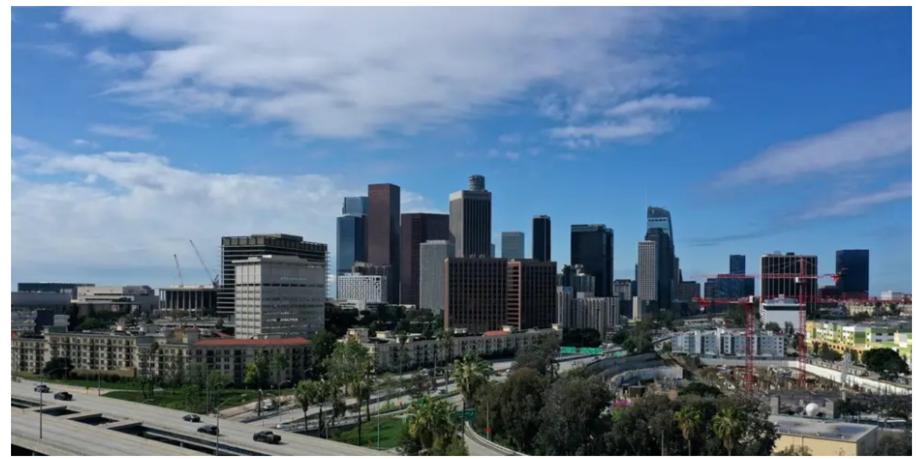
Outdoor air pollution and malignant brain cancer: The Multiethnic Cohort Study



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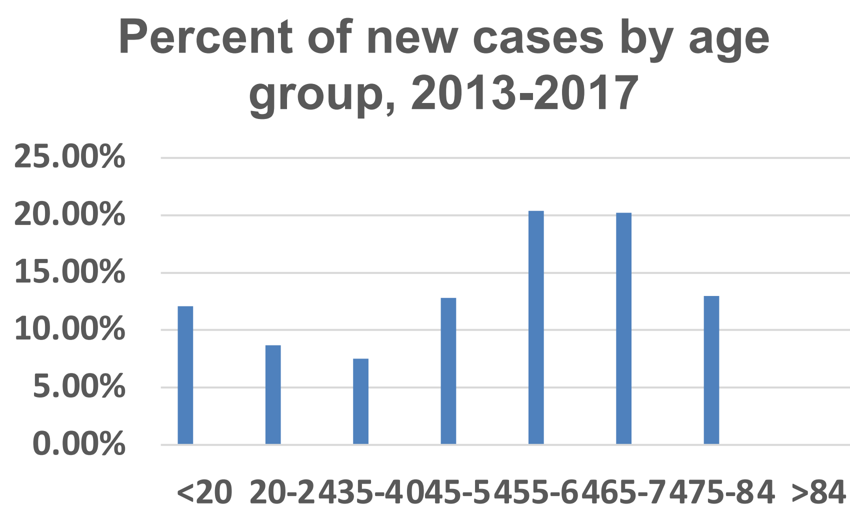
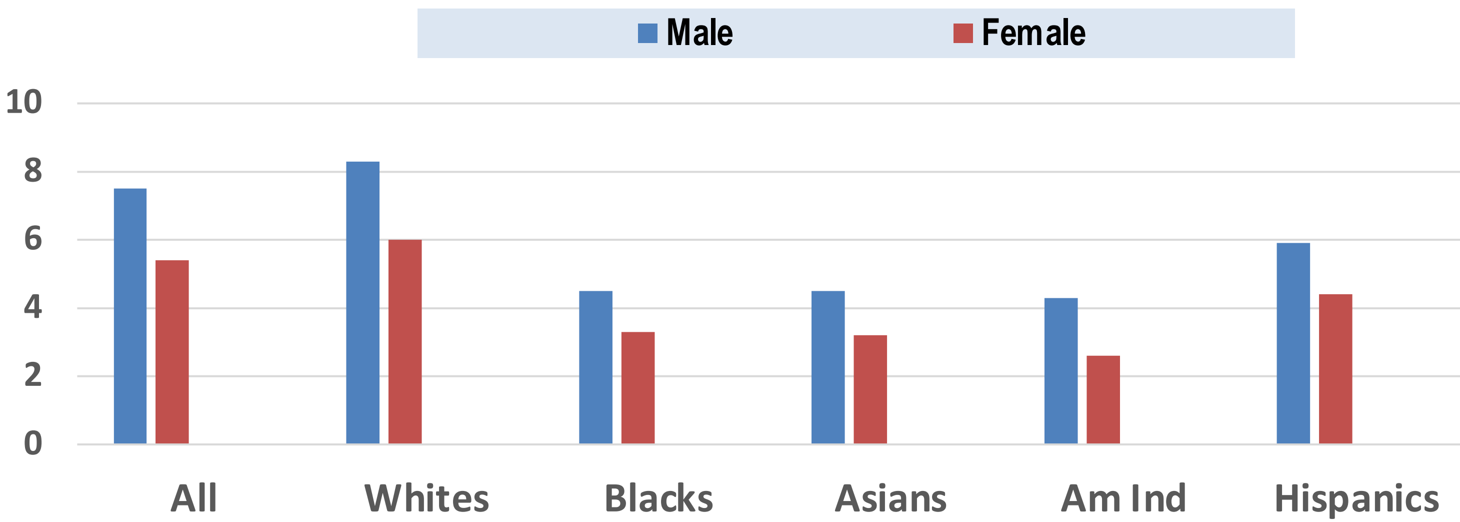
Malignant brain cancers in the U.S.

- Incidence 7.1/100,000/yr
- 24,970 new malignant brain cancers/yr
- ~1.3% of all new cancer cases

- Mortality 4.4/100,00/yr
- 18,020 deaths/year, ~3.0% of all deaths
- 5yr survival rate 36.0%

Ostrom et al. 2020





Risk factors

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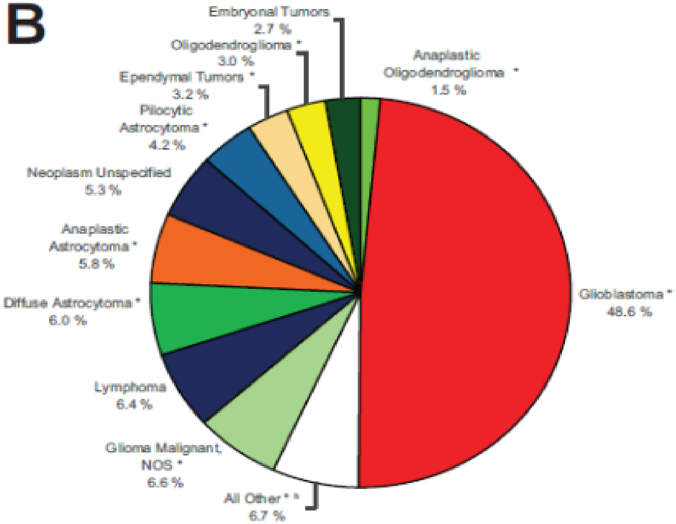

Risk factors	Glioma
Established risk factors	
High-dose radiation	Positive (+++)
Male vs female gender	
White vs African American	Positive (+)
Increasing age	Positive (+++)
Probably risk factors	
Allergies/asthma	Negative (-)
Elevated IgE	Negative (-)
Chickenpox/antivaricella zoster	Negative (-)
Not risk factors: diagnostic radiation, head injury, power lines/EMF, smoking, alcohol, cell phone	

AIR POLLUTION- risk factor?

Air pollution and adult brain cancers

- **3 U.S. studies**
  - gaseous and PM pollutants- exposures were assigned at the census block group level
  - null findings
- **1 Canadian study**
  - ultrafine particles (UFP), $PM_{2.5}$ and NO_2
  - positive association with UFP but not other pollutants
- **6 European studies**
  - gaseous and PM pollutants
  - mixed results

Outdoor air pollution and brain health

- **Air pollutants**
  - **PM pollutant, diesel exhaust and benzene- classified as class 1 carcinogen**

- **Air pollution and central nervous system (CNS):**
  - **Small inhaled particles (<0.1 µm, UFP) may affect the CNS directly through the transport into the CNS or vis systemic inflammation**
  - **Potential effects on chronic brain inflammation, microglia activation, and white matter abnormalities leading to neurodegenerative diseases (e.g., PD, AD), multiple sclerosis, stroke, and autism spectrum (Block et al., 2012)**

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Purpose of Multiethnic Cohort (MEC) Study:

To examine lifestyle and environmental risk factors as well as genetic susceptibility in relation to the causation of cancer.

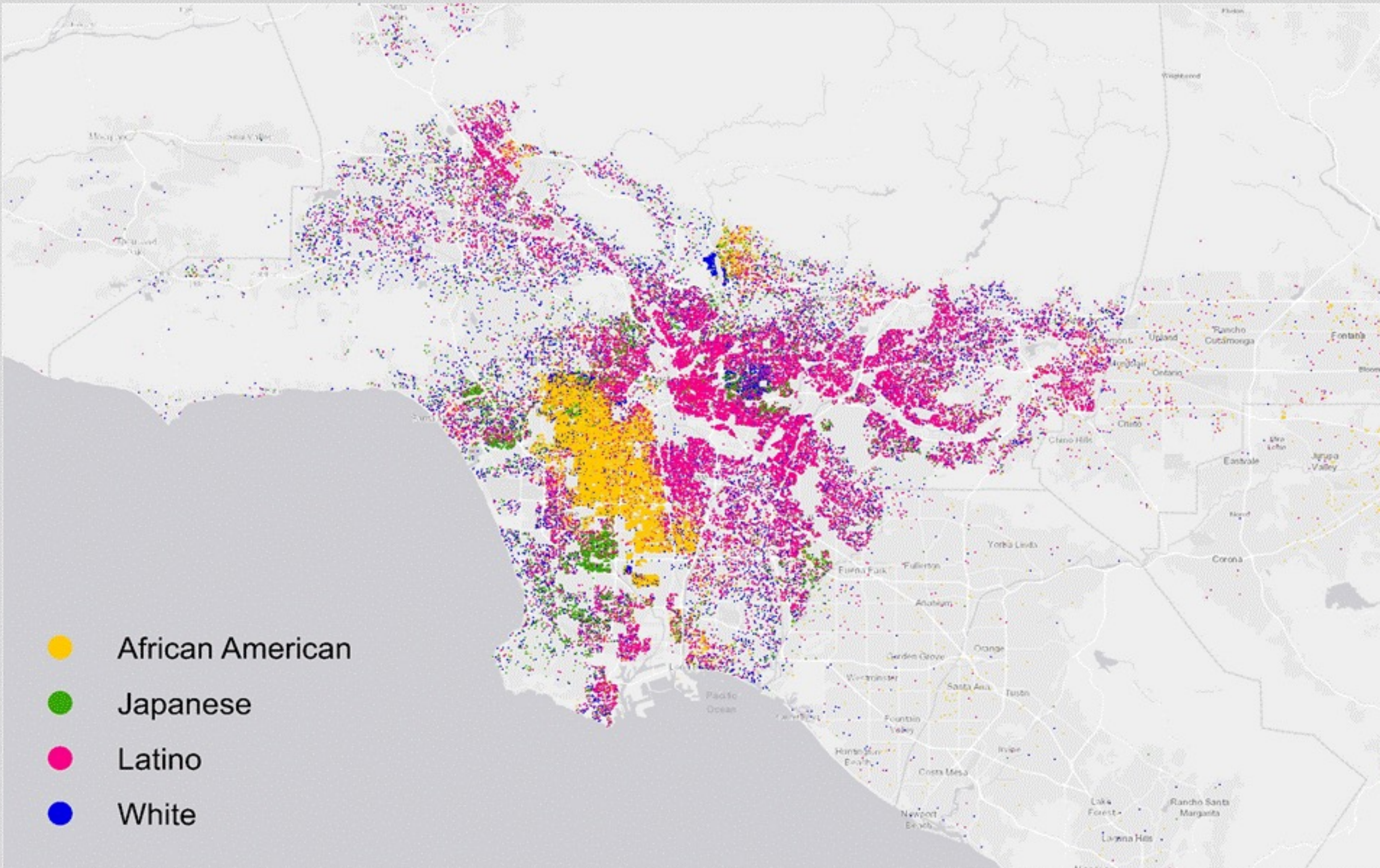
- **Funded by NCI since 1993**
- **Population-based study of >215,000 men & women**
  - **Residents of California (mostly Los Angeles County) and Hawai'i**
  - **African American, Japanese American, Latino American, Native Hawaiian, and White participants**
- **Ages 45-75 at enrollment**

NCI U01 CA164973 MPI: Le Marchand, Haiman, Wilkens

Overall study goals

- **To examine the risk of malignant brain tumors in relation to exposure to gaseous and particulate matter pollutants, ultrafine particles, and benzene in the MEC study**
  - **By sex**
  - **By race and ethnicity**

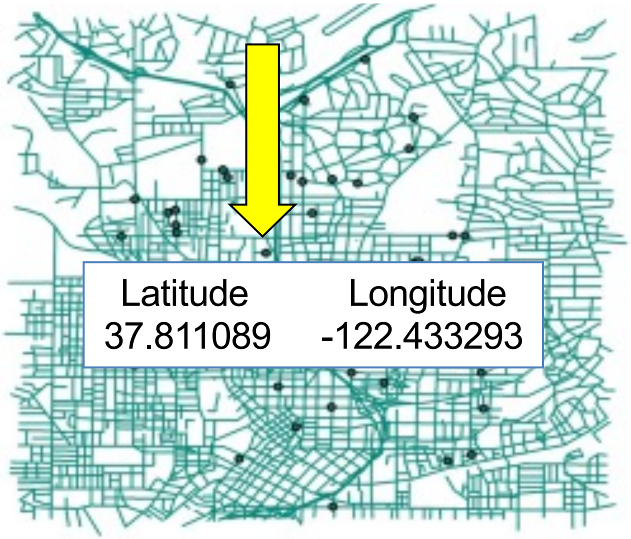
MEC participants: Los Angeles County



Baseline | 1997| 1998| 1999| 2000| 2001| 2002| 2003| 2004| 2005| 2006| 2007| 2008| 2009| 2010| 2011| 2012| 2013

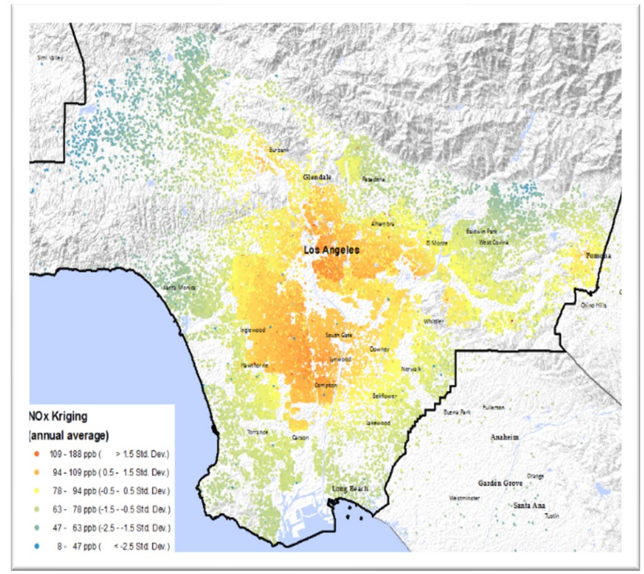
Air pollution exposure assessment

Address	City	State	Zip
342 Royal Dr	Los Angeles	CA	90010



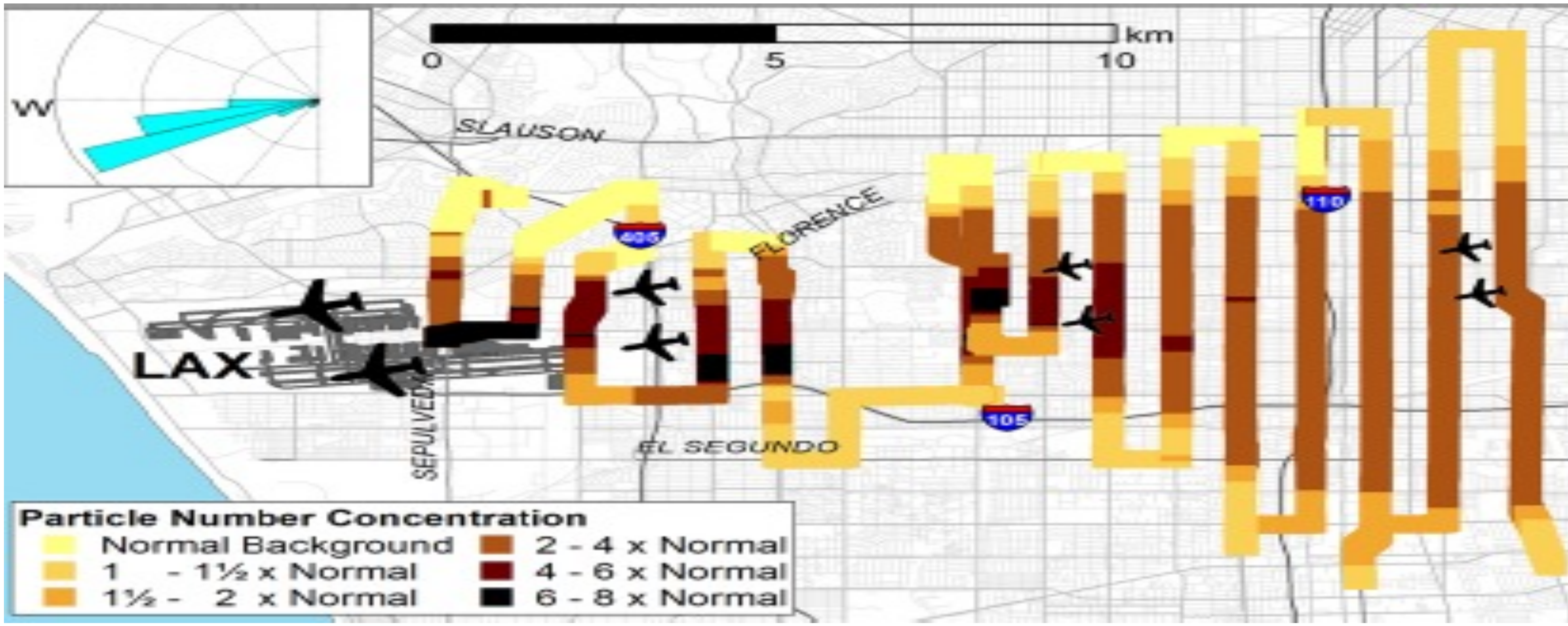
Linkage with state and government air pollution data, capturing factory, traffic, trains, ships, biomass sources

Kriging interpolation:
NO_x, NO_2, PM_{10}, $PM_{2.5}$



Estimate average air pollutant exposure, largely traffic-related, across the residential history for each participant in Los Angeles County

Airport-related UFP- Los Angeles International Airport



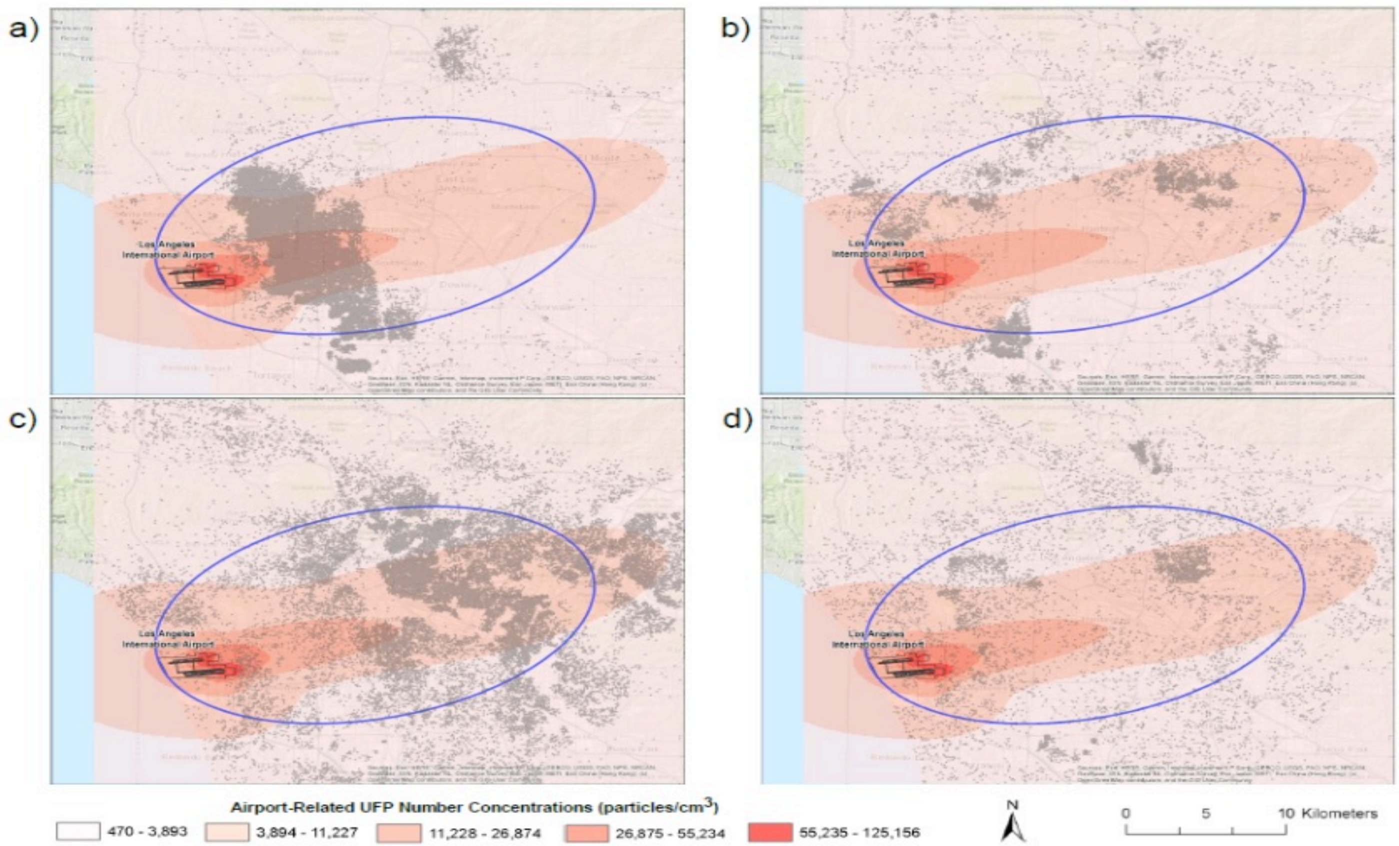
UFP emissions from landing jets at LAX - a doubling of concentrations of UFP in an area of 25 square miles east and downwind of LAX (Hudda 2014)

Obtained average annual UFP concentrations from jet emissions for LA County from 1993 to 2014; model everywhere in LA County with MEC participants within 16 km range

Airport-related ultrafine particles

African Americans n=25,398

Japanese Americans n=9,532



Latino American n=31,568

European Americans n=9,328

Prospective data integration: 1993-2013

Environmental pollutants

Neighborhood socioeconomic status

Questionnaire data

Malignant Brain Cancer Surveillance

California Cancer Registry

Study approach

- Link geocoded addresses across follow-up to monthly/yearly air pollutant exposure estimates
- Calculate monthly/yearly average pollutant exposure from study entry (baseline/diagnosis) to study end date (diagnosis/death/end date) for each participant
- Conduct Cox proportional hazard regression with time-dependent exposures
- Scale HRs to a fix unit change of pollutant or by IQR
- Adjust models for age, race, ethnicity, sex, relevant risk factors, nSES at entry and at exit
- Test for heterogeneity by sex, race/ethnicity, distance from major roads, and moving status

Study population, 1993-2013

Race and ethnicity	Case (n) *	Cohort (n)*
African American	38	25,398
Japanese American	19	9,532
Latino American	72	31,568
White	26	9,328
All groups	155	75,936

* N=210 brain cancer among 100,460 CA MEC participants in analyses of PM and gaseous pollutants

Risk of malignant brain cancer and air pollution exposures

Air pollutant	Unit	Men HR (95% CI)*	Women HR (95% CI)*
Kriging NO_2	20 ppb	2.1 (0.8-6.4)	0.6 (0.3-1.5)
Kriging PM_{10}	10 µg/m^3	1.8 (1.0-3.2)	0.9 (0.5-1.5)
Kriging $PM_{2.5}$	10 µg/m^3	2.2 (0.5-9.8)	0.8 (0.2-2.8)
Benzene	1 ppb	3.5 (1.6-7.6)	0.8 (0.2-2.8)
UFP (All)	5,280 p/m^3	1.1 (0.9-1.3)	1.2 (1.0-1.4)
UFP (African Americans)		1.3 (1.1-1.6)	

*Adjusted for race and ethnicity (all), sex, education, BMI, marital status, asthma, occupation, smoking, nSES at baseline and current

Wu et al., *JNCI Cancer Spectrum* 2020, Cancer Research 2021

Risk of malignant brain cancer and airport-related UFP - co-pollutant models

Air pollutant	HR (95% CI)
UFP particles/cm^3 (per IQR)	1.14 (1.00-1.30)
PM_{10} (per 10 μg/m^3)	1.54 (0.77- 3.10)
UFP particles/cm^3 (per IQR)	1.12 (0.99-1.28)
Benzene (per 1 ppb)	1.42 (0.76- 2.66)

IQR = 5,280 particles/cm3

Ref: Wu et al., *Cancer Research (i2021)*

UFP results- MEC and Canadian study

Factors	MEC	Canadian Study
UFP assessment	Airport related – EPA dispersion (flight patterns, meteorology, etc) address hx 20+yrs	Within city – LUR model assigned to addresses (6-digit postal codes), 3 yrs averages
Brain Cancers	155	1,400
UFP HR (95% CI)	1.14 (1.00-1.30)	1.13 (1.03-1.35)
PM_{10}, $PM_{2.5}$	positive, P>0.05	HR <1.00
Covariates	Sex, race, ethnicity, nSES, education, $PM_{2.5}$, smoking, occupation, BMI, hypertension, reproductive factors	SES, $PM_{2.5}$, NO_2, indirect adjustment for smoking and BMI

Summary

- Need further studies of UFP exposures from aircrafts and within city sources
- Refine UFP measurements from all sources
- Examine UFP and other pollutants in multipollutant models
- Determine the biological effects of UFP and risk of development of brain and other cancers

Study Team

- USC: Anna Wu, Wendy Setiawan, Dan Stram, Chiuchen Tseng, Scott Fruin, Thomas Chen
- UCSF: Iona Cheng, Salma Shariff-Marco, Juan Yang
- UCI: Jun Wu, Shahir Masri
- UCLA: Beate Ritz
- U of Washington: Timothy Larson
- Funded by the Health Effects of Air Pollution Foundation- part of the South Coast Air Management District:

Thank You

Correlations between various air pollutants

Pearson correlation coefficients	Kriging NO_x	Kriging NO_2	Kriging O_3	Kriging CO	Kriging PM_{10}	Kriging $PM_{2.5}$	Benzene	UFP
Kriging NO_x	1.000	0.90	-0.74	0.86	0.56	0.68	0.76	0.07
Kriging NO_2		1.00	-0.56	0.85	0.78	0.73	0.82	-0.12
Kriging O_3			1.00	-0.29	-0.12	-0.44	-0.41	0.05
Kriging CO				1.00	0.60	0.45	0.88	0.05
Kriging PM_{10}					1.00	0.74	0.59	-0.19
Kriging$PM_{2.5}$						1.00	0.41	-0.10
Benzene							1.00	-0.03
UFP								1.00