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Supplemental Material

Long-Term Exposure to Air Pollution and the Occurrence of Metabolic Syndrome and Its Components in Taiwan

Yi-Chuan Chen, Wei-Shan Chin, Shih-Chun Pan, Chih-Da Wu, and Yue-Liang Leon Guo

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Additional File- Excel Document

Table S1. Number of groups in which a participant was enrolled and event occurrence in the present study based on the MJ Health Database Study Population between 2006 and 2016, Taiwan.

Number of groups in which participants were enrolled	Enrollment	Event occurrence
	n (%)	n (%)
0	-	78,786 (84.0)
1	4,766 (5.1)	9,969 (10.6)
2	10,076 (10.7)	3,544 (3.8)
3	17,203 (18.3)	1,130 (1.2)
4	27,154 (29.0)	284 (0.3)
5	34,572 (36.9)	58 (0.1)
Development of MetS [a]	76,349 (81.4)	9,898 (10.6)
Total	93,771 (100)	-

Note: Enrollment in each of six groups was according to participants' baseline status for each component of MetS. For each specific component, only those negative for it were included, e.g., those without abdominal obesity were included in the survival analysis for the development of abdominal obesity, etc. There were 36.9% (n = 34,572) of participants were having zero positive component and included in all five groups. Enrollment in one group did not preclude enrollment in other groups. "Event occurrence" refers to negativity to positivity in a specific component, i.e., abdominal obesity (having a waist circumference of ≥90 cm in men and ≥80 cm in women), elevated TG (having a TG level of ≥150 mg/dL or receiving drug treatment for hypertriglyceridemia), reduced HDL-C (having a HDL-C level of <40 mg/dL [1.0 mmol/L] in males and <50 mg/dL [1.3 mmol/L] in females or receiving drug treatment for decreased HDL-C), elevated BP (having a systolic BP level of ≥130 and/or diastolic BP level of ≥85 mmHg or receiving drug treatment for hypertension), elevated FBG (having an FBG level of ≥100 mg/dL or receiving drug treatment for hyperglycemia), or the occurrence of MetS (the presence of any ≥3 of the above components).

[a] Missing information on covariates were initially represented by the previous value available of each participant. Participants without available value for representation are not eligible for data analysis depends on the covariates in the models, leading to different eligible numbers of participants in different models in Table 3, Table S3, and Table S4.

Table S2. Distribution of annual average concentrations of $PM_{2.5}$ and NO_2 by region between 2005 and 2015, Taiwan.

	North	Middle	South	East
$PM_{2.5}$ ($\mu g/m^3$)				
mean	27.5	33.8	42.6	20.4
SD	4.7	3.8	4.3	2.8
median	28.2	34.2	42.8	21.6
NO_2 (ppb)				
mean	20.3	15.7	20.2	9.8
SD	5.1	3.0	4.8	3.2
median	19.7	16.0	21.1	10.5

Note: $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; NO_2, nitrogen dioxide; SD, standard deviation.

Table S3. Associations of $PM_{2.5}$ and NO_2 with metabolic syndrome and its components between 2006 and 2016, Taiwan, with and without adjustment for baseline body mass index.

MetS and its components	With adjustment for baseline body mass index [a]		Without adjustment for baseline body mass index	
	$PM_{2.5}$	NO_2	$PM_{2.5}$	NO_2
		Adjusted HR	(95% CI)	
Development of abdominal obesity in the no abdominal obesity cohort	n= 70,589 1.07 (1.01, 1.14)	0.97 (0.92, 1.03)	n= 70,594 1.06 (1.00, 1.13)	0.98 (0.93, 1.04)
Development of elevated TG in the normal TG cohort	n= 68,727 1.17 (1.11, 1.23)	0.99 (0.94, 1.03)	n= 68,733 1.16 (1.10, 1.23)	0.99 (0.94, 1.04)
Development of reduced HDL-C in the normal HDL-C cohort	n= 67,587 1.09 (1.02, 1.17)	0.94 (0.88, 1.01)	n= 67,592 1.09 (1.01, 1.17)	0.94 (0.88, 1.01)
Development of elevated BP in the normal BP cohort	n= 63,510 1.15 (1.09, 1.21)	1.04 (0.99, 1.10)	n= 63,514 1.15 (1.09, 1.21)	1.05 (0.99, 1.10)
Development of elevated FBG in the normal FBG cohort	n= 54,269 1.15 (1.10, 1.20)	1.03 (0.99, 1.07)	n= 54,274 1.15 (1.10, 1.20)	1.04 (0.99, 1.08)
Development of MetS based on the number of MetS risk factors exhibited at baseline	n= 69,456		n= 69,460	
0	0.99 (0.89, 1.12)	0.88 (0.76, 1.03)	0.99 (0.89, 1.11)	0.87 (0.75, 1.01)

1	1.12 (1.04, 1.20)	1.01 (0.93, 1.10)	1.12 (1.04, 1.21)	1.02 (0.94, 1.11)
2	1.14 (1.07, 1.22)	1.10 (1.03, 1.18)	1.12 (1.05, 1.19)	1.14 (1.06, 1.21)

Note: All estimates were calculated for every 10 μg/m^3 increase in $PM_{2.5}$ and every 10-ppb increase in NO_2 in the annual average concentrations, determined using time-dependent Cox regression. All models were two-pollutant model, adjusted by age, sex, marital status (single/divorced/separation/widowed, married/cohabitating), education level (junior high school and below, general and vocational high school, college, master degree and above), sleeping time per day (<6, 6–8, >8 hours), smoking habits (never smoking/former smoking, secondhand smoke exposure, frequent smoking/daily smoking), alcohol drinking habits (never drinking/former drinking, occasional drinking, frequent drinking/daily drinking), fried food consumption (none, little or ≤ 1 portion weekly, 2-3 portions weekly, ≥4 portions weekly), processed food consumption (none, little or ≤ 1 portion weekly, 2-3 portions weekly, ≥4 portions weekly), region (north, central, south), and the initial status—baseline waist circumference for abdominal obesity cohort, baseline TG for elevated TG cohort, baseline HDL-C for reduced HDL-C cohort, baseline systolic blood pressure and baseline diastolic blood pressure for elevated BP cohort, baseline FBG for elevated FBG cohort, and baseline number of components of MetS for MetS cohort. $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; NO_2, nitrogen dioxide; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; BP, blood pressure; FBG, fasting blood glucose; MetS, metabolic syndrome; n, number of participants without missing variables in each model; HR, hazard ratio; CI, confidence interval.

[a] Additional adjustment for baseline body mass index (<18.5, 18.5–24, ≥24).

Table S4. Associations of $PM_{2.5}$ and NO_2 with metabolic syndrome and its components between 2006 and 2016, Taiwan, with and without adjustment for sleeping time.

MetS and its components	With adjustment for sleeping time [a]		Without adjustment for sleeping time	
	$PM_{2.5}$	NO_2	$PM_{2.5}$	NO_2
	Adjusted HR (95% CI)			
Development of abdominal obesity in the no abdominal obesity cohort	n= 70,589		n= 70,608	
	1.07 (1.01, 1.14)	0.97 (0.92, 1.03)	1.07 (1.01, 1.14)	0.97 (0.92, 1.03)
Development of elevated TG in the normal TG cohort	n= 68,727		n= 68,746	
	1.17 (1.11, 1.23)	0.99 (0.94, 1.03)	1.17 (1.11, 1.23)	0.98 (0.94, 1.03)
Development of reduced HDL-C in the normal HDL-C cohort	n= 67,587		n= 67,602	
	1.09 (1.02, 1.17)	0.94 (0.88, 1.01)	1.09 (1.02, 1.17)	0.94 (0.88, 1.01)
Development of elevated BP in the normal BP cohort	n= 63,510		n= 63,526	
	1.15 (1.09, 1.21)	1.04 (0.99, 1.10)	1.15 (1.09, 1.21)	1.04 (0.99, 1.10)
Development of elevated FBG in the normal FBG cohort	n= 54,269		n= 54,281	
	1.15 (1.10, 1.20)	1.03 (0.99, 1.07)	1.15 (1.10, 1.20)	1.03 (0.99, 1.07)
Development of MetS based on the number of MetS risk factors exhibited at baseline	n= 69,456		n= 69,469	
0	0.99 (0.89, 1.12)	0.88 (0.76, 1.03)	0.99 (0.89, 1.12)	0.88 (0.76, 1.02)
1	1.12 (1.04, 1.20)	1.01 (0.93, 1.10)	1.12 (1.04, 1.20)	1.01 (0.93, 1.10)

2	1.14 (1.07, 1.22)	1.10 (1.03, 1.18)	1.14 (1.07, 1.22)	1.10 (1.03, 1.18)

Note: All estimates were calculated for every 10 μg/m^3 increase in $PM_{2.5}$ and every 10-ppb increase in NO_2 in the annual average concentrations, determined using time-dependent Cox regression. All models were two-pollutant model, adjusted by age, sex, baseline body mass index (<18.5, 18.5–24, ≥24), marital status (single/divorced/separation/widowed, married/cohabitating), education level (junior high school and below, general and vocational high school, college, master degree and above), smoking habits (never smoking/former smoking, secondhand smoke exposure, frequent smoking/daily smoking), alcohol drinking habits (never drinking/former drinking, occasional drinking, frequent drinking/daily drinking), fried food consumption (none, little or ≤ 1 portion weekly, 2-3 portions weekly, ≥4 portions weekly), processed food consumption (none, little or ≤ 1 portion weekly, 2-3 portions weekly, ≥4 portions weekly), region (north, central, south), and the initial status—baseline waist circumference for abdominal obesity cohort, baseline TG for elevated TG cohort, baseline HDL-C for reduced HDL-C cohort, baseline systolic blood pressure and baseline diastolic blood pressure for elevated BP cohort, baseline FBG for elevated FBG cohort, and baseline number of components of MetS for MetS cohort. $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; NO_2, nitrogen dioxide; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; BP, blood pressure; FBG, fasting blood glucose; MetS, metabolic syndrome; n, number of participants without missing variables in each model; HR, hazard ratio; CI, confidence interval.

[a] Additional adjustment for sleeping time per day (<6, 6–8, >8 hours).

Table S5. Correlation between $PM_{2.5}$ and NO_2 at the township level between 2005 and 2015, Taiwan.

Spearman correlation coefficients between $PM_{2.5}$ and NO_2	In the abdominal obesity development cohort	In the elevated TG development cohort	In the reduced HDL-C development cohort	In the elevated BP development cohort	In the elevated FBG development cohort	In the MetS development cohort
North [a]	0.549	0.551	0.575	0.551	0.548	0.558
Central [b]	0.463	0.461	0.468	0.484	0.464	0.456
South [c]	0.688	0.691	0.697	0.683	0.692	0.688
Total	0.271	0.277	0.291	0.290	0.249	0.272

Note: TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; BP: blood pressure; FBG: fasting blood glucose; MetS: metabolic syndrome. All p <0.001. The Spearman correlation coefficients between $PM_{2.5}$ and NO_2 were measured at the residence of township of participants in each cohort, including participants who were censored, developed and non-developed abdominal obesity, elevated TG, reduced HDL-C, elevated BP, elevated FBG and MetS.

[a] The northern region includes Taipei, New Taipei, Keelung, Hsinchu and Taoyuan Cities, and Hsinchu County.

[b] The central region includes Taichung City, and Miaoli, Changhua, Nantou and Yunlin Counties.

[c] The southern region includes Kaohsiung, Tainan and Chiayi Cities, and Chiayi and Pingtung Counties.

Figure S1. Regions of Taiwan. Western Taiwan was essentially the combination of northern, central, and southern regions. Western Taiwan and eastern region are separated by high-rise mountains. This figure was created using the QGIS Desktop software (version 3.22; Open Source Geospatial Foundation, OSGeo).

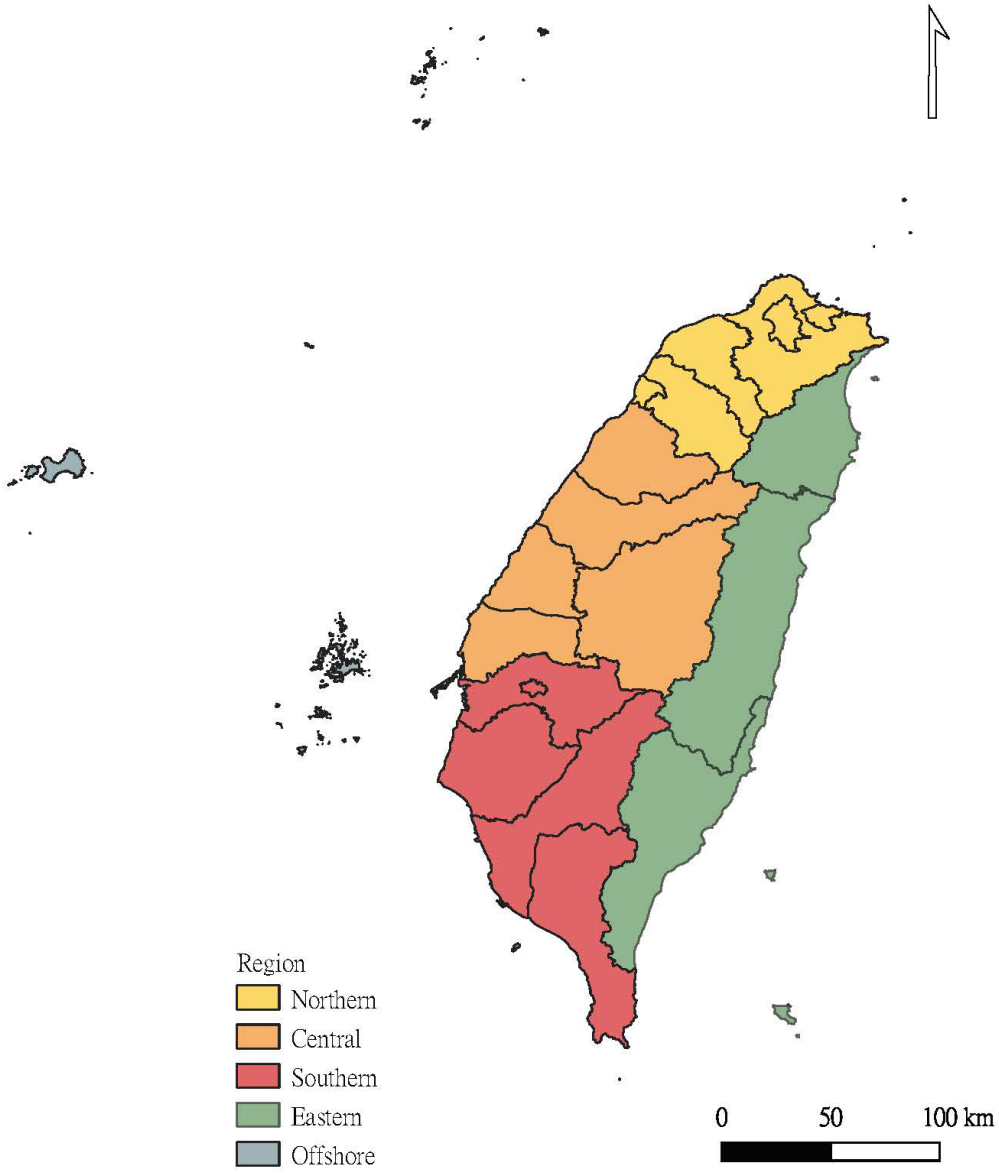
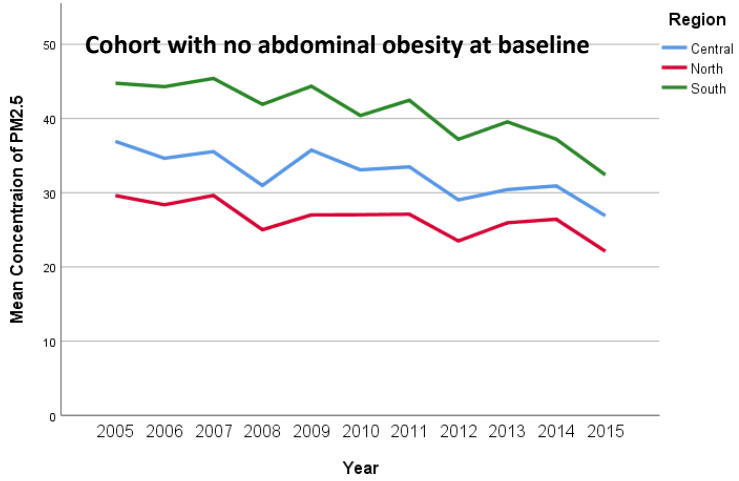
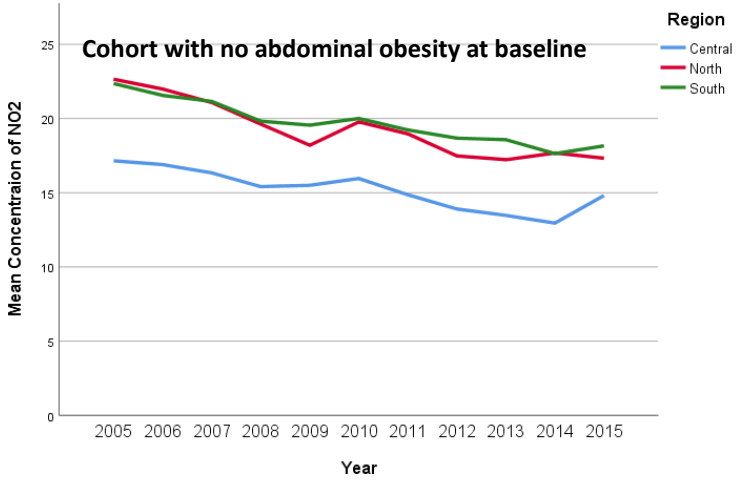
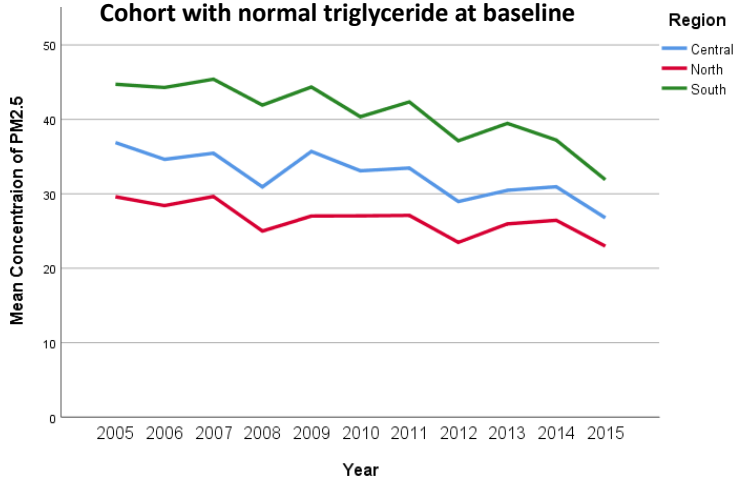
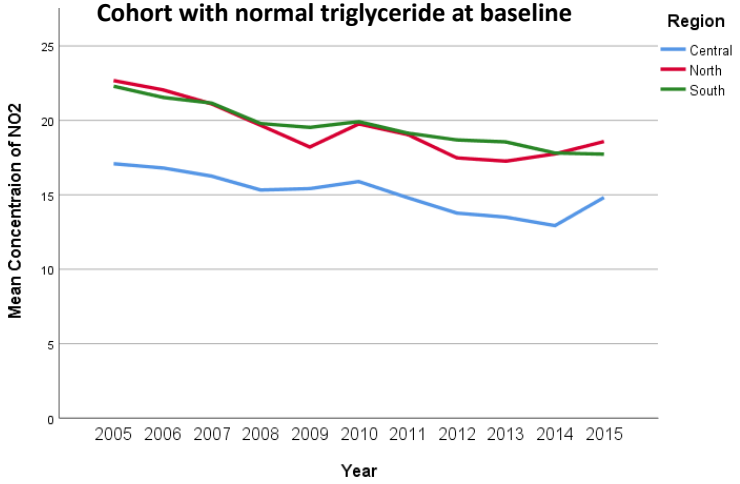


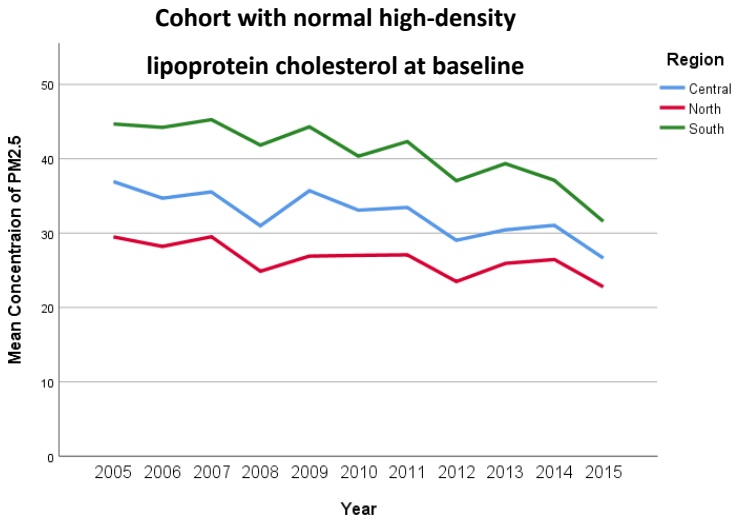
Figure S2. Annual mean concentrations of $PM_{2.5}$ (μg/m^3) and NO_2 (ppb) stratified by regions in the cohorts of metabolic syndrome and its components between 2005 and 2015, Taiwan (N = 93,771). Summary data found in Excel Table S1.

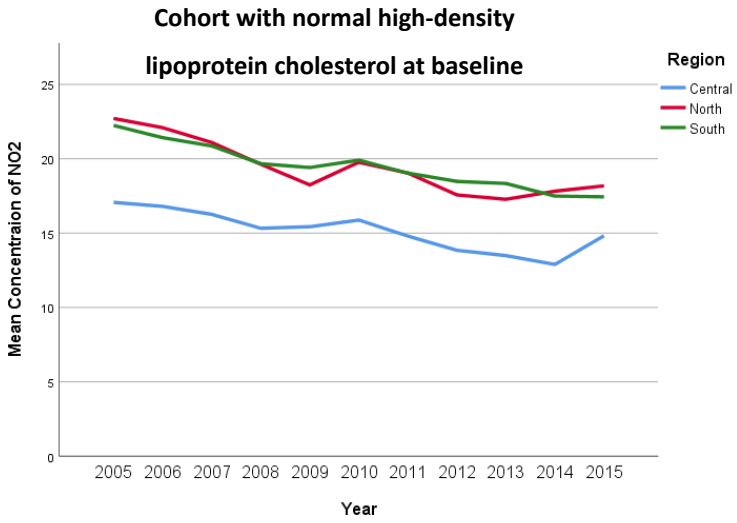


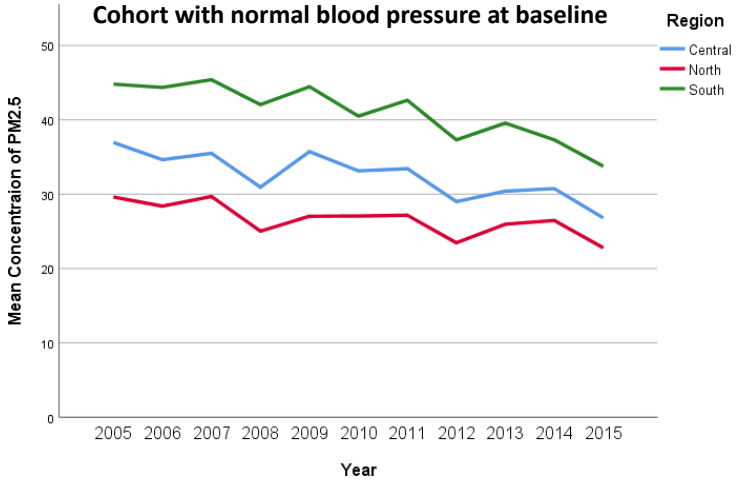


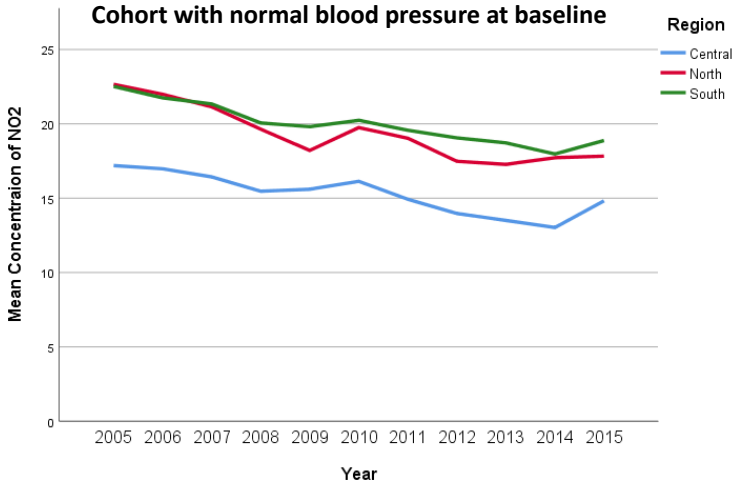


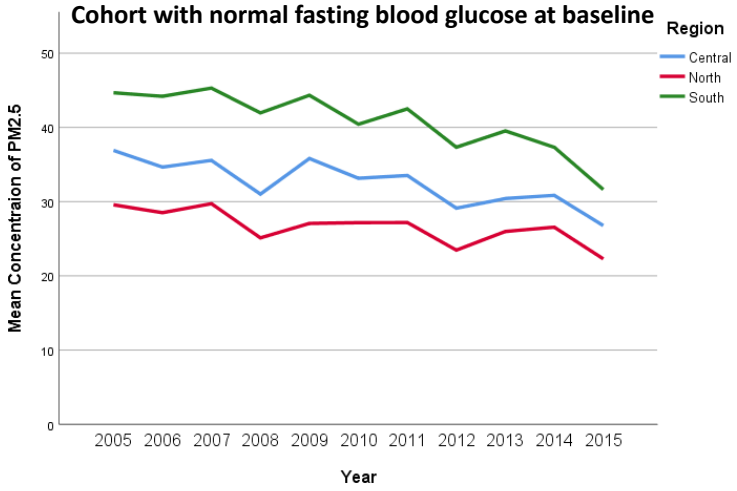


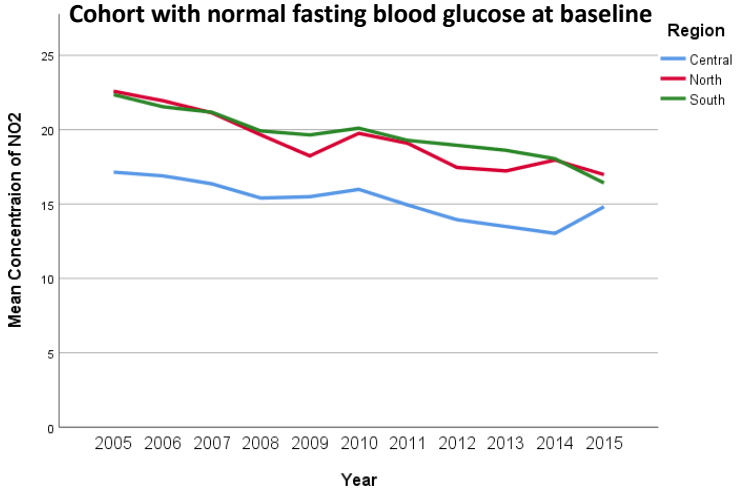

Cohort with normal high-density
lipoprotein cholesterol at baseline
Region
Central
North
South
Mean Concentraion of PM2.5
0
10
20
30
40
50
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year

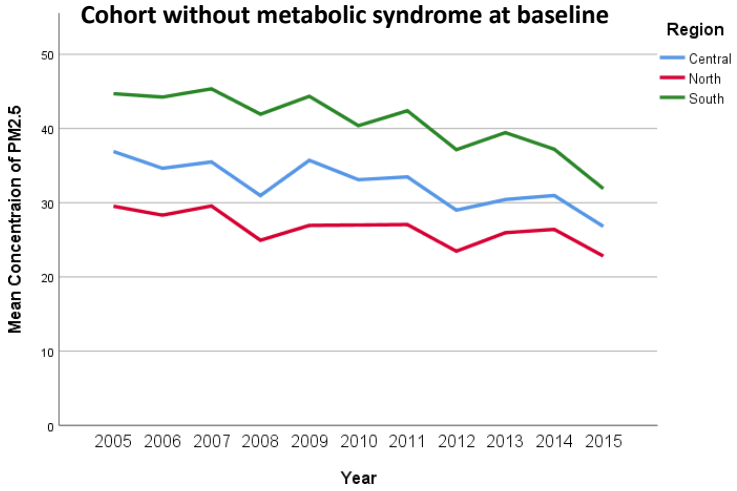

Cohort with normal high-density
lipoprotein cholesterol at baseline
Region
Central
North
South
Mean Concentraion of NO2
0
5
10
15
20
25
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year


Cohort with normal blood pressure at baseline
Region
Central
North
South
Mean Concentraion of PM2.5
0
10
20
30
40
50
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year


Cohort with normal blood pressure at baseline
Region
Central
North
South
Mean Concentraion of NO2
0
5
10
15
20
25
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year


Cohort with normal fasting blood glucose at baseline
Region
Central
North
South
Mean Concentraion of PM2.5
0
10
20
30
40
50
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year


Cohort with normal fasting blood glucose at baseline
Region
Central
North
South
Mean Concentraion of NO2
0
5
10
15
20
25
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year


Cohort without metabolic syndrome at baseline
Region
Central
North
South
Mean Concentraion of PM2.5
0
10
20
30
40
50
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year

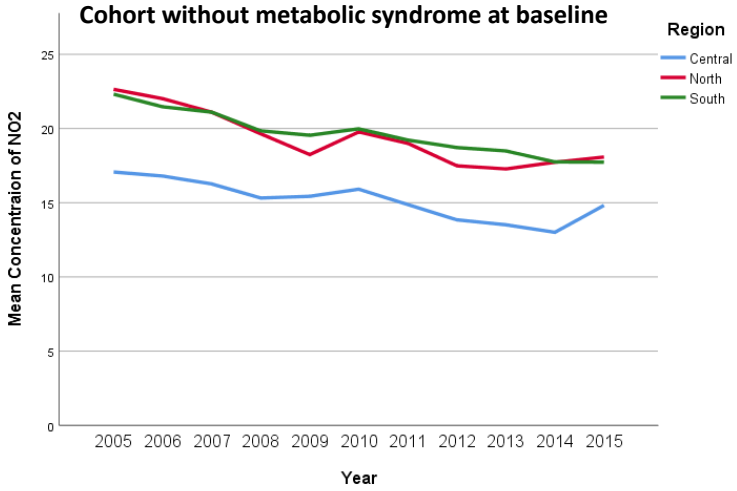
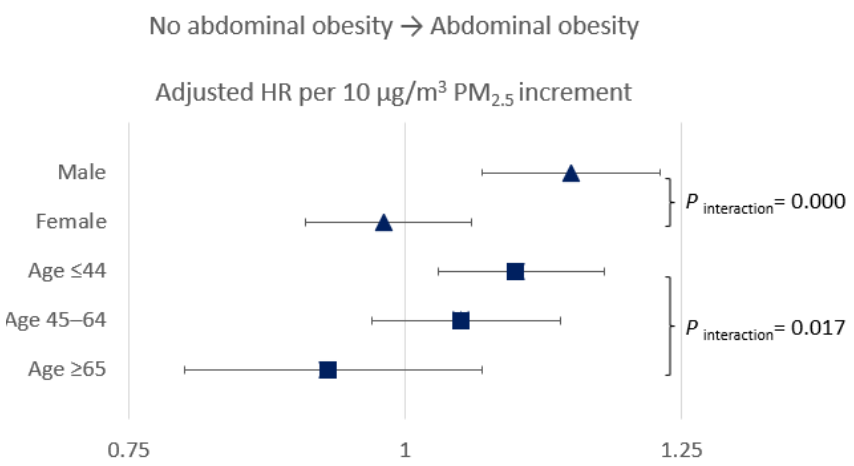
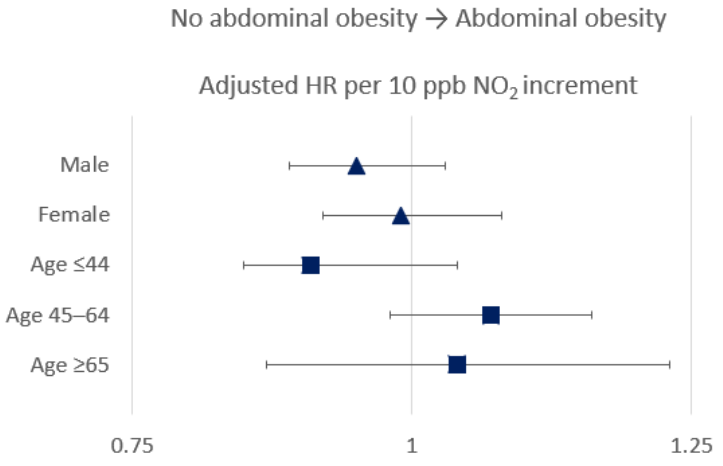
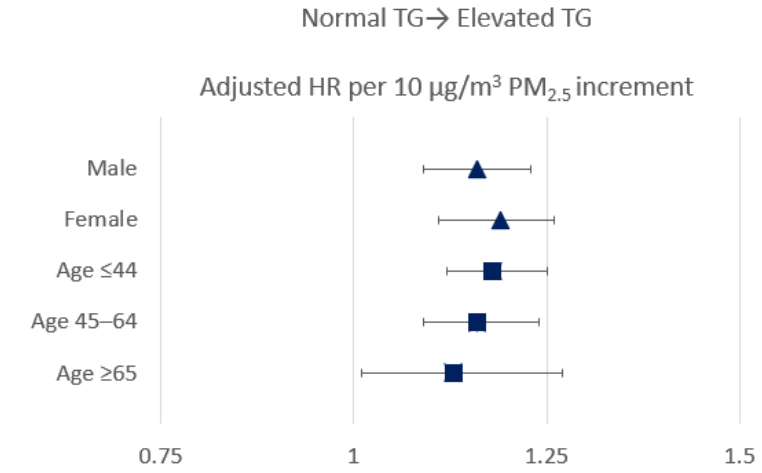
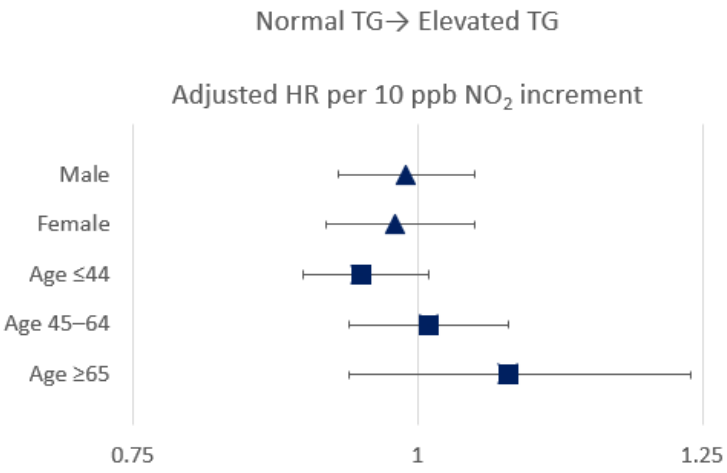

Cohort without metabolic syndrome at baseline
Region
Central
North
South
Mean Concentraion of NO2
0
5
10
15
20
25
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Year

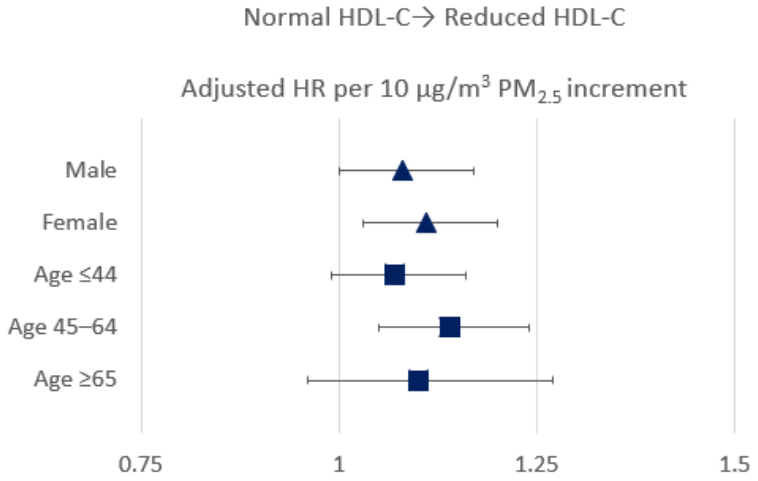
Figure S3. Associations between exposure to $PM_{2.5}$, NO_2 and incident metabolic syndrome and its components between 2006 and 2016, in Taiwan, stratified by sex and age (adjusted HR and confidence intervals graphed). Summary data found in Excel Table S2.

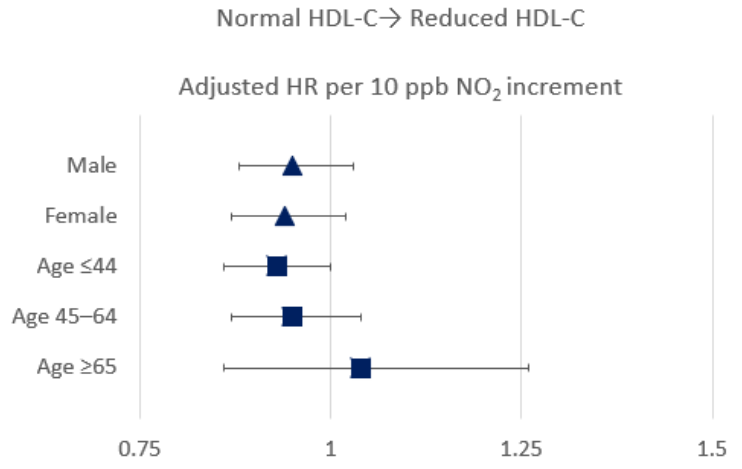


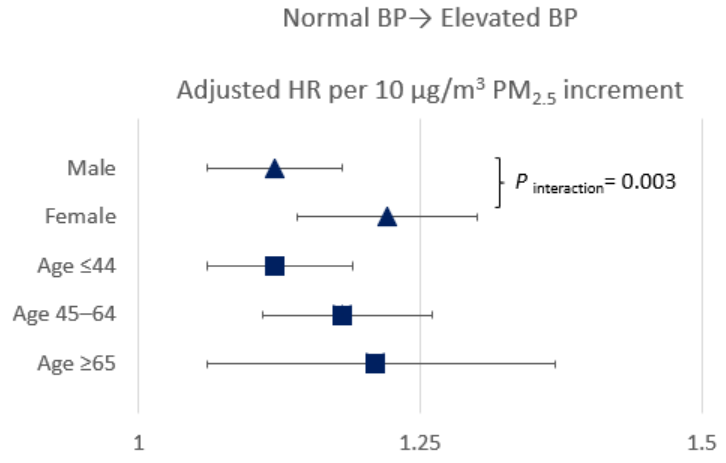


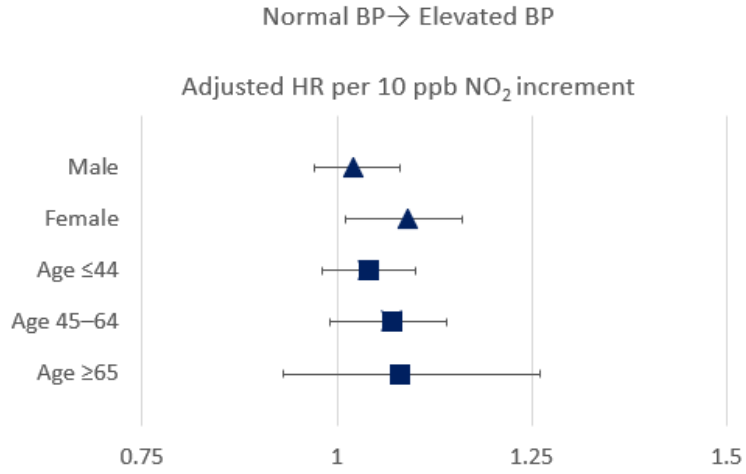


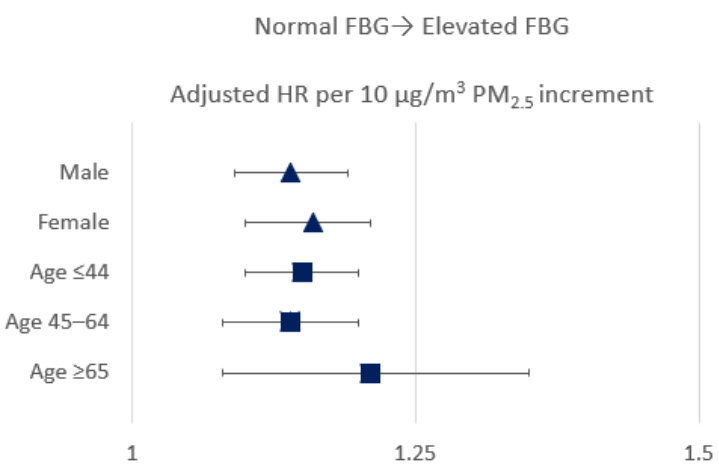



Normal HDL-C→ Reduced HDL-C
Adjusted HR per 10 µg/m3 PM2.5 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


Normal HDL-C→ Reduced HDL-C
Adjusted HR per 10 ppb NO2 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


Normal BP→ Elevated BP
Adjusted HR per 10 µg/m3 PM2.5 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
P interaction= 0.003
1
1.25
1.5


Normal BP→ Elevated BP
Adjusted HR per 10 ppb NO2 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


Normal FBG→ Elevated FBG
Adjusted HR per 10 µg/m3 PM2.5 increment
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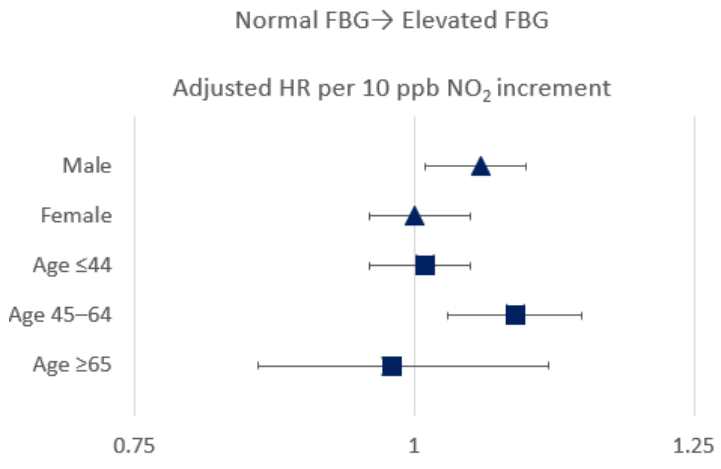
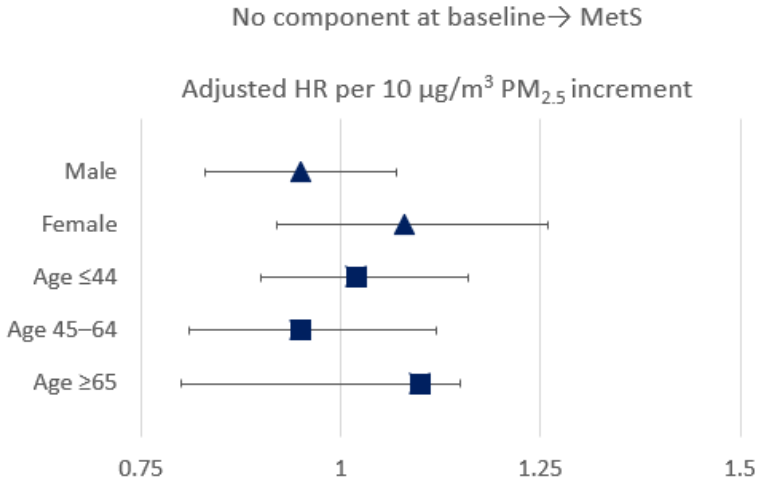
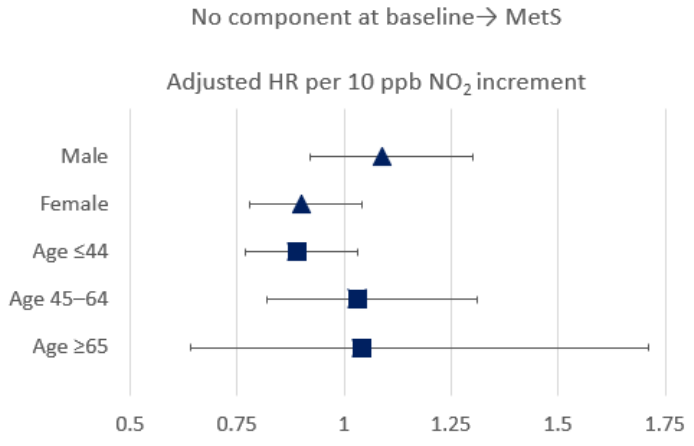
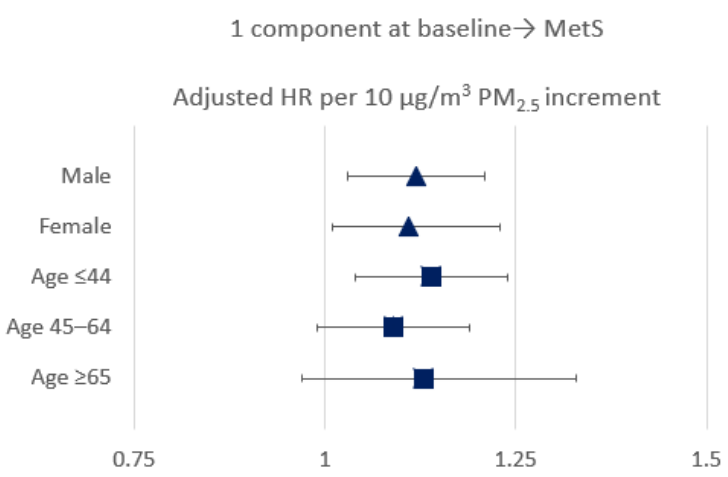
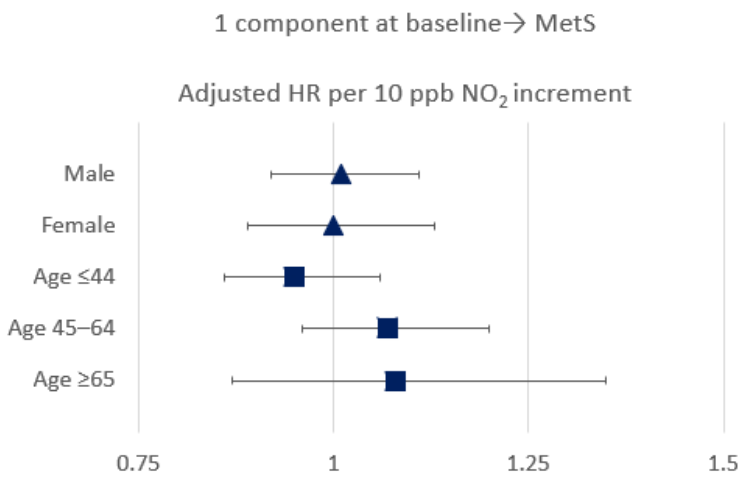
Female
Age ≤44
Age 45–64
Age ≥65
1
1.25
1.5

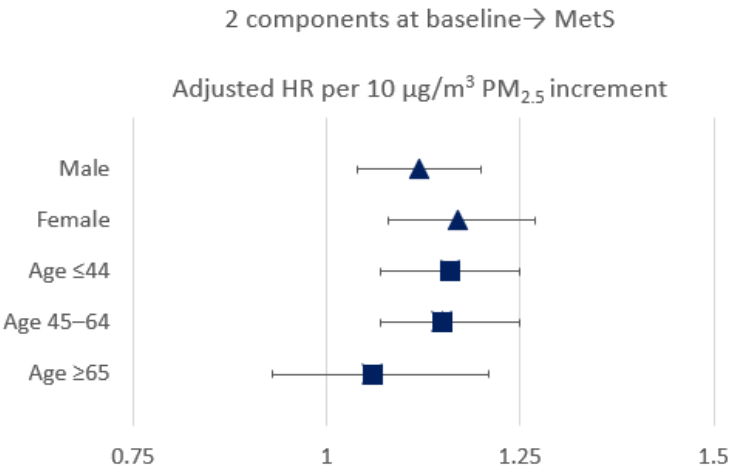

Normal FBG→ Elevated FBG
Adjusted HR per 10 ppb NO2 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25

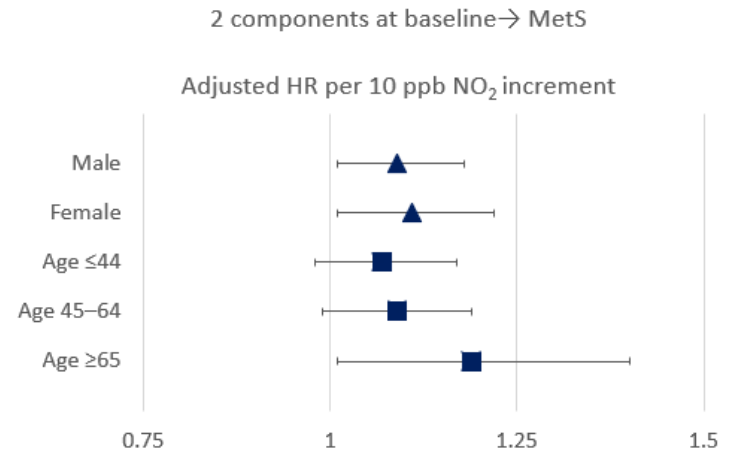

No component at baseline→ MetS
Adjusted HR per 10 µg/m3 PM2.5 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


No component at baseline→ MetS
Adjusted HR per 10 ppb NO2 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.5
0.75
1
1.25
1.5
1.75


1 component at baseline→ MetS
Adjusted HR per 10 µg/m3 PM2.5 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


1 component at baseline→ MetS
Adjusted HR per 10 ppb NO2 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


2 components at baseline→ MetS
Adjusted HR per 10 µg/m3 PM2.5 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5


2 components at baseline→ MetS
Adjusted HR per 10 ppb NO2 increment
Male
Female
Age ≤44
Age 45–64
Age ≥65
0.75
1
1.25
1.5

Note: All estimates were calculated for every 10 μg/m^3 increase in $PM_{2.5}$ and every 10-ppb increase in NO_2 in the annual average concentrations, determined using time-dependent Cox regression. $P_{interaction}$ represented the likelihood ratio test for interaction between $PM_{2.5}$, NO_2, sex, and age. $P_{interaction}$ of greater than 0.05 were not shown. All models were two-pollutant model, adjusted by age, sex, baseline body mass index (<18.5, 18.5–24, ≥24), marital status (single/divorced/separation/widowed, married/cohabitating), education level (junior high school and below, general and vocational high school, college, master degree and above), smoking habits (never smoking/former smoking, secondhand smoke exposure, frequent smoking/daily smoking), alcohol drinking habits (never drinking/former drinking, occasional drinking, frequent drinking/daily drinking), sleeping time per day (<6, 6–8, >8 hours), regular exercise (none, little or < 1 hour weekly, 1-4 hours weekly or once per 2-3 days, ≥5 hours weekly or daily), fried food consumption (none, little or ≤ 1 portion weekly, 2-3 portions weekly, ≥4 portions weekly), processed food consumption (none, little or ≤ 1 portion weekly, 2-3 portions weekly, ≥4 portions weekly), region (north, central, south), and the initial status—baseline waist circumference for abdominal obesity cohort, baseline TG for elevated TG cohort, baseline HDL-C for reduced HDL-C cohort, baseline systolic blood pressure and baseline diastolic blood pressure for elevated BP cohort, baseline FBG for elevated FBG cohort, and baseline number of components of MetS for MetS cohort. $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; NO_2, nitrogen dioxide; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; BP, blood pressure; FBG, fasting blood glucose; MetS, metabolic syndrome; HR, hazard ratio; error bars, 95% confidence intervals.