

Caleb E Finch

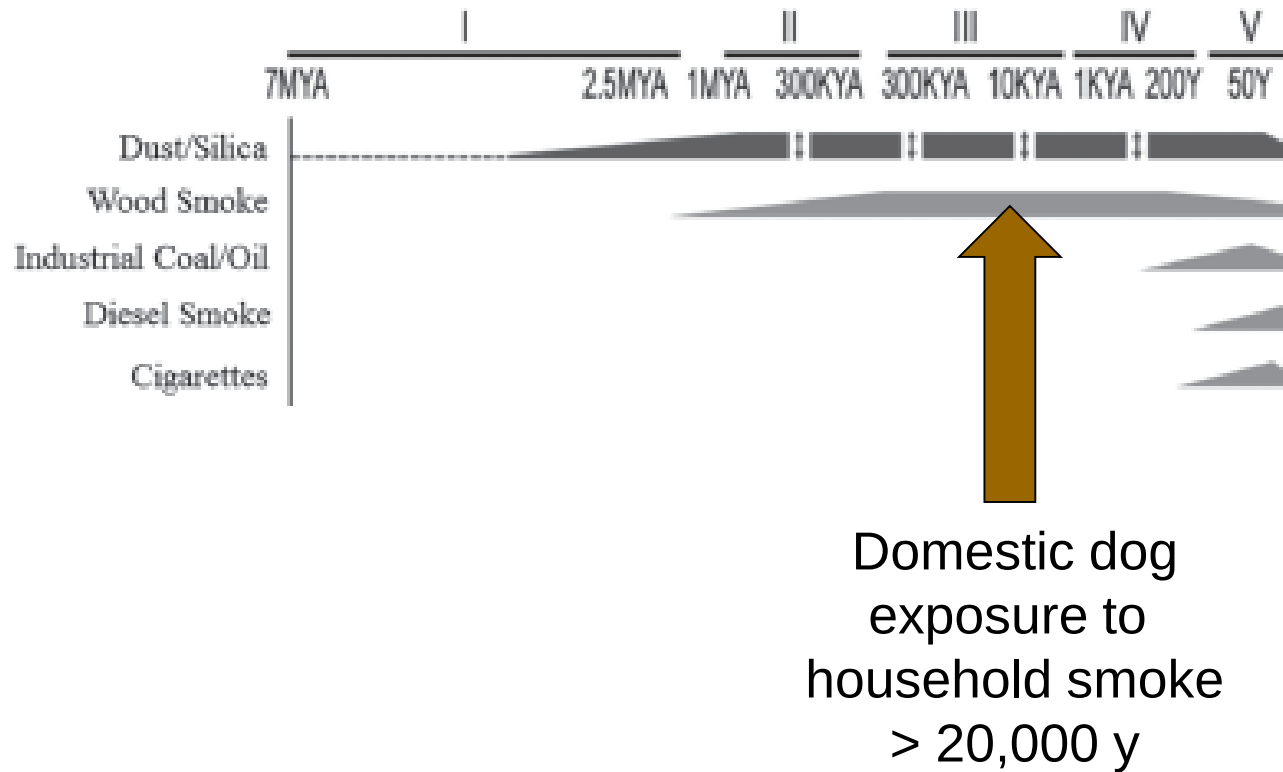


Leonard Davis School
of Gerontology,
Dornsife College

Companion Animals as Sentinels for Predicting Environmental
Exposure Effects on Aging and Cancer Susceptibility in Humans
NAS Workshop Dec 2 2021

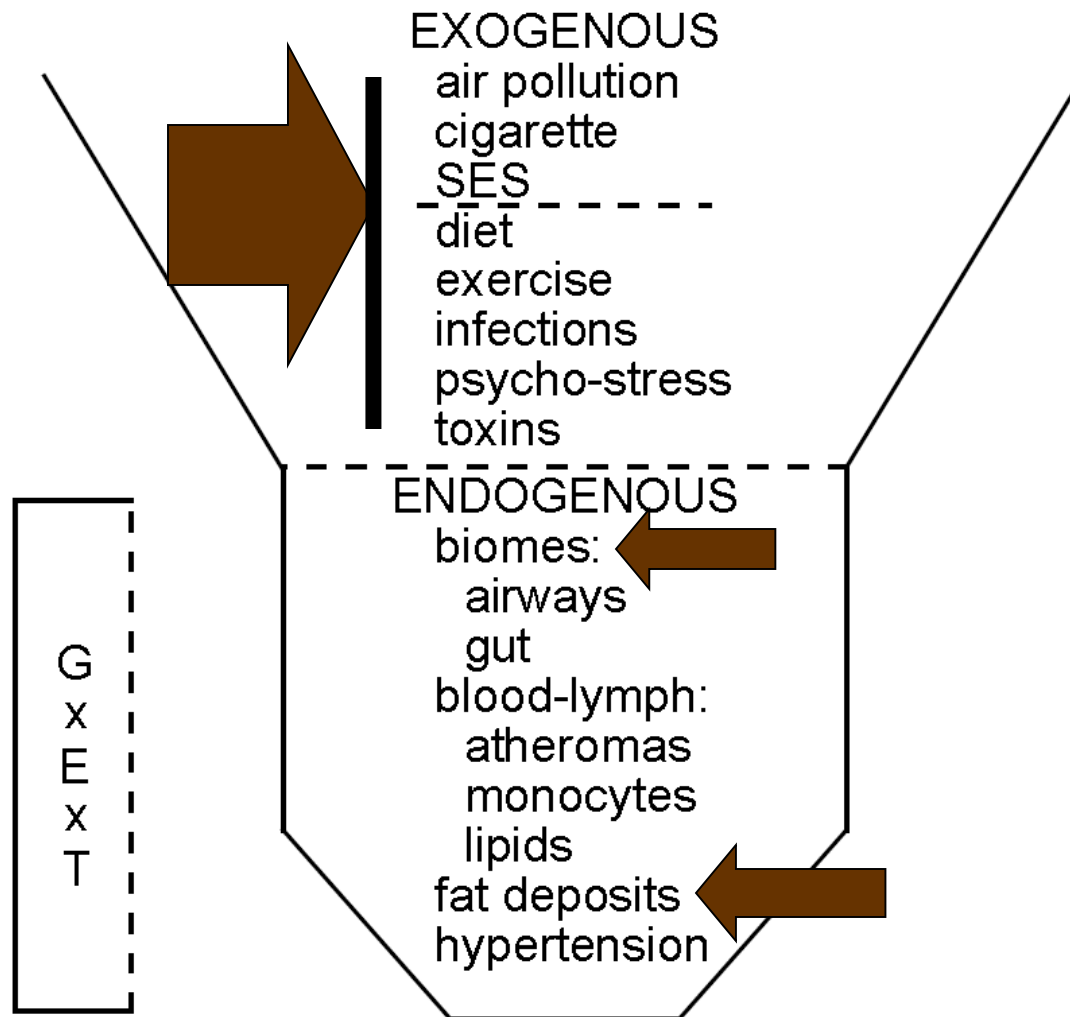
Overview of Outdoor Air, Water, Ground

Exposome Throughout Human Evolutionary History

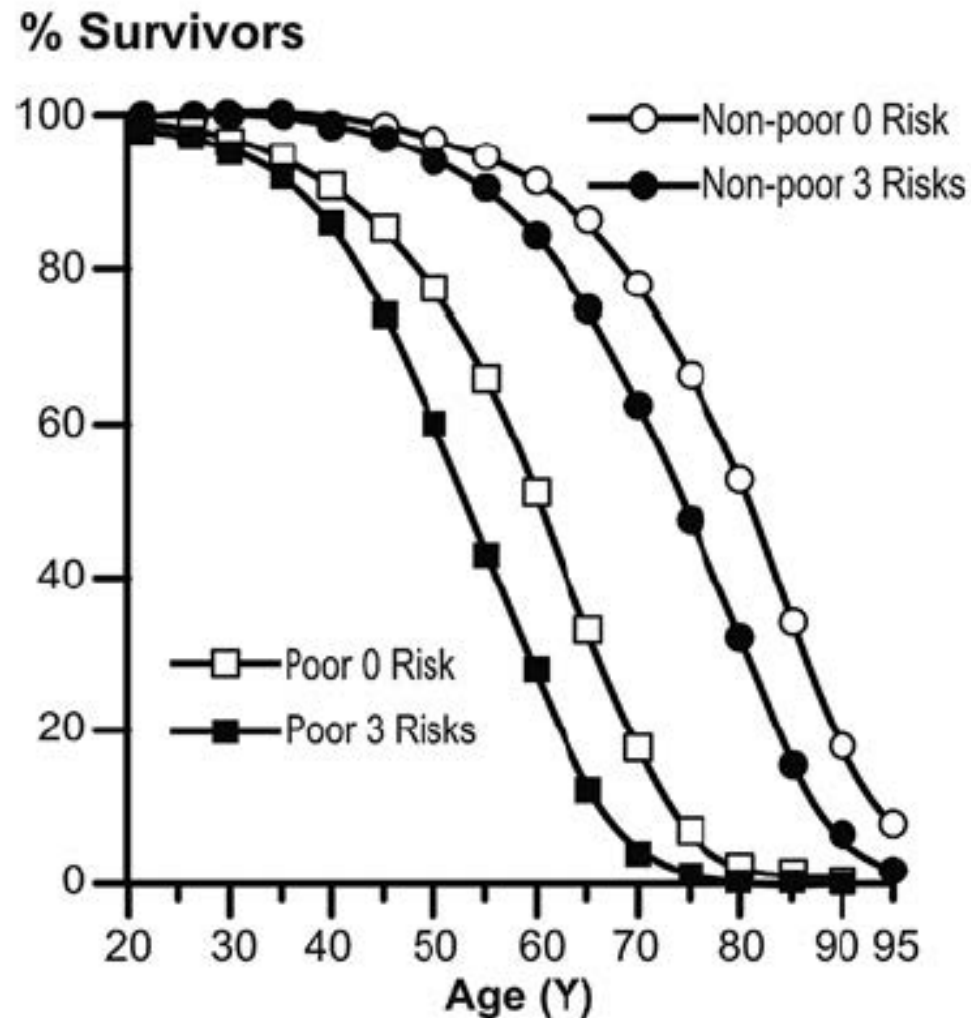


Trumble & Finch *Q Rev Biol* 2019

Gero-Exposome for cats & dogs



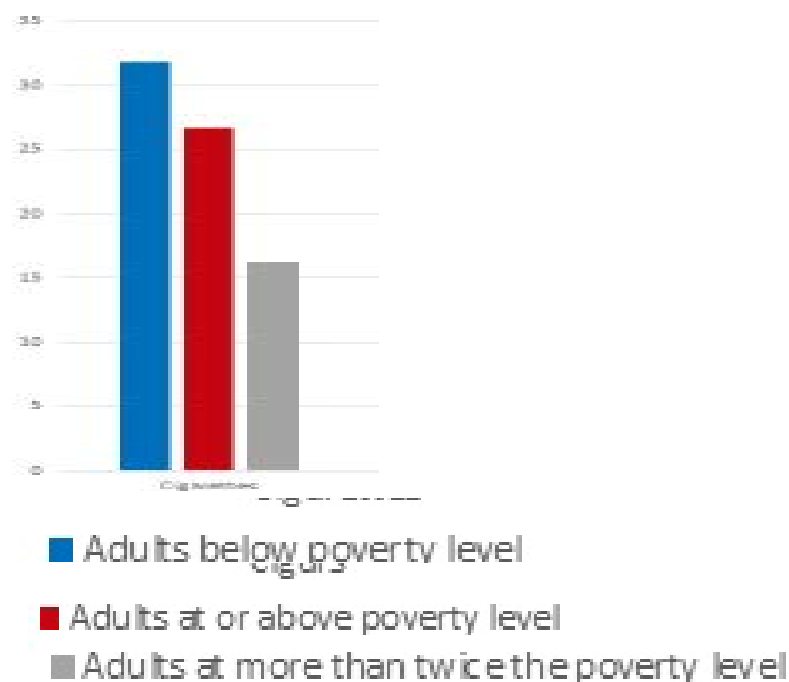
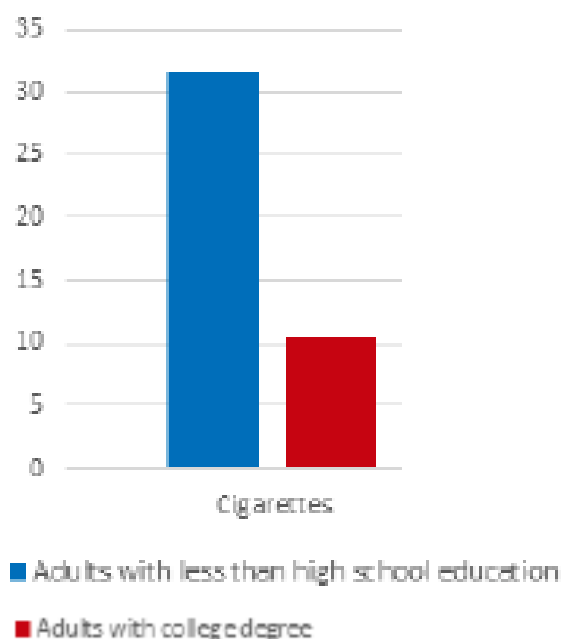
Low SES shortens lifespan: earlier onset of most diseases



Crimmins E.
J Gero 2009

What are the gerogens in poverty?

Cigarette Smoking by SES: education and poverty



<https://www.cdc.gov/tobacco/disparities/low-ses/index.htm>

Factors of companion animal neglect in the family environment in Pinhais Brazil

Monsalve 2018 *Preventive Vet Med*

- Animal abuse reports 2016, cats & dogs

Table 3

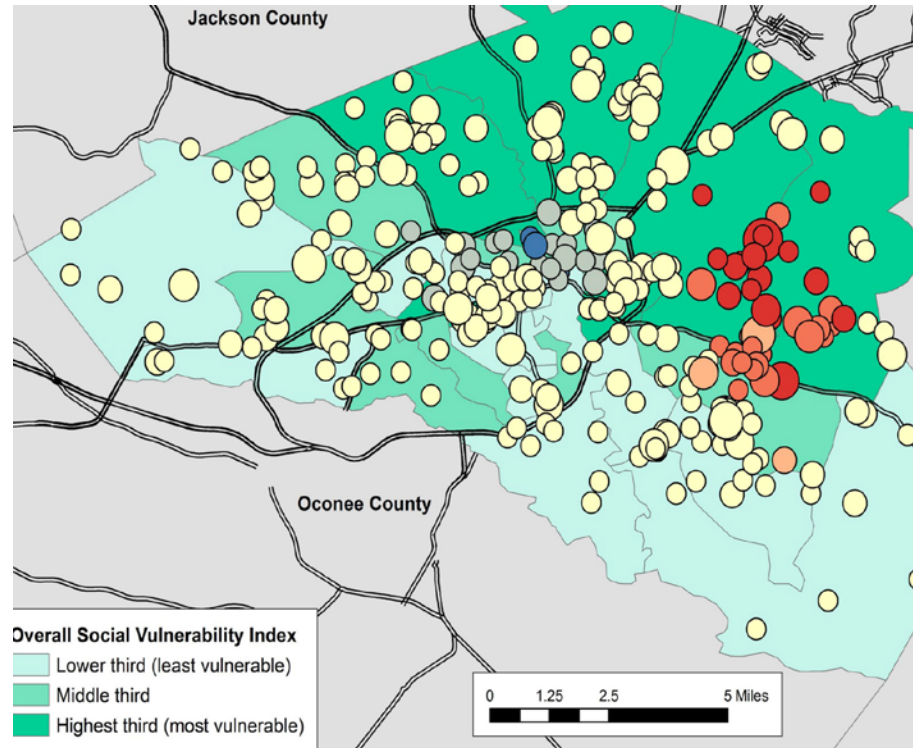
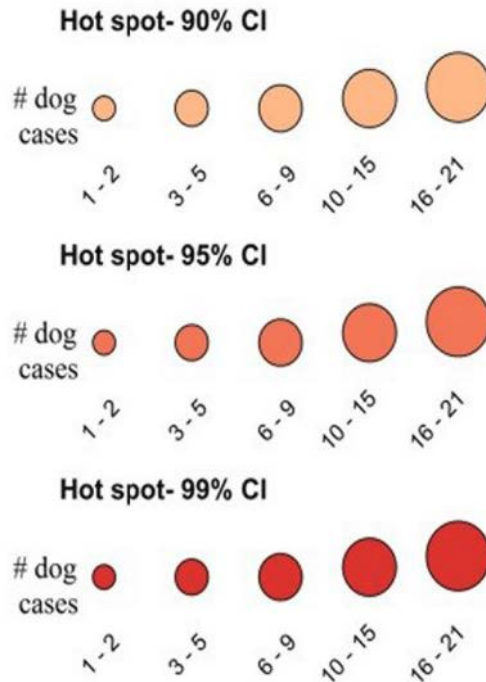
Logistic regression for the occurrence of companion animal neglect of the cases investigated by the Protection Animal Division of Pinhais, Brazil.

Variable	OR	CI - 95%	Wald test P-value
Number of dogs and cats			
1 - 2 animals			
3 - 6 animals	2.72	0.85-8.69	0.092
7 - 10 animals	0.71	0.14- 3.49	0.669
> 10 animals	0.12	0.02- 0.67	0.016
Economic difficulties	5.07	1.07- 24.08	0.041
Presence of disabled person	5.99	1.18-30.27	0.030

OR: Adjusted Odds ratio, CI: Confidence interval.

Animal shelter dog intake varies by owner SES

Georgia

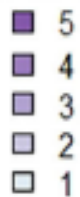


Dyer *PLoS* 2019

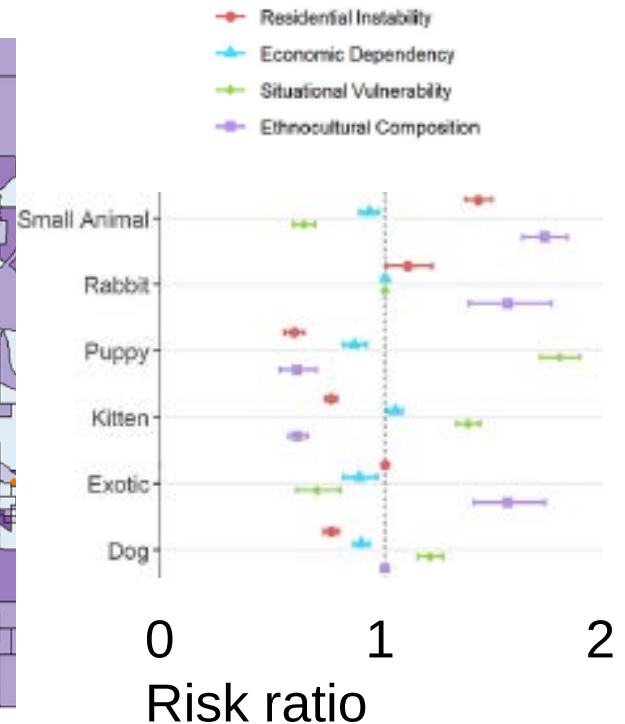
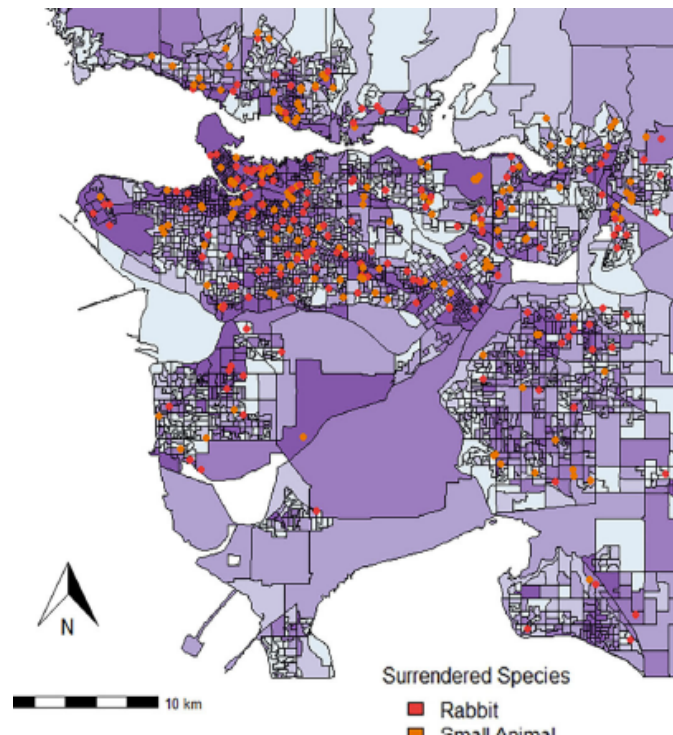
Geospatial analysis of Pet Surrender to Shelters and Human Social Deprivation

British Columbia

CIMD Quintile



*Ly Front Vet
Sci 2021*

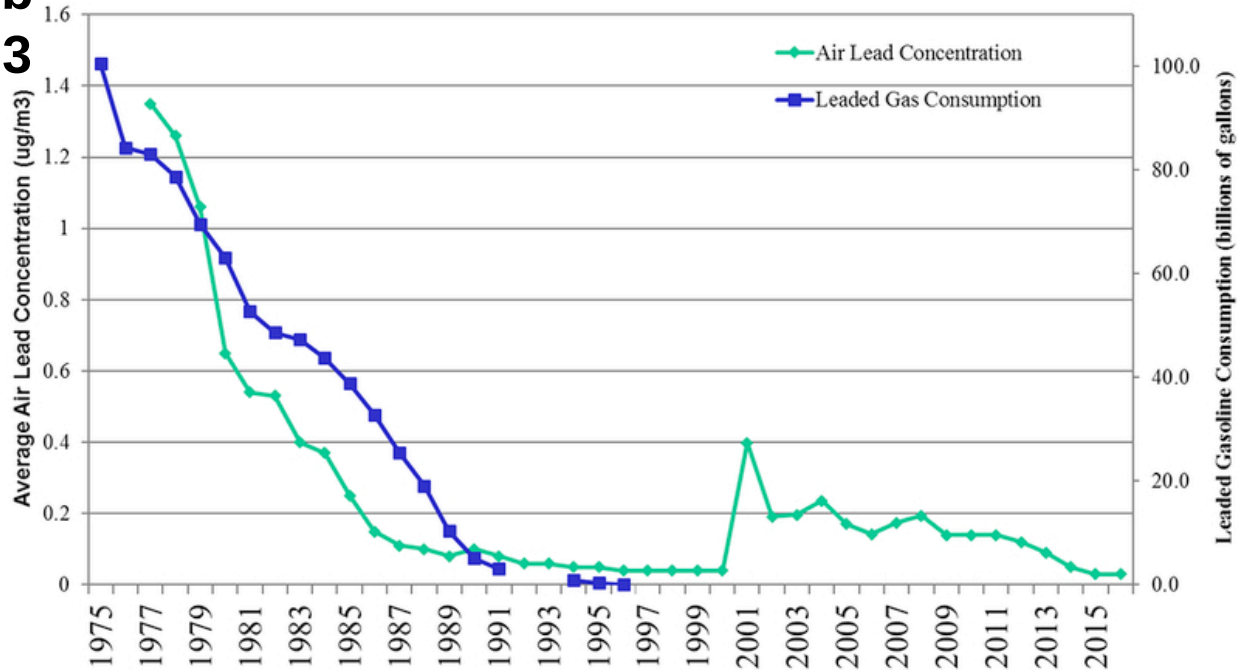


Multi-factorial associations of pet surrender include owner health, housing, income, and ethnicity

Lead exposure

gasoline 1945-1975: 3 gm Pb/gallon

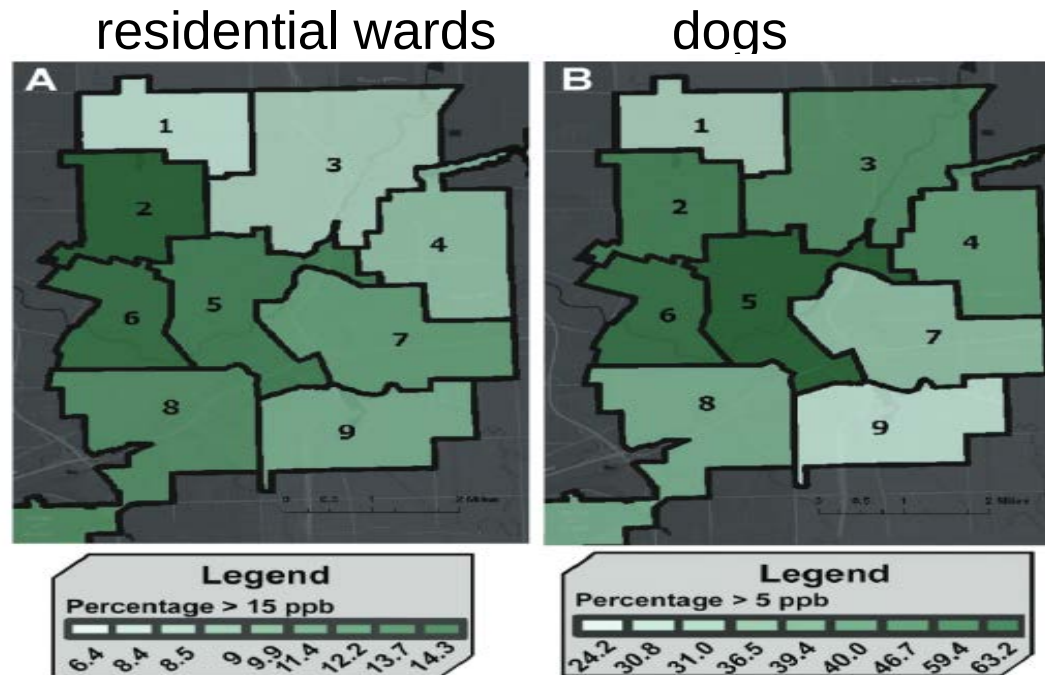
Air Pb
 $\mu\text{g}/\text{m}^3$



2020: paint contributes up to 70% of children's Pb elevations

Dignam *J Publ Health Manag Pract* 2019

- Flint Michigan blood Pb in 284 dogs
blood Pb >50 ppb in 2%; >20 ppb in 7%
no clinical grade lead toxicity



Langlois *J Am Vet Assoc* 2017

Lead poisoning in dog is not common

Stray dogs & cats, Naples Italy

[Esposito *Env Sci Poll Res Int* 2019]

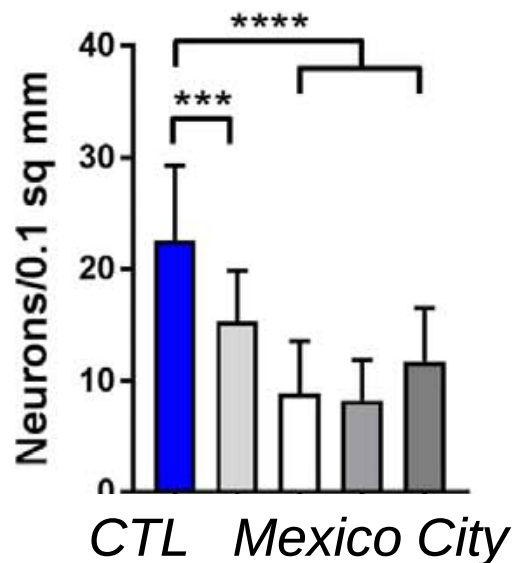
Subgroups had high Pb & Cd in liver & kidney ;
median levels 5-fold > Spanish samples

- Dogs eat lead-shot game. No reports on toxicity
[Hogasen *BMC Vet Res* 2016]
- lead-paint toxicity of dogs-cats: few case reports

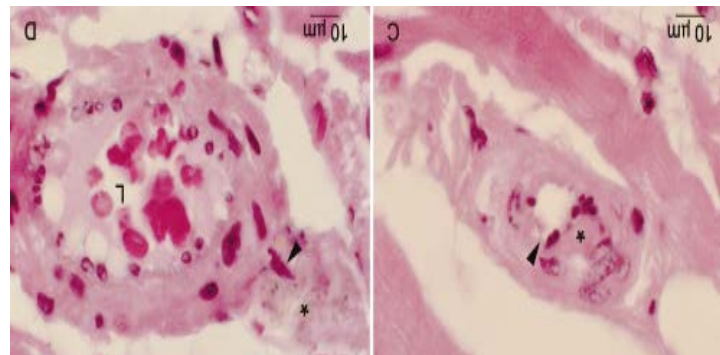
Calderón-Garcidueñas: *Canines as Sentinel Species*

AirPoll in Mexico City (MC) vs coastal city (CTL)
higher PM2.5 & poly aromatic hydrocarbons (PAH)

neuron density,
brain stem olivary nucleus



myocardium
silica-like crystals



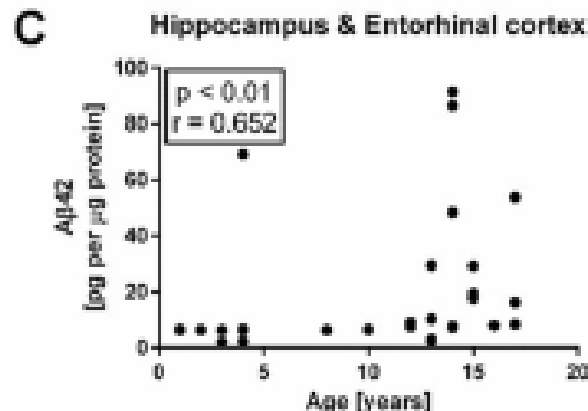
Mexico City

CTL

Canine brain aging

Urfer *GeroScience* 2021

Brain amyloid A β 42 increases with aging



Cognitive dysfunctions correlate with amyloid A β 42

Does 2nd hand cigarette smoke increase A β 42?

Alaskan sled dogs large VO₂ max & high fat diet

- Witkop *Env Intern* 2021

PM_{2.5} exposure from Alaskan wildfire PM_{2.5}>35 µg/m³

plasma SOD: 5-fold transient increase

blunted by anti-oxidant (phycocyanobilin).

- Montrose *Sci Total Env* 2015

Dog kennels differing 6-fold in PM_{2.5} exposures:
(16, 48, 96 µg/m³)

No difference in total DNAm

Global Mortality: Air Pollution and Cigarette Smoke >2x Other Top Causes

	Mortality, million/y	Loss of life expectancy, y	References
air pollution, ambient ^a	8.8 M	2.9	Lelieveld 2020; WHO 2020a
cigarette smoke primary (direct) second-hand	7.2 6 1.2	2.2	Lelieveld 2020 WHO 2020b
Infections ^b	6.7		WHO 2018
Road injuries	1.4		WHO 2018

high PM_{2.5} attributable AD: 10-20%

WIMS-US: Cacciottolo et al *Trans Psychiatr*, 2017

Ontario Canada: Chen et al *Lancet*, 2017

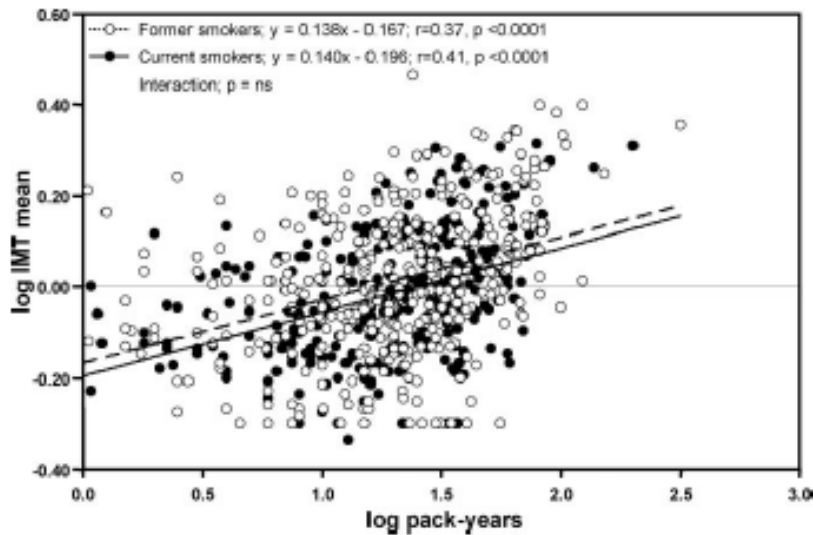
Smoking attributable AD: 11%-14%

meta-analysis **23 prospective studies**,

Barnes & Yaffe, *Lancet Neurol*, 2011

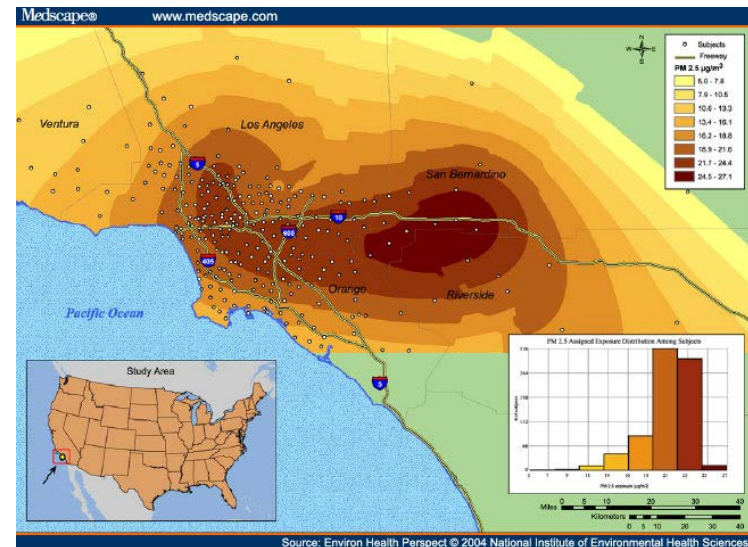
Carotid artery disease: CIMT

tobacco

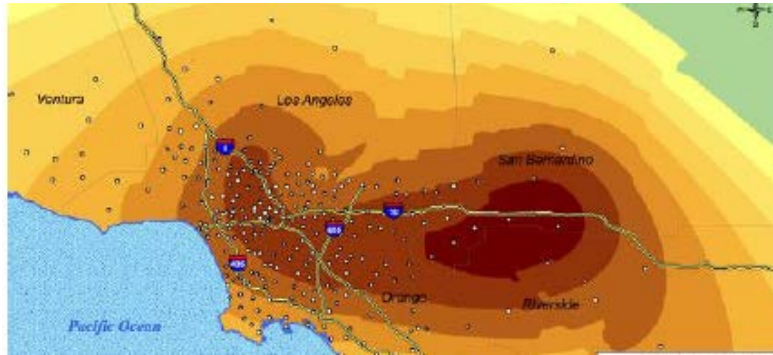


Baldassarre 2009 *Stroke*

PM2.5: 4% thicker/10 $\mu\text{g}/\text{m}^3$



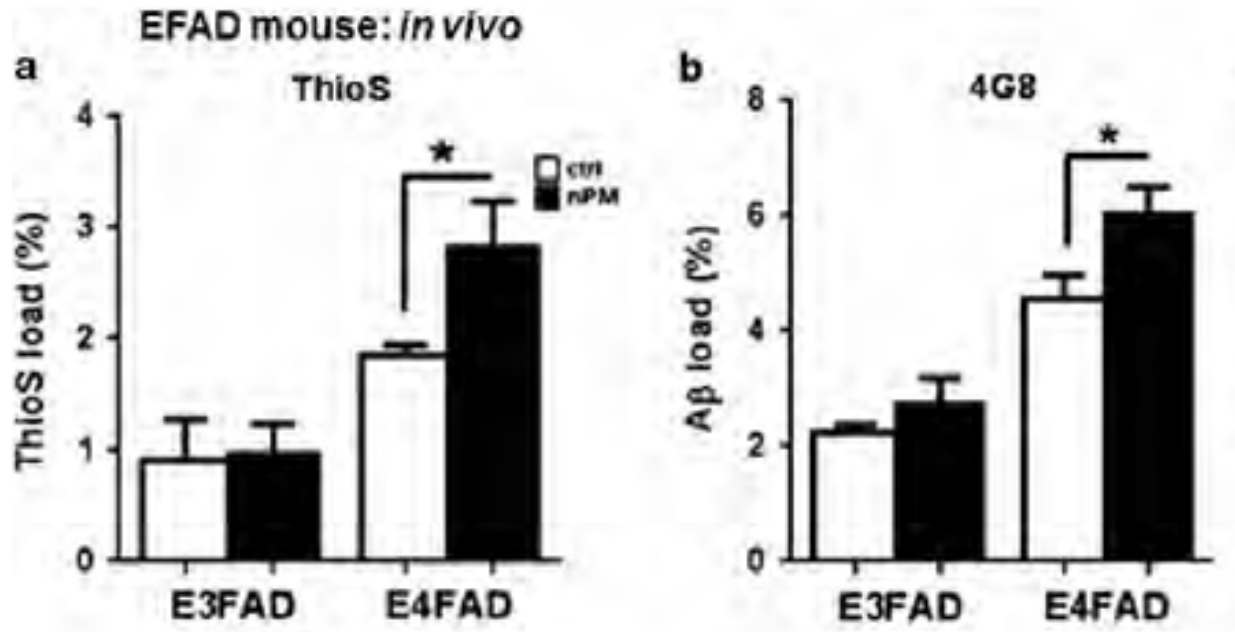
Kunzli 2010 *PLoS*



- PM_{2.5} & with lower verbal learning ($\beta = -0.32$ per $10 \mu\text{g}/\text{m}^3$ PM_{2.5}).
- NO₂ >20 ppb, lower logical memory.
- O₃ >49 ppb, lower executive function

Gatto et al Components of air pollution and cognitive function in middle-aged & older adults in Los Angeles. Neurotoxicology, 2014.

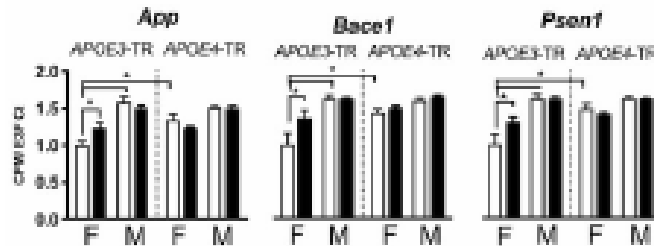
AirPoll increases brain amyloid more in E4FAD mice



Cacciottolo et al 2017, *Transl Psych*

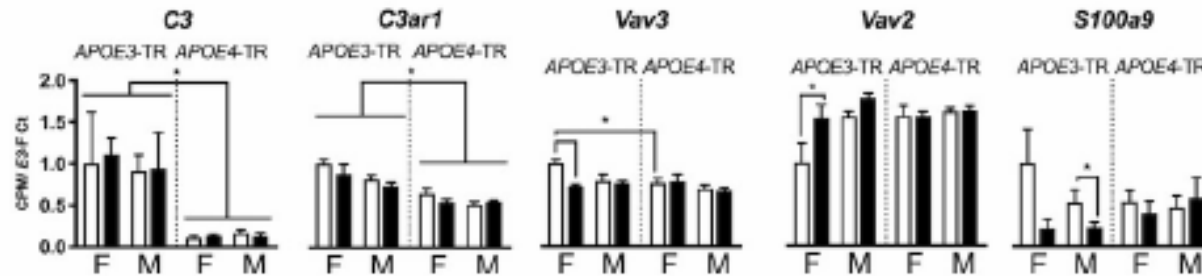
Amyloid metabolism genes in ApoE-TR mice: ApoE3-females respond more to nPM

A. Amyloidogenesis genes



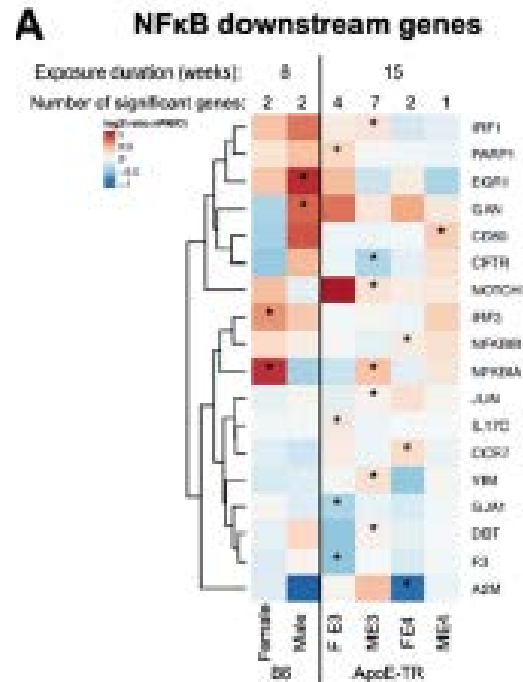
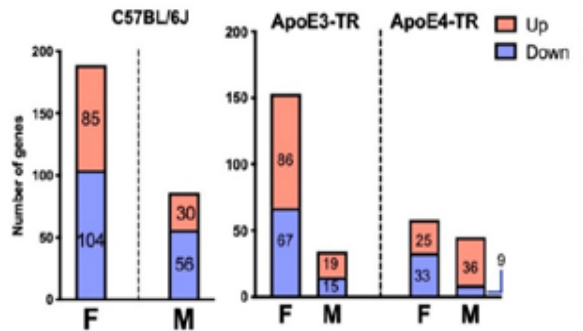
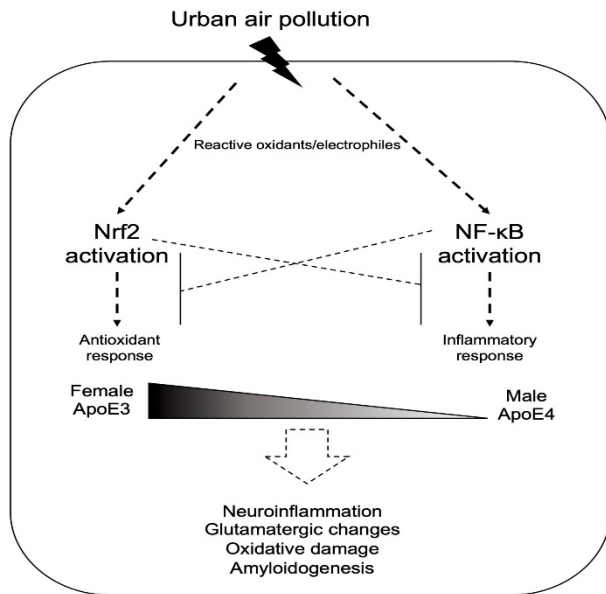
nPM Batch 2012

E. Genes associated with amyloid clearance



Haghani *eLIFE* 2020

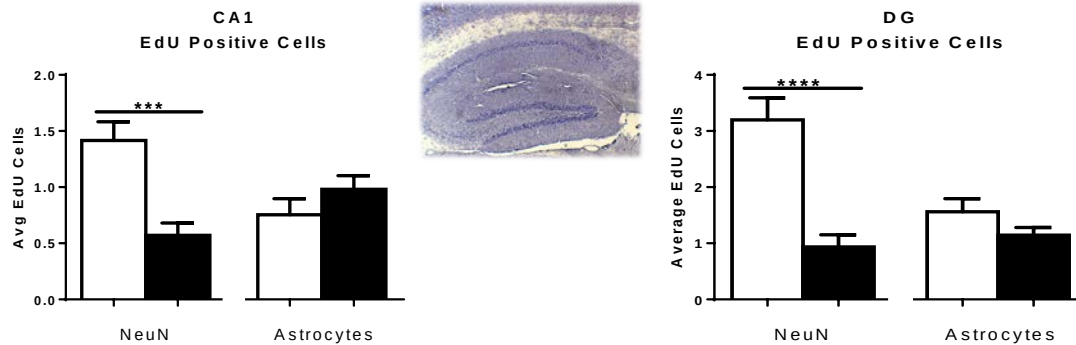
Mouse brain transcriptome responses to inhaled air pollution matter differed by sex & APOE in Nrf2-Nfkb interactions



Gestational AirPoll exposure alters adult neurochemistry, behaviors, & body metabolism by sex

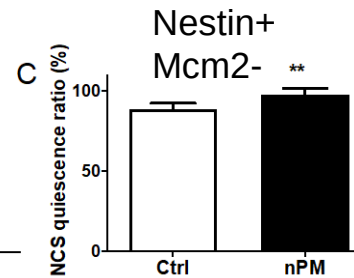
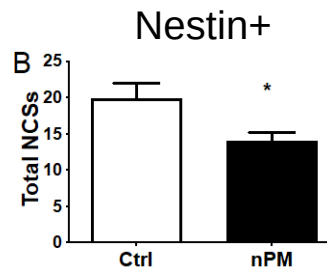
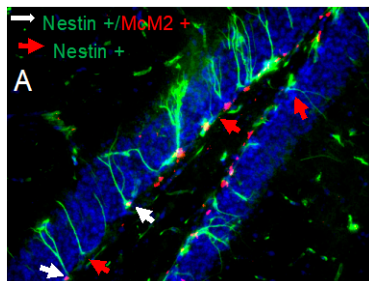
- Adult neurogenesis and neural stem cells
- Adipose depot response to fatty diet
- Cerebral cortex transcriptome
- Anxiety-depressive behaviors

Gestational nPM exposure impairs adult neurogenesis



Haghani [eLife](#) 2020
nPM Batch 2012

Neural stem cells (NSC): Total quiescent



Haghani eLife

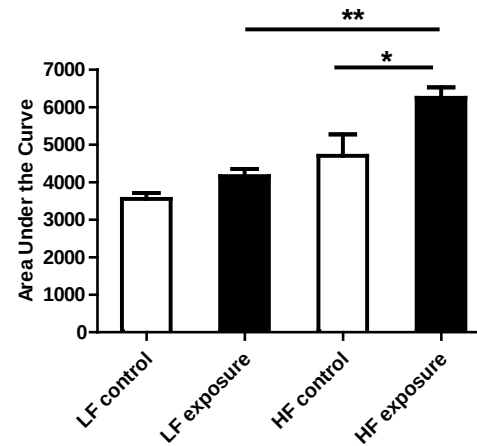
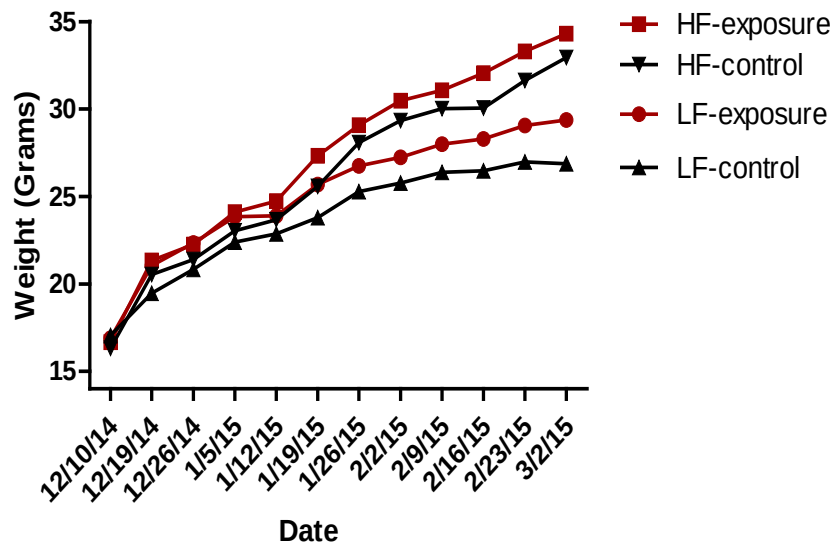
2020

nPM Batch 2012

Gestational PM

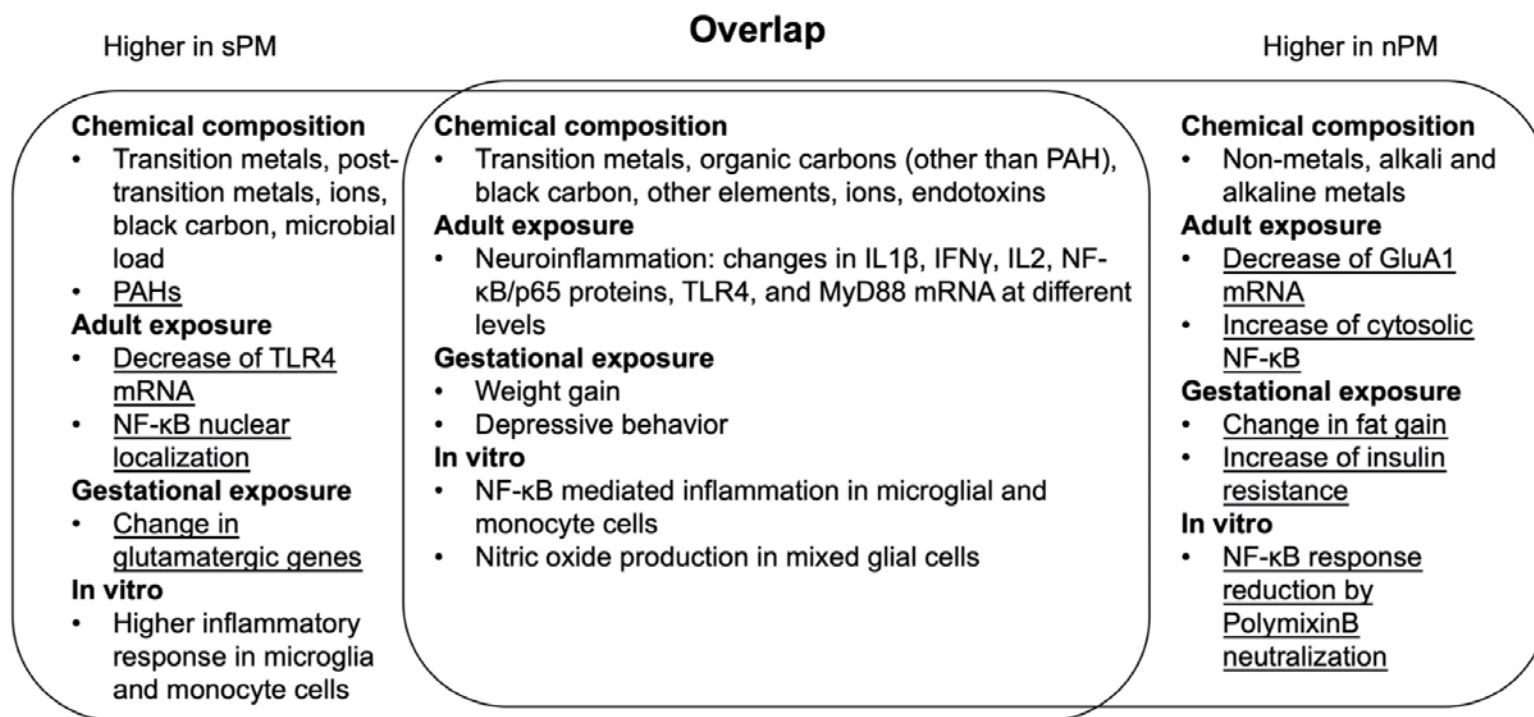
high fat diet induced more adult obesity & glucose intolerance

Males- Weight

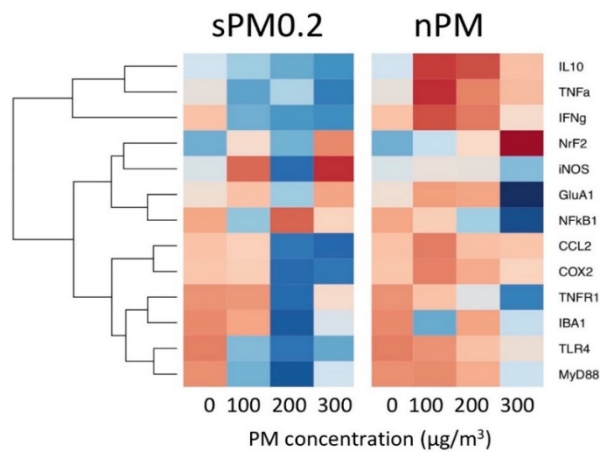


Defining active components in AirPoll polycyclic aromatic hydrocarbons (PAH)

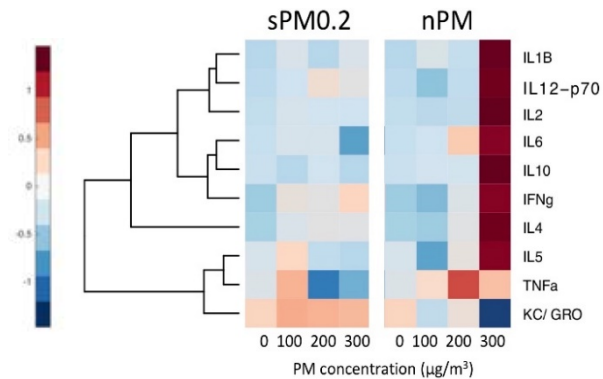
Compare total PM_{2.5} (sPM) vs nPM lacking PAH



Cerebral cortex Nrf2 & NF κ B1
divergent responses to nPM & sPM



Serum cytokines
mostly parallel responses



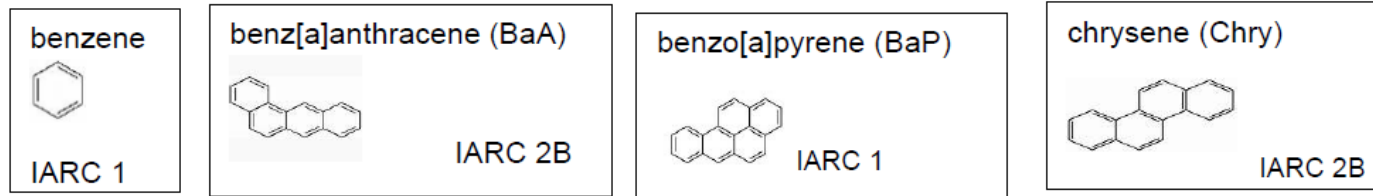
Haghani *Env Int* 2020; nPM Batch 5, 2017

Mal-convergent Smokes in CigPoll: Air pollution (AAP) & Cigarettes (CS)

	AAP	CS	AAP-CS synergies
Atherosclerosis carotid coronary	Aguilera 2016; Liu 2015 Hartiala 2016; Kaufman 2016	Hansen 2016, Huang 2016 Benziger 2016, Nicoll 2016	1.1 fold excess Burnett 2014
Cancer lung	Hamra 2014; Cui 2015	Doll 2004; Chen 2015	2.2fold excess Burnett 2014, Turner 2014
Metabolism insulin sensitivity BMI, children	Wolf 2016, Thiering 2016 McConnell 2015	weak or no association	1.3 fold excess McConnell 2015
Brain aging grey matter atrophy myelin atrophy cognitive decline	Chen 2015 Casanova 2016 Ailshire 2014 Cacciottolo 2017;	Karama 2015; Prom-Wormley 2015	1.9 fold excess Ailshire 2014
Alzheimer disease	Cacciottolo 2016; Oudin 2016; Jung 2015; Kulick 2020	Barnes 2011; Durazzo 2014; Deochand 2016	
Stroke	Sheers 2015; Wang 2014	O'Donnell 2011;	

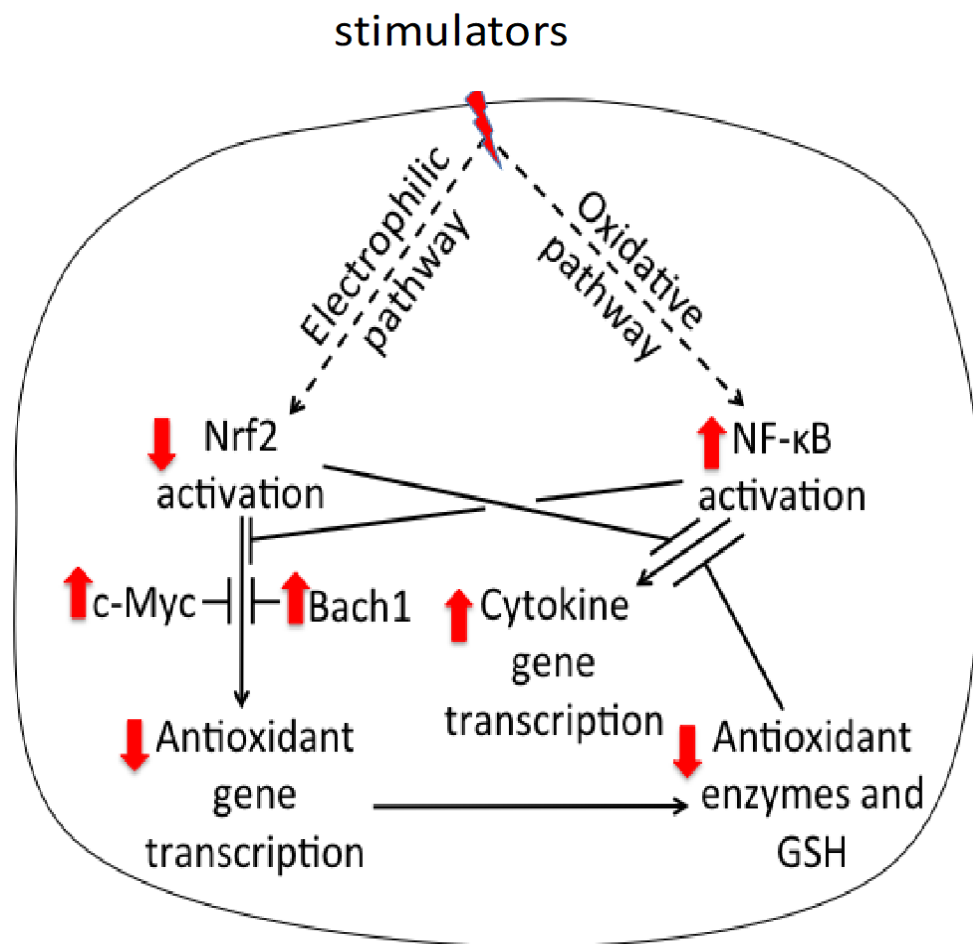
Fossil fuels and cigarettes

- Fine particles (PM_{2.5}) deposited in lungs
- Incompletely burned carbon carcinogens: polyaromatic hydrocarbons (PAH)



- Toxic metals: iron, copper

Detox pathways shared in Cig-Poll



Forman & Finch, *FRBM* 2018