Effects of air pollution and habitual exercise on the risk of death: a longitudinal cohort study

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Appendix

Sources of data

1. Participant selection

Figure E1 (**Supplementary Material**) shows the procedure of participant selection. We selected a total of 442,482 adults (≥18 years old) who joined the medical screening programme between 2001 and 2016, when $PM_{2.5}$ concentration was available. We excluded 3,000 participants with missing $PM_{2.5}$ exposure due to incomplete addresses; 35,041 participants with missing habitual exercise; and 20,311 participants with missing relevant covariates. Finally, we included a total of 384,130 participants with 842,394 complete medical examination records in the main analysis.

2. Outcome ascertainment:

All participants were followed up until 31 May 2019. The entry date was defined as the time of recruitment (i.e., the first medical examination), while the date of study exit was set as 31 May 2019 or the date of death, if earlier. Information on vital status and causes of death was obtained from the National Death Registry, which is maintained by the Ministry of Health and Welfare of Taiwan.[1] The main outcome was death from natural causes [International Classification of Diseases (ICD)-9 codes: 001-779; ICD10 codes: A00–R99]. Participants with an accidental cause of death were censored at the time of death.

3. $PM_{2.5}$ exposure assessment

The Taiwanese government began monitoring ambient $PM_{2.5}$ concentrations in August 2005, and the reported annual concentrations were 33.5, 34.5, 33.7, 33.3, 31.2, 32.3, 28.4, 30.3, 25.1, 21.8 and 20.9 $\mu g/m^3$, respectively, from 2006 to 2016. [2] The major sources of $PM_{2.5}$ pollutants in Taiwan are transportation (such as motor vehicles), construction, power plants and

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heavy industries. The chemical components of particles are complicated. Previous studies observed that secondary aerosols (NH_4^+, NO_3^-, and SO_4^{2-}),[3] natural crustal elements, and the anthropogenic metals (Pb, Ni and Zn)[4] are the main components of $PM_{2.5}$ pollutants in Taiwan.

Details of the $PM_{2.5}$ exposure assessment have been described in our previous publications.[5-7] In brief, a spatiotemporal model was developed at a resolution of 1 km^2 using aerosol optical depth data collected via the Moderate Resolution Imaging Spectroradiometer from the Terra and Aqua satellites carried aboard the U.S. National Aeronautics and Space Administration's Earth Observing System. We obtained ground-level aerosol optical depth data from the aerosol robotic network in Taipei, Taiwan to calibrate the data. Finally, the spatiotemporal model was validated by comparing the estimated $PM_{2.5}$ concentration with the $PM_{2.5}$ concentration from air pollution monitoring stations across Taiwan. The corresponding correlation coefficients ranged from 0.72 to 0.83, and the root mean square error ranged from 3.82 to 5.52 during the study years.[6] The estimated $PM_{2.5}$ exposure was assigned to the participants according to their geo-coded addresses. Long-term exposure to $PM_{2.5}$ was calculated as the two-year average concentration in the year of medical examination and in the previous year. We conducted our analysis using both continuous $PM_{2.5}$ exposure data (per 10 $\mu g/m^3$) and categorical $PM_{2.5}$ exposure (participants were grouped into three categories based on the tertile cut-off points of $PM_{2.5}$, low: <22.4; moderate: 22.4~<26.0; and high: ≥26.0 $\mu g/m^3$).

4. Habitual exercise

Information on habitual leisure-time exercise was collected, and the details have been described in our previous studies. [8-11] Briefly, a standard self-administrated questionnaire was used to collect information on leisure-time exercise. The questionnaire was validated by comparing exercise levels with data from the National Health Interview Survey, and the test-retest approach was used to assess its reliability.[9] We obtained weekly data on the duration and intensity of habitual exercise in the month before each medical examination. Exercise intensity was classified into four categories by asking the question "Which category of exercises did you usually take in the previous month?" with several examples given under each category: light (e.g. walking), moderate (e.g. brisk walking), medium-vigorous (e.g., jogging), or high-vigorous (e.g., running). The four exercise intensity categories were assigned a metabolic equivalent (MET) value (1 MET= 1 kcal/hour/kg bodyweight) of 2.5, 4.5, 6.5 and 8.5, respectively. [9,12] If a participant did not undertake any leisure-time exercise, then a MET value of 0 was assigned. A weighted MET value, based on the time spent in each category, was used for participants who reported activities in more than one intensity category. The exercise volume (MET-h) was calculated as the product of the intensity (MET) and duration (hours). For example, an exercise volume of 8.75 MET-h represented a participant who undertook 3.5 hours/week of light-intensity exercise (e.g., walking), 1.9 hours/week of moderate-intensity exercise (e.g., brisk walking), 1.3 hours/week of medium-vigorous-intensity exercise (e.g., jogging) or 1.0 hours/week of high-vigorous-intensity exercise (e.g., running) or an equivalent combination. For data analysis, participants were grouped into three categories based on the tertile cut-off points of exercise volume (i.e., inactive: MET-h = 0; moderate: 0 < MET-h ≤ 8.75; and high: MET-h > 8.75). The continuous MET-h was not used for data analysis because 0 MET-h was assigned to all participants in the inactive group and previous studies showed a general non-linear association between exercise and various outcomes.[13]

5. Covariates

Details on quality control and data collection for covariates have been described in previous literature[6,14,15] We measured the weight and height of participants with light clothing and without shoes. An overnight fasting blood sample was collected in the

morning. Information on demographics, lifestyles and medical history was collected using a standard self-administered questionnaire. The physical activity intensity at work was also collected using the questionnaire and included in the analysis as a covariate: mostly sedentary (e.g. clerk), sedentary with frequent walking (e.g. seamstress), mostly standing or walking (e.g. retail salesperson), or hard labor (e.g. porter).

In the present study, the following covariates were included in the main analysis: age (years), sex (male or female), education [lower than high school (<10 years), high school (10–12 years), college or university (13–16 years), or postgraduate (>16 years)], body mass index [BMI, calculated as weight divided by height in meters squared (kg/m^2)], physical labor at work (mostly sedentary, mostly standing or walking, or hard labor), cigarette smoking (never, former, or current), alcohol drinking (never/seldom, former, or current), vegetable and fruit intake [seldom (<1 serving/day), moderate (1–2 servings/day), or frequent (>2 servings/day)], occupational exposure (dust or solvent: yes or no), season (spring: March to May; summer: June to August; autumn: September to November; or winter: December to February) and year of enrolment.

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Table E1. The description of the median number of medical visits, time intervals of visits, follow-up duration and the number of person-years

$PM_{2.5}$ × exercise	Median number of medical visits (IQR)	Time intervals of visits (IQR)	Follow-up duration (IQR)	Number of person-years
High-$PM_{2.5}$ & Inactive-exercise	1.0 (1.0, 2.0)	3.8 (1.3, 11.8)	14.3 (11.3, 16.1)	794,603
High-$PM_{2.5}$ & Moderate-exercise	2.0 (1.0, 3.0)	2.9 (1.1, 9.9)	13.5 (10.1, 15.8)	475146
High-$PM_{2.5}$ & High-exercise	2.0 (1.0, 3.0)	2.8 (1.1, 8.4)	12.8 (8.9, 15.8)	384631
Moderate-$PM_{2.5}$ & Inactive-exercise	1.0 (1.0, 2.0)	4.0 (1.3, 11.6)	13.6 (11.0, 16.2)	779429
Moderate-$PM_{2.5}$ & Moderate-exercise	2.0 (1.0, 3.0)	2.9 (1.2, 9.7)	12.9 (9.4, 15.8)	475965
Moderate-$PM_{2.5}$ & High-exercise	2.0 (1.0, 4.0)	2.9 (1.1, 8.7)	12.5 (8.6, 15.8)	364972
Low-$PM_{2.5}$ & Inactive-exercise	1.0 (1.0, 2.0)	4.4 (1.4, 10.4)	14.0 (9.4, 17.3)	730641
Low-$PM_{2.5}$ & Moderate-exercise	2.0 (1.0, 3.0)	3.4 (1.3, 7.7)	12.4 (7.5, 16.9)	457361
Low-$PM_{2.5}$ & High-exercise	2.0 (1.0, 4.0)	3.3 (1.3, 7.0)	10.9 (6.8, 16.8)	395101

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Table E2. Associations of natural-cause mortality with habitual exercise and $PM_{2.5}$ exposures in participants after adjusting for hypertension, diabetes, dyslipidemia and cardiovascular diseases, and chronic obstructive pulmonary disease

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate- exercise / $PM_{2.5}$	0.79 (0.71, 0.89)	<0.001	1.06 (0.95, 1.18)	0.300		
High- exercise /$PM_{2.5}$	0.73 (0.66, 0.81)	<0.001	1.13 (1.02, 1.26)	0.018		
Trend test	0.85 (0.81, 0.90)	<0.001	1.06 (1.01, 1.12)	0.018	1.04 (0.98, 1.12)	0.200 †
Per 10 μg/m^3	–	–	1.12 (1.05, 1.20)	0.001	–	–

131,846 participants with 213,146 medical examinations

The effects were presented as hazard ratio with 95% confidence level, with the participants who were inactive or exposed to low-$PM_{2.5}$ as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, cigarette smoking, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

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Table E3. Associations of natural-cause mortality with habitual exercise and annual $PM_{2.5}$ in the year of medical examination

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate- exercise / $PM_{2.5}$	0.84 (0.8, 0.88)	<0.001	1.1 (1.06, 1.16)	<0.001		
High- exercise /$PM_{2.5}$	0.65 (0.63, 0.68)	<0.001	1.18 (1.16, 1.24)	<0.001		
Trend test	0.81 (0.79, 0.83)	<0.001	1.09 (1.07, 1.12)	<0.001	1.04 (1.01, 1.07)	0.002 †
Per 10 μg/m^3	–	–	1.30 (1.25, 1.35)	<0.001		

384,130 participants with 842,394 medical examinations.

The effects were presented as hazard ratio with 95% confidence level, with the participants who were inactive or exposed to low-$PM_{2.5}$ as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, cigarette smoking, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

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Table E4. Associations of natural-cause mortality with substituted habitual exercise and $PM_{2.5}$

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate- exercise / $PM_{2.5}$	0.83 (0.80, 0.87)	<0.001	1.04 (0.99, 1.08)	0.120		
High- exercise /$PM_{2.5}$	0.64 (0.61, 0.67)	<0.001	1.17 (1.12, 1.22)	<0.001		
Trend test	0.80 (0.78, 0.82)	<0.001	1.08 (1.06, 1.11)	<0.001	1.04 (1.01, 1.06)	0.007 †
Per 10 μg/m^3	–	–	1.29 (1.24, 1.35)	<0.001	–	–

388,272 participants with 958,316 medical examinations.

The effects were presented as hazard ratio with 95% confidence level, with the participants who were inactive or exposed to low-$PM_{2.5}$ as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, cigarette smoking, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

Table E5. Associations of natural-cause mortality with habitual exercise and $PM_{2.5}$ in participants aged 65 years or above

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	***P***	**Hazard Ratio**	***P***	**Hazard Ratio**	***P***
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate- exercise / $PM_{2.5}$	0.67 (0.63, 0.71)	<0.001	1.04 (0.98, 1.11)	0.200		
High- exercise /$PM_{2.5}$	0.64 (0.60, 0.68)	<0.001	1.19 (1.12, 1.27)	<0.001		
Trend test	0.78 (0.76, 0.81)	<0.001	1.09 (1.05, 1.12)	<0.001	1.03 (0.99, 1.07)	0.190 †
Per 10 μg/m^3	–	–	1.24 (1.18, 1.31)	<0.001		

24,817 participants with 47,318 medical examinations.

The effects were presented as hazard ratio with 95% confidence level, with the participants who were inactive or exposed to low-$PM_{2.5}$ as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, cigarette smoking, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

Table E6. Associations of natural-cause mortality with habitual exercise and $PM_{2.5}$ in non-smokers

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate- exercise / $PM_{2.5}$	0.84 (0.79, 0.88)	<0.001	1.01 (0.95, 1.07)	0.810		
High- exercise /$PM_{2.5}$	0.62 (0.59, 0.66)	<0.001	1.16 (1.10, 1.22)	<0.001		
Trend test	0.79 (0.77, 0.81)	<0.001	1.07 (1.04, 1.11)	<0.001	1.04 (1.01, 1.08)	0.010†
Per 10 μg/m^3	–	–	1.22 (1.16, 1.28)	<0.001		

291,529 participants with 635,672 medical examinations.

The effects were presented as hazard ratio with 95% confidence level, with the participants who were inactive or exposed to low-$PM_{2.5}$ as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

Table E7. Associations of all-cause mortality with habitual exercise and $PM_{2.5}$

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	***P***	**Hazard Ratio**	***P***	**Hazard Ratio**	***P***
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate- exercise / $PM_{2.5}$	0.84 (0.81, 0.88)	<0.001	1.02 (0.98, 1.07)	0.350		
High- exercise /$PM_{2.5}$	0.66 (0.63, 0.69)	<0.001	1.15 (1.09, 1.20)	<0.001		
Trend test	0.81 (0.80, 0.83)	<0.001	1.06 (1.04, 1.09)	<0.001	1.03 (1.00, 1.06)	0.022 †
Per 10 μg/m^3	–	–	1.19 (1.14, 1.24)	<0.001		

384,130 participants with 842,394 medical examinations.

The effects were presented as hazard ratio with 95% confidence level, with the participants who were inactive or exposed to low-$PM_{2.5}$ as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, cigarette smoking, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

Table E8. Associations of natural-cause mortality with habitual exercise and $PM_{2.5}$ in participants who provided a home address

Model *	Exercise		$PM_{2.5}$ exposure		$PM_{2.5}$ × exercise	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Inactive/low- $PM_{2.5}$	Reference	–	Reference	–		
Moderate-exercise/ $PM_{2.5}$	0.84 (0.81, 0.88)	<0.001	1.02 (0.98, 1.07)	0.360		
High-exercise/$PM_{2.5}$	0.65 (0.62, 0.68)	<0.001	1.17 (1.11, 1.22)	<0.001		
Trend test	0.81 (0.79, 0.83)	<0.001	1.07 (1.05, 1.10)	<0.001	1.03 (1.00, 1.06)	0.016 †
Per 10 μg/m^3	–	–	1.20 (1.15, 1.25)	<0.001		

This analysis includes 317,232 participants with 699,458 medical examinations.

The effects are presented as hazard ratios with 95% confidence levels. Participants in the inactive and low-$PM_{2.5}$ exposure categories were used as the reference group.

* Model adjusted for age, sex, education, body mass index, physical labor at work, cigarette smoking, alcohol drinking, vegetable intake, fruit intake, occupational exposure, season, year of enrolment, exercise (for the association between $PM_{2.5}$ and death from natural causes) or $PM_{2.5}$ (for the association between exercise and death from natural causes).

† P value for the overall interaction term of "$PM_{2.5}$ (10 μg/m^3) and categories exercise".

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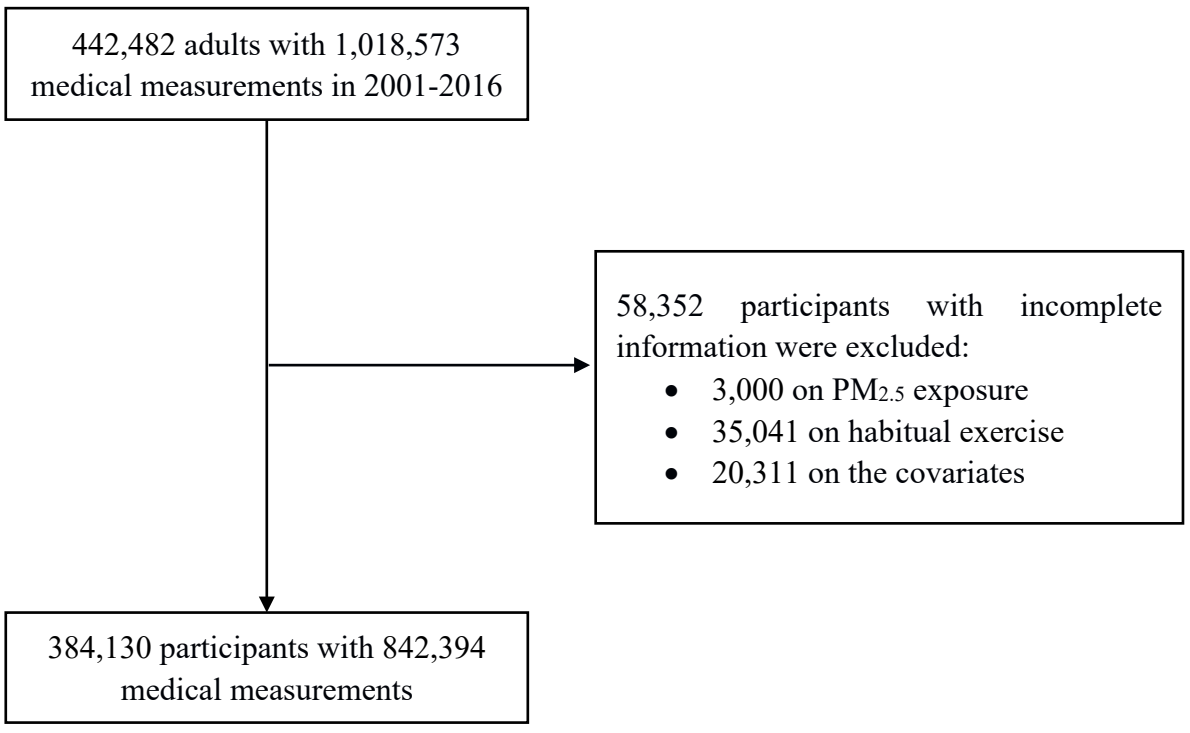

Figure E1. Flow chart of participant selection