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# Occupational vehicle-related particulate exposure and inflammatory markers in trucking industry workers

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ABSTRACT

*Background:* Previous studies have suggested an association between particulate air pollution and cardiovascular disease, but the mechanism is still unclear.
*Objective:* We examined the association between workplace exposure to vehicle-related particles and cardiovascular disease related systemic inflammatory markers, C-reactive protein (hs-CRP), soluble intercellular adhesion molecule-1 (sICAM-1), and interleukin-6 (IL-6) in 137 trucking terminal workers (non-drivers) in the U.S. trucking industry.
*Methods:* We visited two large trucking terminals in 2009 and measured vehicle-related elemental carbon (EC), organic carbon (OC), and particulate matter with aerodynamic diameter $\leq 2.5$ μm ($PM_{2.5}$), for 5 days consecutively at the main work areas. Each participant provided a blood sample and completed a health questionnaire during the sampling period. Individual workplace exposure level was calculated by 12-h time weighted moving averages based on work shift. The association between each blood marker and exposure to each pollutant during 0–12, 12–24, 24–36, and 36–48 h before the blood draw was examined by multivariable regression analyses.
*Results:* In general, OC and EC had a positive association with sICAM-1, especially for exposure periods 12–24 ($lag_{12\text{-}24}$) and 24–36 ($lag_{24\text{-}36}$) h prior to blood draw [$\beta = 54.9$ (95%CI: 12.3–97.5) for $lag_{12\text{-}24}$ and $\beta = 46.5$ (95%CI: 21.2–71.8) for $lag_{12\text{-}24}$; change in sICAM-1 (in ng/mL) corresponding to an IQR increase in OC]. A similar pattern was found for EC and $PM_{2.5}$. We did not find an association between measured pollutants up to 48 h before blood draw and hs-CRP or IL-6.
*Conclusion:* In this group of healthy workers, short-term exposure to vehicle-related air pollutants may be associated with sICAM-1. Our findings may be dependent on the exposure period studied.


## 1. Introduction

Workers in the trucking industry are regularly exposed to exhaust from diesel trucks, light duty gasoline vehicles, and propane fork lift trucks, depending on job duties. Previous studies have suggested that exposure to particulate matter (PM) in general and from vehicle-related exhaust in particular is associated with elevated risks of cardiovascular disease (CVD) (Dockery et al., 1993; Hoek et al., 2013; Laden et al., 2006; Peters et al., 2004; Pope et al., 2004a; Wellenius et al., 2012). Occupational studies suggested that workers in the transportation industry, specifically drivers, have increased risk of CVD (Bigert et al., 2004; Robinson and Burnett, 2005; Shin et al., 2013; Tuchsen et al., 2006), but limited studies have focused on terminal-based workers or non-drivers. In previous work by our research team, we observed

*Abbreviations:* BMI, body mass index; EC, elemental carbon; GSTM1, glutathione S-transferase M1; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; OC, organic carbon; $PM_{2.5}$, particulate matter with aerodynamic diameter $\leq 2.5$ μm; $PM_1$, particle matter with a diameter of $\leq 1.0$ μm; SHS, secondhand smoke; sICAM-1, soluble intercellular adhesion molecule-1

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elevated standardized mortality ratios for ischemic heart disease in both drivers and non-drivers (Hart et al., 2013; Laden et al., 2007).

It has been hypothesized that exposure to PM might induce a low-grade systemic inflammatory response that leads to an increased risk of CVD, and previous studies have suggested that exposure to PM is associated with elevated levels of systemic inflammatory markers (Chen et al., 2015; Dai et al., 2016; Delfino et al., 2009; Riediker et al., 2004; Ruckerl et al., 2007; Schwartz, 2001), the potential predictors of susceptibility to CVD (Blake and Ridker, 2002; Saadeddin et al., 2002; Tousoulis et al., 2007). However, the results have been inconsistent, and recently a growing number of studies have reported null associations (Brauner et al., 2008; Forbes et al., 2009; Mirowsky et al., 2015; Rudez et al., 2009), especially for C-reactive protein (CRP), a widely known acute phase protein produced by the liver in response to proinflammatory cytokines. It is possible that associations between air pollutants and CRP may be stronger in susceptible populations, and may not be as evident among healthy individuals. Positive associations between particulate air pollution and inflammatory markers have been observed among more susceptible populations such as myocardial infarction (MI) survivors (Ruckerl et al., 2007), patients with coronary or ischemic heart disease (Delfino et al., 2009; Siponen et al., 2015), individuals with type 2 diabetes (O'Neill et al., 2007; Ruckerl et al., 2014), and the elderly (Delfino et al., 2009; Pope et al., 2004b; Zeka et al., 2006). On the other hand, a few studies of healthy individuals did not find similar associations (Brauner et al., 2008; Mirowsky et al., 2015; Rudez et al., 2009).

Previous studies have also suggested that the association between air pollution and cardiopulmonary health outcomes might be modified by gene polymorphisms. Glutathione S-trans-ferase M1 (GSTM1), a class member of glutathione S-transferases (GSTs) gene family which is known for their ability to produce enzymes that are involved in detoxification and is part of the antioxidant defense system (Armstrong, 1997), has been reported to modify the association between secondhand smoke exposure and inflammatory markers (Miller et al., 2003). It is also suggested that GSTM1 may modify the association between air pollution and heart rate variability, respiratory illness, as well as pro-inflammatory expression and cell adhesion molecule (Chahine et al., 2007; Madrigano et al., 2010; Ruckerl et al., 2014; Wu et al., 2012; Yang et al., 2008).

The purpose of this study was to examine the short-term relationship between occupational exposure to particulate air pollution and inflammatory markers, including high-sensitivity C-reactive protein (hs-CRP), soluble intercellular adhesion molecule-1 (sICAM-1), and interleukin-6 (IL-6), among trucking terminal workers (non-drivers) in the U.S. trucking industry. Additionally, we assessed gene-environment interaction by GSTM1 gene deletion to identify potential susceptible subpopulations in this relatively healthy working population.

## 2. Materials and methods

### 2.1. Study subjects

We visited two large trucking terminals in Carlisle, PA, and Chicago, IL in March and June 2009, respectively. A total of 178 terminal-based workers (non-drivers) who worked at these two terminals during the sampling periods were recruited to participate in the study. The participants were asked to provide a blood sample and complete a health questionnaire. The detailed job categories in the trucking industry and the corresponding job duties are described elsewhere (Smith et al., 2006). In brief, the job titles of the participants included in the study were mainly dock worker (moving freight within the terminal), hostler (moving trucks in the terminal yard), and clerk (office worker). The protocol was approved by the Human Subjects Committees at the Brigham and Women's Hospital, the Harvard School of Public Health, and VA Boston Healthcare System, and each participant provided informed consent before participating.

### 2.2. Blood sample and health questionnaire

Phlebotomy was offered 24 h per day during the field sampling period in each trucking terminal. At their convenience, participants provided approximately 30 mL of blood either before, during, or after one of their work shifts during the sampling week. Blood samples were stored in a refrigerator in the field and sent back to our laboratory with a coolant by overnight shipping every day. Upon arrival, the blood samples were centrifuged in a refrigerated unit and blood components aliquoted in cryotubes, which were stored in the vapor phase of liquid nitrogen freezers at lower than $-130\,^{\circ}C$. All samples were processed and stored within 24 h of collection. The analyses of inflammatory markers were performed at the Clinical & Epidemiologic Research Laboratory, Department of Laboratory Medicine at Children's Hospital in Boston. Hs-CRP levels were determined by an immunoturbidimetric assay on a Hitachi 917 analyzer (Roche Diagnostics; Indianapolis, IN), using reagents and calibrators from Denka Seiken (Niigata, Japan). Concentrations of sICAM-1 and IL-6 were measured by an enzyme-linked immunosorbent assay (ELISA), which employs the quantitative sandwich enzyme immunoassay technique (R&D Systems, Minneapolis, MN). CRP is a well established non-specific systemic inflammatory marker related to CVD, and IL-6 has been linked to increased risk of stroke and MI, whereas sICAM-1 is directly involved in atherogenesis and has been considered as a good predictor of CVD in healthy individuals (Tousoulis et al., 2007). For the three inflammatory markers analyzed, all the samples were above the laboratory thresholds of detection. In addition, we randomly selected 100 samples from non-smokers to analyze the polymorphisms of an oxidative stress gene, GSTM1, to evaluate the potential for gene-environment interaction. GSTM1 genotyping was performed by polymerase chain reaction (PCR) amplification of exons 4 and 5 of the GSTM1 allele to differentiate between the null polymorphism and the presence of one or more copies of the gene (Schwartz et al., 2005).

A detailed health and exposure questionnaire was completed by each participant at the time of the blood draw. We asked about recent and past smoking habits, recent secondhand smoke (SHS) exposure, job title and job history, date and time of last work shift, specific duties on the day of blood draw, work schedule over the previous week, recent acute and chronic illnesses, medication use, physical activity, alcohol use, weight and height, and waist size.

### 2.3. Exposure assessment

We measured $PM_{2.5}$ (particulate matter with aerodynamic diameter $\leq 2.5\,\mu m$) as an overall measure of air pollution from multiple sources, elemental carbon (EC) in $PM_1$ (particle matter with a diameter of $\leq 1.0\,\mu m$) as a marker of exposure to vehicle related combustion particles, and organic carbon (OC) in $PM_1$. EC and OC were measured in $PM_1$ to focus on exposures to freshly generated exhaust. In this work setting, EC has been shown to originate primarily from diesel exhaust (Davis et al., 2006). Area samples of $PM_{2.5}$, EC, and OC were collected consecutively using 12-h integrated sampling for 5 days and nights, replacing the samplers at 7 a.m. and 7 p.m. every day. The particle collectors and their pumps were mounted in a box sampler connected to an external battery. Area samples were collected at the loading dock