

Research and Policy Needs for Environmental Health

Making the leap from a clinical case series to evidence
based medicine to reduce health impacts of RF
(Radio Frequency)

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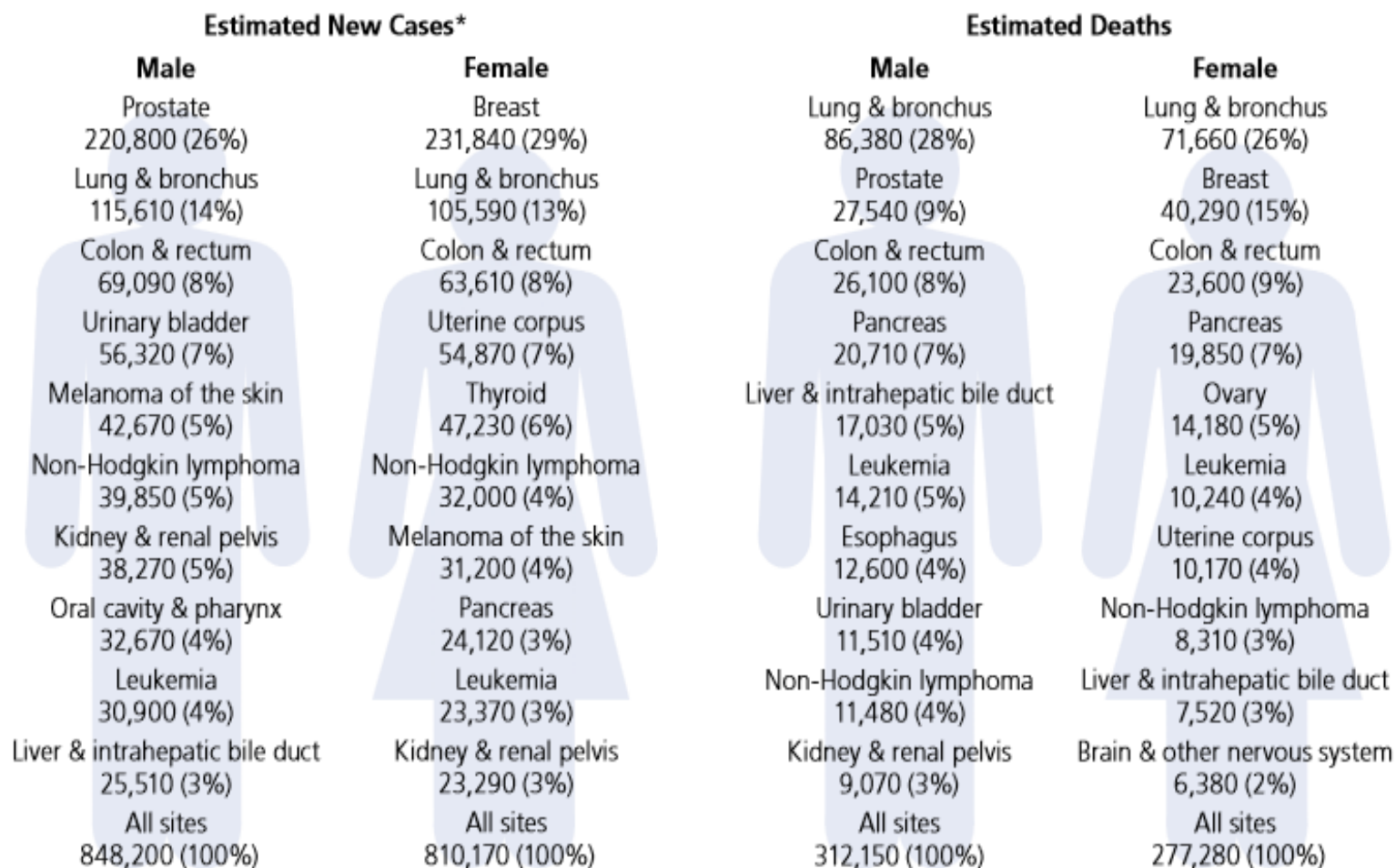
Goals and Objectives

- ▶ Review of Bradford Hill postulates with emphasis on clinical causation of cancer
- ▶ Review concepts of exposure assessment as used in high level acute exposures vs low level chronic exposures
- ▶ Compare study design issues in different types of exposure and understand the limitations
- ▶ Use of evidence based medicine to influence the health care community and the public to decrease exposure to RF

BRADFORD HILL GUIDELINES FOR CAUSATION

1. Temporality
2. Strength (magnitude) of the association
3. Dose-response (biological gradient)
4. Reversibility (cessation of exposure)
5. Consistency with other knowledge
6. Biological plausibility
7. Specificity of the association
8. Analogy
9. Coherence

Leading Sites of New Cancer Cases and Deaths – 2015 Estimates



*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Risk Assessment

- ▶ Identification of a hazard
- ▶ Dose and response assessment (slope, if possible)
- ▶ Exposure Assessment
- ▶ Risk Characterization (mathematical model and/or application of safety factors)

Effective Use of Cohort Studies:

A Comparative Assessment Of Major International Disasters Indicates The Need For Lifetime Health Care Of Affected Populations And Systematic Emergency Preparedness

Roberto G Lucchini^{1,2}, Sushma Acquilla³, Angela Basanets⁴, Pier Alberto Bertazzi⁵, Andrey Bushmanov⁶, Michael Crane¹, Denise J Harrison⁷, Dana Hashim¹, William Holden¹, Philip J Landrigan¹, Benjamin J Luft⁸, Paolo Mocarelli⁹, Nailya Mazitova⁶, James Melius¹⁰, Jacqueline M Moline¹¹, Koji Mori¹², David Prezant¹³, Joan Reibman¹⁴, Dori B Reissman¹⁵, Alexander Stazharau¹⁶, Ken Takahashi¹², Iris G Udasin¹⁷, Andrew C Todd¹

Environmental Disasters

- ▶ Seveso
Trichlorophenol (TCP) and Dioxin
- ▶ Bhopal
Methyl Isocyanate
- ▶ Chernobyl
Ionizing Radiation
- ▶ World Trade Center Health Program
Toxic Soup
- ▶ Fukushima
Ionizing Radiation

Conclusions / Recommendations

- ▶ Surveillance programs found exposure related physical and mental health consequences and identified the need for long term health care of the affected populations
- ▶ The persistence of chronic effects on physical and mental health and quality of life, and the long latency period for solid tumors, highlight the need for lifetime disaster-related health programs
- ▶ Systematic and timely exposure assessment and identification of exposed populations are the key elements of health surveillance of disaster responders

World Trade Center Exposures

March 2016



GENERAL CHARACTERISTICS OF DUST/SMOKE AT WTC

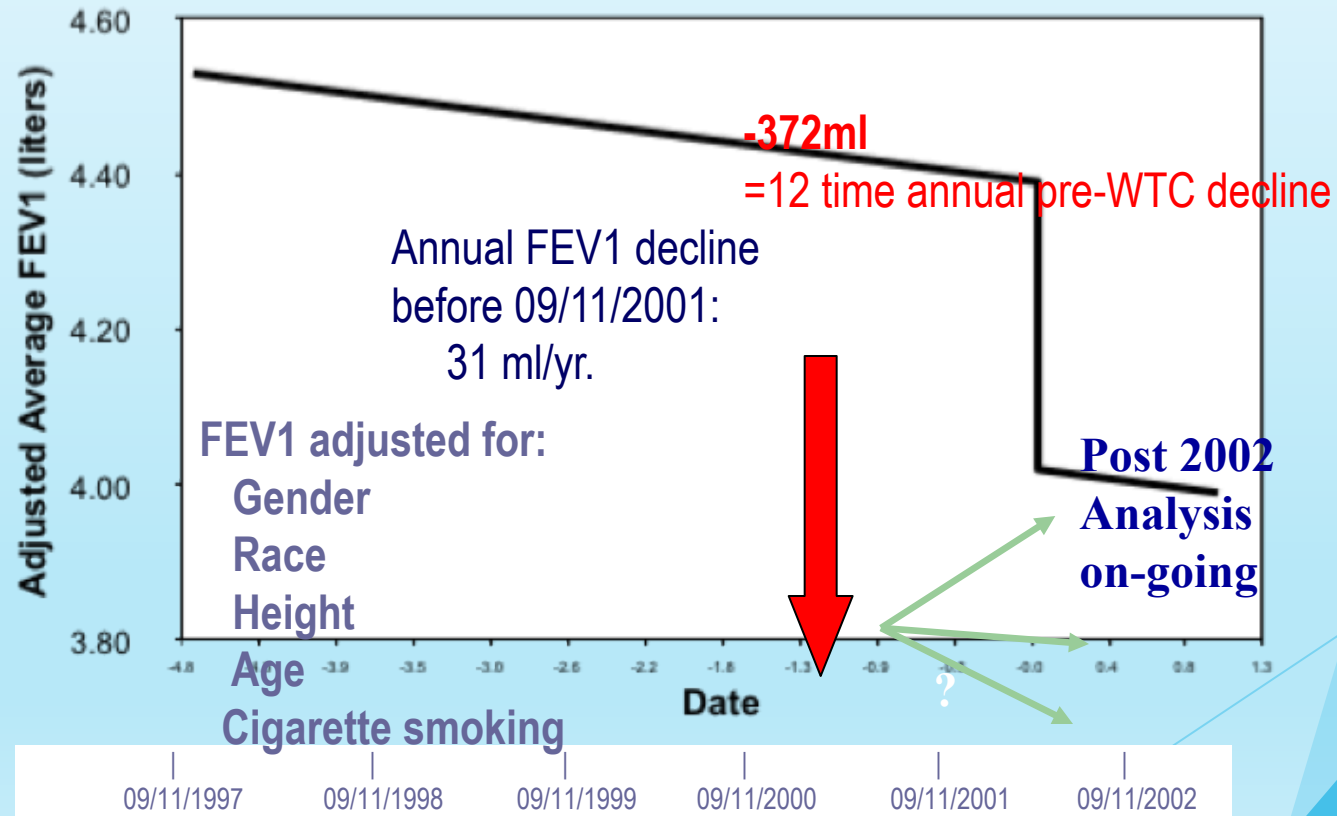
- ▶ Construction Debris (Pulverized vermiculite, plaster, paint, foam, gypsum, cellulose, etc.)
- ▶ Cement
- ▶ Glass Pulverized (Silica)/Fibers
- ▶ Chrysotile Asbestos 0.8%-3.0%
- ▶ Cotton Fibers/Lint
- ▶ Tarry and Charred Wood
- ▶ Soot/PAHs
- ▶ VOCs
- ▶ Heavy metals
- ▶ Initial exposure greater than 100,000 PPM Total Particles

Air Contaminants From Plume

- ▶ Screening conducted to determine presence of combustion byproducts on/above rubble pile
- Workers directly in plume may be exposed to various anticipated fire-related air contaminants

e.g., formaldehyde, benzene, acrylonitrile, acrolein, acetonitrile, phosgene, styrene, toluene, xylene, PAHs, acetaldehyde, 2-butanone, carbofurans, PCBs, ethyl-benzene, Freon R-22, hexane, isocyanates, perchloroethylene, 1-3 butadiene, trichloroethylene, vinyl chloride, glutaraldehyde, and xylene

WTC-Related Longitudinal FEV1 Loss



Banauch, Kelly, Prezant et al; Am J Respir Crit Care Med
2006

Persistence of multiple illnesses in World Trade Center rescue and recovery workers: a cohort study

Juan P Wisnivesky, Susan L Teitelbaum, Andrew C Todd, Paolo Julia Kaplan, Craig Katz, Stephen Levin, Ben Luft, Steven Markowitz, Jacqueline M Moline, Fatih Ozbay, Robert H Pietrzak, Moshe Shapiro, Vansh Sharma, Gwen Skloot, Steven Southwick, Lori A Stevenson, Iris G Udasin, Sylvan Wallenstein, Philip J Landrigan

Lancet, Sept 2011

Association between WTC Exposure and Excess Cancer Risk

- WTC registry is observational study of 55,778 NYS residents including rescue/recovery workers (n= 21,850) and those not involved in rescue/recovery (n=33,928)
- Cancers identified through linkage with 11 state registries 4 years after 9-11 to allow for latency
- Incident cases were identified any time post enrollment through Dec 2008
- 421 cases included in SIR analysis
- Of the 23 cancers analyzed, 3 had statistically significant elevations
Prostate (n=67 SIR 1.43 (95% CI 1.11 - 1.82)
Thyroid (n=13 SIR 2.02 (95% CI 1.07-3.45)
Multiple Myeloma (n=7 SIR 2.85 (95% CI 1.15-5.88)

Li, Cone et al Jama Dec 2012

*We are able to get compensation for our cancer patients because of this

Problematic Use of Cohort Studies which Cast Doubt on Temporality

- ▶ Chapman
- ▶ Sato

Chapman Study Concerning Possible Increase in Incidence of Brain Cancer Since the Introduction of Mobile Phones 29 Years Ago

- ▶ Authors state stability of brain cancer since 1982 except in males over the age of 70
- ▶ **They state this difference is due to improvement in imaging techniques**
- ▶ Methods: Data was obtained on “accounts” not actually individual people
- ▶ No data on heavy use of mobile phones in Australia
- ▶ Discussion by authors states that no cohort studies show excess of brain in other studies including Denmark Cohort and “no evidence of any rise in any age group that can plausibly be attributed to mobile phones”
- ▶ Authors make erroneous conclusion that there is no DNA or cellular data

Chapman, Cancer Epi 2016

Bandora, Wojcik, Cancer Epi 2016

Time Trend In Incidence of Malignant Neoplasms of CNS In Relation to Mobile Phones

- ▶ Cohort of 7550 recruited by distributing leaflets at elementary schools, junior high schools, high schools, universities, and colleges across Japan
- ▶ Increased incidence of malignant neoplasms in men and women age 20-29 and 30-39 from 1993-2010 in Japan
- ▶ Lack of consistency with prevalence data
- ▶ However author states that more accurate estimates of cumulative exposure needed

Can Cohort Studies Be Used to Assess Risk of Cell Phone Use and Brain Cancer?

- ▶ Long latency
- ▶ Rare outcome
- ▶ Selection bias
- ▶ Difficulty in risk assessment and measurement of exposure
- ▶ Studies often don't reflect individual use, length of calls, use of speaker phone or blue tooth or other risk reducing technologies
- ▶ Cohort is useful when defined large exposure has occurred and exposure assessment has already occurred
- ▶ Yet why do health care providers rely on such studies?

Biologic Plausibility

- ▶ Cellular / DNA Data - Levis Meta-Analysis 2011
- ▶ Animal data: NIEHS / NTP Soffritti, Belpoggi - Synergist RF and Formaldehyde
- ▶ Human: Volkow (2011) Abnormal glucose uptake at region of the brain closest to exposure after 50 minute phone calls

Glioblastoma Multiforme

- ▶ Etiology:
- ▶ Genetic
- ▶ Cell phone use (controversial)
- ▶ Head injury, N-nitroso compounds, occupational hazards, electric magnetic field exposure (inconclusive)

Medscape Dec, 2016

Jeffrey Bruce, MD

Case Report: Lt. Bill: NJ State Trooper 2016

48 year old man arrived at 9-11 disaster site of 9-11, coordinated operations for almost 2 years

- ▶ Presents with memory loss
- ▶ 3 months later - abnormal MRI, dx with glioblastoma left temporal lobe, received chemo and radiation
- ▶ Returned to work but only to a desk job until his mental status declined
- ▶ Started hospice care in November and died December 27, 2016



Trooper Bill (Continued)



- ▶ Exposure History - arrived WTC site shortly after planes went into towers, coordinated interagency response and went from place to place in various vehicles
- ▶ Driving with right hand, and holding cellular communication device with his left hand propped on car window
- ▶ During the 2 years of WTC exposure had almost constant exposure to RF
- ▶ Besides Bill, 2 other temporal lobe glioblastoma and 1 temporal lobe astrocytoma in the 2800 people who came to the NJ Clinical Center of WTC, 1 other brain tumor under investigation

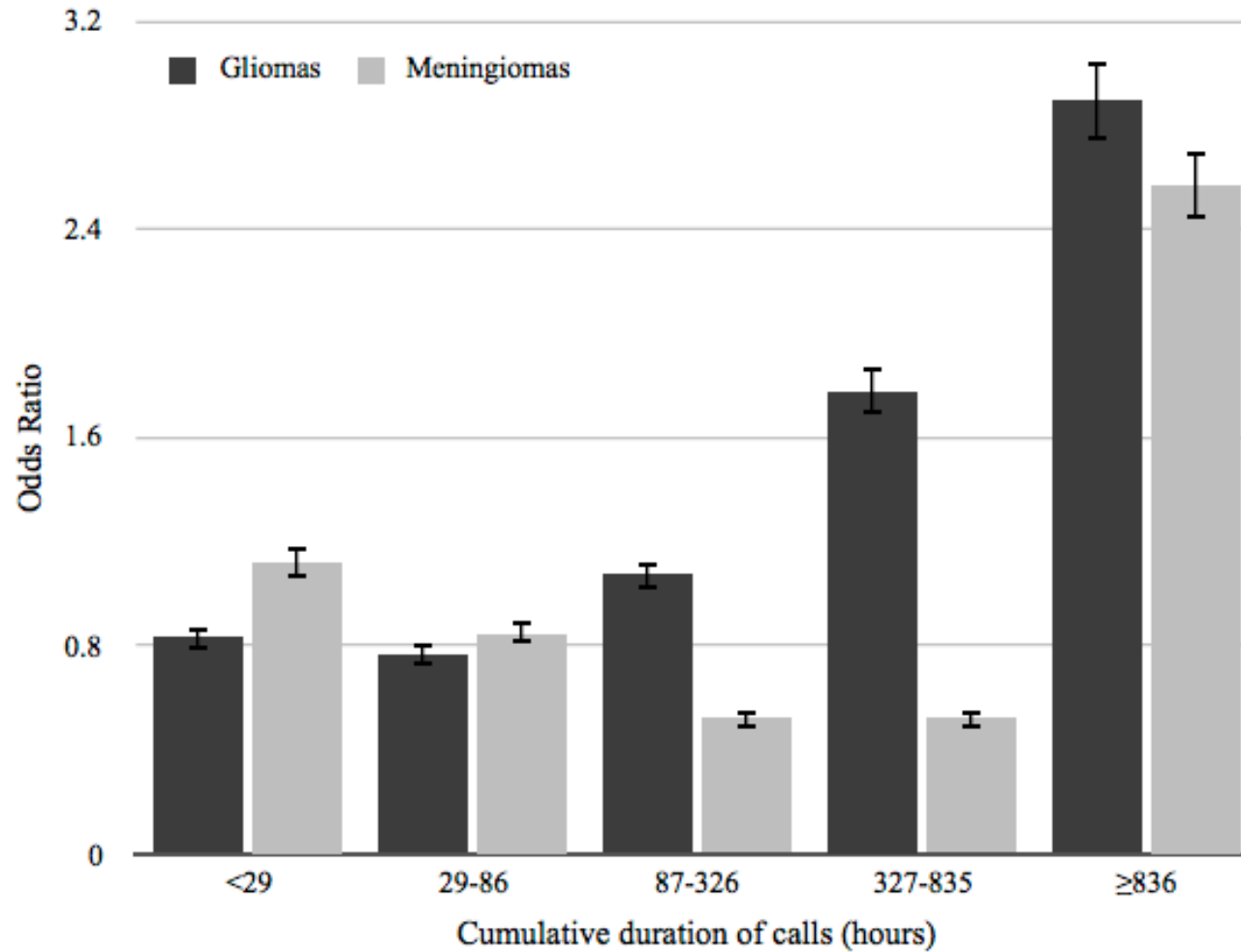
Cancer Cells: Italian Court Rules “ Mobile Phone Can Cause Brain Tumors”

- ▶ Innocente Marrolini - 60 year old retired businessman argued that excessive use of his mobile phone for 6 hours per day for 12 years caused a benign tumor which left his face partially paralyzed
- ▶ Tumor on trigeminal nerve
- ▶ Oncologist Angelo Gino Levis said that the ruling was “extremely significant”

Implications for Future Studies

- ▶ Case control studies with attention to exposure history
- ▶ Attention to other risk factors exposures
- ▶ Selection of appropriate cases
- ▶ Comparability to studies of rare cancers including angiosarcoma of the liver and mesothelioma

Mobile phone use and brain tumours in the CERENAT case-control study



Coureau et al., (2014)

Consistently increased Glioma Risk in Case-control studies

Study		Odds ratio
CERENAT 2014	≥896 h	2.89*
	≥18 360 calls	2.10*
	≥15 h/month	4.04*
2015 reanalysis	ipsilateral – cases only	2.40*
Hardell et al. Meta-analysis 2015	>25 y latency	3.0*
	>1y ipsilateral	1.8*
	first use <20 y old	1.8*
	first use <20 y old	3.1*
	ipsilateral	

* Statistically significant (95%)

CERENAT 2014

CERENAT 2015

Hardell et al. 2015

Implication on Public Policy

- ▶ Workers compensation for highly exposed workers who developed cancers related to their occupational exposures
- ▶ Technical preventive measures to decrease exposure as the science is being performed
- ▶ Health preventive measures: Can risk reduction be incorporated into well child and well adult examinations

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