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# Particulate matter air pollution, physical activity and systemic inflammation in Taiwanese adults

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## ARTICLE INFO

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## ABSTRACT

*Background:* The protective effects of physical activity (PA) against chronic disease can be partially ascribed to its anti-inflammatory effects. On the other hand, long-term exposure to particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) may induce systemic inflammation.

*Objective:* To investigate the joint effects of habitual PA and long-term exposure to $PM_{2.5}$ on systemic inflammation in a large cohort of Taiwanese adults.

*Methods:* We studied 359,067 adult participants from a cohort consisting of Taiwanese residents who participated in a standard medical examination program from 2001 to 2014. Peripheral white blood cell (WBC) and differential counts were measured as indicators of systemic inflammation. Two-year average concentration of $PM_{2.5}$ was estimated at each participant‘s address using a satellite-based spatio-temporal model. Habitual PA level was assessed by questionnaire (inactive, low, moderate and high). Mixed-effects linear regression model was used to examine the associations of WBC counts with $PM_{2.5}$ and PA.

*Results:* Compared with inactive participants, those with low, moderate or high PA levels had 0.36% [95% confidence interval (CI): 0.31%, 0.41%], 0.70% (95%CI: 0.65%, 0.76%) and 1.16% (95%CI: 1.11%, 1.22%) lower WBC counts, respectively, after adjusting for $PM_{2.5}$ exposure and a wide range of confounders. Long-term $PM_{2.5}$ exposure was associated with increased WBC counts at all PA levels. Analyses for differential counts generated similar results. No significant interaction was observed between PA and $PM_{2.5}$ exposure (*P* for interaction = 0.59).

*Conclusions:* Habitual PA was associated with statistically significant lower markers of systemic inflammation across different levels of $PM_{2.5}$. Effects of PA and $PM_{2.5}$ exposure on systemic inflammation are independent.

## 1. Introduction

The health benefits of regular physical activity (PA) have been well documented (Warburton et al., 2006). Even low-volume habitual PA (15 min a day or 90 min a week of moderate-intensity exercise) is associated with reduced mortality from cardiovascular disease, diabetes and cancer (Wen et al., 2011). In contrast to PA, particulate matter (PM) air pollution poses a significant risk to health. According to the Global Burden of Disease Study, ambient PM air pollution was the ninth leading cause of mortality in 2010, responsible for more than 3.2 million deaths (Lim et al., 2013).

Worldwide, 31.1% of adults are estimated to be physically inactive (Hallal et al., 2012). Public health campaigns promoting PA are increasingly being used in an attempt to combat the pandemic of physical

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inactivity. However, enhanced exposure to air pollutants in the lungs due to higher minute ventilation during PA may amplify the adverse health effects of air pollution (Giles and Koehle, 2014). The results of a cross-over experimental study in Barcelona, Spain showed that the beneficial effects of PA on blood pressure and heart rate variability were reduced by exposure to higher traffic-related air pollution, indicating an interaction between PA and short-term exposure to air pollution (Kubesch et al., 2015a; Cole-Hunter et al., 2016). However, such interaction was not found for lung function and inflammatory markers (Kubesch et al., 2015b). Data from epidemiological studies are scarce: A cross-sectional study in Hong Kong reported habitual PA may prevent premature death attributable to short-term exposure to air pollution (Wong et al., 2007); the Danish Diet, Cancer and Health Cohort study that examined the effects of leisure-time PA and long-term exposure to nitrogen dioxide ($NO_2$) on mortality and incidence of asthma and chronic obstructive pulmonary disease (COPD) found no PA-air pollution interactions (Andersen et al., 2015; Fisher et al., 2016).

Balancing the benefits of PA and the potential detrimental effects of enhanced exposure to air pollution during PA has become an important public concern, especially in those regions with significant air pollution. As air pollution is ubiquitous, people need to be clearly aware whether they can benefit from PA despite inhaling a larger amount of air pollution because of the higher minute ventilation during PA.

Systemic inflammation has been recognized as an underlying mechanism for many chronic diseases including cancer and cardiovascular disease. Inflammation induced by PM with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) is hypothesized as a biological link between air pollution and increased morbidity and mortality of chronic diseases, especially for cardiovascular disease (Brook et al., 2010; Pope and Dockery, 2006). On the other hand, the protective effects of PA against chronic disease can be partially ascribed to its anti-inflammatory effects (Nimmo et al., 2013; Beavers et al., 2010). We therefore investigated the joint effects of habitual PA and long-term exposure to $PM_{2.5}$ on systemic inflammation in a large prospective cohort.

## 2. Methods

### 2.1. Study population

The study participants were from a large prospective cohort in Taiwan, which has been documented elsewhere (Wen et al., 2011; Wen et al., 2008; Wu et al., 2017). Briefly, the cohort consisted of more than 0.5 million Taiwanese residents who took part in a standard medical examination program provided by a private firm (MJ Health Management Institution, Taiwan) since 1996. The participants received a series of medical examinations including anthropometric measurements, physical examination, blood and urinary tests and a standard self-administered questionnaire survey during each visit. The participants were encouraged to visit the firm regularly and they gave written informed consent prior to participation. Ethical approval was obtained from the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee.

In the present study, we only included participants aged 18 or above who participated in the cohort from 2001 to 2014, a period for which $PM_{2.5}$ exposure assessment was available. During the study period, white blood cell (WBC) measurements were available for 424,047 participants with 959,280 observations. We excluded 159,733 observations with incomplete information (475 on anthropometric measurements, 44,466 on demographic information, 47,913 on blood tests, 61,667 on PA and other lifestyle factors and 5152 on $PM_{2.5}$ exposure due to missing residential addresses). Compared with all observations, the excluded observations had similar distributions in age (mean: 42.3 vs 42.2 years), sex (male: 49.7% vs 49.8%) and WBC count (median: 5.8 vs $5.8 \times 10^9$/L).

We further excluded 2735 observations with WBC count $< 3.5 \times 10^9$/L and 14,408 observations with WBC count $\geq 12.5 \times 10^9$/L to avoid the potential confounding bias from reduced immune function or acute infections (Tong et al., 2004). The final sample size included in the present data analysis was 359,067 participants with 782,404 observations. Of the 359,067 participants, 158,213 (44.1%) underwent more than one examination.

### 2.2. Medical exanimation

The participants received a series of medical examinations during their visits. Height and weight were measured with participants wearing light indoor clothing without shoes. Body mass index (BMI) was calculated as weight (kg) divided by square of height (m). Seated blood pressure was measured using an auto-sphygmomanometer (Citizen CH-5000, Tokyo, Japan). An overnight fasting blood sample was taken in the morning and Complete Blood Count (CBC) tests were conducted using ABBOTT Cell Dyn 3000/3700 hematology analyzer. Total WBC and differential (neutrophil, lymphocyte and monocyte) counts were retrieved from CBC tests. In addition to CBC, plasma glucose, total cholesterol, triglyceride and high-density lipoprotein cholesterol (HDL-C) were also measured using an automatic biochemical analyzer (7150, Hitachi, Tokyo, Japan). All blood samples were analyzed at the central laboratory of MJ Health Screening Center. All tests were performed by trained technicians and the detailed information including quality control can be accessed in the technical report released by the MJ Health Research Foundation (Chang et al., 2016).

A standard self-administered questionnaire was used to collect information on the demographic characteristics, medical history and lifestyle factors.

### 2.3. Physical activity

Information on habitual PA was collected by questionnaire. The method for assessing PA level has been described in previous publications (Wen et al., 2011; Wu et al., 2017). First, the participants were asked to classify the weekly PAs during the previous month into four intensity categories: light (e.g. walking), moderate (e.g. brisk walking), medium-vigorous (e.g. jogging) and high-vigorous (e.g. rope skipping). A metabolic equivalent value (MET) based on the Compendium of Physical Activities (Ainsworth et al., 2000a) was assigned to each PA category: 2.5 for light, 4.5 for moderate, 6.5 for medium-vigorous and 8.5 for high-vigorous. A weighted MET was assigned to those participants who reported activities in more than one intensity category, depending on the time spent in each category. Afterwards, MET-hour per week was calculated as the product of intensity (MET) and duration (hours) of exercise. In accordance with the guidelines for Americans from the Physical Activity Guidelines Advisory Committee (Physical Activity Guidelines Advisory Committee, 2008), the participants were classified into four groups for data analysis: inactive (< 3.75 MET-hour), low (3.75–7.49 MET-hour), moderate (7.50–16.49 MET-hour) and high (≥16.50 MET-hour).

### 2.4. Air pollution exposure assessment

The details for estimating $PM_{2.5}$ air pollution have been described elsewhere (Zhang et al., 2017). Briefly, we used a spatio-temporal model with high resolution (1 × 1 km) based on satellite aerosol optical depth (AOD) data to retrieve ground-level $PM_{2.5}$ concentrations. The 1-km satellite AOD data was derived from the spectral data from the two Moderate Resolution Imaging Spectroradiometer (MODIS) instruments aboard Terra and Aqua satellites from the U.S. National Aeronautics and Space Administration (Hong Kong University of Science and Technology, 2016). We recently validated the model using data from more than 70 monitoring stations in Taiwan between 2005 and 2014 ($PM_{2.5}$ data were only available for three monitoring stations from 2001 to 2004. Validations were therefore not conducted for this period). The data used for validation were different from the data used