Role of Science and Judgment in Setting National Ambient Air Quality Standards: How Low is Low Enough?

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Presented:
Topical Session: New Developments in Risk Science and Causality
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DECLARATION OF INTEREST

During my career I have been

- a self-employed student farmer

- employed by the

General Electric Co., as contractor to the U.S. government
Battelle Memorial Institute, as contractor to USA
U.S. Government
Lovelace Medical Foundation, as contractor to USA
Chemical Industry Institute of Toxicology, primarily private sector support
Other various private and public entities

- to conduct and manage research oriented to reducing scientific uncertainty on major societal issues and synthesize and interpret scientific information that will inform policy decisions that impact human kind, hopefully in a positive manner

•Served on several dozen EPA Advisory Committees

•Testified to Both Houses of Congress on numerous occasions on air quality issues and EPA operations

Conflicts of Interest

In my opinion conflicts of interest are in the eye of the beholder – not in the words of the declarer

Who is to Blame? The Search for Causality is Ageless!

- **John 9. Verses 1-41:**

As Jesus walked along, he saw a man blind from birth. His disciples asked him, "Rabbi, who sinned, this man or his parents, that he was born blind?

- **Tomasetti, Li and Vogelstein, Stem Cell Divisions, Somatic Mutations, Cancer Etiology, and Cancer Prevention. *Science* (March 24, 2017) 355:1330-1334**

- Cancers are caused by mutations that may be inherited, induced by environmental factors, or results from DNA replication errors (R)

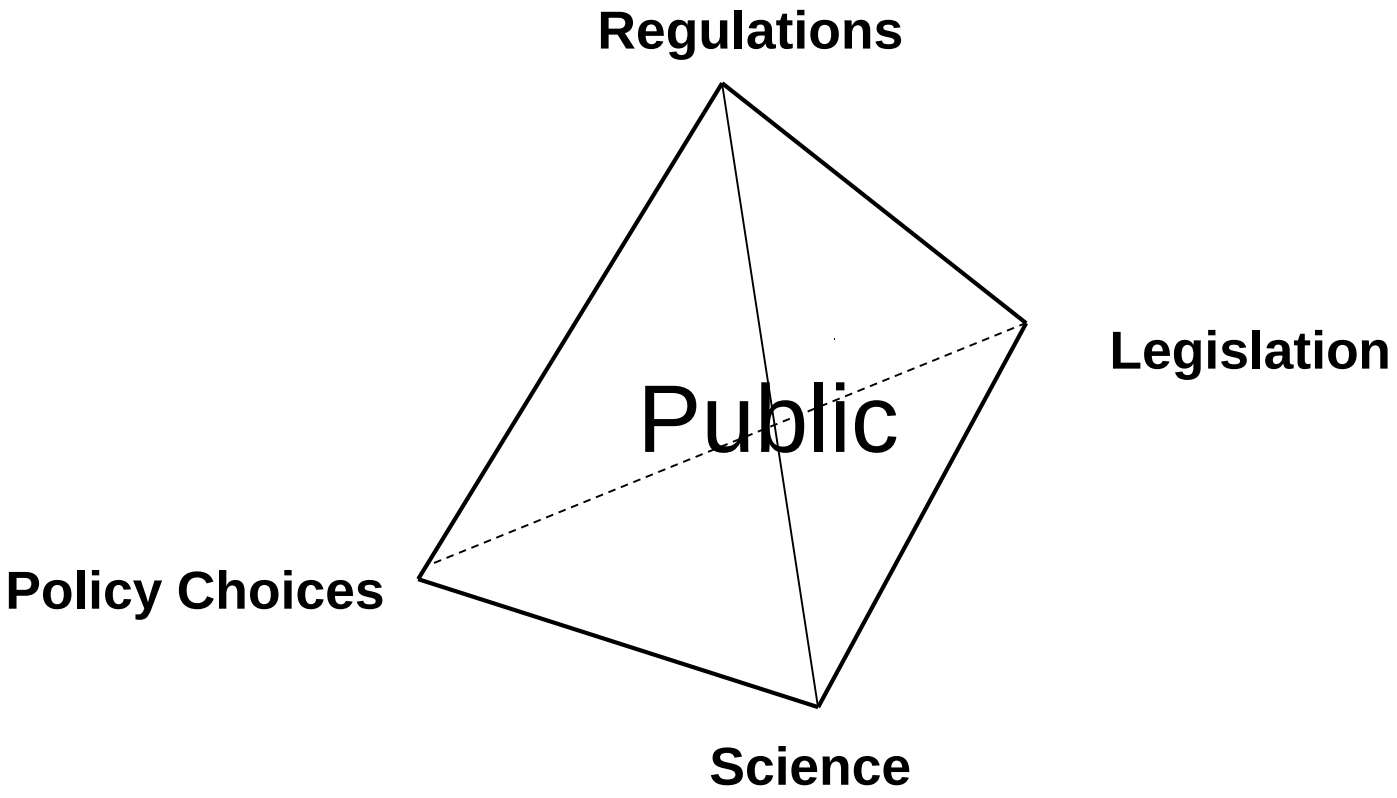
- R Mutations are responsible for two-thirds of the mutations in human cancer

- As a result of the aging of the human population, cancer is today the most common cause of death in the world

- Not all cancers can be prevented by avoiding environmental risk factors

Central Theme:

Policy and regulations should be informed by Science. However, science alone is not sufficient basis for policy and regulatory decisions.



Scientists need to clearly communicate scientific information <u>divorced</u> from their own personal desired policy outcome.

Science: The body of knowledge that has been accumulated by mankind from repeated, confirmed observations and the testing of hypotheses with well-designed experiments that can be replicated, findings reproduced, and conclusions validated.

Policy Choices: Decisions required or allowed by statute that are made using judgment and informed by science and other considerations.

Risks And Risks

"In the United States and some other industrial democracies, where people and their governments tend to be risk averse, legislatures, courts, and administrative entities usually *create a presumption favoring more safety rather than less*. The definitions of risk in law are often vague ("reasonable certainty of no harm" or "adequate margin of safety") and are likely to encourage an unrealistic belief that risks can be minimized or even eliminated altogether.

Donald Kennedy, Editor-in-Chief, Science 309: 2137 (30 September 2005)

Hazard Does Not Equal Risk!

Hazard: The potential for an agent to cause harm at some level of administered dose.

Frequently used in an absolute manner without regard to dose;

xyx causes cancer
abc causes nervous system effects
opq causes reproductive effects

Risk: The likelihood of disease resulting from exposure to a potential hazardous agent.

Requires knowledge of exposure and potency of the agent for causing harm.

DOSE:
The Key Concept in Toxicology

Paracelsus, father of modern toxicology, 1564

"All things are poisonous, only the dose makes it non-poisonous"

All things have the capacity to be toxic

	Beneficial Dose	Toxic Dose
Vitamin A	5000 units/day	50,000 units/day
Aspirin	300-1000 mg	1,000-30,000 mg
Oxygen	20% (Air)	50-80%
Water	2000 cc/day	*

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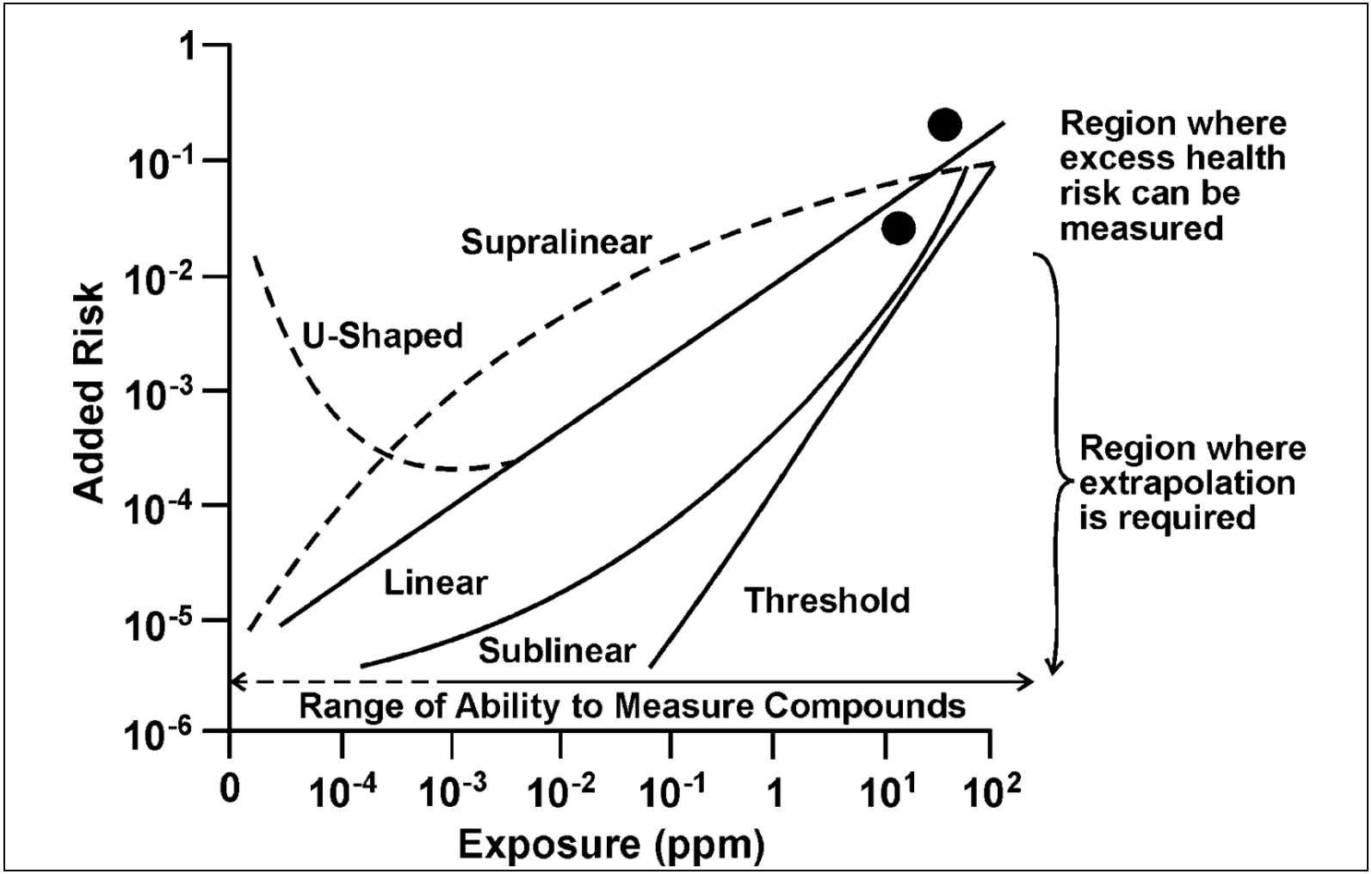
* Woman dies after water drinking contest, water intoxication eyed in "Hold your Wee for a Wii" contest death. AP, January 13, 2007, Sacramento, CA.

Critical Issue: Extrapolation Of Added Risks To Low Exposures



EPA National Ambient Air Quality Standards for "Criteria Air Pollutants"*

Carbon Monoxide
Lead
Nitrogen Dioxide
Ozone
Particulate Matter
Sulfur Dioxide

***Original 1970 Clean Air Act included "hydrocarbons"**

History of Ozone NAAQS (Primary Only)

Final Rule	Indicator	Averaging Time	Level
1971	Total Photochemical Oxidants	1 hr	0.08 ppm
1979	O_3	1 hr	0.12 ppm
1993	EPA Administrator decided no revisions were warranted		
1997	O_3	8 hr	0.08 ppm (by rounding convention is equal to 0.084 ppm)
2008	O_3	8 hr	0.075 ppm
2015	O_3	8 hr	0.070 ppm

History of Particulate Matter NAAQS* (Primary Only)

Final Rule	Indicator	Averaging Time	Level ($\mu g/m^3$)
1971	TSP	24 hr	260
		annual	75
1987	PM_{10}	24 hr	150
		annual	50
1997	$PM_{2.5}$	24 hr	65
		annual	15
	PM_{10}	24 hr	150
		annual	50
2006	$PM_{2.5}$	24 hr	35
		annual	15
	PM_{10}	24 hr	150
2012	$PM_{2.5}$	24 hr	35
		annual	12
	PM_{10}	24 hr	150

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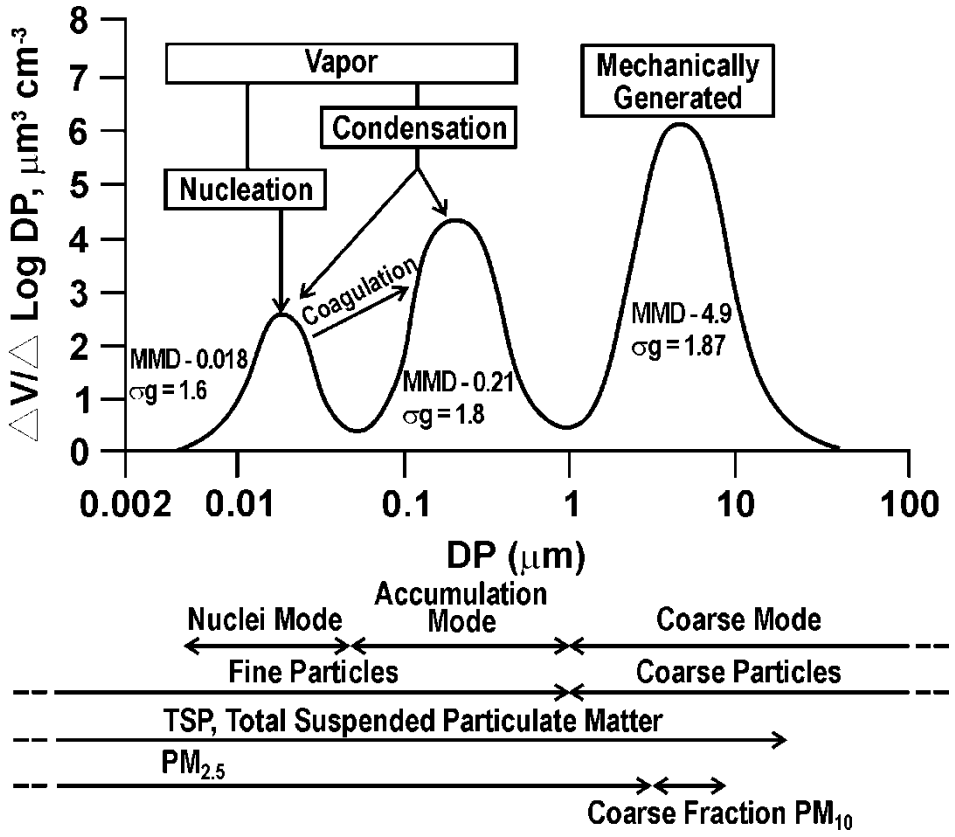
*Specified only as to mass concentration without regard to chemical composition

TRI-MODAL MEASURED VOLUME OR MASS SIZE DISTRIBUTION OF AIRBORNE PARTICLES



MAJOR ISSUE: Role of Clean Air Scientific Advisory Committee (CASAC) – Offering Advice or Prescribing Bounds for Policy Decisions

- **Pre-2004: CASAC commented on adequate descriptions of the science and offered "closure letters"**

- **Post-2004: CASAC offered "bright line" statements on specific levels for policy decisions on the level (and form) of the NAAQS**

- **Impact varied with EPA Administrators**

  - Some saw it as an intrusion on their policy judgment authority
  - Some welcomed the opportunity to defer to CASAC, "I am just following the science!"

2006-2008 Decisions on the NAAQS for $PM_{2.5}$ and Ozone

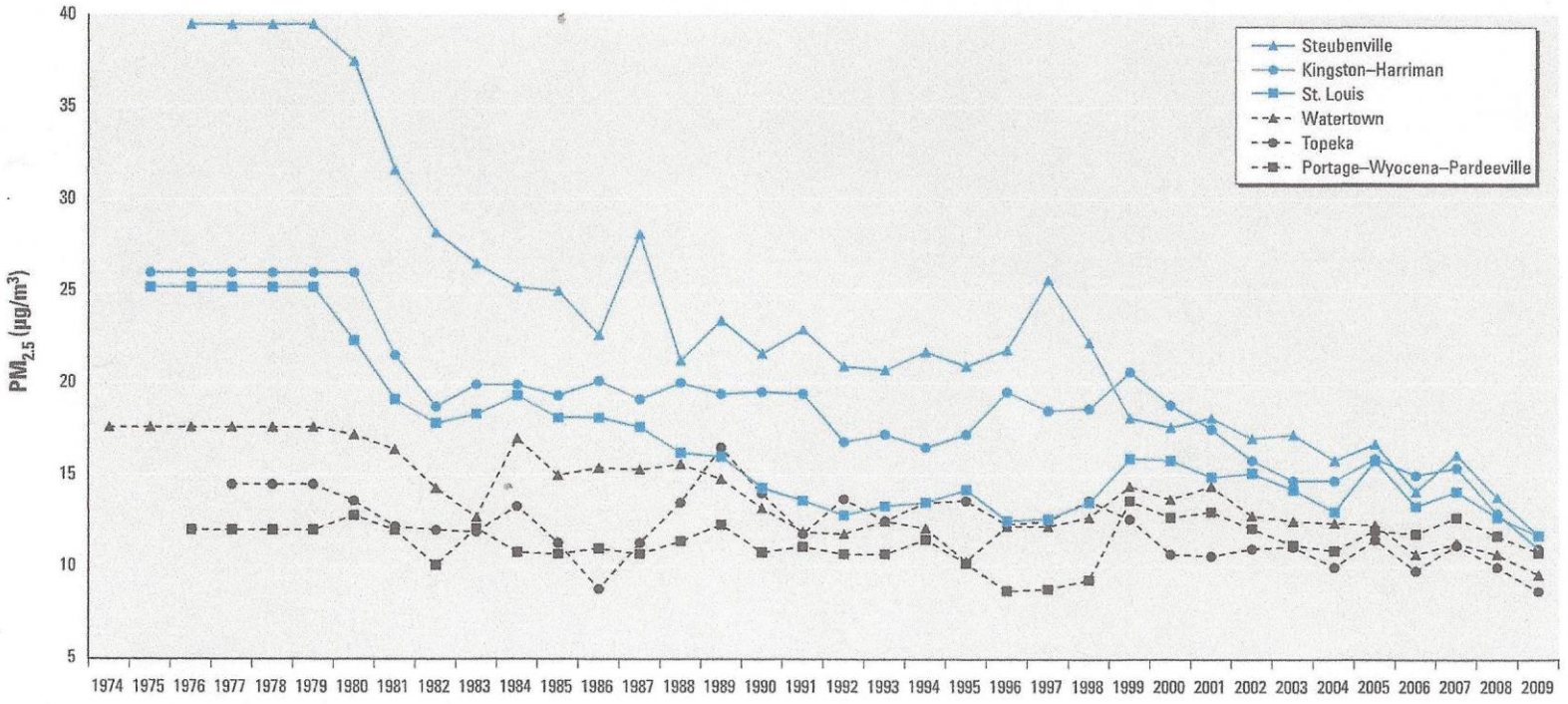
Indicator (unit)	Old NAAQS	CASAC	New Standard
$PM_{2.5}$ – 24 hr ($\mu g/m^3$)	65	30-35	35
$PM_{2.5}$ – annual ($\mu g/m^3$)	15	13-14	15
Ozone – 8 hr (ppb)	84*	60-70	75

*Set at .080 ppm, by rounding convention equal to 0.084 ppm or 84 ppb

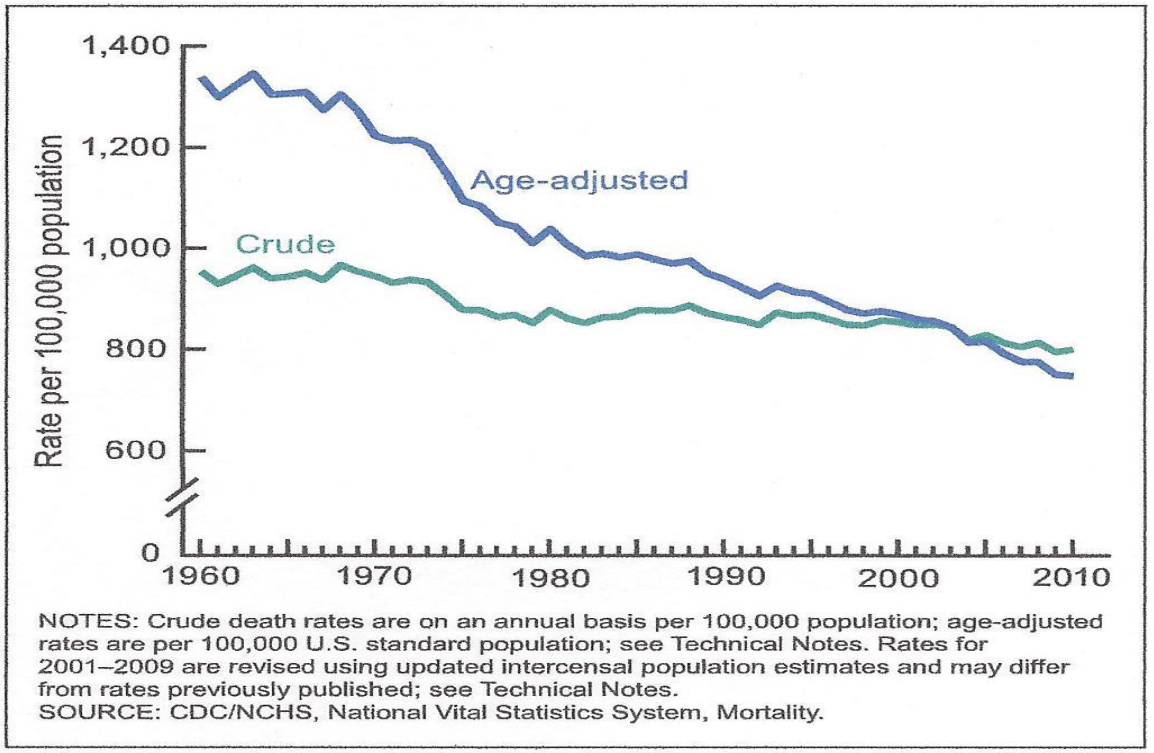
MAJOR ISSUE: Improvements in both air quality and mortality rates for interpreting epidemiological findings

- **Major improvements in air quality across the US:A and especially in areas most polluted in 1950s and 1960s**
- **Major improvements in both crude and age-adjusted mortality rates for USA**
- **Changing pattern of disease associated with changes in life style and aging (cancer, heart disease, and neurological disease)**

Annual Mean $PM_{2.5}$ Levels During 1974-2009 in the Harvard Six Cities Study. (Adapted from Lepeule *et al*. The data points pre-1997 for $PM_{2.5}$ have been extrapolated from TSP and PM_{10} measurements)



Crude and Age-Adjusted Death Rates: United States, 1960-2010 (Adapted from Murphy *et al*.)



NOTES: Crude death rates are on an annual basis per 100,000 population; age-adjusted rates are per 100,000 U.S. standard population; see Technical Notes. Rates for 2001–2009 are revised using updated intercensal population estimates and may differ from rates previously published; see Technical Notes.
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

MAJOR ISSUE: Should very small statistical associations at low pollutant levels be extrapolated to even lower levels and interpreted as "causal"?

- **Some key data sets are heavily influenced by high levels and protracted exposures of 1950s and 1960s**
- **With few exceptions, air pollutants do not cause unique diseases**
- **Diseases of greatest impact are common diseases of aging populations**

EPA Created Five-Level Causality Hierarchy Based on Overall Weight of Evidence

(1) Causal
(2) Likely to be causal
(3) Suggestive of causal
(4) Inadequate to infer causal relationship
(5) Not likely to be causal relationship

- Very similar to IARC cancer hazard categorization scheme

Causes of Death for USA for 2010 by Major Causes (Murphy et al, 2013)

Rank	Cause of Death (based on ICD-10, 2004)	Number
…	All causes	2,468,435
1	Diseases of heart	597,689
2	Malignant neoplasms	574,743
3	Chronic lower respiratory diseases	138,080
4	Cerebrovascular diseases	129,476
5	Accidents (unintentional injuries)	120,859
6	Alzheimer's disease	83,494
7	Diabetes mellitus	69,071
8	Nephritis, nephrotic syndrome and nephrosis	50,476
9	Influenza and pneumonia	50,097
10	Intentional self-harm (suicide)	38,364
11	Septicemia	34,812
12	Chronic liver disease and cirrhosis	31,903
13	Essential hypertension and hypertensive renal disease	26,634
14	Parkinson's disease	22,032
15	Pneumonitis due to solids and liquids	17,011
…	All other causes	483,694

Comparison of Original Conditional Logistic Regression Results (Silverman[7]) with Results of Similar Analyses Except Based on New REC Estimates Defined Using HP and CFM

All Subjects Who Ever Worked Underground						
Silverman *et al.*[7]	0 to <81	29	92	1.0 (referent)	0.004	0.00065[a]
	81 to <325	29	52	2.46 (1.01–6.01)		(0.00020,0.0011)[a]
	325 to <878	29	69	2.41 (1.00–5.82)		
	≥878	29	51	5.10 (1.88–13.87)		
REC estimates from Silverman *et al.*[7] and "without radon" controls[12]	0 to < 97	31	158	1.0 (referent)	0.01	0.00073
	97 to < 384	31	90	1.90 (0.78–4.63)		(0.00022,0.0012)
	384 to < 903	31	80	2.73 (1.08–6.88)		
	≥ 903	31	84	5.04 (1.77–14.30)		
HP-CFM REC estimates and "without radon" controls	0 to <130	31	144	1.0 (referent)	0.16	0.00014
	130 to <531	31	99	2.03 (0.83–4.96)		(–0.000062,0.0003)
	531 to <2,149	31	99	3.45 (1.27–9.41)		
	≥2,149	31	70	3.84 (1.07–13.74)		
HP-CFM REC estimates and "with radon" controls	0 to <130	31	144	1.0 (referent)	0.69	0.00005
	130 to <531	31	99	1.83 (0.73–4.61)		(–0.00020,0.00030)
	531 to <2,149	31	99	2.47 (0.79–7.73)		
	≥2,149	31	70	2.5 (0.49–12.79)		

Estimates of Avoided Premature Deaths in California in 2020 Estimated for $PM_{2.5}$ NAAQS with a Reduction in the Annual Standard from 15 to 12 µg/m^3 projected using BenMAP (A Smith, personal communication, 2016).

	Population		Baseline Mortality (#)		Avoided Deaths (#)	
	Krewski[a] (30-99)	Lepeule[b] (25-99)	Krewski (30-99)	Lepeule (25-99)	Krewski (30-99)	Lepeule (25-99)
Not attaining/above margin (>13 µg/m^3)	763,104	875,086	7,574	7,681	21	47
Not attaining/in margin (>12 to 13 µg/m^3)	3,841,464	4,419,703	41,853	42,342	117	266
Already attaining (≤12 µg/m^3)	7,560,163	8,537,984	86,913	87,735	318	721
Total	12,164,732	13,832,773	136,340	137,758	456	1,034

[a] Krewski et al (2009) evaluates the population from age 30 to 99 years;
[b] Lepeule et al (2012) evaluates the population from age 25 to 99 years.

MAJOR ISSUE: A lack of "public access" to key data sets for replication and extended analyses by other scientists under-mines credibility of original analyses by "closed circle" of investigators

- This is a real issue that can be resolved
- Recent experience with Diesel Exhaust in Miners Study (DEMS) data set illustrates problems and solutions
  - Original analyses of DEMS data drove decision of International Agency for Research in Cancer (IARC) to classify diesel exhaust as a human carcinogen
  - Replication and extended analyses of DEMS data by independent scientists provide alternative results and interpretations
  - This is the way science should work!

Comparison of Original Conditional Logistic Regression Results (Silverman[7]) with Results of Similar Analyses Except Based on New REC Estimates Defined Using HP and CFM

Analysis	Quartiles of Cumulative REC, Lagged 15 Years ($\mu g/m^3$-yr)	Cases	Controls	OR (95% CI)	p_{trend}	Slope $(\mu g/m^3\text{-yr})^{-1}$ 95% CI
			All Subjects			
Silverman *et al.*[7]	0 to <3	49	158	1.0 (referent)	0.001	0.00073[a]
	3 to <72	50	228	0.74 (0.40–1.38)		(0.00028,0.0012)[a]
	72 to <536	49	157	1.54 (0.74–3.20)		
	≥536	50	123	2.83 (1.28–6.26)		
REC estimates from Silverman	0 to <3	49	158	1.0 (referent)	0.0006	0.00082
et al.[7] and "without	3 to <72	50	228	0.79 (0.41–1.52)		(0.00035,0.0013)
radon" controls[12]	72 to <536	49	157	1.62 (0.75–3.49)		
	≥536	50	123	3.24 (1.40–7.55)		
HP-CFM REC estimates and	0 to <6.6	49	172	1.0 (referent)	0.06	0.00016
"without radon" controls	6.6 to <129	50	191	1.05 (0.58–1.93)		(–0.000012,0.0003)
	129 to <891	49	168	1.60 (0.79–3.24)		
	≥891	50	135	2.37 (1.02–5.50)		
HP-CFM REC estimates and	0 to <6.6	49	172	1.0 (referent)	0.63	0.00005
"with radon" controls	6.6 to <129	50	191	1.02 (0.55–1.90)		(–0.00016,0.00026)
	129 to <891	49	168	1.20 (0.56–2.56)		
	≥891	50	135	1.37 (0.5–3.77)		

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MAJOR ISSUE: Excess emphasis on ENVIRONMENTAL factors in "causing" disease may be misleading

- Major improvements in air quality during last half century provide the opportunity to refocus research efforts (and public expenditures) using an attributable risk orientation to studying diseases
- It is time to return "environmental health" to the "public health" arena
- Increasing expenditures on health care as fraction of gross domestic product (current – 1 of every 6 dollars) will increase the need to better understand the multiple factors influencing the occurrence of major diseases
- Increasing concern for social equity will move attention to other factors influencing health, including jobs

The Impact of Socio-Economic Status on Mortality Rate Ratio[a] (adapted from Steenland et al, 2004)

Mortality	Men	Women
All causes	2.02 (1.95-209)[b]	1.29 (1.25-1.32)
Heart Disease	1.88 (1.83-193)	1.84 (1.76-1.93)
Stroke	2.25 (2.14-2.37	1.53 (1.44-162)
Diabetes	2.19 (2.07-2.32)	1.85 (1.72-2.00)
COPD	3.59 (3.35-3.83)	2.09 (1.91-230)
Lung Cancer	2.15 (2.07-2.23)	1.31 (1.25-1.39)
Breast Cancer	-	0.76 (0.73-0.79)
Colorectal Cancer	1.21 (1.16-1.27)	0.91 (0.86-0.96)
External Causes	2.67 (2.58-2.78)	1.41 (1.35-1.48)

[a] Mortality rate ratio = Mortality for lowest quartile of socioeconomic status / Mortality for highest quartile of socioeconomic status

[b] 95% Confidence Interval

CONCLUSIONS

- **The air quality community is at a critical juncture**
- **Tremendous progress has been made in the last half century improving air quality and developing new technologies with ultra-low emissions of pollutants**
- **The question of how low is low enough must be addressed by Society at Large, not just by scientists**
- **The era of separate “environmental health” is likely to be replaced by a more holistic view of public health**
- **Assumptions of causal linkages should be viewed with caution**
- **Quantitative estimates of costs and benefits are useful inputs to decision making, however, 5 significant figure estimates are most assuredly wrong!**