The Future of Low-Dose Radiation Risk Modeling

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November 16,2021

Public Meeting #5
Developing a Long-Term Strategy for
Low-Dose Radiation Research In the United States

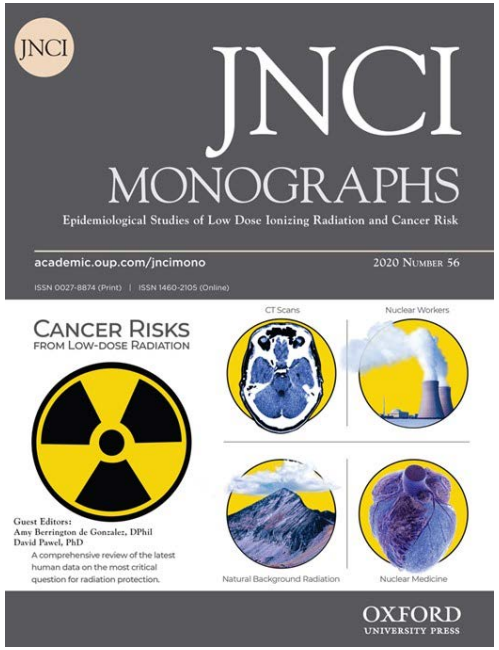
Understanding Low Dose Radiation Effects Is Important

- Low dose exposures are common
  - Diagnostic medical procedures
  - Occupational exposures
  - Environmental exposure (radon, elevated natural background levels)
- Low dose exposures of broad (if often exaggerated) concern to the general public
  - Nuclear accidents
  - Nuclear terrorism (e.g. “dirty” bombs)

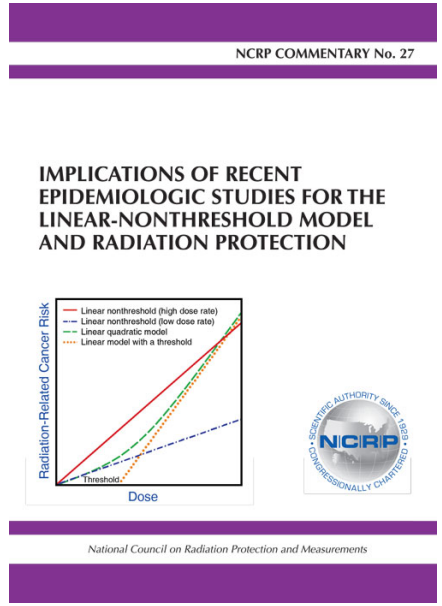
Low Dose Radiation Effect Studies Are of Great Interest

- Many studies exist
  - Occupational exposures
    - INWORKS (and its component studies), UK NRRW, USRT, US Million Person Study cohorts, Mayak workers
  - Medical Exposures
    - CT studies
  - Accidental population exposures
    - Techa River, Chernobyl, Taiwan Contaminated Buildings
  - Environmental exposure
    - Kerala, Chinese High Background Areas, UK background radiation
  - Atomic bomb survivors (low dose portion)

Low Dose Radiation Effect Studies Are of Great Interest



- NCI Low dose monograph (Berrington et al 2018)
  - Review of statistical issues affecting analysis and interstation
  - Sign-test based assessment of evidence from a range of epi studies in populations with mean doses < 100 mGy
- NCRP Commentary 27 (NCRP, 2018)
  - Considered study-by-study degree of support the LNT paradigm for many low dose studies



Challenges and Limitations of (Epi) Studies of Low Dose Effects

- Compelling evidence of radiation effects at higher doses (e.g., > 0.2 Gy)
  - Clear evidence of persistent increases in rates
  - Effects at a given dose depend on effect modifiers
    - e.g. sex, attained age, age at exposure and other factors
- However, direct evidence for effects at lower doses less clear
  - Limited statistical power
  - Large potential for bias due to confounding, unrepresentative comparison groups, or shared dose uncertainties
  - Virtually impossible to characterize effect modification

The Low Dose Radiation Effect Challenge: Recognize the Limitations

- No single study can provide a definitive characterization of low dose effects
- Low dose studies provide little or no information on
  - Dose response shape
  - Effect modification
  - Biological mechanisms

The Low Dose Radiation Effect Challenge: What Can Be Done

- Consider the full spectrum of low dose /low dose rate studies
  - Minimize subjective ranking/weighting (e.g. by quality score)
  - Use low dose information from studies with higher and lower doses
  - Use information from high dose studies to help characterize effect modification
- Do not emphasize statistical significance
  - Low power does not necessarily mean bias
  - Significant risk estimates in a given study are likely to be biased upward
- Do not be too dismissive on the grounds of **potential** bias or confounding
    - The likelihood of an apparent effect being due to confounding is greatly reduced if there is a trend with dose
    - (Non-differential) Dose uncertainty is unlikely to cause a spurious dose response

Epi Studies of Low Dose Radiation Effects: Needs (1)

- Support for continuation of existing studies
  - Extended follow-up
  - Sub-studies to help understand likelihood of significant confounding
- Studies of newly exposed populations
  - Individual/individualized doses with some characterization of uncertainty
  - An appropriate internal comparison group
  - Careful follow-up
  - A component to assess psychological impacts of mass low dose exposure events.
- Better methods for combining evidence from multiple studies
  - Pooled analyses can be useful
    - Data access can be an issue
    - Random effect models are essential
  - Development of Empirical Bayes and Fully Bayesian methods
- Methods to allow the direct use of information on risk obtained from low dose studies in the development of radiation protection standards

Epi Studies of Low Dose Radiation Effects: Needs (2)

- Better methods for combining evidence from multiple studies
  - Pooled analyses can be useful
    - Data access can be an issue
    - Random effect models are essential
  - Development of Empirical Bayes and Fully Bayesian methods
- Methods to allow the direct use of information on risk obtained from low dose studies in the development of radiation protection standards