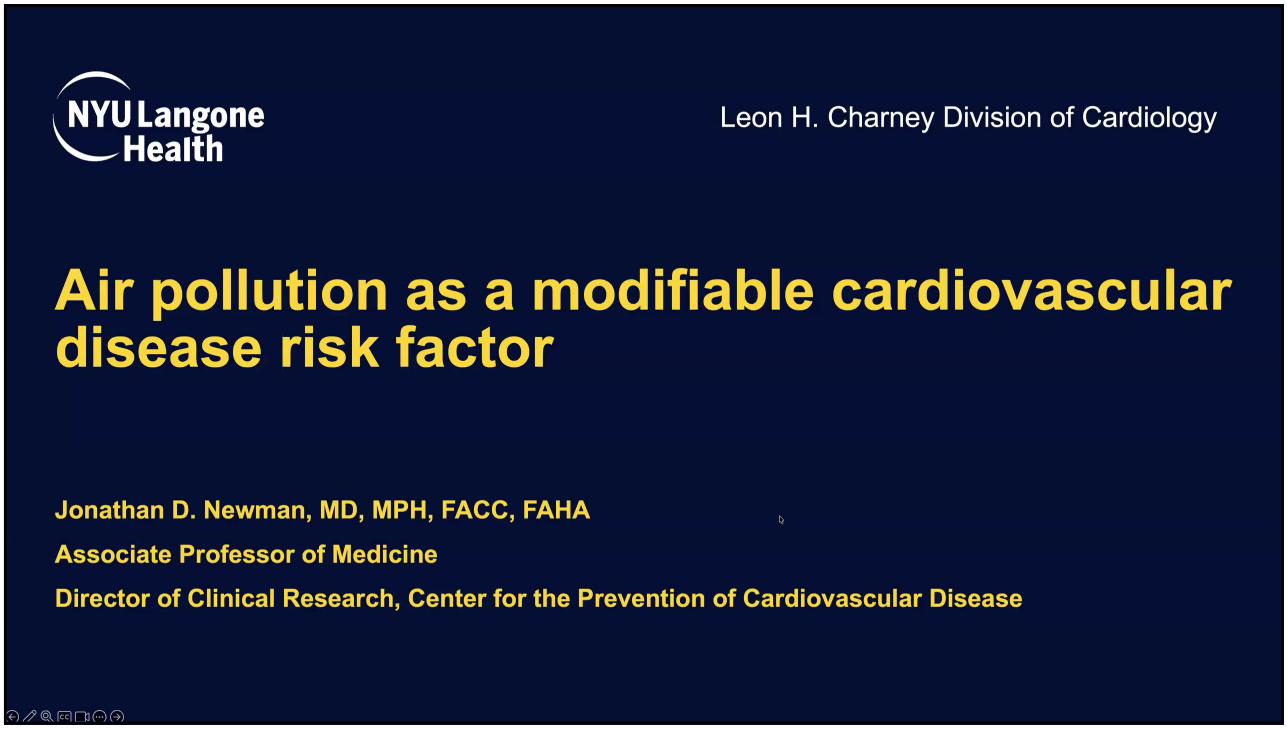

Minneapolis Heart Institute Foundation
GRAND ROUNDS

1


NYU Langone Health
Leon H. Charney Division of Cardiology
Air pollution as a modifiable cardiovascular disease risk factor
Jonathan D. Newman, MD, MPH, FACC, FAHA
Associate Professor of Medicine
Director of Clinical Research, Center for the Prevention of Cardiovascular Disease

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Disclosures

Jonathan D. Newman, MD, MPH, FAHA, FACC

Financial Disclosure: Grant support from the NIH: NHLBI/NIEHS/NCCIH, American Heart Association, Doris Duke Charitable Foundation

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Overview

- Recent data and conceptual models
  - Twin epidemics and feedback loops
- Preventive strategies
  - Personal strategies
  - Public policies
- Ongoing studies
- Lessons learned (and learning)

3

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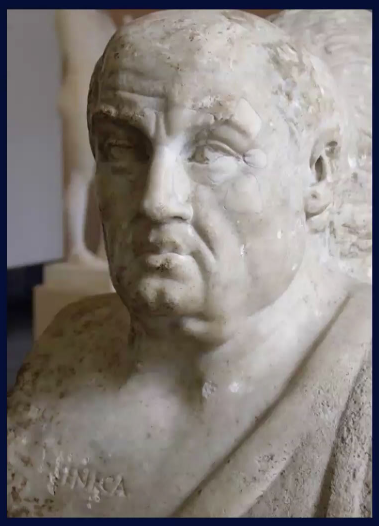
Gravioris Caeli (Air Pollution) in Ancient Rome



- ***Gravioris caeli*** (heavy heaven):

  "Who indeed could breathe his last for long?"
- ***Infamis aer*** (infamous air)
- *"…heavy air of Rome…the stench of its smoky chimneys, which…poured forth…soot they held enclosed, I felt a change in my disposition"*

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King Edward I (1272) "Malleus Scotorum"

"Whosoever shall be found guilty of burning coal shall suffer the loss of his head"

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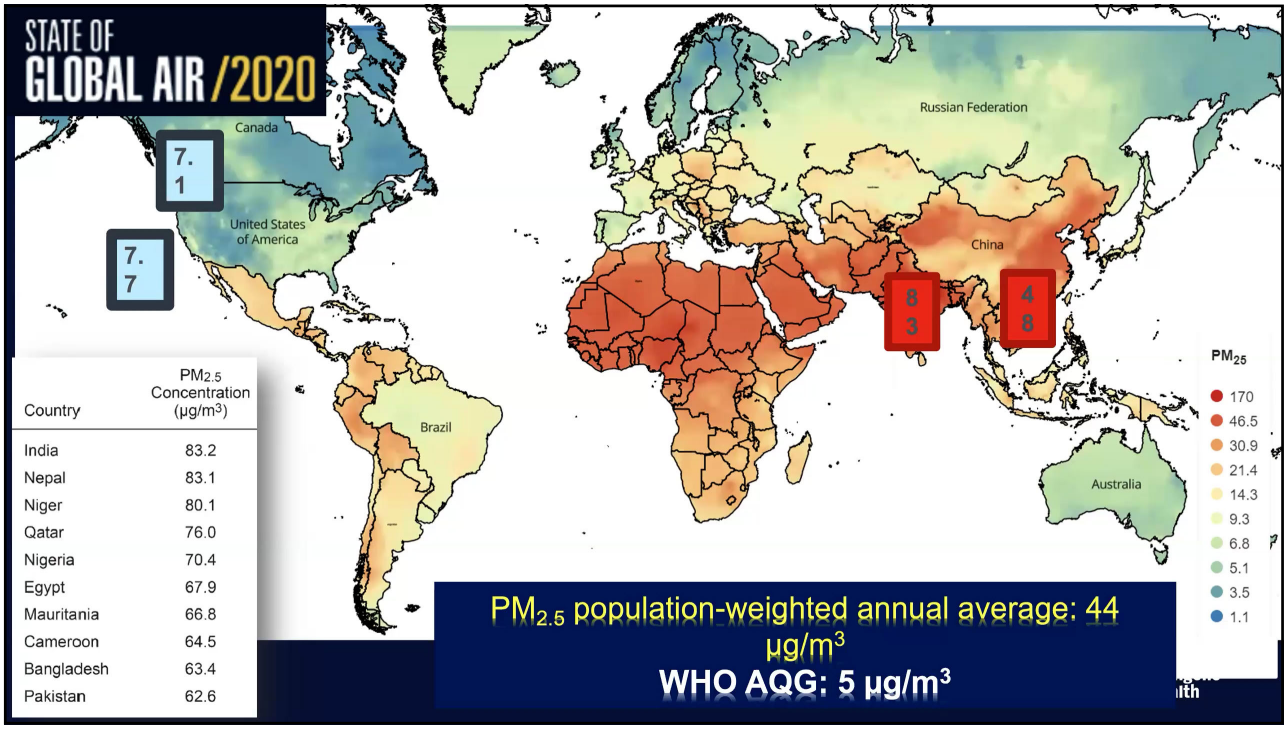
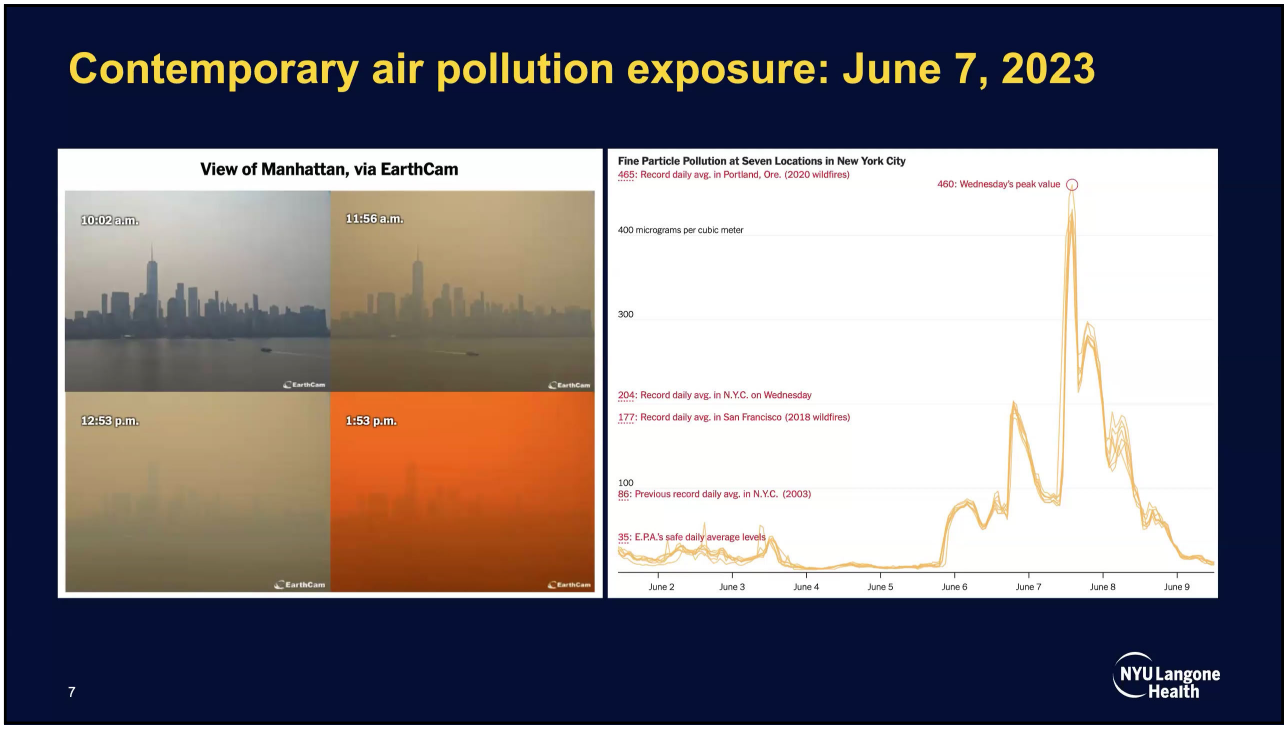

STATE OF
GLOBAL AIR /2020
Canada
7.1
United States of America
7.7
Russian Federation
China
83
48
Brazil
Australia
PM25
170
46.5
30.9
21.4
14.3
9.3
6.8
5.1
3.5
1.1
Country
PM2.5 Concentration (µg/m3)
India 83.2
Nepal 83.1
Niger 80.1
Qatar 76.0
Nigeria 70.4
Egypt 67.9
Mauritania 66.8
Cameroon 64.5
Bangladesh 63.4
Pakistan 62.6
PM2.5 population-weighted annual average: 44 µg/m3
WHO AQG: 5 µg/m3

7


Contemporary air pollution exposure: June 7, 2023
View of Manhattan, via EarthCam
10:02 a.m.
11:56 a.m.
12:53 p.m.
1:53 p.m.
Fine Particle Pollution at Seven Locations in New York City
465: Record daily avg. in Portland, Ore. (2020 wildfires)
460: Wednesday's peak value
400 micrograms per cubic meter
300
204: Record daily avg. in N.Y.C. on Wednesday
177: Record daily avg. in San Francisco (2018 wildfires)
100
86: Previous record daily avg. in N.Y.C. (2003)
35: E.P.A.'s safe daily average levels
June 2
June 3
June 4
June 5
June 6
June 7
June 8
June 9
7
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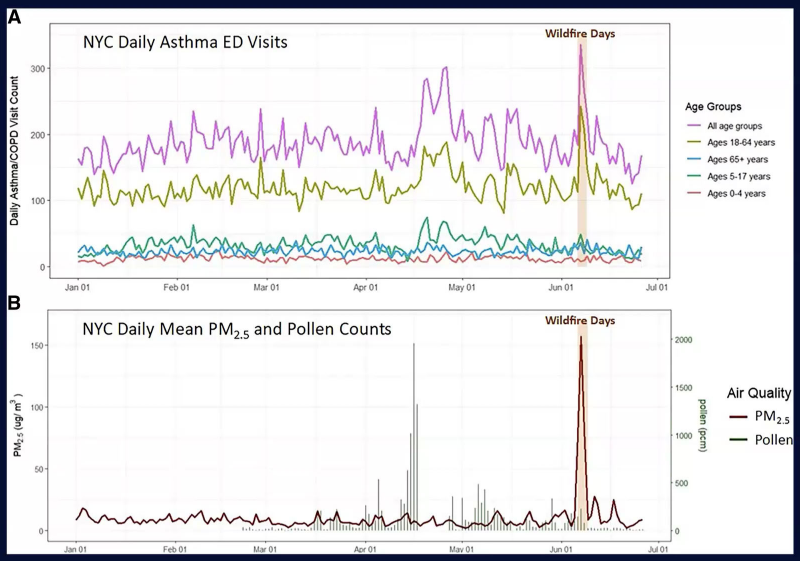
Wildfire PM and asthma presentations in 2023



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Composition of wildfire smoke in NYC → varying health effects?

Table 1. $PM_{2.5}$, Elemental Constituent Concentrations, and Composition Fractions on Wildfire Peak Day and in 2019 in NYC

	$PM_{2.5}$	Cu	S	Cr	Na	Si	Ca	K
Airborne concentrations, μg/m³								
Wildfire: June 7–8, 2023	111.5	0.006	1.214	0.003	0.084	0.534	0.618	0.838
NYC mean, 2019	7.6	0.003	0.311	0.002	0.078	0.030	0.035	0.037
$PM_{2.5}$ constituent percentage								
Wildfire: June 7–8, 2023	—	0.005%	1.09%	0.003%	0.08%	0.48%	0.56%	0.75%
NYC mean, 2019	—	0.043%	4.14%	0.027%	1.05%	0.40%	0.47%	0.50%
Wildfire day: NYC mean ratio	—	12%	26%	9%	7%	121%	119%	151%

Definition of abbreviations: NYC = New York City; $PM_{2.5}$ = particulate matter ≤2.5 μm in aerodynamic diameter.

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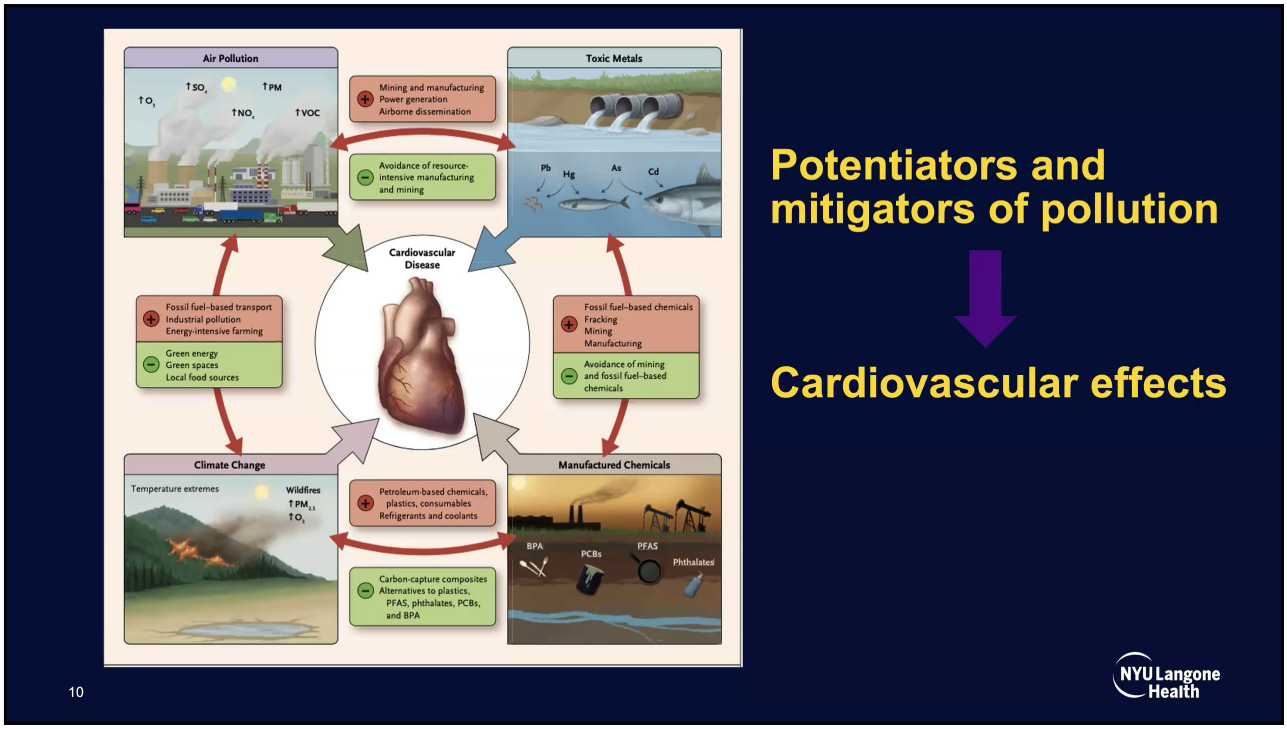
Air Pollution
↑SO2
↑PM
↑O3
↑NO2
↑VOC
Mining and manufacturing
Power generation
Airborne dissemination
Avoidance of resource-intensive manufacturing and mining
Toxic Metals
Pb
Hg
As
Cd
Cardiovascular Disease
Fossil fuel–based transport
Industrial pollution
Energy-intensive farming
Green energy
Green spaces
Local food sources
Fossil fuel–based chemicals
Fracking
Mining
Manufacturing
Avoidance of mining and fossil fuel–based chemicals
Climate Change
Temperature extremes
Wildfires
↑PM2.5
↑O3
Petroleum-based chemicals, plastics, consumables
Refrigerants and coolants
Carbon-capture composites
Alternatives to plastics, PFAS, phthalates, PCBs, and BPA
Manufactured Chemicals
BPA
PCBs
PFAS
Phthalates
Potentiators and mitigators of pollution
Cardiovascular effects
10
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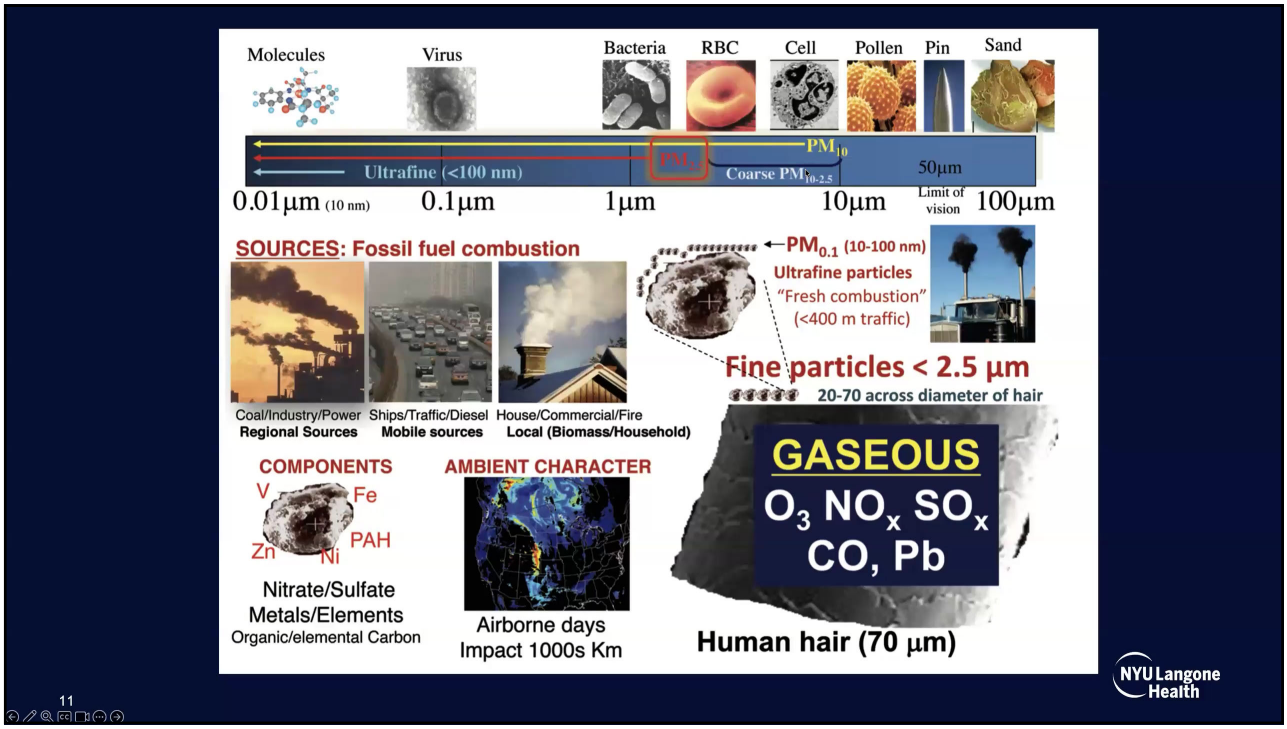
Molecules
Virus
Bacteria
RBC
Cell
Pollen
Pin
Sand
PM10
PM2.5
Ultrafine (<100 nm)
Coarse PM10-2.5
50µm
0.01µm (10 nm)
0.1µm
1µm
10µm
Limit of vision
100µm
SOURCES: Fossil fuel combustion
PM0.1 (10-100 nm)
Ultrafine particles
"Fresh combustion"
(<400 m traffic)
Fine particles < 2.5 µm
20-70 across diameter of hair
Coal/Industry/Power
Regional Sources
Ships/Traffic/Diesel
Mobile sources
House/Commercial/Fire
Local (Biomass/Household)
GASEOUS
O3 NOx SOx
CO, Pb
COMPONENTS
V
Fe
Zn
Ni
PAH
Nitrate/Sulfate
Metals/Elements
Organic/elemental Carbon
AMBIENT CHARACTER
Airborne days
Impact 1000s Km
Human hair (70 µm)
11
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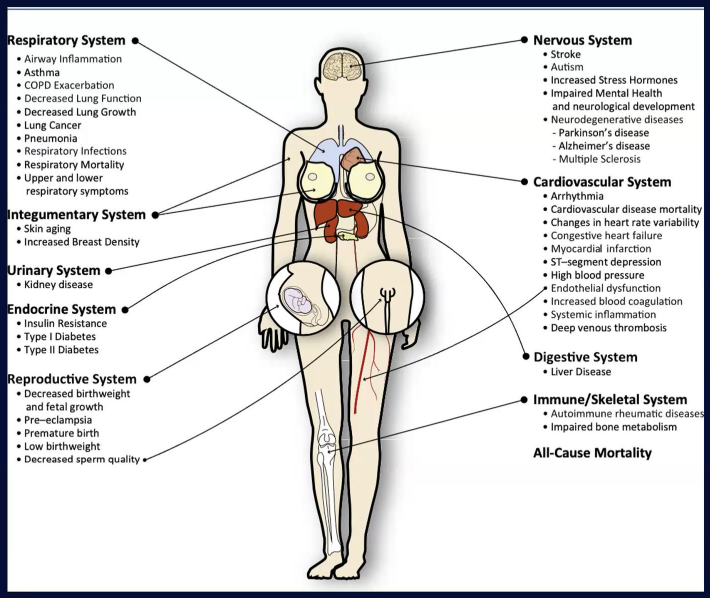
Organ Systems Vulnerable to Air Pollution



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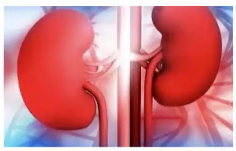
HTN 15-20%

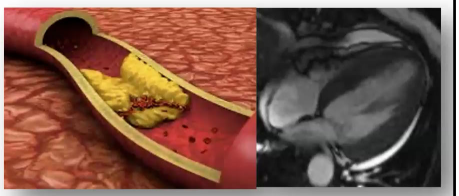
Int J Environ Health Res 2023; 33: 268-83
Environ Res 2022; 204: 112352
Sci Total Environ 2021: : 796: 148620



Kidney Disease 31-42%

3.3 million new CKD/yr

J Biol Mol Toxicol 2024; 38: e2361
Sci Rep 2024; 14: 1048
BMJ Global Health 2020; 5: e002063



ATHEROSCLEROSIS / CARDIAC

CAC, carotid plaque / LVH, LV remodeling

Athero Thromb Vasc Biol 2021;41:628-37

CHRONIC DISEASES

DM 11-15% **↓HDL** **Obesity**

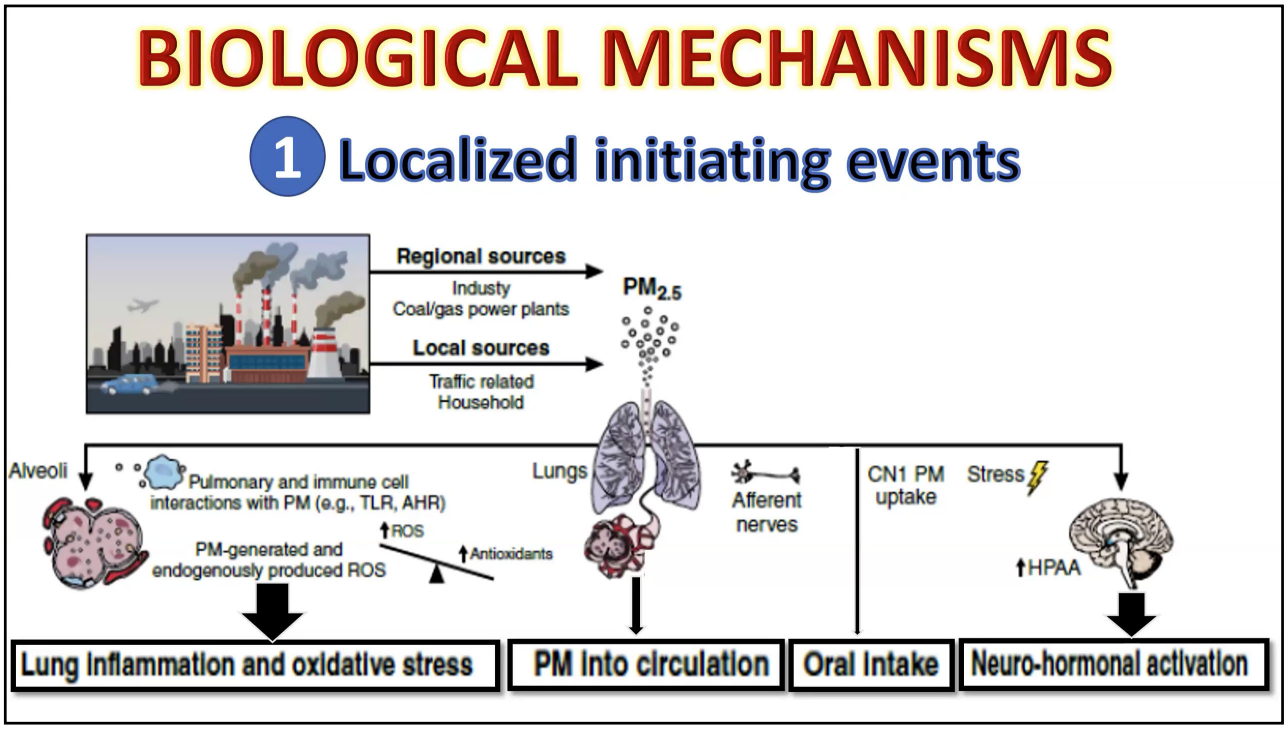
20% of DM due to PM2.5
3.2 million new DM/yr

Environ Sci Pollut Res Int 2020; 27: 798-811
Lancet Planet Health 2018; 2: e301

Neurocognitive Decline

BMJ 2023: 381: e071620

14


BIOLOGICAL MECHANISMS
1 Localized initiating events
Regional sources
Industry
Coal/gas power plants
Local sources
Traffic related
Household
PM2.5
Alveoli
Pulmonary and immune cell interactions with PM (e.g., TLR, AHR)
PM-generated and endogenously produced ROS
↑ROS
↑Antioxidants
Lungs
Afferent nerves
CN1 PM uptake
Stress
↑HPAA
Lung Inflammation and oxidative stress
PM into circulation
Oral Intake
Neuro-hormonal activation

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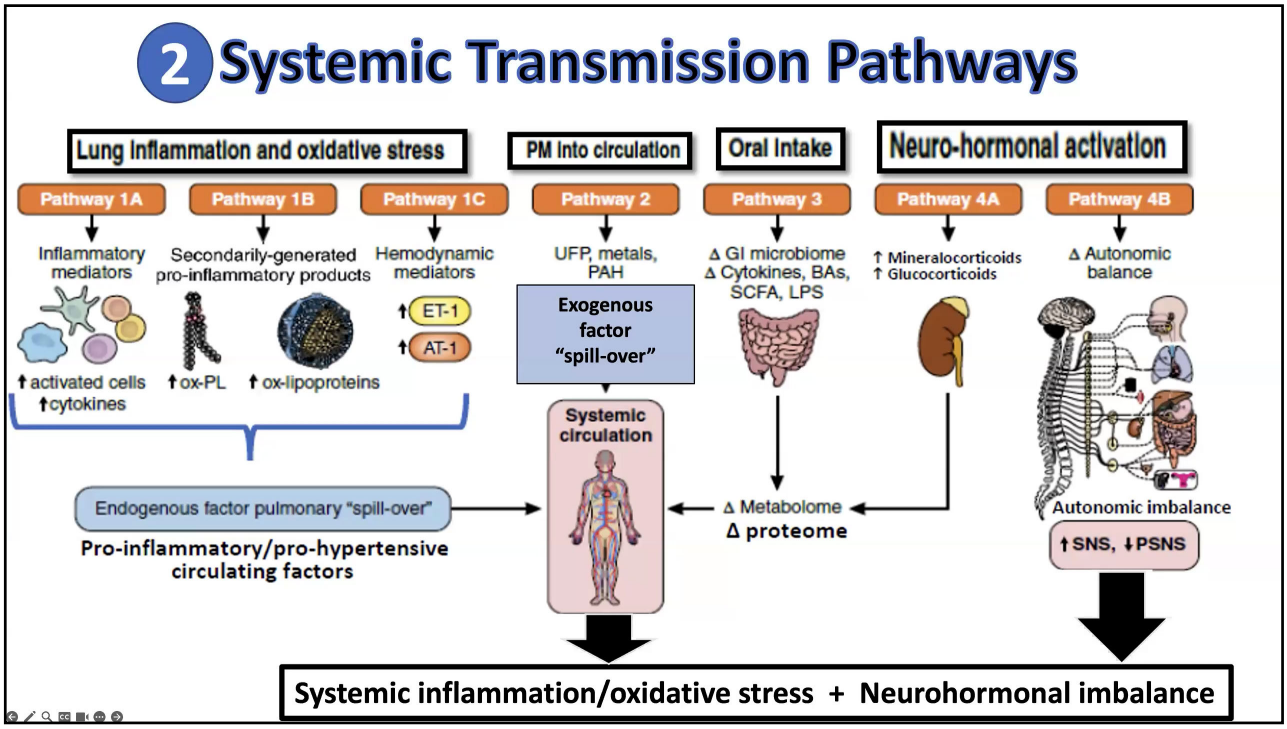
2 Systemic Transmission Pathways
Lung Inflammation and oxidative stress
PM into circulation
Oral Intake
Neuro-hormonal activation
Pathway 1A
Pathway 1B
Pathway 1C
Pathway 2
Pathway 3
Pathway 4A
Pathway 4B
Inflammatory mediators
Secondarily-generated pro-inflammatory products
Hemodynamic mediators
UFP, metals, PAH
Δ GI microbiome
Δ Cytokines, BAs, SCFA, LPS
↑ Mineralocorticoids
↑ Glucocorticoids
Δ Autonomic balance
↑activated cells
↑cytokines
↑ox-PL
↑ox-lipoproteins
↑ET-1
↑AT-1
Exogenous factor "spill-over"
Systemic circulation
Endogenous factor pulmonary "spill-over"
Pro-inflammatory/pro-hypertensive circulating factors
Δ Metabolome
Δ proteome
Autonomic imbalance
↑SNS, ↓PSNS
Systemic inflammation/oxidative stress + Neurohormonal imbalance

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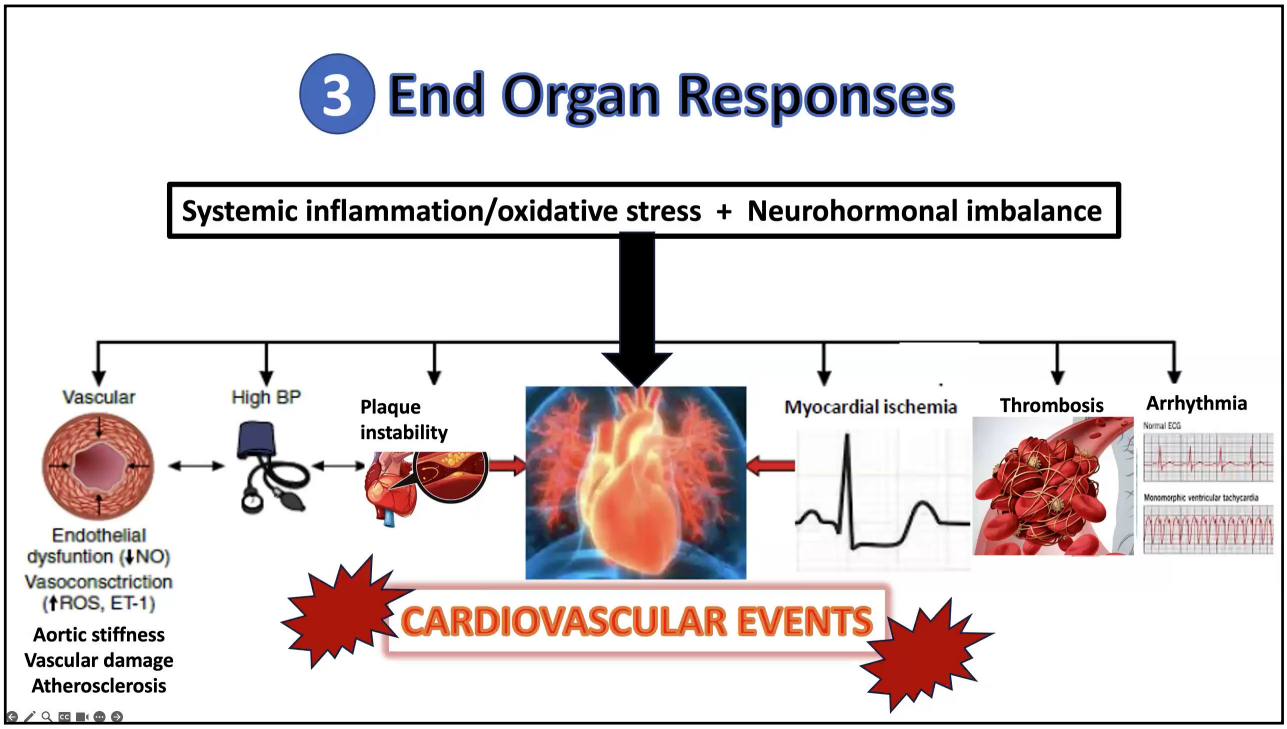
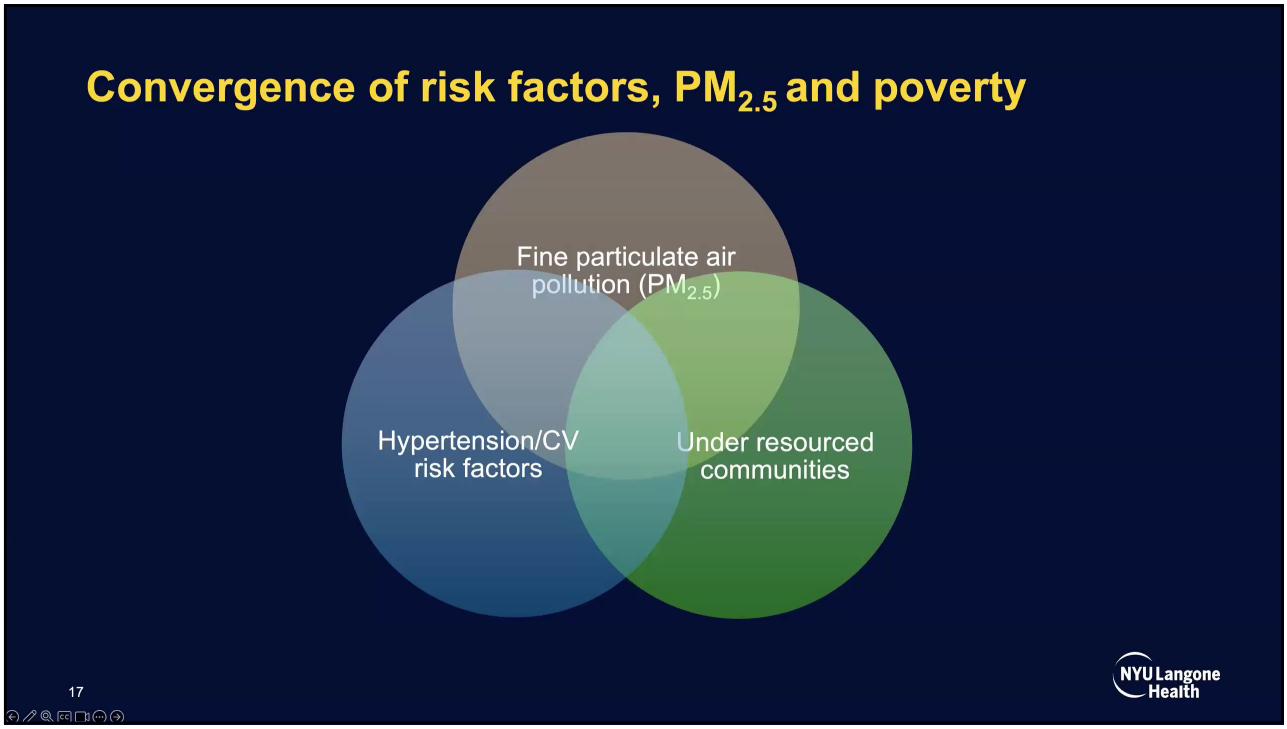

3 End Organ Responses
Systemic inflammation/oxidative stress + Neurohormonal imbalance
Vascular
High BP
Plaque instability
Myocardial ischemia
Thrombosis
Arrhythmia
Endothelial dysfuntion (↓NO)
Vasoconsctriction (↑ROS, ET-1)
Aortic stiffness
Vascular damage
Atherosclerosis
CARDIOVASCULAR EVENTS

17


Convergence of risk factors, PM2.5 and poverty
Fine particulate air pollution (PM2.5)
Hypertension/CV risk factors
Under resourced communities
17
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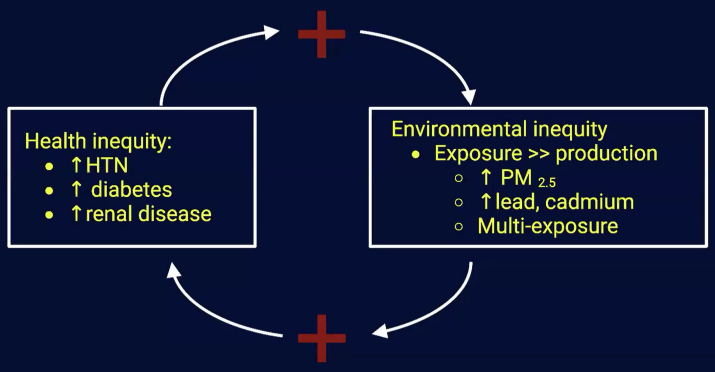
A positive feedback loop
The twin epidemics environmental and health inequities



HEALTH INEQUITY in NYC communities

- >70% hypertension (≈50% US)
- >35% diabetes (≈30% US)

ENVIRONMENTAL INEQUITY

- Increased exposure relative to production
- Increased air pollution
- Multi-exposure

18

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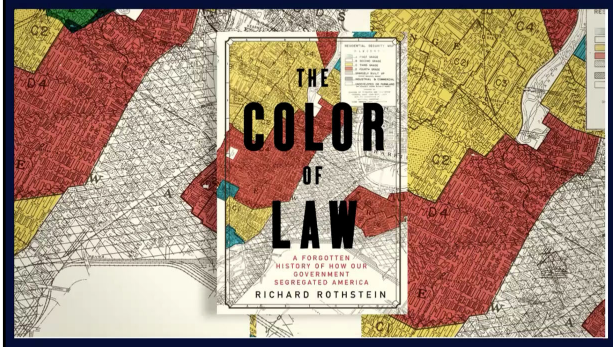
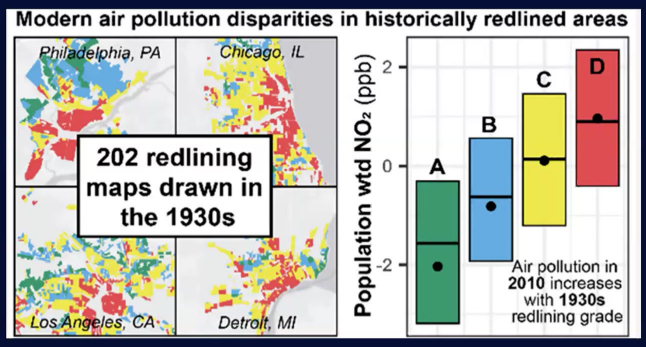
Historical "redlining" and current air pollution disparities





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Lane, Env. Sci Tech Letters, 2022

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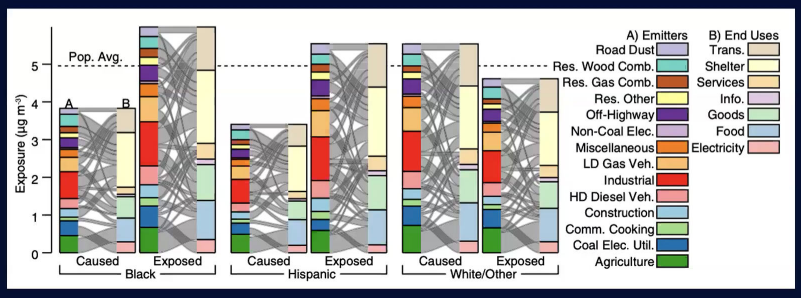
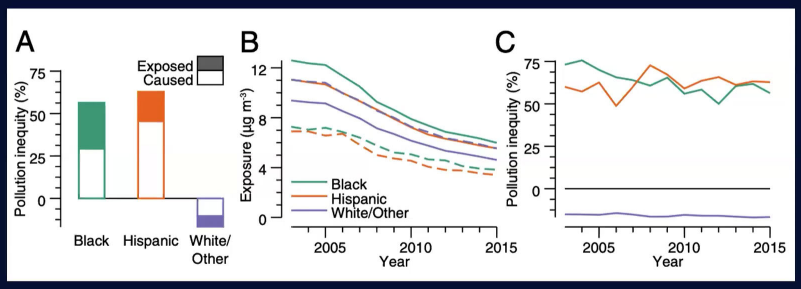
Inequity in production vs. exposure





20

Tessum et. al. Proc Natl Academy Sci, 2019, Science Advances, 2021

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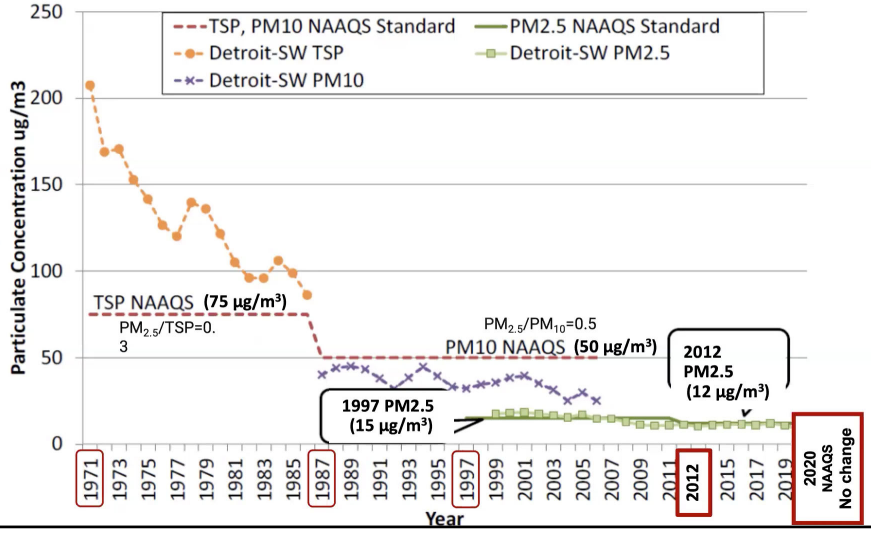
Clean Air Act

National Ambient Air Quality Standards (NAAQS)

December 31, 1970

Detroit 1970-2020



Courtesy Rob Brook, MD

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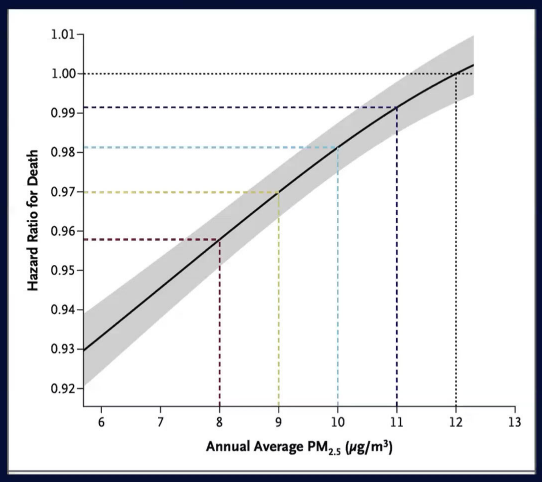
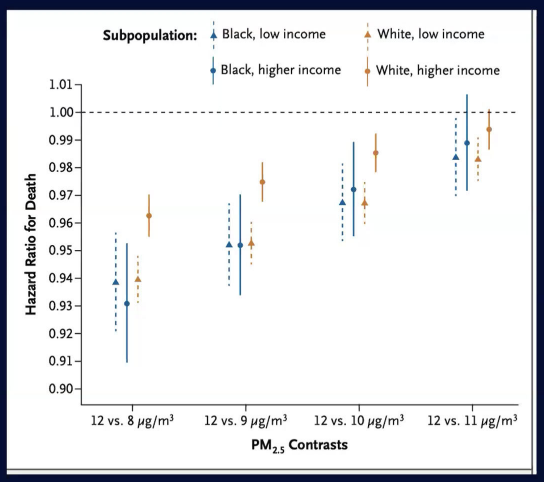
Race, income and impact of lower $PM_{2.5}$





22 Josey et. al. N Engl J Med, 2023

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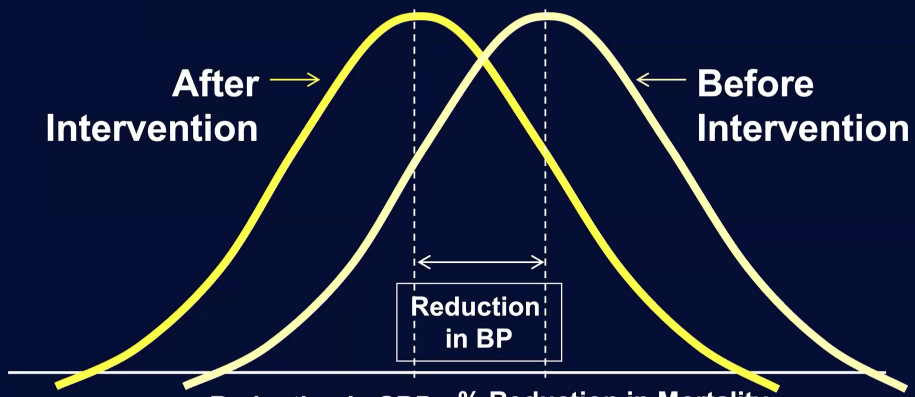
Sick individuals, sick populations

SBP Distributions



Reduction in SBP mmHg	% Reduction in Mortality Stroke	CHD	Total
2	–6	–4	–3
3	–8	–5	–4
5	–14	–9	–7

Rose, Int J Epi, 2001; JAMA 2003

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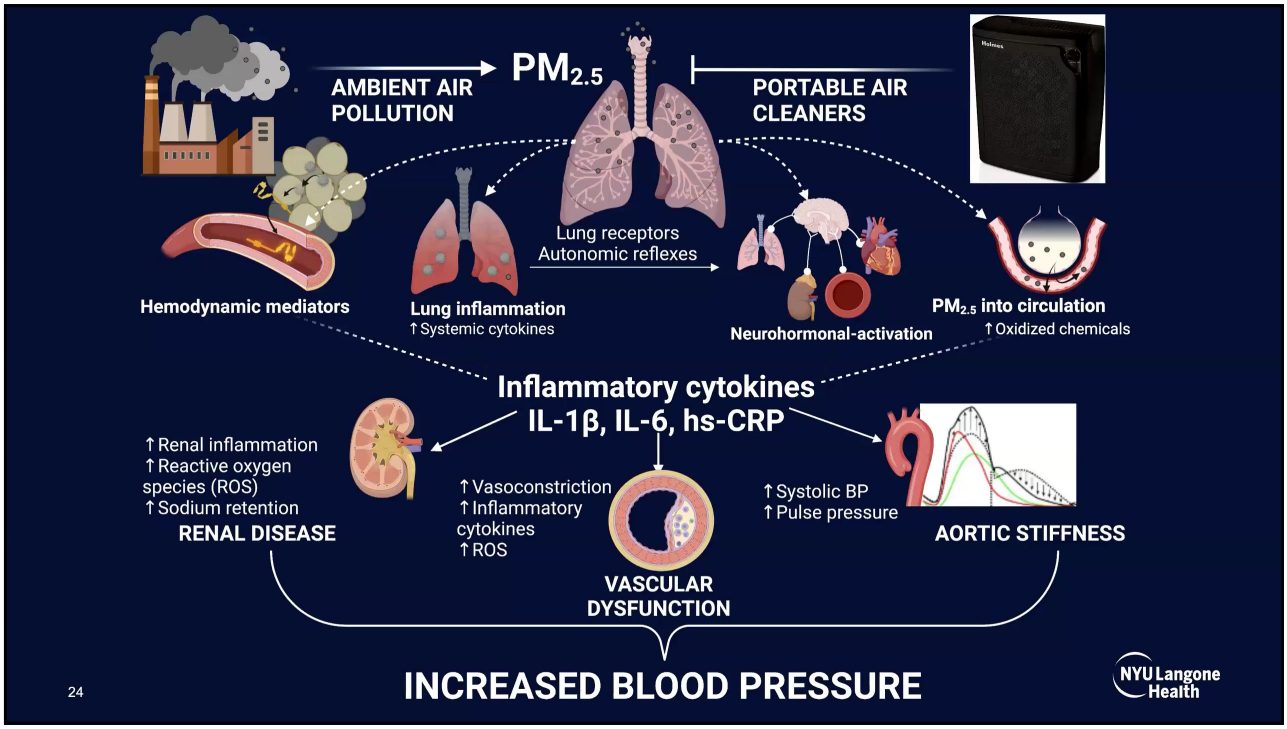

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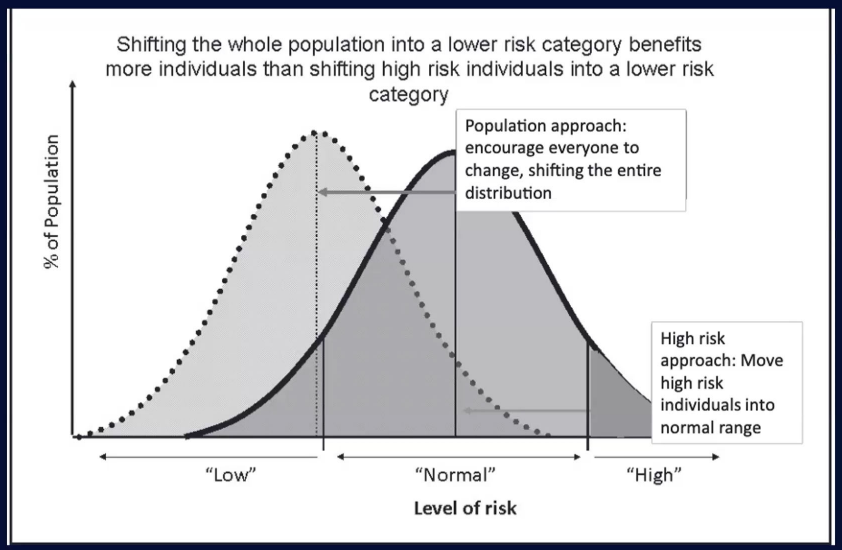
Prevention strategies applied to air pollution ($PM_{2.5}$)



25 Rose, G. Int J Epi, 1985

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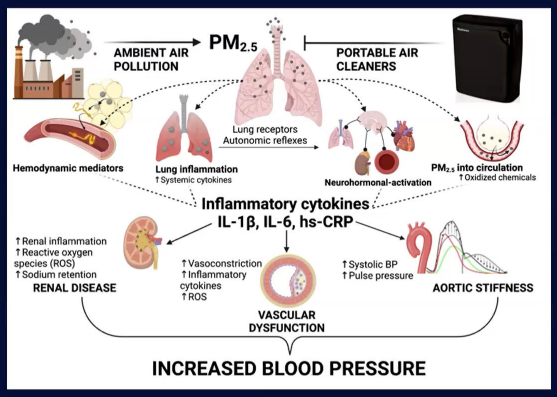
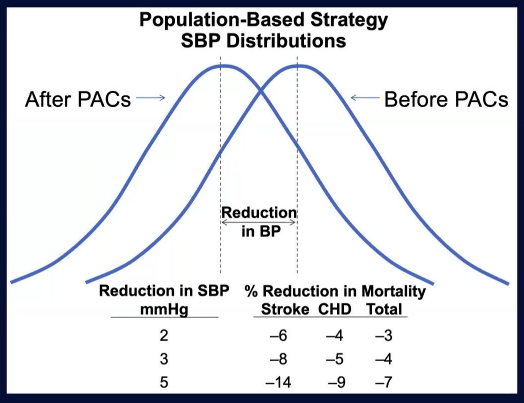
Air pollution ($PM_{2.5}$) – Adverse health effects & risk trajectories

Many risk pathways → **By lowering (indoor) $PM_{2.5}$, can we improve SBP and health outcomes?**





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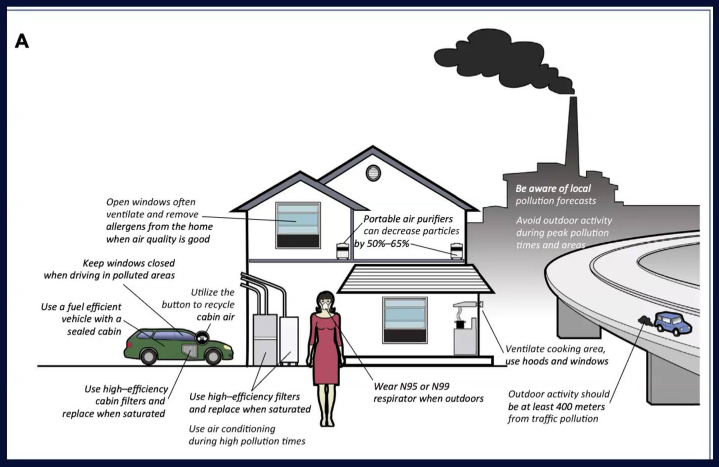
Approaches to Limit Health Effects of Air Pollution



- Personal strategies
  - Portable air cleaners
- Building interventions
  - Windows
  - Building HEPA filters
- Policy interventions

Newman…Brook NHLBI/NIEHS/CDC/EPA White Paper, JACC 2020; Newman…Brook, J Human Hypertension,

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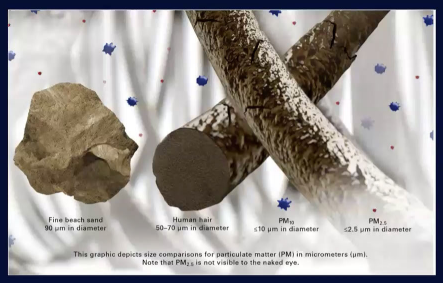
Portable air cleaners (PACs)

- PACs are “affordable” (<$100/device), using high efficiency particle arrestance (HEPA) filtration, capture >99% of small particles
- Reduce indoor $PM_{2.5}$ by 50-70%
- Largest health impacts overnight (in bedroom PAC)
- Studies show:
  - Decreased odds of respiratory symptoms
  - Emerging benefits for other non-pulmonary outcomes:
    - Blood pressure, heart rate variability, oxidative stress/inflammation, peri-natal/fetal outcomes
  - Favorable benefit-cost ratio, could prevent ≈64,000 deaths/year
  - Benefits exceed costs by >$1,000/person



28 https://www.epa.gov/sites/default/files/201807/documents/guide_to_air_cleaners_in_the_home_2nd_edition.pdf

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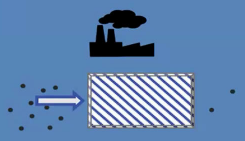
Effects of home particulate air filtration on blood pressure: a meta-analysis

Do **personal air cleaners** which filter fine particulate matter ($PM_{2.5}$)...



...reduce Systolic and Diastolic Blood Pressure?

5 databases and **330 studies** screened

10 studies selected
(N = 604 participants)

Include:
- All states of health
- HEPA or dielectric cleaners

Exclude:
- Non-home settings
- Cigarette smokers

Personal air cleaner use associated with
≈4 mmHg lower systolic blood pressure
and
≈56% lower indoor $PM_{2.5}$

No significant association with diastolic blood pressure

No heterogeneity of effect for health status, age, or $PM_{2.5}$ concentration

29 Walzer...Newman, Hypertension, 2020

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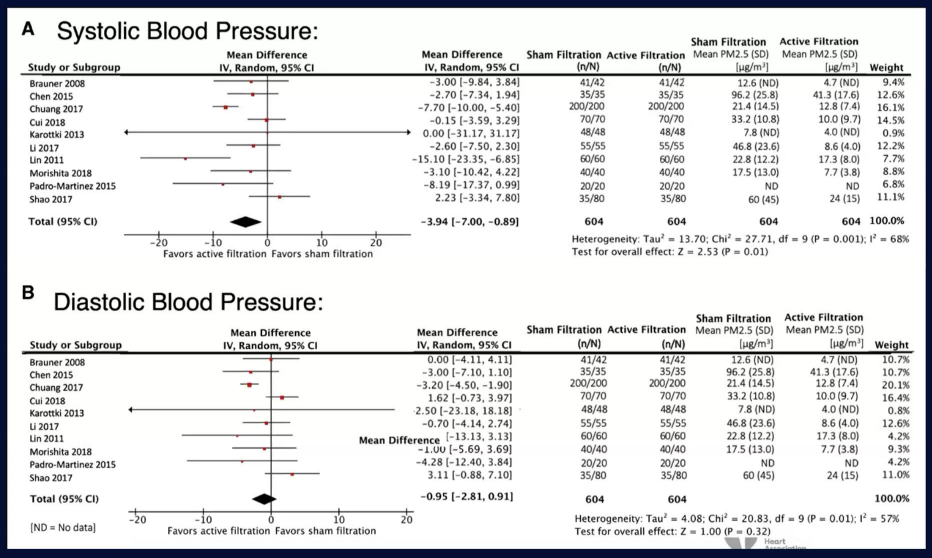
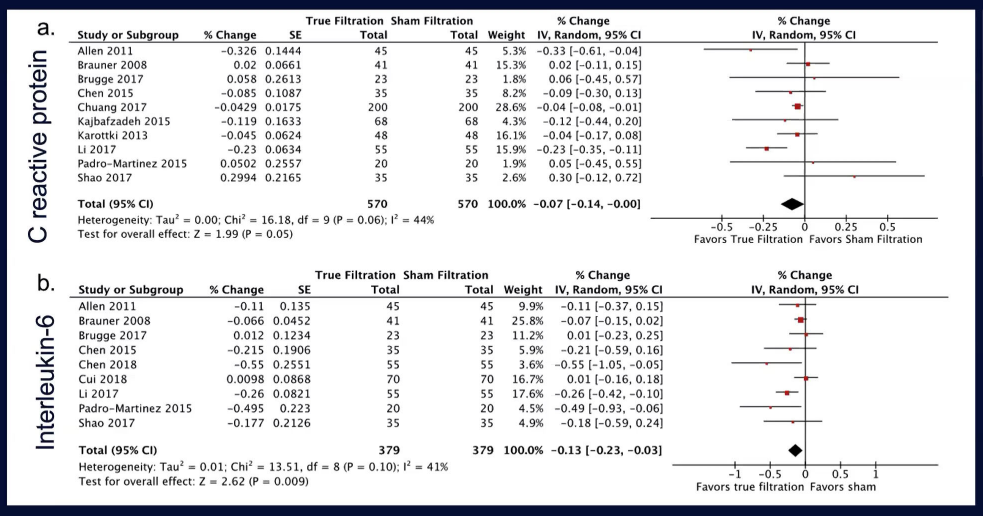
Air filters to reduce blood pressure…



30 Walzer…Newman, Hypertension, 2020

31

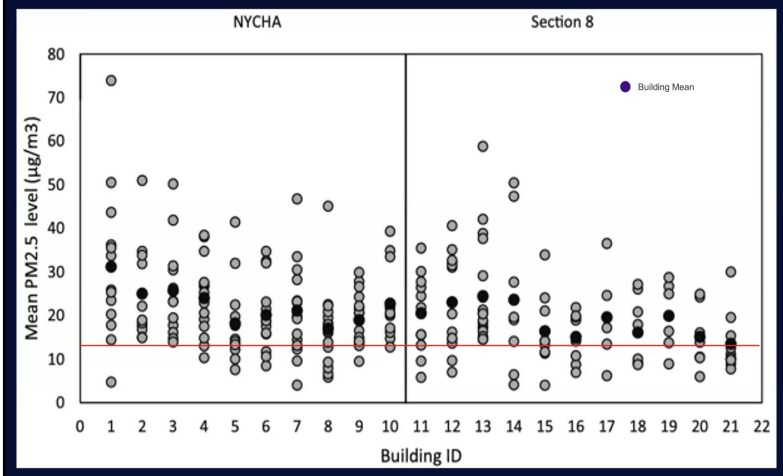
and inflammatory markers…



31 Wittkopp….Newman Am Heart J Plus, 2022

32

NYCHA residents have increased PM2.5 exposures relative to other public housing (and NYC overall)



	NYCHA: HHAP	NYC reference
Female	80%	≈50%
Hypertension	83%	≈35%
Diabetes	≈45%	≈15%

Source: NYC Community Health Survey 2013, adults aged 35+

Anastasiou….Thorpe, *Sci Total Environ*, 2020; Lopez et al / Am J Prev Med 2017;

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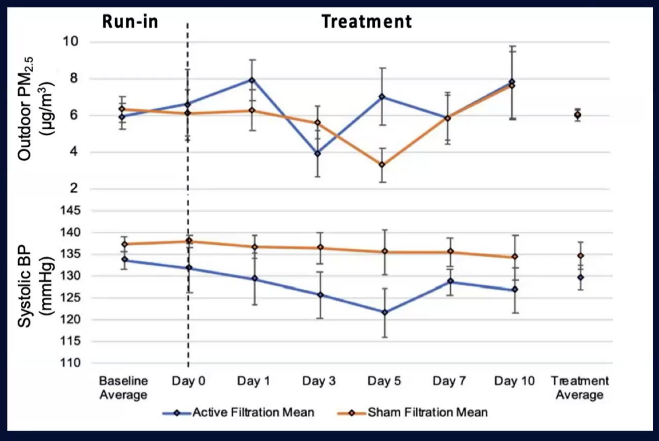
PACs may lower home blood pressure in NYCHA residents with HTN: NYU pilot study

	All (n=20) mean (SD) or N (%)	Sham (n=10) mean (SD) or N (%)	Active (n=10) mean (SD) or N (%)
Age (nearest yr.)	55 (14)	50 (14)	61 (13)
Female	14 (70)	7 (70)	7 (70)
BMI	34 (6)	35 (7)	32 (5)
Waist Circumference (inches)	43 (6)	44 (7)	42.8 (5)
Race/ethnicity			
Non-Hispanic Black	9 (45)	5 (50)	4 (40)
Hispanic/Latino	6 (30)	3 (30)	3 (30)
American Indian/Alaska Native	1 (5)	0 (0)	1 (10)
Asian	1 (5)	1 (10)	0 (0)
More than one race	2 (10)	1 (10)	1 (10)
Unknown/ not reported	1 (5)	0 (0)	1 (10)
Comorbidities			
History of MI	1 (5)	0 (0)	1 (10)
History of CVA	6 (30)	2 (20)	4 (40)
History of Diabetes	10 (50)	5 (50)	5 (50)
Years since HTN Diagnosis			
0-2 years	3 (15)	2 (20.0)	1 (10.0)
2-5 years	2 (10)	2 (20.0)	0 (0.0)
5-10 years	2 (10)	0 (0.0)	2 (20.0)
>10 years	13 (65)	6 (60.0)	7 (70.0)
Proportion ≥1 BP Medication	17 (85)	8 (80.0)	9 (90.0)
Current Antihypertensive medication use (YES)			
ACEI/ARN/ARB	8 (40)	2 (20.0)	6 (60.0)
Beta Blocker	2 (10)	1 (10.0)	1 (10.0)
Diuretic	5 (25)	1 (10.0)	4 (40.0)
CCB	6 (30)	4 (40.0)	2 (20.0)
Baseline SBP*	135 (13)	136 (10)	134 (14)



Wittkopp…Newman *J Am. Heart Assoc*, 2023

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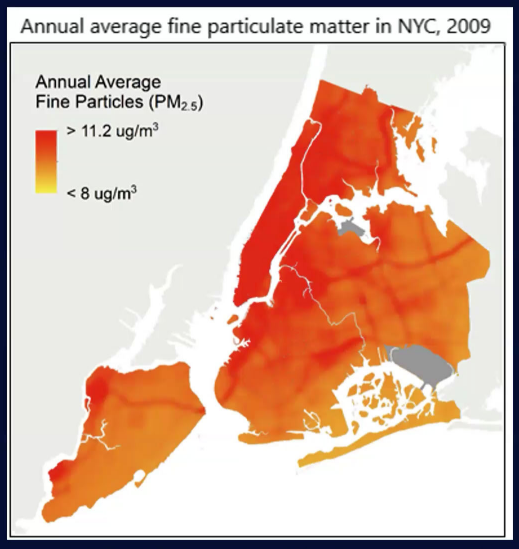
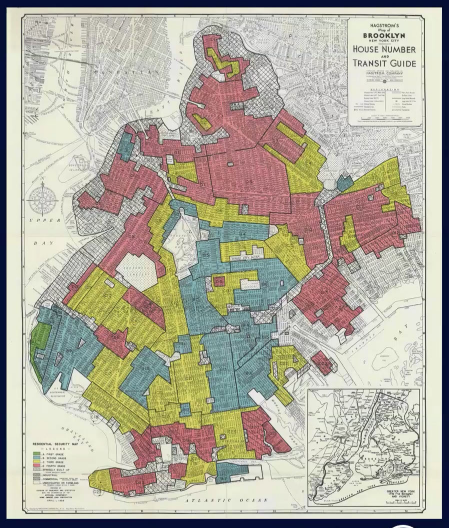
Persistence of economic inequality in NYC



NYC DOH New York City Community Air Survey (NYCCAS) report



Mapping Inequality Project

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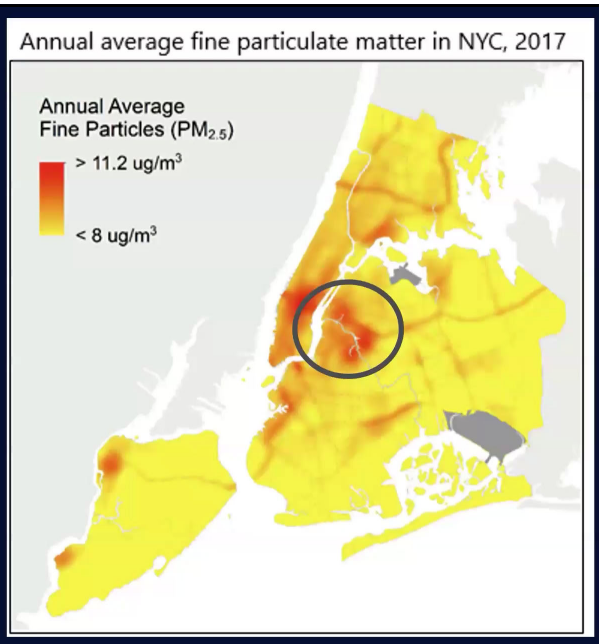
Persistence of economic inequality in NYC



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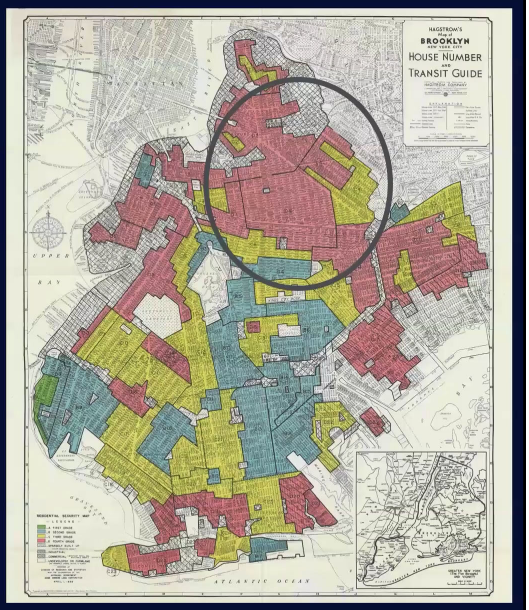

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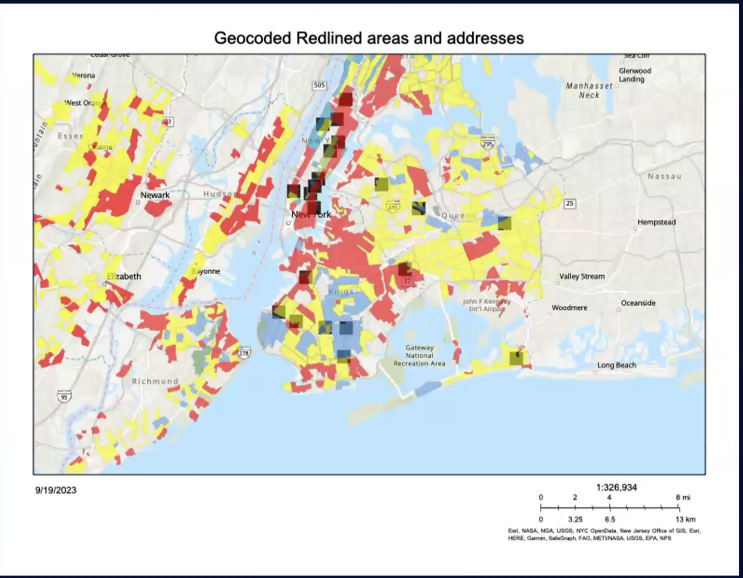
Results



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Results – PM across HOLC grade in NYC

Table 1. Characteristics by HOLC Grade

	All (n=44)	C/D (n=25)	Others (n=19)
True	22	11	11
Sham	22	14	8
$PM_{2.5}$ $\mu g/m^3$ mean (SD)	5.92 (13.43)	8.48 (17.24)	3.12 (6.12)

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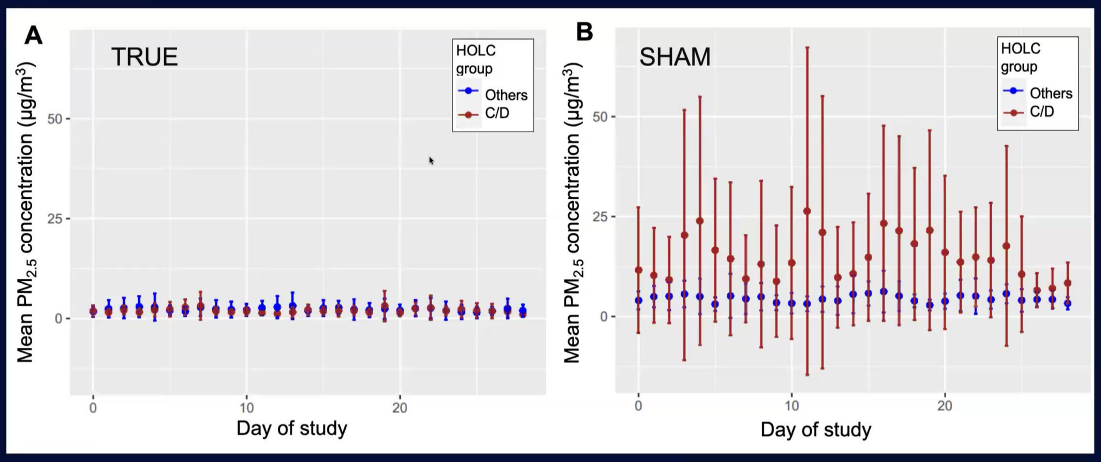
Daily mean $PM_{2.5}$ by Study Arm



Significant interaction between study arm and HOLC group
($\beta_{interact}$ = -7.07576 p = 0.027)

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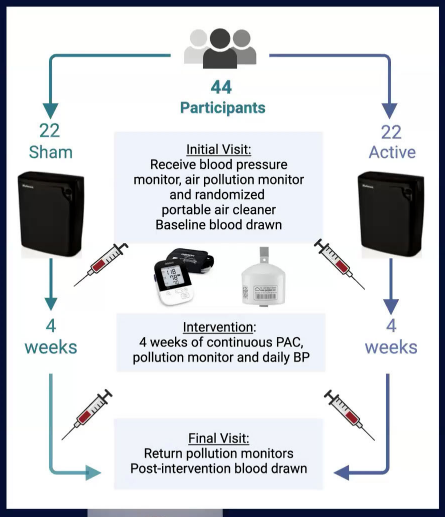
Glycemic effects of $PM_{2.5}$ and PACs

- Randomized double-blind sham-controlled trial
- English-speaking adults with hypertension
- Living in Greater NYC area
- Randomized to TRUE or SHAM (HEPA removed) air filtration



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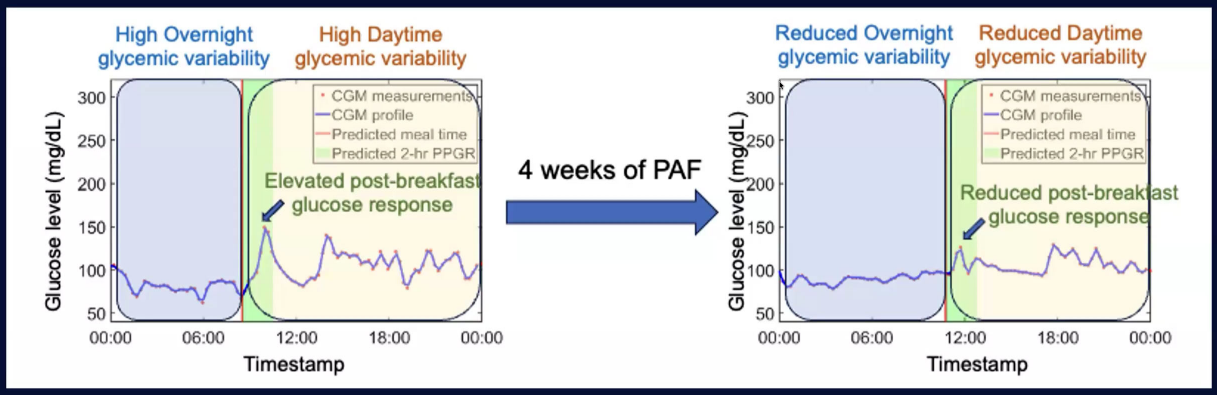
Reduced glycemic variability with PACs



40 Wittkopp, Barua, Newman, unpublished data

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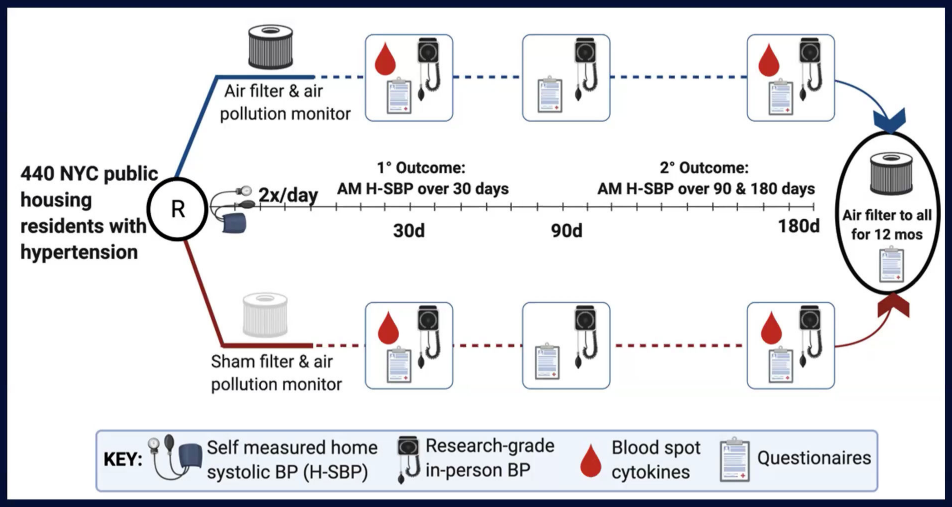
AirPressureNYC: Reducing AIR pollution to lower blood PRESSURE among NYC public housing residents



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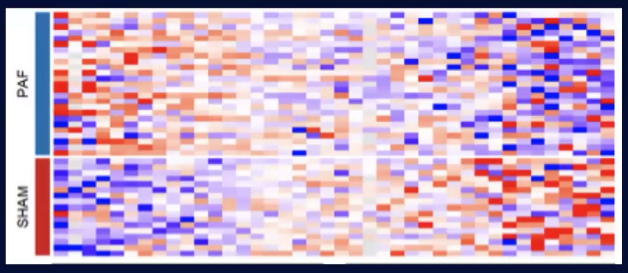
Preliminary data - AirPressureNYC



- N=50 participants, dried blood spots at baseline and day 30
- Unbiased metabolomics (Metabolon, ≈1100 metabolites)
  - Global metabolic differences between PAF and sham
  - Reductions in exposure-related forever chemicals (PFAS) and glucose-related metabolites

Newman, Barua, Grams, upublished data

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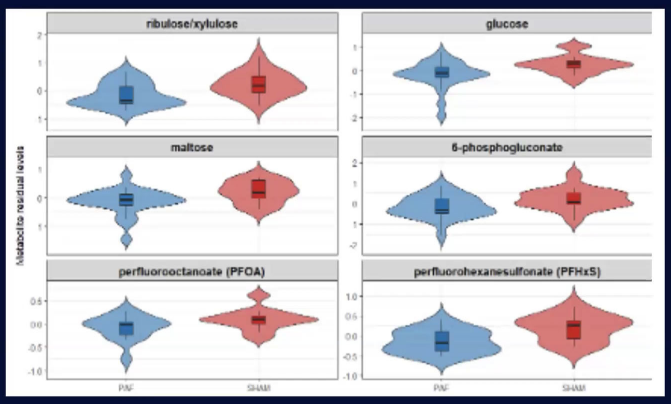
Preliminary data - AirPressureNYC



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Newman, Barua, Grams, upublished data

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AirPressureNYC: lessons & questions (thus far…)

- Community based research/trials
- Remote patient monitoring (RPM)
- Studying interventions, observing risk factors
- Clinical trials vs. advocacy

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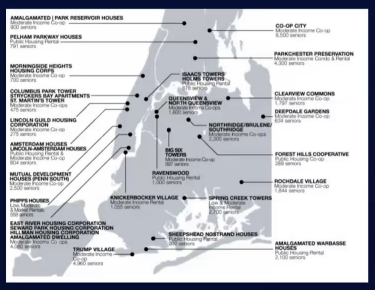
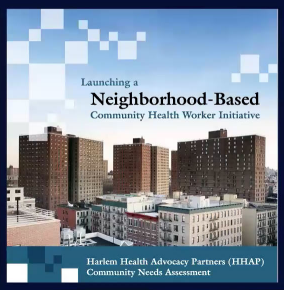
AirPressureNYC: Community partnerships are crucial





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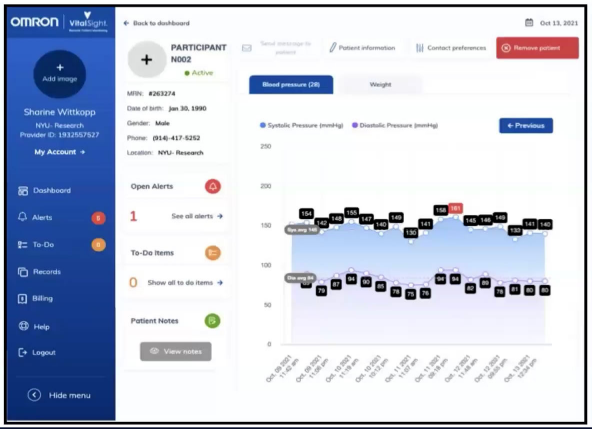
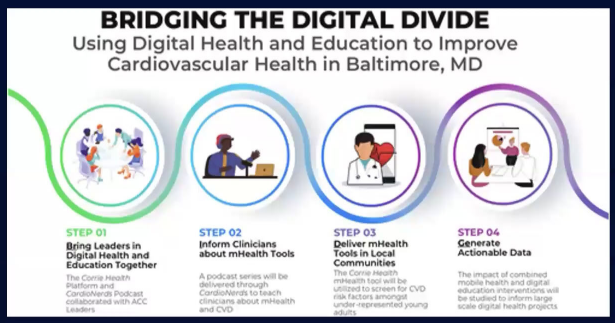
Bridging the digital divide…in pragmatic trials

Figure 1. HBP Dashboard





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$PM_{2.5}$ interventions in patients with CV risk: Navigating between Scylla and Charybdis?

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How to balance priorities: risk factor control in $PM_{2.5}$ studies

Issue

1) (Un)controlled risk factors
2) Differential treatment bias
   1) Dilution of treatment effect - bias to null
   2) Surrogate endpoints (e.g. biomarkers)
3) Air purifiers as medical devices?

Potential solution

1) Enrollment of stable patients
   1) Guidelines & clinical safety
   2) Referral protocols
      1) Outreach detracts from pragmatic approach
2) Limit med titration if possible
3) Convince your IRB they are not!

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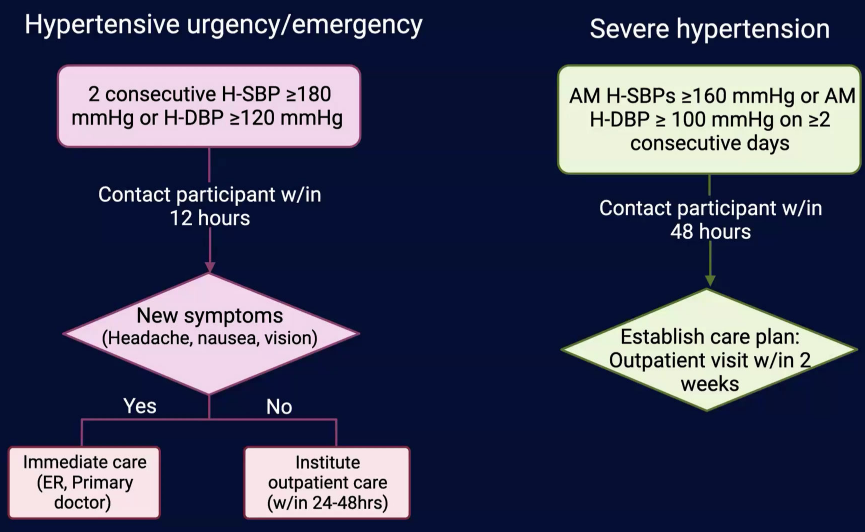
Example referral pathway – AirPressureNYC



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Clinical trials vs. advocacy: what is the right stance?

Clinical trial

Advocacy

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Collaborators/support

- **NYU**
  - Division of Cardiology:
  - Dr. Fishman, Hochman, Katz
    - Center for the Prevention of CVD
      - Drs Fisher, Berger, Goldberg
  - Department of Population Health
    - Dr. Thorpe + team
  - Division of Environmental Medicine
    - Drs. Gordon and Thurston
  - CTSI
  - Environmental research group
    - Dr. Wittkopp, Dr. Walzer, Dr. Bonnani
    - Elle Anastasiou, MPH, Albert Tovar, Emily Gill
- **Wayne State**
  - Dr. Brook
- **Cardiovascular Research Center**
  - Dr. Moore

- **NIH R01HL168597**
- **NIH R01HL165208**
- **Doris Duke Charitable Foundation, Physician Scientist Fellowship** (PI: Wittkopp)

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Questions/discussion?

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