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**CLINICAL RESEARCH**
*Epidemiology and Prevention*

# Association of the combined effects of air pollution and changes in physical activity with cardiovascular disease in young adults

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**Aims** Little is known about the trade-off between the health benefits of physical activity (PA) and the potential harmful effects of increased exposure to air pollution during outdoor PA. We examined the association of the combined effects of air pollution and changes in PA with cardiovascular disease (CVD) in young adults.

**Methods and results** This nationwide cohort study included 1 469 972 young adults aged 20–39 years. Air pollution exposure was estimated by the annual average cumulative level of particulate matter (PM). PA was calculated as minutes of metabolic equivalent tasks per week (MET-min/week) based on two consecutive health examinations from 2009 to 2012. Compared with the participants exposed to low-to-moderate levels of PM2.5 or PM10 who continuously engaged in ≥1000 MET-min/week of PA, those who decreased their PA from ≥1000 MET-min/week to 1–499 MET-min/week [PM10 adjusted hazard ratio (aHR) 1.22; 95% confidence interval (CI) 1.00–1.48] and to 0 MET-min/week (physically inactive; PM10 aHR 1.38; 95% CI 1.07–1.78) had an increased risk of CVD (*P* for trend <0.01). Among participants exposed to high levels of PM2.5 or PM10, the risk of CVD was elevated with an increase in PA above 1000 MET-min/week.

**Conclusion** Reducing PA may lead to subsequent elevation of CVD risk in young adults exposed to low-to-moderate levels of PM2.5 or PM10, whereas a large increase in PA in a high-pollution environment may adversely affect cardiovascular health.

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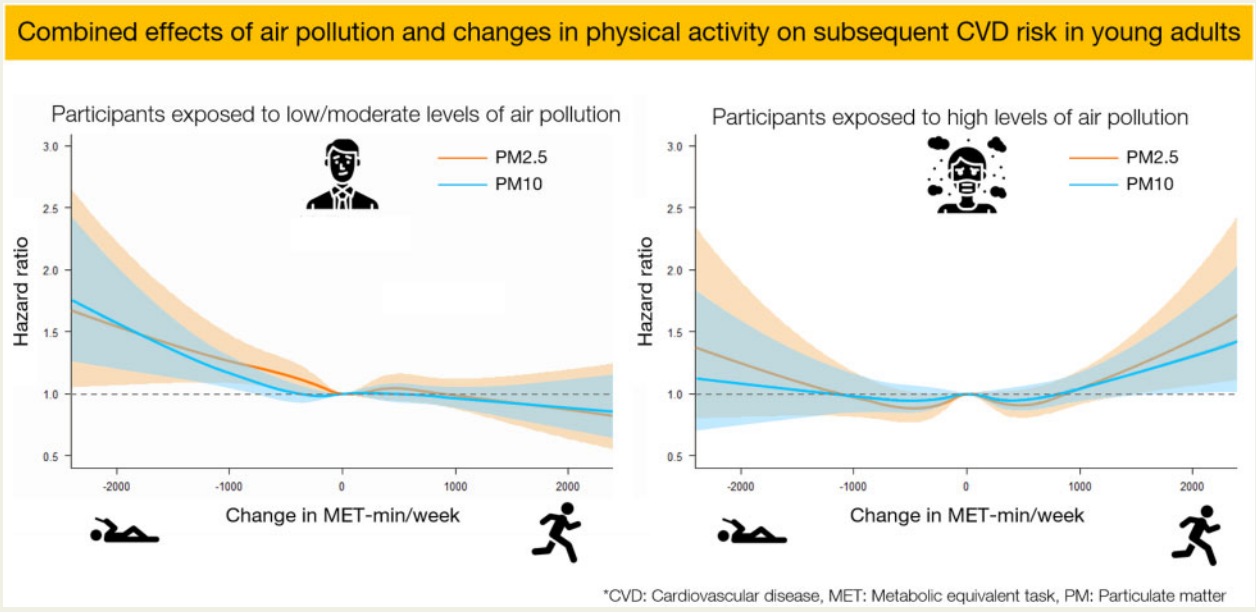
## Graphical Abstract




Combined effects of air pollution and changes in physical activity with cardiovascular disease in young adults.

**Keywords** Physical activity • Air pollution • Young adults • Cardiovascular disease

# Introduction

Cardiovascular disease (CVD) is the most common cause of death worldwide.[1] The Global Burden of Disease study reported that ~17 million global deaths per year between 2006 and 2016 were attributable to CVD, which surpasses the number of deaths from any other disease.[1] Therefore, the risk factors for CVD should be managed properly considering its clinical importance.

Among CVD-related factors, the association of the combined effects of air pollution and physical activity (PA) with CVD is becoming one of the most important public health issues. PA is well known for its protective effects on CVD,[2–5] whereas exposure to particulate matter (PM) in air pollutants, such as PM2.5 and PM10, has been reported to have detrimental effects on CVD.[6–9] These reports imply that outdoor PA in the presence of high levels of ambient air pollution may attenuate the protective effects of PA on CVD or even increase CVD risk. The trade-off between the health benefits of PA and its potential detrimental effects due to increased exposure to air pollutants during outdoor PA remains controversial.[6]

To date, only one study has investigated the combined effects of air pollution and PA on CVD. The study found that engaging in a higher frequency of moderate to vigorous PA decreased the risk of CVD in participants exposed to both high and low levels of air pollution,[10] but this study was conducted on middle-aged and older adults. No study has examined the effects of changes in PA combined with the effects of air pollution on cardiovascular health. Young adults are more likely to have fewer cardiovascular risk factors and to be physically active than middle-aged and older adults.[11,12] For these reasons, young adults might be more sensitive to air pollution, which is a risk factor for CVD, especially as a result of increased exposure to air pollution when performing outdoor PA.

Using a large, nationwide database of young adults 20–39 years of age from the National Health Insurance Service (NHIS) in South Korea, we examined the association of the combined effects of air pollution and changes in PA with CVD risk and also assessed whether the cardiovascular health benefits of changes in PA outweigh the potential detrimental effects of increased exposure to air pollution.

# Methods

## Study population

The NHIS provides universal health insurance for the Korean population, with an enrolment of 97%,[13] covering nearly all kinds of healthcare services, such as hospital admission, outpatient hospital use, and pharmaceutical prescriptions. The NHIS also provides biennial health screening examinations for all employed and self-employed insured citizens aged 20 years or older, including all dependents aged 40 years or older.[14] Health screening examinations include anthropometric measurements, laboratory tests, and health behaviours collected from a self-reported questionnaire. Several epidemiological studies have used NHIS data because NHIS provide its database for research purposes, and its validity has been described elsewhere.[13]

Among 1 486 758 Korean young adults aged between 20 and 39 years without a previous history of CVD living in all metropolitan cities in South Korea who underwent two consecutive biennial health examinations during the first (2009 and 2010) and second (2011 and 2012) health screening periods, data from 430 subjects who died and 16 356 subjects

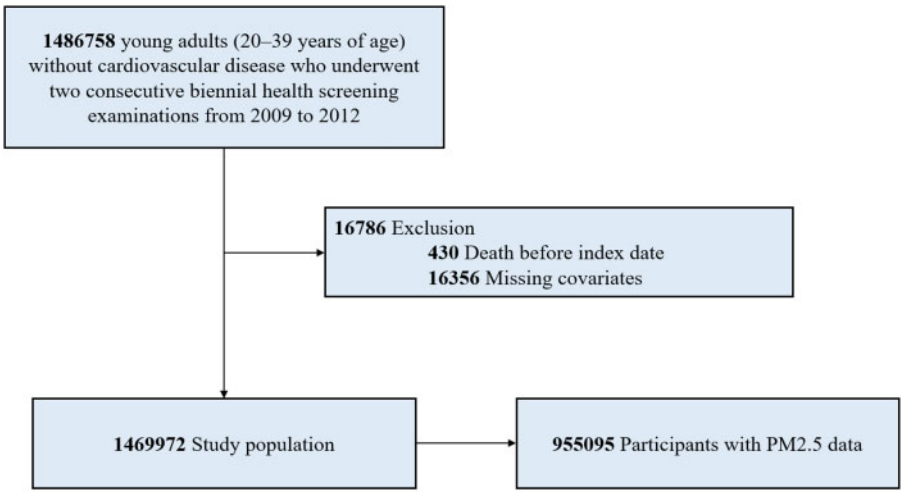



**Figure 1** Flow diagram of selection of study participant.

with missing covariate values before the index date of 1 January 2013, were excluded. Finally, a total of 1 469 972 participants were enrolled and followed up from 1 January 2013 to 31 December 2018. *Figure 1* shows the selection flow diagram of the study population.

The Institutional Review Board of the Seoul National University Hospital (IRB number: E-1911-133-1080) approved the study. The requirement for informed patient consent was waived because the NHIS cohort database is anonymized according to strict confidentiality guidelines.

## Assessment of physical activity

PA was measured by a series of self-administered questionnaires during the consecutive health examinations using a last 7-day recall method which is reliable for monitoring PA levels of the population.[15,16] Using the responses to the NHIS survey from the two consecutive biennial health examinations (2009–2010 and 2011–2012), we extracted the weekly frequencies of light-intensity (≥30 min/day; e.g. light exercise, walking for leisure), moderate-intensity (≥30 min/day; e.g. fast/brisk walking, tennis, slow cycling), and vigorous-intensity (≥20 min/day; e.g. running, aerobics, fast cycling, mountain hiking) PA. Ratings of 2.9, 4.0, and 7.0 metabolic equivalent tasks (METs) were applied to light, moderate, and vigorous PA, respectively, based on a previous study.[17] The total PA energy expenditure values in minutes of metabolic equivalent tasks per week (MET-min/week) were calculated by summing the MET-min/week values for each kind of PA considering frequency, intensity, and duration. We categorized individuals into four groups of 0, 1–499, 500–999 (current guideline recommendations[18,19]), and ≥1000 MET-min/week of PA during the two consecutive screening periods, and the MET-min/week values for the first and second screening periods were used to determine changes in PA. The changes in PA were calculated by subtracting MET-min/week values obtained during the first health screening period from those obtained during the second health screening period.

## Estimation of individual exposure to air pollution

The National Ambient Air Monitoring System (NAMIS) (https://www.airkorea.or.kr) in South Korea provides monitoring data on ambient levels of PM10 and PM2.5. Daily air pollution data are collected from ~280 nationwide atmospheric monitoring sites. The monitoring sites are allocated based on the number of residents, location of the residential area, source of emissions, and area of the target monitoring site. Usually at least one atmospheric monitoring station is allocated to each administrative residential district in metropolitan cities. This study included 73 administrative residential districts located in all metropolitan cities in South Korea. Most people lived in residential districts that were covered by atmospheric monitoring stations, except for those living in two residential districts (0.8% of the total population) that were not monitored for PM10. PM2.5 was only monitored in three major metropolitan cities (Seoul, Busan, and Incheon) from 2009 to 2012. Therefore, a total of 955 095 individuals living in 50 administrative residential districts in three major metropolitan cities were included and were covered by atmospheric monitoring stations, except for eight residential districts (7.9% of the total population) that were not monitored for PM2.5. Air pollution levels in these unmonitored districts were estimated using information from the closest monitoring station. The baseline characteristics of participants with PM2.5 data compared to the those without PM2.5 data were assessed using descriptive statistics in Supplementary material online, *Table S1*.

The air pollution data on each administrative residential district from NAMIS were linked with each participant using the residential district codes provided by the NHIS database. In particular, in this process, we collected data on the residences of each participant on a yearly basis and linked them with the yearly average annual PM2.5 or PM10 levels based on the residential districts of each year to accurately assess the exposure levels to air pollution among migrant populations. Then, according to a previous study's method,[20] we calculated the 4-year average annual cumulative PM2.5 or PM10 levels for each individual by computing the mean of the annual PM2.5 or PM10 levels from 2009 to 2012, which were linked based on the residential district of each participant and were estimated as the level of air pollution exposure for each subject. The amount of exposure to air pollution was categorized into two levels (low to moderate vs. high) based on a cut-off value of the 66th percentile (3rd tertile) of the range of exposure in this cohort.

## Cardiovascular disease events

Hospitalization records from the NHIS database and the International Classification of Diseases, Tenth Revision (ICD-10) were used to identify CVD events, including coronary heart disease (CHD) and stroke. Based

on the American Heart Association guidelines, we used ICD-10 codes to determine CVD events (ICD-10 codes I20–I25 and I60–I69), including CHD (ICD-10 codes I20–I25) and stroke (ICD-10 codes I60–I69).[21] To include only genuine cases of CVD, we defined CVD outcomes in patients with at least 2 days of hospitalization with ICD-10 codes related to CVD.

## Statistical analysis

The participants were followed up from 1 January 2013, and their data were censored at the date of the first CVD event, death, or 31 December 2018, whichever came first. We conducted Cox proportional regression analysis to assess the hazard ratios (HRs) and 95% confidence intervals (CIs) for CVD including CHD and stroke according to the combined effects of exposure to air pollution and changes in PA. Restricted cubic splines of changes in PA according to the level of exposure to PM2.5 or PM10 were suggested to graphically estimate the association of the combined effects of air pollution and changes in PA with CVD.[22] In accordance with previous studies, five knots were located at the 5th, 25th, 50th, 75th, and 95th percentiles of the change in MET-min/week of PA.[17,23] Subgroup analyses of CVD risk according to changes in PA stratified by sex, body mass index (BMI), smoking status, Charlson comorbidity index (CCI), and presence of hypertension, diabetes, and hypercholesterolaemia were also performed. We adjusted for the following covariates in the Cox proportional regression model: age (continuous, years), sex (categorical, male or female), district (categorical, metropolitan city), household income (categorical, 1st, 2nd, 3rd, and 4th quartiles), smoking status (categorical, never, past, and current smokers), alcohol intake (categorical, 0, 1 or 2, 3 or 4, and ≥5 times per week), BMI (continuous, kg/m$^2$), systolic blood pressure (SBP) (continuous, mmHg), fasting serum glucose (FSG) (continuous, mg/dL), total cholesterol (TCHO) (continuous, mg/dL), and CCI (continuous). Household income was assessed according to each individual's insurance premium, and smoking status and alcohol consumption were measured by a self-administered questionnaire during the health examination. CCI was estimated using an algorithm based on a previous study.[24]

In addition, four types of sensitivity analyses were conducted. First, analyses were performed after excluding subjects with hypertension, diabetes, hypercholesterolaemia, and atrial fibrillation to strictly exclude the possible influences of cardiovascular risk factors. We defined hypertension (SBP ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of antihypertensive mediation such as beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blocker), diabetes (FSG level ≥126 mg/dL or use of antidiabetic medication), and hypercholesterolaemia (TCHO level ≥ 240 mg/dL or use of antiatherosclerotic medication such as statin) using laboratory tests and the use of medication according to previous studies and atrial fibrillation in patients with ICD-10 codes related to atrial fibrillation (ICD-10 code I48).[25,26] Second, we additionally conducted sensitivity analysis by adding patients with <2 days of hospitalization and with ICD-10 codes related to CVD as CVD outcomes to consider the possibility of the true events in patients with <2 days of hospitalization. Third, sensitivity analysis was conducted after considering the change in levels of exposure to air pollution and adjusting the baseline smoking status, alcohol intake, BMI, SBP, FSG, TCHO, and CCI and their changes to consider the time-varying characteristics of the variables. Finally, we performed additional analyses using two-pollutant model. The single-pollutant model used in this study is the simplest model to identify the influence of a single air pollutant; however, it may not be able to consider the impacts of the other air pollutants. In the two-pollutant model, however, PM2.5 and PM10 levels were mutually adjusted; although the two-pollutant model has potential for collinearity, it enables the simultaneous consideration of the effects of air pollutants (PM2.5 and PM10) and further the results from this model might also be more likely to be valid than those from the single-pollutant model of each pollutant.[27,28]

A two-sided *P*-value of <0.05 was considered to indicate statistical significance. All analyses, data collection, and data mining were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R programming version 3.5.3 (the R Foundation for Statistical Computing, Vienna, Austria).

# Results

A total of 8706 CVD events occurred during 8 779 364 person-years of follow-up. The descriptive characteristics of study participants are listed in *Table 1*. Among 1 469 972 participants, the mean (SD) age was 32.3 (4.8) years and 886 844 were men. About one-fifth of the participants were reported as physically inactive (18% in the first health examination and 16% in the second health examination). Women tended to be more physically inactive than men in both health examinations. In addition, participants with PM2.5 data tended to be more physically active, be exposed to higher level of PM10, have higher household income, do not smoke, drink more alcohol, and have lower SBP, FSG, and CCI compared with those without PM2.5 data (Supplementary material online, *Table S1*). The data of average annual cumulative PM2.5 or PM10 exposure levels from 2009 to 2012 and their changes from 2009 to 2012 are presented in Supplementary material online, *Table S2*.

*Figure 2* shows that a decrease in PA was associated with a higher risk of CVD among participants with low-to-moderate levels of exposure to PM2.5. Among participants exposed to high levels of PM2.5 or PM10, an increase in PA above 1000 MET-min/week had a negative effect on cardiovascular health. Indeed, the significant effect modification of the association between changes in PA and CVD risk was identified by the level of PM2.5 exposure (*P* for interaction = 0.09, marginally attenuated). According to *Figure 3*, the association of the combined effects of PM10 exposure and changes in PA with CVD showed similar results and trends to that of PM2.5 exposure and changes in PA with CVD. In particular, the significant effect modification of the association between changes in PA and CVD risk was also identified by the level of PM10 exposure (*P* for interaction = 0.01) (Graphical Abstract).

The association of changes in PA strata with CVD risk stratified by level of air pollution is depicted in *Tables 2* and *3*. Among participants exposed to low-to-moderate levels of air pollution, those who increased their PA from 0 MET-min/week (physically inactive) to ≥1000 MET-min/week [PM2.5 adjusted HR (aHR) 0.73; 95% CI 0.52–1.03; *P* for trend 0.04] had a reduced risk of CVD compared with participants who were continuously physically inactive. Participants who decreased their PA from ≥1000 MET-min/week to 1–499 MET-min/week (PM10 aHR 1.22; 95% CI 1.00–1.48) and 0 MET-min/week (PM10 aHR 1.38; 95% CI 1.07–1.78) had an increased risk of CVD compared with participants who maintained ≥1000 MET-min/week of PA. On the other hand, among groups exposed to high levels of air pollution, increasing PA from physically inactive to ≥1000 MET-min/week tended to negate the risk-reducing effect of PA on CVD (PM2.5 aHR 1.33; 95% CI 0.96–1.84). For CHD and stroke, the association of changes in PA strata with these outcomes stratified by level

**Table 1 Characteristics of the study participants**

| | Total | Men | Women |
|---|---|---|---|
| Number of people | 1 469 972 | 886 844 | 583 128 |
| Physical activity at health examination Period I (2009–10), MET-min/week, *n* (%) | | | |
| 0 (physically inactive) | 263 822 (18.0) | 144 060 (16.2) | 119 762 (20.5) |
| 1–499 | 548 395 (37.3) | 309 032 (34.9) | 239 363 (41.1) |
| 500–999 | 463 983 (31.6) | 294 338 (33.2) | 169 645 (29.1) |
| ≥1000 | 193 772 (13.1) | 139 414 (15.7) | 54 358 (9.3) |
| Physical activity at health examination Period II (2011–12), MET-min/week, *n* (%) | | | |
| 0 (physically inactive) | 241 545 (16.4) | 132 224 (14.9) | 109 321 (18.8) |
| 1–499 | 540 688 (36.8) | 307 123 (34.6) | 233 565 (40.1) |
| 500–999 | 471 611 (32.1) | 296 697 (33.5) | 174 914 (30.0) |
| ≥1000 | 216 128 (14.7) | 150 800 (17.0) | 65 328 (11.1) |
| PM10 (μg/m$^3$), mean (SD)[a] | | | |
| Low/moderate (<49.9 2 μg/m$^3$) | 45.54 (3.64) | 45.55 (3.63) | 45.52 (3.67) |
| High (≥49.92 μg/m$^3$) | 53.29 (3.48) | 53.40 (3.49) | 53.12 (3.45) |
| PM2.5 (three major metropolitan cities), mean (SD)[b] | | | |
| Low/moderate (<26.43 μg/m$^3$) | 24.11 (1.75) | 24.09 (1.77) | 24.13 (1.72) |
| High (≥26.43 μg/m$^3$) | 29.70 (2.29) | 29.78 (2.28) | 29.56 (2.30) |
| Age, mean (SD) | 32.3 (4.8) | 33.1 (4.5) | 31.1 (5.0) |
| Household income, quartile, *n* (%) | | | |
| 1st (highest) | 387 666 (26.4) | 284 551 (32.1) | 103 115 (17.7) |
| 2$^{nd}$ | 560 851 (38.2) | 359 560 (40.5) | 201 291 (34.5) |
| 3$^{rd}$ | 343 672 (23.4) | 169 582 (19.1) | 174 090 (29.9) |
| 4th (lowest) | 177 783 (12.0) | 73 151 (8.3) | 104 632 (17.9) |
| Smoking, *n* (%) | | | |
| Never | 801 633 (54.5) | 257 007 (29.0) | 544 626 (93.4) |
| Former | 193 633 (13.2) | 176 695 (19.9) | 17 038 (2.9) |
| Current | 474 606 (32.3) | 453 142 (51.1) | 21 464 (3.7) |
| Alcohol intake, times per week, *n* (%) | | | |
| 0 | 539 086 (36.7) | 211 199 (23.8) | 327 887 (56.2) |
| 1–2 | 753 540 (51.3) | 528 591 (59.6) | 224 949 (38.6) |
| 3–4 | 152 025 (10.3) | 125 579 (14.2) | 26 446 (4.5) |
| ≥5 | 25 321 (1.7) | 21 475 (2.4) | 3846 (0.7) |
| Body mass index (kg/m$^2$), mean (SD) | 23.3 (3.6) | 24.5 (3.3) | 21.4 (3.2) |
| Systolic blood pressure (mmHg), mean (SD) | 117.8 (13.5) | 122.5 (12.5) | 110.7 (11.7) |
| Fasting serum glucose (mg/dL), mean (SD) | 92.1 (17.0) | 94.6 (18.9) | 88.4 (12.5) |
| Total cholesterol (mg/dL), mean (SD) | 189.5 (34.4) | 194.9 (35.1) | 181.2 (31.6) |
| Charlson comorbidity index, *n* (%) | | | |
| 0 | 903 736 (61.5) | 568 885 (64.2) | 334 851 (57.4) |
| 1 | 450 567 (28.6) | 253 947 (28.6) | 196 620 (33.7) |
| ≥2 | 115 669 (7.9) | 64 012 (7.2) | 51 657 (8.9) |

PM, particulate matter; MET, metabolic equivalent task; SD, standard deviation.
[a]A total of 1 469 972 participants with PM10 data.
[b]A total of 955 095 participants with PM2.5 data.

of air pollution exhibited similar results and trends, which are shown in Supplementary material online, *Tables S3* and *S4*.

The combined effects of changes in PA and exposure to PM2.5 on CVD risk are depicted in *Figure 4*. Compared with participants who were continuously physically inactive while exposed to high levels of PM2.5, participants who were exposed to lower levels of PM2.5 and increased their PA from physically inactive to ≥1000 MET-min/week had a reduced risk of CVD (aHR 0.63; 95% CI 0.44–0.90). On the contrary, compared with participants who continuously engaged in ≥1000 MET-min/week of PA while exposed to low-to-moderate levels of PM2.5, participants who were exposed to higher levels of PM2.5 and decreased their PA from ≥1000 MET-min/week to physically inactive had an elevated CVD risk (aHR 1.67; 95% CI 1.14–2.43).

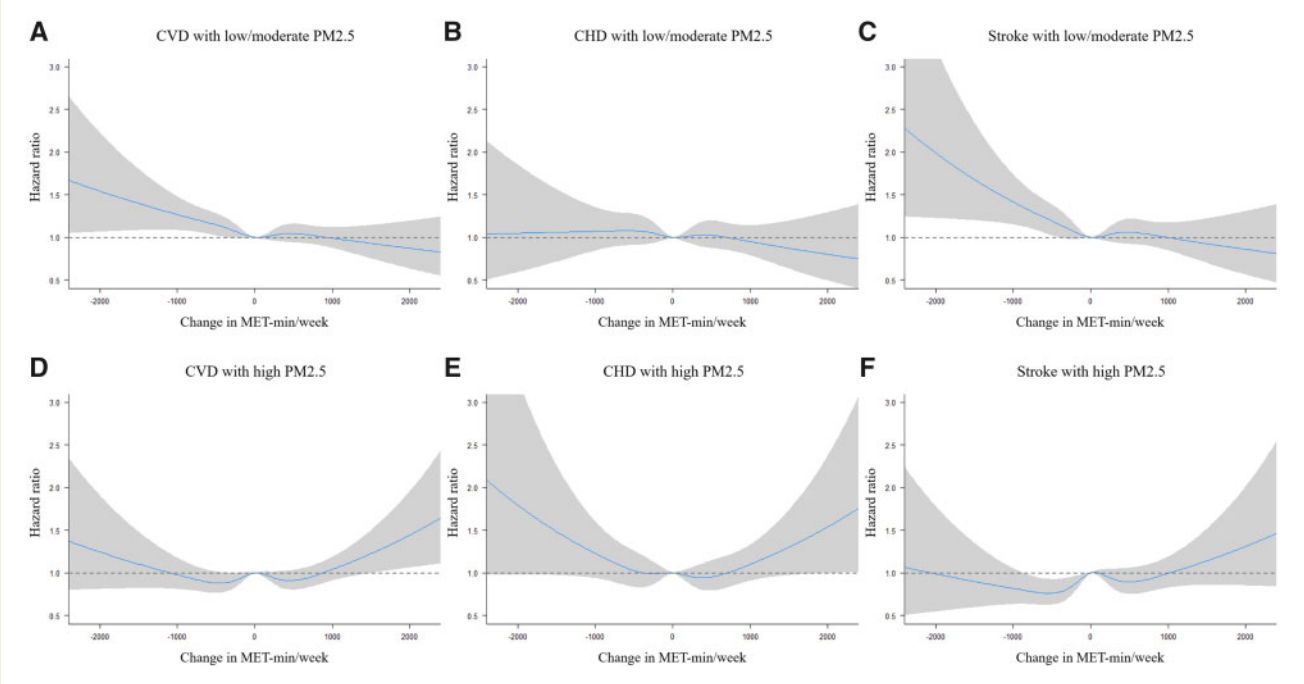



**Figure 2** Association of the change in physical activity (metabolic equivalent task-min/week) with cardiovascular disease including coronary heart disease and stroke according to the level of particulate matter 2.5 among young adults. Solid lines represent adjusted hazard ratios, and the shaded region indicates the 95% confidence intervals from restricted cubic spline regression. Restricted cubic splines were constructed with five knots located at the 5th, 25th, 50th, 75th, and 95th percentiles of the change in metabolic equivalent task-min/week. Adjusted hazard ratios (95% confidence interval) were calculated using Cox proportional hazards regression analysis after adjusting for baseline metabolic equivalent task-min/week, age, sex, district, household income, body mass index, smoking, alcohol intake, systolic blood pressure, fasting serum glucose, total cholesterol, and Charlson comorbidity index. The cut-off value of particulate matter 2.5 (low to moderate vs. high) was 26.43 μg/m$^3$.

Supplementary material online, *Tables S5* and *S6* show the results of subgroup analyses stratifying the subjects by sex, BMI, smoking status, comorbidity (CCI), and presence of hypertension, diabetes, and hypercholesterolaemia. The trends of association between the combined effects of air pollution and increase or decrease in PA and CVD risk were similar in most subgroups.

The results of sensitivity analyses after excluding subjects with cardiovascular risk factors (hypertension, diabetes, hypercholesterolaemia, and atrial fibrillation) (Supplementary material online, *Figure S1*), adding patients with <2 days of hospitalization and with ICD-10 codes related to CVD as CVD outcomes (Supplementary material online, *Figure S2*), considering the change in levels of exposure to air pollution and the time-varying characteristics of various variables (Supplementary material online, *Figures S3* and *S4*), and using the two-pollutant model (Supplementary material online, *Figure S5*) are presented. In all sensitivity analyses, the results and trends were consistent with the main results. In particular, according to Supplementary material online, *Figure S4*, a decrease in PA was associated with a greater risk of CVD in participants with reduced levels of exposure to PM10 or PM2.5 in 2012 as compared to 2009. Among participants with increased levels of exposure to air pollution in 2012 as compared to 2009, a large increase in PA had a negative impact on cardiovascular health, although the statistical significance was attenuated in participants with PM10 exposure probably due to a relatively small sample size.

# Discussion

In this large, population-based, nationwide study, we showed real-world evidence that physically active young adults who decreased their PA had an increased risk of CVD compared with those who maintained their frequency of PA within groups with low-to-moderate levels of exposure to PM2.5 or PM10. In contrast, among young adults exposed to high levels of PM2.5 or PM10, participants who increased their PA above 1000 MET-min/week were at an increased risk of CVD. We found a significant effect modification of the association between changes in PA and CVD risk by the level of exposure to PM2.5 or PM10. This is the first study to examine the association of the combined effects of air pollution and changes in PA with CVD in young adults.

Until now, there has been little information on the trade-off between the cardiovascular health benefits of PA and the potential harmful effects of increased exposure to air pollution during outdoor PA. Furthermore, no study has examined the trade-off between the potential cardiovascular harm caused by a decrease in PA and the benefits to cardiovascular health from decreased exposure to air pollutants due to decreased outdoor PA. Multiple studies have focused on the harmful impact of increased inhalation and deposition of air pollutants due to rapid breathing during outdoor PA.[29,30] In the direct pathway, fine particles of PM2.5 are directly transmitted into the blood stream and are deposited on target organs, causing

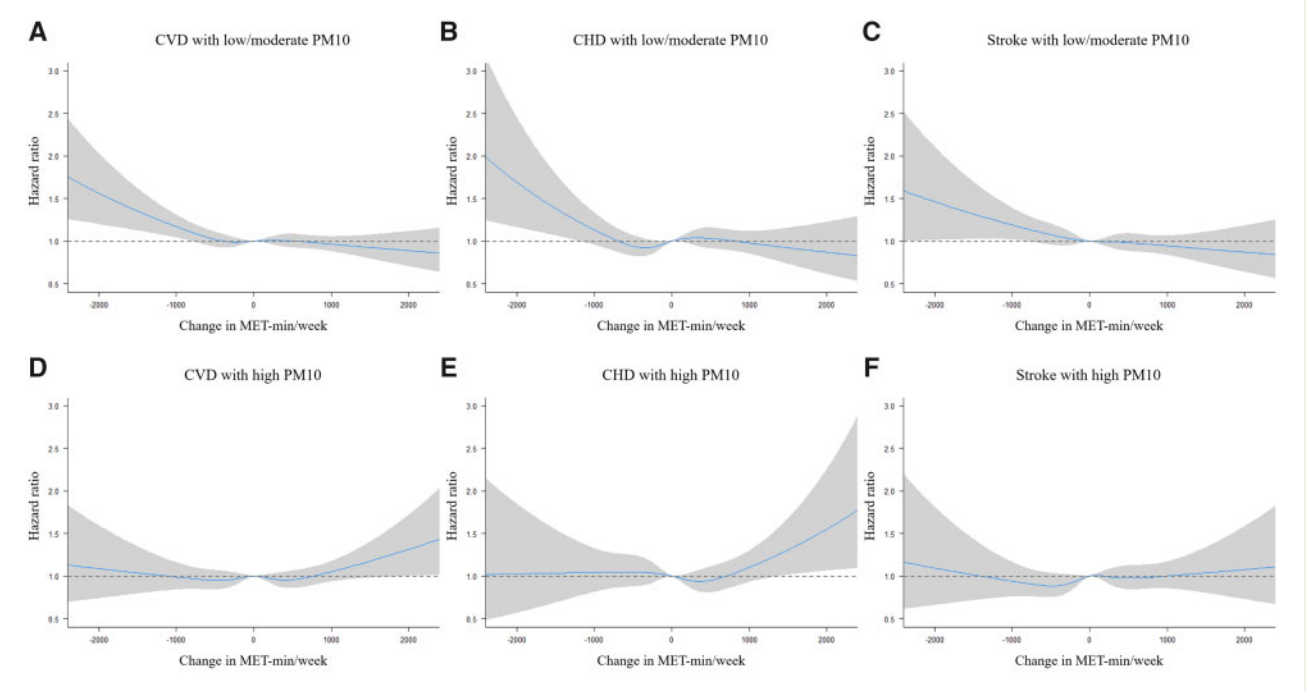



**Figure 3** Association of the change in physical activity (metabolic equivalent task-min/week) with cardiovascular disease including coronary heart disease and stroke according to the level of particulate matter 10 among young adults. Solid lines represent adjusted hazard ratios, and the shaded region indicates the 95% confidence intervals from restricted cubic spline regression. Restricted cubic splines were constructed with five knots located at the 5th, 25th, 50th, 75th, and 95th percentiles of the change in metabolic equivalent task-min/week. Adjusted hazard ratios (95% confidence interval) were calculated using Cox proportional hazards regression analysis after adjusting for baseline metabolic equivalent task-min/week, age, sex, district, household income, body mass index, smoking, alcohol intake, systolic blood pressure, fasting serum glucose, total cholesterol, and Charlson comorbidity index. The cut-off value of particulate matter 10 (low to moderate vs. high) was 49.92 μg/m$^3$.

vasoconstriction, endothelial dysfunction, elevated blood pressure, and platelet aggregation.[31] In the indirect pathway, PM activates the pulmonary oxidative stress and systemic inflammatory pathways, which contribute to increasing the risk of CVD.[32,33] The autonomic nervous system is also activated by PM through specific lung receptors, resulting in imbalance of the autonomic nervous system and potentially elevated cardiac arrhythmia.[32] Therefore, engaging in outdoor PA in a polluted atmosphere might have detrimental effects on cardiovascular health due to the increased inhalation of air pollutants in spite of the cardiovascular benefits of PA.[30]

In spite of the detrimental effects of air pollution on CVD described above, PA may diminish the risk of CVD by improving cardiopulmonary function.[34–36] Engaging in PA is helpful for enhancement of aerobic capacity and physical function, and it also reinforces cardiorespiratory fitness.[37] PA, especially aerobic training, improves the compliance and reactivity of blood vessels, systemic immune function, and cardiac output.[38] Moreover, engaging in PA regularly is a highly effective way to manage a variety of metabolic risk factors for CVD, such as controlling body weight and reducing blood pressure, systemic inflammation, atherogenic lipid profiles, haemoglobin A1C, and insulin resistance.[39] Decreased PA may reduce all these cardiovascular health benefits of regular PA and also damage peroxisome proliferator-activated receptors, which contribute to myocyte inflammation and insulin resistance.[40] Currently, the European Society of Cardiology and US Department of Health and Human Services have reemphasized the importance and positive impacts of PA, and engaging in at least 500–1000 MET-min/week of PA is recommended by current PA guidelines.[11,18,19]

It is clinically very important to determine the optimal patterns of PA behaviours according to air pollution levels because air pollution is an obstacle to active exercise, despite the clinical importance of PA for young adults who have peak aerobic capacity.[41,42] Our findings showed that decreased PA was associated with elevated risk of CVD in participants with low-to-moderate levels of exposure to PM2.5 or PM10. Thus, our results support the need to encourage the maintenance of PA among young adults who are already physically active in order to reduce the risk of CVD, especially for those with low-to-moderate levels of exposure to PM2.5 or PM10. However, the risk-elevating effects upon decreasing PA tended to be attenuated in participants with high PM2.5 or PM10 exposure levels, implying that the harmful effects of reducing PA, such as chronic reduction in cardiorespiratory fitness, may be attenuated by the positive effects of reducing exposure to PM by reducing outdoor PA. Further studies are warranted to compare the effects of these two factors.

In contrast, cardiovascular health deteriorated when PA was increased above 1000 MET-min/week, which is above the current PA

**Table 2 Hazard ratios for cardiovascular disease according to changes in physical activity stratified by the level of particulate matter 2.5 among young adults**

| | Physical activity at second health examination (MET-min/week) | | | | *P* for trend |
|---|---|---|---|---|---|
| | 0 | 1–499 | 500–999 | ≥1000 | |
| Low/moderate PM2.5 (<26.43 μg/m$^3$) | | | | | |
| Initial 0 MET-min/week (physically inactive) | | | | | |
| Events, *n* | 180 | 234 | 132 | 40 | |
| Person-year | 173 905 | 249 859 | 146 922 | 48 390 | |
| aHR (95% CI) | 1.00 (reference) | 0.92 (0.76–1.12) | 0.85 (0.68–1.07) | 0.73 (0.52–1.03) | 0.04 |
| Initial 1–499 MET-min/week | | | | | |
| Events, *n* | 200 | 569 | 334 | 101 | |
| Person-year | 212 566 | 673 678 | 422 658 | 109 721 | |
| aHR (95% CI) | 1.13 (0.96–1.33) | 1.00 (reference) | 0.94 (0.82–1.07) | 1.04 (0.84–1.29) | 0.17 |
| Initial 500–999 MET-min/week | | | | | |
| Events, *n* | 112 | 328 | 451 | 177 | |
| Person-year | 118 655 | 385 790 | 560 790 | 206 163 | |
| aHR (95% CI) | 1.22 (0.99–1.51) | 1.08 (0.94–1.24) | 1.00 (reference) | 1.05 (0.8–1.25) | 0.15 |
| Initial ≥1000 MET-min/week | | | | | |
| Events, *n* | 37 | 90 | 145 | 162 | |
| Person-year | 36 259 | 88 119 | 178 721 | 182 155 | |
| aHR (95% CI) | 1.22 (0.85–1.75) | 1.19 (0.92–1.54) | 0.97 (0.77–1.21) | 1.00 (reference) | 0.14 |
| High PM2.5 (≥26.43 μg/m$^3$) | | | | | |
| Initial 0 MET-min/week (physically inactive) | | | | | |
| Events, *n* | 147 | 164 | 81 | 49 | |
| Person-year | 117 023 | 135 268 | 70 082 | 26 954 | |
| aHR (95% CI) | 1.00 (reference) | 0.94 (0.75–1.18) | 0.88 (0.67–1.15) | 1.33 (0.96–1.84) | 0.49 |
| Initial 1–499 MET-min/week | | | | | |
| Events, *n* | 142 | 380 | 219 | 71 | |
| Person-year | 119 884 | 329 945 | 194 493 | 59 173 | |
| aHR (95% CI) | 1.03 (0.85–1.25) | 1.00 (reference) | 0.99 (0.84–1.17) | 1.03 (0.80–1.32) | 0.88 |
| Initial 500–999 MET-min/week | | | | | |
| Events, *n* | 62 | 177 | 248 | 128 | |
| Person-year | 65 713 | 183 857 | 246 925 | 103 594 | |
| aHR (95% CI) | 0.94 (0.71–1.25) | 0.98 (0.80–1.18) | 1.00 (reference) | 1.19 (0.96–1.47) | 0.11 |
| Initial ≥1000 MET-min/week | | | | | |
| Events, *n* | 33 | 47 | 102 | 119 | |
| Person-year | 22 620 | 49 379 | 88 742 | 97 327 | |
| aHR (95% CI) | 1.30 (0.88–1.91) | 0.84 (0.60–1.18) | 1.00 (0.76–1.30) | 1.00 (reference) | 0.71 |

aHR (95% CI) were calculated using Cox proportional hazards regression analysis after adjusting for age, sex, district, household income, body mass index, smoking, alcohol intake, systolic blood pressure, fasting serum glucose, total cholesterol, and Charlson comorbidity index.
aHR, adjusted hazard ratio; CI, confidence interval; MET, metabolic equivalent task; PM, particulate matter; PA, physical activity.

guidelines, in environments with a high level of PM2.5 or PM10. Our results indicate that damages to the cardiovascular system caused by increased exposure to air pollutants during a large amount of outdoor PA may negate the health benefits of PA for CVD and rather aggravate the cardiovascular health of young adults. Therefore, for young adults who are exposed to high levels of ambient air pollution, engaging in PA while reducing exposure to air pollution by methods such as air filtration systems should be encouraged to prevent the negation of the benefits of PA to cardiovascular health. Furthermore, our findings indicated that the change in levels of exposure to air pollution, especially an increase in levels of exposure to air pollution, may also negate the positive effects of PA on CVD. Thus, at the national level, policy intervention for reducing air pollution levels would be necessary to maximize the health benefits of PA on CVD in young adults.

Our study has multiple strengths. It is the first large, population-based study to investigate the association of the combined effects of air pollution and changes in PA with CVD in young adults aged 20–39 years. Our findings are especially valuable because we suggest whether young adults should increase or decrease their PA depending on the level of air pollution. The large number of participants increases the generalizability of these results, and the reliable medical claims record supports the validation of CVD events. In addition, the analyses were performed after adjusting for significant metabolic

**Table 3 Hazard ratios for cardiovascular disease according to changes in physical activity stratified by the level of particulate matter 10 among young adults**

| | Physical activity at second health examination (MET-min/week) | | | | *P* for trend |
|---|---|---|---|---|---|
| | 0 | 1–499 | 500–999 | ≥1000 | |
| Low/moderate PM10 (<49.92 μg/m$^3$) | | | | | |
| Initial 0 MET-min/week (physically inactive) | | | | | |
| Events, *n* | 349 | 422 | 207 | 87 | |
| Person-year | 334 893 | 409 590 | 223 675 | 81 872 | |
| aHR (95% CI) | 1.00 (reference) | 0.99 (0.86–1.14) | 0.86 (0.72–1.02) | 0.93 (0.74–1.18) | 0.15 |
| Initial 1–499 MET-min/week | | | | | |
| Events, *n* | 377 | 978 | 564 | 162 | |
| Person-year | 361 882 | 1 034 154 | 614 256 | 177 349 | |
| aHR (95% CI) | 1.14 (1.01–1.29) | 1.00 (reference) | 0.97 (0.88–1.08) | 0.93 (0.79–1.10) | 0.02 |
| Initial 500–999 MET-min/week | | | | | |
| Events, *n* | 200 | 490 | 715 | 318 | |
| Person-year | 192 229 | 567 851 | 776 227 | 310 368 | |
| aHR (95% CI) | 1.17 (1.00–1.37) | 0.95 (0.85–1.07) | 1.00 (reference) | 1.07 (0.94–1.23) | 0.94 |
| Initial ≥1000 MET-min/week | | | | | |
| Events, *n* | 79 | 163 | 274 | 281 | |
| Person-year | 63 540 | 146 555 | 269 939 | 288 437 | |
| aHR (95% CI) | 1.38 (1.07–1.78) | 1.22 (1.00–1.48) | 1.11 (0.94–1.31) | 1.00 (reference) | <0.01 |
| High PM10 (≥49.92 μg/m$^3$) | | | | | |
| Initial 0 MET-min/week (physically inactive) | | | | | |
| Events, *n* | 207 | 215 | 122 | 59 | |
| Person-year | 173 339 | 203 085 | 108 091 | 40 773 | |
| aHR (95% CI) | 1.00 (reference) | 0.89 (0.73–1.08) | 0.94 (0.75–1.18) | 1.15 (0.86–1.53) | 0.71 |
| Initial 1–499 MET-min/week | | | | | |
| Events, *n* | 184 | 523 | 305 | 100 | |
| Person-year | 183 698 | 512 389 | 301 815 | 90 082 | |
| aHR (95% CI) | 0.98 (0.82–1.15) | 1.00 (reference) | 1.01 (0.87–1.16) | 1.04 (0.84–1.29) | 0.61 |
| Initial 500–999 MET-min/week | | | | | |
| Events, *n* | 94 | 271 | 391 | 179 | |
| Person-year | 99 417 | 283 443 | 386 997 | 154 800 | |
| aHR (95% CI) | 0.96 (0.77–1.20) | 0.97 (0.83–1.13) | 1.00 (reference) | 1.12 (0.94–1.34) | 0.15 |
| Initial ≥1000 MET-min/week | | | | | |
| Events, *n* | 33 | 71 | 136 | 150 | |
| Person-year | 33 224 | 72 729 | 135 843 | 146 840 | |
| aHR (95% CI) | 1.03 (0.71–1.51) | 1.02 (0.77–1.35) | 1.03 (0.82–1.31) | 1.00 (reference) | 0.85 |

aHR (95% CI) were calculated using Cox proportional hazards regression analysis after adjusting for age, sex, district, household income, body mass index, smoking, alcohol intake, systolic blood pressure, fasting serum glucose, total cholesterol, and Charlson comorbidity index.
aHR, adjusted hazard ratio; CI, confidence interval; MET, metabolic equivalent task; PA, physical activity; PM, particulate matter.

mediators of CVD, including SBP, FSG level, and TCHO level. We also conducted extensive subgroup analyses and sensitivity analyses to enhance the reliability of the results and provided real-world evidence to encourage young adults not to decrease their PA when exposed to low-to-moderate levels of air pollution and to increase their PA in an environment considering the reduction of air pollutants.

The study has some limitations. First, the survey of PA was not sufficient to estimate the amount of outdoor PA because of the absence of data on whether the participants engaged in PA outdoors (e.g. running in a park) or indoors (e.g. running in a gym). There may be also discordances between a participant's residence and where they engage in PA regularly. However, according to the nationwide 2010 and 2012 Survey on Citizens' Sports Participation conducted biennially by the Ministry of Culture, Sports and Tourism and Korea Institute of Sports Science,[43,44] the sports facilities or locations of physical performance that Korean people often use are generally those that are close to their residence. Furthermore, it was estimated that approximately 90% of the Korean population engages in outdoor PA, such as walking, mountain hiking, playing football, or cycling, close to their residence. The majority of the contents of the questionnaires used in our study also refer to outdoor PA, such as cycling, mountain hiking, and tennis. Further studies are necessary to estimate the amount of outdoor and indoor PA and validate the concordance

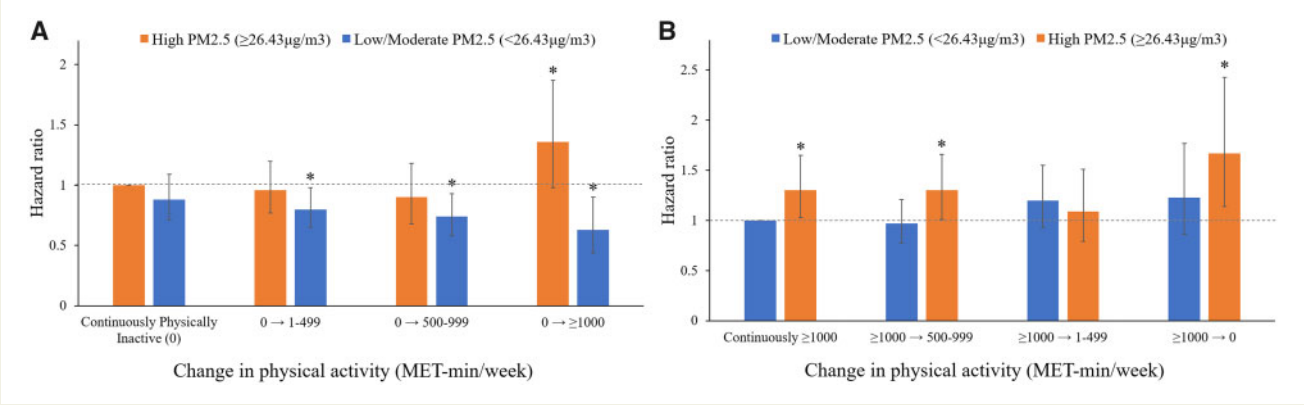



**Figure 4** Combined effects of change in physical activity and particulate matter 2.5 on cardiovascular disease. adjusted hazard ratio (95% confidence interval) were calculated using Cox proportional hazards regression analysis after adjusting for age, sex, district, household income, baseline body mass index, smoking, alcohol intake, systolic blood pressure, fasting serum glucose, total cholesterol, and Charlson comorbidity index (where $*P < 0.05$). (*A*) Young adults who were continuously physically inactive (0 metabolic equivalent task-min/week) while exposed to high levels of particulate matter 2.5 are the reference group for all adjusted hazard ratios. (*B*) Young adults who continuously engaged in >1000 metabolic equivalent task-min/week while exposed to low-to-moderate levels of particulate matter 2.5 are the reference group for all adjusted hazard ratios.

between the residence and location where PA is performed to precisely identify the combined effect of air pollution and changes in PA on CVD in young adults. Second, recall bias may occur because the data on the PA level were collected using self-reported questionnaires. However, because the validity and feasibility of the 'last 7-day recall' method based on a self-reported PA questionnaire have been confirmed by multiple researches monitoring PA levels of population,[15,16] the data on the PA of participants in this study may be reliable. Third, population selection bias may occur when conducting analyses using participants with PM2.5 data because PM2.5 was only monitored in the three major metropolitan cities. Finally, we did not investigate the short-term effects of exposure to air pollution. Therefore, further studies are necessary to identify the association of the combined effects of short-term exposure to air pollution and changes in PA with CVD risk.

# Conclusion

Among young adults with exposure to low-to-moderate levels of PM2.5 or PM10, decrease in PA from continuously physically active was associated with a greater risk of CVD. In contrast, cardiovascular health deteriorated when PA was increased to a fairly high level, above 1000 MET-min/week, among young adults with exposure to high levels of PM2.5 or PM10. Therefore, at least maintaining PA levels is recommended for young adults who are already physically active with exposure to low-to-moderate levels of air pollution. In addition, engaging in more PA in an environment considering the reduction of air pollutants would be necessary to prevent the adverse impacts on cardiovascular health for young adults who are exposed to high levels of ambient air pollution.

# Supplementary material

Supplementary material is available at *European Heart Journal* online.

# Data availability

Additional data are not available, because only authorized researchers can assess the database at the Big Data Research Center of the NHIS.

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