Radiation Hormesis:
Real or Not?

22.01 – Intro to Radiation

December 7th, 2015

What Is the Idea of Hormesis?

- A little bit of a bad thing can be good

- What are some examples?

Selenium: Helps or Hurts?
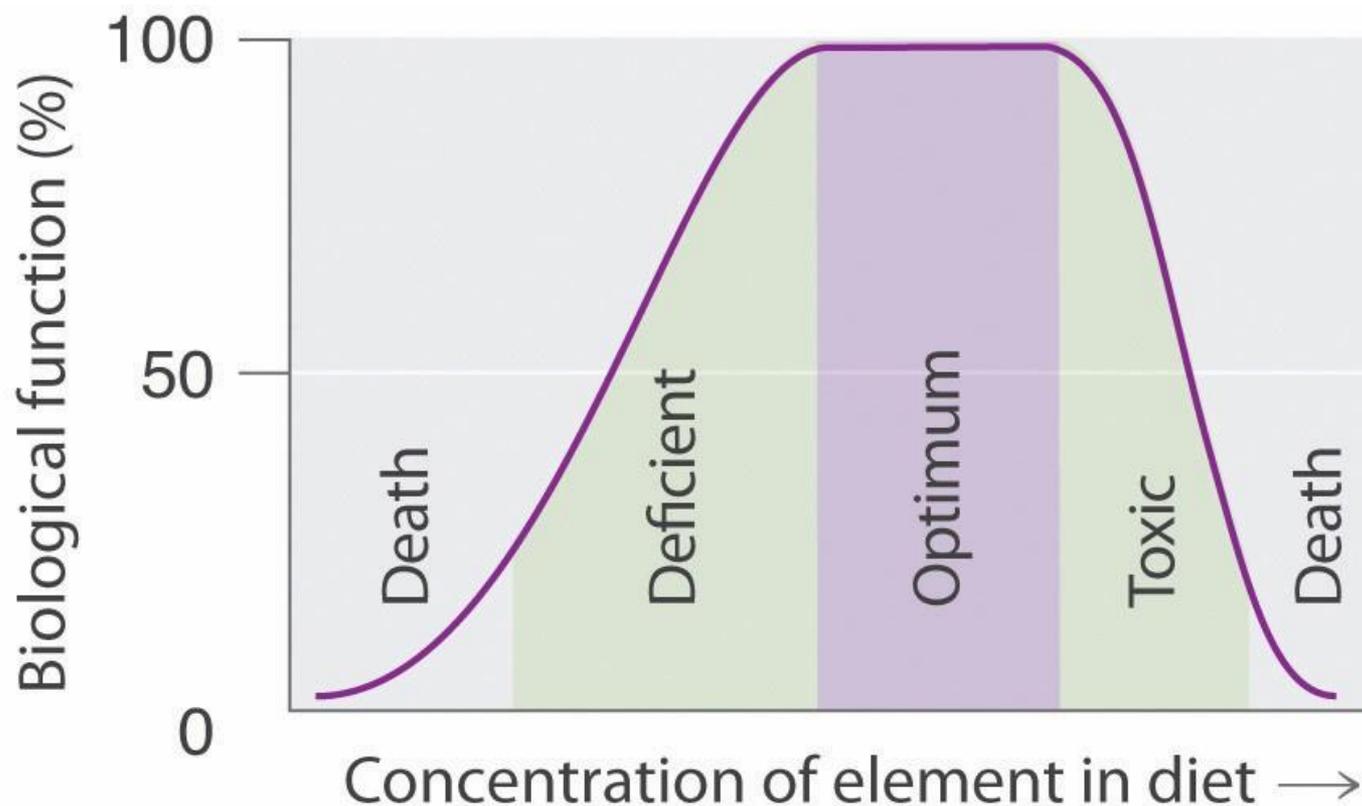
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Selenium: Helps or Hurts?

Table 3. Published reports discussed in text (with emphasis on serum selenium)

| Report	Age & Gender (yr, M/F)	Dosing pattern	Serum Se (µg/L)	Notes
3	24 M	acute	30000	ingestion ~ 1 hr, fatal ~ 4 hr
7	52 F	acute	2435	ingestion at 4 d, fatal at 6 d
11	15 F	acute	3100	ingestion ~ 1 hr
12	56 M	acute	2716	ingestion ~ 3 hr
13	48 F	acute	2400	ingestion ~ 2 hr
14	2 F	acute	1580[a]	ingestion ~ 5 hr
15	29 M	acute	931[a]	ingestion ~ 3 hr
16	2 M	acute	420	ingestion at 1 d, fatal at 18 d
17	adults	chronic	650-1400[b]	no toxicity in 54 of 86
18	36 M	chronic	680	vitamin therapy for fatigue
19	57 F	chronic	528	nutritional supplement
20	adults	-	123-363[c]	without toxicity
21	≥14 M	-	101-151[d]	NHANES III reference interval

Arguments For/Against Selenium Hormesis

- Taking megadoses of 200 mcg/day (4x the RDA) of selenium may have acute toxic effects, and showed no decreased incidence of prostate cancer mortality for low doses, and increased high-grade prostate cancer rates (~35,533 men)

    - Refs: Brasky TM, Kristal AR. J Natl Cancer Inst (2015) 107(1): dju375, Kenfield SA, et al. *J Natl Cancer Inst* (2015) 107 (1): dju360

- Selenium supplements of 200 mcg/day (4x the RDA) greatly reduced (63%) secondary prostate cancer evolution (974 men, 13 Se vs. 35 placebo cases, 11 years follow-up)

    - Ref: L. C. Clark et al. British Journal of Urology [1998, 81(5):730-734]

Models of Dose-Response

Linear-threshold model

Linear-no threshold model
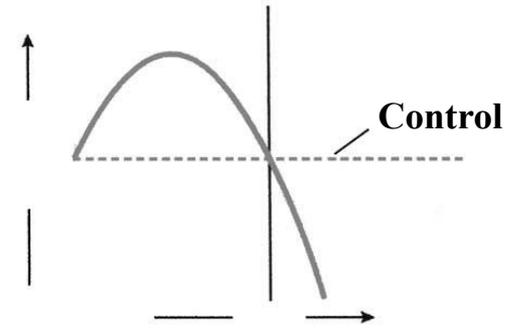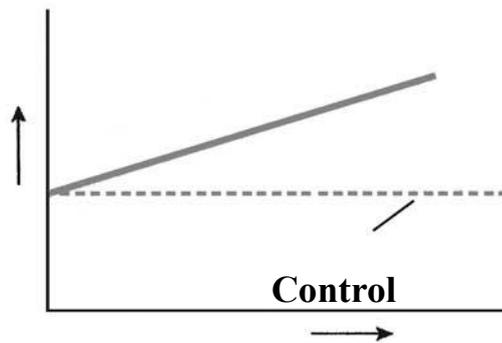
Inverted U-shaped hormesis
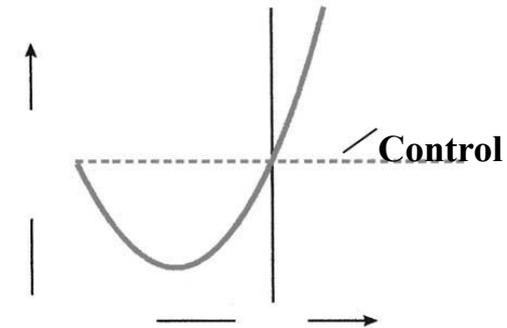
Hormesis model

Courtesy of Macmillan Publishers Ltd.

Is Radiation Hormetic?

D. P. Hayes. *European Journal of Clinical Nutrition* (2007) 61, 147–159
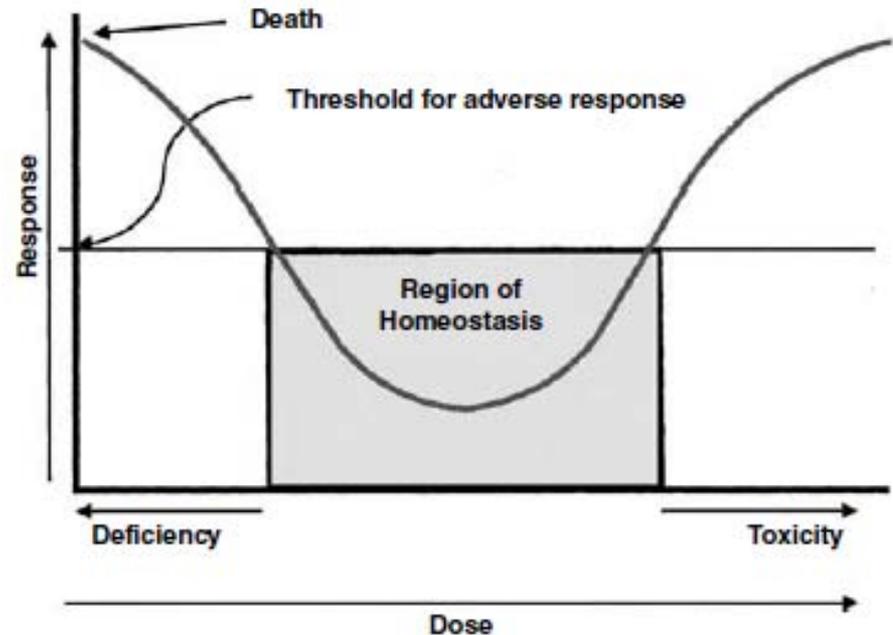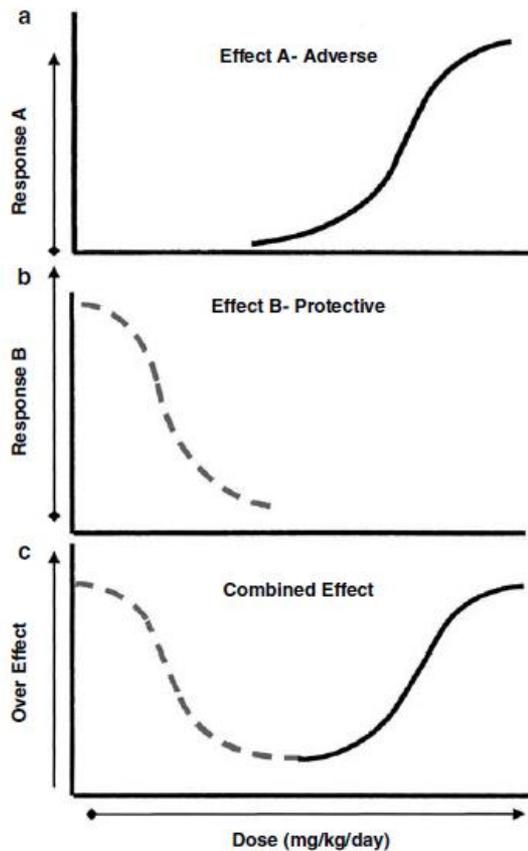
Figure 3 Depiction of dose–response relationships for essential vitamin or mineral nutrients. The U-shaped hormetic response is shown with a Region of Homeostasis (the dose range with neither nutrient deficiency nor toxicity) being contiguous to both the low-dose Deficiency region and the high-dose Toxicity region. See text for further discussion. Adapted from Eaton and Klaassen (2001).

Courtesy of Macmillan Publishers Ltd.

History of Non-Hormetic Models
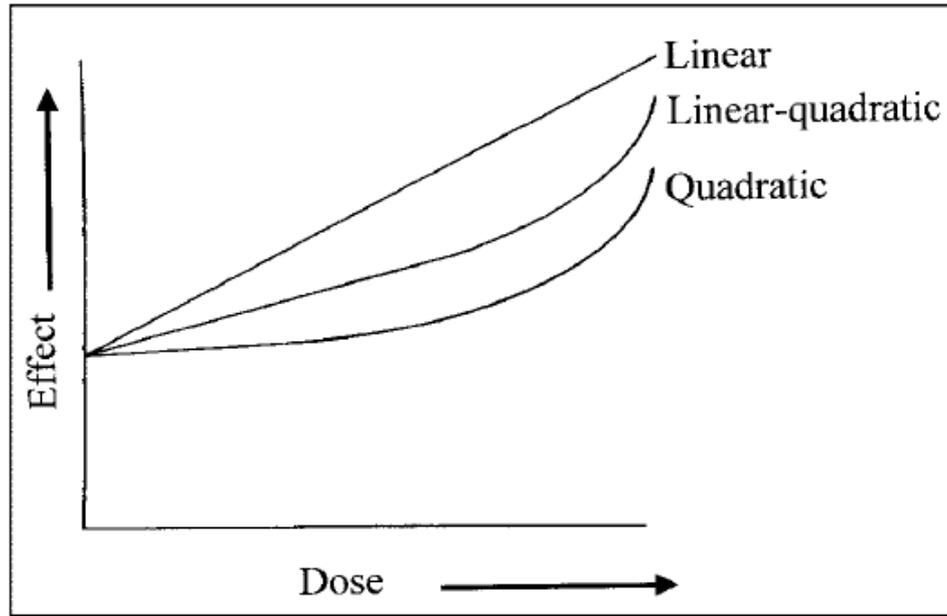
FIGURE 1. Three hypotheses of radiation dose–response relationship, as proposed by the United Nations Scientific Committee on the Effects of Atomic Radiation in 1958. (Reprinted with permission of (*3*).)

Original image source: Mettler, F.A., and A.C. Upton. *Medical Effects of Ionizing Radiation*. 2nd ed. W.B. Saunders, 1995.

History: The LNT Model

Linear No-Threshold model states that:

- Radiation exposure is harmful;

- Radiation exposure is harmful at all exposure levels;

- Each increment of exposure adds to the overall risk;

- The rate of accumulation of radiation exposure has no bearing on risk.

Checking the LNT Model

<u>Linear No-Threshold</u> model states that:

- Radiation exposure is harmful;

  We know this from LOTS of accidental exposure data

- Radiation exposure is harmful at all exposure levels;

- Each increment of exposure adds to the overall risk;

- The rate of accumulation of radiation exposure has no bearing on risk.

Checking the LNT Model

<u>Linear No-Threshold</u> model states that:

- Radiation exposure is harmful;

- Radiation exposure is harmful at all exposure levels;

- Each increment of exposure adds to the overall risk;

- The rate of accumulation of radiation exposure has no bearing on risk.

> **The ICRP-99 study showed this to be false**
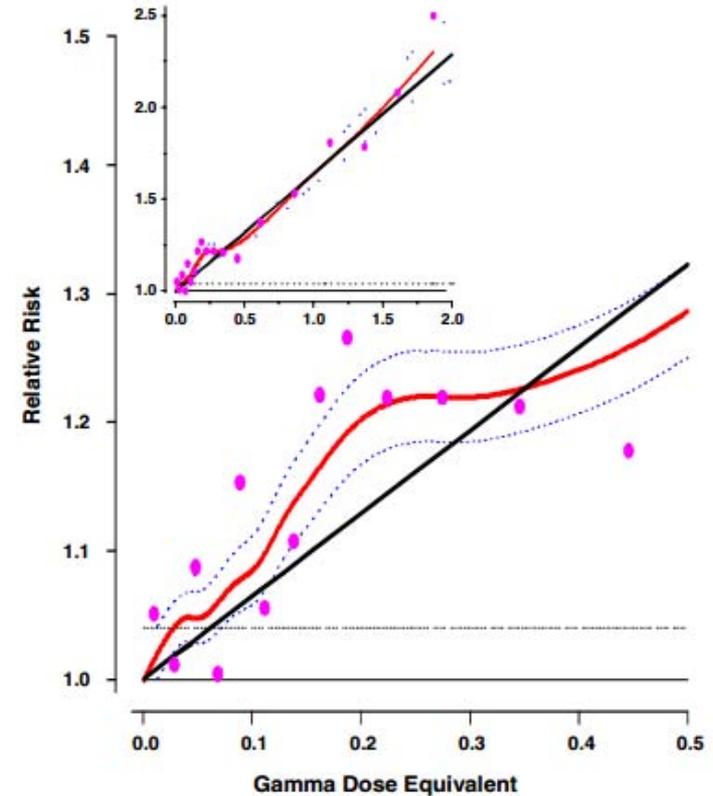
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.

Checking the LNT Model

<u>Linear No-Threshold</u> model states that:

- Radiation exposure is harmful;

- Radiation exposure is harmful at all exposure levels;

- Each increment of exposure adds to the overall risk;

These are the open questions today!

- The rate of accumulation of radiation exposure has no bearing on risk.

Evidence for Hormesis

- Ask yourself:

  - What study size was used?

  - How were the error bars defined?

  - Can hormesis be conclusively shown from this study?
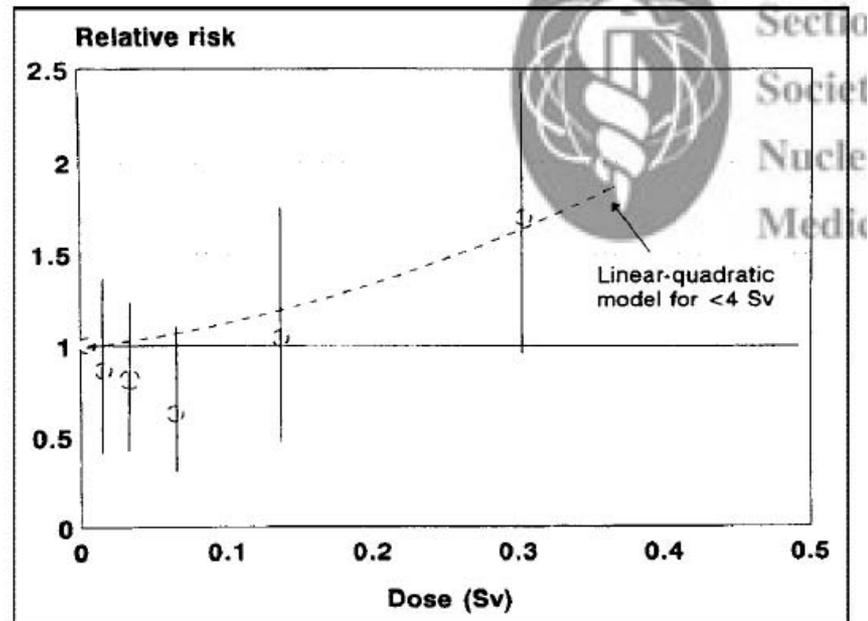
FIGURE 3. Incidence of leukemia as function of radiation dose in atomic bomb survivors in Japan. (Reprinted with permission of (*3*).)

Original image source: Mettler, F.A., and A.C. Upton. *Medical Effects of Ionizing Radiation*. 2nd ed. W.B. Saunders, 1995.

Evidence for Hormesis
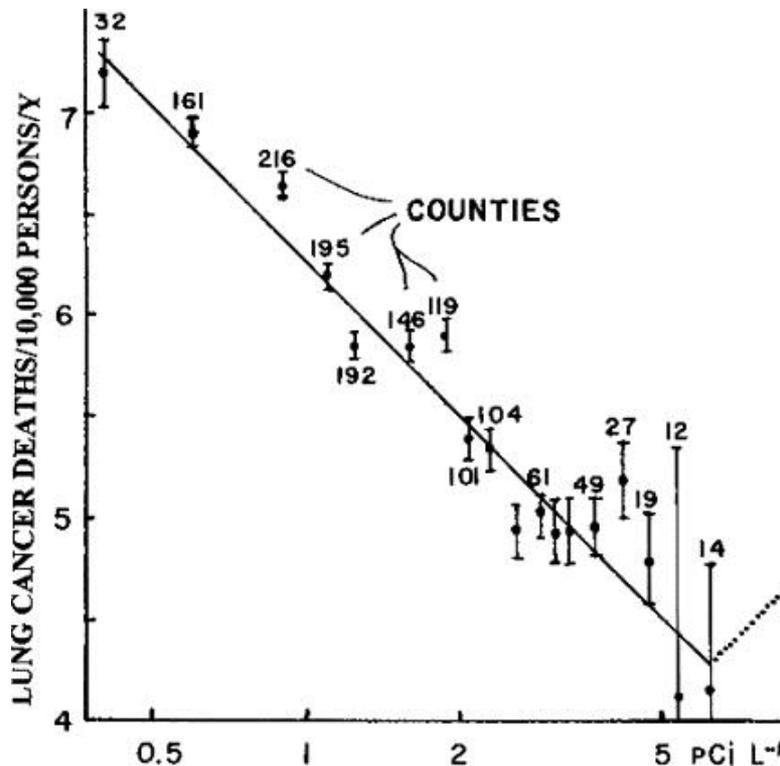
- To a point, radon levels in homes were found to *decrease* lung cancer deaths
  - 200,000 radon samples
  - 1,600 counties, comprising 90% of the U.S. population

Evidence for Hormesis
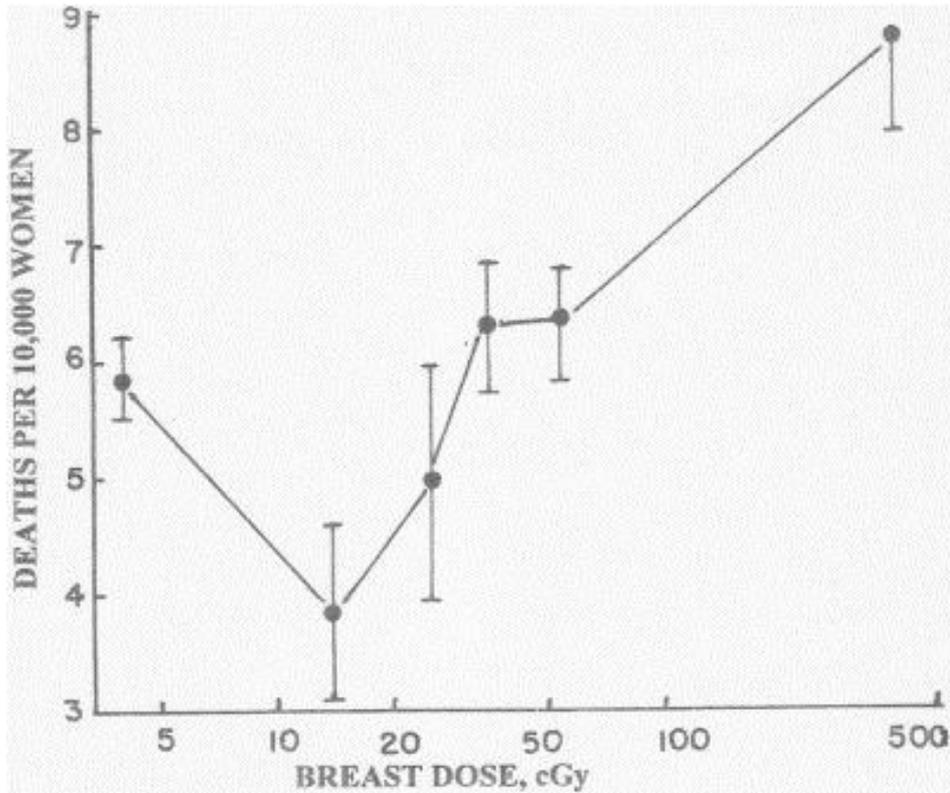
- Women who received multiple x-rays to monitor lung collapse during tuberculosis treatment experienced less breast cancer
 - One standard deviation displayed

CAN Hormesis Be Real?

- Certainly at the cellular level

- Maybe not at the multicellular/organism level

- More data needed?

Evidence for a Threshold Model

Lung cancer deaths from radon in miners. Pooled analysis of the relative risks of lung cancer deaths, with 95% confidence limits, from 11 underground miner studies

Evidence for a Threshold Model

Courtesy of National Academies Press. Used with permission.
Source: National Research Council. *Health Effects of Exposure to Radon: BEIR VI*. The National Academies Press, 1999. doi:10.17226/5499.
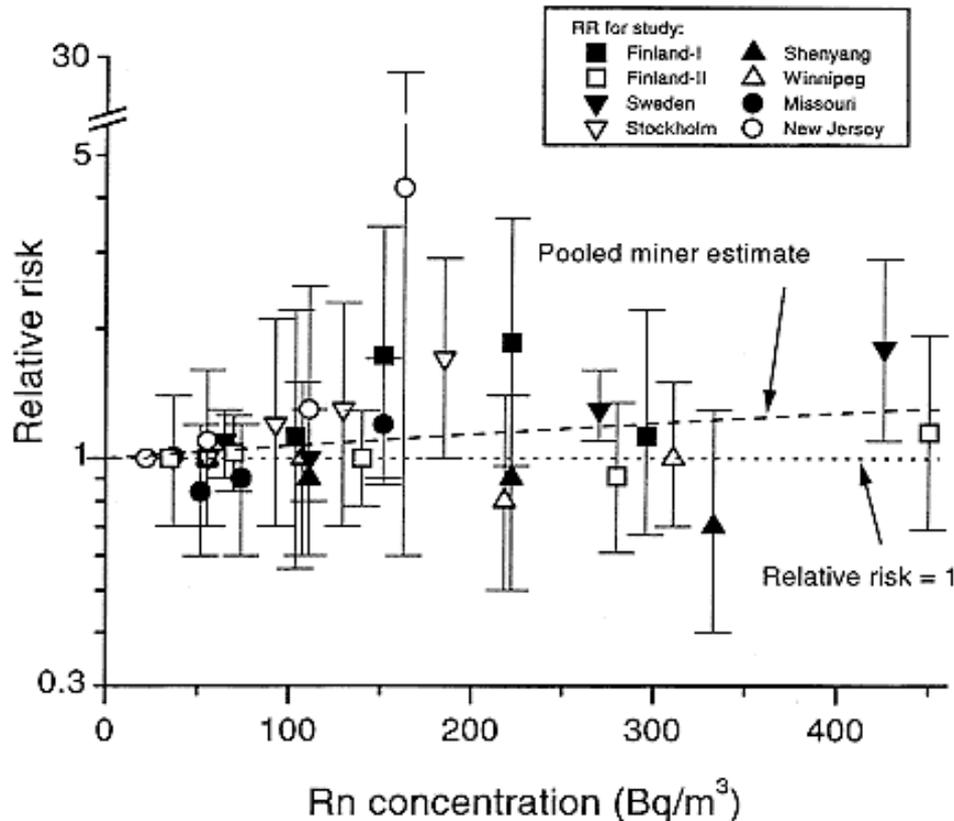
Lung cancer deaths from radon in homes. Eight case control studies of relative risks for lung cancer death rates of people in homes. One standard deviation shown.

The 22.01 Hormesis Debate

Together, we will debate whether hormesis can actually exist

1. Split into two groups: Pro and Against

2. Spend ~30 minutes to find evidence, papers, and construct arguments for/against hormesis

3. Present your findings in 10 minutes each, with 5 minutes each to rebut

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