COULD EXPOSURE TO AIR POLLUTION INFLUENCE DEMENTIA RISK?

The state of the science

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What we mean by “dementia”

Deficits in **memory**, language, problem-solving and other **cognitive abilities** that affect a person's **ability to perform everyday activities**.
Cognitive function, cognitive decline, and dementia

1. Cognitive level
2. Rate of cognitive decline
3. Dementia incidence

Adapted from M. Maria Glymour
No drug has been shown to alter the clinical course of Alzheimer’s dementia.

2002-2014: 1 new FDA-approved medication


Anti-amyloid agents: reduce amyloid, but do not markedly stall cognitive decline
The neuropathologic causes of dementia often overlap

- Alzheimer's disease
- Cerebrovascular factors
- Lewy body disease, FTD, PD or other pathology
- Other?
Most Alzheimer’s dementia occurs with other pathologies.
Most Alzheimer’s dementia occurs with other pathologies.

Percentage of probable Alzheimer’s dementia cases (N=447)

Kapasi, DeCarli, & Schneider. Acta Neuropathol. 2017
Potential **pleiotropy**

*not just amyloid beta plaques and tau tangles*

**Air Pollution**

- Oxidative stress
- Inflammation
- Synapse toxicity
- BBB injury
- Cerebrovascular pathology
- Other pathology?
- Apoptosis
- Amyloid beta pathology

**Effects in Periphery**

**Dementia**
State of the science
UPDATE TO

A SYSTEMATIC REVIEW

of published epidemiologic research
on the relation of air pollution exposure
with dementia, its precursors and its correlates

NeuroToxicology 56 (2016) 235–253

Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research

Melinda C. Power, Sara D. Adar, Jeff D. Yanosky, Jennifer Weuve, MPH, ScD
Studies identified

1. Cognitive level
2. Rate of cognitive decline
3. Incident dementia/impairment
4. Brain imaging

Adapted from M. Maria Glymour
Study locations
Pollutants investigated

- fine PM
- coarse PM
- thoracic PM
- ozone
- woodsmoke PM
- chemical species in PM
- black carbon
- nitrogen dioxide
- nitrogen oxide
- traffic-related indices
Summary of findings

Most studies reported an **adverse association** of at least one pollutant exposure with a dementia-related outcome.

**Most consistent** results involve:

- PM$_{2.5}$
- NO$_2$
- NO$_x$
- Cognitive level
- Dementia
- Infarcts on MRI

**Mixed/sparse** results involve:

- PM$_{10}$
- PM$_{coarse}$
- Ozone, Sources
- Cognitive decline
- Other MRI outcomes
Is this good enough?
Of the 10 dementia studies,

• 6 relied solely on claims/medical records to identify cases and non-cases.

• 2 relied partially on these data sources
Audience quiz

What is the approximate positive predictive value of medical records and insurance claims for classifying people with dementia?

(a) 95%  (b) 83%  (c) 75%  (d) 64%  (e) 56%

Wait, what? Surely it’s better in [insert non-US country].

(a) It is not.  (b) Nope.  (c) Even worse for dementia “types.”  (d) All of these.
Misclassification: Dementia diagnoses via “passive surveillance”

85% have a dementia diagnosis in Medicare claims (sensitivity)

89% do not have a dementia diagnosis in Medicare claims (specificity)

Positive predictive value: 56%
(of Medicare beneficiaries who have dementia claims, 56% actually have dementia)

All positive claims

Misclassification of dementia diagnoses via "passive surveillance".

CONCERN: Misclassification of dementia status that depends on air pollution exposure.

Air pollution exposure → Cardiovascular disease → Dementia diagnosis

UPSHOT? Overestimation of air pollution's adverse effect on dementia.
Selection bias: e.g., healthy volunteers

Cognitive function

Air pollution exposure

Selection (lower exposure OR better function)

Cognitive decline/dementia

UPSHOT?

underestimation of air pollution’s adverse effect
Selection bias: e.g., high-burden protocol attracting high-risk volunteers

Air pollution exposure

Selection (lower exposure OR family history)

Adverse brain imaging findings

UPSHOT?

overestimation of air pollution’s adverse effect

Family history

-
Attention to mechanism: to **make informed decisions about adjustment**

- Adjust for smoking?
- ... BMI?
- ... for diabetes?

**Effects of exposure**
- cardiovascular disease, diabetes, depression

**Air pollution exposure**

SES → smoking → BMI₁ → Incipient illness → BMI₂ → DEMENTIA

Adjust for smoking?...

- for diabetes?

APOE genotype

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State of the science: summary

Suggestion of **adverse association**
Method deployed have improved, but ...

**Needs:**
- Studies using *uniform, standardized dementia assessments*
- Attention to *misclassification, selection bias*
- Realistic *time scales*
- Adequate *exposure contrasts*
- Involvement of *researcher disciplines, diverse populations*
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- And the posse of other people who have bravely dared to cross disciplinary lines to ply their combined superpowers to investigate matters of air pollution and dementia risk.
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