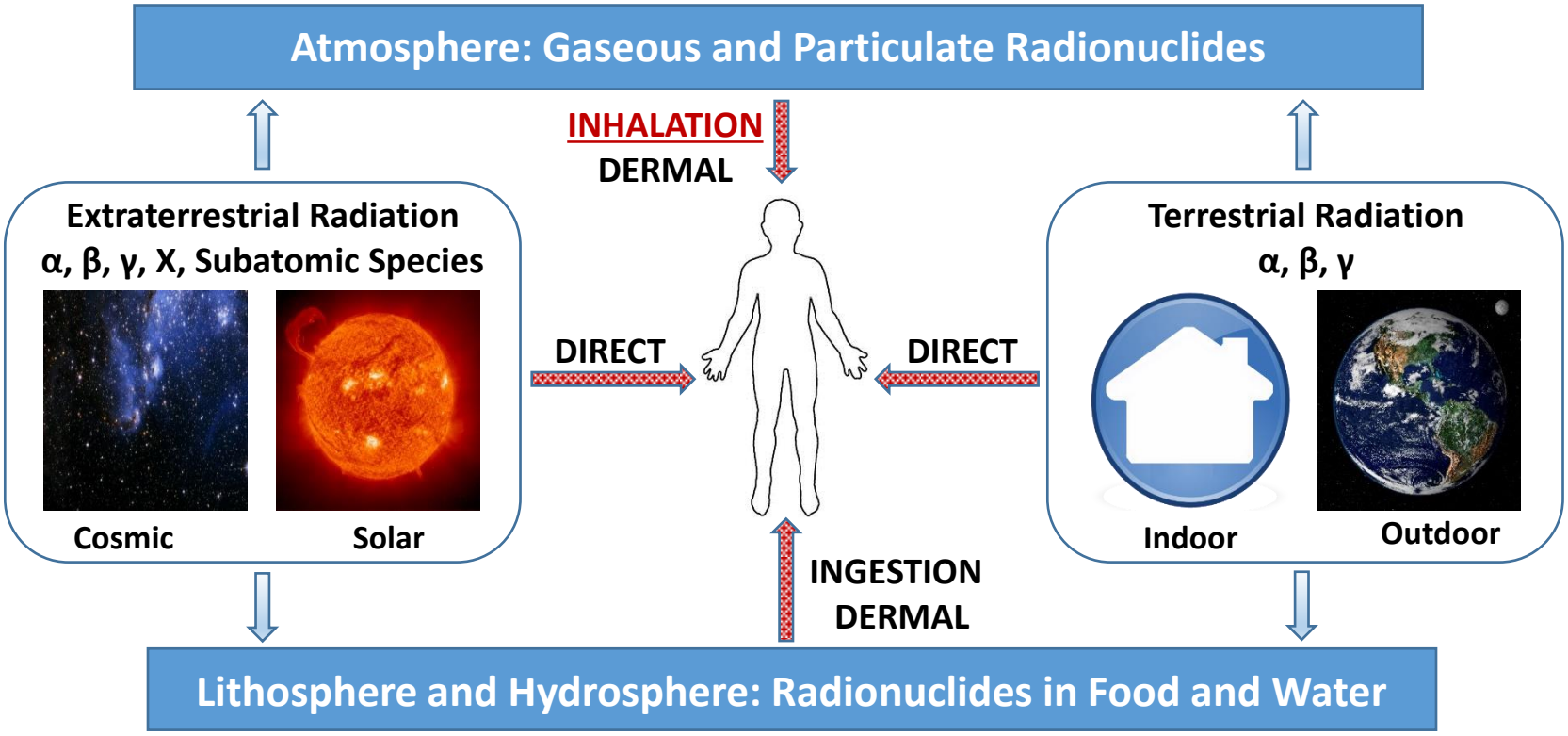
Health Effects of Ambient Particle Radioactivity

Petros Koutrakis,
Harvard University

ACE SAC, June 30 2018

Exposures to Environmental Radiation



Our Hypothesis

- PM carry radioactive nuclides that that emit α, β and γ
- PM have α, β and γ activity → Particle Radioactivity (PR)
- PM - attached radioactive nuclides can deposit onto the lungs or translocate

α – particles emitted by PM are toxic

- Large mass (two protons and two neutrons) and large positive charge
- Some of the radionuclides ^{214}Po and ^{210}Po have high energies (2 to 5 MeV)
- High Linear Energy Transfer (LEF) (Amount of energy released per distance)
- α-particles may result in greater damage in nearby cells
- The equivalent absorbed dose of radiation from α-particles is 20 times than that of β-particles (Youn et al)
- α particles do not penetrate the epidermis
- α exposure pathways are inhalation and digestion

Yoon JY, Lee JD, Joo SW, Kang DR. Ann. Occup. Environ Med 2016;28:15. PMCID:PMC4807540

Radon Exposure Enhances PM Effects on Mortality: A Time Series Analysis on Air Pollution Mortality in 109 U.S. Cities

Annelise Blomberg et al.

Submitted to Environment International

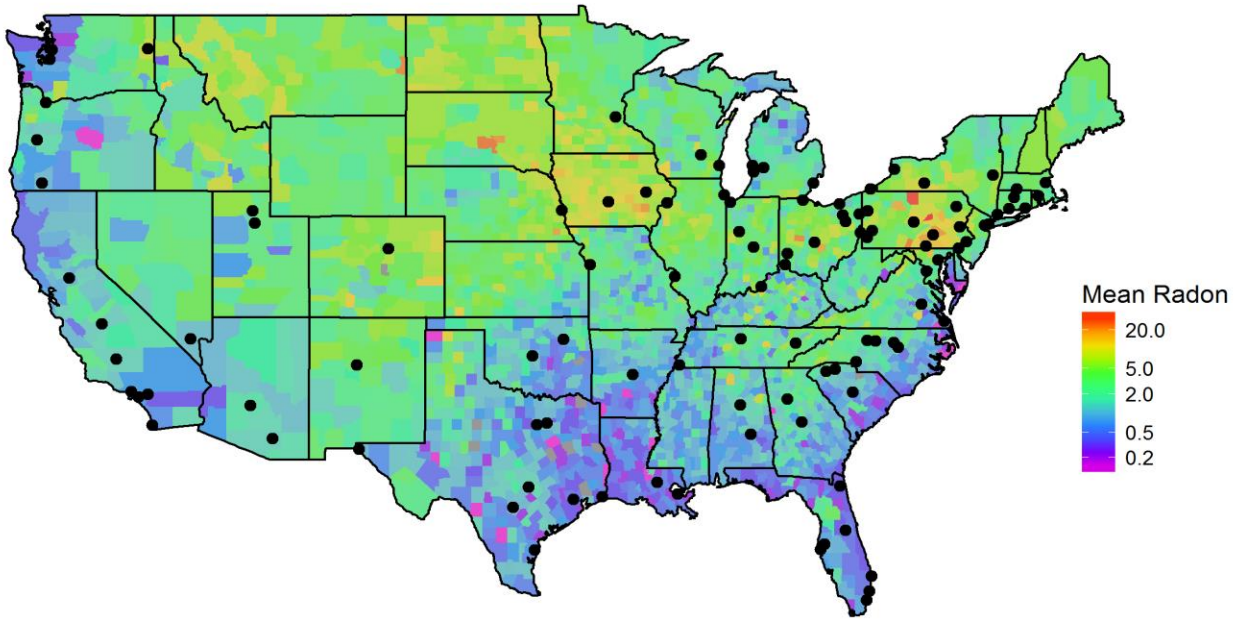
Poster this afternoon

U.S. Rn Concentrations

State Residential Radon Survey:

- 60,000 measurements collected 1987-1992
- Short-term charcoal canister samplers located in lowest level of house
- Calculate **mean-county** radon concentrations

U.S. Rn Concentrations (pCi/L)



- **Cities with PM2.5 and mortality data 3,007 counties in the U.S.**

Analysis: Stage 1

City- and season-specific $PM_{2.5}$ mortality risk:

- Exposure: two-day averaged $PM_{2.5}$ concentrations
  - Measurements from Air Quality Systems monitors within each city
- Outcome: total, cardiovascular and respiratory mortality by city and season
- Covariates: temperature, relative humidity, DOW and long-term time

Analysis: Stage 2

Overall $PM_{2.5}$ effects by season and modification by ln(Rn):

- Three-level mixed effects meta-regression
  - Accounts for potential correlation of seasonal effect estimates within cities
- Effect estimates: %change in mortality for a 10 $\mu g/m^3$ increase in $PM_{2.5}$

Results

- Significant associations between $PM_{2.5}$ and all mortality outcomes in spring and fall
- Overall $PM_{2.5}$ effect estimates agree with previous studies
- Rn significantly modifies $PM_{2.5}$ effects in the spring and fall

Example:

10 $\mu g/m^3$ increase in $PM_{2.5}$ at 10^{th} Rn percentile (0.6 piC/L):

1.95% increase in total mortality (95% CI: 1.32, 2.59)

10 $\mu g/m^3$ increase in $PM_{2.5}$ at 90^{th} Rn percentile (6.3 piC/L):

3.69% increase in total mortality (95% CI: 2.84, 4.56)

Residential radon exposure and all-cause mortality risk among Medicare beneficiaries

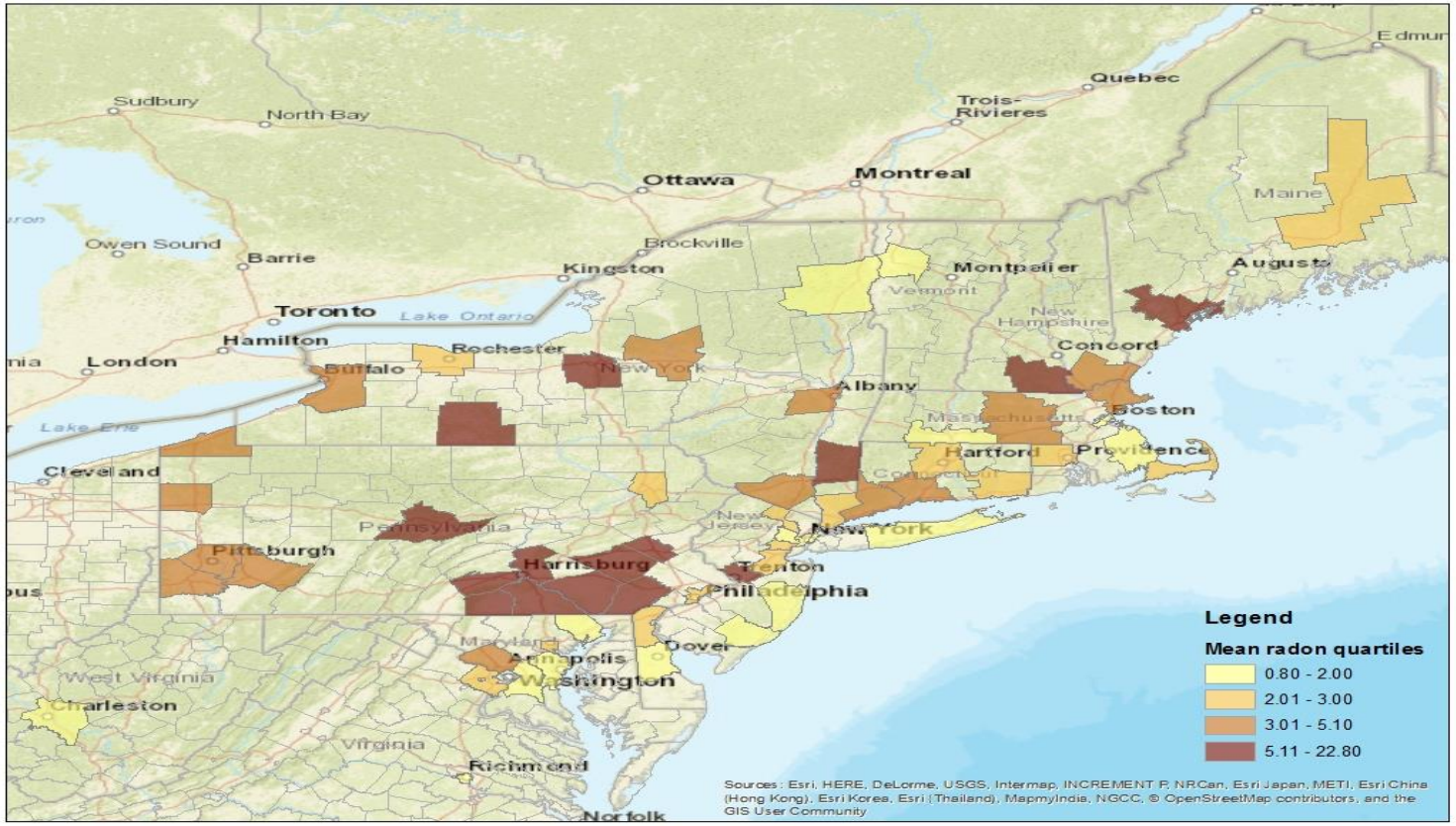
Maayan Yitshak Sade, Annelise J. Blomberg, Antonella Zanobetti, Joel D. Schwartz, Brent A. Coull, Itai Kloog and Petros Koutrakis

To be submitted soon

Methods

- **Design:** Population based cohort study with 14 years of follow-up (2000-2013)
- **Participants**: 42,663,005 person years of Medicare beneficiaries 65 years and older from 63 counties in 14 Middle-Atlantic and Northeastern states, traced until death or the end of follow-up period
- **Exposures**: We obtained radon levels from the State/EPA Residential Radon Survey. Annual, ZIP code level, fine particle ($PM_{2.5}$) levels were estimated using a spatiotemporal Aerosol Optical Depth-based model
- **Main outcome:** The association between the logarithm of county mean radon (log(Rn)) and mortality were assessed using Poisson survival analysis, both among all participants and separately in sub-cohorts of potentially susceptible individuals

County mean Rn by quartiles in the 63 study counties included in the analysis (had both Rn and $PM_{2.5}$ available)



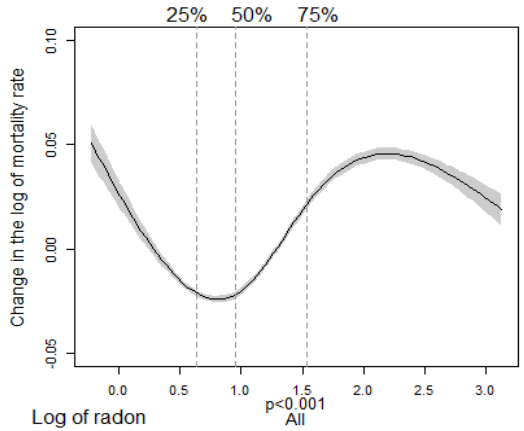
Results: Population Characteristics

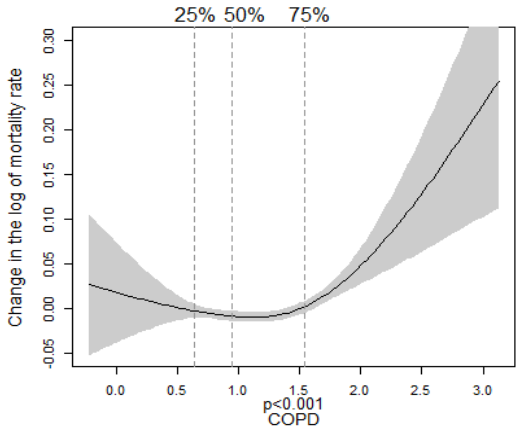
Population characteristics	N=42,663,005 person years
Male gender, No. (%)	17,564,996 (41.2)
Race, No. (%)	
White	36,642,683 (85.9)
Black	3,830,490 (9.0)
Other	1,409,648 (3.3)
Age, Mean (SD), years	75.86 (7.97)
Comorbidities, No. (%)	
COPD	849,034 (2.0)
MI	378,191 (0.9)
CHF	963,689 (2.3)
Ischemic stroke	501,163 (1.2)
Diabetes mellitus	1,005,990 (2.4)
Death, No. (%)	2,004,660 (4.7)

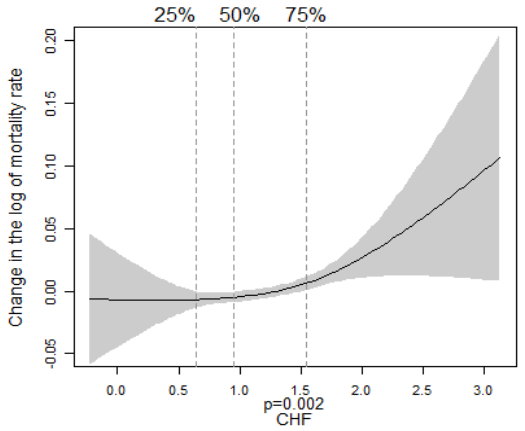
Results: %change in all-cause mortality associated with IQR increase in log(Rn) (0.9 pCi/L) among all study participants and in sub cohorts

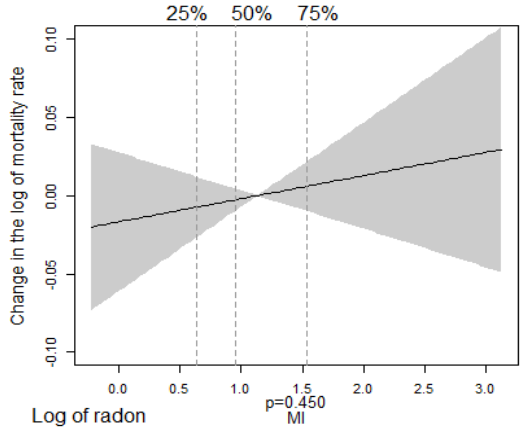
	Percent change (95% CI)	P value
All available data	0.61% (0.42%; 0.80%)	<0.001
COPD	1.72% (0.56%; 2.84%)	0.003
CHF	1.67% (0.66%; 2.67%)	<0.001
MI	1.08% (-2.34%; 4.52%)	0.541
Stroke	2.83% (-0.39%; 6.06%)	0.085
DM	2.31% (1.04%; 3.56%)	<0.001

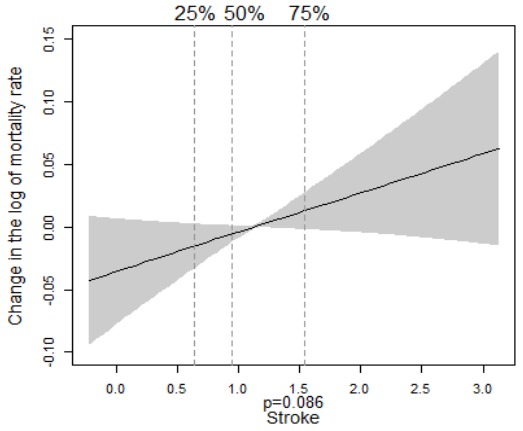
The association between Rn and mortality among all study participants, and sub cohorts of susceptible individuals

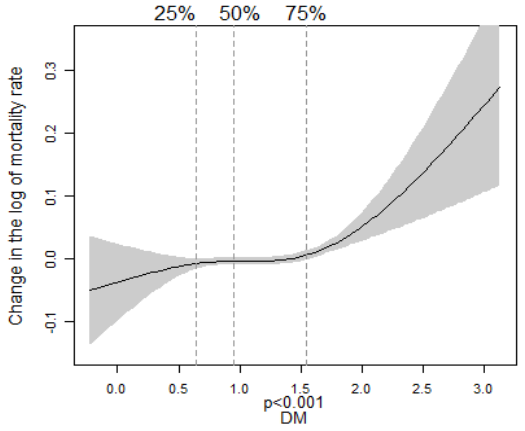












Conclusions

- We found an increased risk for all-cause mortality associated with residential Rn exposure
- The correlation between the Rn and $PM_{2.5}$ was low and the association with each exposure was not confounded by the other
- People with respiratory, circulatory or metabolic diseases appeared to be more susceptible
- The dose response curve for all-cause mortality was nonlinear, and higher mortality risks with increasing Rn levels were found only for exposures around the mean of log(Rn)
- Among COPD, CHF and diabetes patients, higher mortality risks were observed only for log(Rn) increases within the highest quartile of the log(Rn) distribution

Can we refine exposures?

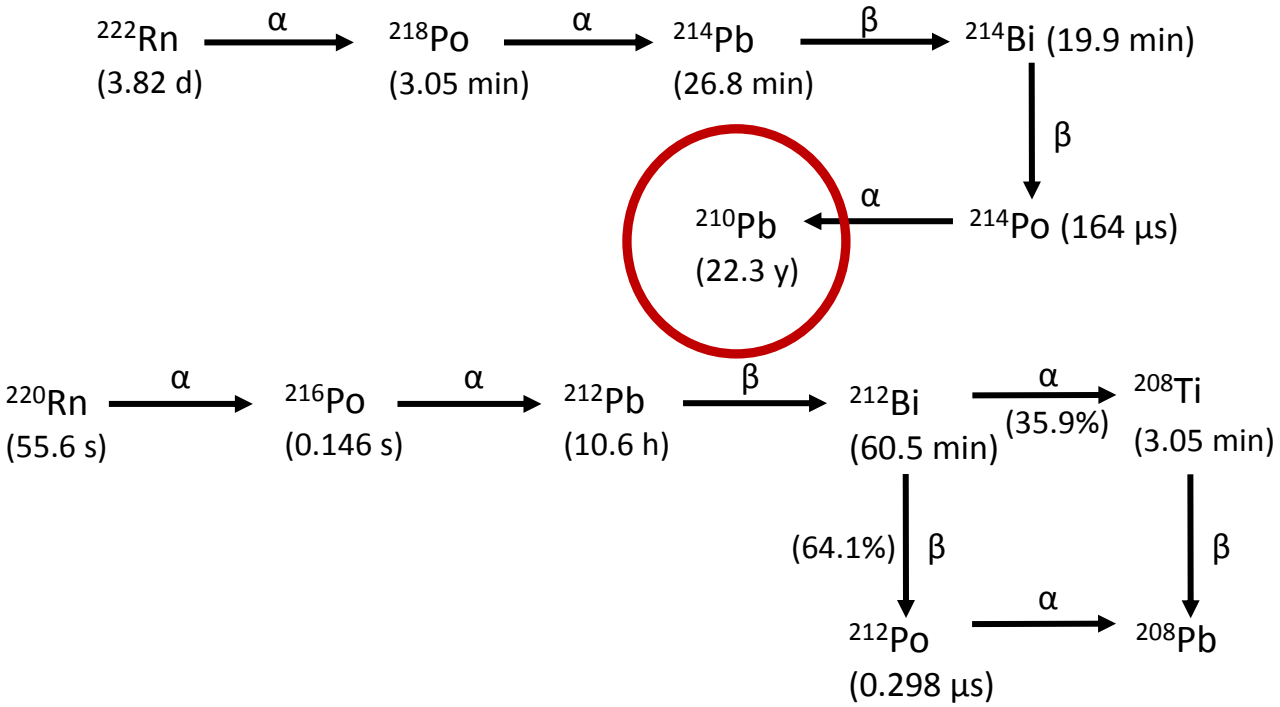
- If Rn enhances PM toxicity then we should be able to see effects for some related PM properties, for example
  - Filter gross radiation activity for α, β and γ
  - Specific Radionuclides (e.g., ^{214}Bi, ^{212}Pb. ^{210}Pb)

- We have tested our hypothesis using non ideal concentration data
  - Networks do not focus on Rn chemistry (terrorist activities and nuclear accidents)
  - Physical limitations (many of the Rn progenies have **short half-lives**)

RadNet Monitoring Network

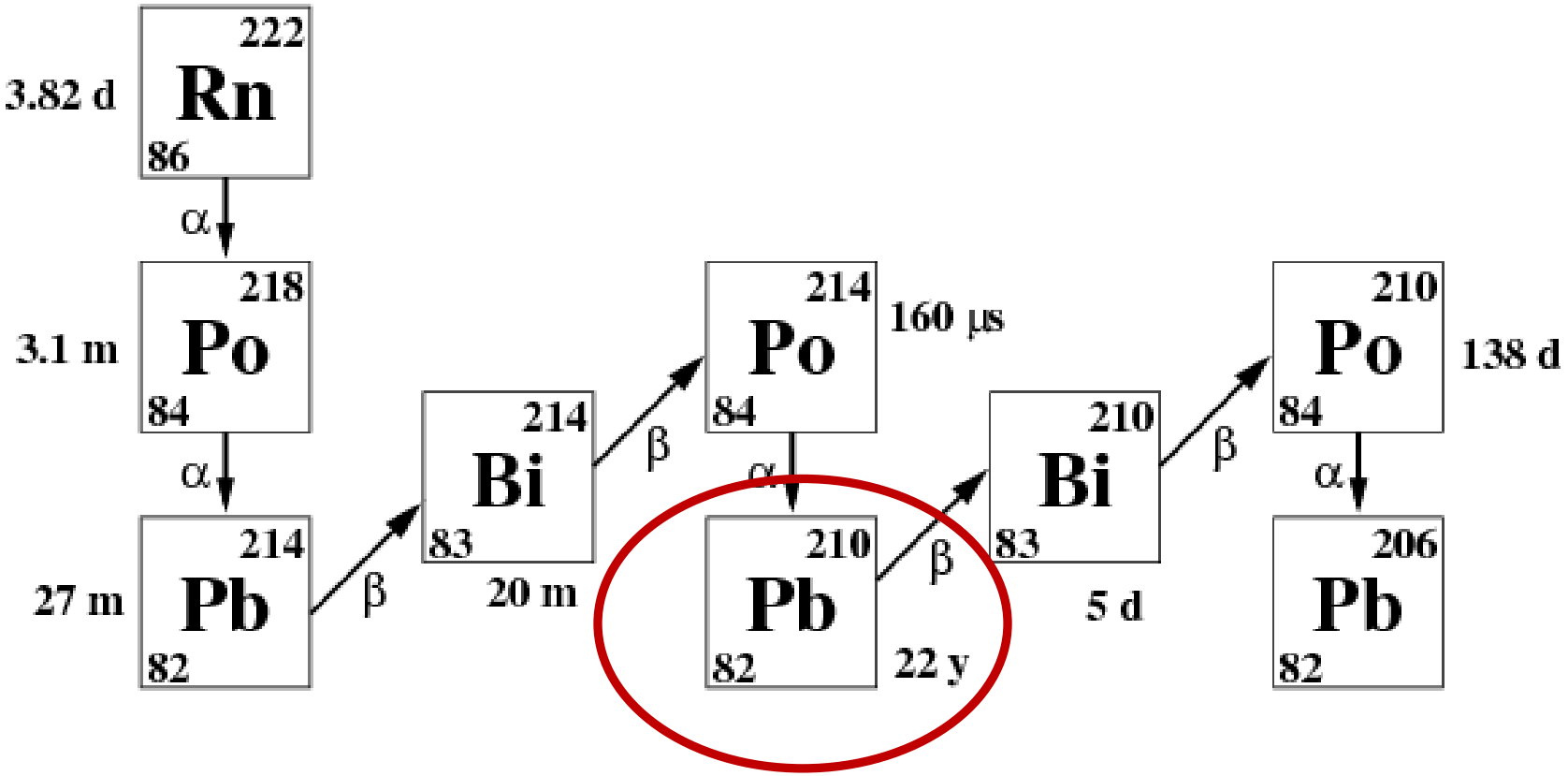
- Purpose (nuclear accidents, terrorism)
- TSP samples collected over 5-7 days since 1981
- Over 100 sites across USA
- Radionuclides on composite samples
- Gross beta measurements as a screening tool
- Beta counting is done several days after the sampling ends
- Use of beta activity as a surrogate of PR
  - Most activity is expected to be related to Rn

Radon (^{222}Rn) and Thoron (^{220}Rn) chains reactions

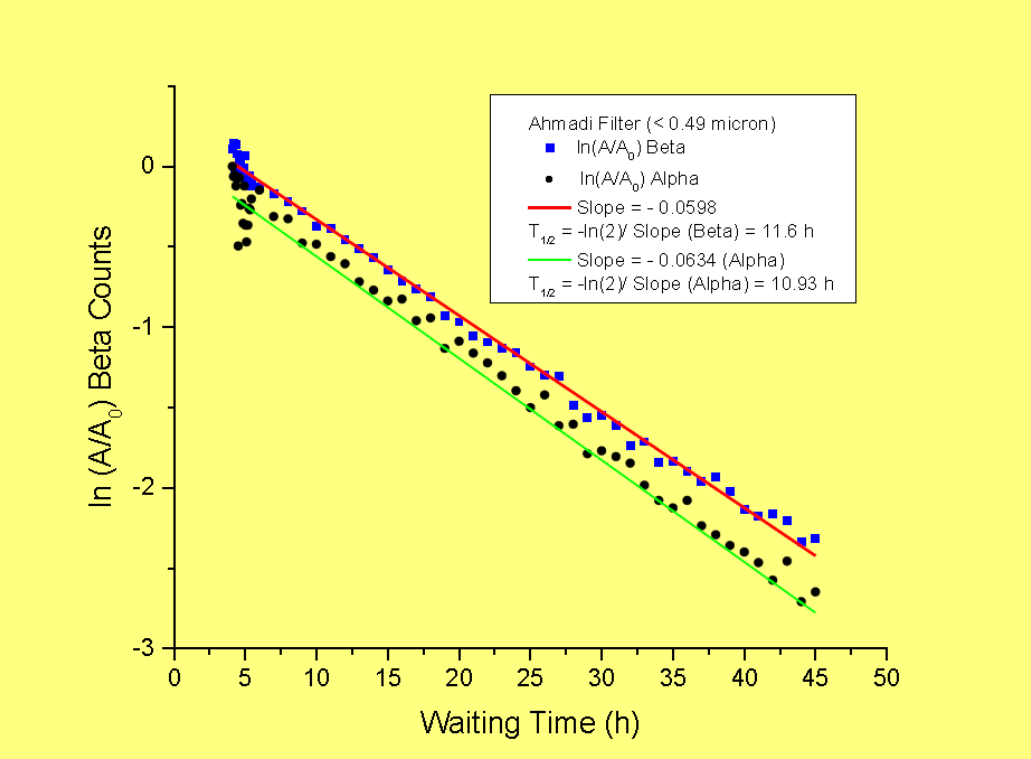


^{222}Rn >> ^{220}Rn

^{210}Pb Emits Beta



Estimated gross α and β PM filter activity half lives



Courtesy of Dr. Abdulaziz Aba; Kuwait Institute of Scientific Research

Association between particle radioactivity, $PM_{2.5}$, BC and PN with blood pressure in the Veterans Administration Normative Aging Study

Marguerite Nyhan, Ph.D.
T. H. Chan School of Public Health,
Harvard University

Published by the Journal of American Heart Assciation, 2018

Data

Air Pollution – Countway Library

- BC from 1999 – 2015; $PM_{2.5}$ and PN from 1998 - 2015

Normative Aging Study (NAS) Cohort Data
US army Veterans followed up since 1970s

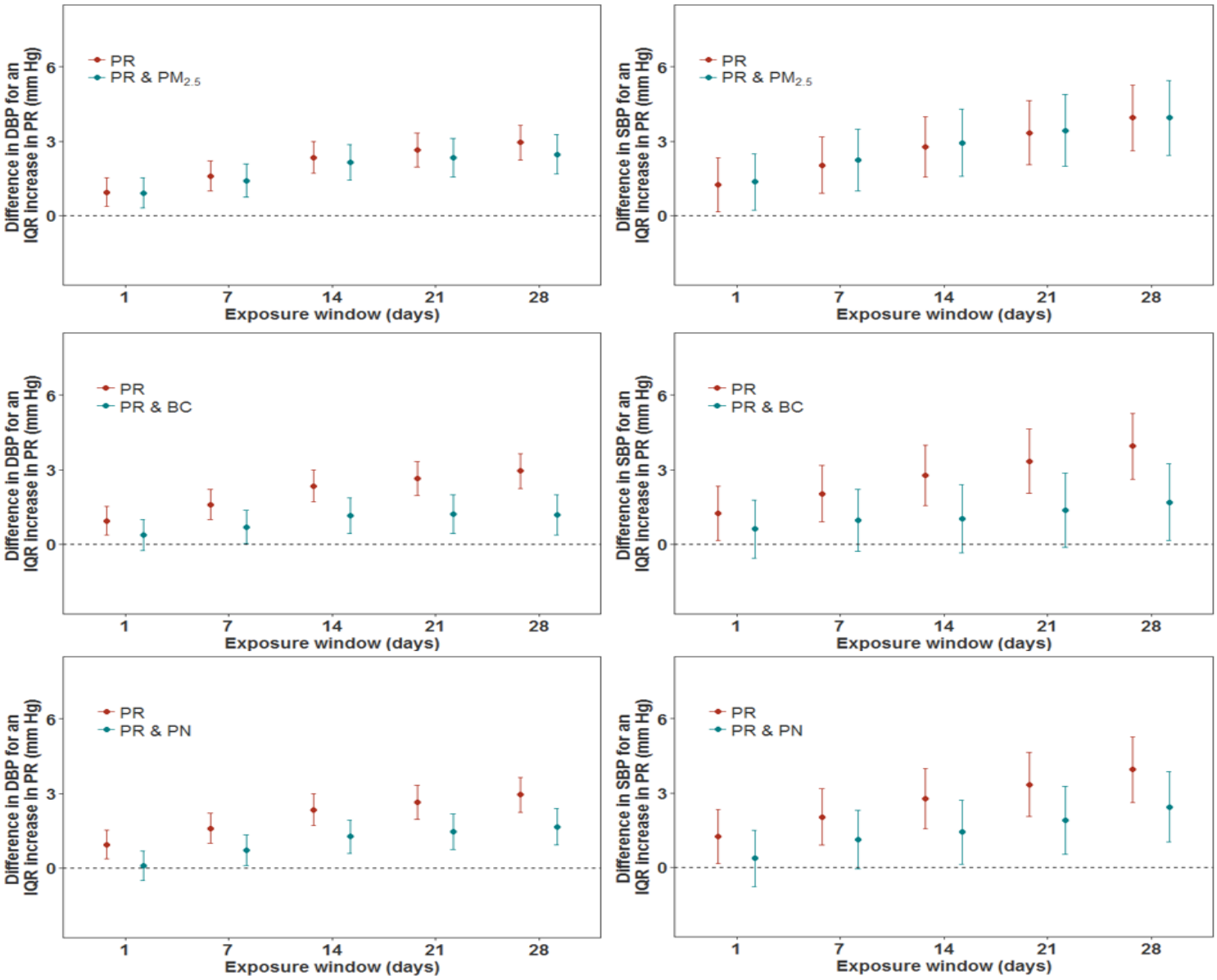
- Regular Hospital Visits every few years (many tests)

Radiation – RadNet Monitoring Network

- PR = Beta Activities from 1981 – 2016
- Cities: Albany, Worcester, Boston and Providence
- Predicted PR levels in each city where there are missing values
- Calculated the regional mean

Statistical methods

- Analyzed associations between exposure to PR, $PM_{2.5}$, BC, PN and blood pressure (SBP and DBP)
  - using linear mixed effects models with a random intercept for each subject
- Evaluated SBP and DBP as dependent variables.
- Exposure metrics – moving averages from 1 to 28 days.



Nyhan, M. et al., Association between PM radioactivity and BP: the NAS. JAHA, 2018.

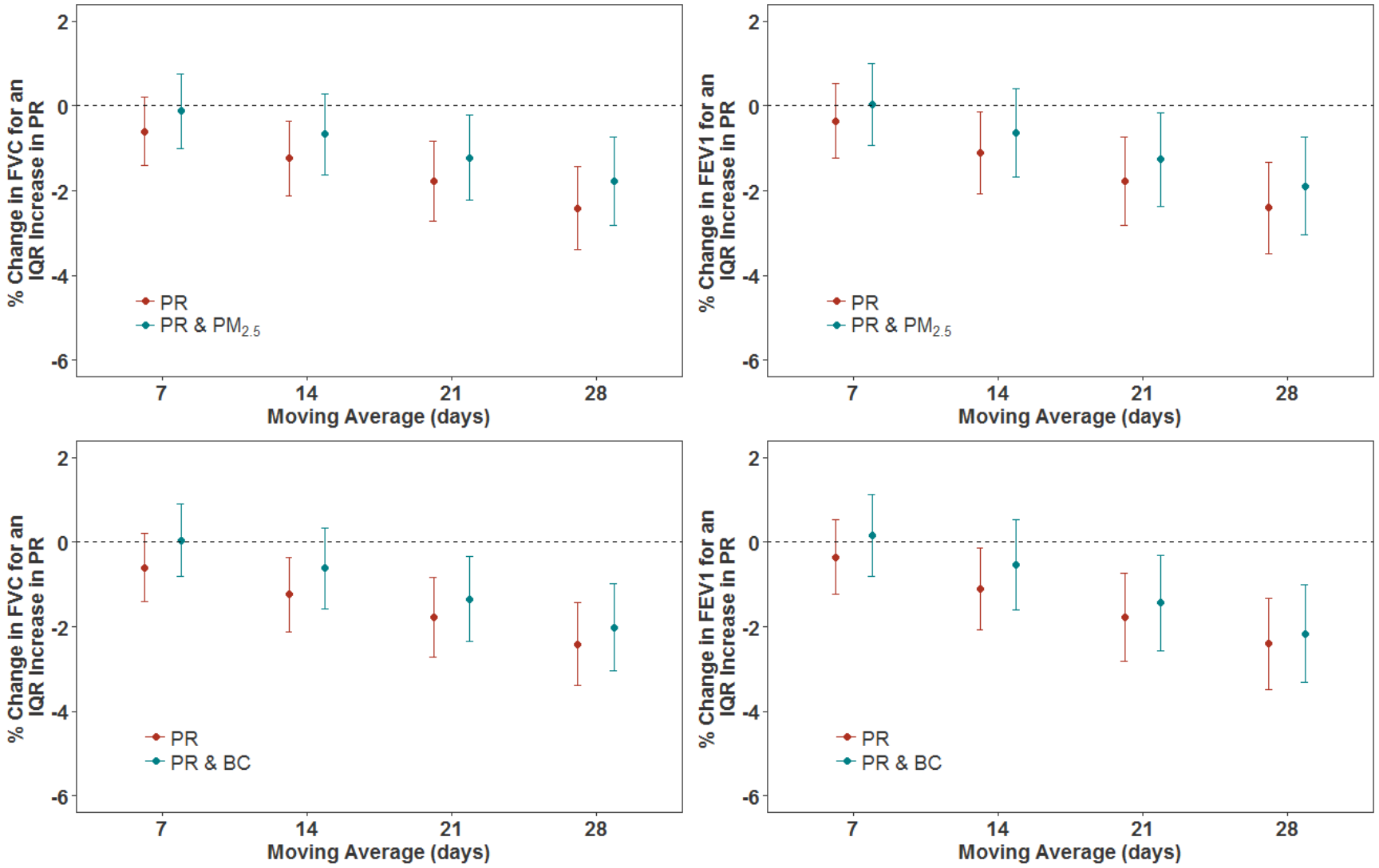
Association between particle radioactivity, $PM_{2.5}$, BC and PN, and lung function in the Veterans Administration Normative Aging Study

Marguerite Nyhan, Ph.D.
T. H. Chan School of Public Health,
Harvard University

Ready to be submitted

Statistical methods

- Analyzed associations between exposure to PR, $PM_{2.5}$, BC, PN and lung function (FEV1 and FVC)
  - using linear mixed effects models with a random intercept for each subject
- Evaluated FEV1 and FVC as dependent variables.
- Exposure metrics – moving averages from 7 to 28 days.



Nyhan, M. et al., 2018. Association between PM radioactivity and lung function: the NAS. AJRCCM, under review.

Thanks

Air Pollution and Health

- Ambient Particle exposures have been associated with mortality (over 7,000,000) deaths per year, 6% of the total global mortality

- Ambient Particle exposures have been associated with many morbidity outcomes, e.g., blood pressure, lung function, cognitive function etc.

- There is a knowledge gap on which are the properties of the PM air pollution responsible for the well-documented short- and long-term effects of cardiovascular outcomes

What is the role of particle radioactivity?

Radon and Birth Weight

Man Liu et al.
T. H. Chan School of Public Health,
Harvard University

Spectra of typical air filter after 24 h filtration

(A) 1 min delay; 3 h counting **(B) 3 h delay; 3 h counting**

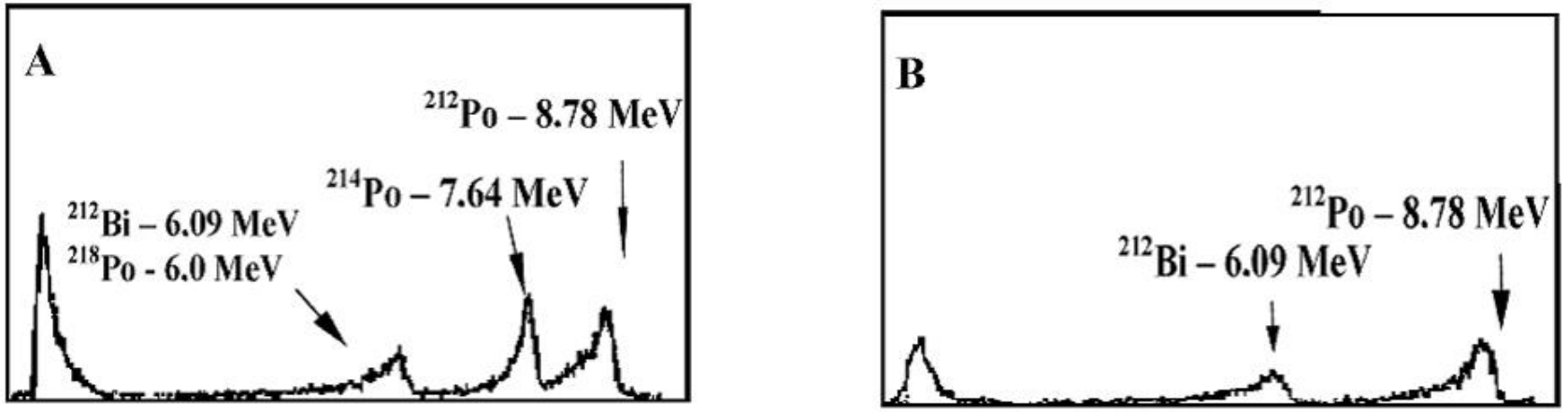
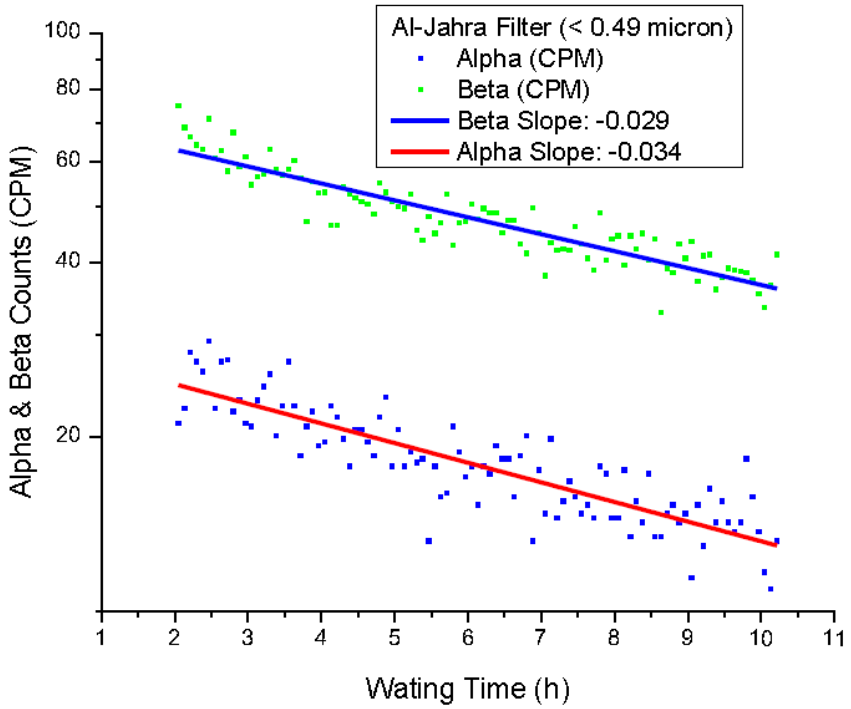


Fig. 3. The α spectra of a typical air filter obtained after 24 h filtration. A – 24 h filtration, 1 min delay time, 3 h counting (with a metal net collimator); B – 24 h filtration, 3 h delay time, 3 counting (with a metal net collimator).

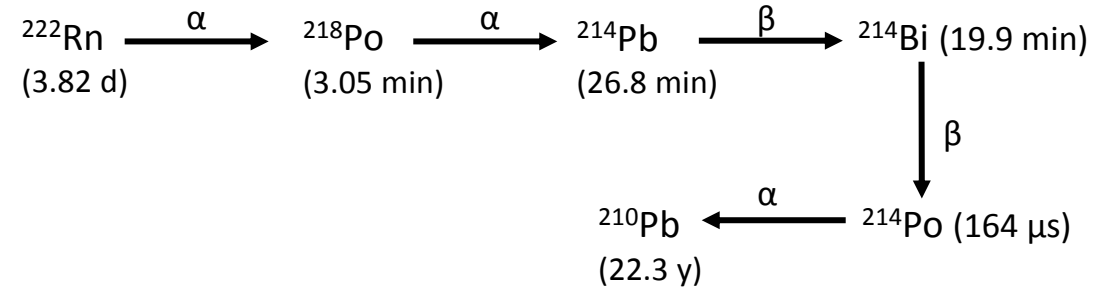
Courtesy of Dr. Abdulaziz Aba; Kuwait Institute of Scientific Research

Gross α and β filter activity measurements starting 5 h after the end of PM_{10} sampling

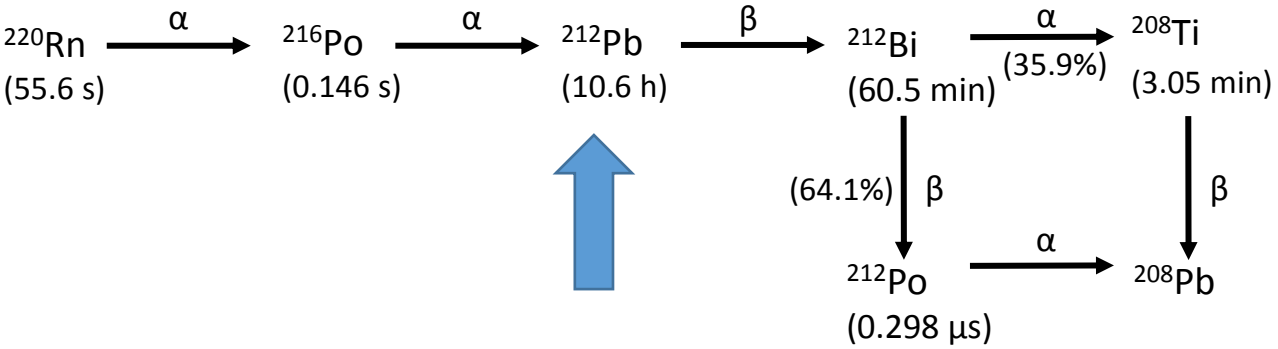


Courtesy of Dr. Abdulaziz Aba; Kuwait Institute of Scientific Research

Radon (^{222}Rn) and Thoron (^{220}Rn) chains reactions



Faster Decay Chain
More radiation

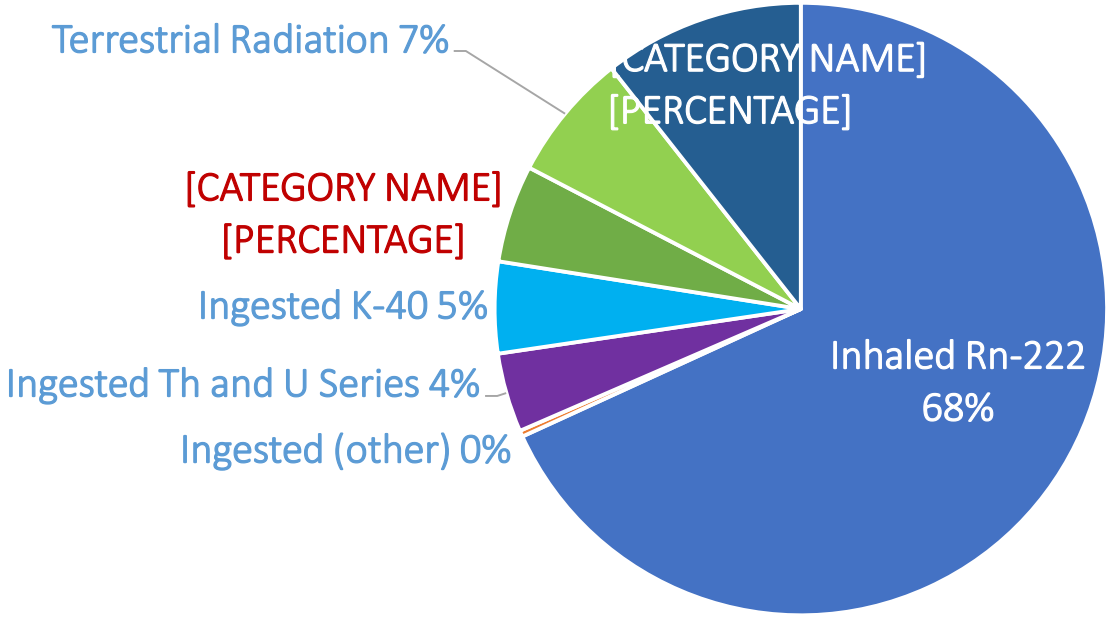


Slower Decay Chain
Less radiation

^{222}Rn >> ^{220}Rn

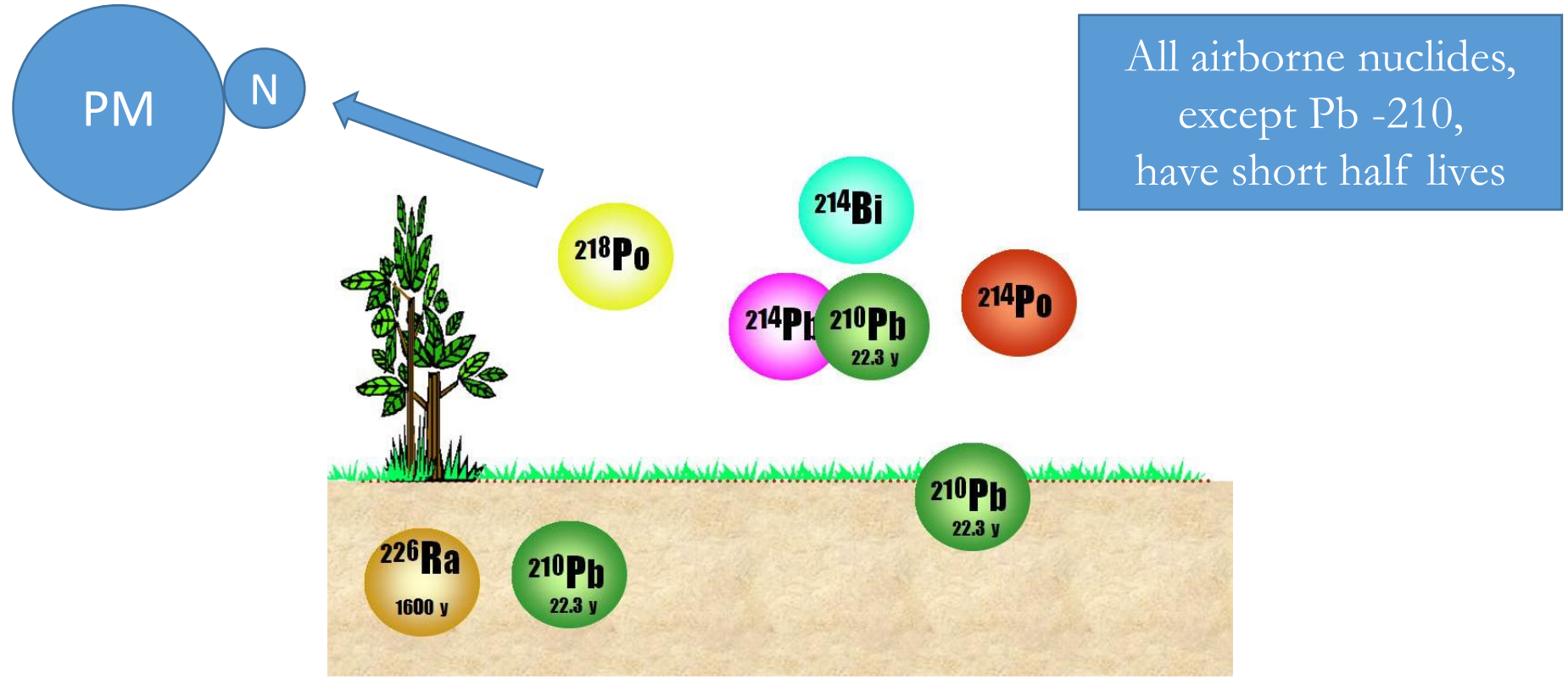
At a specific location
could be assumed correlated

Estimated Average U.S. Radiation Dose

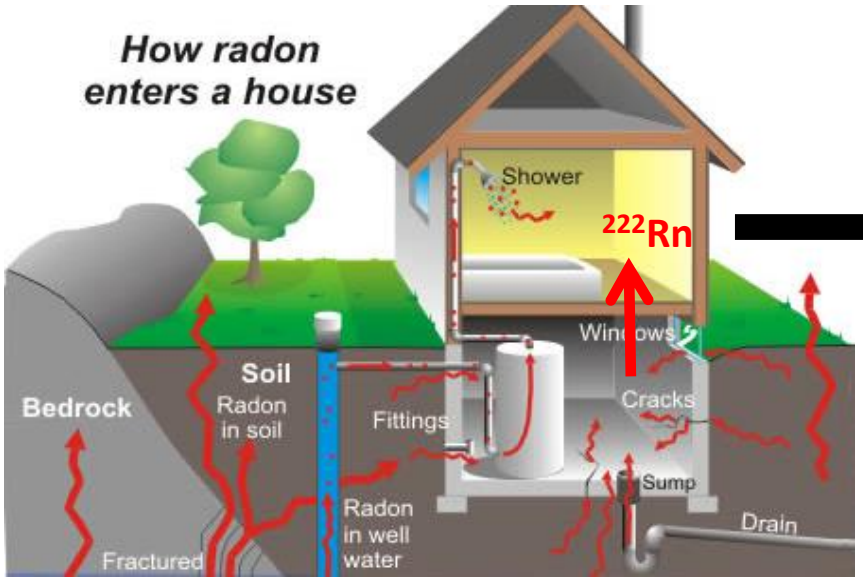


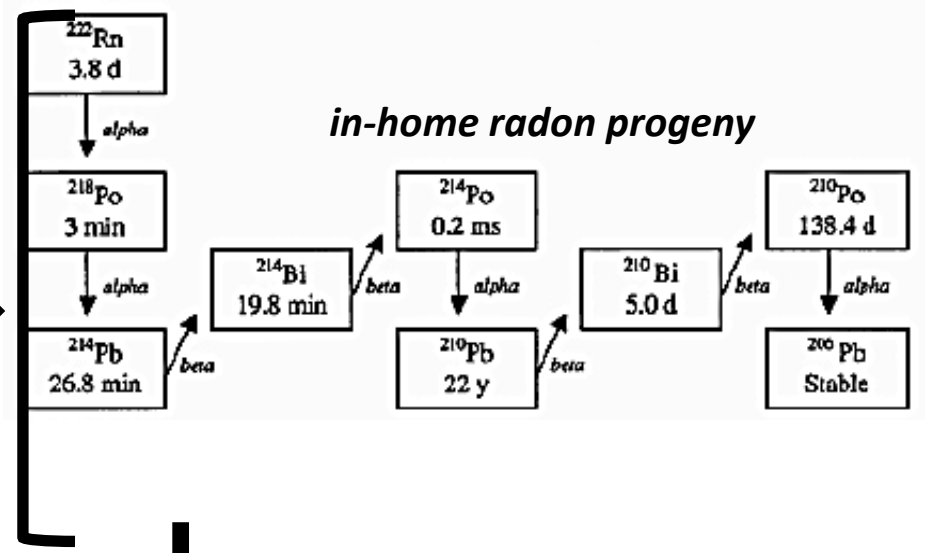
Source: NCRP 160, Figure 3-19

Radon Emanation and Exhalation

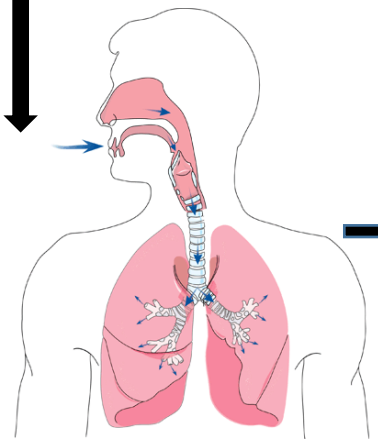


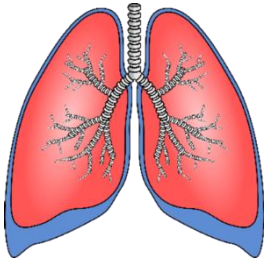
Courtesy of Dr. Abdulaziz Aba; Kuwait Institute of Scientific Research





Inhale $PM_{2.5}$ attached progeny





Impaired lung function



Blood markers of inflammation and oxidative damage

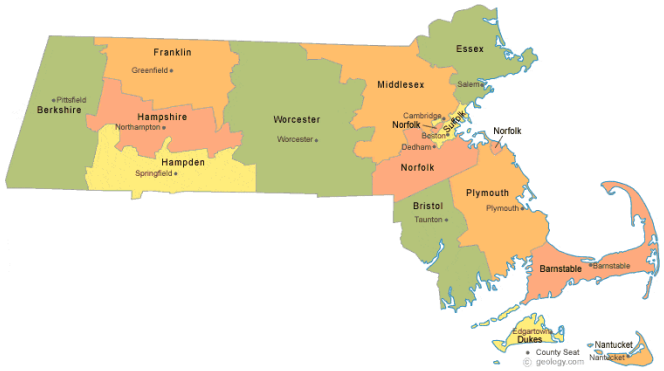
Data

Outcome: Birth Weight

- Birth data: MA, 2000 ~ 2009 (Final data include: 444,493 observations)

Exposure: Rn

- Rn level for 13 Massachusetts Counties
- Two Rn metrics: mean / geometric mean
- Rn exposure is considered stable over time



Other predictors and effect modifiers:

- 24 individual-level variables (e.g., pre-existing diseases, smoking, method of delivery, etc.)
- Three county-level SES variables: population density, median income and race
- Temperature, Relative humidity, $PM_{2.5}$ (average through pregnancy)

County Rn levels in Massachusetts

County	Radon Levels (pCi/L)				
	Mean	Geometric Mean	Median	Maximum	Standard Deviation
Barnstable	2.1	2.0	1.6	12.5	1.5
Berkshire	3.3	3.8	1.9	15.7	1.8
Bristol	2.8	3.4	1.8	28.8	1.8
Dukes	**4.6**	**7.4**	1.2	19.5	1.9
Essex	4.1	5.1	2.8	52.4	2.6
Franklin	3.3	3.4	1.6	12.6	2.1
Hampden	2.0	2.4	1.3	22.9	1.4
Hampshire	2.6	2.6	1.6	14.1	1.8
Middlesex	4.1	7.0	2.2	61.3	2.3
Norfolk	3.0	3.5	1.9	30.1	2.0
Plymouth	2.0	2.0	1.4	14.7	1.4
Suffolk	**1.7**	**1.3**	1.2	8.0	1.4
Worcester	**4.6**	5.3	2.8	41.1	2.9

Mixed Effect Models

(zipcode as random intercept)

Models	Exposures	Remarks
Model 1	Only Rn	-
Model 2	Rn + Rn * Parity	Parity = 1, 2 or 3
Model 3	Rn + Rn * Mother's Age	6 Categories
Model 4	Rn + Rn * Gestational Hypertension	Yes or No
Model 5	Rn + Rn * Gestational Diabetes	Yes or No
Model 6	Rn + Rn * $PM_{2.5}$	Average $PM_{2.5}$

Results

IQR of Geo. Mean = 1.7

Model	Variable	Mean Rn		Geometric Mean Rn	
		Coefficient	p-value	Coefficient	p-value
Model 1	Rn	-5.45	0.01	-5.90	<0.0001
Model 2	Rn	-6.65	0.003	-6.86	<0.0001
	Rn * Parity (=1)	Ref	-	Ref	-
	Rn * Parity (=2)	2.75	0.06	1.84	0.02
	Rn * Parity (=3)	0.92	0.63	1.59	0.12
Model 3	Rn	-5.02	0.11	-5.61	0.002
	Rn * Mage (=1)	Ref	-	Ref	-
	Rn * Mage (=2)	1.40	0.60	0.63	0.69
	Rn * Mage (=3)	-1.98	0.45	-1.73	0.25
	Rn * Mage (=4)	-0.68	0.80	-0.46	0.76
	Rn * Mage (=5)	-0.54	0.86	0.49	0.77
	Rn * Mage (=6)	4.83	0.32	2.42	0.32
Model 4	Rn	-5.36	0.01	-5.82	<0.0001
	Rn * Hypertension	-3.28	0.42	-3.00	0.16
Model 5	Rn	-5.26	0.01	-5.81	<0.0001
	Rn * Diabetes	-6.84	0.08	-3.65	0.08
Model 6	Rn	-6.72	0.01	-6.42	<0.0001
	Rn * $PM_{2.5}$	0.12	0.27	0.05	0.40

Particle Beta Activity and Birth Weight

Stefania Papatheodorou et al.
T. H. Chan School of Public Health,
Harvard University

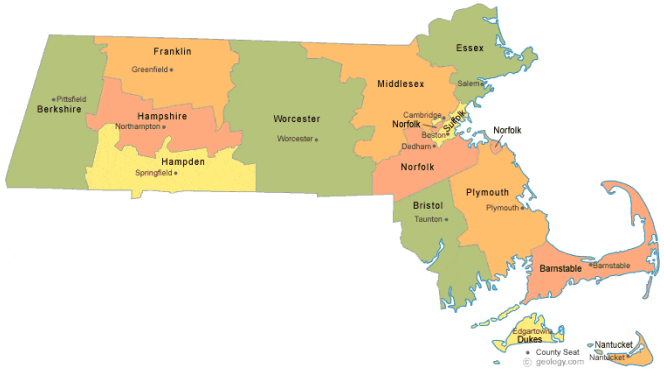
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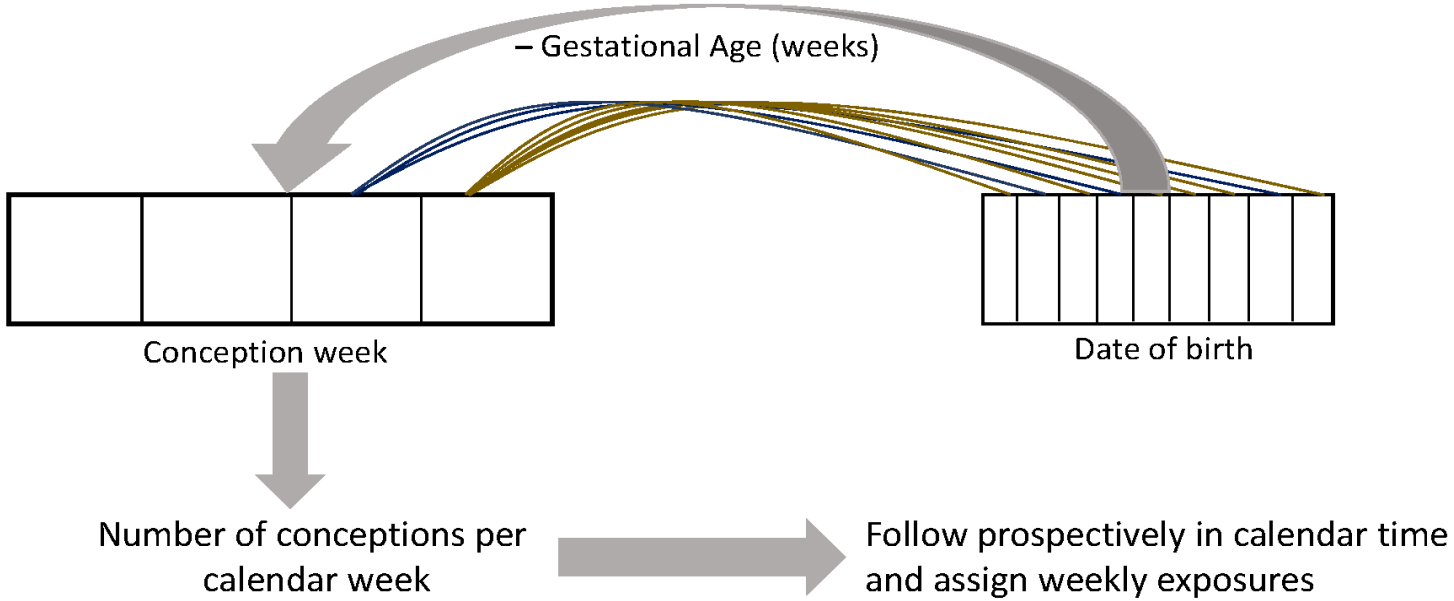


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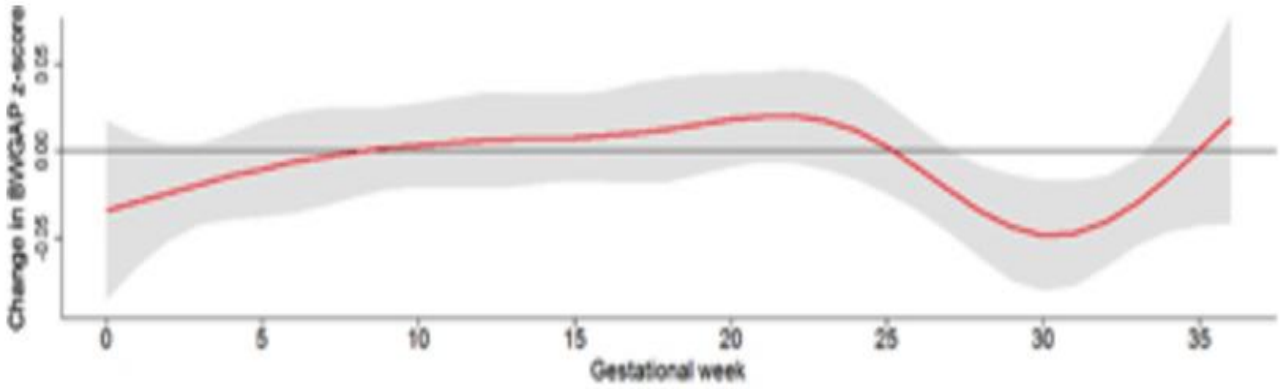
Methods, cont.

- **U**se distributed lag linear and non-linear models to assess the effect of weekly exposures of radionuclides during pregnancy



Preliminary Data

- Maternal weekly PM beta activity exposure and birth weight (data from MA birth registry)

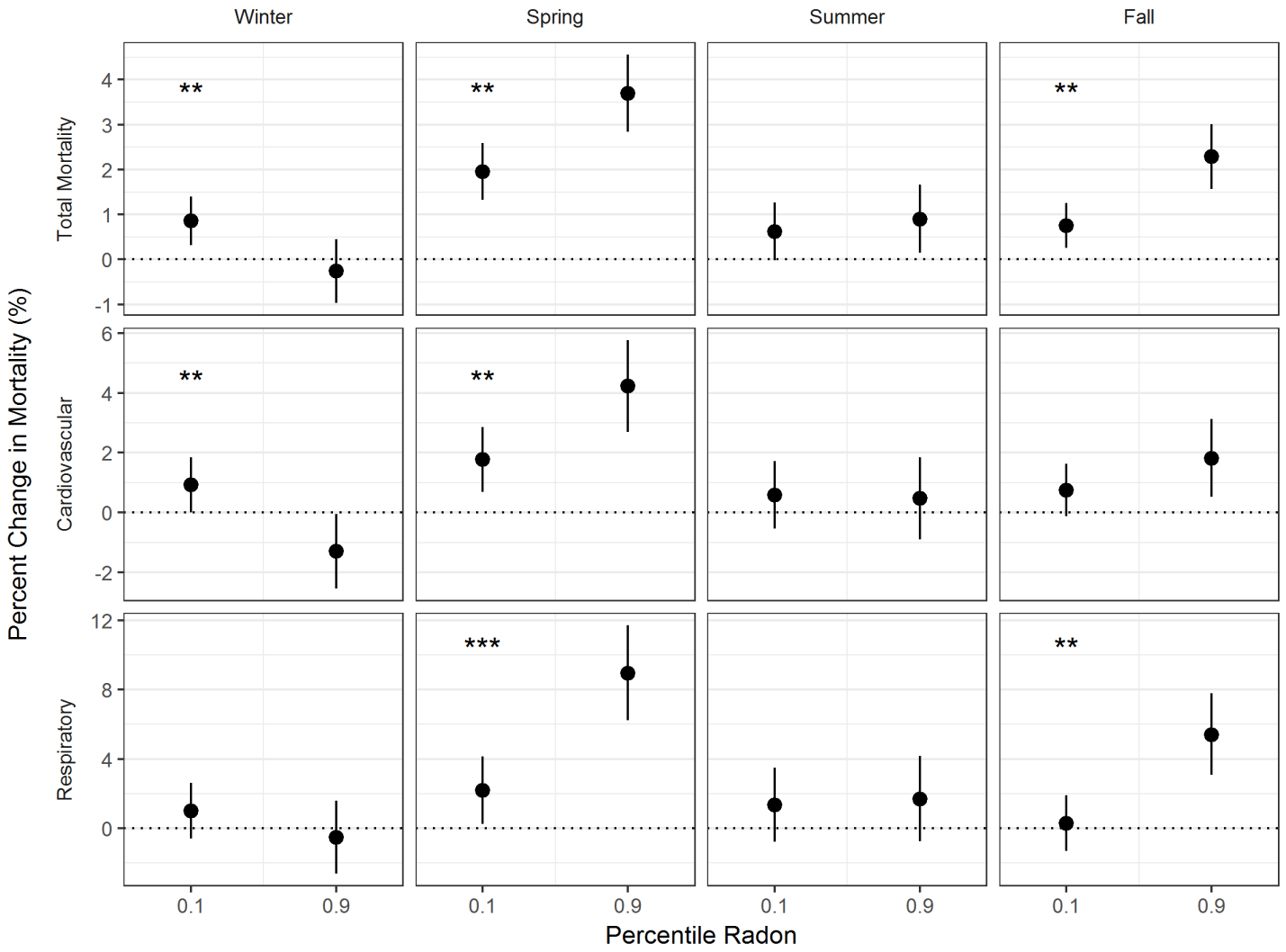


Conclusions (Rn effects)

- There is evidence that Rn can modify the effects of $PM_{2.5}$ on mortality or increase mortality
- There is evidence that Rn county levels are associated with birth weight loss
- PM β activity is associated with:
  - an increase in diastolic and systolic blood pressure and
  - a decrease in FEV1 and FVC
- The effects are to a great extent independent of those caused by Black carbon, $PM_{2.5}$ mass and Particle number
- We have shown a high correlation between β and α activity of particles collected on a Teflon filter
  - This supports our hypotheses that α particles may be responsible for the observed effects

Conclusions (Particle Radioactivity)

- Investigating the effects of PM radioactivity will become an emerging research area
- Today we presented a few studies
  - About **Rn** and the ^{222}**Rn** and ^{220}**Rn** reactions
  - There are other radionuclides of terrestrial origin e.g., ^{40}**K** not an α emitter
  - Finally, there are other sources of radionuclides of solar or cosmic origin


Winter
Spring
Summer
Fall
Total Mortality
Cardiovascular
Respiratory
Percent Change in Mortality (%)
Percentile Radon
0.1
0.9
**
***

Strengths and Limitations

Strengths:

- Biologically plausible (PM radioactivity)
- Application of well-established statistics
- Important scientific implications (e.g., regional NAAQS)

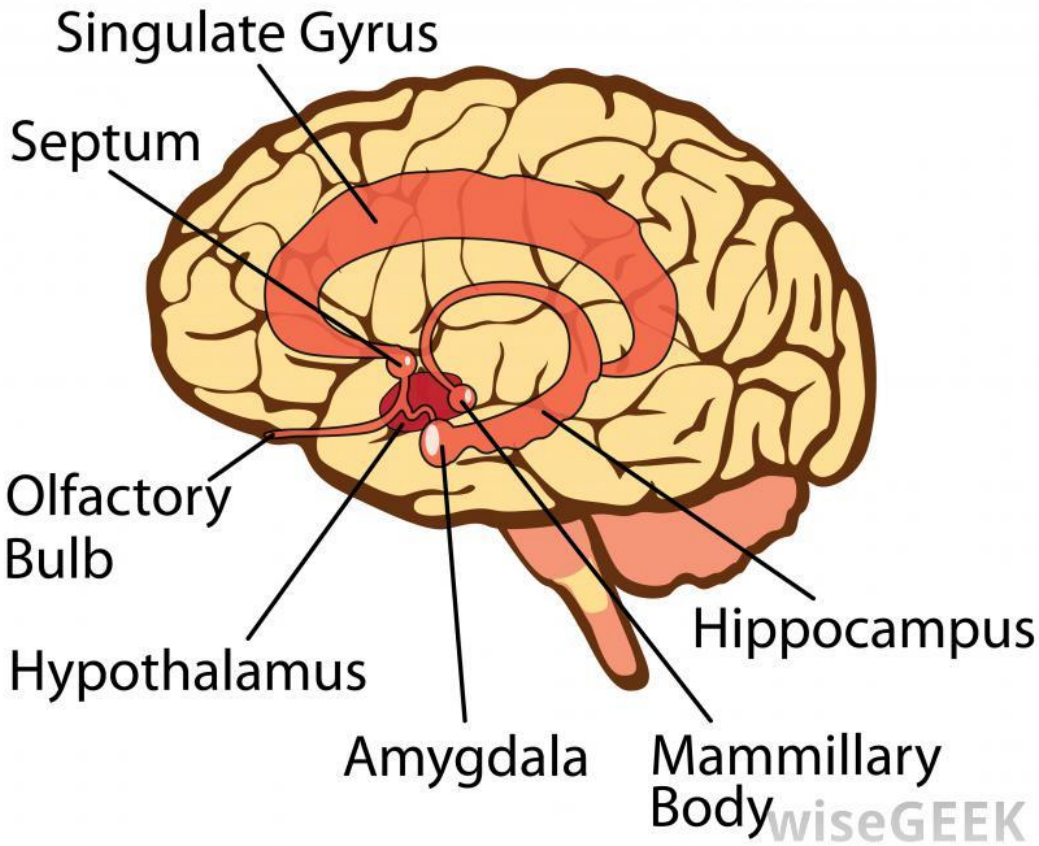
Limitations:

- County-level Rn estimates based on short-term measurements
- No temporal variability in Rn: how does it change with season and year
- Assumes no unmeasured confounding

Radon a precursor of α-emitting nuclides

- Radon-222 formed by decay of uranium-238 (Radon Chain - **major**)
- Radon-220 formed by decay of thorium-238 (Thoron Chain - **minor**)
- Radon:
  - Radioactive noble gas
  - Accumulates in mines and houses but exists outdoors as well
  - Decays into radon progeny
  - Second highest cause of lung cancer
- Factors that impact formation and advection to surface:
  - Source concentrations
  - Temperature
  - Soil saturation
  - Pressure changes

LIMBIC SYSTEM STRUCTURES



Thanks

Thanks

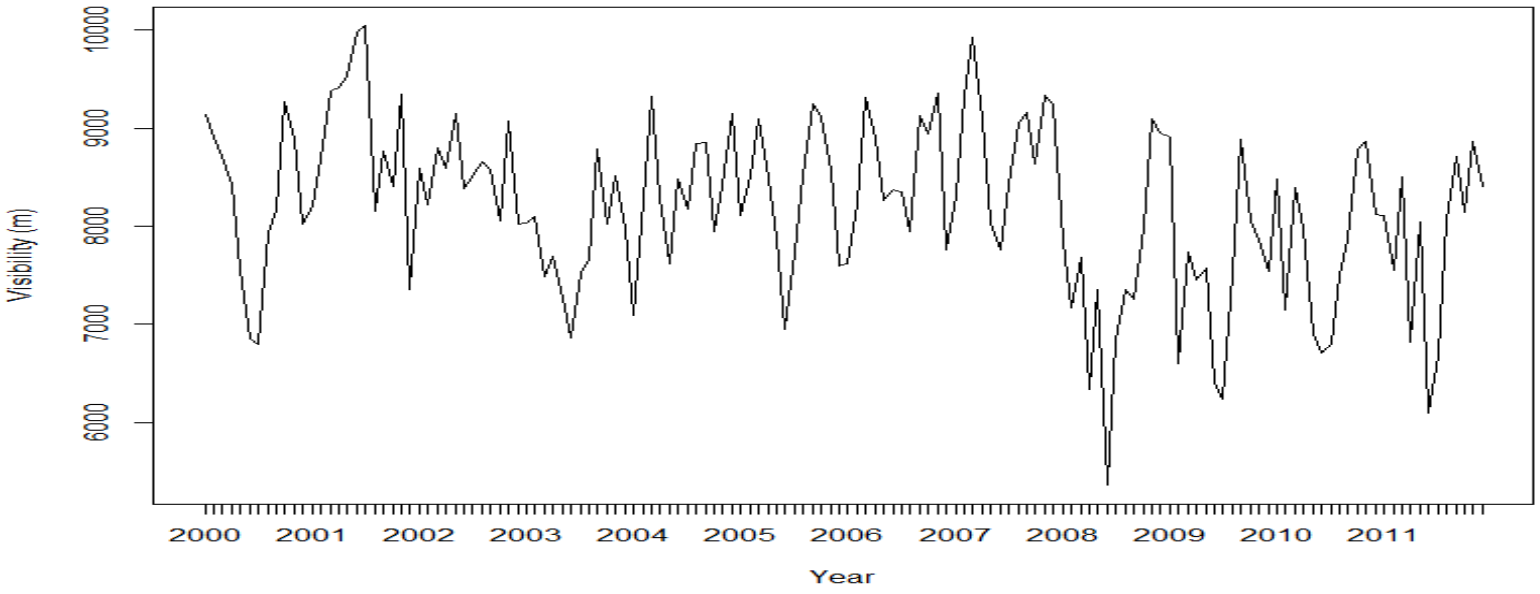
Acute effects of air pollution on mortality: a 12-year analysis in Kuwait

Souzana Achilleos, Ebaa Al Ozairi, Eric Garshick, Andreas M. Neophytou, Mohamed F. Yassin, Walid Bouhamra, and Petros Koutrakis

Dataset

- Mortality data
  - Daily records for Kuwait
  - January 2000 – December 2011
  - Causes: all non-accidental, cardiovascular, and respiratory
  - Stratify by gender (male, female) and nationality (Kuwaitis, non-Kuwaitis)
- Exposure data
  - Hourly measurements
  - Visibility (m), Temp (^{o}C), RH (%), and wind speed (m/s)
  - Kuwait International Airport by the U.S. Air Force
  - 24-hr average if >12 hourly observations were available

Monthly visibility average across the study period



Daily visibility: Mean ± SD: 8,185 ± 1,881 m; Lowest during summer months

Data analysis

- Low visibility (yes/no) was used as an indicator of poor air quality days: defined as visibility < than the 25th percentile (7,160 m)

$$\log E(Y_i) = \text{intercept} + s(\text{time}_i, df=60) + \text{day of week} + s(\text{temperature}_i, df=3) + s(\text{relative humidity}_i, df=3) + \text{visibility}_i$$

Daily mortality, visibility, temperature, relative humidity, and wind speed in Kuwait during 2000-2011

Variable	All days (n=4,383)	Low visibility days (n=1,095)	High visibility days (n=3,287)
Mortality (deaths/day)			
Total	12.02 ± 3.96	12.24 ± 3.92	11.95 ± 3.97
Cardiovascular	6.56 ± 3.02	6.62 ± 2.97	6.54 ± 3.04
Respiratory	0.49 ± 0.74	0.52 ± 0.77	0.48 ± 0.72
Daily Visibility (m)	8,185 ± 1,881	5,468 ± 1,355	9,091 ± 910
Weather			
Temperature,T (°C)	27.0 ± 9.8	28.3 ± 9.6	26.6 ± 9.8
Relative Humidity, RH (%)	34.5 ± 21.6	38.0 ± 26.3	33.4 ± 19.7
Wind speed, ws (m/s)	7.9 ± 3.6	9.5 ± 4.3	7.4 ± 3.1

Summary statistics (mean ± SD) of daily mortality across Kuwait in 2000-2011 by nationality

Mortality (deaths/day)	All days (n=4,383)	Low visibility days (n=1,095)	High visibility days (n=3,287)
Kuwaitis			
Total	6.83 ± 2.82	6.84 ± 2.79	6.83 ± 2.83
Cardiovascular	3.56 ± 2.13	3.47 ± 2.12	3.59 ± 2.14
Respiratory	0.26 ± 0.53	0.29 ± 0.56	0.26 ± 0.52
Non-Kuwaitis			
Total	5.19 ± 2.50	5.40 ± 2.58	5.12 ± 2.47
Cardiovascular	3.00 ± 1.89	3.14 ± 1.92	2.96 ± 1.88
Respiratory	0.22 ± 0.49	0.23 ± 0.51	0.22 ± 0.48

Summary statistics (mean±SD) of daily mortality across Kuwait in 2000-2011 by gender

Mortality (deaths/day)	All days (n=4,383)	Low visibility days (n=1,095)	High visibility days (n=3,287)
Males			
Total	7.25 ± 2.94	7.38 ± 2.98	7.20 ± 2.92
Cardiovascular	4.12 ± 2.69	4.17 ± 2.19	4.11 ± 2.29
Respiratory	0.27 ± 0.55	0.30 ± 0.61	0.26 ± 0.53
Females			
Total	4.78 ± 2.35	4.86 ± 2.44	4.75 ± 2.32
Cardiovascular	2.44 ± 1.71	2.45 ± 1.75	2.43 ± 1.69
Respiratory	0.22 ± 0.48	0.22 ± 0.47	0.22 ± 0.48

Estimated rate ratio (95% CI) comparing mortality rates on low visibility days to mortality rates on high visibility days at lag 0

	Total	Cardiovascular	Respiratory
All	1.02 (1.00,1.04)	1.02 (0.99,1.06)	1.04 (0.93,1.15)
Kuwaitis	1.01 (0.98,1.04)	1.00 (0.96,1.04)	1.10 (0.95,1.27)
Non-Kuwaitis	**1.03 (1.00,1.07)** ‡	**1.06 (1.01,1.10)** †	0.96 (0.82,1.13)
Males	1.02 (1.00,1.05)	1.02 (0.99,1.06)	**1.17 (1.01,1.35)** †
Females	1.01 (0.97,1.05)	1.02 (0.97,1.07)	0.89 (0.75,1.04)

† Statistically significant at 0.05 level; ‡ Statistically significant at 0.10 level

Conclusions

- Exposure to poor air quality conditions in Kuwait was associated with an increased risk of mortality
- Non-Kuwaitis, and males (Kuwaitis and non-Kuwaitis) are at higher risk
- Probably because of exposure heterogeneity among the population. For example, most non-Kuwaitis and males spend more time outdoors because of their occupation (agriculture, fishery, craft and related trades, monitor production, domestic servants, etc.) (source: Public Authority for Civil Information, Government of Kuwait, 2017)
- Further research is needed to improve the exposure assessment and study the association between indoor and outdoor exposure to specific air pollutants