Regulatory Dose Limits:

Significance of Additional Data Sets and New Analysis Techniques

David J. Brenner and Igor Shuryak

Columbia University Center for Radiological Research, New York, NY

Research Team*:

Eric Wang, Xiao Wu, Robert Ullrich, Columbia University, New York

Zhenqiu Liu, Munechika Misumi, Alina Brenner, RERF, Hiroshima Japan

**View and opinions expressed here are those of the authors (DJB, IS)*

Current Radiation Protection Limits – Background

What <u>really</u> controls radiation protection are the two annual dose limits:

- ➔ **Occupational limit: 50 mSv/y**
- ➔ **Public limit: 1 mSv/y**

The 50 mSv/y limit comes from analyses (1977; 1990; 2007) only of A-bomb survivor data

- ➔ ***The great majority of the A-bomb exposures took place in <u>much less than 1 microsecond</u>***
- ➔ ***The 1 mSv/y limit comes from adding an extra "public acceptance factor" to the 50 mSv/y limit***

Since these earlier analyses, there have been two key developments:

1. **Large-scale high-quality epidemiological data have become available for cohorts exposed to *<u>prolonged</u>* radiation exposures**
2. **New advanced epidemiological data analysis techniques have been developed such that we can now assess the *<u>causal</u>* effects of radiation exposures, independent of any *a-priori* assumptions about dose-response shapes**

1. Epidemiological Data

What sorts of data sets do we need?

- ➔ We need large data sets incorporating a wide range of radiation doses, ages, and both sexes
- ➔ We need data sets where we have reliable retrospective dose estimates that are specific for each ***individual***, not just for groups
- ➔ We need long-term follow up of individual outcome
- ➔ *We want data sets for short-term and long-term exposures*

1. Epidemiological Data

What useful data sets do we have now?

➔ **A-bomb survivor data**

- **Exposures largely in less than 1 microsecond**
- **All ages, both sexes**
- **Long-term follow up**
- **Wide dose range**
- **Credible individualized radiation dosimetry**

➔ **Nuclear worker data**

- **Prolonged (years) radiation exposures**
- **Long-term follow up**
- **Wide dose range (generally no very high doses)**
- **Reliable individualized radiation dosimetry**

2. Analysis of Radiation Epidemiological Data

Traditional Analysis Methods

➔ **The effects of radiation on disease induction or mortality, especially at low doses, are fundamentally <u>causal</u> inference questions**

- **Traditional analysis methods look for correlations rather than causes**
- **For example, when non radiation features like age and sex have a strong influence on the outcome, traditional analysis methods will prioritize these, resulting radiation effect estimates being distorted**
- **Traditional analysis methods of necessity need to make a-priori assumptions about the shape of the dose-effect relation (linear, LQ, etc)**

2. Analysis of Radiation Epidemiological Data

Causal Machine Learning

- **A new approach for analyzing low-dose epi data**
- **Assesses causal effects of radiation doses, rather than simply associations**
- **Does not require a-priori assumptions such as LNT, LQ**
- **Very flexible, can handle complex multi-dimensional datasets incorporating any new features such as ‘omics data**
- **Better estimates of risk estimate uncertainties**

2. Analysis of Radiation Epidemiological Data

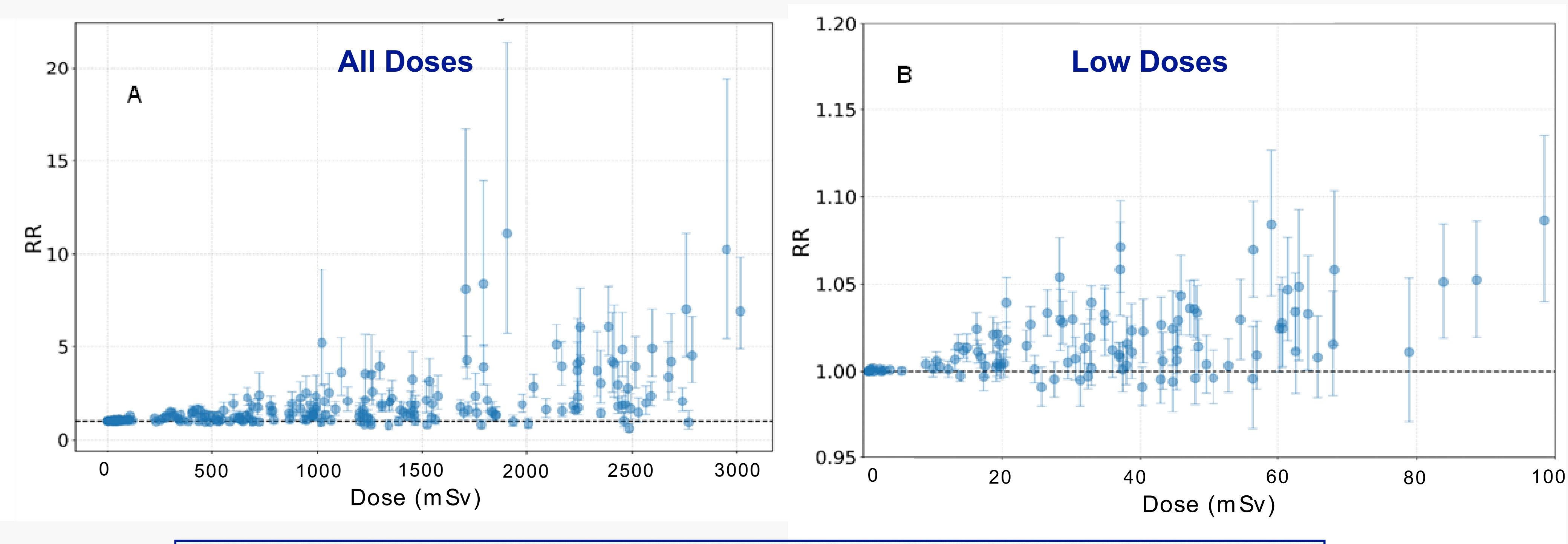
Causal Machine Learning

- **Double/debiased Machine Learning (DML)**
- **Causal Forest DML**
- **Bag-of-Little-Bootstraps method for estimating confidence intervals**

- **<u>Extensive</u> testing of the methodology using synthetic artificial data sets**

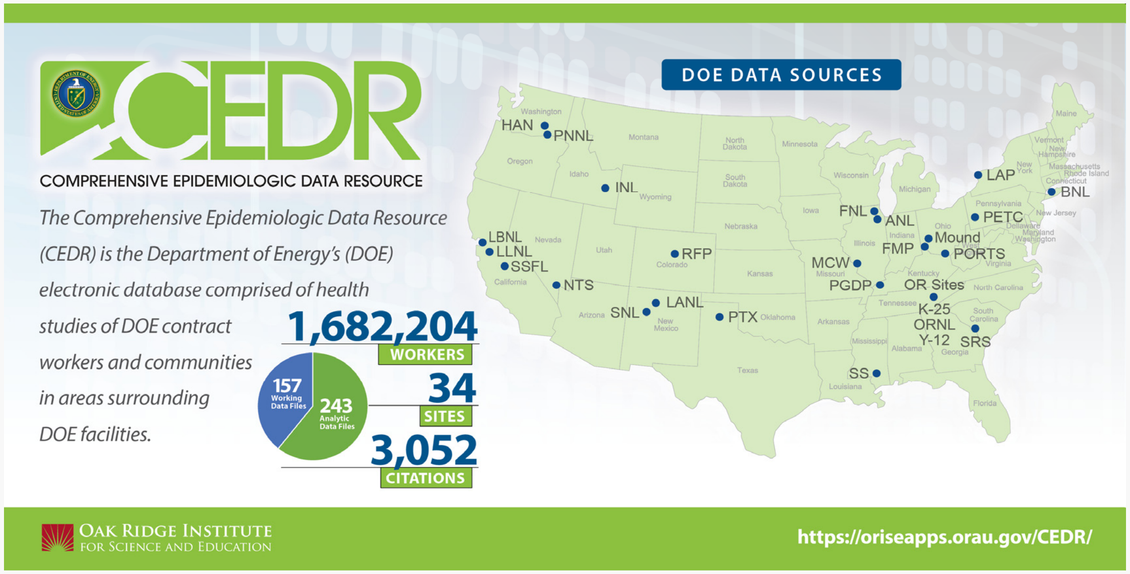
All Cause Mortality Among A-Bomb Survivors:
CML-Estimated Relative Risks

* Each data point correspond to a small number of individuals who have roughly the same characteristics (dose, sex, age, city, etc)



- ♦ **Evidence for a causal relation between dose and risk at higher doses**
- ♦ **No evidence of a causal relation between dose and risk at lower doses**

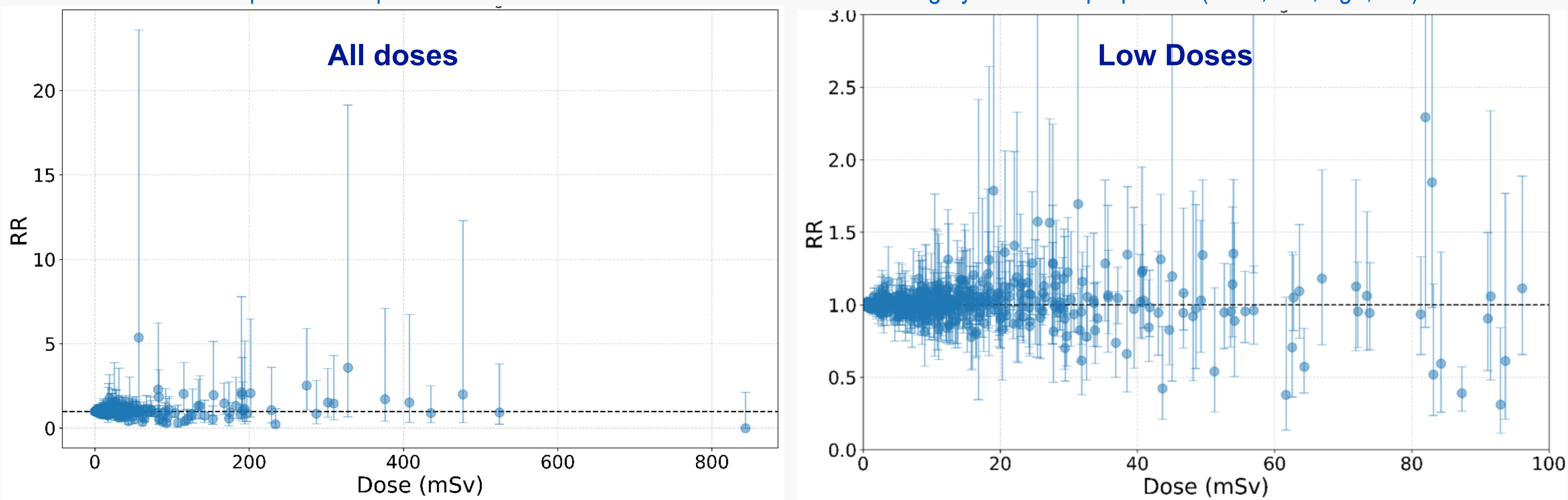
Prolonged Radiation Exposures



Data set	# of subjects in analysis	Yrs when subjects worked with radiation		Yr when followup ended	Total dose (mSv)		
					median	mean	max
ORX10A05, Expanded Oak Ridge National Laboratory (ORNL) cohort	10,742	1943	1973	1988	3.1	19.3	1144
HFWC94A1, Hanford Workers Cohort Study Follow-up through 1994	26,389	1944	1978	1994	4.3	27.9	860
MFFEGWA1, Mortality study among female nuclear workers at multiple DOE facilities	21,445	1943	1979	1994	0.5	3.9	296

All-Cause Mortality in ORNL cohort:
CML-Estimated Relative Risks

* Each data point correspond to a small number of individuals who have roughly the same properties (dose, sex, age, etc)



♦ **No evidence of a causal relation between dose and risk in any dose range within the cohort**

Regulatory Dose Limits:

Significance of Additional Data Sets and New Analysis Techniques

- **Current dose limits based on A-bomb survivor data, where exposures were essentially instantaneous**
  - **We now have corresponding high-quality epidemiological data from prolonged radiation exposures**

- **Current dose limits are based on "old school" data analysis approaches, which**
  - **a) look for correlations between dose and risk, not causal relations between dose and risk**
  - **b) of necessity make a-priori assumptions about the shape of the dose-risk relationship**

- **Discussed here is a new approach for analyzing radiation epidemiological data, *Causal Machine Learning* (CML), which does not have the problems of a) and b)**

- **CML analysis of A-bomb data (instantaneous exposure) suggests:**
  - **Evidence for a causal relation between dose and risk at higher doses (above about ~50-100 mSv)**
  - **No evidence of a causal relation between dose and risk at lower doses**

- **CML analysis of nuclear worker data (prolonged exposure) suggests:**
  - **No evidence of a causal relation between dose and risk in <u>any</u> dose range within the studied 3 cohorts**

These results might suggest that the current annual occupational dose limit of 50 mSv may be too low for non-instantaneous exposures – a conclusion that can be reached without the need to get immersed in the debates about LNT and ALARA…