Supplemental Material: Chapter 12 (Populations Potentially at Increased Risk for PM-Related Health Effects) Integrated Science Assessment for Particulate Matter

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Center for Public Health and Environmental Assessment
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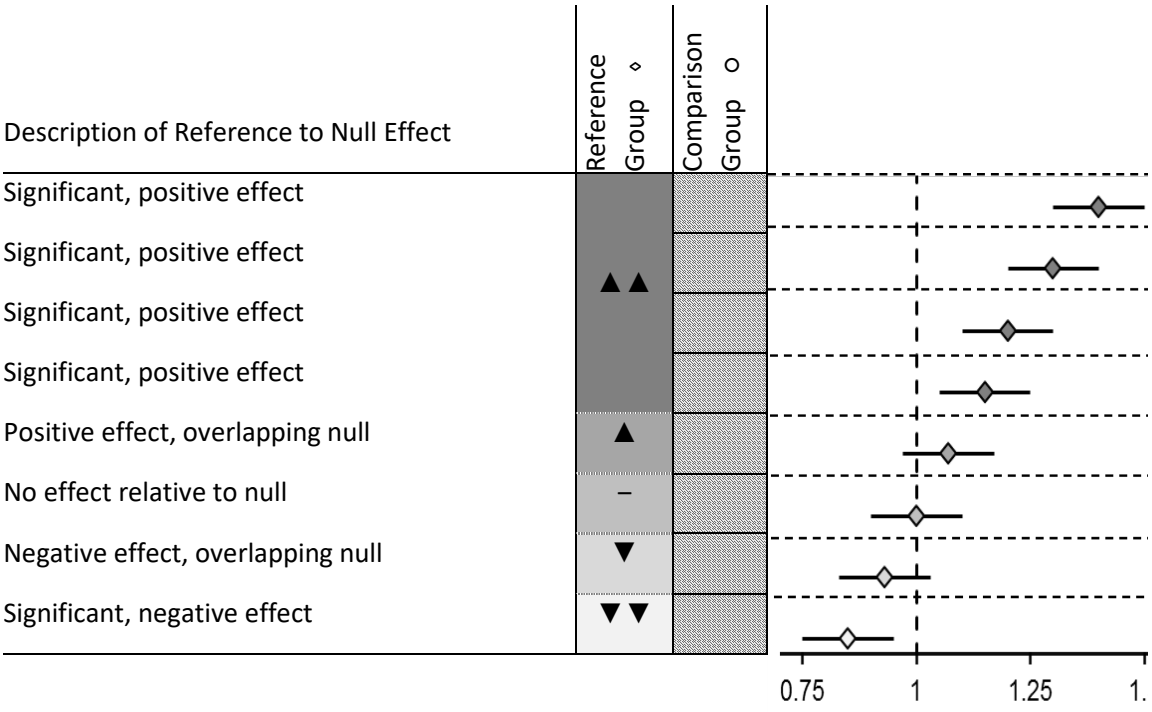
Contents

1.1 Consideration of evidence from stratified analyses

As discussed above, characterizing the overall body of evidence to determine whether a population or lifestage is at increased risk of an air pollutant-related health effect includes an evaluation epidemiologic studies that conduct stratified analyses. Stratified analyses examine whether there is evidence of differential risk between two populations within the same study design, by specifically examining effect measure modification between a potential at-risk population (e.g. those with a pre-existing disease) and a pre-determined reference group (e.g. those with no pre-existing disease—not the overall population). In this chapter, heatmaps are used to depict results from stratified analyses across the range of studies and outcomes available for each at-risk factor.



Each row in this figure is a representation of a result from a hypothetical example study. In the heatmaps throughout this chapter, the gray indicates the direction and strength of the association relative to the null.

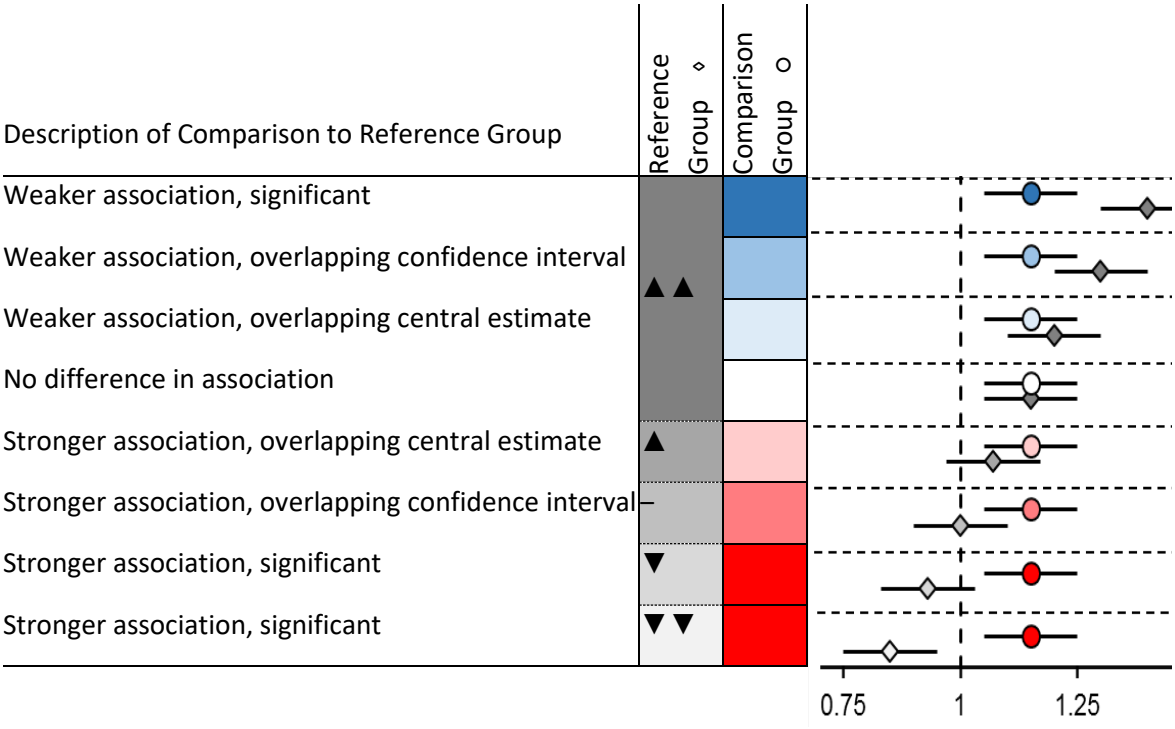
Supplemental Figure S12-1 Example of presentation of health effects in reference group

Figures 12-1 and 12-2 illustrate this chapter's approach to characterizing evidence across studies that conducted stratified analyses using heatmaps. These heatmaps visually indicate (1) the presence or absence of an effect in the reference group and (2) a modification of that effect by the at-risk factor; the approach to depicting the evidence is further described below.

Figure 12-1: The presence of a positive, negative, or null association with a health effect in the reference group is depicted in each row with both grayscale and arrows indicating the direction of the effect. Positive and negative associations are further split into two groups each: those with confidence intervals distinct from the null effect (i.e. 95% CIs not including 0) and those overlapping the null (i.e., 95% CIs including 0).

Each row in this figure is a representation of a reference result from a hypothetical example study. In the heatmaps throughout this chapter, the gray scale and arrows indicate the strength of the association in the reference group relative to the null effect.

Figure 12-2: Examination of effect measure modification of a health effect by the at-risk factor is depicted in the heatmaps with a red-to-blue scale. The color-coding for a particular at-risk group and health outcome represents the strength and direction of association compared to that of the reference group. Differences in association compared to reference groups are either increases, decreases, or neither. Increases and decreases are each further divided into three categories from strongest to weakest: those with no overlap in confidence intervals; those in which confidence intervals overlap each other but do not overlap the central estimates; and those in which the central estimate of at least one association is overlapped by the confidence interval of the other. Notably, a particular group may have a weaker association relative to the reference group, which would be indicated by the blue scale, while retaining a positive overall association to the health effect in question. This example reiterates that the red-to-blue color scale only provides information for the comparison of groups and not the presence or absence of a PM2.5 association.



Each row in this figure is a representation of a reference result and its corresponding comparison group result from a hypothetical example study. In the heatmaps throughout this chapter, the gray scale and arrows indicate the strength of the association in the reference group relative to the null effect, while the red-blue color scale indicates the modification of the effect in the comparison group relative to the reference group.

Supplemental Figure S12-2 Key to heatmaps of stratified analyses for at-increased-risk factors.

The presence of a positive or negative effect in the reference column and an increased or decreased effect in the comparison column are distinct and can be considered hierarchically: the category of the reference is determined by its relationship to the null effect; the category of the comparison is determined by its relationship to the reference effect. The forest plot presented in Figure 12-2- displays example associations and corresponding confidence intervals that would result in the coloring depicted in the provided heatmap.

Studies that conduct stratified analyses vary in methodology, health outcome, and quality. Furthermore, a study that contributes high-quality evidence for the overall population may be less valuable to at-risk characterization (e.g., small sample sizes for comparison groups), and vice versa. As discussed above and in the Preamble (U.S. EPA, 2015), the evaluation and characterization of whether a population or lifestage is at increased risk of a PM-related health effect involves the integration of

evidence across disciplines. The heatmaps provided in this chapter should be considered visual guides to one element of the conclusions that are drawn regarding the extent to which a population or lifestage may be at increased risk for a PM2.5-related health effect.

1.2 Supplemental Heatmaps for Stratified Analysis for At-Increased-Risk Factors

Supplemental Table S12-1 Stratified analyses of pre-existing cardiovascular disease and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	No Pre-existing	Condition Present
					Pre-existing CVD Condition		
Puett et al. (2009)	LT	Midwest and Northeast U.S.	(1992-2002)	Mortality	Hypertension	▲▲	
				Fatal CHD	Hypertension	▲	
				First CHD	Hypertension	▲	
Goldberg et al. (2013)	ST	Montreal, Quebec		Mortality	Hypertension	▲	
Wellenius et al. (2012a)	ST	Boston, MA	(1999-2008)	Ischemic stroke	History of hypertension	▲▲	
O'Donnell et al. (2011)	ST	8 cities in Ontario, Canada	(2003-2008)	Ischemic stroke	Hypertension	▲	
Hansen et al. (2016)	LT	Denmark	(2003-2013)	Diabetes incidence	Hypertension	▲	
Chen et al. (2013)	LT	Ontario	(1996-2010)	Diabetes incidence	Hypertension	▲▲	
Auchincloss et al. (2008)	LT	6 U.S. cities	(2000-2002)	PP	Hypertension	▲	
				BP	Hypertension	▲	
Krishnan et al. (2012)	LT	6 U.S. cities	(2000-2002)	BAD	Hypertension	▲	
				FMD	Hypertension	▲	
Wellenius et al. (2013)	LT	Boston, MA	(2005-2009)	Flow velocity	Hypertension	▲▲	
				Cerebrovascular resistance	Hypertension	▲	
Hajat et al. (2015)	LT	6 U.S. cities	(2000-2002)	IL-6	Hypertension	▲	
Ostro et al. (2014)	LT	6 U.S. cities	(1999-2005)	CRP	High BP	▲	

Study	Exp	Location	Time	Outcome	Notes	No Pre-existing	Condition Present
Hennig et al. (2014)	LT	Ruhr area, Germany	(2000-2008)	CRP	CHD	▲	
Hertel et al. (2010)	ST	Ruhr area, Germany	(2000-2003)	CRP	CHD	▲	
					CHD	▲▲	
Hoffmann et al. (2009a)	ST	Ruhr area, Germany	(2000-2003)	CRP	CHD - Men	▲▲	
				CRP	CHD - Women	▲	
				Fibrinogen	CHD - Men	▲▲	
				Fibrinogen	CHD - Women	▲	
Viehmann et al. (2015)	ST	Ruhr area, Germany	(2000-2008)	CRP	CHD	▲▲	
				Platelets	CHD	▲▲	
Fuks et al. (2011)	LT	Ruhr area, Germany	(2000-2003)	BP	CHD	▲▲	
O'Donnell et al. (2011)	ST	8 cities in Ontario, Canada	(2003-2008)	Ischemic stroke	Atrial fibrillation	▲	
Wellenius et al. (2012a)	ST	Boston, MA	(1999-2008)	Ischemic stroke	History of atrial fibrillation	▲	
O'Donnell et al. (2011)	ST	8 cities in Ontario, Canada	(2003-2008)	Ischemic stroke	Prior stroke	▲	
Wellenius et al. (2012a)	ST	Boston, MA	(1999-2008)	Ischemic stroke	History of stroke	▲	
Chen et al. (2013)	LT	Ontario	(1996-2010)	Diabetes incidence	MI	▲	
Hansen et al. (2016)	LT	Denmark	(2003-2013)	Diabetes incidence	MI	▲▲	
Bunch et al. (2011)	ST	Utah	(1993-2008)	HA for atrial fibrillation	Prior MI	▲	
Goldberg et al. (2013)	ST	Montreal, Quebec		Mortality	Any CVD	▲	
Goldberg et al. (2013)	ST	Montreal, Quebec		Mortality	CHF	▲	
Chen et al. (2013)	LT	Ontario	(1996-2010)	Diabetes incidence	CHF	▲	
Goldberg et al. (2013)	ST	Montreal, Quebec		Mortality	Acute CAD	▲	
					Chronic CAD	▲	
Haley et al. (2009)	ST	New York	(2001-2005)	CVD admissions	Atherosclerosis	▲▲	
				CVD admissions	Previous heart failure	▲▲	
				CVD admissions	Ischemic heart disease	▲▲	
				CVD admissions	Conduction disorder	▲▲	

Study	Exp	Location	Time	Outcome	Notes	No Pre-existing	Condition Present
Bauer et al. (2010)	LT	Ruhr area, Germany	(2000-2003)	CIMT	Coronary artery disease	▲▲	

BP=blood pressure; BAD=brachial artery diameter; CAD=coronary artery disease; CVD=cardiovascular disease; CHF=congestive heart failure; HA=hospital admissions; MI = myocardial infarction; CVD = cardiovascular disease, CIMT = carotid intima media thickness; FMD=flow-mediated dilation; CRP=C-reactive protein; CHD=coronary heart disease

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-2 Stratified analyses of pre-existing diabetes and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	No Diabetes	Diabetes	Borderline*	Untreated
Mortality									
Pope et al. (2014)	LT	US (ACS CPS-II)	(1999-2004)	CVD Mortality		▲▲			
Puett et al. (2009)	LT	11 US States (NHS)	(1992-2002)	Non-accidental Mortality	Women	▲▲			
	LT			Fatal CHD	Women	▲			
Lipsett et al. (2011)	LT	CA (CTS)	(2000-2005)	IHD Mortality	Women	▲			
Goldberg et al. (2013)	ST	Montreal, Canada	(1990-2003)	Non-accidental Mortality	Any CVD, Age > 65	▲			
Wang et al. (2017)	LT	SE US (Medicare)	(2000-2013)	Mortality	Age > 65	▲▲			
Cardiovascular									
Hart et al. (2015)	LT	11 US States (NHS)	(1989-2006)	Incident CVD	Women	▼			
Chen et al. (2014)	LT	Ontario, Canada (CCHS)	(1996-2010)	Incident Hypertension		▲▲			

Study	Exp	Location	Time	Outcome	Notes	No Diabetes	Diabetes	Borderline*	Untreated
Johnson and Parker (2009)	LT	US (NHIS)	(1999-2005)	Self-reported Hypertension	Age >= 30	▲			
	LT			Self-reported Heart Disease	Age >= 30	▲			
Hoffmann et al. (2009b)	LT	Germany (GHNRC)	(2000-2003)	Prevalence PAD	Age 45-75	▲			
	LT		(20002003)	ABI	Age 45-75	▼			
Chan et al. (2015)	LT	US (Sister Study)	(2003-2009)	SBP	Women, Age 35-76	▲▲			
Fuks et al. (2011)	LT	Germany (GHNRC)	(2000-2003)	SBP	Age 45-75	▲▲			
	LT			DBP	Age 45-75	▲▲			
Wellenius et al. (2012b)	ST	Boston, MA	(2005-2008)	SBP (supine)	Age >= 70	▲			
	ST			DBP (supine)	Age >= 70	▲			
Hoffmann et al. (2012)	ST	Boston, MA	(2006-2010)	SBP	Age 40-85, (HbA1c)	▲			
Haley et al. (2009)	ST	NY	(2001-2005)	Heart Failure HA/ED	Age >35	▲▲			
O'Donnell et al. (2011)	0-48	Ontario, Canada	(2003-2008)	Ischemic Stroke HA/ED	Stroke Registry	▼			
Wellenius et al. (2012a)	0-24	Boston, MA	(1999-2008)	Ischemic Stroke HA/ED	Age >= 21	▲			
Rich et al. (2010)	0-24	NJ	(2004-2006)	Transmural Infarction HA/ED	Age >= 18	▲▲			
Allen et al. (2009)	LT	5 US Cities (MESA)	(2000-2002)	Detectable Calcium	Age 45-84	▲			
Bauer et al. (2010)	LT	Germany (GHNF)	(2000-2003)	CIMT	Age 45-73	▲▲			
Wellenius et al. (2013)	0-28	Boston, US	(2005-2008)	Difference in Resistance	Age >= 65	▲▲			
	0-28			Blood Flow Velocity	Age >= 65	▼			
Van Hee et al. (2011)	LT	6 US Cities (MESA)	(2000-2002)	QT Prolongtation	Age 45-84	▲			
Hajat et al. (2015)	LT	6 US Cities (MESA)	(2000-2002)	IL-6	Age 45-84	▲▲			
Hoffmann et al. (2009a)	LT	Germany (GHNRC)	(2000-2003)	Fibrinogen	Men, Age 45-75	▼			
	LT			Fibrinogen	Women, Age 45-75	▲			
	LT			hs-CRP	Men, Age 45-75	▲			
	LT			hs-CRP	Women, Age 45-75	▲▲			
Ostro et al. (2014)	LT	6 US Cities (SWAN)	(1999-2005)	hs-CRP	Women, Age 42-52	▲▲			
Hertel et al. (2010)	0-28	Germany (GHNRC)	(2000-2003)	hs-CRP	Age 45-75	▲			

BP=blood pressure; CVD=cardiovascular disease; ED=emergency department visit; HA=hospital admissions; CIMT = carotid intima media thickness; IL-6=interleukin 6; CRP=C-reactive protein; PAD=peripheral artery disease; IHD=ischemic heart disease

***Van Hee et al. (2011) examined "impaired fasting glucose" while Chan et al. (2015) examined "borderline".**

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) **Positive association with PM2.5, CI does not overlap null,** **Positive association with PM2.5, CI overlaps the null;** **Null association;** **Negative association with PM2.5, CI overlaps the null;** **Negative associations with PM2.5, CI does not overlap the null.**

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): **Stronger association than reference group, no overlap in CIs;** **Stronger association than reference group, overlapping CIs;** **Stronger association than reference group, CIs overlap with central estimates;** **Weaker association than reference group, no overlap in CIs;** **Weaker association than reference group, overlapping CIs;** **Weaker association than reference group, CIs overlap with central estimates**

Supplemental Table S12-3 Stratified analyses of pre-existing obesity and PM2.5-related health effects.

Study	Exposure	Location	Time	Outcome	Notes	Normal/Non-Obese BMI*	Underweight	Overweight**	Obese***
Mortality									
Pope et al. (2014)	LT	50 US States (ACS CPS-II)	(1994-2004)	CVD Mortality	BMI: <25, 25-29.9, 30-34.9	▲▲			
Turner et al. (2011)	LT	50 US States (ACS CPS-II)	(1982-2008)	Lung Cancer Mortality	Age > 30, non-smokers, BMI: 18.5-24.9, 25-29.9, >=30	▲▲			
Puett et al. (2009)	LT	11 US States (NHS)	(1992-2002)	Non-accidental Mortality	Women, BMI: <30, >=30	▲▲			
	LT			Fatal CHD		▲			
Pinault et al. (2016)	LT	Nationwide, Canada (CCHS)	(2000-2011)	Non-accidental Mortality	BMI: 18.5-25, >=30	▲▲			
	LT			Circulatory Mortality		▲			
	LT			Respiratory Mortality		▲▲			
Villeneuve et al. (2015)	LT	Nationwide, Canada (CNBSS)	(1980-2005)	Non-accidental Mortality	Women, age > 40 BMI: <30, >= 30	▲▲			
	LT			Cancer Mortality		▲			
	LT			CVD Mortality		▲▲			
	LT			IHD Mortality		▲			
Beelen et al. (2014a)	LT	19 European Cohorts (ESCAPE)	(2008-2011)	Non-accidental Mortality	BMI: <25, 25-30, >=30	▲			
Beelen et al. (2014b)	LT	19 European Cohorts (ESCAPE)	(2008-2011)	CVD Mortality	BMI: <25, 25-29.9, >=30	▼			
Dimakopoulou et al. (2014)	LT	6 European Cohorts (ESCAPE)	(2008-2011)	Respiratory Mortality	BMI: <25, 25-29.9, >=30	▼			
Lipsett et al. (2011)	LT	California (CTS)	(2000-2005)	IHD Mortality	Women, BMI: 20-24.9, <20, 25-29.9, >=30	▲			
Weichenthal et al. (2014)	LT	Iowa & North Carolina (AHS)	(1993-2009)	CVD Mortality	Men in Agricultural Industry BMI: 12-26.5, >26.5	▲			
Cardiovascular									
Hart et al. (2015)	LT	11 US States (NHS)	(1989-2006)	Incident CVD	Women, Underweight/Normal, Overweight, Obese	▼			
Chen et al. (2014)	LT	Ontario, Canada (CCHS)	(1996-2010)	Incident Hypertension	BMI: <25, 25-29.9, >=30	▲▲			
Johnson and Parker (2009)	LT	Nationwide, US (NHIS)	(1999-2005)	Self-reported Hypertension	Age >= 30, BMI: <30, >=30	▲			
	LT			Self-reported Heart Disease		▲			
Chan et al. (2015)	LT	50 US States (Sister Study)	(2003-2009)	SBP	Women, Age 35-76, BMI: <25, 25-29.9, >=30	▲			
Fuks et al. (2011)	LT	3 Cities Germany (GHNRC)	(2000-2003)	SBP	Age 45-75, BMI: <27.4, >=27.4	▲▲			
				DBP		▲▲			

Wellenius et al. (2012b)	ST	Boston, MA	(2005-2008)	SBP (supine)	Age >= 70, BMI: <30, >=30	▲
	ST			DBP (supine)		▲
Hoffmann et al. (2012)	ST	Boston, MA	(2006-2010)	SBP	Diabetes, Age 40-85, BMI: <30.6, >=30.6	▲
Hoffmann et al. (2009b)	LT	3 Cities Germany (GHNRC)	(2000-2003)	Prevalence PAD	Age 45-75, BMI: <30, >=30	▼
	LT			ABI		▼
Allen et al. (2009)	LT	5 US Cities (MESA)	(2000-2002)	Detectable Calcium	Age 45-84, BMI: <30, >=30	▲
Bauer et al. (2010)	LT	3 Cities Germany (GHNF)	(2000-2003)	CIMT	Age 45-73, BMI: <27, >=27	▲▲
Hajat et al. (2015)	LT	6 US Cities (MESA)	(2000-2002)	IL-6	Age 45-84, Obese/Non-Obese	▲▲
Hoffmann et al. (2009a)	LT	3 Cities Germany (GHNRC)	(2000-2003)	Fibrinogen	Men, Age 45-75, BMI: <30, >=30	▲▲
	LT			Fibrinogen	Women, Age 45-75, BMI: <30, >=30	▲
	LT			CRP	Men, Age 45-75, BMI: <30, >=30	▲▲
	LT			CRP	Women, Age 45-75, BMI: <30, >=30	▲
Ostro et al. (2014)	LT	6 US Cities (SWAN)	(1999-2005)	CRP	Menopausal Women, Age 42-52, BMI: <25, >=25	▲
Hertel et al. (2010)	0-28	3 Cities Germany (GHNRC)	(2000-2003)	CRP	Age 45-75, BMI: <27, >=27	▲▲
Reproductive						
Mobasher et al. (2013)	1st Tri.	Los Angeles, CA	(1996-2008)	Preeclampsia	Women, Hispanic, BMI: <30, >=30	▲▲
	2nd Tri.			Preeclampsia		▲
	3rd Tri.			Preeclampsia		▲
Robledo et al. (2015)	Pre-Concep.	12 US Clinical Centers (CSL)	(2002-2008)	Gestational Diabetes	Women, BMI: <25, >=25	▲
	1st Tri.			Gestational Diabetes		–
Mahalingaiah et al. (2014)	LT	14 US States (NHS-II)	(1993-2007)	Endometriosis	Women, Age >=25, BMI: <25, >=25	▼
Diabetes						
Chen et al. (2013)	LT	Ontario, Canada	(1996-2010)	Incident Diabetes	Age >= 35, BMI: <25, 25.0-29.9, >=30	▲
Hansen et al. (2016)	LT	Nationwide, Denmark (DNC)	(1993-2013)	Incident Diabetes	Women, Age > 44, BMI: <18.5, 18.5-25, 25.0-29.9, >=30	▲
Weinmayr et al. (2015)	LT	3 Cities Germany (GHNRC)	(2000-2003)	Incident Diabetes	Age 45-75, BMI: <=30, >30	▼

*Some studies specified a normal or healthy range BMI group (BMI: 18.5-24.9), while some studies included all BMI values below a cutpoint (e.g. <25). Furthermore, some studies did not distinguish between overweight and obese, and grouped normal/healthy BMI (18.5-24.9) with overweight (variable definitions).
** Underweight is typically defined as a BMI of 25-29.9. Studies that dichotomized BMI at a value of 25 were included in this column as "overweight & obese"
*** Obese typically defined as a BMI >= 30, though definition of obese varied across studies (27-30.6) as indicated in the Notes column.

ABI=ankle brachial index; BP=blood pressure; CVD=cardiovascular disease; CIMT = carotid intima media thickness; IL-6=interleukin 6; CRP=C-reactive protein; PAD=peripheral artery disease; IHD=ischemic heart disease; CHD=coronary heart disease

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-4 Stratified analyses evaluating elevated cholesterol and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Reference	Potentially At-Increased-Risk Population
Mortality and CVD by Hypercholesterolemia Status						No Lipid Disorder	Lipid Disorder
Puett et al. (2009)	LT	11 US States (NHS Cohort)	(1992-2002)	Non-accidental Mortality	Women	▲▲	
	LT			Fatal CHD	Women	▲▲	
Gardner et al. (2014)	ST	Rochester, NY	(2007-2010)	STEMI		▲▲	
Atherosclerosis, Systemic Inflammation by Statin Usage						No Statins	Statins
Allen et al. (2009)	LT	5 US Cities (MESA)	(2000-2004)	Detectable Calcium	Age 45-84	–	
	LT			Agatston Score	Age 45-84, all population	▲▲	
Künzli et al. (2010)	LT	Los Angeles, CA (Meta-analysis)	(Varied)	CIMT	Never/Past Lipid Medication	▲▲	
Bauer et al. (2010)	LT	3 Cities Germany (GHNR Cohort)	(2000-2003)	CIMT	Age 45-75	▲▲	
Hoffmann et al. (2009b)	LT	3 Cities Germany (GHNR Cohort)	(2000-2003)	History PAD	Age 45-75	▼	
Krishnan et al. (2012)	LT	6 US Cities (MESA Cohort)	(2000-2002)	FMD %	Age 45-84	▼	
Viehmann et al. (2015)	LT	3 Cities Germany (GHNR Cohort)	(2000-2003)	Platelets	Age 45-75	▲▲	
	LT			hs-CRP	Age 45-75	▲▲	

Ostro et al. (2014)	LT	6 US Cities (SWAN Cohort)	(1999-2005)	hs-CRP	Women, Age 42-52	▲▲	
Hertel et al. (2010)	ST	3 Cities Germany (GHNR Cohort)	(2000-2003)	hs-CRP	Age 45-75	▲▲	

CHD=coronary heart disease; FMD=flow-mediated dilation; STEMI=ST-elevation myocardial infarction; CIMD=carotid media intima thickness; CRP=C-reactive protein; PAD=peripheral artery disease

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-5 Stratified analyses of pre-existing respiratory disease (asthma and COPD) and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	No Pre-existing	Condition Present
Asthma							
Bunch et al. (2011)	ST	UT	(1992-2008)	AF hospitalizations		▲	
Turner et al. (2011)	LT	Multi-city US	(1982-2008)	Lung cancer mortality		▲	
Watanabe et al. (2015)	ST	Matseu, Japan	(2012-2013)	PEF	Children	▲▲	
Chen et al. (2013)	LT	Ontario, Canada	(1996-2010)	Diabetes incidence		▲▲	
Klümper et al. (2015)	ST	Germany	(2002-2005)	IL-10	Children	–	
				IL-12p70	Children	–	
				MCP-1	Children	▼	
				TNFalpha	Children	▲▲	
				IFNgamma	Children	–	
				IL-6	Children	▲▲	
				IL-8	Children	▲	
COPD							
Wang et al. (2017)	LT	Southeastern US	(2000-2013)	Mortality		▲▲	
Turner et al. (2011)	LT	Multi-city US	(1982-2008)	Lung cancer mortality		▲▲	

Study	Exp	Location	Time	Outcome	Notes	No Pre-existing	Condition Present
Bunch et al. (2011)	ST	UT	(1992-2008)	AF hospitalizations		▲	
Haley et al. (2009)	ST	NY	(2001-2005)	CVD hospitalizations		▲▲	
Rich et al. (2010)	ST	NJ	(2004-2006)	MI hospitalizations		▲▲	
Belleudi et al. (2010)	ST			HA for acute coronary syndrome		▲▲	
				HA for heart failure		▲	
Chen et al. (2014)	ST	Ontario, Canada	(1996-2010)	Incident hypertension		▲▲	
Chen et al. (2013)	LT	Ontario, Canada	(1996-2010)	Diabetes incidence		▲	

AF=antrial fibrillation; IL-6=interleukin 6; CRP=C-reactive protein; IL-10=interleukin 10; IL-8=interleukin 8; IL-12p70=interleukin 12 (p70 – active heterodimer); MCP-1=monocyte chemotactic protein 1; PEF=peak expiratory flow; TNFalpha=tumor necrosis factor alpha; IFNgamma=interferon gamma;

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-6 Stratified analyses of genetic background and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Wild-Type	Mutation/variant
Fuertes et al. (2013)	LT	Europe - 6 cohorts	(1994-1999)	Allergic rhinitis	GSTP1 rs1138272 C/T	▲	
				Allergic rhinitis	GSTP1 rs1695 A/G	▲	
Chen et al. (2016)		New Taipei City, Taiwan	(2007-2009)	Leukocytes (nasal lavage)	GSTM1 null	▼	
	ST			Neutrophils (nasal lavage)	GSTM1 null	▼	

Study	Exp	Location	Time	Outcome	Notes	Wild-Type	Mutation/variant
*Breton et al. (2011)	LT	Southern California	(1993-2004)	FVC	GSS haplotype 0100000	▲	
				FEV1	GSS haplotype 0100000	▲	
				MMEF	GSS haplotype 0100000	▼▼	
Hampel et al. (2010)	ST	Augsburg, Germany	(2003-2004)	QTc	NFE2L2 rs2364725 T/G	–	
Fuertes et al. (2013)	LT	Europe - 6 cohorts	(1994-1999)	Allergic rhinitis	TNF rs1800629 G/A	▼	
				Allergic rhinitis	TLR2 rs4696480 T/A	▲	
				Allergic rhinitis	TLR4 rs10759930 C/T	▼	
				Allergic rhinitis	TLR4 rs10759931 G/A	▲	
				Allergic rhinitis	TLR4 rs10759932 T/C	▲	
				Allergic rhinitis	TLR4 rs1927911 C/T	▲	
				Allergic rhinitis	TLR4 rs2737190 A/G	▲	
				Allergic rhinitis	TLR4 rs2770150 T/C	▲	
Wilker et al. (2011)	ST	Boston, MA		ICAM-1	GEMIN4 (rs1062923)	▲▲	
				VCAM-1	GEMIN4 (rs1062923)	▲▲	
Ren et al. (2010)	LT	Boston, MA	(2000-2007)	SDNN	ApoE (rs7412)	▲▲	
				SDNN	ApoE (rs405509)	▲	
				SDNN	ApoE (rs429358)	▲▲	
				SDNN	ApoE (rs440446)	▲	
				SDNN	ApoE (rs449647)	▲▲	
				SDNN	ApoE (rs769446)	▲▲	
				SDNN	LPL (rs328)	▲	
				SDNN	VEGF (rs2010963)	▲	
Hampel et al. (2012)	ST	Augsburg, Germany	(2007-2008)	SDNN	CHT1 rs333229	▲	
				SDNN	rs2966762	▲	
				SDNN	rs1871841	▲▲	

GSTP1= Glutathione S-transferase P; GSTM1=Glutathione S-transferase Mu 1; GSS=glutathione synthetase; TNF=tumor necrosis factor; NFE2L2= Nuclear factor-like 2; TLR4=toll-like receptor 4; GEMIN4=Gem-associated protein 4; ApoE=Apolipoprtein E; LPL=Low density lipoprotein; VEGF=vascular endothelial growth factor; CHT1=High-affinity choline transporter 1; FVC=forced vital capacity; FEV1=forced expiratory volume in 1 second; MMEF=maximal mid-expiratory flow; QTc=QT interval; ICAM-1=intracellular adhesion molecule; VCAM=vascular cell adhesion molecule; SDNN=standard deviation of the NN interval

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-7 Stratified analyses evaluating lifestage: children and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Reference: Adults	Children
Respiratory					Child Age		
Samoli et al. (2016)	ST	London, UK	(2011-2012)	HA/ED - all resp	0-14	▼	
Atkinson et al. (2016)	ST	London, UK	(2011-2012)	HA/ED - all resp	0-14	▼	
Youngquist et al. (2016)	ST	Utah, US	(2009-2012)	Emergency calls - all respiratory	0-17	▲	
Lavigne et al. (2012)	ST	Windsor, CA	(2002-2009)	HA/ED – asthma	2-14	▲	
Haikerwal et al. (2015)	ST	Victoria, Australia	(2006-2007)	HA/ED – asthma	0-19	▲▲	
Alman et al. (2016)	ST	Colorado, US	(2012)	HA/ED - all resp	0-18	▲▲	
	ST			HA/ED – asthma	0-18	▲▲	
Cardiovascular							
Youngquist et al. (2016)	ST	Utah, US	(2009-2012)	Emergency calls - cardiac arrest	0-17	▲	

HA=hospital admissions; ED=emergency department visits; ST=short term; LT=long term

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-8 Stratified analyses evaluating lifestage: older adults and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Ref	Group 1	Group 2	Group 3	Group 4	Group 5
Cardiovascular					Reference Age						
Atkinson et al. (2016)	ST	London, UK	(2011-2012)	HA/ED - All CVD	15-64	▲					
Youngquist et al. (2016)	ST	Utah, US	(2009-2012)	Emergency calls - cardiac arrest	18-39	▼					
Belleudi et al. (2010)	ST	Rome, Italy	(2001-2005)	HA/ED - acute coronary	35-64	▲					
	ST			HA/ED - heart failure	35-64	▼					
Bunch et al. (2011)	ST	Utah, US	(1994-2006)	HA/ED - Atrial Fib	<55	▲					
Dales et al. (2010)	ST	Santiago, Chile	(1998-2005)	HA/ED – VT	<65	▲▲					
	ST			HA/ED – PE	<65	▲▲					
Ensor et al. (2013)	ST	Houston, TX	(2004-2011)	Cardiac arrest	35-64	▲					
Lanzinger et al. (2016)	ST	Multicity, Europe	(2011-2014)	HA/ED - All CVD	<75	▲					
Rich et al. (2010)	ST	New Jersey, US	(2004-2006)	HA/ED - TIA	<65	▲▲					
Silverman and Ito (2010)	ST	New York City, NY	(2002-2006)	Cardiac arrest	40-69	▲					
Wellenius et al. (2012a)	ST	Boston, MA	(1999-2008)	HA/ED - stroke	<75	▲					
Huang et al. (2016b)	ST	Beijing, China	(2013-2014)	HA/ED- ischemic stroke	<65	▲					
	ST			HA/ED- hem stroke	<65	▼					
Huang et al. (2016a)	ST	Shanghai, China	(2013-2014)	HA/ED - CHD	<65	▲▲					
Samoli et al. (2016)	ST	London, UK	(2011-2012)	HA/ED - All CVD	15-64	▲					
Weichenthal et al. (2016)	ST	Ontario, Canada	(2004-2011)	HA/ED - MI	<56	▲▲					
Ye et al. (2016)	ST	Shanghai, China	(2005-2012)	HA/ED - CHD	41-65	▲▲					
Yitshak Sade et al. (2015)	ST	Multicity, Israel	(2005-2012)	HA/ED- ischemic stroke	<55	▲					
Milojevic et al. (2014)	ST	Multicity, UK	(2001-2010)	Mortality - CVD	<70	▼					
Su et al. (2015)	ST	Beijing, China	(2008)	Mortality - CVD	<75	▲▲					
Chen et al. (2014)	LT	Ontario, Canada	(1996-2005)	Hypertension	<60	▲					
Fuks et al. (2011)	LT	Multicity, Germany	(2000-2003)	SBP	<60	▲▲					
Bauer et al. (2010)	LT	Multicity, Germany	(2000-2003)	CIMT	<60	▲▲					

Study	Exp	Location	Time	Outcome	Notes	Ref	Group 1	Group 2	Group 3	Group 4	Group 5
Allen et al. (2009)	LT	Multicity, US	(2000-2002)	Ca+	<65	▲					
	LT			Agatston scorew/ Ca+	<65	▼					
	LT			Agatston score	<65	–					
Hoffmann et al. (2009b)	LT	Multicity, Germany	(2000-2003)	ABI	<60	▼					
	LT			PAD	<60	▲					
Krishnan et al. (2012)	LT	Multicity, US	(2000-2002)	BAD	45-54	▼					
	LT			FMD	45-54	▼▼					
Cesaroni et al. (2014)	LT	Multicity, Europe	(1997-2007)	Coronary events	<60	▼					
Hajat et al. (2015)	LT	Multicity, US	(2000-2012)	IL-6	<65	▲					
Hennig et al. (2014)	LT	Multicity, Germany	(2000-2003)	CRP	<65	▲▲					
Hertel et al. (2010)	ST	Multicity, Germany	(2000-2003)	CRP	<60	▼					
Hoffmann et al. (2009a)	LT	Multicity, Germany	(2000-2003)	CRP	<60 (Men)	▲					
	LT			CRP	<60 (Women)	▲					
	LT			Fibrinogen	<60 (Men)	▲					
	LT			Fibrinogen	<60 (Women)	▲					
Viehmann et al. (2015)	LT	Multicity, Germany	(2000-2008)	CRP	<60	▲					
	LT			Platelets	<60	▲▲					
Beelen et al. (2014b)	LT	Multicity, Europe	(2008-2011)	Mortality - CVD	<60	▼					
Cesaroni et al. (2013)	LT	Multicity, Italy	(2001-2010)	Mortality - CVD	<60	▲▲					
Crouse et al. (2015)	LT	Multicity, Canada	(1991-2006)	Mortality - CVD	<60 (Men)	▲▲					
	LT			Mortality - CVD	<60 (Women)	▲▲					
Pinault et al. (2016)	LT	Multicity, Canada	(2000-2011)	Mortality - CVD	<75	▲▲					
Thurston et al. (2016)	LT	Multicity, US	(2000-2009)	Mortality - CVD	<65	▲▲					
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Mortality - CVD	<71	▲▲					
Cesaroni et al. (2013)	LT	Multicity, Italy	(2001-2010)	Mortality - IHD	<60	▲▲					
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Mortality - IHD	<71	▲▲					
	LT			Mortality - CBVD	<71	▲					
Respiratory											
Belleudi et al. (2010)	ST	Rome. Italy	(2001-2005)	HA/ED - Respiratory Inf	35-64	▲					
	ST			HA/ED – COPD	35-64	▲					
Xu et al. (2016)	ST	Beijing, China	(2013)	HA/ED - All Respiratory	35-59	▲					

Study	Exp	Location	Time	Outcome	Notes	Ref	Group 1	Group 2	Group 3	Group 4	Group 5
Samoli et al. (2016)	ST	London, UK	(2011-2012)	HA/ED - All Respiratory	15-64	▼					
Atkinson et al. (2016)	ST	London, UK	(2011-2012)	HA/ED - All Respiratory	15-64	▼					
Lavigne et al. (2012)	ST	Windsor, Canada	(2002-2009)	HA/ED - Asthma	15-39	▲					
Alman et al. (2016)	ST	Colorado, US	(2012)	HA/ED - All Respiratory	19-64	▲▲					
	ST			HA/ED - Asthma	19-64	▲▲					
Lanzinger et al. (2016)	ST	Multicity, Europe	(2011-2014)	HA/ED - All Respiratory	<75	▲▲					
Youngquist et al. (2016)	St	Utah, US	(2009-2012)	Ambulance call - Respiratory distress	18-39	▲					
Hwang et al. (2017)	ST	Taiwan	(2006-2012)	HA/ED - COPD	<65	▲					
Dimakopoulou et al. (2014)	LT	Multicity, Europe	(2008-2011)	Mortality – Respiratory	<60	▼					
Pinault et al. (2016)	LT	Multicity, Canada	(2000-2011)	Mortality – Respiratory	<75	▲▲					
Thurston et al. (2016)	LT	Multicity, US	(2000-2009)	Mortality – Respiratory	<65	▲					
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Mortality – Respiratory	<71	▲					
Cesaroni et al. (2013)	LT	Multicity, Italy	(2001-2010)	Mortality - Lung Cancer	<60	▲					
Turner et al. (2011)	LT	Multicity, US	(1982-2008)	Mortality - Lung Cancer	<70	▲					
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Mortality – Pneumonia	<71	▲					
	LT			Mortality - COPD	<71	▲▲					
Mortality											
Huang et al. (2012)	ST	Xi'an, China	(2004-2008)	Mortality - Total	45-64	▲					
Lee et al. (2015a)	ST	Multicity, Asia	(2001-2009)	Mortality - Total	<65	▲▲					
Lee et al. (2015b)	ST	Multicity, Asia	(2001-2009)	Mortality - Total	<65	▲▲					
Madsen et al. (2012)	ST	Oslo, Norway	(1992-2001)	Mortality - Total	50-64	▲▲					
Pascal et al. (2014)	ST	Multicity, France	(2000-2006)	Mortality - Total	15-74	▲▲					
Samoli et al. (2013)	ST	Multicity, Europe	(2001-2010)	Mortality - Total	<75	▲					
Beelen et al. (2014a)	LT	Multicity, Europe	(2008-2011)	Mortality - Total	<60	▲					
Cesaroni et al. (2013)	LT	Multicity, Italy	(2001-2010)	Mortality - Total	<60	▲▲					
Crouse et al. (2015)	LT	Multicity, Canada	(1991-2006)	Mortality - Total	<60 (Men)	▲▲					
	LT			Mortality - Total	<60 (Women)	▲▲					

Study	Exp	Location	Time	Outcome	Notes	Ref	Group 1	Group 2	Group 3	Group 4	Group 5
Pinault et al. (2016)	LT	Multicity, Canada	(2000-2011)	Mortality - Total	<75	▲▲					
Thurston et al. (2016)	LT	Multicity, US	(2000-2009)	Mortality - Total	<65	–					
Wang et al. (2016)	LT	Multicity, US	(2004-2009)	Mortality - Total	<65	▲					
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Mortality - Total	<71	▲▲					

LT=long term; S=short term; COPD=chronic obstructive pulmonary disease;

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-9 Stratified analyses evaluating sex and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Reference: Females	Males
Mortality							
Di et al. (2017a)	LT	US	(2000-2012)	All-cause	All	▲▲	
	LT				Medicaid Eligible	▲▲	
	LT				Medicaid Ineligible	▲▲	
Zeger et al. (2008)	LT	US	(2000-2005)	All-cause	Eastern US	▲	
	LT				Central US	▲	
	LT				Western US	–	
Thurston et al. (2016)	LT	US	(2000-2009)	All-cause	All	▲	
	LT				< 65 years	▲	
	LT				>= 65 years	▲	

Study	Exp	Location	Time	Outcome	Notes	Reference: Females	Males
Wang et al. (2017)	LT	Southeast US	(2000-2013)	All-cause		▲▲	
Weichenthal et al. (2014)	LT	IA and NC	(1993-2009)	Non-accidental		▼	
Crouse et al. (2015)	LT	Canada	(1991-2006)	Non-accidental	All	▲▲	
	LT				< 60 years	▲▲	
	LT				60-69 years	▲	
	LT				70-79 years	▲▲	
	LT				80-89 years	▲	
Beelen et al. (2014a)	LT	Europe	(1991-2007)	Natural-cause		▼	
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Natural-cause		▲▲	
Son et al. (2017)	LT	MA	(2001-2007)	Infant Mortality	First-year exposure	▲▲	
Huang et al. (2012)	ST	Xi'an, China	(2004-2008)	All-cause		▲	
Samoli et al. (2013)	ST	Europe	(2001-2010)	All-cause		▲▲	
Madsen et al. (2012)	ST	Oslo, Norway	(1992-2001)	Non-accidental		▲▲	
Cardiovascular							
Thurston et al. (2016)	LT	US	(2000-2009)	Cardiovascular mortality	All	▲▲	
	LT				< 65 years	▲	
	LT				>= 65 years	▲▲	
Weichenthal et al. (2014)	LT	IA and NC	(1993-2009)	Cardiovascular mortality		▼	
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	Cardiovascular mortality		▲▲	
	LT			IHD mortality		▲▲	
	LT			Cerebrovascular mortality		▲	
Johnson and Parker (2009)	LT	US	(1999-2005)	Heart disease		▲	
	LT			Hypertension		▲	
Crouse et al. (2015)	LT	Canada	(1991-2006)	Cardio-metabolic disease	All	▲▲	
	LT				< 60 years	▲▲	
	LT				60-69 years	▲	
	LT				70-79 years	▲▲	
	LT				80-89 years	▲▲	
Chen et al. (2014)	LT	Ontario, Canada	(1996-2010)	Hypertension		▲▲	
Fuks et al. (2011)	LT	Germany	(2000-2003)	BP		▲▲	

Study	Exp	Location	Time	Outcome	Notes	Reference: Females	Males
Su et al. (2015)	ST	Beijing, China	(2008)	Cardiovascular mortality	Lag 0	▲	
	ST				Lag 1	▲▲	
	ST				5-day avg	▲▲	
Milojevic et al. (2014)	ST	England	(2003-2009)	Cardiovascular HAs		▼▼	
	ST			Mortality		▲▲	
Bell et al. (2015)	ST	US	(1999-2010)	Acute myocardial infarction		▲	
	ST			Heart failure		▲▲	
	ST			Heart rhythm disturbance		▲▲	
	ST			Peripheral vascular disease		▲▲	
	ST			Cardiovascular		▲▲	
	ST			Ischemic heart disease		▲	
Rodopoulou et al. (2015)	ST	Little Rock, AR	(2002-2012)	Cardiovascular		▼▼	
Kloog et al. (2014)	ST	Mid-Atlantic US	(2000-2006)	Cardiovascular		▲▲	
Lanzinger et al. (2016)	ST	Europe	(2011-2014)	Cardiovascular		▲	
Silverman et al. (2010)	ST	New York City, NY	(2002-2006)	Cardiac arrest		▲	
Haley et al. (2009)	ST	NY	(2001-2005)	Heart failure		▲▲	
Rich et al. (2010)	ST	NJ	(2004-2006)	Transmural infarction		▲	
Brook and Kousha (2015)	ST	Alberta, Canada	(2010-2011)	Hypertension	Lag 0	▲	
	ST				Lag 1	▲	
	ST				Lag 8	▲	
Weichenthal et al. (2016)	ST	Ontario, Canada	(2004-2011)	Myocardial infarction		▲	
Ye et al. (2016)	ST	China	(2005-2012)	Congenital heart disease		▲▲	
Dales et al. (2010)	ST	Chile	(2001-2005)	Pulmonary embolism		▲▲	
	ST			Venous thrombosis		▲▲	
Respiratory							
Thurston et al. (2016)	LT	US	(2000-2009)	Respiratory mortality	All	▲	
	LT				< 65 years	▲	
	LT				>= 65 years	▲	
Dimakopoulou et al. (2014)	LT	Europe	(1985-2007)	Respiratory mortality		▼▼	

Study	Exp	Location	Time	Outcome	Notes	Reference: Females	Males
Wong et al. (2015)	LT	Hong Kong	(1998-2011)	COPD		▲	
	LT			Pneumonia		▼	
	LT			Respiratory		▼	
Bell et al. (2015)	ST	US	(1999-2010)	Asthma		▲	
	ST			COPD		▲	
	ST			Respiratory		▲▲	
	ST			RTI		▲▲	
	ST			Cerebrovascular		▲▲	
Rodopoulou et al. (2015)	ST	Little Rock, AR	(2002-2012)	Respiratory		▲	
Liu et al. (2016b)	ST	Jinan, China	(2013-2014)	Respiratory	Urban	▲▲	
	ST				Suburban	▲	
Lanzinger et al. (2016)	ST	Europe	(2011-2014)	Respiratory		▲▲	
Gleason et al. (2014)	ST	NJ	(2004-2007)	Pediatric asthma		▼	
Watanabe et al. (2015)	ST	Matsue, Japan	(2012-2013)	PEF	Year 2012	▼▼	
	ST				Year 2013	▼	
Diabetes							
Brook et al. (2013)	LT	Canada	(1991-2001)	Diabetes mortality		▲▲	
Park et al. (2015)	LT	Multi-City US	(2000-2012)	Diabetes incidence		▲	
	LT			Diabetes prevalence		▲	
Chen et al. (2013)	LT	Ontario, Canada	(1996-2010)	Incident diabetes		▲▲	
Liu et al. (2016a)	LT	China	(2011-2012)	Type 2 diabetes		▲▲	

BP=blood pressure; COPD=chronic obstructive pulmonary disease; HA=hospital admissions; PEF=peak expiratory flow; ST=short term; LT=long term

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates.

Supplemental Table S12-10 Stratified analyses evaluating SES (Educational Measures) and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	College Degree	Reference: More than HS	HS Diploma	Incomplete HS	Less than HS
Mortality										
Thurston et al. (2016)	LT	US	(2000-2009)	All-cause			▲			
Kloog et al. (2013)	LT	MA	(2000-2008)	CVD and Respiratory	Ref = No College		▲▲			
Beelen et al. (2014a)	LT	Europe	(1991-2007)	Natural-cause			▲			
Son et al. (2017)	LT	MA	(2001-2010)	Infant Mortality	First-year exposure		▲▲			
Turner et al. (2011)	LT	US	('79-'83; '99-'00)	Lung cancer			▲			
Cardiovascular										
Thurston et al. (2016)	LT	US	(2000-2009)	Cardiovascular mortality			▲▲			
Johnson and Parker (2009)	LT	US	(1999-2005)	Heart disease			▲			
	LT			Hypertension			▲			
Coogan et al. (2016)	LT	US	(1995-2011)	Hypertension			▲			
Chen et al. (2014)	LT	Ontario	(1996-2005)	Hypertension			▲▲			
Fuks et al. (2011)	LT	Germany	(2000-2003)	BP			▲▲			
Respiratory										
Thurston et al. (2016)	LT	US	(2000-2009)	Respiratory mortality			▲			
Strickland et al. (2014)	ST	Atlanta, GA	(2002-2010)	Pediatric asthma	Maternal education		▲▲			
Reproduction										
Vinikoor-Imler et al. (2012)	LT	NC	(2000-2003)	Gestational hypertension	Maternal education		▼			
Green et al. (2015)	LT	CA	(1999-2009)	Stillbirth	Maternal education		▲			
Diabetes										
Coogan et al. (2016)	LT	US	(1995-2011)	Diabetes			▼			
Chen et al. (2013)	LT	Ontario	(1996-2010)	Incident diabetes			▲			

BP=blood pressure; CVD=cardiovascular disease

Heatmap legend:

Reference group (no pre-existing cardiovascular disease); Positive association with PM2.5, CI does not overlap null; Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates.

Supplemental Table S12-11 Stratified analyses evaluating SES (Non-Educational Measures) and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Reference: High SES	Medium	Low
Mortality					(SES Metric)			
Di et al. (2017a)	LT	US	(2000-2012)	All-cause	Medicaid Eligibility	▲▲		
Kioumourtzoglou et al. (2016)	LT	207 US cities	(2000-2010)	All-cause	Area poverty rate	▲▲		
Zeger et al. (2008)	LT	US (Eastern)	(2000-2005)	All-cause	Composite Index	▲▲		
	LT	US (Central)				▲▲		
	LT	US (Western)				▼▼		
Puett et al. (2009)	LT	Northeast and Midwest US	(1992-2002)	All-cause	Area income (quartile 1;3;4)	▲		
Wang et al. (2017)	LT	Southeast US	(2000-2013)	All-cause	Area income	▲▲		
Crouse et al. (2015)	LT	Canada	(1991-2006)	Non-accidental	Income (quintile 1;5)	▲▲		
Brook et al. (2013)	LT	Canada	(1991-2001)	Diabetes-related	Income (quintile 1;3;5)	▲▲		
Madsen et al. (2012)	ST	Norway	(1992-2001)	Non-accidental	Area income	▲▲		
Cardiovascular								
Johnson and Parker (2009)	LT	US	(1999-2005)	Heart disease	Above/Below Poverty	▲		
	LT			Hypertension		▲		
Coogan et al. (2016)	LT	US	(1995-2011)	Hypertension	Area income (quintile 1;3;5)	▼▼		
Kloog et al. (2014)	ST	Mid-Atlantic US	(2000-2006)	CVD Hospital admissions	Income	▲▲		
Haley et al. (2009)	ST	NY	(2001-2005)	Heart failure	Area poverty rate	▲▲		
Fuks et al. (2011)	LT	Germany	(2000-2003)	Diastolic BP	Employed/Unemployed	▲		
	LT			Systolic BP		▲		
Respiratory								
O'Lenick et al. (2017)	ST	Atlanta, GA	(2002-2008)	Pediatric asthma	Area poverty rate	▲▲		
Sarnat et al. (2013)	ST	Atlanta, GA	(1999-2002)	Asthma	Area poverty rate	▲		
Strickland et al. (2014)	ST	Atlanta, GA	(2002-2010)	Pediatric asthma	Medicaid status	▲▲		
Gleason et al. (2014)	ST	NJ	(2004-2007)	Pediatric asthma	Composite Index	▼		
Reproduction								
Vinikoor-Imler et al. (2012)	LT	NC	(2000-2003)	Gestational hypertension	Composite Index (quartile 1;3;4)	–		
Stieb et al. (2015)	LT	Canada	(1999-2008)	Low birthweight	Area low-income rate	–		
	LT			Preterm birth		▼▼		
	LT			Small for gestational age		▲		
Diabetes								
Coogan et al. (2016)	LT	US	(1995-2011)	Diabetes	Area income (quintile 1;3;5)	▼		

BP=blood pressure; ST=short-term; LT=long term

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates.

Supplemental Table S12-12 Stratified analyses evaluating Race and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Reference: White	Nonwhite	Black	Hispanic	Asian
Mortality										
Di et al. (2017b)	LT	US	(2000-2012)	All-cause		▲▲				
Kioumourtzoglou et al. (2016)	LT	US	(2000-2010)	All-cause	City-level race	▲▲				
Wang et al. (2017)	LT	Southeast US	(2000-2013)	All-cause		▲▲				
Parker et al. (2017)	LT	US	(1997-2009)	All-cause		▲				
				Heart disease		▲▲				
Lee et al. (2015b)	ST	GA, NC, SC	(2007-2011)	Non-accidental		▲▲				
Cardiovascular										
Johnson and Parker (2009)	LT	US	(1999-2005)	Heart Disease		▲				
	LT			Hypertension		▲▲				
Hicken et al. (2016)	LT	Six US cities	(2000-2002)	LVEF		–				
	LT			LVMI		–				
Rodopoulou et al. (2015)	ST	Little Rock, AR	(2002-2012)	Cardiovascular ER		▲				
Rich et al. (2010)	ST	NJ	(2004-2006)	Transmural Infarction		▲▲				
Respiratory										
Nachman and Parker (2012)	LT	US	(2002-2005)	Asthma	Attack in past year	▼				
	LT				Still has asthma	▼				
	LT			Chronic Bronchitis	Attack in past year	▲				
Alhanti et al. (2016)	ST	Three US cities	(1993-2009)	Asthma	0-4 yrs	▲				
	ST	(Atlanta, GA /			5-18 yrs	▲				
	ST	Dallas, TX /			19-39 yrs	▼				
	ST	St. Louis, MO)			40-64 yrs	▲				
	ST				65+ yrs	▼				
Glad et al. (2012)	ST	Pittsburgh, PA	(2002-2005)	Asthma	18-64 yrs	▼				
	ST				All ages	▼				

Study	Exp	Location	Time	Outcome	Notes	Reference: White	Nonwhite	Black	Hispanic	Asian
Strickland et al. (2014)	ST	Atlanta, GA	(2002-2010)	Pediatric Asthma	Ref = Not Black	▲				
Gleason et al. (2014)	ST	NJ	(2004-2007)	Pediatric Asthma		▲				
	ST				Ref = Not Hispanic	▼▼				
Rodopoulou et al. (2015)	ST	Little Rock, AR	(2002-2012)	Respiratory ER		▲				
Reproduction										
Bell et al. (2007)	LT	CT; MA	(1999-2002)	Birthweight		▲▲				
Pereira et al. (2014)	LT	CT	(2000-2006)	Preterm Birth		▲				
Green et al. (2015)	LT	CA	(1999-2009)	Stillbirth		▲				
Vinikoor-Imler et al. (2012)	LT	NC	(2000-2003)	Gestational Hypertension		–				

ER=emergency room visits; LVEF=left ventricular ejection fraction; LVMI=left ventricular mass index

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates.

Supplemental Table S12-13 Stratified analyses evaluating residential location and PM2.5-related health effects.

Study	Location	Exp	Time	Outcome	Notes	Categorization	Ref: Urban	Moderately Urban	Less Urban	Rural
Mortality										
Di et al. (2017a)	Nationwide, US (Medicare)	LT	(2000-2012)	Mortality	Age > 65	High | Med-High | Med-Low | Low Density	▲▲			
Kioumourtzoglou et al. (2016)	207 US Cities (Medicare)	LT	(2000-2010)	Mortality	Urbanicity, Age > 65	75th | 25th %ile	▲▲			
		LT		Mortality	Pop Den., Age > 65		▲▲			
Shi et al. (2015)	6 NE States (Medicare)	LT	(2003-2008)	Mortality	Age > 65	Above | Below Median Zip Code Pop.	▲▲			
		LT		Mortality	Age > 65, <10ug/m3		▲▲			
Lee et al. (2015b)	3 SE States	ST	(2007-2011)	Mortality		Metro Urban Core | Rural (RUCA*)	▲▲			
Wang et al. (2017)	7 SE States (Medicare)	LT	(2000-2013)	Mortality	Age > 65	80th | 20th %ile Density	▲▲			
Kloog et al. (2013)	Massachusetts	LT	(2000-2008)	CVD & Resp. Mortality		Urban (<20km) | Rural (>20km)	▲▲			
Brook et al. (2013)	Multicity, Canada	LT	(1991-2001)	Diabetes-Related	Age >25	>500k|30-500k|Farm & Rural Population	▲▲			
Cardiovascular										
Bravo et al. (2017)	708 U.S. Counties(Medicare)	ST	(2002-2006)	CVD HA/ED	Age > 65	>90% | 41-60% | <40% Urban Population	▲▲			
Kloog et al. (2014)	7 NE Mid-Atlantic States (Medicare)	ST	(2000-2006)	CVD HA/ED	Age > 65	Urban (<30km) | Rural (>30km)	▼			
Johnson and Parker (2009)	Nationwide, US	LT	(1999-2005)	Self-Report. CVD	Age > 30	Large Metro | Large Fringe Metro |	▲▲			
		LT		Self-Report. Hypertension		Medium Metro | Other	–			
Respiratory										
Bravo et al. (2017)	708 U.S. Counties (Medicare)	ST	(2002-2006)	Respiratory HA/ED	Age > 65	>90% | 41-60% | <40% Urban Population	▲▲			
Strickland et al. (2015)	Georgia, U.S.	ST	(2002-2010)	Asthma/wheeze HA/ED	Age 2 -18	Large Metro | Med or Small Metro |	▲			
		ST		Upper Resp. Infect. HA/ED		Non-Metro	▲			
		ST		Bronchitis HA/ED			▼			

		ST		Otitis media HA/ED			▲			
		ST		Pneumonia HA/ED			▼			
		ST		Sinusitis HA/ED			▼			
Yap et al. (2013)	12 California Counties	ST	(2000-2005)	All Respiratory HA/ED	Children, Age 1 - 9	Los Angeles County, CA | Kern County, CA	▲▲			
		ST		Respiratory Infect. HA/ED			▲▲			
		ST		Pneumonia HA/ED			▲▲▲			
		ST		Asthma HA/ED			▲			
Reproductive										
Hu et al. (2015)	Florida		(2004-2005)	Gestational Diabetes	Trimester 1	Urban | Rural	▲▲			
				Gestational Diabetes	Trimester 2		▲▲			
				Gestational Diabetes	Full pregnancy		▲▲			
Stieb et al. (2015)	Canada		(1999-2008)	Preterm Birth	Full pregnancy	Urban Postal Codes | Rural Postal Codes	▼			
				Low Birth Weight	Full pregnancy		–			
				Small for Gestational Age	Full pregnancy		▲			
				Term Birth Weight	Full pregnancy		▲▲			

* RUCA = Rural-Urban Commuting Area Codes based on U.S. 2010 Census Data. 1 = Metropolitan Urban Core, 10 = Rural

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates.

Supplemental Table S12-14 Stratified analyses evaluating smoking and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Ref	Form. Smokers	Curr. Smokers	Ever Smokers
Mortality									
Lepeule et al. (2012)	LT	Multicity, US	(1974-2009)	Mortality - Total		▲			
Puett et al. (2009)	LT	Multicity, US	(1988-2002)	Mortality - Total		▲▲			
Thurston et al. (2016)	LT	Multicity, US	(2000-2008)	Mortality - Total		▲			
Beelen et al. (2014a)	LT	Multicity, Europe	(2008-2011)	Mortality - Total		▲			
Pinault et al. (2016)	LT	Multicity, Canada	(1998-2011)	Mortality - Total		▲▲			
Villeneuve et al. (2015)	LT	Multicity, Canada	(1998-2006)	Mortality - Total		▲			
Cardiovascular									
Lepeule et al. (2012)	LT	Multicity, US	(1974-2009)	Mortality - CVD		▲▲			
Thurston et al. (2016)	LT	Multicity, US	(2000-2008)	Mortality - CVD		▲▲			
Beelen et al. (2014a)	LT	Multicity, Europe	(2008-2011)	Mortality - CVD		–			
Puett et al. (2009)	LT	Multicity, US	(1988-2002)	Mortality - CVD		▲▲			
Puett et al. (2011)	LT	Multicity, US	(1988-2002)	Mortality - CVD		▲▲			
Pinault et al. (2016)	LT	Multicity, Canada	(1998-2011)	Mortality - CVD		▲▲			
Villeneuve et al. (2015)	LT	Multicity, Canada	(1998-2006)	Mortality - CVD		▲▲			
	LT			Mortality - IHD		▲▲			
Roux et al. (2008)	LT	Multicity, US	(2000-2002)	CVD-CIMT		▲▲			
	LT			CVD - Coronary Ca		▲▲			
	LT			CVD - Coronary Ca w/Ca		▼			
Hoffmann et al. (2009b)	LT	Multicity, Germany	(2000-2003)	CVD-PAD		▼			
Krishnan et al. (2012)	LT	Multicity, US	(2000-2002)	CVD-FMD		▼▼			
Johnson and Parker (2009)	LT	Multicity, US	(1999-2005)	CVD-hypertension		▲			
	LT			CVD-heart disease		▲			
Respiratory									

Study	Exp	Location	Time	Outcome	Notes	Ref	Form. Smokers	Curr. Smokers	Ever Smokers
Dimakopoulou et al. (2014)	LT	Multicity, Europe	(2008-2011)	Mortality – Respiratory		▲			
Thurston et al. (2016)	LT	Multicity, US	(2000-2008)	Mortality – Respiratory		▲▲			
Pinault et al. (2016)	LT	Multicity, Canada	(1998-2011)	Mortality – Resppiratory		▲▲			
Lepeule et al. (2012)	LT	Multicity, US	(1974-2009)	Mortality - Lung Cancer		▲			
Villeneuve et al. (2015)	LT	Multicity, Canada	(1998-2006)	Mortality - Lung Cancer		▼			
Lepeule et al. (2012)	LT	Multicity, US	(1974-2009)	Mortality - COPD		▼			
Metabolic									
Weinmayr et al. (2015)	LT	Multicity, Germany	(2000-2003)	Metabolic		▲			
Hansen et al. (2016)	LT	Multicity, Denmark	(1993-2012)	Diabetes		▲▲			
Liu et al. (2016a)	LT	Multicity, China	(2011-2012)	Diabetes		▲▲			
Reproductive									
Mahalingaiah et al. (2014)	LT	Multicity, US	(1993-2007)	Endometriosis		▲			
Fleisch et al. (2016)	LT	MA, US	(2003-2008)	Gestational Diabetes		▼			

CVD=cardiovascular disease; COPD=chronic obstructive pulmonary disease; PAD=peripheral artery disease; FMD=flow-mediated dilation; CIMT=carotid intima media thickness

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

Supplemental Table S12-15 Stratified analyses evaluating dietary patterns and PM2.5-related health effects.

Study	Exp	Location	Time	Outcome	Notes	Reference	Comparison Group 1	Comparison Group 2
Alcohol Use							No Use	Reg Use
Mortality								
Pinault et al. (2016)	LT	Canada, multicity	(2000-2011)	Non-accidental		▲▲		
				Circulatory		▲▲		
				Respiratory		▲		
Inflammation								
Ostro et al. (2014)	LT	6 US cities		CRP	Women, ages 42-52	▲▲		
Fruit/Vegetable or Fat Intake						Low Intake*	Medium Intake*	High Intake*
Mortality								
Pope et al. (2014)	LT	US (ACS CPS-II)	(1994-2004)	LT CVD Mortality	ref: Q1 vs. Q4 fruit/veg	▲▲		
Turner et al. (2011)	LT	Multi-city US	(1984-2008)	Lung Cancer	Age > 30	▲		
Pinault et al. (2016)	LT	Canada, multicity	(2000-2011)	Non-accidental		▲▲		
				Circulatory		▲		
				Respiratory		▲▲		
Beelen et al. (2014a)	LT	Europe (ESCAPE)	(1985-2007)	Non-accidental	Meta-analysis, 10 cohorts	▲		
				Circulatory	Meta-analysis, 10 cohorts	▲		
Dimakopoulou et al. (2014)	LT	Europe (ESCAPE)	(1985-2007)	Respiratory	Meta-analysis, 7 cohorts	▼		
B Vitamins							No B Vit.	B Vit. Use
Biomarkers								
Zhong et al. (2017a)	ST	Toronto, Canada	(2013-2014)	Change in SDNN	Age 19-49, post exposure	▲		
				Change in LF/HF	Age 19-49, post exposure	▲		
				Change in WBC	Age 19-49, post exposure	▲		
Zhong et al. (2017b)	ST	Toronto, Canada	(2013-2014)	Mitochondrial DNA Copy Number	Age 19-49, 24 hours later	▲▲		
Fish Oil								
Biomarkers							Olive Oil	Fish Oil
Tong et al. (2012)	ST	Chapel Hill. NC	(2 hr CAPs)	nLF HRV	Age 50-72, next morning	▲▲		
				QTp	Age 50-72, next morning	▲▲		

Study	Exp	Location	Time	Outcome	Notes	Reference	Comparison Group 1	Comparison Group 2
				Triglycerides	Age 50-72, next morning	▲		
							Fish Oil	Olive Oil
Tong et al. (2015)	ST	Chapel Hill. NC	(2 hr CAPs)	FMD	Age 50-72, post exposure	▼		
				tPA	Age 50-72, post exposure	▲		
				Endothelin-1	Age 50-72, next morning	▲▲		

***Intake is either fruit or fruit/vegetable. Low Intake = <150g/day or <5 servings/day. Medium Intake = 150-300 g/day. High Intake = >=300 g/day or >= 5 servings/day; CHD=coronary heart disease; FMD=flow-mediated dilation; STEMI=ST-elevation myocardial infarction; CIMD=carotid media intima thickness; CRP=C-reactive protein; PAD=peripheral artery disease**

Heatmap legend:

Reference group (no pre-existing cardiovascular disease) Positive association with PM2.5, CI does not overlap null, Positive association with PM2.5, CI overlaps the null; Null association; Negative association with PM2.5, CI overlaps the null; Negative associations with PM2.5, CI does not overlap the null.

At-risk group examined (pre-existing cardiovascular disease, indicated in the notes column): Stronger association than reference group, no overlap in CIs; Stronger association than reference group, overlapping CIs; Stronger association than reference group, CIs overlap with central estimates; Weaker association than reference group, no overlap in CIs; Weaker association than reference group, overlapping CIs; Weaker association than reference group, CIs overlap with central estimates

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