effect meta-estimate of association is indicated by vertical point of diamond and 95% CI is represented by horizontal point. Squares represent individual effect size of primary studies and the bars the 95% CI; size of squares is proportional to weight in calculating random-effect summary estimates. A pooled effect size was estimated per 10 $\mu g/m^3$ increase in PM_4.

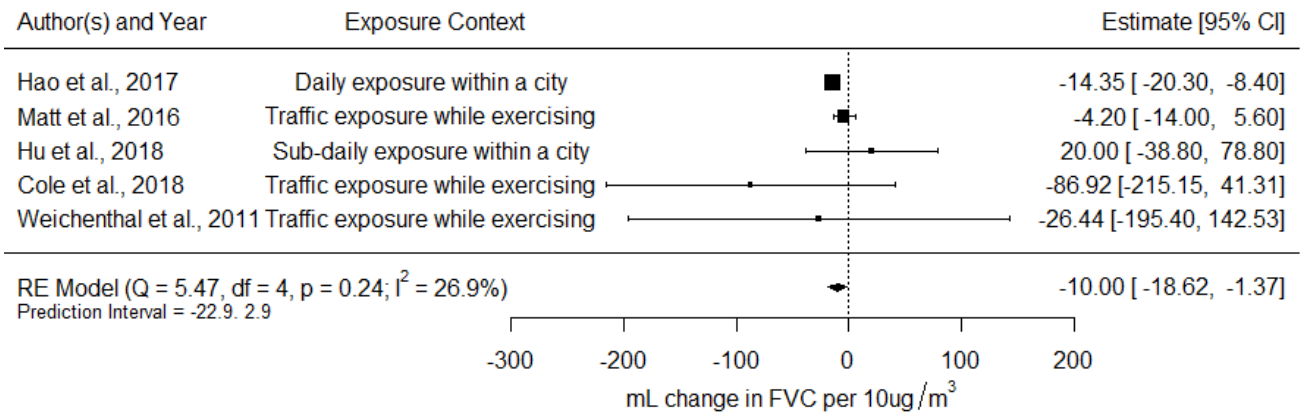

Figure 4: Meta-analysis of the association between environmental $PM_{2.5}$ and FVC (mL changes). Random-effect meta-estimate of association is indicated by vertical point of diamond and 95% CI is represented by horizontal point. Squares represent individual effect size of primary studies and the bars the 95% CI; size of squares is proportional to weight in calculating random-effect summary estimates. A pooled effect size was estimated per 10 $\mu g/m^3$ increase in $PM_{2.5.}$ Daily exposure is defined as a 24h exposure duration, while sub-daily is defined as an exposure duration <24h.

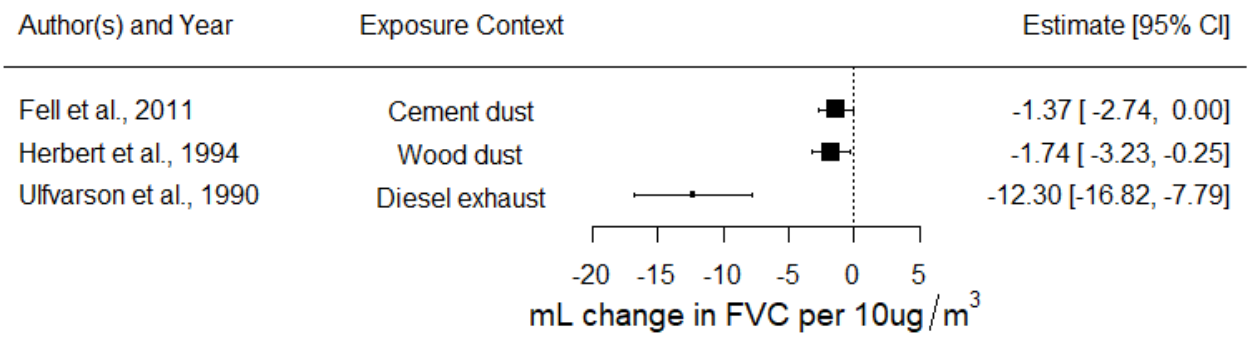

Figure 5: Forest plot of the association between occupational PM_4 and FVC (mL changes) per 10 $\mu g/m^3$ increase in exposure level. Squares represent individual effect size of primary studies and the bars the 95% CI.

7.12 Supplementary Material

PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	143
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	144
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	145
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	145
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	146
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	146 and 147
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	146
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	146 and 176

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	147
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	148
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	148
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	148
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	148 and 149
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	148 and 149
Section/topic	**#**	**Checklist item**	**Reported on page #**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	148
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	149
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	150 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	150, 151, Table 1 and Table S2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	151 and 154

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table S2 and Figures 2 to 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	152, 153, 154 and Figures 2 to 5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	151 and 154
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	152, 153 and 154
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	154
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	156
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	157
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	157

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 .

Search Strategy and Keywords:

#1 TOPIC: ("Lung Inflammation*") OR TOPIC: ("Pulmonary Inflammation*") OR TOPIC: ("Respiratory Inflammation*") OR TOPIC: ("Exhaled nitric oxide") OR TOPIC: (FeNO) OR TOPIC: (eNO)

#2 TOPIC: ("Lung Function*") OR TOPIC: (Spirometry) OR TOPIC: ("Pulmonary Function*") OR TOPIC: ("Airway Function*") OR TOPIC: ("Forced Expiratory Volume") OR TOPIC: ("Respiratory function*")

#3 TOPIC: ("ultrafine particle*") OR TOPIC: ("Particulate matter*") OR TOPIC: (particulate*) OR TOPIC: (UFP) OR TOPIC: (particle*) OR TOPIC: ("diesel exhaust*") OR TOPIC: (fume) OR TOPIC: (dust*) OR TOPIC: (PM2.5)

#4 #2 OR #1

#5 #4 AND #3

#6 TOPIC: (chronic) OR TOPIC: ("long term")

#7 TOPIC: (rat) OR TOPIC: (mice) OR TOPIC: (animal) OR TOPIC: (mouse)

#8 TOPIC: (cell) OR TOPIC: ("cell culture")

#9 TOPIC: (children)

#10 #5 NOT #6

#11 #10 NOT #7

#12 #11 NOT #8

#13 #12 NOT #9

Table S1: Metrics of respiratory outcomes used across the studies.

	Outcome Unit	Example of Codification	Definition
Absolute change	Absolute change	mL change	The difference between the value post-exposure and the value pre-exposure is calculated and included in the model
Percent change	Percent change (not log-transformed model)	% change	The difference between the post-exposure value and the pre-exposure (or mean) value is calculated, transformed in % change and then included in the model
	Percent change (log-transformed model)	log % change	The outcome is first log-transformed and then the difference post – pre exposure is calculated, transformed in % change and then included in the model
	Percent change from predicted value (PV)	%PV change	The absolute value of the outcome is transformed to % deviation from a mean predicted value from a reference population. The difference between post-exposure and the pre-exposure is calculated and then included in the model
	Percent change from PV (log-transformed model)	Log %PV change	The absolute value of the outcome is transformed to % deviation from a mean predicted value from a reference population. The difference between post-exposure and the pre-exposure is calculated, log-transformed and then included in the model

Additional FEV_1 results

FEV_1 (% change) and $PM_{2.5}$ in environmental studies

Figure S1 presents the association between environmental $PM_{2.5}$ exposures and FEV_1 measured in % change from a baseline value. Six studies were evaluated, and a negative but not significant association was found: -0.04% (95% CI: -0.14 to 0.06%; I^2 = 68%). The exclusion of Wu et al. (2013a) in the leave-one-out test resulted in a reduction in the value of the estimate: -0.07% (95% CI: -0.15 to 0.02%; I^2 = 60%).

Studies that could not be pooled in the meta-analyses

Seven environmental and six occupational studies could not be pooled in the meta-analyses because their outcomes (i.e. log % change from predicted value, log % change and % change from predicted value) or exposures metrics (i.e. log-transformed exposure, no information about IQR) were not comparable and could not be combined with at least three studies. Estimates and confidence intervals of these studies are presented in Table S2. Among the environmental studies, Dales et al. (2013) and Cakmak et al. (2014) reported negative association, Jarjour et al. (2013); Kubesch et al. (2015) and Mirabelli et al. (2015) reported a negative but non-statistically significant relationship and Baccarelli et al. (2014) and Liu et al. (2018) found a positive but non-statistically significant association between FEV_1 and fine particles. In occupational studies using a cross-shift design, Mandryk et al. (1999), Mandryk et al. (2000) and Neghab et al. (2018) found a statistically significant negative association in workers occupationally exposed to the respirable fraction of wood dust, while Hu et al. (2006) and Mitchell et al. (2015) reported a negative non-statistically significant exposure-outcome relationship.

Additional FVC results

FVC (% change) and $PM_{2.5}$ in environmental studies

No relationship was found for the % change in FVC after exposure to $PM_{2.5}$ in five environmental studies: 0.04% (95% CI: -0.32 to 0.40; I^2: 85%) (Figure S2). The exclusion of Wu et al. (2013a) caused a reduction in heterogeneity and resulted in a negative but not statistically significant association: -0.14% (95% CI: -0.51 to 0.24%; I^2: 49%).

Studies that could not be pooled in the meta-analyses

Five environmental and five occupational studies could not be pooled in the meta-analysis because their outcomes (i.e. log % change and % change from log-predicted value) or exposures metrics (i.e. log-transformed exposure, no information about IQR) were not comparable with other researches and could not be combined with at least three studies. In the environmental studies, Cakmak et al. (2014); Dales et al. (2013) and Jarjour et al. (2013) reported a negative but non-statistically significant association, while Baccarelli et al. (2014) and Kubesch et al. (2015) found a positive but non-statistically relationship between fine particles and FVC. In the occupational studies with a cross-shift design, Mandryk et al. (1999), Mandryk et al. (2000) and Neghab et al. (2018) found a statistically significant negative association between FVC and exposure to the respirable fraction of wood dust, while Hu et al. (2006) and Mitchell et al. (2015) did not report a statistically significant exposure-response relationship (Table S2).

Table S2: Descriptive results of the studies selected in the systematic review according to their outcomes.

Authors and Year	Pollutant	Statistical Approach	Outcome Unit	Outcome Change (SE or 95% CI or p- value)
Forced Expiratory Volume in 1 Second (FEV_1)				
Baccarelli et al. (2014)	$PM_{2.5}$	Change per 83.9 µg/m^3	log % change	0h: 1.11% (-1.31 to 3.59)
Cakmak et al. (2014)	$PM_{2.5}$	Change per 9 µg/m^3	log % PV	Lag 1: -0.42% (-0.83 to -0.004)
Cole et al. (2018)	$PM_{2.5}$	Change per 4.7 µg/m^3	mL change	0h: -32mL (-66 to 3.0)
Dales et al. (2013)	$PM_{2.5}$	Change per 9 µg/m^3	log % PV	Lag 1: -0.42% (-0.83 to -0.004)
Girardot et al. (2006)	$PM_{2.5}$	Change per 1 µg/m^3	% change	0h: 0.003% (0.033)
Hao et al. (2017)	$PM_{2.5}$	Change per 10 µg/m^3	mL change	Lag 0: -9mL (-14 to -3.6) // Lag 0-1: -1.7mL (-5.9 to 2.4)
Hu et al. (2018)	$PM_{2.5}$	Change per 10 µg/m^3	mL change	Lag 1: -20 mL (20)
Huang et al. (2016)	$PM_{2.5}$	Change per 10 µg/m^3	% change	During exposure: -0.13% (-0.24% to -0.05%) 0h: -0.15% (-0.3 to -0.02) // 3h: 0.19% (-0.02 to 0.38%) 5h: 0.14%(-0.09 to 0.35%) // 7h: 0.04%(-0.16 to 023%) 20h: 0.01% (-0.35 to 0.35%)
Jarjour et al. (2013)	$PM_{2.5}$	Change compared to baseline (T-test)	mL change	Low Traffic-0h: 20mL (p>0.05) // 4h: 40mL (p>0.05) High traffic-0h: 50mL (p>0.05) // 4h: -10mL (p>0.05)
Kubesch et al. (2015)	$PM_{2.5}$	IQR not informed	mL change	Pooled analysis for 30 min, 3h and 6h: -2mL (-23 to 18)
Liu et al. (2018)	$PM_{2.5}$	Change per 17.4 µg/m^3	% PV	0.3% (-5.1 to 5.7)
Matt et al. (2016)	$PM_{2.5}$	Change per 1 µg/m^3	mL change	0h: -0.55mL (-1.4 to 0.3) // 7h: 0.43mL (-0.5 to 1.4)
Mirabelli et al. (2015)	$PM_{2.5}$	Change per 20.9 µg/m^3	% PV	Non-asthmatics: 0h: −0.42% (−2.2, 1.3)
Mirowsky et al. (2015)	$PM_{2.5}$	Change per 1µg/m^3	% change	0h: -0.11% (-0.2 to -0.01) // 24h: -0.04% (-0.15 to 0.06)
Vilcassim et al. (2019)	$PM_{2.5}$	Change per 10 µg/m^3	mL Change	Evening: -7 mL (-11 to-3)
Weichenthal et al. (2011)	$PM_{2.5}$	Change per 8.7 µg/m^3	mL change	0h: -16mL (-90 to 58) // 1h: 32mL (-46 to 110) // 2h: 4.9 mL (-81 to 90) // 3h: 10mL (-50 to 69)
Wu et al. (2013a)	$PM_{2.5}$	Change per 51.2 µg/m3	% change	Lag 1: 1.7% (0.1 to 3.3)
Wu et al. (2013b)	$PM_{2.5}$	Change per 63.4 µg/m^3	% change	Morning: -0.5% (-1.0 to -0.07) // evening: -0.49% (-0.93 to -0.05)
Zuurbier et al. (2011)	$PM_{2.5}$	Changer per 68.1 µg/m3	% change	0h: 0.02% (-0.41 to 0.45) // 6h: 0.21% (-0.26 to 0.67)
Altin et al. (2002)	PM_4	Change compared to baseline (T-test)	mL change	Workers-0h: -102mL (p=0.56) Controls-0h: -60mL (p=0.56)
Bakirci et al. (2006)	PM_4	Change compared to baseline (Mann-Whitney)	mL change	Workers-0h: -120mL (-65 to -185) Controls-0h: 20mL (-65 to 105)
Bakirci et al. (2007)	PM_4	Change compared to baseline (T-test)	mL change	Cross-shift 1st day: -102mL (-137 to -67) Cross-shift 1st month: -78mL (-104 to -52) Cross-shift 3rd month: -50mL (-73 to -27)

				Cross-shift 6th month: -55mL (-85 to -25) Cross-shift 12th month: -67mL (-100 to -34)
Fell et al. (2011)	PM_4	Change compared to baseline (T-test)	mL change	Non-asthmatics: 0h: -46 mL (-86 to 6.3)
Gaughan et al. (2014)	PM_4	Change compared to baseline (T-test)	mL change	0h: -45mL (25.7mL)
Herbert et al. (1994)	PM_4	Change compared to baseline (T-test)	mL change	0h: -39mL (p=0.044)
Hu et al. (2006)	$PM_{2.5}$	1% change in log dust	% PV	0h: -1.31% (0.85)
Mandryk et al. (1999)	PM_4	% change in log dust	% PV	0h after exposure: 6.3% reduction in workers compared to 1.78% reduction in controls (P<0.001)
Mandryk et al. (2000)	PM_4	% change in log dust	% PV	0h after exposure: 6.44% reduction for green mill 21.8% reduction in dry mill workers (P<0.001 compared to control)
Mitchell et al. (2015)	$PM_{2.5}$	1% change in log dust	mL change	0h: -0.05ml (-27.76 to 27.66)
Neghab et al. (2018)	PM_4	Cross-shift change. Exposed versus Controls	% PV	0h: -10.5% (-14.3 to -6.8)
Slaughter et al. (2004)	PM_4	Change per 1,000 $\mu g/m^3$	mL change	0h: -30mL (-87 to 26)
Ulfvarson and Alexandersson (1990)	PM_4	Cross-shift change. Exposed versus Controls	mL change	Workers-0h: -105.8mL (92mL) Controls-0h: -44.8mL (45mL)
Forced Vital Capacity (FVC)				
Baccarell et al. (2014)	$PM_{2.5}$	Change per 83.9 $\mu g/m^3$	log % change	0h: 0.12% (-2.79 to 3.11)
Cakmak et al. (2014)	$PM_{2.5}$	Change per 9 $\mu g/m^3$	log % PV	Lag 1: -0.27% (-0.69 to 0.16)
Cole et al. (2018)	$PM_{2.5}$	Change per 4.7 $\mu g/m^3$	mL change	0h: -41mL (-102 to 19)
Dales et al. (2013)	$PM_{2.5}$	Change per 9 $\mu g/m^3$	log % PV	Lag 1: -0.41% (-0.88 to 0.05)
Girardot et al. (2006)	$PM_{2.5}$	Change per 1 $\mu g/m^3$	% change	0h: 0.007% (0.04)
Hao et al. (2017)	$PM_{2.5}$	Change per 10 $\mu g/m^3$	mL change	Lag 0: -14.3mL (-19.5 to -7.6) // Lag 0-1: -2.8mL (-12 to 0.39)
Hu et al. (2018)	$PM_{2.5}$	Change per 10 $\mu g/m^3$	mL change	Lag 1: 20mL (30)
Jarjour et al. (2013)	$PM_{2.5}$	Change compared to baseline (T-test)	mL change	Low Traffic-0h: -20mL (p>0.05) // 4h: -30mL (p>0.05) High traffic-0h: 0mL (p>0.05) // 4h: -50mL (p>0.05)
Kubesch et al. (2015)	$PM_{2.5}$	IQR not informed	mL change	Pooled analysis for 30 min, 3h and 6h: 14mL (-11 to 38)
Matt et al. (2016)	$PM_{2.5}$	Change per 1 $\mu g/m^3$	mL change	0h: -0.42mL (-1.4 to 0.56) // 7h: 0.38mL (-0.56 to 1.32)
Mirowsky et al. (2015)	$PM_{2.5}$	Change per 1$\mu g/m^3$	% change	0h: 0.01% (-0.1 to 0.13) // 24h: 0.05% (-0.07 to 0.17)
Wu et al. (2013a)	$PM_{2.5}$	Change per 51.2 µg/m3	% change	Lag 1: 2.5% (1.5 to 3.5)
Thaller et al. (2008)	$PM_{2.5}$	Change per 10 $\mu g/m^3$	% change	Non-asthmatics: 0h: -0.80% (-1.4 to -0.09)
Weichenthal et al. (2011)	$PM_{2.5}$	Change per 8.7 $\mu g/m^3$	mL change	0h: -23mL (-170 to 124) // 1h: 46mL (-84 to 175) // 2h: -17mL (-90 to 56) // 3h: 2.5mL (-75 to 79)

Zuurbier et al. (2011)	$PM_{2.5}$	Changer per 68.1 µg/m3	% change	0h: 0.10% (-0.40 to 0.61) // 6h: 0.396% (-0.13 to 0.84)
Fell et al. (2011)	PM_4	Change compared to baseline (T-test)	mL change	Non-asthmatics: 0h: -41mL (-80 to 23)
Herbert et al. (1994)	PM_4	Change compared to baseline (T-test)	mL change	0h: -47mL (p=0.022)
Hu et al. (2006)	$PM_{2.5}$	1% change in log dust	% PV	0h: -1.42% (0.76)
Mandryk et al. (1999)	PM_4	% change in log dust	% PV	0h after exposure: 4.3% reduction in workers compared to 2.1% reduction in controls (P<0.01)
Mandryk et al. (2000)	PM_4	% change in log dust	% PV	0h after exposure: 1.46% reduction for green mill and 4.54% reduction in dry mill workers (P<0.001)
Mitchell et al. (2015)	$PM_{2.5}$	1% change in log dust	mL change	0h: -6.78 ml (-39.6 to 26.1)
Neghab et al. (2018)	PM_4	Cross-shift change. Exposed versus Controls	% PV	0h: -10.38% (-14.67 to -6.09)
Ulfvarson et al. (1990)	PM_4	Cross-shift change. Exposed versus Controls	mL change	Workers-0h: -283ml (53mL) Controls-0h: 55mL (110mL) P=0.01

Abbreviations: % change: percent change from a baseline or mean value; log % change: percent change of a log-transformed outcome; % PV: percent change from a predicted value; log % PV: percent change from a log-transformed predicted value.

$PM_{2.5}$: Particulate matter with median diameter of less than 2.5 µm; PM_4: Particulate matter with median diameter of less than 4 µm; SE: Standard error; 95% CI: 95% confidence interval.

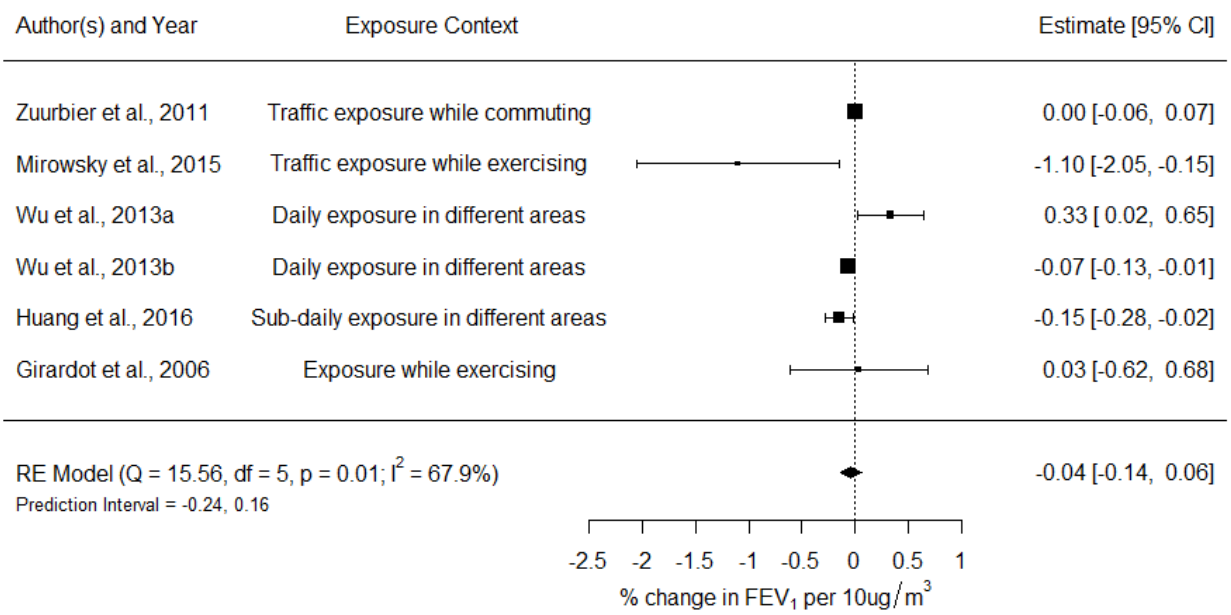

Figure S1: Meta-analyses of the association between environmental $PM_{2.5}$ and FEV_1 (% change). Random-effect meta-estimate is indicated by vertical point of diamond and 95% CI is represented by horizontal point. Squares represent individual effect size of primary studies and the bars the 95% CI; size of squares is proportional to weight in calculating random-effect summary estimates.

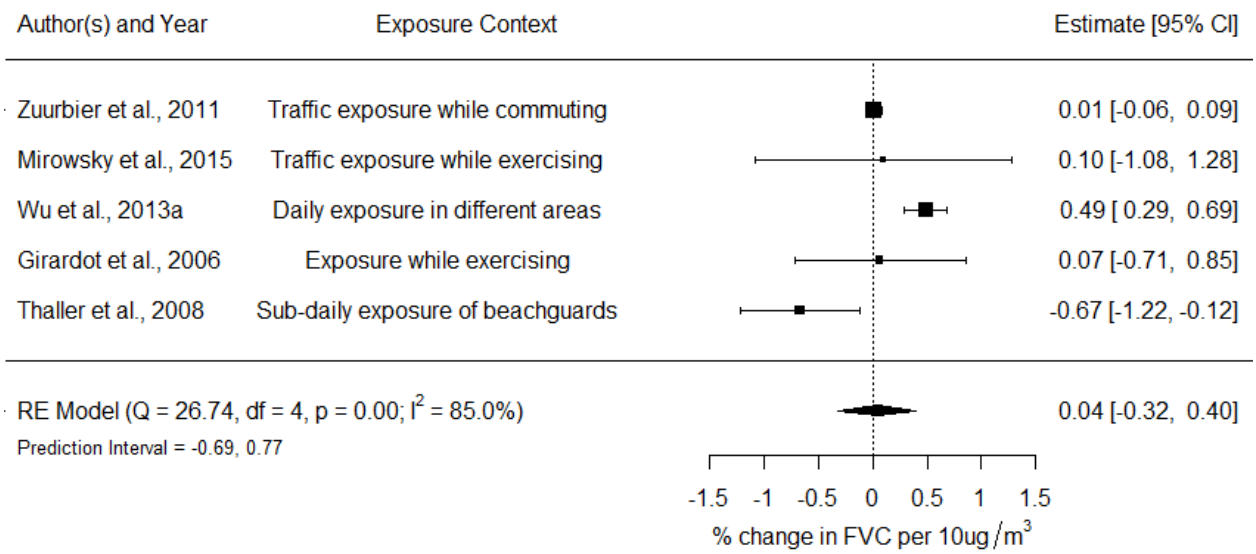

Figure S2: Meta-analyses of the association between environmental $PM_{2.5}$ and FVC (% change). Random-effect meta-estimate of association is indicated by vertical point of diamond and 95% CI is represented by horizontal point. Squares represent individual effect size of primary studies and the bars the 95% CI; size of squares is proportional to weight in calculating random-effect summary estimates.

Table S3: Quality assessment of the studies included in the meta-analyses.

Criteria	Low risk	Medium risk	High risk
Exposure assessment: List of major considerations: 1) Adequacy of the method of exposure assessment to detect individual exposures. Personal and quasi-personal measurements are preferred to central station measurements 2) Equipments and direct-reading instruments were well described in the methods and are suitable for the type of measurement aimed. **- Low risk:** There is high confidence that the exposure to particles is the true exposure. **- Medium risk:** There is incertitude if the exposure measured represents the true exposure to particles, or one of the listed considerations is not applied. **- High risk**: There is direct evidence of high risk of misclassification bias, or the two listed considerations are not applied	**Zuurbier et al. (2011); Gaughan et al. (2014); Weichenthal et al. (2011); Hao et al. (2017); Cole et al. (2018); Bakirci et al. (2007); Slaughter et al. (2004); Ulfvarson et al. (1990); Mirowsky et al. (2015); Huang et al. (2016); Hu et al. (2018); Mirabelli et al. (2015)**	Risk of exposure misclassification due to the use of respirators: **Fell et al. (2011)** Measurements were not personal: **Wu et al. (2013a); Matt et al. (2016); Herbert et al. (1994); Wu et al. (2013b)**; **Girardot et al. (2006)**; **Dales et al. (2013)**; **Thaller et al. (2008); Vilcassim et al. (2019)**	**Bakirci et al. (2006)** (exposure based on historical records). **Altin et al. (2002)** (measurements for 60 min, no information if exposure and health outcomes were measured concomitantly, no details about methodology)
Outcome assessment: Outcome assessment methods lack accuracy. List of major considerations: 1) Spirometry was performed by a trained technician. 2) Spirometry was performed according to an official guideline. **- Low risk:** We have confidence that the outcome assessment reflects the true value of the physiological outcome. **- Medium risk:** There is incertitude if the outcome assessment represents the true value of the physiological outcome measured, or one of the listed	**Zuurbier et al. (2011); Wu et al. (2013a); Gaughan et al. (2014); Bakirici et al. (2006); Weichenthal et al. (2011); Matt et al. (2016); Hao et al. (2017); Bakirci et al. (2007); Slaughter et al. (2004); Huang et al. (2016); Girardot et al. (2006); Dales et al. (2013); Thaller et al. (2008); Wu et al. (2013b); Hu et al. (2018)**	Tests were not performed by a trained person or there is no information about it: **Fell et al. (2011); Cole et al., 2018; Altin et al. (2002); Matt et al. (2016); Mirowsky et al. (2015); Vilcassim et al. (2019); Mirabelli et al. (2015)**	No information if test was performed by a trained technician and if procedure followed an official guideline: **Ulfvarson et al. (1990); Herbert et al. (1994)**

considerations is not applied. **-High risk**: There is direct evidence of high risk of misclassification bias, or the two listed considerations are not applied.			
Confounding bias: Study appropriately accounted for all important well studied potential confounders and modifiers in the design or in the statistical analysis: Important effect confounders and modifiers: individual variables (e.g. age, sex, BMI (or height and weight)), health status (asthma, COPD), smoking status, temperature. **-Low risk**: study accounted for all important categories of confounders and modifiers which were measured consistently. **-Medium risk**: study accounted for some but not all of confounders and modifiers, and this may introduce bias. - **High risk:** study did not account for potential confounders and modifiers OR were inappropriately measured	**Zuurbier et al. (2011); Matt et al. (2016); Hao et al. (2017); Huang et al. (2016); Wu et al. (2013b); Girardot et al. (2006); Weichenthal et al. (2011); Mirowsky et al. (2015); Dales et al. (2013); Herbert et al. (1994); Thaller et al. (2008); Hu et al. (2018)**	No adjustment for individual variable between subjects, although controlled for within subjects by design: **Wu et al. (2013a)** Occupational studies where it is not possible to differentiate co-exposure as cause of the effects: **Bakirci et al. (2006); Altin et al. (2002) ; Ulfvarson et al. (1990); Gaughan et al. (2014), Fell et al. (2011); Bakirci et al. (2007)** No adjustment for temperature: **Cole et al., 2018; Slaughter et al. (2004); Vilcassim et al. (2019); Mirabelli et al. (2015)**	
Selection bias: Does the selection of participants into the study was done in a manner that might introduce bias in the study? **-Low risk:** The descriptions of the studied population were sufficiently detailed and the risk of selection bias was minimal. **-Medium risk:** The description of the population is not complete or there is a possibility that the selection of the population may introduce bias. However, there is insufficient information about population to permit a judgment of high risk of bias. **-High risk:** There were indications from descriptions of the population of high risk of bias.	**Zuurbier et al. (2011); Wu et al. (2013a); Gaughan et al. (2014); Weichenthal et al. (2011); Matt et al. (2016); Hao et al. (2017); Cole et al. (2018); Slaughter et al. (2004); Altin et al. (2002); Mirowsky et al. (2015); Huang et al. (2016); Girardot et al. (2006); Dales et al. (2013); Thaller et al. (2008); Fell et al. 2011; Bakirci et al. (2007); Hu et al. (2018);**	Only male subjects: **Bakirci et al. (2006); Ulfvarson et al. (1990); Wu et al. (2013b)** Employment duration not described: **Slaughter et al. (2004); Bakirci et al. (2006); Herbert et al. (1994); Ulfvarson et al. (1990)**	

	Vilcassim et al. (2019); Mirabelli et al. (2015)		
Selective reporting: Selective reporting of outcomes or analyses. **-Low risk:** all of the studies pre-specified outcomes and findings were reported in the article or supplementary material **-Medium risk**: there was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report. **-High risk**: not all pre-specified outcomes and findings were reported, or at least one of the primary outcomes was assessed with other methods than the pre-specified one, or at least one of the reported outcomes was not pre-specified	**Zuurbier et al. (2011); Wu et al. (2013a); Weichenthal et al. (2011); Matt et al. (2016); Hao et al. (2017); Cole et al. (2018); Bakirci et al. (2007); Slaughter et al. (2004); Altin et al. (2002); Herbert et al. (1994); Ulfvarson et al. (1990); Mirowsky et al. (2015); Wu et al. (2013b); Girardot et al. (2006); Dales et al. (2013); Thaller et al. (2008); Bakirci et al. (2006); Huang et al. (2016); Hu et al. (2018); Vilcassim et al. (2019); Mirabelli et al. (2015)**		Regression models described in the methods but results not presented: **Gaughan et al. (2014); Fell et al. (2011)**
Conflict of interest: Potential source of bias in reporting through source of funding **-Low risk:** the study did not receive funding from an entity with financial interest in the outcome of study **-Medium risk**: there is insufficient information to judge for low risk, but indirect evidence suggests study was free of financial interest **-High risk**: study received support from an entity with financial interest in the outcome of study	**Zuurbier et al. (2011); Wu et al. (2013a); Gaughan et al. (2014); Bakirci et al. (2006); Weichenthal et al. (2011); Matt et al. (2016); Hao et al. (2017); Cole et al. (2018); Bakirci et al. (2007); Slaughter et al. (2004); Herbert et al. (1994); Mirowsky et al. (2015); Huang et al. (2016); Wu et al. (2013b); Girardot et al. (2006); Dales et al. (2013); Thaller et al. (2008); Hu et al. (2018); Vilcassim et al. (2019); Mirabelli et al. (2015)**	No information: **Altin et al. (2002); Ulfvarson et al. (1990)**	**Fell et al. (2011):** Funding from a possible interested organization (The European Cement Association)
Incomplete outcome data: Was incomplete data adequately addressed? **-Low risk:** no missing outcome data or missing data is	**Zuurbier et al. (2011); Wu et al. (2013a); Gaughan et al. (2014); Bakirci et al. (2006); Fell et al.**		

unrelated to true outcome **-Medium risk:** there was insufficient information about incomplete data to judge for low risk, but indirect evidence suggests that incomplete data may introduce bias. **-High risk**: missing outcome data is related to true outcome	**(2011); Weichenthal et al. (2011); Matt et al. (2016); Hao et al. (2017); Cole et al. (2018); Barkirci et al., 2007; Slaughter et al. (2004); Altin et al. (2002); Herbert et al. (1994); Ulfvarson et al. (1990); Mirowsky et al. (2015); Huang et al. (2016); Wu et al. (2013b); Girardot et., 2006; Dales et al. (2013); Thaller et al. (2008); Hu et al. (2018); Vilcassim et al. (2019); Mirabelli et al. (2015)**		

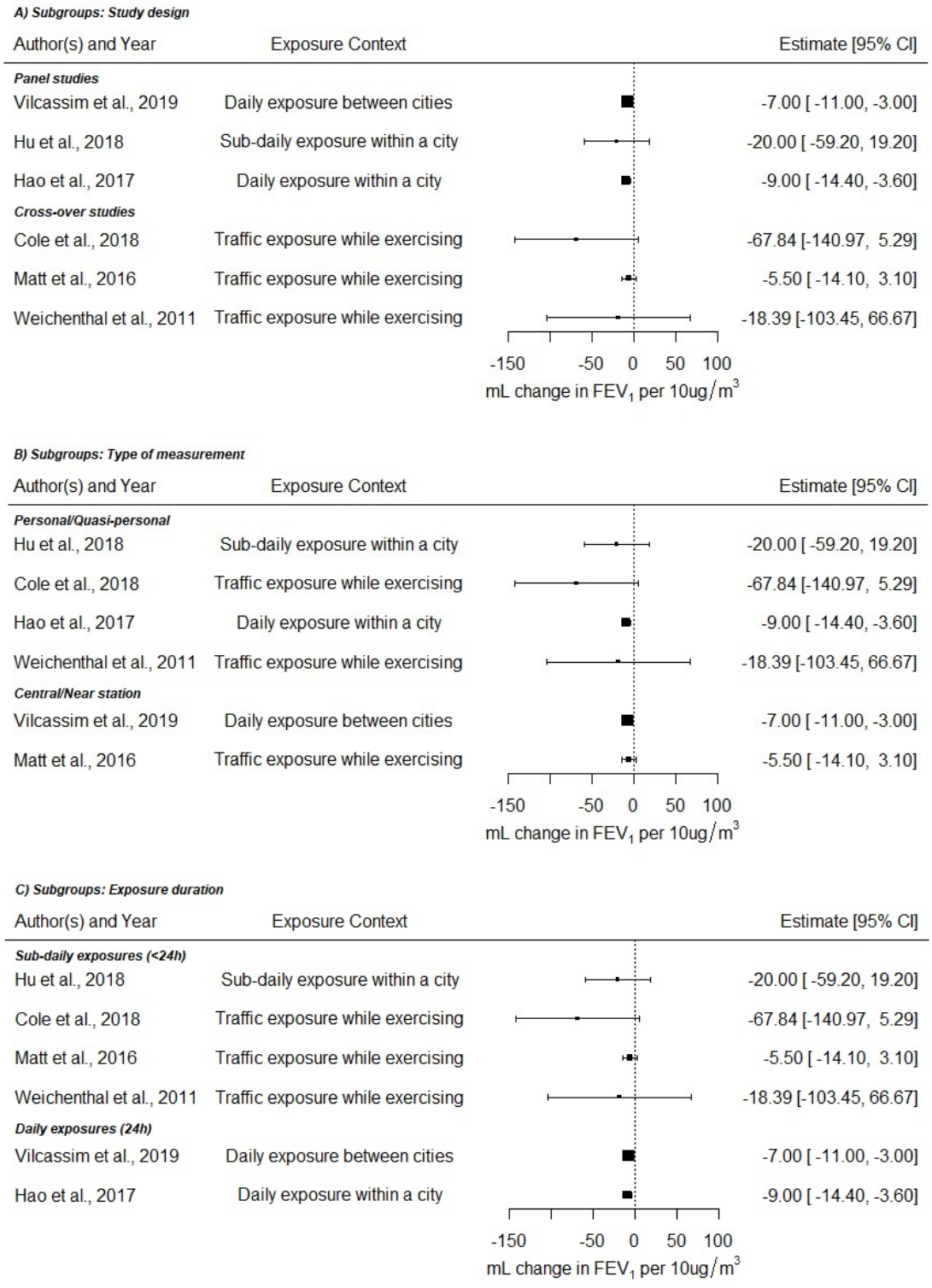

Figure S3: Forest plot of the association between environmental $PM_{2.5}$ and FEV_1 (mL change) grouped by (A) study design, (B) type of measurement and (C) exposure duration. Squares represent individual effect size of primary studies and the bars the 95% CI.

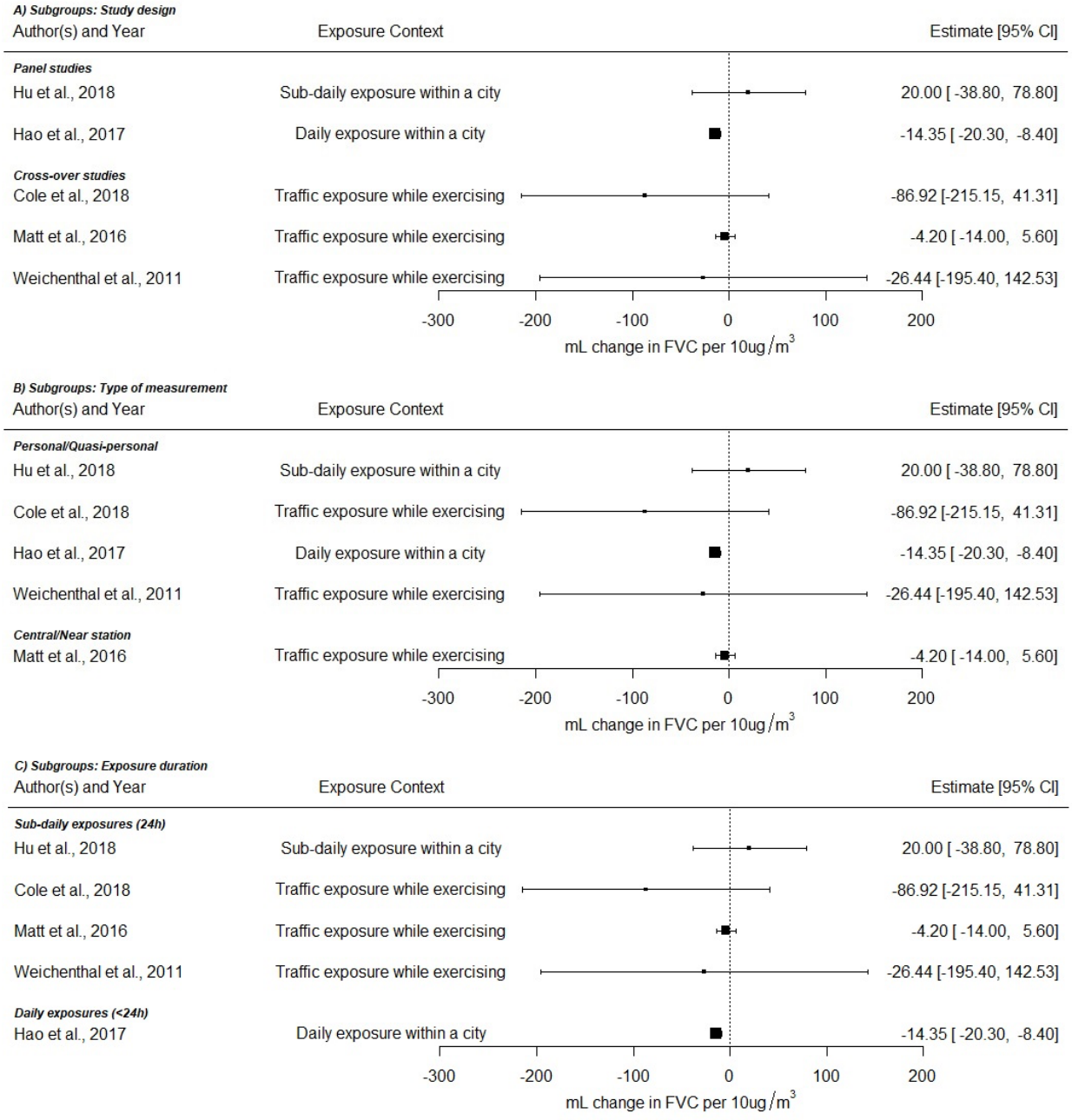

Figure S4: Forest plot of the association between environmental $PM_{2.5}$ and FVC (mL change) grouped by (A) study design, (B) type of measurement and (C) exposure duration. Squares represent individual effect size of primary studies and the bars the 95% CI.

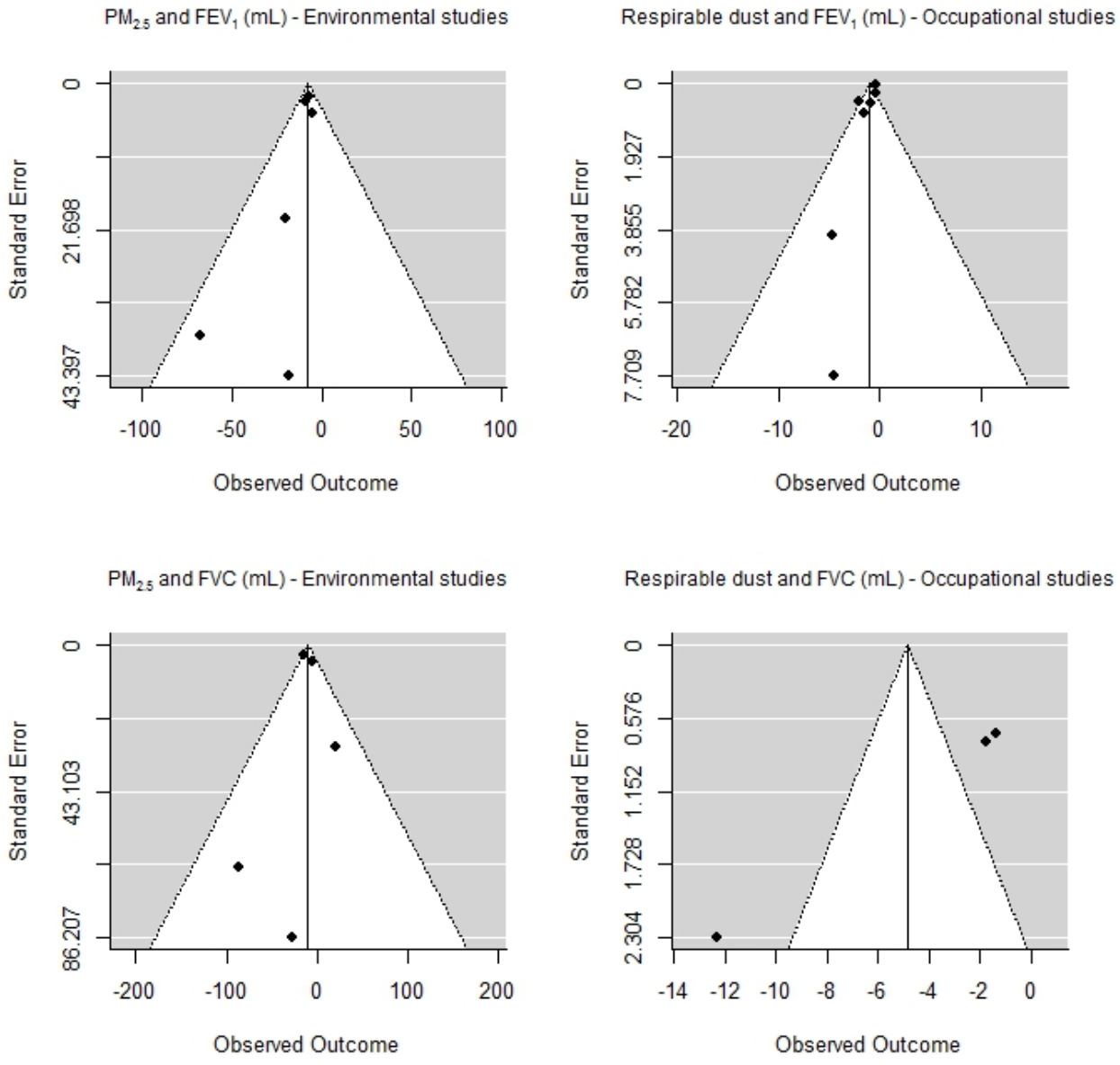

Figure S5: Funnel plots of FEV_1 and FVC (mL change) meta-analyses for environmental and occupational studies.

Chapter 8 - Discussion and Conclusion

A general discussion of the thesis is presented in the next sections of this chapter. At first, we discuss the results of the estimation of occupational levels of fine and ultrafine particles by a multi-metric sampling strategy (Chapter 5). Then, we focus on the assessment of the oxidative potential and oxidative burden from occupational exposures to particulate matter (Chapter 6). Next, the meta-analysis results associating environmental and occupational short-term exposures to fine particles and lung function are discussed. Finally, the limitations, contributions to the advancement of the knowledge and perspectives for future studies in the field are presented.

8.1 Estimation of occupational levels of fine and ultrafine particles by a multi-metric sampling strategy

As mentioned in Chapter 2, studies investigating levels of fine and ultrafine fractions of particulate matter in occupational settings are few and lack comparability in terms of sampling strategy to allow a general conclusion about workers' exposure. Therefore, the harmonization of sampling strategies, the measurement of exposure during multiple full work shifts, and the assessment of additional information related to the size distribution, metrics of exposure and the particles' composition in different workplaces is essential to generate more reliable and comparable data on exposure. These questions were initially addressed in the first article of Chapter 5, where we assessed the number concentration, mass concentration and carbonaceous components of diesel particulate matter in underground mines by an innovative sampling strategy that combines DRI and filter-based methods. Exposures in this environment were sourced by the presence of diesel-powered vehicles in a restricted and poorly ventilated space, which allowed us to assess the above-mentioned parameters and validate our sampling strategy in an environment considered a worst-case scenario compared to other workplaces with lower diesel exposure levels. Next, we extended the scope of these analyses in the second article of Chapter 5 by performing additional measurements in another mine, by including analyses such as the size distribution and transmission electron microscopy, and by expanding this sampling strategy to other workplaces with intermediate and low levels of exposure, namely a subway

tunnel and a truck workshop, respectively. Finally, as reported in Chapter 6, fine and ultrafine particles were also measured during welding and bricklaying activities in a construction trades school.

Levels of the respirable fraction of particulate matter in the three workplaces ranged from 13 to 2,190 μg/m^3, with the highest mean concentration found in the underground mines (521 μg/m^3). We found a strong and positive correlation between aerosols' mass concentration measured by the laser photometer and EC concentrations measured by the NIOSH 5040 method (i.e. the reference method for DPM). This result agrees with the study of Miller et al. (2007), and it suggests that the photometer can be an inexpensive and reliable method to estimate real-time DPM exposure when other sources of particulate matter are not present (78). However, although DRIs are interesting devices for ranking exposures and making an initial and immediate estimation of the exposures, this type of measurement is not specific and can be affected by aerosols from other sources. Thus, the calibration of laser photometers against a reference method should be performed for each workplace, and the use of a standard calibration factor is not recommended (79).

One exception regarding the non-specificity of DRIs for DPM measurement was the Airtec. We found strong and positive correlations between EC concentrations measured by the Airtec and the NIOSH 5040 method across all workplaces and comparable concentrations between these two methods in the underground mine. Since this instrument is specific for EC measurements, it could be used as an alternative and simpler method to the filter-based NIOSH 5040 method in the mining industry.

Work shift OEL for DPM are expressed as mass concentrations of the carbonaceous components, and they vary between and within countries. In Quebec, an OEL of 400 μg/m^3 of TC is implemented in the mining industry. The province of Ontario has a limit of 400 μg/m^3 of TC, which is transposable to EC via a conversion factor of 1.3 for the mining industry. In the USA, the U.S Mine Safety and Health Administration has prescribed an OEL of 160 μg/m^3 of TC, while in the European Union, a recent regulation was approved, and the OEL will be set at 50 μg/m^3 of EC for all diesel emissions, without distinguishing between sources or workplaces. Geometric means of TC and EC in our study were 174 μg/m^3 and 125 μg/m^3 in the underground mines, and they

were significantly higher than concentrations reported for the subway tunnel (TC= 59.1 μg/m^3; EC = 24.7 μg/m^3) and the truck workshop (TC = 16 μg/m^3; EC = 2.7 μg/m^3). Most of these TC measurements in the mines were lower than Quebec's OEL of 400 μg/m^3. Nonetheless, if our results are compared with the OEL of 50 μg/m^3 of EC recently approved in the European Union, 87.5% of EC samples would exceed the limit concentration in the underground mine. Moreover, CAREX Canada recommended that Canadian jurisdictions move towards an OEL based on EC of 20 μg/m^3 for the mining industry and 5 μg/m^3 for other workplaces (47). If compared with these values, all EC concentrations measured in the underground mine and the subway tunnel—as well as one-third of the truck workshop measurements—would be above recommendations. This indicates that, although regulations that are currently in place (i.e. Quebec's OEL of 400 μg/m^3 of TC) are generally being respected, many workplaces would have difficulties complying with the more restrictive OEL being currently discussed worldwide and more extensive actions for the control of emissions are needed.

The TC/EC ratio of 1.4 in the underground mine suggests that EC is an important part of DPM; this ratio is similar to the value reported in the literature for this workplace (80). In contrast, the ratios of 2.5 found in the subway tunnel and 8.7 in the truck workshop indicate a significant presence of OC in TC's mass. Such high ratios suggest non-diesel-related OC from other sources such as oil mist and environmental emissions (e.g. gasoline vehicles) that interfere with the characterization of DPM exposure (81, 82). These results support the idea that, due to interferences related to non-diesel OC sources, EC is a more reliable mass-based surrogate of exposure than TC to estimate diesel emissions.

The highest particle number concentration levels - measured by the P-Trak - were found in the underground mine (GM = 134,000 particles/cm^3) and are among the highest reported in the literature for occupational DPM exposure (54). These levels are comparable with those measured in environments with diesel-powered trains (126,000 particles/cm^3) and tunnel constructions (97,600 particles/cm^3) (52, 83). Particle number concentrations found in the subway tunnel and truck repair workshop (GM = 32,800 particles/cm^3 and 22,700 particles/cm^3, respectively) are comparable with concentrations found in a port facility (36,000 particles/cm^3) and for bus/tram drivers (between 10,000 and 24,000 particles/cm^3) (49, 84). EEPS/CPC ratios were 1.96, 1.24 and

1.24 for the underground mine, subway tunnel and truck repair workshop, respectively; indicating a significant difference between the particle number concentration reported by these instruments, especially for the underground mine. The size distribution, measured by the EEPS 3090, showed a bimodal distribution of particles with a small nucleation mode with a mean diameter of 10.8 nm and an accumulation mode where the agglomerates were concentrated. Results about particles' size were confirmed by the TEM analysis that showed individual carbon spheres between 10 and 56.5 nm organized in agglomerates. These results are in line with the findings of Burtscher et al. (2005), who reported that typical diesel particles are formed mainly by agglomerates of spherical primary particles between 15 and 40 nm and that the accumulation mode could be accompanied by a nucleation mode consisting of smaller particles (85). In addition, as reported in Chapter 6, although the number concentration during bricklaying activities was close to background levels, concentrations in the welding shop were 128,000 particles/cm^3. These levels are comparable to the ones measured in the mining industry, which indicates that very high concentrations of UFP are also emitted during welding activities. These concentrations are comparable to other studies that evaluated number concentration by CPC measurements during welding activities, where mean concentrations ranged between 67,000 particles/cm^3 and 171,000 particles/cm^3 (54, 86, 87).

The above-mentioned results from diesel emissions indicate that a significant portion of DPM emissions is in the ultrafine size range. As exposure to UFP is best captured by measuring number concentration, this could be a more appropriate metric to estimate the risks of DPM exposures than the current limits of exposure expressed in mass concentrations of EC and TC. This point is further discussed by Landwehr et al. (2020) that reported that although the introduction of new diesel engine technologies in the past years contributed to a reduction of around 90% of the mass concentration of EC, this had little to no impact on measured health effects; thus, limiting the feasibility of using mass-based limits for DPM. The authors completed by saying that additional limits, such as in particle number concentration, are needed for occupational exposures to DPM to be reliably monitored (88). Thus, future epidemiological studies should also consider using number concentration to assess associations with health effects. However, it is essential to note the limitation of the current particle counters, which may

contribute to the lack of routine measurements of ultrafine particles in industrial settings. Such limitations could be mitigated by the development of instruments specifically for the industrial hygiene context, such as portable instruments suitable for personal measurements, with the capacity of accurately measuring number concentration at very high exposure levels that are frequently found in industrial settings (i.e. above 100,000 particles/cm^3), and that are also able to measure particles smaller than 20 nm.

We also investigated topics that are complementary to the DPM sampling strategy presented in Chapter 5. The two studies resulted from these investigations are presented in the appendix of this thesis. In Appendix 1, we compared two methodologies to assess DPM in mines: the measurement of TC_1 with the correction for the vapor phase organic carbon (method currently recommended by the Mine Safety and Health Administration for regulations in the U.S.); and the measurement of the TC_R with field blank correction (method currently employed in some provinces of Canada, such as Quebec and Ontario). Significant differences between side-by-side TC_R and TC_1 samples were observed, while EC levels were not extensively affected by the different methodologies. This suggests that, as opposed to TC, using of EC as an indicator of DPM exposure could increase the comparability of exposure data between different workplaces and countries. In Appendix 2, we validated the use of a dual-port system for simultaneous sampling of DPM and crystalline silica, pollutants that are common in workplaces like underground mines and construction sites. While most tests supported the use of the dual-port for evaluating concomitant exposures, results also highlighted the possibility of filter overloading as a cause of flow rate changes. The collection of these particles using the same sampling train can minimize workers' physical burden (by using only one personal pump instead of two). This can also reduce sampling time and cost of analyses and ultimately promote exposure assessments. However, occupational hygienists should test the flow rates' stability under worst-case conditions before including the dual-port sampling system in an exposure assessment study.

As mentioned in Chapter 1, It is estimated that around 900,000 workers are exposed to particles from diesel engine exhaust in Canada, which is the second most common carcinogen that Canadians are exposed to (10). This justifies why the measurements and implementation of the sampling strategy from Chapter 5 were performed in these workplaces. However, high levels

of exposure to fine and ultrafine particles may occur in many other types of industries (57). For this reason, we also characterized exposures in a workplace with emissions of metallic particles, namely in two sectors of a smelting industry: a foundry and a machining shop (Appendix 3). Significant levels of particles - with mass and number concentrations higher than the subway tunnel but lower than the underground mine – were found, especially in the foundry. The size distribution, measured by the EEPS, showed that most of these particles were 10 nm and smaller. As mentioned in Chapter 5, the P-Trak cannot detect particles smaller than 20 nm, explaining why the values for ratios EEPS/P-Trak (i.e. 4.6 for the foundry and 3.8 for the machining shop) are much higher than the ones found for the diesel workplaces. These results are in line with the study of Jarvela et al. (2016) in a ferrochromium and stainless-steel production facility. The authors reported that the main mode of the size distribution of the particles emitted in this industry was below 10 nm (55). Thus, due to the risk of underestimating the number concentration in these workplaces, particle counters with the capacity of measuring particles smaller than 20 nm and that can quantify concentrations higher than 500,000 particles/cm^3 are suggested. However, as mentioned, DRI suitable for occupational hygiene measurements are limited.

8.2 Assessment of the oxidative potential and oxidative burden from occupational exposures to particulate matter

As mentioned previously, at present, occupational PM is regulated in terms of mass concentration (i.e. $\mu g/m^3$ or mg/m^3), and it has been historically used as a metric of exposure for associations with adverse health effects. This is usually done by selecting a specific size fraction of PM (i.e. respirable dust, $PM_{2.5}$) and/or by collecting and analyzing individual components that serve as surrogates of exposure (i.e. Fe, Mn and Cr for welding fumes; EC and TC for diesel emissions; crystalline silica). This strategy, however, does not provide an integrative measurement of multiple components or information regarding the synergistic interactions between chemical species; it also does not provide information on the potential toxicity of particles that may result from their oxidative potential. To address this gap, in Chapter 6, we evaluated the OP^{AA} and OB^{AA} from occupational exposures to PM, including the comparison between workplaces, activities, sampling strategies and size fractions.

To our knowledge, this was one of the few studies that assessed the oxidative potential of occupational PM. Significant levels of OP^{AA} and OB^{AA} were observed, especially in the welding shop where particulate concentrations up to 6,030 $\mu g/m^3$ resulted in OB^{AA} median levels 3.6 times higher than in the construction site. However, comparing these results with other studies is difficult due to the different OP techniques reported in the literature and the lack of standardization of the methods. Some of these challenges include the use of different types of assays (i.e. cellular versus acellular), antioxidants (i.e. AA, GSH and DTT), units of depletion (i.e. % depletion/µg versus pmol/min/µg) and incubation medium (i.e. RTLF versus single antioxidant). Because of these methodological differences, our results could not be quantitatively compared with other occupational studies which used a different method (62, 89).

Nonetheless, the methodology used in our study - namely the acellular OP^{AA} assay in synthetic RTLF – passed by an inter-laboratory validation and is comparable to the technique employed in some environmental studies (90-92). These environmental OP^{AA} values were generally within the same range reported in our study for the construction activities but lower than those measured in the welding shop, indicating that metallic particles from welding fumes can have a higher oxidative potential compared to particles from the general environment. Interestingly but not surprisingly, OB levels from both workplaces – driven by the higher PM concentrations, especially in the welding shop – considerably exceeded those from environmental studies by more than 100x.

The comparison of size fractions showed no difference in terms of oxidative potential between $PM_{2.5}$ and PM_4. This result is in line with the findings of Sauvain et al. (2016), who reported that 97% of the oxidative potential of PM_4 was already present in the $PM_{2.5}$ fraction (62). However, it is suggested that smaller size fractions - namely the ultrafine size range - may be associated with a highest potential of ROS generation and oxidative stress due to their high number and surface to mass ratio compared to larger particles (93). Thus, results found for $PM_{2.5}$ and PM_4 should not be extrapolated to other size fractions that were not evaluated in our study (e.g. PM_1).

The sampling strategy (i.e. personal versus area) also did not influence the values of OP^{AA}. However, we found higher OB levels from personal samples - driven by the higher mass

concentration - compared to area samples in the welding shop. This suggests that some particles collected by the personal samplers were not captured by the area samplers. Also, although the distance from the source did not influence the oxidative potential of the particles, it may have influenced the mass concentration of the particles and, consequently, the OB levels. In this regard, Cena et al. (2016) have demonstrated that the mass concentration of particles from welding fumes significantly decreases as the distance from the welding source increases (94).

Although exposure to PM from diesel emissions was extensively studied in this thesis, the oxidative potential of diesel particles was not evaluated. This information can be retrieved from the results of studies in ambient and chamber conditions that have been reviewed by Bates et al. (2019). The authors found that the OP^{DTT} from diesel sources is comparable to values from other environmental sources such as traffic, biomass burning and gasoline (i.e. between 10 and 100 ρmol/min/µg) (15). While these studies were not conducted in real occupational contexts, their results suggest that - at least for OP^{DTT} – occupational diesel particles could also have an OP comparable to environmental sources. As reported in Chapter 5, the mass concentration of $PM_{2.5}$ in the mining industry (i.e. 486 µg/m^3) is around 30 times higher than what is considered a typical urban background. Since the OB is a product of the OP and the mass concentration, this marker would also be expected to be the same magnitude higher in the mines than environmental values.

Our study suggests that the OP can be an important tool in the process of hazard identification, while OB can be used as an indicator of risk that combines an indicator of hazard (i.e. OP) and the levels of exposure (i.e. PM concentration). Thus, OP and OB can be used to guide the decision-making process about control strategies in industrial hygiene. In this regard, Martin et al. (2019) evaluated the oxidative potential of PM from biodiesel versus petroleum diesel emitted from a non-road heavy-duty engine. The authors found that the biodiesel particles had lower OP, suggesting that the substitution of petroleum diesel to biodiesel may reduce risk to human health (95). Besides, these assays could be used in future occupational epidemiological studies as exposure metrics to explore associations between PM and respiratory outcomes; thus, supplementing the information currently given by associations with mass concentration alone. Besides, since these assays evaluate the potential of PM in generating reactive oxygen species,

which can also trigger inflammatory processes, they can be used to investigate the associations with biomarkers of effects related to these mechanisms, such as FeNO for lung inflammation or 8-hydroxy-2'-deoxyguanosine (8-OHdG) for oxidative damages in the DNA. Finally, these indicators could be used to compare exposure levels from particles of different compositions.

8.3 Associations between daily and sub-daily PM exposures with lung function

By performing a systematic review and meta-analysis, Chapter 7 of this thesis investigated the associations currently reported in the literature between short-term (i.e. daily and sub-daily) exposures to fine particles and its acute respiratory effects, namely the lung function parameters FEV_1 and FVC.

Results showed that, for occupational studies, an increment of 10 $\mu g/m^3$ of PM_4 was associated with a reduction of 0.87 mL (95% CI: -1.36 to -0.37 mL) in FEV_1. A similar tendency was observed for associations with FVC. Although distinct sources of PM exposure were present (e.g. particles from cement, diesel cotton and wood), the fact that only a moderate heterogeneity of the meta-estimate was found (i.e. $I^2 = 54\%$) suggests consistency of the association across varying particulate types. For environmental studies, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ exposure was associated with a FEV_1 reduction of 7.62 mL (95% CI: -10.62 to -4.63 mL). Although the results of the individual environmental studies were more inconsistent compared to occupational studies, this meta-estimate is in line with another recent meta-analysis that showed a reduction of 7.02 mL (95% CI: -11.75 mL to -2.29 mL) in FEV_1 after short-term environmental exposures to $PM_{2.5}$ in healthy adults (96). Thus, for a similar exposure increment, a significantly stronger effect was observed in environmental studies compared to occupational studies. However, it is important to note that total daily declines in individuals' lung function can be more significant in occupational settings because exposure levels to fine particles in the workplace are substantially higher than in the general environment. Two hypotheses may explain the 10-fold difference in the magnitude of the occupational and environmental meta-estimates of FEV_1 for the same exposure increment. Firstly, this difference may reflect the distinct characteristics between occupational and environmental studies, notably in the composition of particles due to the varied sources of ambient versus workplace exposures, size fraction (i.e. $PM_{2.5}$ versus PM_4), sampling strategy (i.e. personal monitoring versus central station), study design (i.e. cross-shift versus

panel studies), study population (i.e. sex and smoking status), exposure duration (i.e. daily versus hourly) and the healthy worker effect (97). However, although these factors may explain a portion of the observed difference, they may not fully explain the almost 10-fold difference between both meta-estimates. In this regard, another hypothesis may be related to the difference in the range of PM concentrations between occupational (i.e. between 270 $\mu g/m^3$ and 2,390 $\mu g/m^3$) and environmental (i.e. between 2 $\mu g/m^3$ and 146.5 $\mu g/m^3$) studies. This could indicate a potential nonlinear relationship linking PM exposure to lung function, with a steeper slope at lower concentrations (i.e., environmental exposure) that may flatten in the higher ranges, as observed in some mortality studies with ambient fine particles (98, 99). Biologically, this could indicate that high short-term exposure levels – such as observed in occupational studies – could lead to the saturation of cellular and biochemical mechanisms involved in acute lung inflammation and oxidative stress, resulting in a plateau in the exposure-response relationship at these concentrations (99, 100).

To our knowledge, this was one of the first studies to separately calculate and compare meta-estimates for the associations between occupational and environmental exposures to PM and respiratory health effects. In our understanding, occupational and environmental exposures to particles are not entirely independent fields but areas that overlap in many aspects; thus, these results can have important public health implications. For instance, for the general population, results indicate that healthy individuals are susceptible to acute respiratory responses after daily and sub-daily environmental exposures during everyday situations. For the workers' population, results suggest that cross-shift declines in lung function occur at current exposure levels.

8.4 Limitations

The studies in this thesis also had some limitations. In Chapter 5, mostly area measurements were performed. Although this strategy is adequate for comparing several surrogates measured with different instruments, these concentrations may not be representative of the personal exposure of workers. Secondly, the influence of several determinants of exposure (i.e. ventilation systems, vehicles and fuel types) could not be estimated. Finally, we did not use a dynamic blank to correct the vapor phase OC, which may overestimate TC concentrations.

Regarding Chapter 6, although a general characterization of the metals from a few samples was performed at each workplace, we could not determine the elemental composition of all individual samples, which precluded us from correlating the OP^{AA} with individual chemical species. Furthermore, the ascorbate assay - which only identifies elements that react with this antioxidant - was the only technique used to measure the oxidative potential. In this context, the OP^{GSH} is also sensitive to metals and could complement the information given by the OP^{AA} assay. Furthermore, OP^{DTT} is also sensitive to organic components like quinones, PAHs and organic carbon and could be used to assess the OP of occupational exposures from combustion sources (i.e. diesel) (15). Thus, future studies would also benefit from evaluating additional acellular tests, especially when comparing different settings or with multiple sources of exposure.

Finally, in Chapter 7, although the comparison between environmental and occupational studies was possible because these studies share a comparable population (i.e. healthy adults), exposure duration (i.e. hourly exposures), and PM size fractions (i.e. fine particles and respirable dust), the tasks and processes which workers are subjected to are not present in the general environment. In addition, levels of exposure, study designs and statistical methods also differ. To account for this limit in comparability, we have presented separate estimates for environmental and occupational studies. Second, the impacts of PM composition were not assessed by this systematic review and meta-analysis. In addition to the size fraction and concentration, the particles' composition is also involved in the development of adverse effects and could explain some of the heterogeneity among study results. Finally, several studies – especially in the environmental area – could not be pooled in the meta-analysis. This limitation can be explained by the different units of outcomes (i.e. mL change, % change, log % change, % change from predicted value and log % change from predicted value) reported by the studies, which resulted in a small number of estimates per category in our meta-analyses. This also precluded us from exploring in depth the impact of important factors that could also influence associations, such as the types of measurements (i.e. personal versus central station measurements), study designs (i.e. panel versus crossover versus cross-shift studies) and exposure sources. Thus, future studies could benefit from standardization on the report of the outcome units.

8.5 Contributions to knowledge and suggestions for future studies

Despite these limitations, the studies in this thesis resulted in important contributions to the knowledge in the field. Firstly, our sampling strategy enabled us to accurately characterize fine and ultrafine particles emitted in the workplaces regarding number and mass concentrations, size distribution, morphology, and chemical composition. To our knowledge, the study presented in Chapter 5 is the first to provide such an extensive assessment of occupational exposures to fine and ultrafine particles using a comprehensive sampling strategy in different workplaces. For the ultrafine fraction, the reported results add important information in terms of number concentration and size distribution to the limited literature available regarding measurements in real work conditions and can guide the design of future studies and interventions to reduce occupational exposure. For mass concentration, specifically for the mining industry, our results support the argument that EC should be considered in regulations as the marker for DPM exposure in opposition to TC, which is currently regulated in Quebec and other Canadian provinces. Secondly, results of the oxidative potential and oxidative burden, which indicated levels higher than what is found in environmental studies, were unique for an occupational context. The important contrasts observed between settings suggest that this technique – which integrates mass concentration and particle composition in a single exposure metric - can be implemented in future sampling strategies to complement the information regarding occupational exposure assessment to particles currently given by mass concentrations alone. Finally, the systematic review and meta-analysis contributed to the understanding that daily and sub-daily occupational and environmental exposures to fine particles can result in declines in lung function at current exposure levels. Together, this thesis' findings converged to a better and broader understanding of workers' exposure to fine and ultrafine particles and their respiratory health effects.

The contributions generated by this thesis can be expanded in future studies. For instance, panel studies with repeated measurements across different days could also be developed for occupational settings to further explore the relationship between exposures during work shifts and respiratory effects. This type of study design would be fundamental to understand how occupational exposures across different days (i.e. with different lags for effects)

impact the duration and transience of lung function reductions in workers. In addition, associations with particle number concentration, oxidative potential and oxidative burden – currently not explored by occupational epidemiological studies – could complement the information regarding associations given only by mass concentration and further improve our knowledge about occupational exposures to particulate matter and respiratory health effects.

8.6 Conclusions

The work presented in this thesis showed that workers are exposed to important levels of fine of and ultrafine particles, especially for mining, smelting and welding activities where mass and number concentrations highly exceed the levels from other workplaces and where airborne particles are largely dominated by the ultrafine fraction. Also, these particles can have an important oxidative potential, namely welding particles, and - when combined with the high levels of exposure - result in an oxidative burden that is much higher than what is observed in environmental studies. Additionally, daily and sub-daily occupational and environmental exposures differ in terms of health risks for a similar exposure increment but are both associated with respiratory health effects described in terms of lung function declines. Given the magnitude of the levels of fine PM and UFP, their oxidative potential and health effects, it is concerning that these particles are not systematically monitored in the workplace. Based on our results, improvements in industrial hygiene practices and the surveillance of exposure to fine and ultrafine particles in the workplace are needed to control and limit potential health risks of daily exposures to these contaminants.

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Appendix

Appendix 1: Comparison between personal sampling methodologies for evaluating diesel particulate matter exposures in mines: submicron total carbon corrected for the adsorption of vapor-phase organic carbon versus respirable total carbon

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A1. 1 Abstract

In the mining industry, personal measurements of elemental and total carbon are frequently used as surrogates of diesel particulate matter (DPM) exposure, and the respirable or submicron fractions are usually measured. However, vapour-phase organic carbon (OC) can be adsorbed in the filters, interfering with total carbon results. This study presents a comparative evaluation between the submicron fraction of DPM concentrations corrected for the adsorption of the vapor-phase OC (dynamic blank), and the respirable fraction of DPM corrected for a field blank. Respirable and submicron fractions of total carbon (TC_R and TC_1) and elemental carbon (EC_R and EC_1) concentrations were sampled in parallel, in the workers' breathing zone, in an underground gold mine. A total of 20 full-shift personal samples were taken for each size fraction. Field blanks were collected each day for both the submicron and respirable fractions, while dynamic blank correction was also applied for the submicron fraction. TC_R presented a larger and statistically different geometric mean concentration compared to TC_1 (98 µg/m^3 versus 72 µg/m^3; p=0.01), while the concentrations of EC_R and EC_1 were not statistically different (58 µg/m^3 versus 54 µg/m^3; p=0.74). Average TC_R/EC_R ratio was 1.7, while the TC_1/EC_1 ratio was 1.3. In addition, 93% of EC had an aerodynamic size lower than 1 µm, while the proportion of TC particles in the submicron fraction was lower (73%). Finally, a similar quantity of OC was found when analysing the dynamic and field blanks of the filters with the submicron fraction selective size (24 µg and 22 µg, respectively). In conclusion, this study suggests that the differences in TC may be explained by the different aerodynamic fractions of DPM collected. In addition, elemental carbon measurements did not seem to be extensively affected by the aerodynamic size of the particles collected.

Keywords: Diesel Exposure, Elemental Carbon, Total Carbon, DPM, mining industry

A1. 2 Introduction

Short-term exposure to diesel exhaust (DE) has been associated with pulmonary inflammatory response, eye irritation, nasal irritation and cardiovascular effects (1-3). In addition, epidemiological studies have evaluated the association between long-term exposure to DE and increased lung cancer risk (4, 5). DE refers to the complex mixture of chemical substances found in solid, liquid or gaseous states resulting from the incomplete combustion of diesel fuel. Diesel particulate matter (DPM) is the particulate phase of DE and it is primarily composed of elemental carbon (EC) and onto which organic carbon (OC) compounds and other particles (unburnt fuel, lubricant droplets, metallic additives, etc.) are adsorbed. The sum of the elemental carbon and organic carbon is defined as total carbon (TC = EC + OC).

Occupational exposure limits (OEL) for DPM vary. In Quebec, a limit value of 400 $\mu g/m^3$ of total carbon (TC) is implemented in the mining industry (6). The Canadian province of Ontario also has a regulatory time-weighted limit value of 400 $\mu g/m^3$ of TC transposable to EC via a conversion factor of 1.3 (i.e. about 310 $\mu g/m^3$ for EC) for the mining industry (7). However, changes for an 8-h OEL of 160 $\mu g/m^3$ of TC have been proposed (8), based on the U.S. Mine Safety and Health Administration 8-h OEL of 160 $\mu g/m^3$ of TC (9).

Monitoring strategies for DPM measurement can involve a size-selective sampler to measure TC and EC levels based on the National Institute for Occupational Safety and Health (NIOSH) method (NIOSH 5040) (10). In this context, the respirable and submicron fractions can be sampled to avoid interferences from carbonaceous dust with larger aerodynamic size. The respirable fraction can be collected using a cyclone, while the submicron fraction, in addition to the cyclone, can be sampled by using a precision jeweled impactor.

Quartz fiber filters (QFFs) are used to sample DPM according to the NIOSH 5040 method. However, QFFs have been found to adsorb vapor-phase organic carbon, which derives from sources other than DPM such as oil mist and environmental tobacco smoke (11-13). This vapor-phase organic carbon is not traditionally recognized as part of DPM. As indicated by Noll et al. (2007), the adsorbed vapor-phase organic carbon can be a positive bias in TC results. Thus, a tandem filter correction procedure for taking into account this phenomenon was proposed. DPM cassettes (SKC Inc.) include tandem QFFs for correction purposes. Noll et al. (2007) demonstrated

that, when sampling in an area not contaminated with DPM, the two filters collected approximately the same amount of vapor-phase OC since, for 92% of the samples, the concentration of OC on the second filter did not exceed by more than 5 µg/m^3 the concentration on the first (11). In this tandem filter correction procedure, the first filter (QFF1) collects the DPM and the vapour phase OC while the second tandem filter (QFF2) collects only the vapour phase OC, and therefore constitutes a dynamic blank. The difference between TC concentrations (TC(QFF1) - TC(QFF2)) represents the TC associated with the DPM.

Different strategies for DPM sampling are thus described in the literature. These strategies can include the measurement of the respirable fraction of DPM with the use of field blanks (14-16) or the measurement of the submicron fraction of DPM with a dynamic blank correction (11, 17). However, according to the author's knowledge, no study has been carried out to compare these different strategies and their impact on the assessment of DPM concentrations. Thus, the present paper presents a comparative evaluation between submicron total carbon concentrations corrected for the adsorption of vapor-phase organic carbon, and respirable total carbon concentrations corrected for a field blank.

A1. 3 Methods

The present study was performed in an underground gold mine in Quebec, Canada. The mine operates at a maximum depth of around 1,700 m below the surface and the presence of off-road, diesel-powered mobile machinery contributes to workers' diesel exposure.

Respirable and submicron fractions of total carbon (TC_R and TC_1, respectively) and elemental carbon (EC_R and EC_1, respectively) were sampled in parallel in an underground gold mine. For the respirable fraction, Dorr-Oliver nylon cyclones were used with 25-mm QFF cassettes to collect particles with a 4 µm cut-point in the aerodynamic diameter. For the submicron fraction, 37-mm QFF cassettes equipped with jeweled impactors (SKC Inc, Eighty-Four, PA, USA) were used in addition to cyclones to collect particles with a 0.8 µm cut-point in the aerodynamic diameter. To achieve these cut-points, GilAir pumps (Sensidyne, LP, St. Petersburg, FL, USA) set at a flow rate of 1.7 L/min were used.

A total of 20 full-shift personal samples were taken for each method. Side-by-side personal samples were taken in the workers' breathing zone during their full shift (between 8 and 10 hours). The pumps were calibrated before and after each sampling period using a DryCal volumetric flow meter (Mesa Labs Inc., Lakewood, CO, USA). Samples were analyzed by the laboratories of Galson (Ontario, Canada) following the NIOSH 5040 method (10). Field blank samples were collected each day for both submicron and respirable fraction methods, while dynamic blank correction was also applied for the submicron fraction.

Results are expressed as geometric mean (GM) and geometric standard deviation (GSD). The statistical difference between the respirable and submicron fractions of TC and EC concentrations were assessed by the Student's T-test. A linear regression analysis was used to evaluate the relationship between respirable and submicron concentrations. The Pearson correlation coefficient was computed for each association.

This project was approved by the Ethics Committee for Health Research of the University of Montreal (Project Number: 16-057-CERES-D).

A1.4 Results

Table 1 presents the concentrations, for each worker, of the submicron and respirable fractions of total carbon and elemental carbon. The mean sampling duration was 566 minutes per worker. The samples covered several job titles like truck operators, load haul dump (LHD) operators and boom truck operators. The GM concentration of TC_R was 98 µg/m^3, while the GM concentration of TC_1 was 72 µg/m^3. In addition, the GM concentration of EC_R was 58 µg/m^3, while the GM of EC_1 was 54 µg/m^3. The analysis of the data shows that the mean concentrations of personal TC_R and TC_1 were statistically different (p=0.01). However, the mean concentrations of personal EC in both fractions were not statistically different (p=0.74). The average ratio between respirable TC and EC (TC_R/EC_R) was 1.7, while the average ratio between submicron TC and EC (TC_1/EC_1) was 1.3.

By comparing the values of the respirable fractions of both indicators with their respective values of the submicron fraction, results suggest that 73% of TC measured was in the submicron

fraction, while 93% of the respirable EC had an aerodynamic size lower than 1 µm. Results of the linear regression (Figure 1) confirm these values. In addition, the Pearson correlation coefficient for the EC association was 0.89, while the Pearson correlation coefficient for the TC association was 0.85, indicating strong and positive relationships.

The six QFF filters of the three 37-mm QFF cassette field blanks (submicron fraction) were analyzed for OC quantity. Average OC on these filters was 22 µg (ranged from 14 to 32 µg). Comparatively, average OC measured in the dynamic blank of the 20 personal sampling cassettes was 24 µg (ranged from 16 to 47 µg). There was no statistical difference between both quantities of OC (T-test; p=0.473).

A1. 5 Discussion

This study compared two different methodologies for assessing DPM in mines: the measurement of submicron total carbon with the correction for the vapor-phase organic carbon (method currently recommended by the Mine Safety and Health Administration (MSHA) for regulations in the US), and the measurement of the respirable fraction of total carbon with field blank correction (method currently employed in some provinces of Canada, such as Quebec and Ontario). Significant differences between side-by-side TC_R and TC_1 samples were observed, with higher GM concentrations reported for the respirable fraction. These differences could be attributed to the size selection and also to the correction for the adsorption of vapor-phase organic carbon. However, the six filters of the three 37-mm QFF cassettes used as field blanks for the submicron fraction presented quantities of OC that were comparable to the ones measured by the dynamic blank of the 20 personal 37-mm QFF sampling cassettes (submicron fraction). This result suggests that the main difference observed between side-by-side measurements would be mostly due to the size-selective sampler (the jewelled impactor) removing a significant fraction of TC. However, EC levels do not seem to be significantly affected by the size-selective sampler, which suggests that EC is most largely related to submicron particles. In consequence, we estimated that in our study 93% of EC had an aerodynamic size lower than 1 µm, while the proportion of TC in the submicron fraction was lower (73%).

In addition to the mean concentration of TC, the ratio TC/EC is also higher for the respirable fraction compared to the submicron fraction (1.7 versus 1.3). These values are in accordance with ratios provided in other studies with personal measurements of DPM. In this regard, Debia et al. (2017) reported an average TC_R/EC_R ratio of 1.8 in 120 personal samples collected in two underground mines in Quebec (14). In addition, the ratio TC_1/EC_1 of 1.3 found in this study is very similar to the value of 1.27 reported by Noll et al. (2015) (18). Furthermore, Fleck et al. (2018) also performed parallel measurements of both submicron and respirable fractions of DPM (15). The authors reported a TC_R/EC_R ratio of 1.50 and TC_1/EC_1 ratio of 1.37. However, the comparability with the present study is limited because the authors performed ambient measurements and the samples were not corrected for the vapor-phase OC in the above-mentioned study.

Both the higher mean concentration of TC_R and the higher TC/EC ratio in the respirable fraction reinforces the hypothesis that the measurement of the respirable fraction is more susceptible to the influence of OC than the methodology used for the submicron fraction analysis. However, we have shown that the correction for the vapor phase OC by the dynamic blank was not a significant correction in our study design compared to the field blank samples. This suggests that the added TC_R is attributable to OC associated with particles, but this study was not designed for identifying the sources of the OC contributing to the additional TC collected in the respirable fraction.

Finally, our results suggest that exposure data expressed in TC concentrations depends on the sampling strategy used, but exposure data expressed in EC concentrations could be comparable regardless of the sampling strategy used.

A1.6 Conclusion

In conclusion, the present study showed a difference in the concentrations of total carbon between the respirable and submicron fractions. Organic carbon levels in the dynamic blank were similar to the levels found in the field blanks, suggesting that the differences in the concentrations of total carbon may be explained by the different aerodynamic fractions of DPM

collected. In addition, elemental carbon measurements did not seem to be extensively affected by the aerodynamic size of the particles collected.

A1.7 Contributions

ASF contributed to the study design, measurements, data analysis and manuscript preparation. CC, PER, VC and RT contributed to the measurements. GL contributed to the study design and implementation. MD contributed to the study design and preparation of the manuscript.

A1.8 References

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A1.9 Tables and Figures

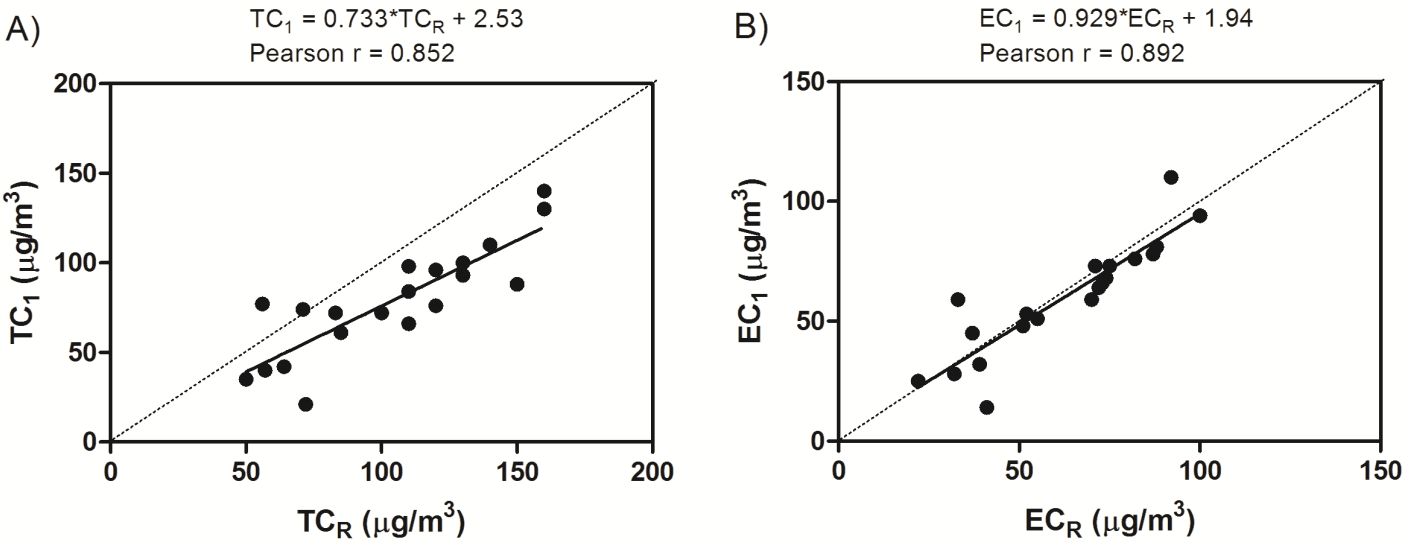

Figure 1: Relationship between TC_1 and TC_R (A), and EC_1 and EC_R (B) concentrations. Dotted lines represent a slope = 1. Solid lines represent the linear model.

Table 1: Concentrations of TC and EC (μg/m^3) for the respirable and submicron fractions.

Worker	Job Title	TC (μg/m^3) Respirable Fraction*	TC (μg/m^3) Submicron Fraction**	EC (μg/m^3) Respirable Fraction*	EC (μg/m^3) Submicron Fraction**
1	Truck Operator	83	72	52	53
2	LHD Operator	110	98	74	68
3	Buggy Operator	56	77	33	59
4	Truck Operator	57	40	32	28
5	Buggy Operator	130	93	87	78
6	Boom Truck Operator	120	96	88	81
7	LHD Operator	110	66	73	66
8	LHD Operator	64	42	39	32
9	Truck Operator	72	21	41	14
10	LHD Operator	160	140	92	110
11	Safety Advisor	140	110	82	76
12	Hammer Operator	130	100	75	73
13	Buggy Operator	150	88	71	73
14	Long Hole Blaster	100	72	51	48
15	Rock Bolter Operator	160	130	100	94
16	LHD Operator	50	35	22	25
17	Truck Operator	85	61	55	51
18	LHD Operator	110	84	72	64
19	LHD Operator	71	74	37	45
20	Boom Truck Operator	120	76	70	59
GM (GSD)		98† (1.5)	72 (1.6)	58 (1.6)	54 (1.7)

* Respirable fraction corrected with a field blank; ** Submicron fraction corrected for the adsorption of vapor-phase organic carbon

† p=0.01 compared to TC-submicron fraction. Student's T-test.

Appendix 2: Parallel personal measurements of diesel engine exhaust and crystalline silica using dual sampling port

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A2.1 Abstract

Diesel engine exhaust (DEE) and crystalline silica exposures occur simultaneously in the mining industry, and occupational sampling campaigns can be time and cost-consuming. The authors evaluated a dual-port system for simultaneous sampling of DEE and crystalline silica in laboratory and field conditions. Laboratory tests evaluated the operation of pumps during 8 h sampling and the intensity of the flow variation for various filter loading conditions and for different modes of operation. Field validation was performed in an underground mine. Pumps operated in constant flow or constant pressure modes. Tests in constant flow mode showed that when the flow rate increased on one side of the system, it decreased on the opposite side according to the loading intensity. Tests in constant pressure mode showed that flow rates systematically decreased when using loaded cassettes. However, the higher the backpressure setting, the lower the flow variation was. Flow variations during field tests were generally within the acceptable ±5% range. However, significant flow variations were identified in higher concentrations. A significant negative correlation was found between flow rate variation and total carbon concentration. While the majority of tests support the use of the dual-port for evaluating concomitant exposures, results highlight the possibility of filter overloading as a cause of flow rate changes.

Keywords: Crystalline silica; Diesel engine exhaust; Dual-port; Mining; Monitoring

A2.2 Introduction

Diesel engine exhaust (DEE) and crystalline silica are contaminants of concern regarding workers' health. Since 1997, crystalline silica has been classified as a human carcinogen (Group 1) by the International Agency for Research on Cancer (IARC) (1). Exposure to this contaminant increases the risk of bronchopulmonary cancer and is associated with occupational diseases such as silicosis. In addition, since 2012, DEE has also been classified as a human carcinogen (Group 1) by the IARC. Exposure to these fumes increases the risk of lung cancer and may increase the risk of bladder cancer (2). DEE and crystalline silica are the second and third most commonly known and suspected carcinogens that Canadian workers are exposed to and the first and second most common in the mining industry (3). Maintaining good air quality in order to minimize exposure to these contaminants is therefore a major issue for the exploitation and sustainable development of mines.

In June 2016, following a regulatory amendment to the Regulation Respecting Occupational Health and Safety in Mines in Quebec, the indicator used to assess DEE exposure changed from respirable combustible dust (RCD) to total carbon (TC) (4). Until then, it was possible to measure RCD and crystalline silica from the same sampling filter using the CANMET SOP 2703 method (5). However, it is no longer the case with the NIOSH 5040 method for TC quantification (6). Because of this regulatory modification, two separate sampling methods are required, which is more time- and cost-consuming.

A dual-port, high-flow manifold system (Sensidyne, St. Petersburg, FL) has been developed for the simultaneous sampling of two contaminants using a single pump operating in constant pressure mode. Dual-port systems allow for adjusting the flow rate of each sample independently, and the constant pressure mode means that a change in the flow rate of one sample should not affect the flow rate of the other sample (7). Tests performed by the manufacturer with different dual-port assemblies have shown that pumps can maintain a constant flow over full work shift periods (8). The authors did not recommend using this dual-port system for sampling contaminants that might lead to filter overloading as this could cause the flow rates to change. Key basic requirements for pump performance are that the nominal flow rate remains constant within narrow bounds over the sampling period, within the

acceptable ± 5% range (9). Only tests conducted in controlled environments by the manufacturer have been done under the constant pressure mode and no tests have been done using pumps set to the constant flow mode (8). In addition, no workplace studies have been conducted to evaluate the dual-port system in real-case scenarios.

This study aims to evaluate the dual-port sampling system for simultaneous sampling of DEE and crystalline silica. Laboratory tests were carried out under different sampling conditions and a field validation took place in an underground gold mine.

A2.3 Methods

The general framework of laboratory and field tests is presented in Fig. 1. Laboratory tests evaluated the operation of pumps during a sampling period of 8 h and the intensity of the flow variation for various filter loading conditions. Field tests took place in an underground gold mine in Quebec (Canada) in April 2018. As shown in Fig. 1, PVC is the poly vinyl chloride and QFF is the quartz fiber filter.

Laboratory tests for the measurements of backpressures and flow rates for different sampling assemblies

A diagram representing the assembly of the equipment is presented in Fig. 2. For diesel assemblies, the laboratory tests were performed using 37 mm cassettes equipped with QFF and a cellulose support pad. For crystalline silica assemblies, 37 mm cassettes with PVC filters (5 µm pore size and cellulose support pad) were used. New and used cassettes (loaded cassettes) were used. The loaded diesel cassettes (37 mm QFF) came from previous sampling carried out in an underground mine over several days. The loaded silica cassettes (37 mm PVC filter) were provided by the laboratory of Robert-Sauvé Research Institute for Occupational Health and Safety (IRSST), but no information on the sampling conditions was available. Dorr-Oliver nylon cyclones were used to simulate the collection of the respirable fraction. Flow rates were measured using 4040 mass flow meters (TSI Inc., Shoreview, MN). GilAir-5 pumps (Sensidyne, St. Petersburg, FL) were run in constant flow mode, and GilAirPlus pumps (Sensidyne, St. Petersburg, FL) were run in constant flow mode or constant pressure mode. In constant flow mode, the pump

controls the flow rate regardless of changes in the filter load (i.e. pressure drop). In constant pressure mode, the pump controls the inlet pressure regardless of the flow, and it can be adjusted in the pump settings (10).

Sampling time test

The effect of operation time on the flow was evaluated in both constant flow and constant pressure modes. Pumps ran for 8 h while connected to a dual sampling port equipped with a diesel cassette (37-mm 1QFF) on one side and a silica cassette (37 mm PVC filter) on the other side. Both cassettes were unloaded and were connected to Dorr-Oliver nylon cyclones. In order to simulate real sampling conditions, flow rates were chosen in accordance to the manufacturer's recommendations for nylon cyclone. The pump flow rates were set around 3.4 L/min and each side of the dual-port was adjusted to 1.7 L/min. For constant pressure mode, the pump performance was tested using the GilAirPlus pumps at backpressure settings of 3.75 and 5 kPa (corresponding to 15 and 20 inches of water). Flow rates were measured before and after sampling and the percentage of variation was calculated. Each test was repeated twice to ensure the reproducibility of the results.

Filter loading test

Filter loading was simulated to evaluate its effects on the stability of the flow rates. Three scenarios were reproduced: (1) where the 37 mm PVC filter (silica) loads up faster than the 37 mm QFF (diesel) during sampling; (2) where 37 mm QFF (diesel) loads up faster than the 37 mm PVC filter (silica) during sampling; and (3) where both filters load up during sampling. The flow rate was set to 1.7 L/min on each side of the dual-port.

Loading intensities (i.e. low, medium and high) were determined by measuring the pressure drop of each cassette in the diesel and silica samplers. For the constant flow mode, three pre-loaded PVC filters (silica) were used to simulate an unbalanced sampling. Tests started with an unloaded (new) silica cassette and the flow rate on each side of the dual-port was adjusted to 1.7 L/min. After 5 min of running, the pumps were paused, and the unloaded silica cassette was replaced with a pre-loaded silica cassette and the new flow rates in both sides were noted after stabilization (around 10 s). The same procedure was repeated using pre-loaded diesel cassettes.

For constant pressure mode, backpressures were first adjusted to 2.5 kPa on the GilAirPlus pump settings and the flow rate on each side of the dual-port was adjusted to 1.7 L/min using unloaded cassettes. After 5 min of running, the silica cassette was replaced with a highly loaded silica cassette and the resulting flow rates on both sides of the dual-port were noted after stabilization (around 10 s). The backpressure setting was then increased in increments of 1.25 kPa up to 7.5 kPa, and the same procedure was repeated using the same sampling trains (unloaded silica cassette followed by highly loaded cassette) at this new constant backpressure setting. The whole procedure was then repeated by loading the diesel side (unloaded diesel cassette replaced by highly loaded cassette).

For tests where both filters were loaded during sampling, the same sampling trains were used for constant flow mode and constant pressure mode (3.75 kPa). Tests were performed with high, medium and low cassette loading intensities.

Workplace measurements in a mining environment

Before field measurements, all pumps were tested for a running period of at least 12 h and no problems were detected.

Measurements were carried out in an underground gold mine in Quebec (Canada) on randomly selected groups of workers with different exposure conditions for crystalline silica and DEE. Twenty diesel and silica samples using one pump with the dual-port connector were collected during full work shifts over five consecutive working days. Of these 20 tests, ten pumps were programmed using constant flow mode and ten using constant pressure mode. Crystalline silica samples were collected using 37 mm cassettes with PVC filters with 5 µm pore size and support pads, and DEE samples were collected using 25 mm cassettes equipped with 2QFFs. Dorr-Oliver nylon cyclones were used on both sides. The samples were placed in the workers' breathing zone, as shown in Fig. 3. At the start of the sampling event, flow rates on each side of the dual-ports were adjusted to 1.7 L/min to collect respirable fractions. Flow rates were measured before and after the work shift using 4040 mass flow meters (TSI Inc., Shoreview, MN). For constant pressure pumps (GilAirPlus), backpressures were adjusted to 3.75 kPa. The flow rate adjustment screws of the dual-port systems were capped to avoid any disturbance during sampling (except for one device which was missing its cap). Samples were sent to the IRSST

laboratories for TC, respirable dust and crystalline silica analyses. Concentrations of respirable dust were measured because the quantity of dust may be more directly associated with the loading of the cassette compared to the quantity of crystalline silica.

Statistical analysis

Results from the field measurements in the mine were summarized as arithmetic mean and standard deviation (SD) (i.e. average flow rate, flow rate variation and sampling time) and geometric mean and geometric standard deviation (i.e. TC, crystalline silica and respirable dust concentrations).

The degree of association between the flow rate variation and the concentrations of TC and respirable dust was assessed by Pearson correlation. The level of significance for these analyses was set at 5%. Analyses were performed using the software SPSS version 24 (IBM Corp., Armonk, NY, USA).

A2.4 Results

Laboratory tests

Sampling time test

Results of sampling time testing at constant pressure and constant flow modes are presented in Table 1. Flow rates at constant pressure modes were constant (less than 5% of variation) at the two backpressures tested (3.75 and 5 kPa) during the 8 h tests with no particle loading, indicating that all assemblies were functional over an 8 h sampling time. Similar results were observed with the tests at constant flow mode with no particle loading, indicating that flow rates were constant over the sampling time.

Filter loading test

Tests that simulated filter loading on the silica and diesel samplers, with pumps running in constant flow mode, are presented in Fig. 4. In general, flow rates on the loaded side decreased while those on the opposite side increased. The variation depended on the level of filter loading (low, medium or high). For instance, in the first measurement (low loading intensity in the silica sampler and diesel sampler unloaded), the flow variation was 0% for the diesel side and -1.17%

for the silica side. For the third measurement (high loading intensity in the silica sampler and diesel sampler unloaded), the flow variation was 6.43% for the diesel side and -8.24% for the silica side.

Tests that simulated filter loading on the silica and diesel samplers, with pumps running in constant pressure mode with different backpressure settings, are presented in Fig. 5. Measurements indicate that regardless of the backpressure used in the pump settings, flow rates systematically decreased when using the loaded cassette on the dual-port. However, the higher the backpressure, the lower the percentage of flow variation was. No flow rate variation was observed on the opposite side (unloaded cassette).

Fig. 6 presents the results for filter loading simulations on both sides with pumps running in constant flow mode and constant pressure mode. During the tests performed in constant flow mode, when a flow rate increased on one side, the flow rate on the opposite side decreased in accordance to the loading intensity. However, during the tests performed in constant pressure mode, the flow rates of both diesel and silica samplers decreased during the test. For low and medium filter loading intensities, flow rate variations were within the acceptable ±5% range. However, for high filter loading intensity, flow rate variations were beyond the acceptable ±5% range in one side of the dual-port sampler.

Workplace measurements in a mining environment

Tables 2 and 3 show the sampling time, average flow rates measured at the end of each sampling day for diesel and silica cassettes, as well as the flow rate variations (in %) for the two running modes.

For constant flow mode (Table 2), all the flow variations were within the acceptable ±5% range, except for Test 7 which was characterized by the highest TC concentration (284 $\mu g/m^3$). The mean flow rate variation in the diesel side was 2.0% ± 1.9%, while the flow rate variation in the silica side was 2.1% ± 2.6%. The mean sampling time was 7 h 52 min.

Larger variations were observed for pumps running in constant pressure mode (Table 3), with five tests (Tests 1, 2, 7, 9 and 10) characterized by variations higher than the acceptable ±5% range. Tests 1 and 7 used the dual-port device without caps to protect the adjustment screws. For this reason, these tests were not included in the calculation of the mean flow rate variation.

For Tests 2, 9 and 10 no methodological problems were noted. However, Test 9 was characterized by a high TC concentration (160 µg/m³). The mean flow rate variation in the diesel side was 3.0% ± 2.3%, while the flow rate variation in the silica side was 4.2% ± 4.4%. The mean sampling time was 9 h 51 min.

Fig. 7 shows a negative significant correlation between flow rate variation and TC concentration (Pearson *r*=-0.62; *p* value=0.007). Although in our study only two samples show flow rate variation larger than 5%, this result suggests that larger variations in the flow rate are expected in the diesel sampler of the dual-port when high concentrations of total carbon are collected. On the other hand, no association was found between crystalline silica concentration and flow rate variation or respirable dust concentration and flow rate variation (data not shown).

A2.5 Discussion

The performance of the pumps in relation to the use of the dual-port was evaluated. Two modes of pumps were tested. The constant pressure mode is recommended when using the dual-port system. Under the constant pressure mode, it is possible to adjust the flow rate of each side independently. However, only few pumps are able to operate under the high flow constant pressure mode. In consequence, the authors also tested the constant flow mode with the hypothesis that filter loading could be negligible to cause flow rate changes. In the constant flow mode, it is yet more difficult to regulate flow rates. Indeed, under this operation mode, adjusting the flow rate of one side will affect the flow rate of the other side.

In the laboratory experiments, results showed that the pumps with unloaded cassettes could operate for a sampling period of at least 8 h, whether they operated in constant flow mode or constant pressure mode. For the tests performed with loaded cassettes and pumps in constant pressure mode, results show that the higher the backpressure is, the lower the changes in the flow rate are. These results suggest that using a high backpressure setting for pumps in constant pressure mode will limit possible effects of filter loading on the flow rate.

Results of the laboratory simulation tests confirmed also the filter loading effect on the flow rate. When pumps ran in constant pressure mode, flow rates systematically decreased when using loaded cassettes. The higher the concentration, the higher is the possibility of a decrease

in flow rate. For constant flow mode, flow rates on the loaded side decreased while those on the opposite side increased.

Field sampling put the dual-port system into action in an underground gold mine. Most of the time, the sampling was satisfactory, and results suggest that the dual-port system could be adequate for simultaneously measuring worker exposure to different dust contaminants in this environment. However, results also showed the filter loading effect on the flow rate at the highest concentrations. In the present study, geometric mean (GM) concentrations of 104 and 15.6 $\mu g/m^3$ were reported for TC and quartz crystalline silica, respectively. These concentrations fall within the same range as the TC concentrations reported by Fleck et al. (2018) in an underground mine (GM of 148 $\mu g/m^3$) and as the quartz crystalline silica concentrations reported by Scarselli et al. (GM of 46 $\mu g/m^3$, and median of 20 to 90 $\mu g/m^3$, depending on the mine) (11-13). In consequence, the acceptable ±5% range is expected to be surpassed in some cases in underground mines. Fleck et al. (2018) also showed that differences are expected between exposure levels of different similar exposure groups (SEGs) in underground mines (11). Thus, a well-advised occupational hygienist could use the dual sampling port system for evaluating exposures of workers who are the least likely to have highest exposure levels.

Based on a few unplanned events that occurred during sampling, the authors recommend the following: It is essential to lock the flow adjustment screws of the dual-port system by capping them to avoid significant changes in flow rates through involuntary friction of the screws on the worker's clothing. In addition, the authors have selected a backpressure of 3.75 kPa as the maximum backpressure which allowed the pumps to work properly for field sampling. According to Breuer, the filter material, pore size, thickness, composition of the filter supports (pads), and effective filter surface area are all important contributors to the backpressure and can influence pump performance (9). For this reason, the authors recommend testing backpressure settings before sampling, and selecting the highest functional backpressure to limit the variation due to filter loading. Finally, nylon cyclones operated at 1.7 L/min were used to select the respirable fraction. These cyclones were chosen because of the relative low flow necessary to provide the respirable fraction. The use of other types of cyclones, requiring higher flow rates, could present technical difficulties for the use of the dual-port.

Different cassettes and size-selective sampling devices were tested in parallel to this project. Results indicate that using a cyclone has a slight influence on the variation of the pressure drop (Table 4). Breuer found that in a few worst-case conditions, measured pressure drop can be severe for some membrane filters at high flow rate (9). Results presented in Table 4 show that Diesel Particulate Matter (DPM) Cassettes (SKC, Eighty Four, PA) have higher average pressure drops which can affect pump performance. DPM cassettes were not evaluated in this study neither in the field portion of this study nor in the filter loading part of the laboratory tests. Fleck et al. (2019) performed a comparative evaluation of the submicron fraction of TC, measured using DPM cassettes, and the respirable fraction of TC measured using a cyclone (14). Different TC concentrations were obtained with each sampling method, which may be explained by the different aerodynamic fractions of DEE collected. According to Fleck et al. (2019), the level of filter loading for DPM and 25 mm cassettes is suspected to be different and, thus, the impact on the stability of the flow is unknown (14). Before including DPM cassettes in a dual-port sampling strategy, new evaluations should be performed to validate the stability of the flow rates.

Because the surface of the 37 mm filter is about twice that of the 25 mm filter, particles will be more evenly distributed over the surface of the 37 mm filter, which will cause less clogging. In addition, backpressures measured with the 37 mm 1-QFF cassettes were slightly lower than those measured with the 25 mm 1-QFF cassettes (Table 4). For these reasons, we recommend using 37 mm cassettes rather than 25 mm cassettes when sampling with the dual-port device for DEE evaluation.

Although the field part of this study was conducted in a mining environment, it is reasonable to believe that sampling using dual-port system could be transposed to other working environments.

A2.5 Conclusions

The use of a dual-port system for simultaneously measuring DEE and crystalline silica can reduce sampling time and cost, and ultimately promote exposure assessments. While most of the experiments conducted in this study to evaluate the dual-port sampling system supports its use for evaluating concomitant occupational exposures to diesel engine exhaust and crystalline

silica, results highlight the possibility of filter overloading as a cause of flow rate changes. Before including the dual-port sampling system in an exposure assessment study, occupational hygienists must test the stability of the flow rates under their specific conditions. Worst case evaluations will inform the occupational hygienist on the stability of the flow rates and thus on the possibility to use the dual port system.

A2.6 Acknowledgements

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G.L works for Agnico Eagle Mines, the company where the field measurements of this study were performed.

The authors declare no other conflict of interest relating to the material presented in this article.

A2.7 Contributions

ASF contributed to the study design, measurements, data analysis and manuscript preparation. CC, PER and RT contributed to the measurements. VC contributed to the measurements and data analysis. GL and HC contributed to the study design and implementation. MD contributed to the study design and preparation of the manuscript.

A2.8 References

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A2.9 Tables and Figures

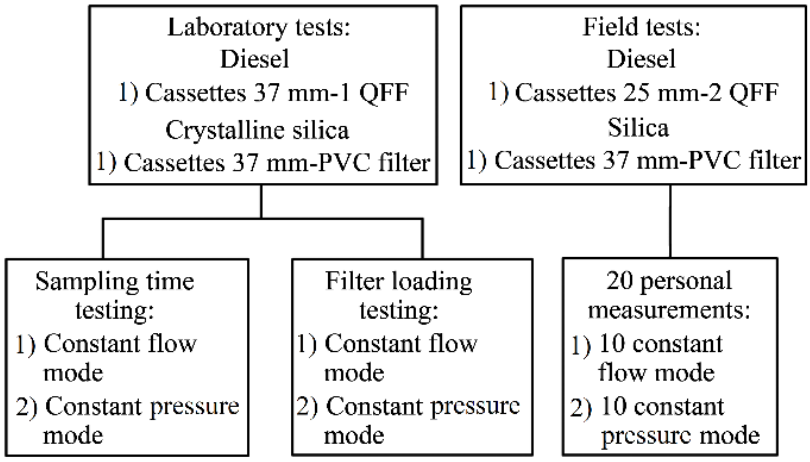

Figure 1: General framework of laboratory and field tests.

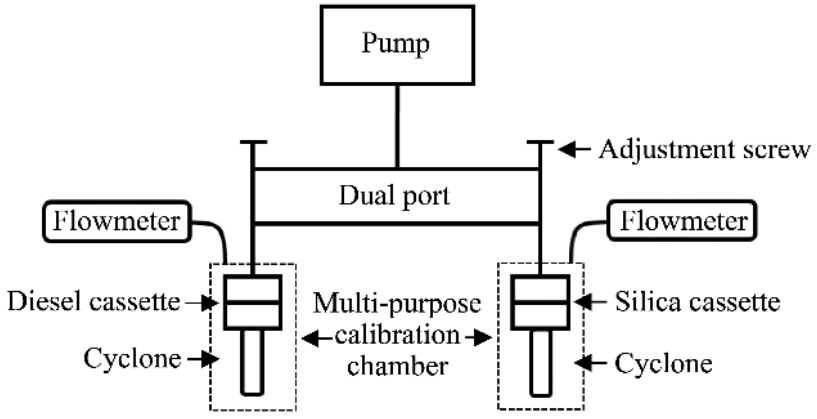

Figure 2: Diagram for the assembly of the laboratory tests.

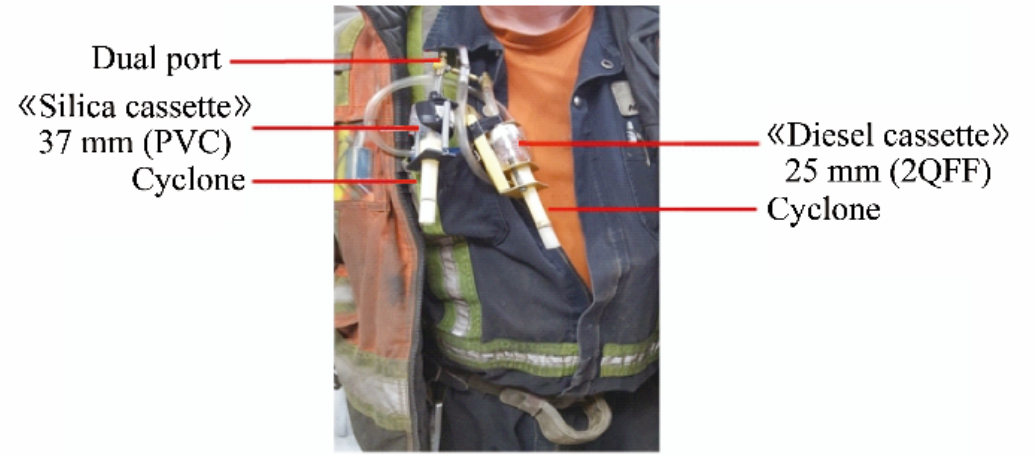

Figure 3: Worker wearing a dual-port sampling train.

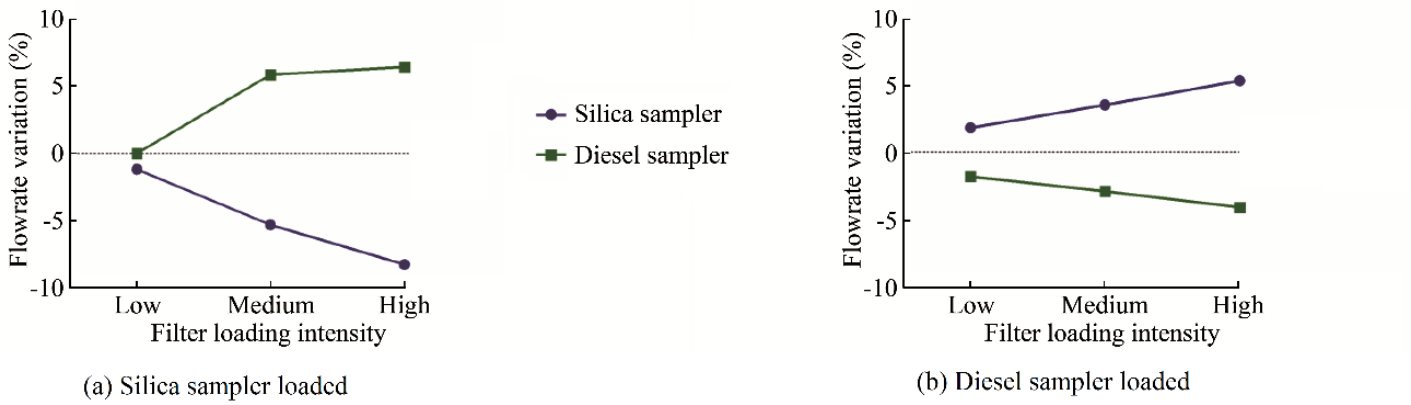

Figure 4: Filter loading test with pumps running in constant flow mode.

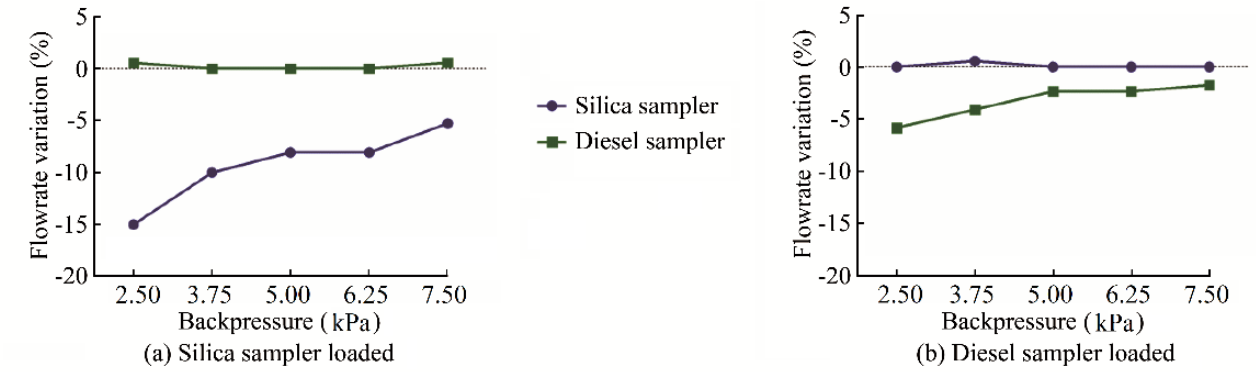

Figure 5: Filter loading test with pumps running in constant pressure mode.

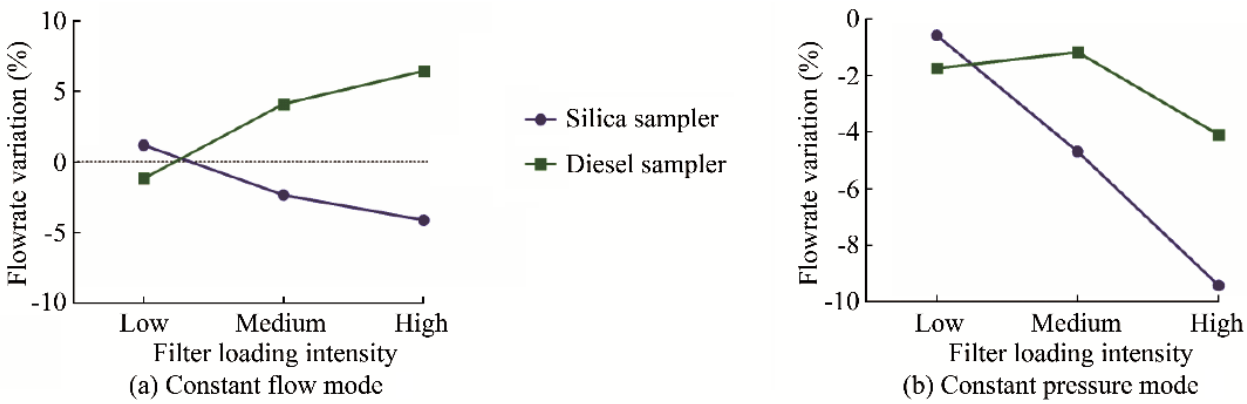

Figure 6: Filter loading test (both samplers loaded).

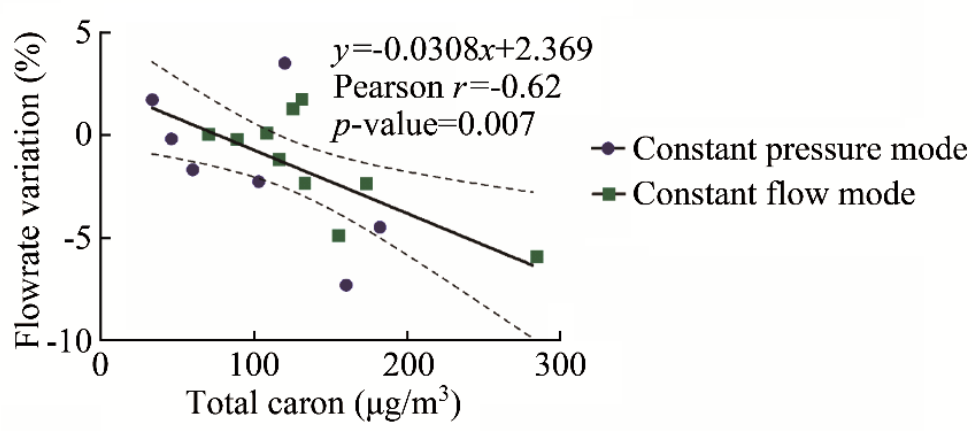

Figure 7: Scatter plot and Pearson correlation between flow rate variation and total carbon concentration of samples measured in constant pressure mode and constant flow mode.

Table 1: Flow rate variations over 8 h for pumps running in constant pressure and constant flow modes (no particle loading).

Backpressure setting (kPa)	Cassette	Initial flow rate (L/min)	Flow rate after 4 h (L/min)	Flow rate after 8 h (L/min)	Average flow rate (L/min)	8 h flow rate variation (%)
			Constant Pressure Mode			
3.75	D	1.72	1.70	1.70	1.71	-1.16
	S	1.71	1.68	1.68	1.69	-1.75
3.75	D	1.71	1.69	1.69	1.70	-1.17
	S	1.72	1.71	1.70	1.71	-1.16
5	D	1.71	1.68	1.68	1.69	-1.75
	S	1.71	1.68	1.60	1.66	-3.43
5	D	1.74	1.71	1.71	1.72	-1.72
	S	1.72	1.68	1.68	1.69	-2.33
Mean±SD	-	1.72±0.1	1.69±0.1	1.68±0.1	1.7±0.1	1.8±0.7
			Constant Flow Mode			
-	D	1.73	1.74	1.73	1.73	0.00
	S	1.71	1.72	1.73	1.72	1.17
-	D	1.70	1.72	1.74	1.72	2.35
	S	1.70	1.68	1.67	1.68	-1.76
-	D	1.72	1.72	1.72	1.72	0.00
	S	1.73	1.71	1.72	1.72	-0.58
-	D	1.70	1.74	1.74	1.73	2.35
	S	1.73	1.70	1.68	1.70	-2.89
-	D	1.74	1.66	1.66	1.69	-4.60
	S	1.75	1.75	1.75	1.75	0.00
-	D	1.72	1.69	1.72	1.71	0.00
	S	1.72	1.72	1.69	1.71	-1.74
-	D	1.73	1.75	1.71	1.73	-1.16
	S	1.70	1.67	1.68	1.68	-1.18
-	D	1.73	1.68	1.67	1.69	-3.47
	S	1.73	1.70	1.70	1.71	-1.73
Mean±SD	-	1.72±0.1	1.71±0.1	1.68±0.1	1.71±0.1	1.5±1.6

Notes: “D” is the diesel; and “S” the silica.

Table 2: Results of field tests in the mine with pumps running in constant flow mode.

Test number	TC (µg/m³)	Average flow rate (L/min)	Flow rate variation (%)	Cristalline silica (µg/m³)	Respirable dust (µg/m³)	Average flow rate (L/min)	Flow rate variation (%)	Time (hh:mm)
1	116	1.71	-1.16	8.50	210	1.70	-1.17	9:46
2	173	1.69	-2.34	21.0	1400	1.70	-2.33	5:30
3	131	1.73	1.75	9.60	840	1.72	1.17	9:17
4	133	1.71	-2.31	28.0	420	1.71	-0.58	4:52
5	88.9	1.70	-0.18	14.0	150	1.69	-2.87	10:05
6	155	1.71	-4.86	-	-	1.71	-1.34	9:45
7	284	1.65	-5.88	15.0	2100	1.76	5.54	9:07
8	125	1.73	1.28	19.0	280	1.73	2.51	6:37
9	108	1.72	0.12	23.0	270	1.74	2.98	8:02
10	70.2	1.72	0.06	<7.0	83	1.74	0.75	8:04
Mean (SD)	129(1.4)[a]	1.71±0.02[b]	2.0±1.9[b]	14.1(1.7)[a]	389(2.9)[a]	1.72±0.02[b]	2.1±2.6[b]	7:52

Notes: “a” means the geometric mean (geometric standard deviation); and “b” means the arithmetic mean±standard deviation. All values were considered positive for the calculation of the mean flow rate variation.

Table 3: Results of field tests in the mine with pumps running in constant pressure mode.

Test number	TC (µg/m³)	Average flow rate (L/min)	Flow rate variation (%)	Cristalline silica (µg/m³)	Respirable dust (µg/m³)	Average flow rate (L/min)	Flow rate variation (%)	Time (hh:mm)
1[#]	74.4	1.35	-45.4	17.0	270	1.73	0.00	10:40
2	33.7	1.75	1.73	12.0	140	1.62	-13.8	10:33
3*	62.7			14.0	120			10:11
4	120	1.74	3.51	130	1000	1.70	-2.91	10:03
5	46.3	1.76	-0.17	14.0	120	1.74	-2.16	9:54
6	103	1.72	-2.24	6.50	150	1.72	-1.56	9:53
7[#]	132	1.89	16.5	16.0	420	1.65	-9.48	10:24
8	182	1.71	-4.46	12.0	1100	1.76	1.90	9:25
9	160	1.67	-7.27	32.0	450	1.73	1.87	9:40
10	60.1	1.73	-1.67	10.0	150	1.77	5.52	7:55
Mean (SD)	85(1.7)[a]	1.7±0.1[b]	3.0±2.3[b]	17 (2.2)[a]	276(2.3)a	1.7±0.04[b]	4.2±4.4[b]	9:51

Notes: "*" means that pump stopped after 10:11 in test; and "#" means that the test used the dual-port device without caps to protect the adjustment screws. ''[a]" means the geometric mean (geometric standard deviation); and ''[b]" means the arithmetic mean ± standard deviation. All values were considered positive for the calculation of the mean flow rate variation.

Table 4: Backpressure measurements for various sampling trains.

Cassette	Backpressure without cyclone (kPa)	Backpressure with cyclone (kPa)
2QFFs (25 mm) - 1	1.44	1.71
2QFFs (25 mm) - 2	1.32	1.64
1QFF (25 mm) - 1	1.36	1.69
1QFF (25 mm) - 2	1.39	1.72
1QFF (37 mm) - 1	0.94	1.27
1QFF (37 mm) - 2	0.94	1.27
2QFFs (DPM)[a]	1.57	1.84
Mean (SD)	1.28 (0.24)	1.59 (0.22)*

Notes: “a” means that DPM cassette has an integrated jeweled impactor; “*” means that T-test; and p is 0.03.

Appendix 3: Results of occupational exposures to particles in a foundry and a machining shop.

The section below shows the result of the measurements in the two sectors of a smelting industry (i.e. foundry and machining shop) during 12 full work shifts. Table 1 presents the mass and number concentration of particles measured by the DRIs. The GM (GSD) of the mass concentration of particles from different size fractions, measured by the DustTrak DRX, ranged between 101 (2.1) $\mu g/m^3$ (PM_1) and 147 (2.1) $\mu g/m^3$ (PM_{TOTAL}) in the foundry, and 79 (1.5) $\mu g/m^3$ (PM_1) and 142 (1.5) $\mu g/m^3$ in the machining shop. The geometric means of PM_4 was 125 (2.1) $\mu g/m^3$ in the foundry and 106 (1.5) $\mu g/m^3$ in the machining shop.

Mean particle number concentration, measured by the P-Trak, was 80,400 particles/cm^3 in the foundry. These levels were considerably higher than the mean number concentration of 41,000 particle/cm^3 reported in the machining shop. Table 1 also shows ratios EEPS/P-Trak of 4.6 in the foundry and 3.8 in the machining shop. Figure 1 shows the size distribution of the ultrafine particles measured by the EEPS 3090. Results show that the main mode of the size distribution was around 10 nm in both workplaces.

Nearly 800 particles or particle agglomerates were analyzed by TEM. Figure 2 shows representative TEM bright field images and EDS spectra of particles collected during activities in the smelting industry. The particles identified in the foundry (Figure 2A) were of spherical shape ranging from 50 to 500 nm, isolated or in agglomerates, composed mostly of metal oxides. The elements identified were: iron (in 66% of the particles analyzed), chromium (64%), silicon (61%), manganese (59%), zinc (29%), copper (22%), aluminum (9%), nickel (8%) and lead (8%). Two main types of particles were identified in the machining shop. The first type consisted of particles on the order of a few nanometres that were highly agglomerated (Figure 2B). These particles were detected mainly on sample grids taken near welding and arc cutting areas. The second category consisted of particles of various shapes (i.e. non-specific or non-spherical) and rather coarse (0.5 to 5 µm). They were mainly found on sample grids taken near grinding activities (Figure 2C). The main elements identified in the machining shop were iron (in 77% of the particles analyzed),

chromium (48%), silicon (41%), manganese (35%), nickel (28%), aluminum (26%), copper (13%), zinc (8%), and lead (3%).

Table 1: Ambient mass and number concentrations of aerosols measured by direct reading instruments in a foundry and machining shop.

Instrument	Indicator	Foundry			Machining Shop		
		N	**GM (GSD)**	**Min–Max**	**N**	**GM (GSD)**	**Min–Max**
DustTrak DRX	**PM_1 (µg/m³)**	12	101 (2.1)	30–260	12	79 (1.5)	50–160
	$PM_{2.5}$ (µg/m³)	12	115 (2.1)	30–300	12	94 (1.5)	50–200
	PM_4 (µg/m³)	12	125 (2.1)	40–330	12	106 (1.5)	60–220
	PM_{10} (µg/m³)	12	142 (2.1)	40–330	12	132 (1.5)	70–260
	PM_{TOTAL} (µg/m³)	12	147 (2.1)	40–380	12	142 (1.5)	70–280
DustTrak 8520	**PM_4 (µg/m³)**	12	157 (2.1)	40–420	12	148 (1.5)	80–290
P–Trak 8525	**Particles/cm³**	12	80,400 (2.3)	23,700–262,200	12	41,000 (1.5)	17,000–63,600
		Foundry			**Machining Shop**		
Ratio EEPS 3090/P-Trak 8525		4.6			3.8		

N: Number of measurements; **GM:** Geometric mean; **GSD:** Geometric standard deviation; **Min–Max:** Minimum and maximum daily values.

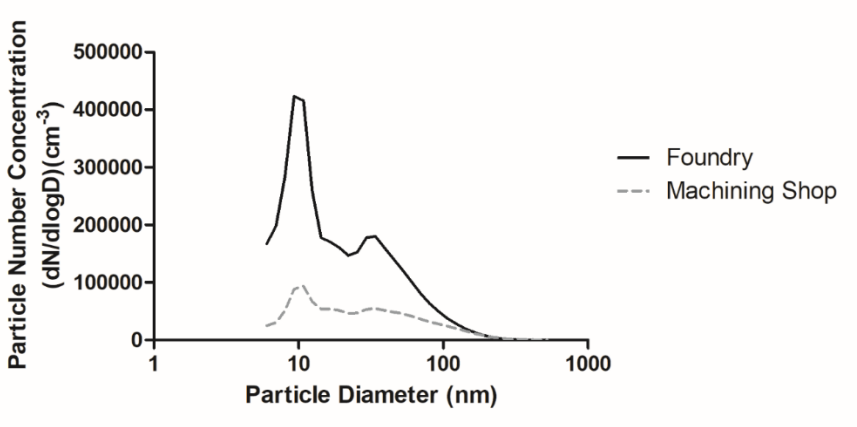

Figure 1: Size distribution of the ultrafine particles measured by the EEPS 3090 in the foundry and machining shop.

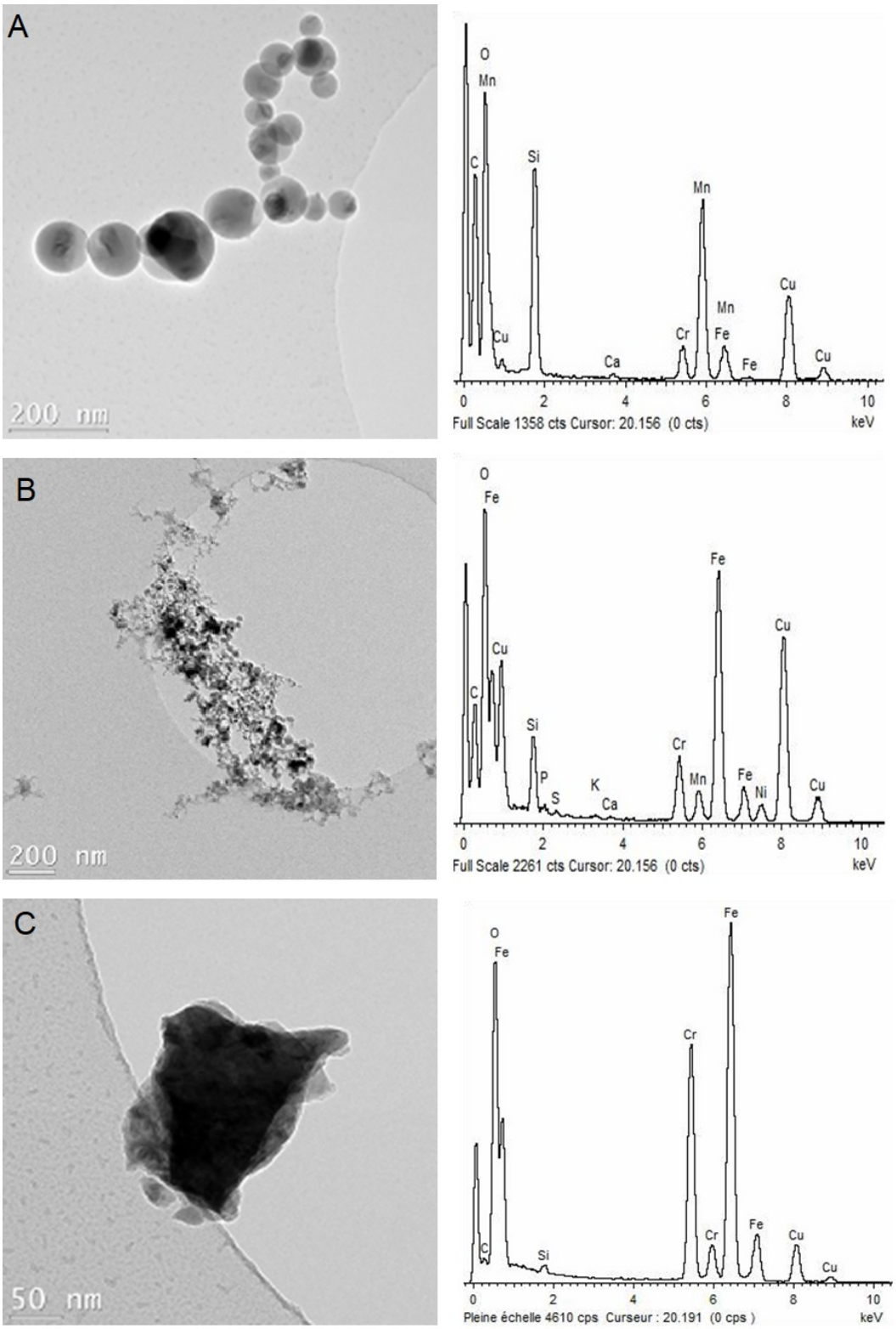

Figure 2: TEM bright field images and EDS spectra of particles collected in the foundry (A) and machining shop during cutting/welding (B) and grinding (C) activities.