Impact of Air Pollutant Exposures and Social Connectedness on Cognitive Function and Mood Disorders

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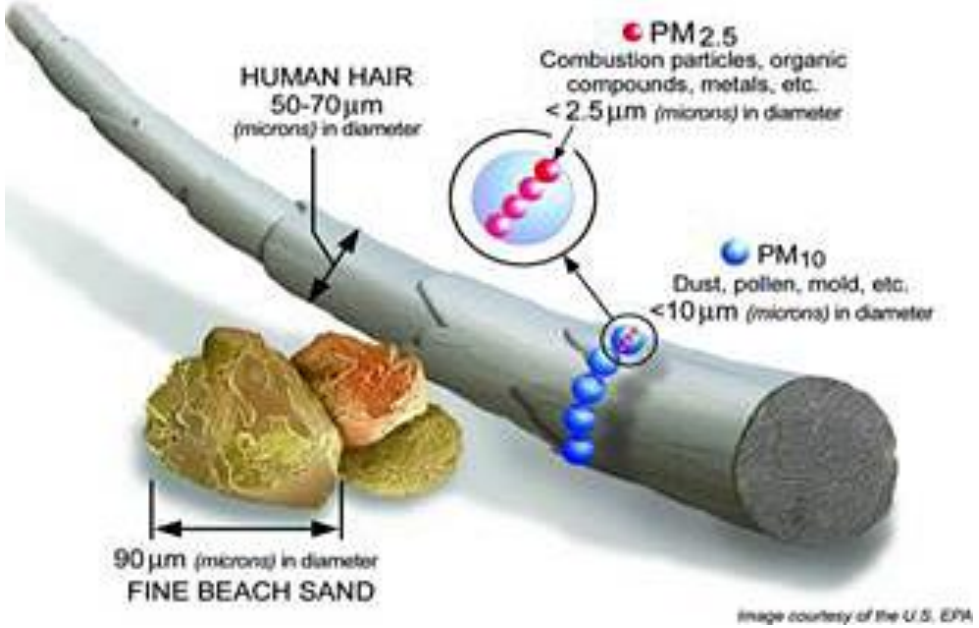
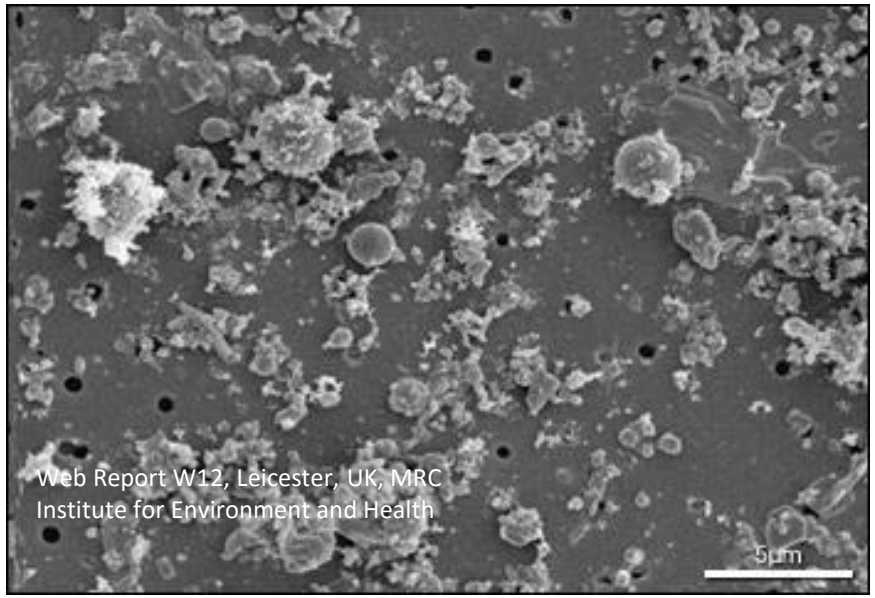
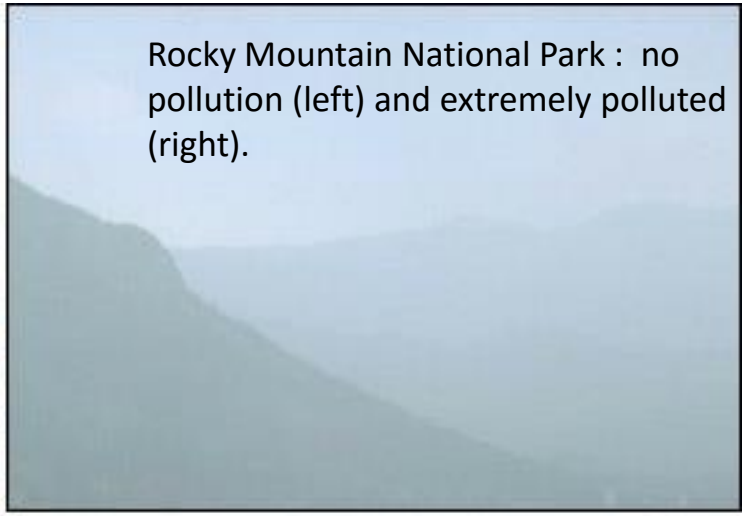
Fine Particulate Matter or $PM_{2.5}$





220 km visibility



Rocky Mountain National Park : no pollution (left) and extremely polluted (right).

20 km visibility

Early Severe Air Pollution Episodes

1930: Meuse River Valley, Belgium

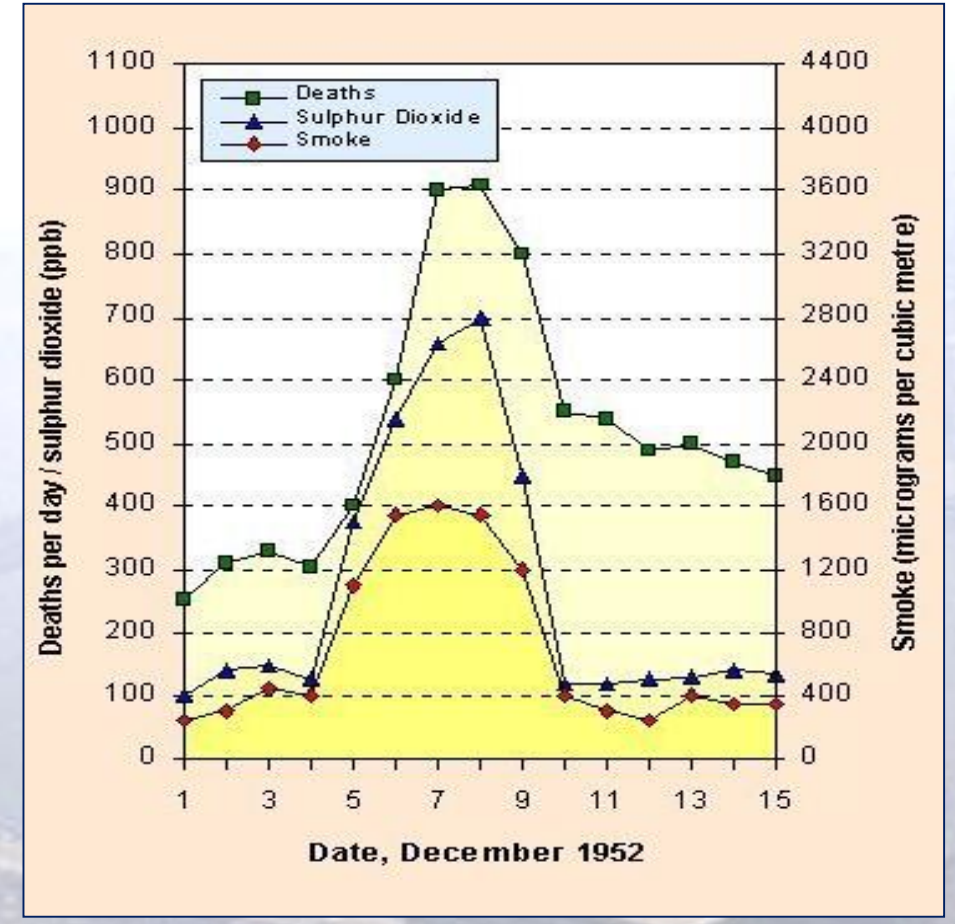
- Cold, damp weather
- Main sources: zinc smelter, H_2SO_4 factory, glass manufacturers
- 60 deaths recorded

1948: Donora, Pennsylvania

- Cold weather
- Main sources: iron, steel plants, zinc smelting, acid plant
- 20 deaths observed

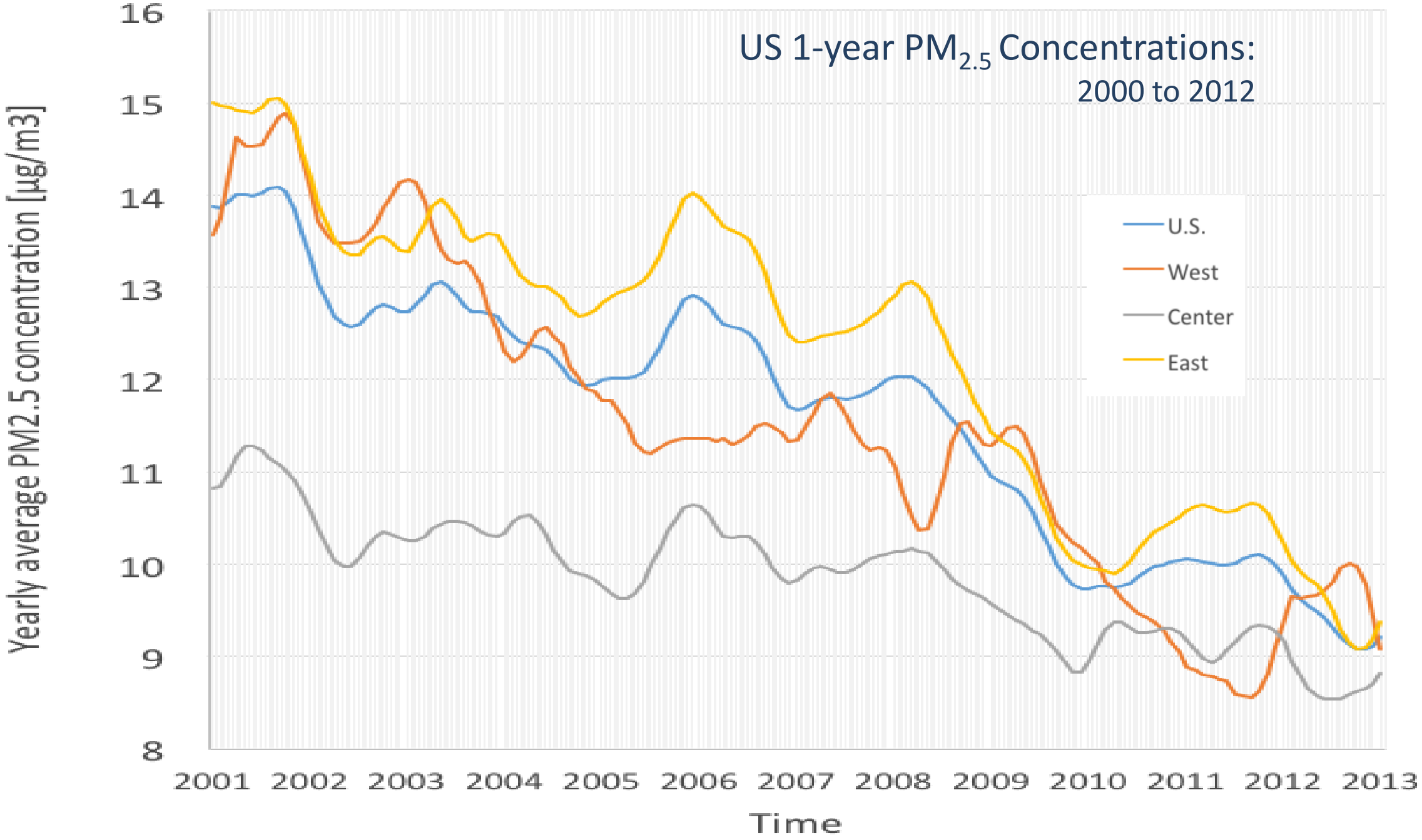
1952: London

- Killer fog (right)
- Main source: domestic coal burning
- 4,500 excess deaths during December week

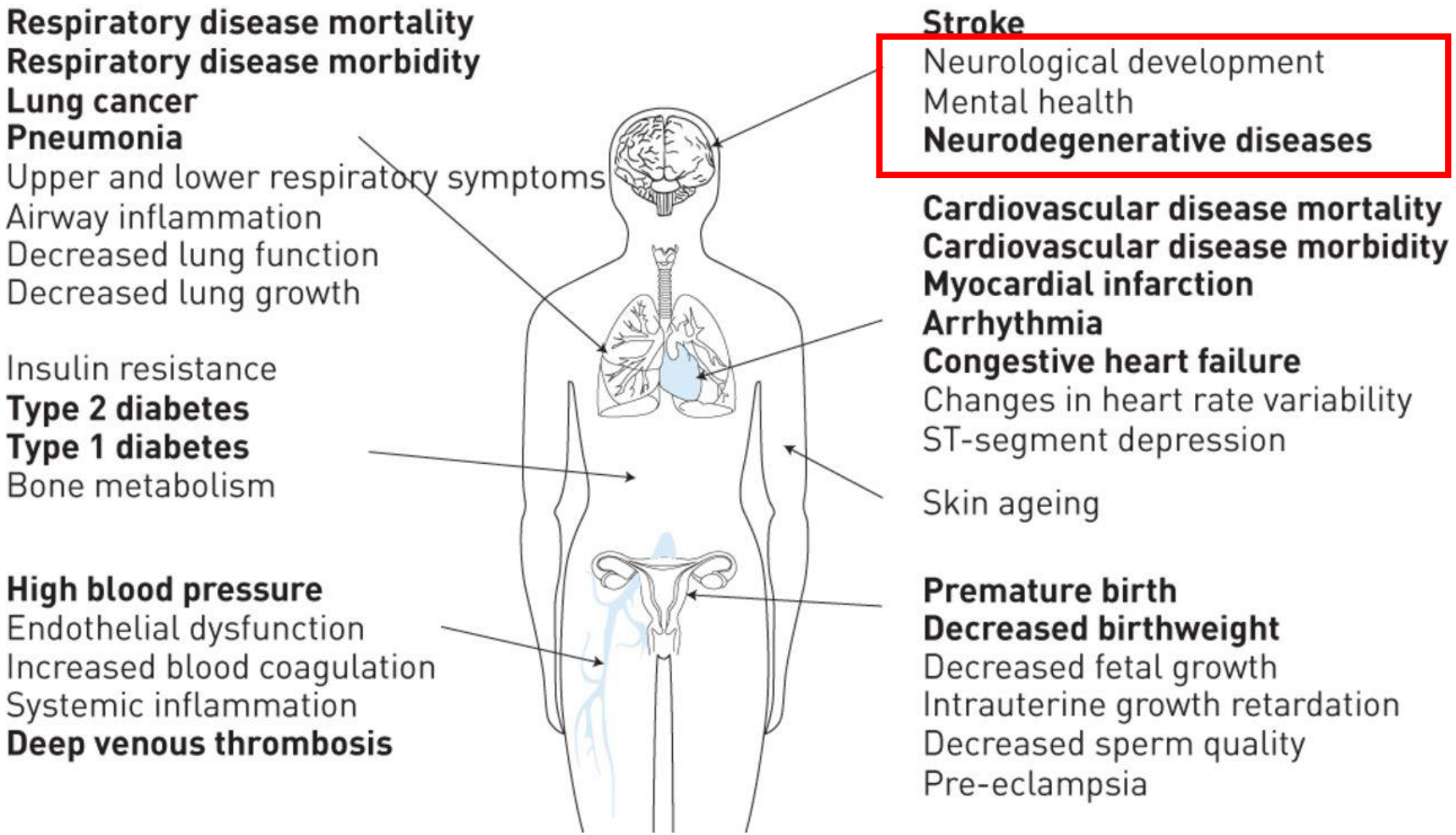


The Great London Smog (1952)

Source: http://www.portfolio.mvm.ed.ac.uk/studentwebs/session4/27/greatsmog52.htm


US 1-year PM2.5 Concentrations:
2000 to 2012
Yearly average PM2.5 concentration [µg/m3]
16
15
14
13
12
11
10
9
8
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Time
U.S.
West
Center
East

Overview of diseases, conditions and biomarkers affected by outdoor air pollution



Am. Thoracic/Eur. Respiratory Society assessment of established and emerging air pollution adverse effects. Outcomes in bold are included in GBD estimates of health effects of air pollution. George D. Thurston et al. Eur Respir J 2017;49:1600419

Study Rationale

- By 2050, US will have approx. 84 million adults over 65 years, more than double the current population
- Older adults disproportionately affected by chronic diseases such as cognitive decline and mood disorders
  - 5.3 million older adults have Alzheimer's disease; 13.2 million by 2050 (http://www.alz.org/facts/)
  - 15-20% of US elderly have experienced depression, 11% anxiety (http://www.apa.org/about/gr/issues/aging/mental-health.aspx)
  - Cognitive disorders: $1.1 trillion in 2050
  - Mood disorders: 140+ million disability-adjusted life years worldwide in 2010

Study Rationale

- Air pollution shown to be important risk factor for cognitive decline; less evidence for mood disorders
  - $PM_{2.5}$ linked to memory deficits, cognitive decline, more cognitive errors, lower verbal scores
  - May occur via oxidative stress, inflammation, cerebrovascular damage, neurodegeneration
- Older individuals may be more susceptible to environmental hazards, possibly due to combined effects of
  - Lack of social connection and poor physical health
  - Higher air pollution exposures

➢ Significant questions remain regarding possible mediating pathways and combined impacts of social connectedness, health and pollution

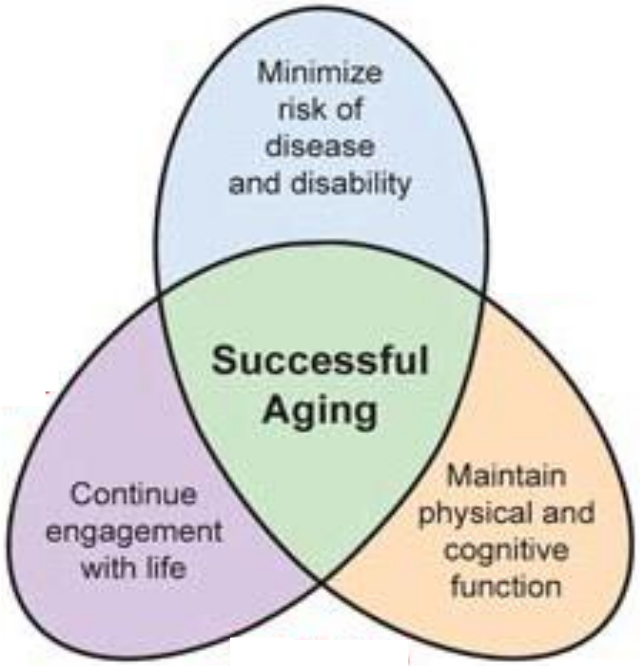
Study Objective

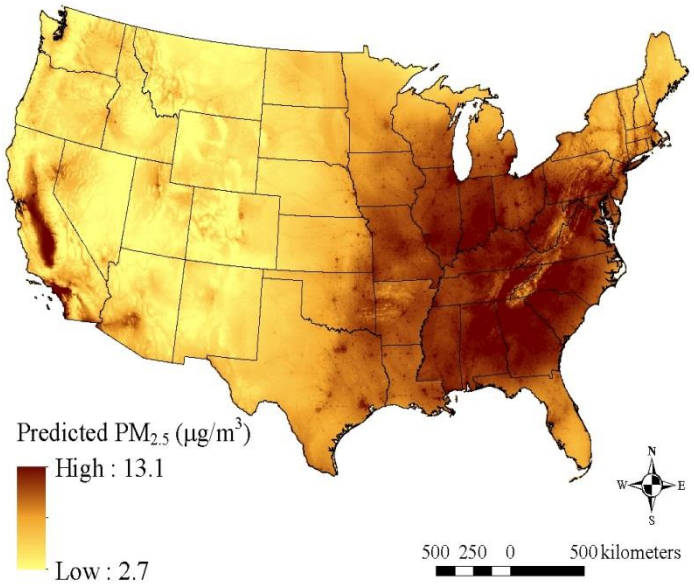
To examine the impact of air pollution and lifestyle on cognitive function and mood disorders in a nationally representative sample of community dwelling older Americans

- Is exposure to air pollution associated with decreased cognitive function and increased mood disorders?
- Do physical and emotional health modify the relationship between air pollution and cognitive function and mood disorders?
- Does air pollution impact cognition through emotional health pathways?

Air Pollution, Lifestyle and Health in NSHAPs

- **Participants**: 4,119 nationally representative sample of community-dwelling older Americans (57-95 yrs)
- **Data Collection**: 2 waves (2004-5, 2010-11)
- **Measures**:
  - *Mental*: cognitive function
  - *Emotional* : stress, depression, anxiety
  - Social: Loneliness, social connectedness
  - *Functional*: mobility
  - *Physical*: blood pressure, CRP, HbA1c, pre-existing disease

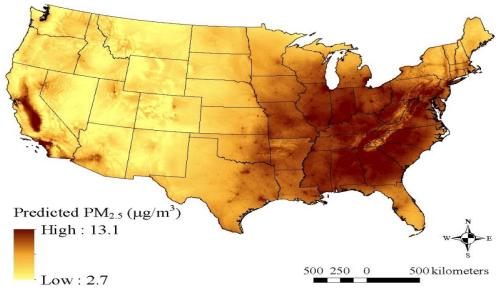




Outcome Measures

- **Cognitive Function** using Chicago Cognitive Function Measure: measures 8 cognitive domains on a 20-point scale
- **Depression** using Center for Epidemiological Studies Depression Scale: widely used to assess self-reported depression in older persons
  - Participants reported frequency in past week of having poor appetite, restless sleep, feeling of depression, that everything was an effort; feeling happy, lonely, sad, that people were unfriendly; enjoying life; people disliked me, could not get "going"
  - *Moderate-to-severe* depressive symptoms: ≥9 out of 33
- **Anxiety** using Hospital Anxiety and Depression Scale – Anxiety: widely used to detect state of generalized anxiety
  - Participants reported frequency in past week of feeling tense, having worrying thoughts, getting a frightened feeling like butterflies in stomach, getting frightened feeling as if something awful was about to happen, having sudden feeling of panic, feeling relaxed, feeling restless
  - *Moderate-to-severe* anxiety symptoms: ≥8 out of 21

Participant-Specific Exposure Measures



- **Air pollution**: $PM_{2.5}$, NO_2 exposures
  - Estimated at each participant's home using GIS-based spatio-temporal models
  - Accounted for residential moves

- **Roadway Distance**: U.S. Census Feature Class A1-A3
  - Calculated distance from each participant's home to the nearest segment
  - Created categorical (0–49, 50–199, ≥200 meters) distance measure

- **Urbanicity**: percent of urban land use (US Census)
  - Calculated within 1 km of each NSHAP participant home
  - Create categorical (<75, ≥75 percentile) urbanicity measure

Key Covariates

- **Demographic**: Age, gender, race
- **SES**: Individual educational attainment, family income, census-level median household income, percent of population below poverty level
- **Health History**: BMI, diabetes, hypertension, stroke, heart failure, emphysema, COPD, asthma, blood pressure, CRP, HbA1c
- **Behaviors**: Alcohol consumption, current smoking status
- **Physical Health**: Physical activity (e.g., frequency of walking, physical exercise, etc.); physical function (difficulty performing daily living activities (e.g., walking one block and across a room, using the toilet))
- **Social**: loneliness (revised 9-point UCLA Loneliness Scale), social connectedness (self-reported frequency of socializing with friends or relatives past year)

Statistical Analysis

Examine association of:

- Air pollution ($PM_{2.5}$ and NO_2) and cognitive function
- Air pollution ($PM_{2.5}$ and NO_2) and mood disorders
- Living near roadway and mood disorders
- Urbanicity of residence and mood disorders

Using linear mixed models, accounting as necessary for repeated measurements of participants and households

- ➢ Examine whether risks differ by participant characteristics
- ➢ Investigate whether associations occur via environmental emotional (e.g., loneliness, social connectedness), and physical (e.g., physical activity) pathways

NSHAP Participant Characteristics

Characteristic	Study population*	
	Wave 1	Wave 2
No. of participants	3,005	3,377
Age (year, mean ± SD[a])	69.3 ± 7.8	72.4 ± 8.1
Male (%)	48.4	45.5
Race (%)		
White	70.5	71.5
Black	17.0	15.4
Hispanic non-black	10.2	10.9
BMI (kg/m^2, mean ± SD)	29.1 ± 6.1	29.3 ± 6.1
Obesity (% ≥30 BMI)	35.1	36.7
Current smoking (%)	14.8	13.3
Physical activity (%)		
3+ times per week	61.4	40.9
1-2 times per week	15.4	15.5
1-3 times per month	6.3	8.7
<1 time per month	6.4	9.3
Never	10.4	25.6
Hypertension (%)	57.3	61.6
Diabetes (%)	21.4	23.8
Antidepressant use (%)	12.5	15.2

Characteristic	Study population*	
	Wave 1	Wave 2
Socioeconomic status		
Education attainment (%)		
College degree or greater	21.9	24.5
High school or vocational school	54.9	56.4
< high school	23.3	19.1
Family income ($ in thousands, mean ± SD)	51.3 ± 64.4	59.3 ± 74.2
Median census household income[1] ($thousands)	52.7 ± 25.1	56.4 ± 27.3
Census population w/income <poverty level[1] (%)	15.3	14.4
Loneliness score (mean ± SD)	4.0 ± 1.4	3.1 ± 2.3
Feeling lonely (%)	26.2	23.4
Social support (frequency of socializing) (%)		
Never or less than once a year	2.4	3.0
Several times a year	18.6	20.3
Once a month	32.0	30.6
Every week	33.4	32.0
Several times a week	13.6	14.1
Having difficulty with **get-up-and-go** (%)	22.4	21.1
Moderate-to-severe depression (number, %)[2]	730 (24.3)	703 (20.8)
Moderate-to-severe anxiety (number, %)[3]	378 (13.5)	605 (21.3)
$PM_{2.5}$ annual concentration (μg/m^3, mean ± SD)	11.1 ± 3.0	8.8 ± 2.3

* 2,261 participants were in both wave 1 and wave 2; [1] US Census Bureau (2010). [2] Assessed using Center for Epidemiological Studies – Depression; [d] Assessed using Hospital Anxiety and Depression Scale – anxiety (HADS-A) subscale

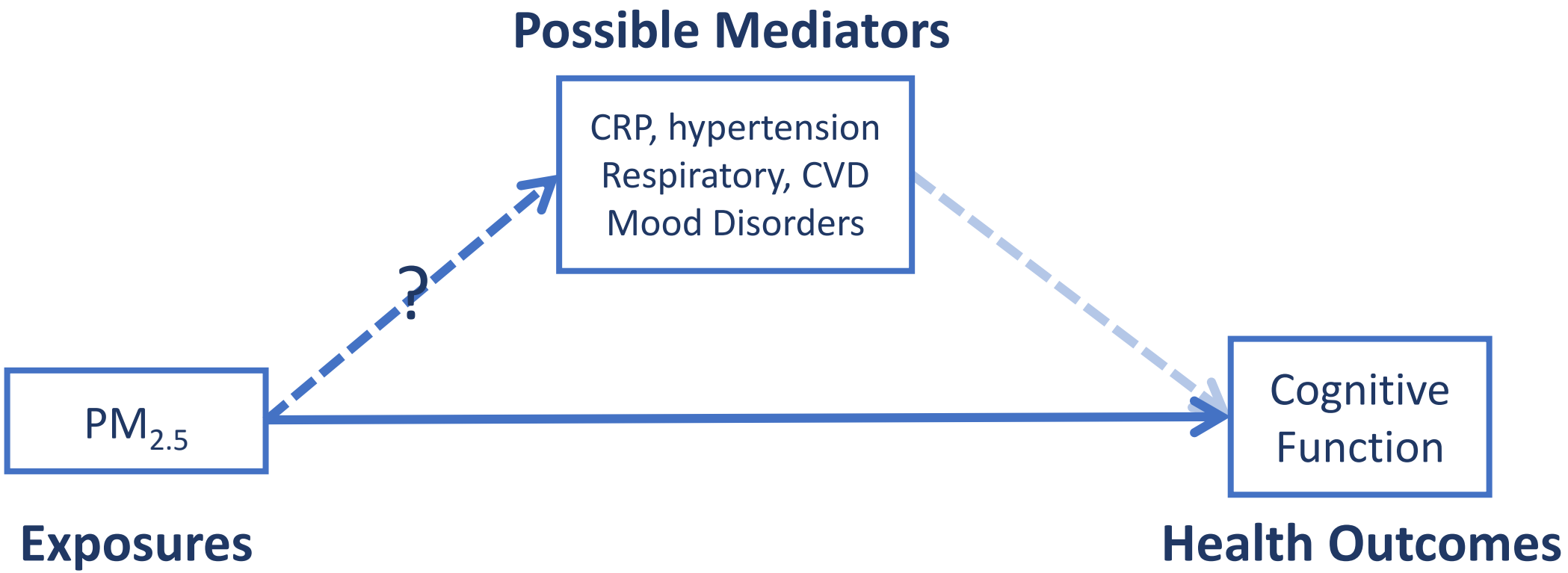
Change in CCFM Score per IQR Increase in Ambient Air Pollutants over 1-6 year Moving Average Exposures[a]

Moving Average	$PM_{2.5}$		NO_2	
	Base	Fully Adjusted [f]	Base[e]	Fully Adjusted[f]
1 year	-0.27 (-0.47, -0.07)*	-0.22 (-0.44, -0.01)*	-0.06 (-0.24, 0.12)	-0.13 (-0.34, 0.08)
2 years	-0.23 (-0.43,-0.04)*	-0.22 (-0.42, -0.01)*	-0.13 (-0.29, 0.04)	-0.26 (-0.45, -0.06)*
3 years	-0.21 (-0.40, -0.03)*	-0.21 (-0.40, -0.02)*	-0.13 (-0.30, 0.03)	-0.27 (-0.46, -0.07)*
4 years	-0.23 (-0.41, -0.05)*	-0.22 (-0.40, -0.04)*	-0.14 (-0.31, 0.02)	-0.29 (-0.48, -0.09)*
5 years	-0.25 (-0.43, -0.07)*	-0.23 (-0.42, -0.05)*	-0.17 (-0.34, -0.01)*	-0.32 (-0.52, -0.12)*

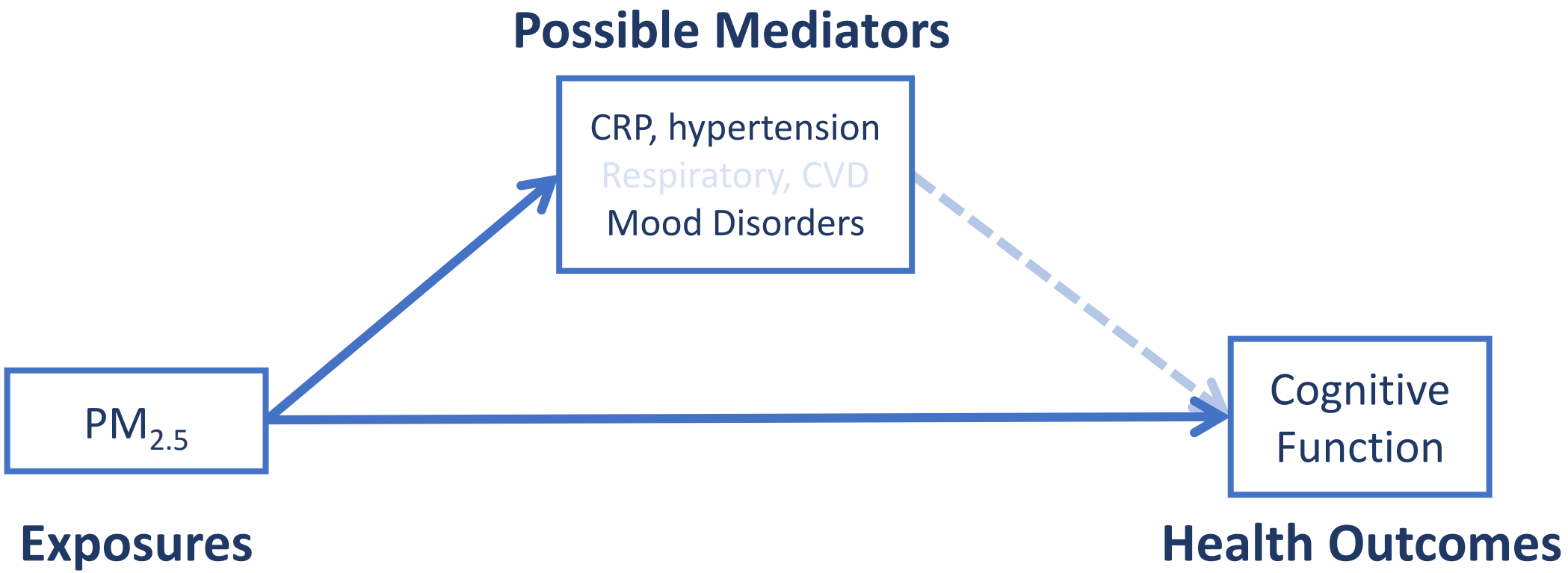
- An IQR increase in $PM_{2.5}$ is associated with a decrease in cognitive function equal to aging 1.6 years.

Contains participants in Wave 2 who completed CCFM cognitive test; [b] $PM_{2.5}$ 1-7yr IQR=4.25, 4.03, 3.93, 3.99, 4.10, 4.18, 4.33 ug/m^3, respectively; [c] NO_2 1-7yr IQR=8.37, 6.66, 6.68 6.90, 6.99, 7.28, 7.42 ppb, respectively; [e] Base model adjusts for gender, age, race/ethnicity, education; [f] Fully adjusted model additionally adjusts for season, smoking, region, median census tract household income; * $p<0.05$

Possible Pathways



Possible Pathways

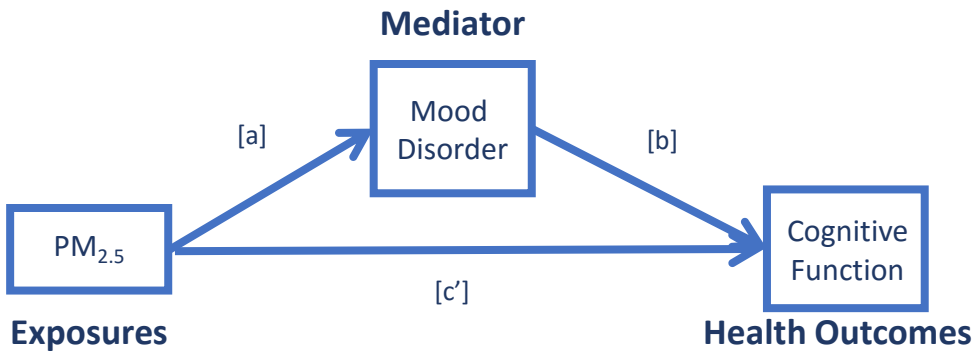


ORs (95% CIs) for mental illness per 5 μg/m^3 increment in $PM_{2.5}$: over various moving averages.

$PM_{2.5}$ moving averages	Depression: CESD-11 ≥ 9 vs < 9		Anxiety: HADS-A ≥ 8 vs < 8	
	Basic[1]	Multivariable adjusted[2]	Basic[1]	Multivariable adjusted[2]
7-days	1.09 (1.01, 1.17)*	1.08 (1.00, 1.16)**	1.14 (1.05, 1.24)*	1.14 (1.05, 1.24)*
30-days	1.20 (1.08, 1.33)*	1.16 (1.05, 1.29)*	1.34 (1.19, 1.50)*	1.31 (1.20, 1.51)*
180-days	1.10 (0.94, 1.28)	1.04 (0.89, 1.22)	1.55 (1.31, 1.85)*	1.61 (1.35, 1.92)*
365-days	1.10 (0.93, 1.31)	1.06 (0.89, 1.27)	1.33 (1.10, 1.61)*	1.39 (1.15, 1.69)*
4-years	1.17 (1.00, 1.38)**	1.14 (0.97, 1.34)	1.29 (1.08, 1.54)*	1.34 (1.12, 1.61)*

[1] Basic models adjust for age, gender, race/ethnicity, year, season, day of week, region, MSA.
[2] Multivariable models adjusted for age, gender, race/ethnicity, year, season, day of week, region, MSA, education attainment and family income of the participants, median household income, percentage of population below poverty level in the census tract of residence.
* P<0.05; ** P<0.10.

Mediation of $PM_{2.5}$-Cognition Association



Analysis Step[1]	Effect Estimates for Mediators		
	Depression	Anxiety	Stress
[a] $PM_{2.5}$ → Mediators[2]	0.42 (0.16, 0.68)	0.02 (-0.21, 0.25)	-0.04 (-0.21, 0.14)
[b] Mediator → CCFM[3]	-0.09 (-0.11, -0.06)	-0.12 (-0.16, -0.08)	-0.21 (-0.27, -0.15)
[c'] $PM_{2.5}$ → CCFM[4]	-0.16 (-0.42, 0.10)**	-0.13 (-0.40, 0.13)	-0.11 (-0.37, 0.16)

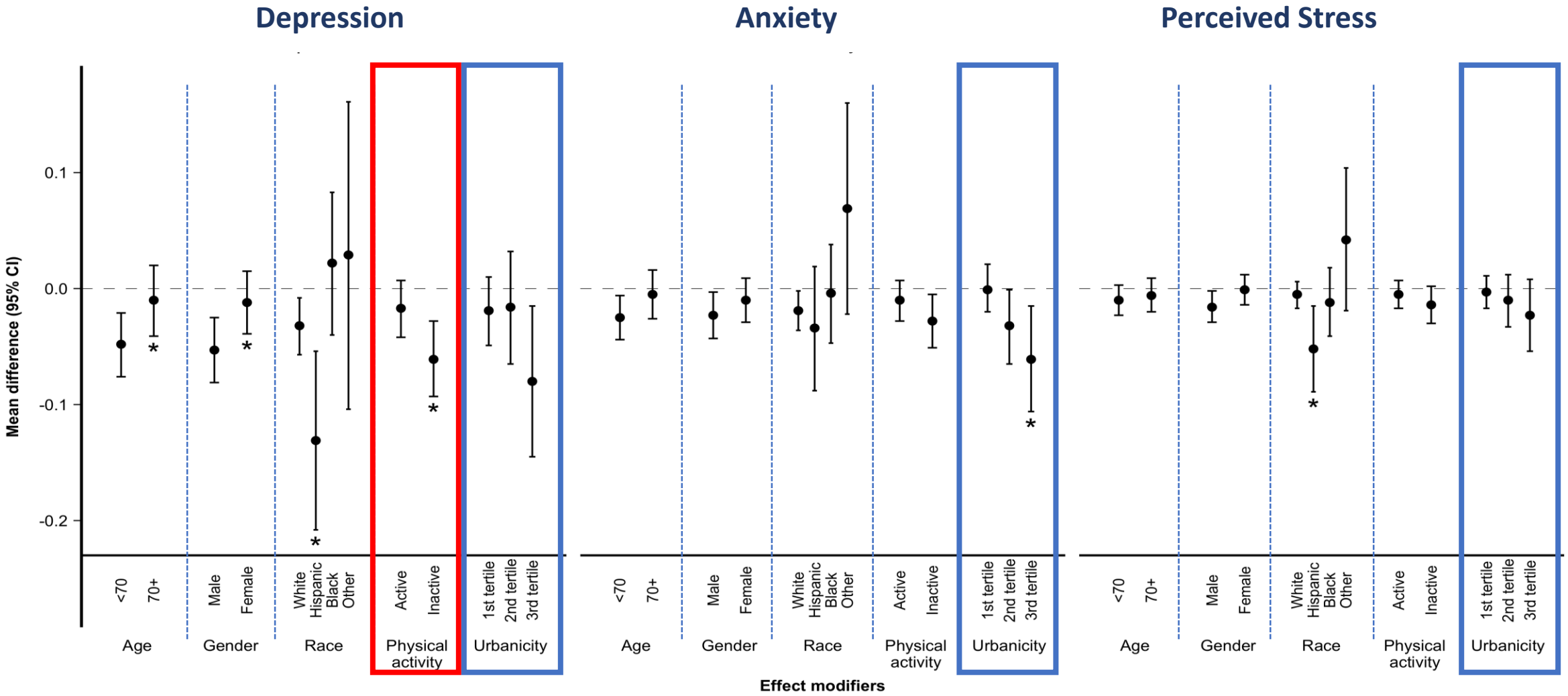
[1] Contains participants in Waves 1 and 2 who completed CCFM and SPMSQ cognitive tests and had mediator data; models adjusted for race/ethnicity, gender, education, age, season, smoking, region, median household income of census tract
[2] Mediator test run on mediators in Wave 2, controlling for mediators in Wave 1, results per IQR increase in 1 year moving average $PM_{2.5}$ from Wave 1
[3] Test run between mediator in Wave 1 and CCFM outcome in Wave 2, controlling for SPMSQ results in Wave 1
[4] Results per IQR increase in 1 year moving average $PM_{2.5}$ in Wave 2, controlling for SPMSQ results in Wave 1
** $p<0.05$ for Sobel test.

Difference (95% CI) in Depression, Anxiety, Perceived Stress per 50 m Increment in Roadway Distance

Roadway Distance	Mental health condition		
	Depression	Anxiety	Perceived stress
Base model [a]	−0.033 (−0.055, −0.010)**	−0.017 (−0.032, −0.002)**	−0.009 (−0.019, 0.001)*
Multivariable model [b]	−0.030 (−0.052, −0.008)**	−0.016 (−0.031, −0.001)**	−0.007 (−0.018, 0.003)
Indirect effect via [c]			
Loneliness	**40.7%**	**42.2%**	–
Social support	3.5%	3.0%	–
Physical activity	2.1%	1.3%	–
Get-up-and-go	4.4%	2.3%	–
Respiratory illnesses	3.1%	2.2%	–
$PM_{2.5}$	**5.5%**	**8.7%**	–
NO_2 [d]	**5.8%**	**9.3%**	–
Temperature	3.4%	−2.1%	–

[a] Base models adjusted for age, sex, race/ethnicity, year, season, day of week, MSA and region. [b] Multivariable Model 1 adjusted for age, sex, race/ethnicity, year, season, day of week, MSA, region, education attainment, family income of the participants, median household income. [c] Mediation analysis was performed for statistically significant associations in multivariable models. Bold text refers to statistically significant percent of mediation using Sobel test ($p_{indirect}<0.05$). [d] Restricted to subset of NSHAP participants that resided within 90 kilometers from a U.S. EPA ambient monitor that measured NO_2 concentrations. * P<0.10; ** P<0.05

Effect Modification in Mental Health and Roadway Distance



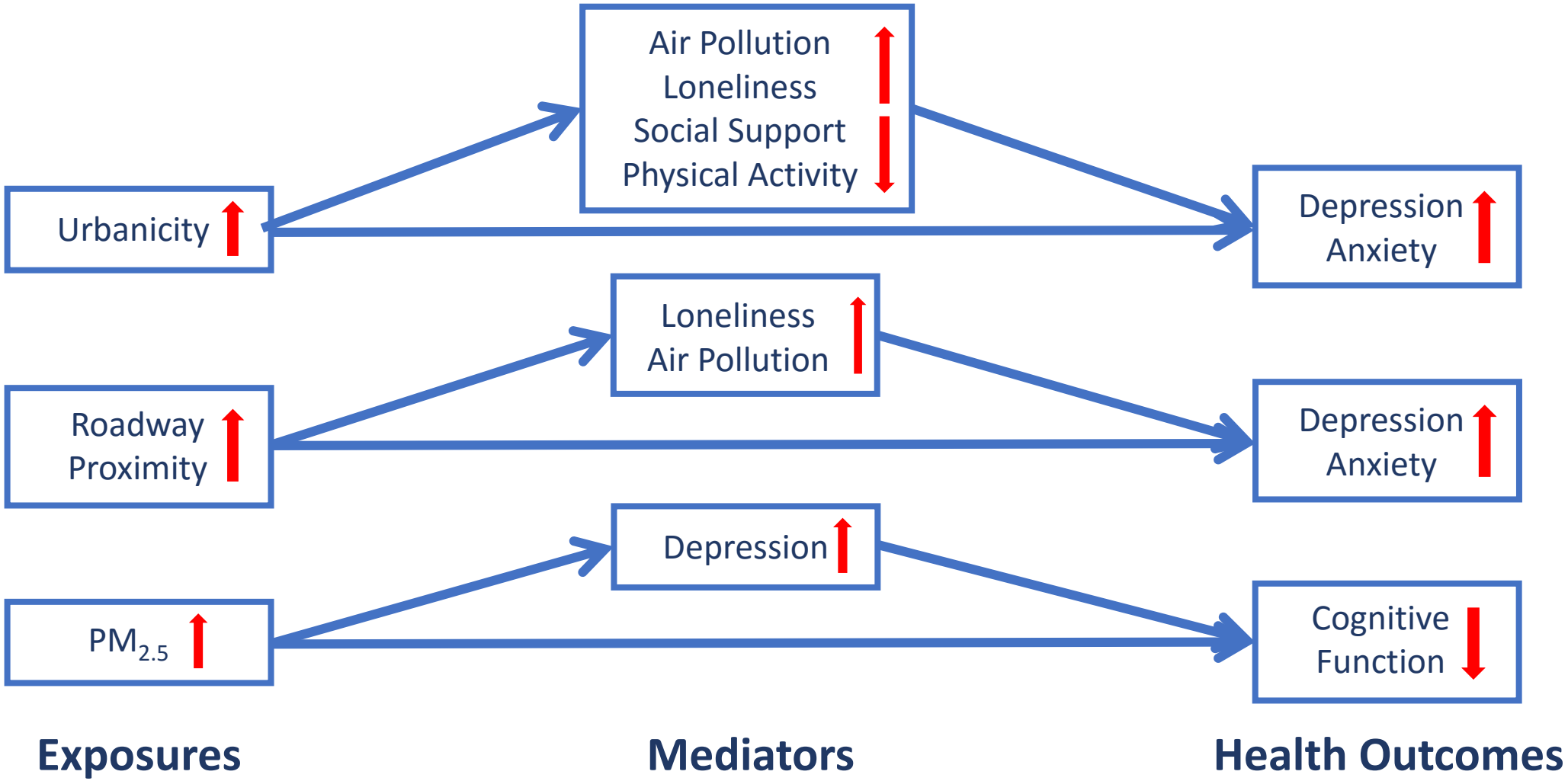
Outcomes log-transformed; results from multi-variate models per 50 m increment in roadway distance

Difference (95% CI) in Depression, Anxiety and Perceived Stress Symptoms per IQR (57%) increment in Urbanicity

Urbanicity	Mental health condition		
	Depression	Anxiety	Perceived stress
Base model [a]	0.370 (0.078, 0.663)**	0.140 (−0.056, 0.337)	0.133 (−0.002, 0.267)*
Multivariable model [b]	0.288 (0.101, 0.574)**	0.117 (−0.079, 0.246)	0.098 (−0.035, 0.232)
Indirect effect via [c]			
Loneliness	**67.0%**	–	–
Social support	**15.9%**	–	–
Physical activity	**22.6%**	–	–
Get-up-and-go	−6,1%	–	–
Respiratory illnesses	−5.0%	–	–
$PM_{2.5}$	**29.4%**	–	–
NO_2 [d]	**26.9%**	–	–
Temperature	8.8%	–	–

[a] Base models adjusted for age, sex, race/ethnicity, year, season, day of week, MSA and region. [b] Multivariable Model 1 adjusted for age, sex, race/ethnicity, year, season, day of week, MSA, region, education attainment, family income of the participants, median household income. [c] Mediation analysis was performed for statistically significant associations in multivariable models. Bold text refers to statistically significant percent of mediation using Sobel test ($p_{indirect}$<0.05). [d] Restricted to subset of NSHAP participants that resided within 90 kilometers from a U.S. EPA ambient monitor that measured NO_2 concentrations. * P<0.10; ** P<0.05

Mediation: Summary



Summary

- $PM_{2.5}$ significantly associated with decreased cognitive function, increased anxiety and to a lesser extent depression
  - $PM_{2.5}$ impacts on cognitive function may occur in part through impact on depression
  - Magnitude of $PM_{2.5}$-mental health association larger in individuals with less education, living in poorer areas, in poorer health
- Roadway proximity and urbanicity significantly associated with increased anxiety and depression, but not perceived stress
  - Associations partially mediated through $PM_{2.5}$, loneliness, and physical activity
  - Associations were greatest among individuals who were physically inactive

➢ Consistent with evidence that individuals may be more vulnerable due to joint lack of social support, poorer physical health, greater air pollution exposure

➢ Further research is needed to examine their combined impacts

Acknowledgements

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