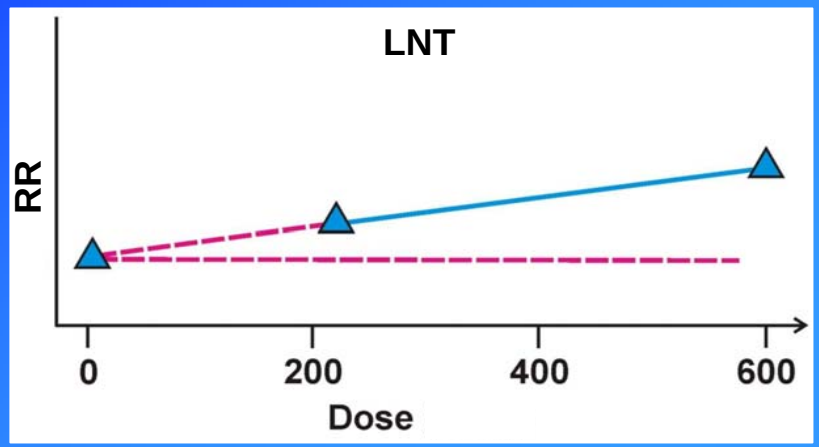
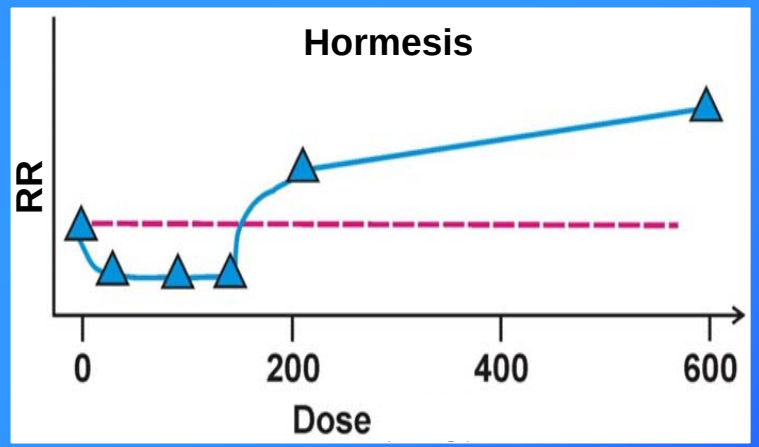
The LNT Hypothesis vs. Radiation Hormesis: Implications for Managing Radiological Terrorism Events





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Rio Grande Chapter HPS Meeting

Albuquerque, NM, June 2, 2006

http://www.radiation-scott.org

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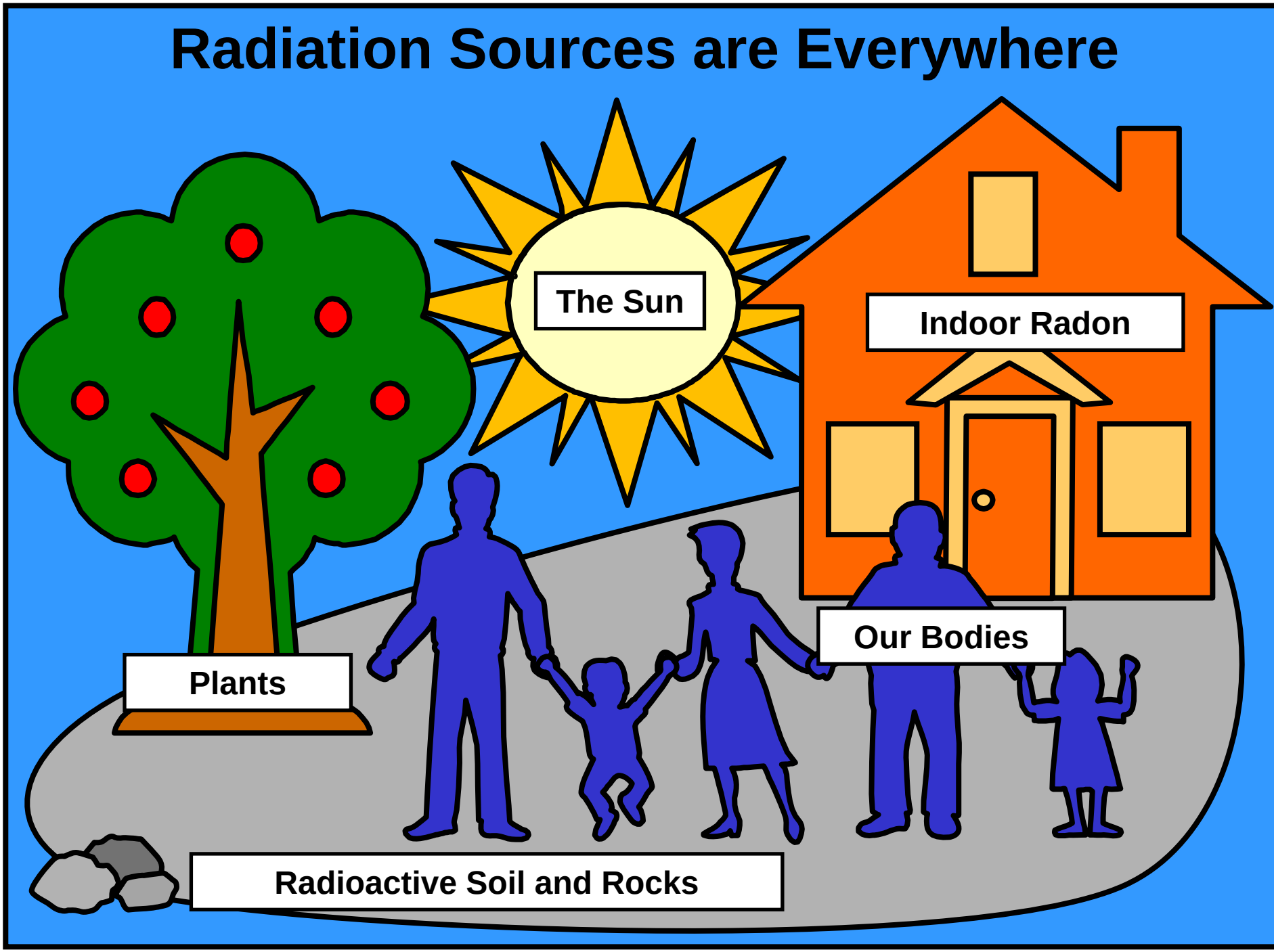
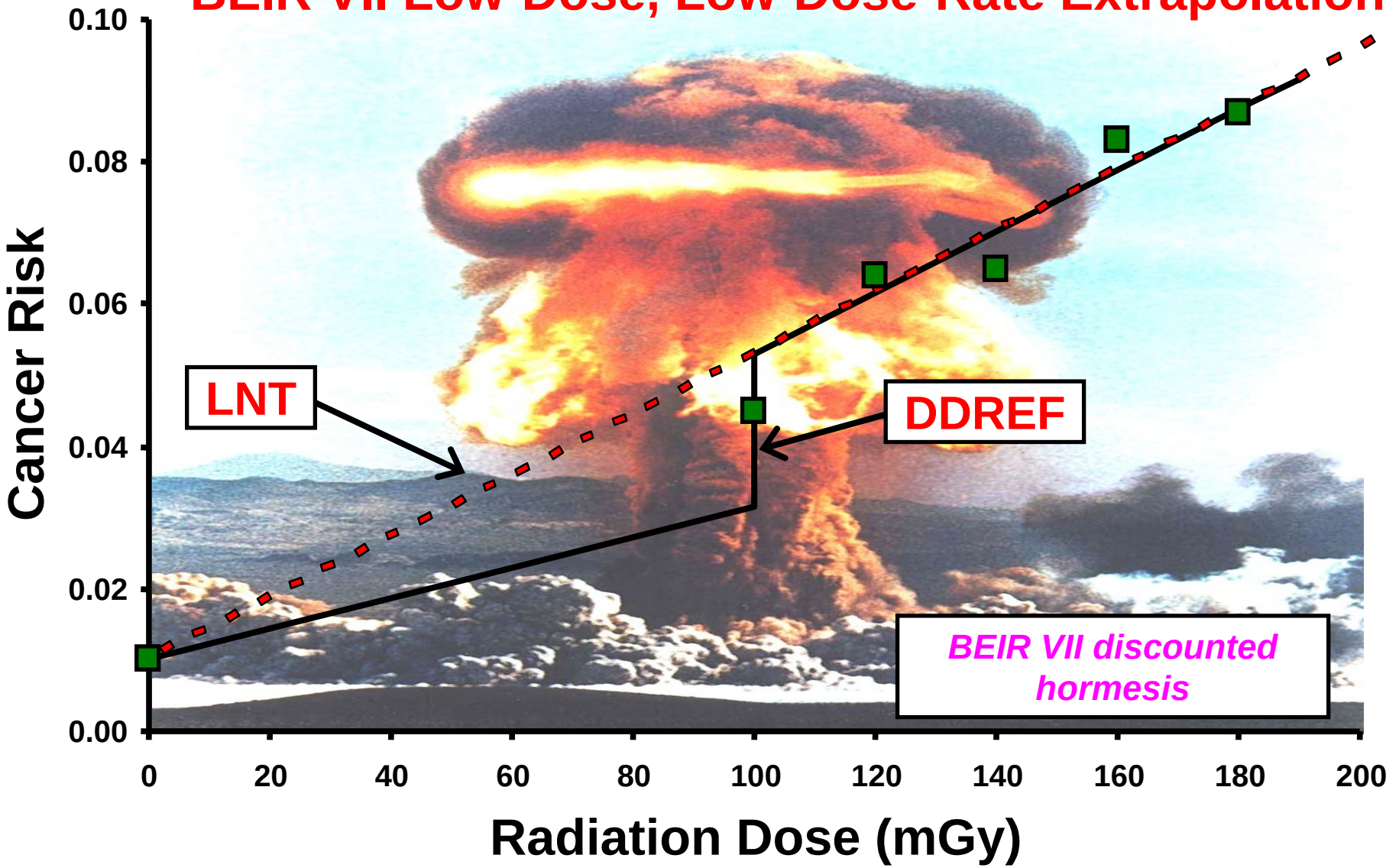

Radiation Sources are Everywhere
The Sun
Indoor Radon
Plants
Our Bodies
Radioactive Soil and Rocks

LNT Approach to Low Dose Cancer Risk Assessment

- **LNT hypothesis: cancer risk increases as a linear, no-threshold (LNT) function of dose.**
- **Applies to both single and combined radiation exposures (via use of dose weighting factors).**
- **Hypothesis has remained controversial for years.**

Current Regulatory Risk Assessment Paradigm

BEIR VII Low-Dose, Low-Dose-Rate Extrapolation



Radiation Hormesis

- **Hormesis: low dose stimulation and high dose inhibition (Calabrese, 2003).**
- **Radiation hormesis: low doses of radiation protect, high doses harm.**

Calabrese EJ. Annu. Rev. Pharmacol. Toxicol 43:175-197, 2003.

BEIR VII vs. French Academies on LNT and Radiation Hormesis

BEIR VII	French Academies
Selectively-chosen A-bomb survivor cancer data was consistent with LNT	LNT may not apply to low-LET doses < 100 mGy
Even natural background low-LET radiation harms	No evidence of harm from natural background radiation; may be beneficial
Radiation hormesis dismissed	Radiation hormesis not dismissed
Looked at basic research results and ignored	Considered implications of basic research results

Incorrect Implications of BEIR VII Use of LNT

- Any radiation (e.g., a single CT scan, chest X-ray, or diagnostic nuclear medicine) is harmful.
- Natural and man-made background radiation increases cancer risk.
- A gamma-ray dose < 1 mGy to first responders after a radiological terrorist attack increases cancer risk.
- A protracted gamma-ray dose < 100 mGy to the public over a lifetime after a radiological terrorist attack increases cancer risk.
- Any residual radiation exposure in a government building after a terrorist attack will increase cancer risk to inhabitants.

Radiation Hormesis: Low-Dose and Low-Dose-Rate, Low-LET Radiation Protects Us:

- **Protects against mutation induction (Pam Sykes' group).**
- **Protects against neoplastic transformation (Les Redpath's group).**
- **Protects against cancer occurrence (epidemiological and animal data).**
- **Suppresses metastasis of existing cancer (Kiyohiko Sakamoto's group)**
- **Extends tumor latent period (Ron Mitchel's group).**
- **Protects against diseases other than cancer (Kazuo Sakai's group).**

Low-LET Radiation-Induced Adapted Protection

- **Normal DNA repair/apoptosis competition (presumed *p53*-dependent).**
- **Auxiliary PAM process (presumed *p53*-independent) involving selective apoptosis.**
- **Immune system stimulation.**

Activation thresholds for these processes vary for different individuals and are therefore stochastic.

Our new hormetic relative risk (HRR) model accounts for the indicated system of protection.

The PAM Process

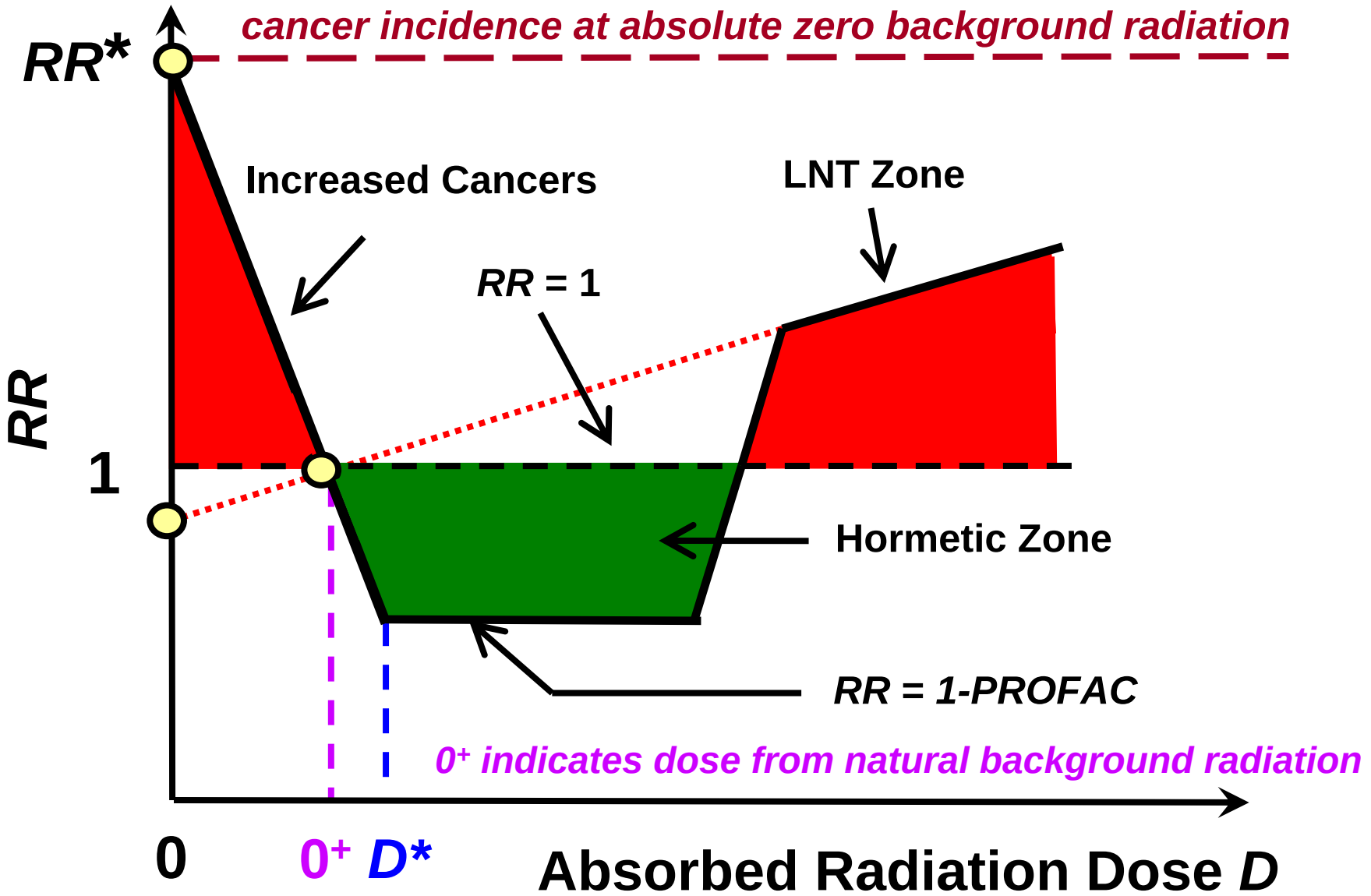
- **Eliminates cells transformed by radiation, chemicals, oncogenic retroviruses, herpes simplex virus, and viral oncogenes such as *ras* and *src* (Scott *et al*., 2004).**
- **Recognizes a variety of DNA damage and may also remove mutant and other aberrant cells (e.g., cells with virally altered DNA).**
- **Does not require *p53* (Hipp and Bauer, 1997).**
- **Appears to be induced by low doses of radioprotectors such as amifostine and resveratrol.**

Scott BR et al. Nonlinearity 2(3):185-211, 2004.

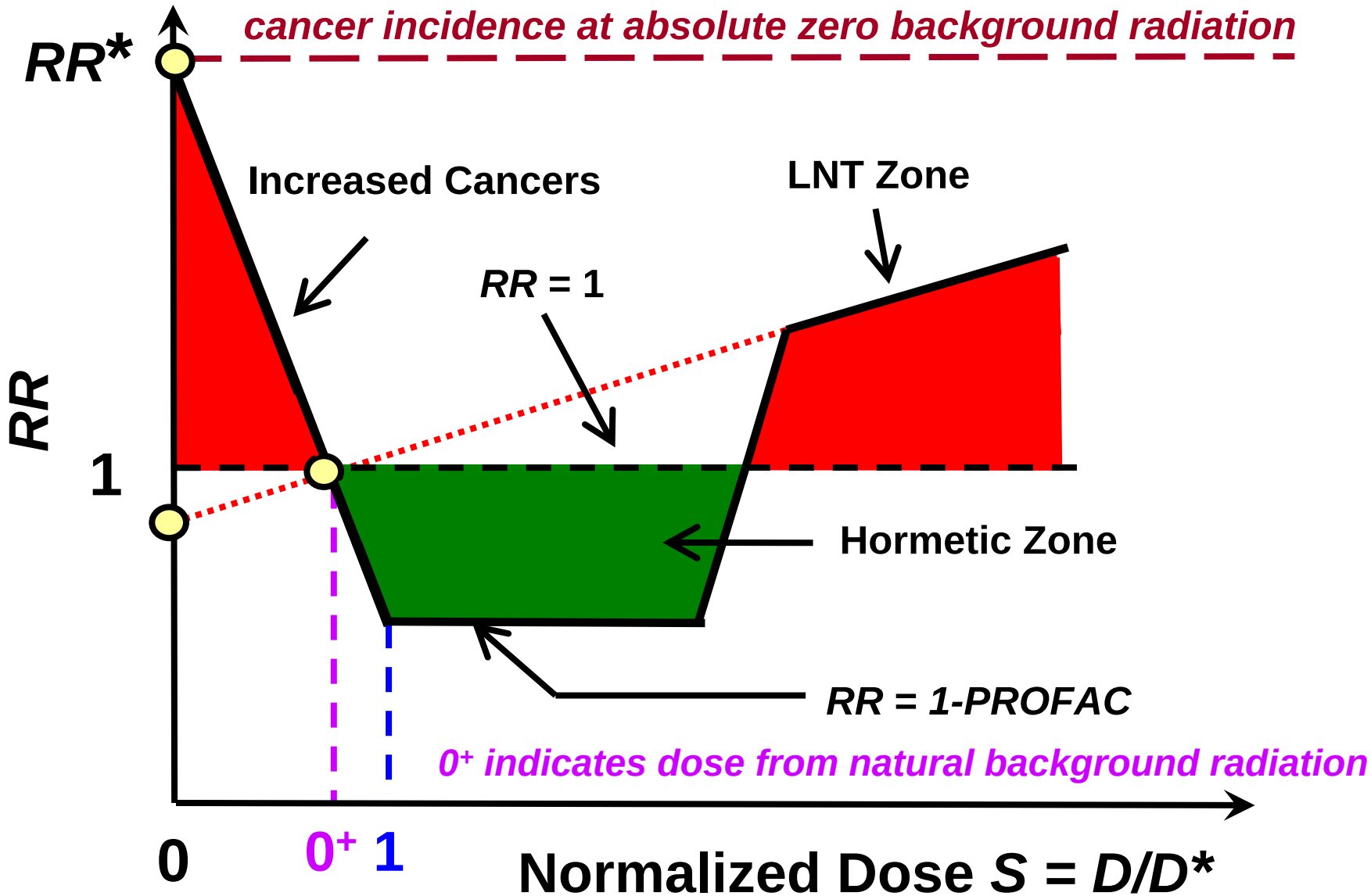
Hipp ML and Bauer G. Oncogene 17(7):791-797, 1997.

Relative Risk Modeling to Account for Hormetic Effects

Novel Cancer Hormetic Relative Risk (HRR) Model: Absorbed Radiation Dose Perspective



Novel Cancer HRR Model: Normalized Dose (*S*) Perspective

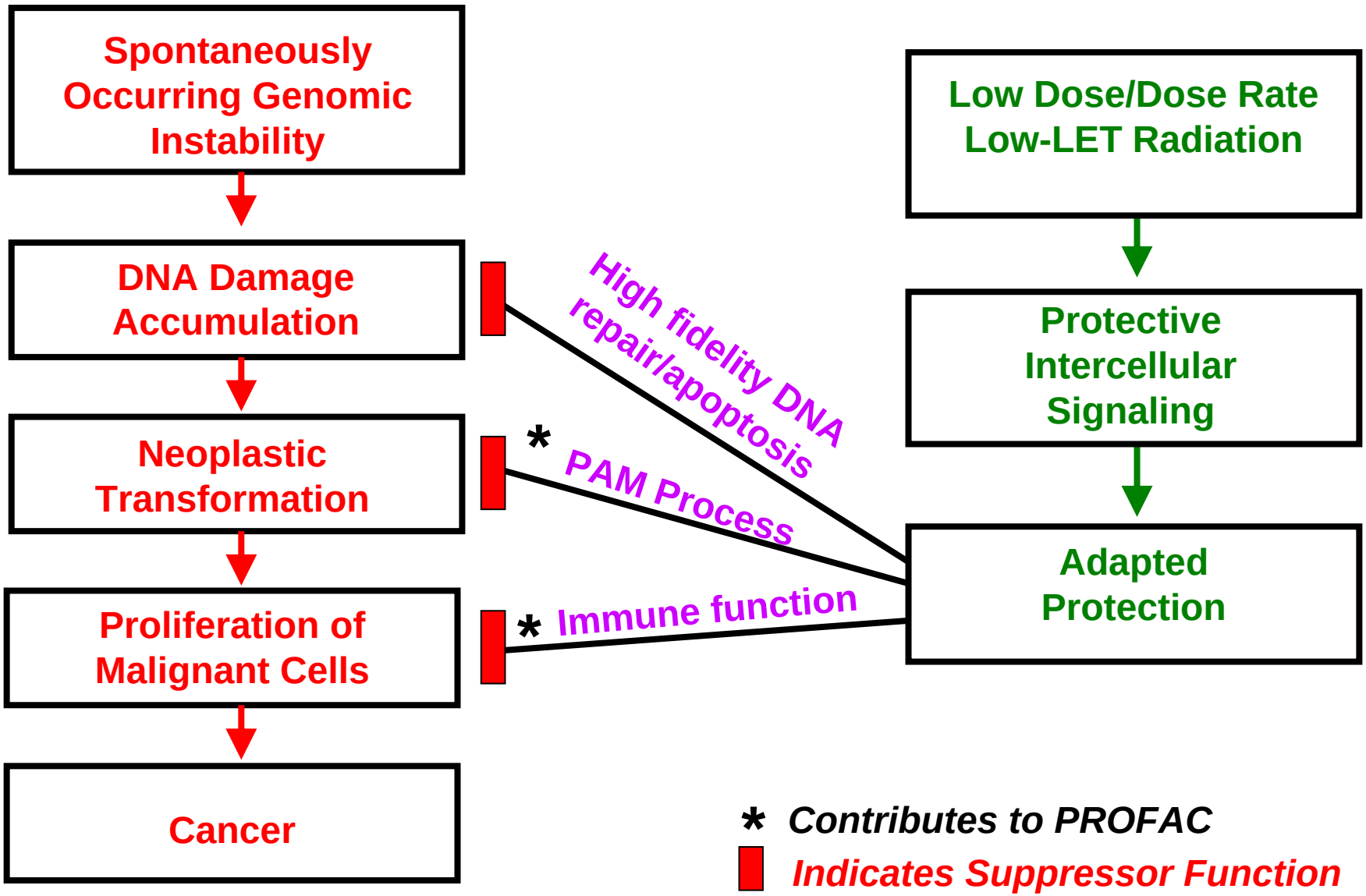


PROFAC

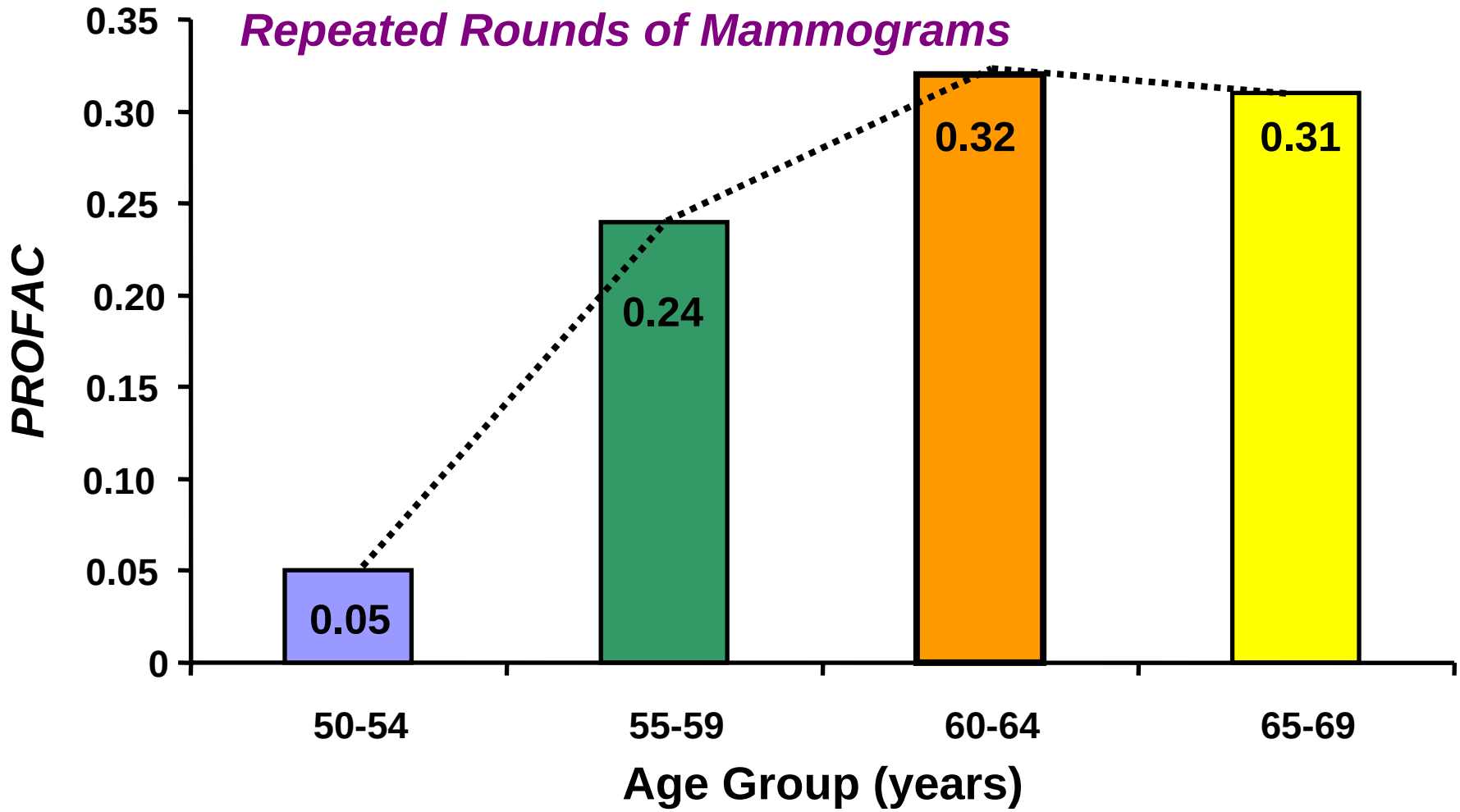
- **For cancer induction, the *PROFAC* gives the proportion of cancer cases prevented due to radiation hormesis.**
- **Ranges from 0 to 1.**
- **The product *100*PROFAC* gives the expected percentage of lives saved (cancer deaths avoided) due to radiation hormesis among the irradiated population.**

Scott BR. Dose-Response (in press), 2006a.

Radiation Hormesis Related System of Protection Against Cancer: Adapted Protection



PROFAC is Age-dependent: Breast Cancer



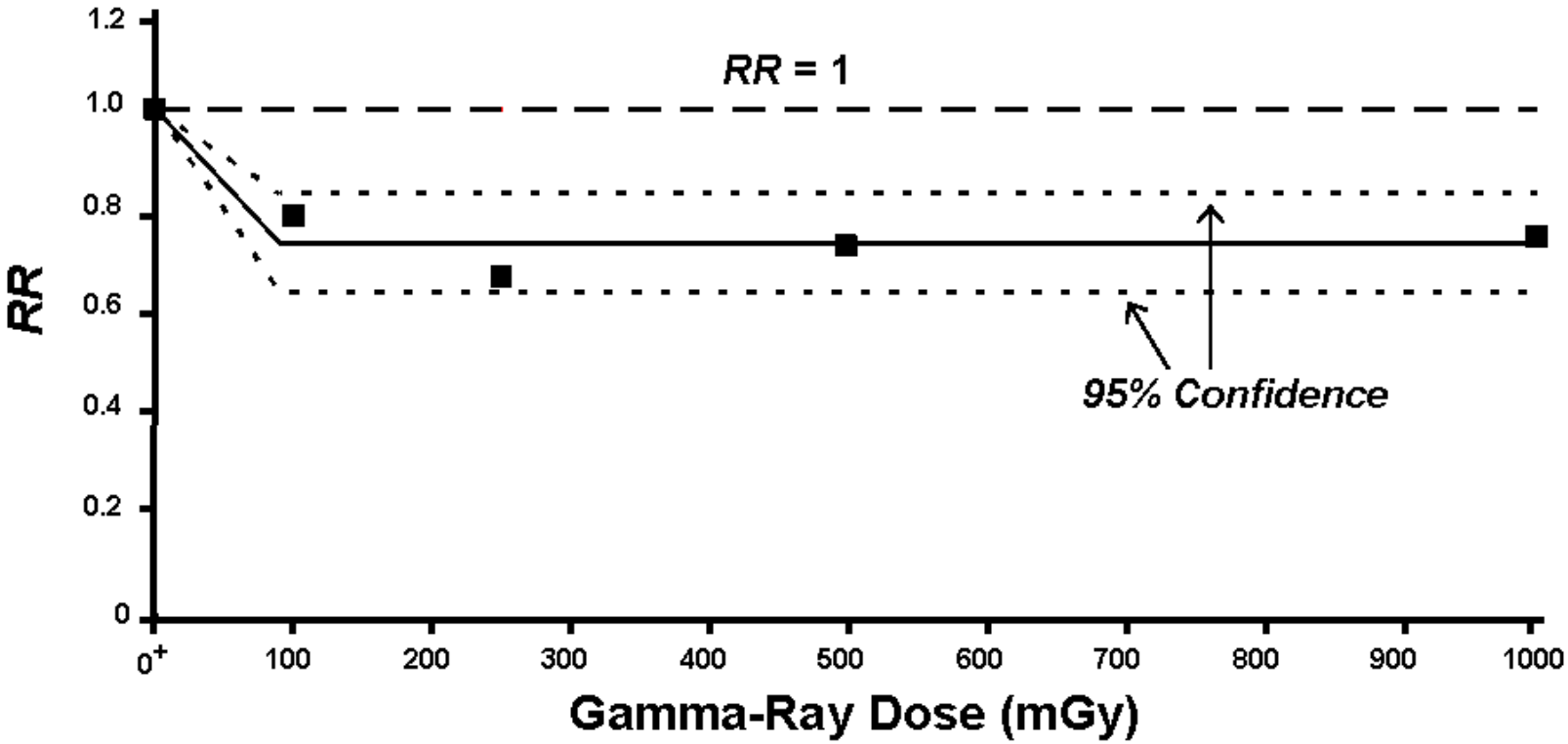
Based on data from Nyström et al. 2002.

Radiation Doses from Typical Diagnostic Radiation Sources Fall in The Hormetic Zone

Source	mGy
Dental, full-mouth (X-ray)	0.17
Chest X-ray	0.25
Mammograms (X-ray)	4
CT scan, head (X-ray)	20
CT scan, body (X-ray)	60
Thyroid scans:	
Iodine-131 (β + γ radiation)	50-100
Iodine-123 (γ radiation)	30-50
Technetium-99 (β radiation)	10

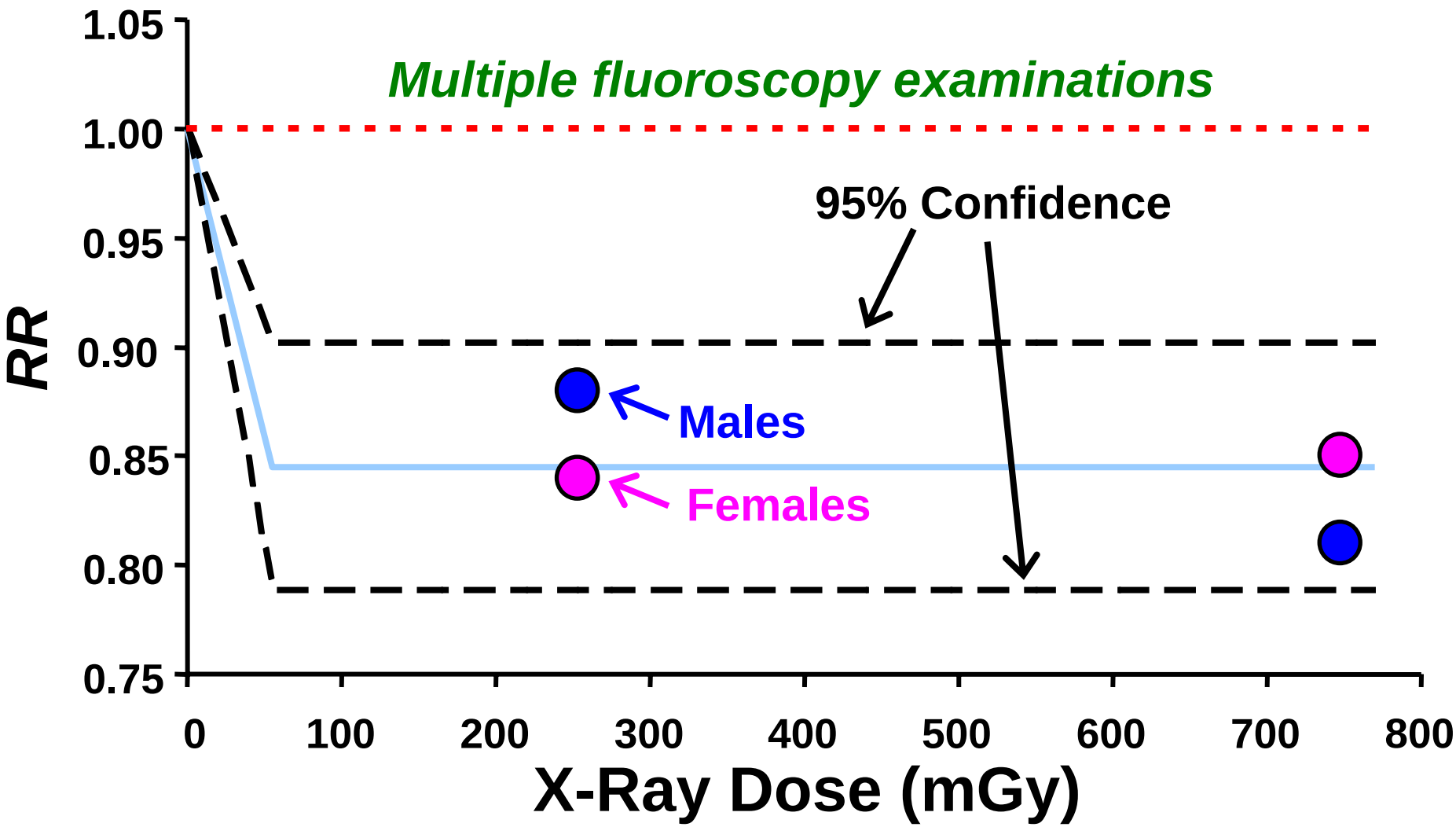
Kauffman. Journal of American Physicians and Surgeons 8(2):54-55, 2003.

Lung Cancer *RR* Based on HRR Model: Mouse Data from R. Ulrich *et al.* (1976)

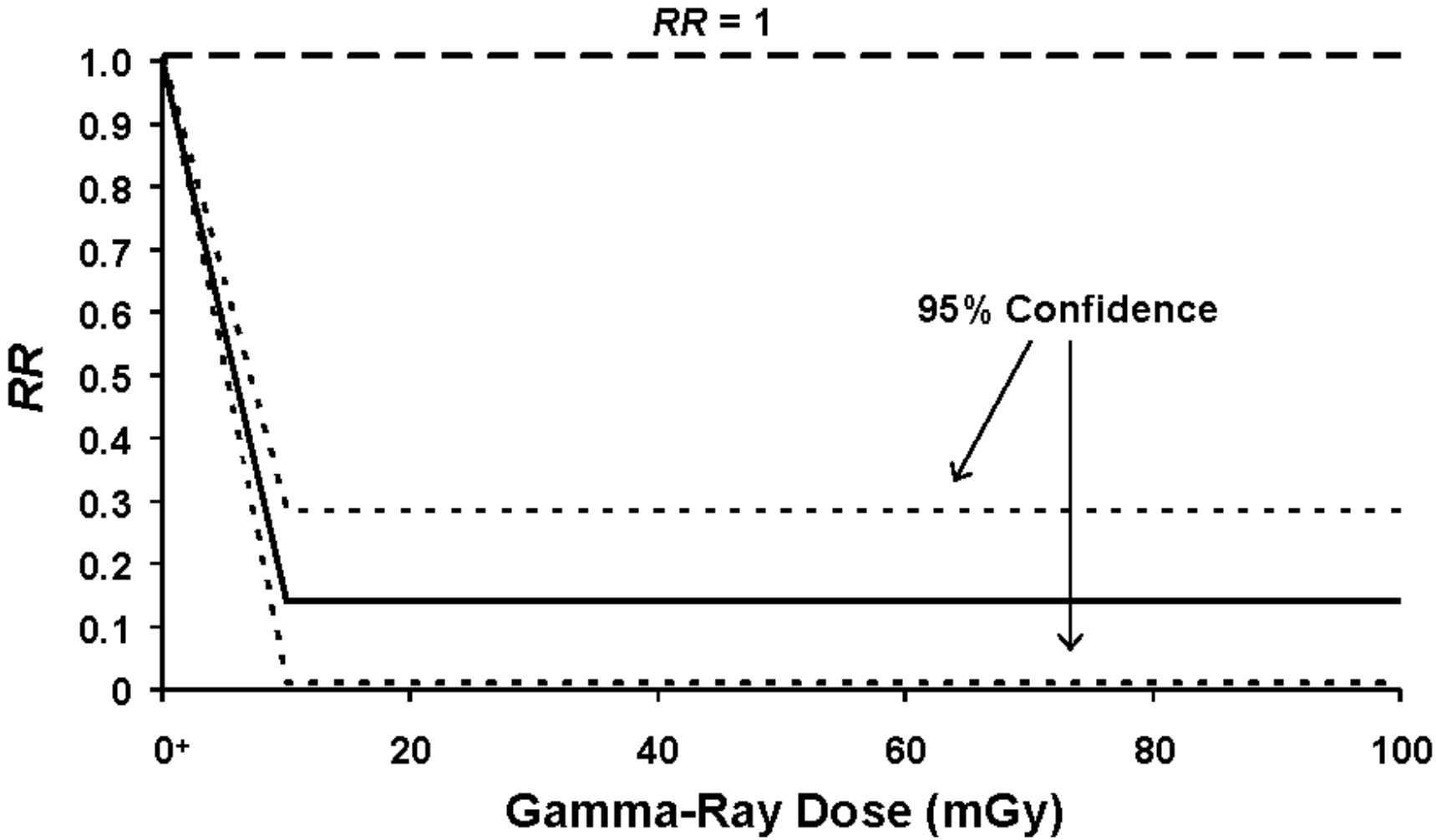


Study involved more than 15,000 mice.

Lung Cancer RR Based on HRR Model: Humans Exposed to Fractionated Diagnostic X-Rays (Howe, 1995)

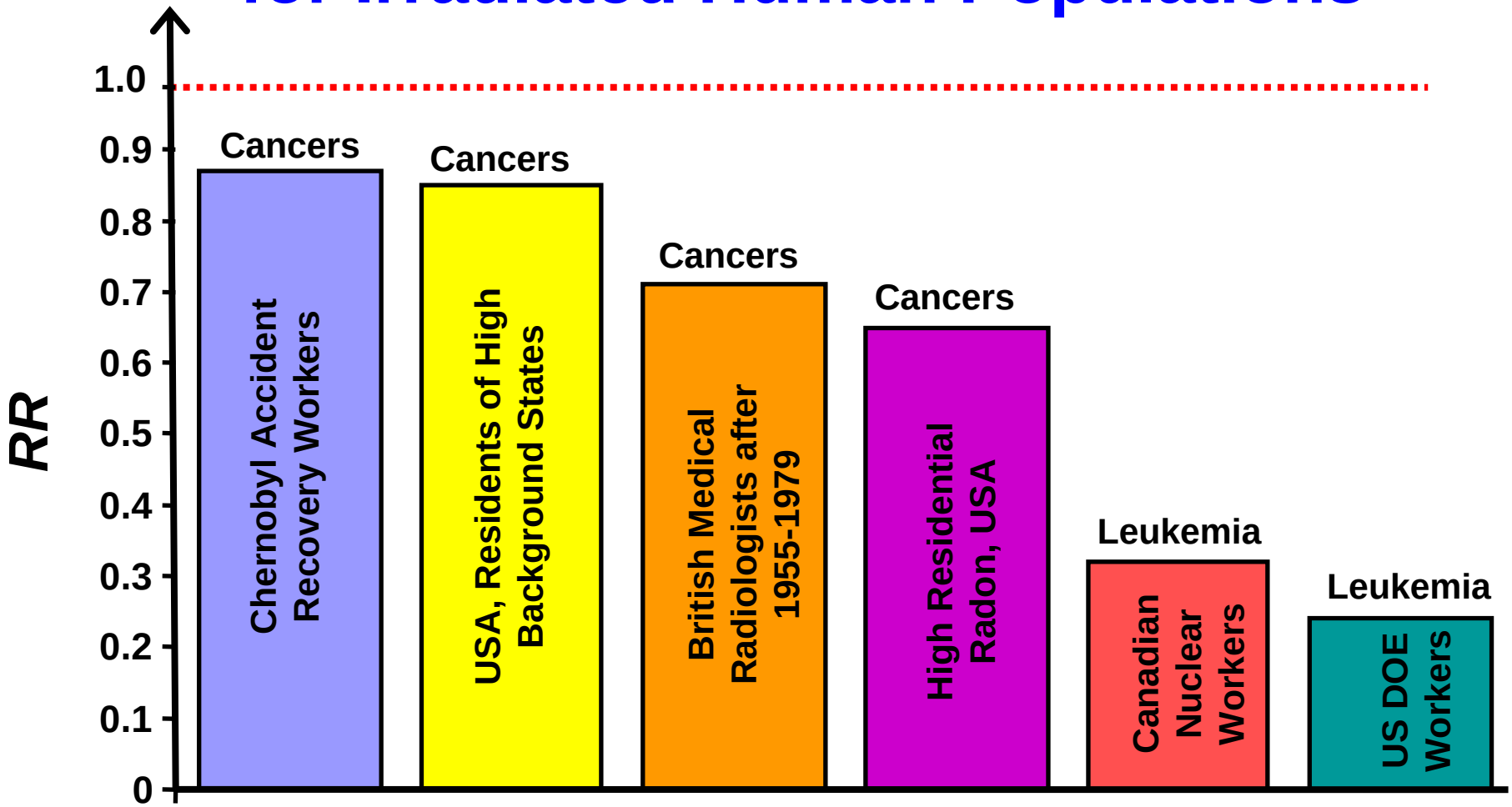


Lung Cancer Relative Risk Based on HRR Model: Mayak Plutonium Facility Workers (Scott, 2006a)



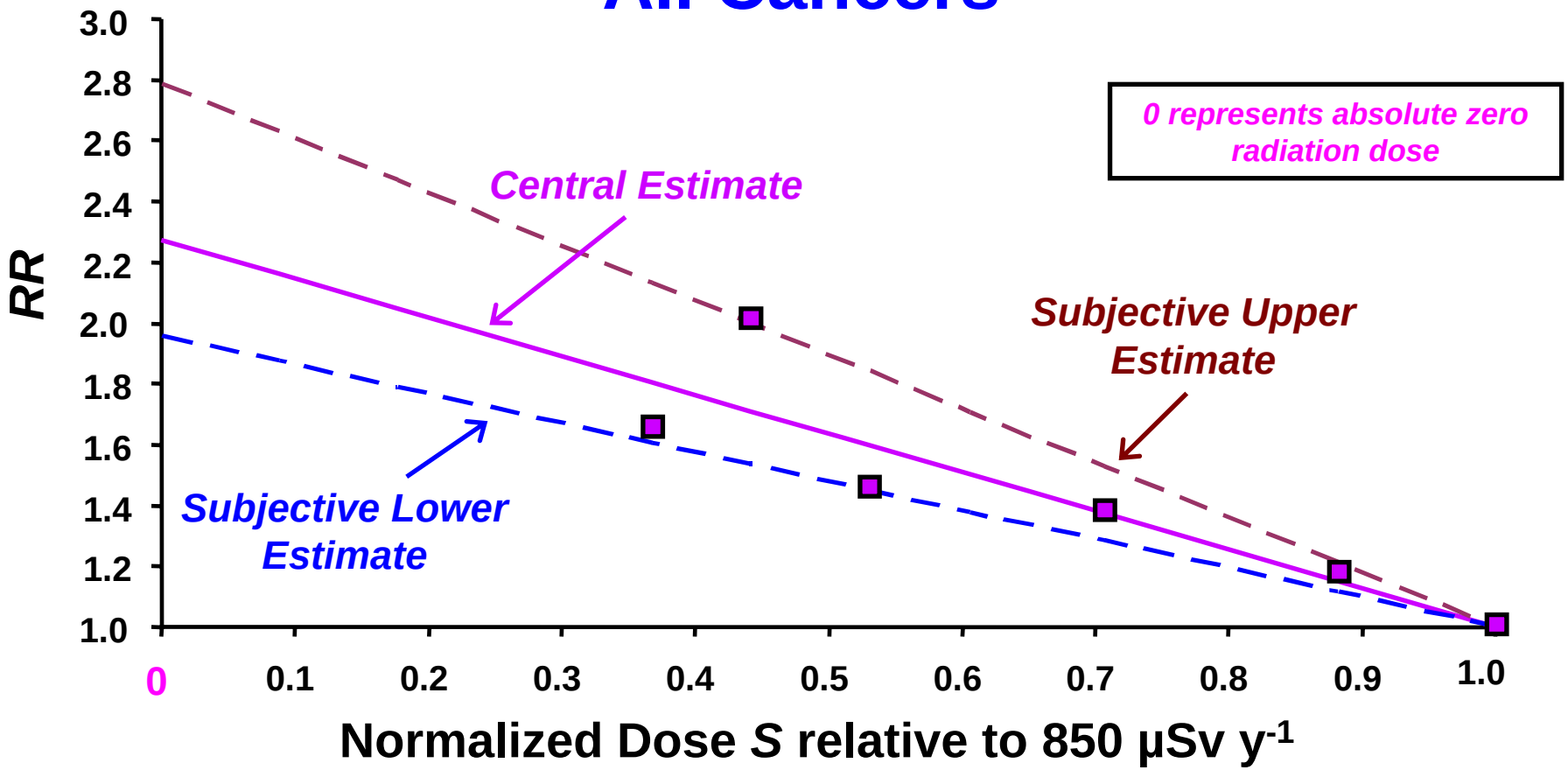
Data corrected for influence of alpha radiation.

Cancer Relative Risk In Hormetic Zone for Irradiated Human Populations



Healthy worker effect does not explain RR < 0.85 for workers (Sponsler and Cameron, 2005)

Expected Impact of Reducing Natural Background Radiation on Relative Risk for All Cancers



Data are based on various cities and states of India. Only gamma- ray exposures were evaluated. *RR = 1* at *0+* = 850 μSv y^{-1}.

Data from Nambi KSV and Soman SD. Health Physics 53(5):653-657, 1987

Amifostine and Diagnostic X-Ray Protection After Radiological Terrorism Events

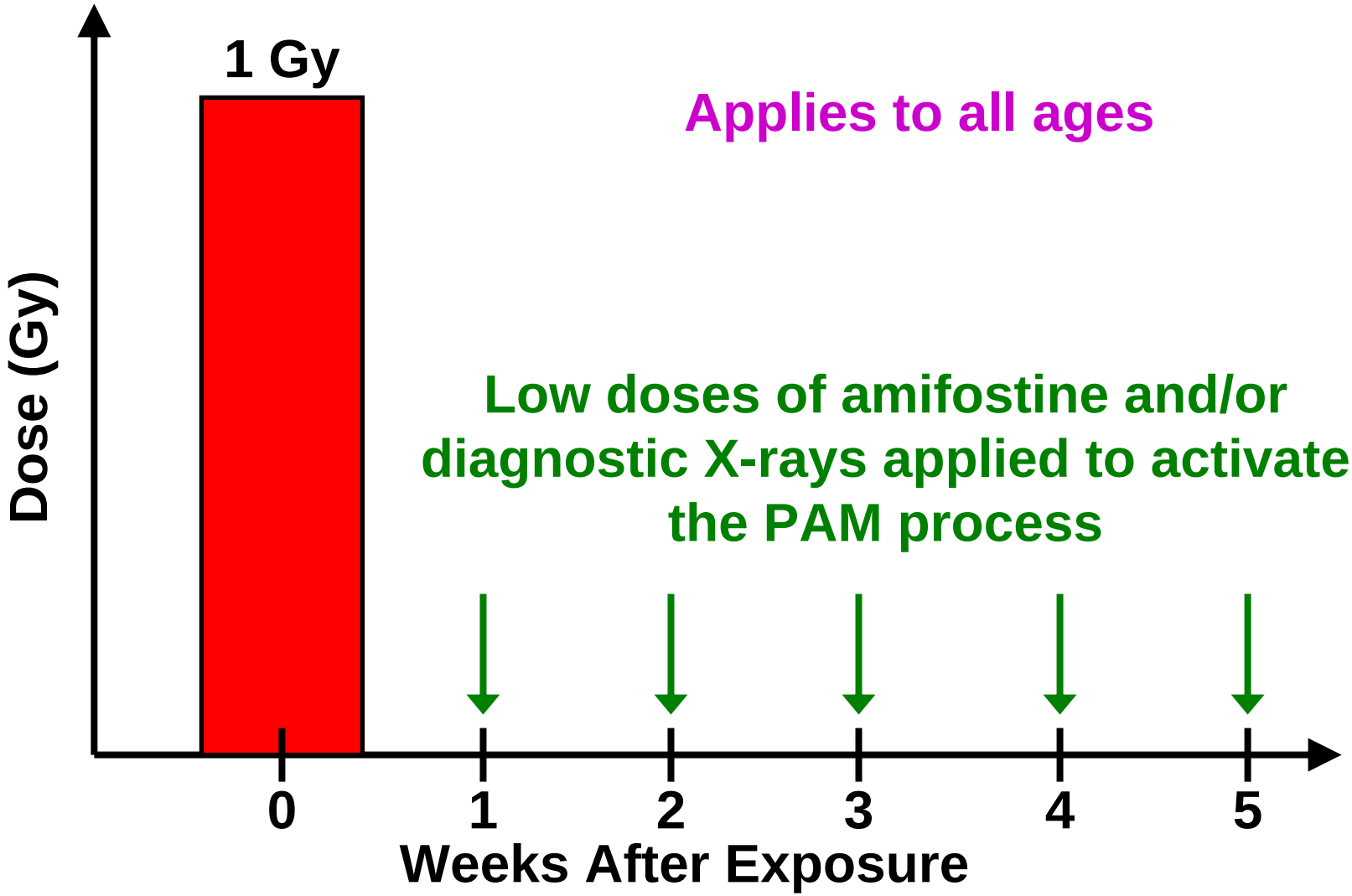
Low-Dose Protection Against Harm From a Prior Mutagenic Dose

- **Low-dose X-rays suppress mutations in mice when given after a mutagenic dose of X-rays (Day *et al.*, 2005).**
- **Low-doses of amifostine (WR-2721) suppress mutations in mice after a mutagenic dose of neutrons (Grdina *et al.*, 1992).**
- **Multiple applications of these agents could protect from cancer after exposure to a carcinogenic radiation dose during a radiological terrorist attack.**

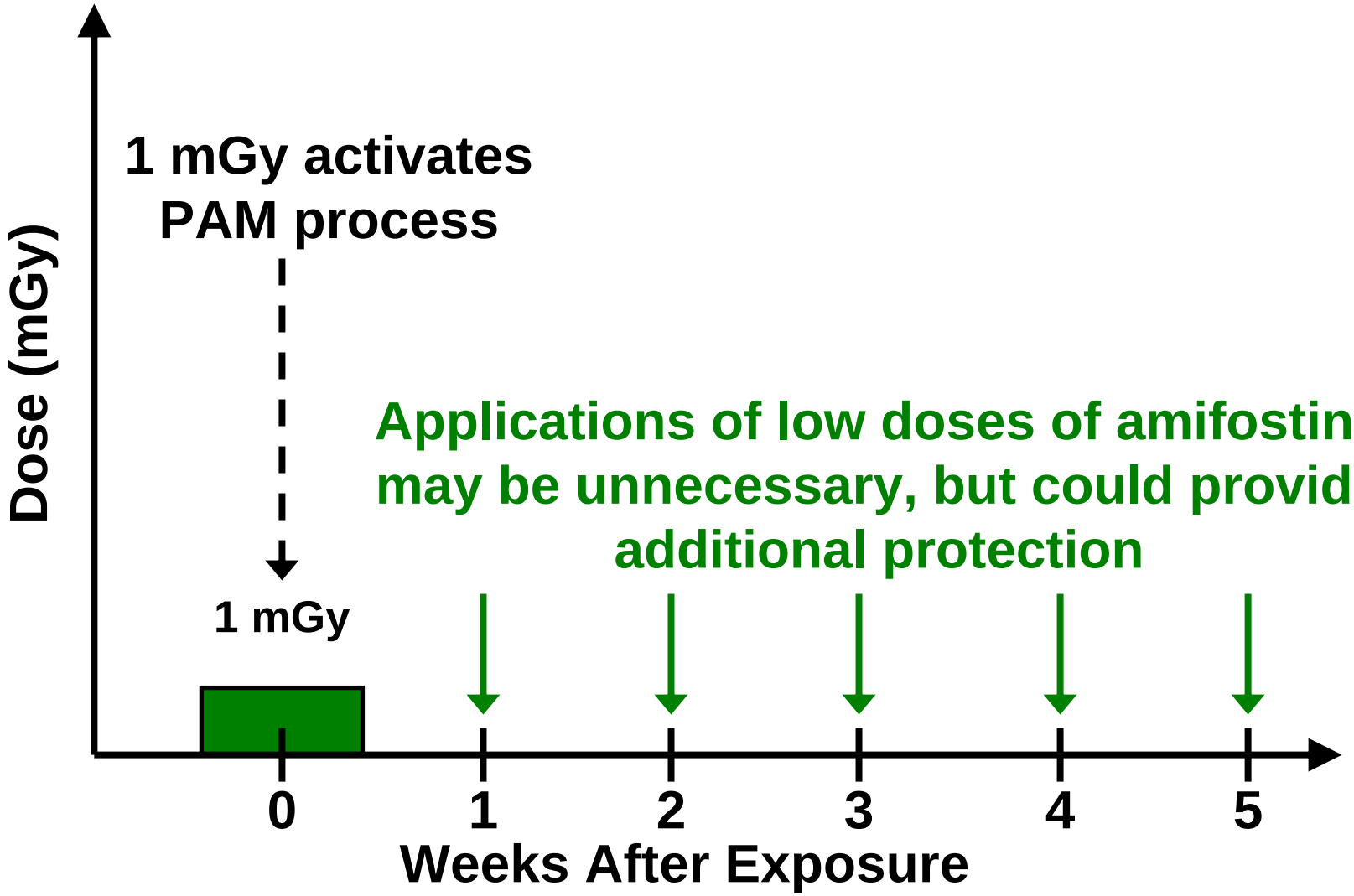
Day T. et al. EMS Meeting presentation, 2005.
Grdina D. et al. Carcinogenesis 13(5):811-814, 1992.

Hidden Gamma-Ray Source Exposure Scenarios: Protecting from Stochastic Effects

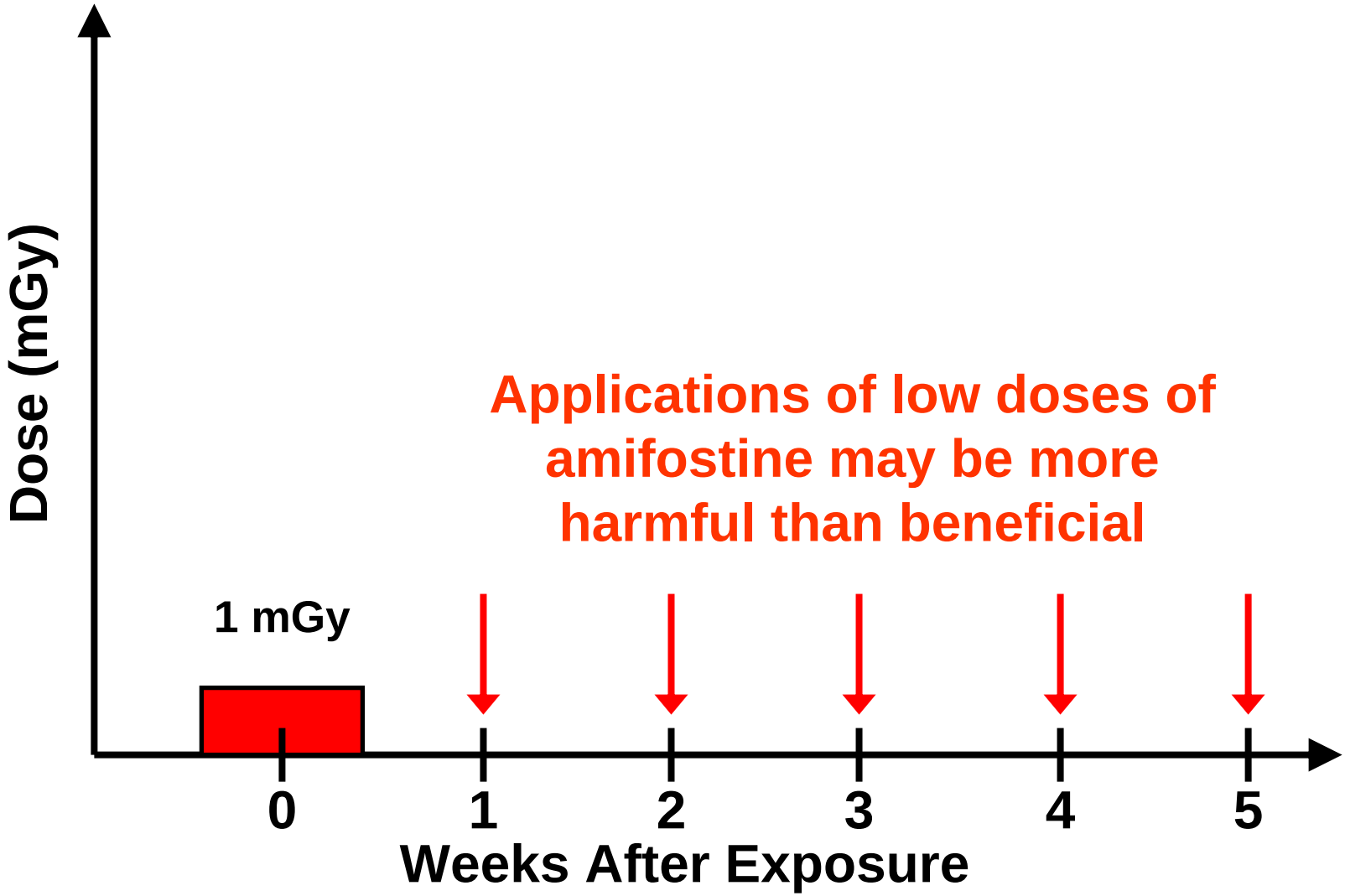
Hidden Gamma-Ray Source Scenario 1: Post-Exposure Protection



Hidden Gamma-Ray Source Scenario 2: Low Radiation Dose to an Adult



Hidden Gamma-Ray Source Scenario 3: Low Radiation Dose to a Child



Radiation Phobia and Managing Radiological Terrorism Events

LNT-Associated Radiation Phobia Following a Dirty Bomb Incident

Radiation Phobia Associated Impacts:

- **Loss of lives associated with frantic evacuations.**
- **Severe injuries during evacuations.**
- **Increased suicides and abortions.**
- **Increased psychosomatic disorders.**
- **Increased drug/alcohol/cigarette abuse.**
- **Permanent abandonment of properties with low-level contamination.**

Chernobyl-Associated Radiation Phobia

- **"The psychosomatic disorders observed in the 15 million people in Belarus, Ukraine, and Russia… who were affected by the April 1986 Chernobyl accident are probably the accident's most important effect on public health…[1]**
- **Radiation phobia caused over 100,000 deaths by abortions in Western Europe, a tragic loss of life.[2]**

[1] *Zbigniew Jaworowski. Physics Today, September 1999, pp. 24-29.*

[2] *Ketchum LE. J. Nucl. Med. 28:413-422, 1987.*

Implications for Managing Low-Dose* Radiological Terrorism Events

LNT Model	HRR Model
Harm to 1st responders	No harm to 1st responders
↑ cancers for public	↓ cancers for public
High remediation costs	Lower remediation costs
Abandoning of expensive facilities (e.g., government buildings)	Continued use of expensive facilities after cleanup
Many radiation-phobia-associated casualties	Fewer radiation-phobia-associated casualties

*Doses of low-LET radiation < 100 mGy.

Conclusions

- **The LNT hypothesis is wrong for low doses and dose rates of low-LET radiation and for mixed low- and high-LET irradiations.**
- **A hormetic risk vs. dose relationship with a dose-rate-dependent effective threshold for excess cancer more likely applies.**
- **LNT may apply to exposure only to high-LET radiation such as pure alpha sources (which excludes radon in the home).**
- **The gamma-ray component of radon in the home is likely protecting us from cancer and other diseases. Thus, eliminating radon from the home may be causing harm via loss of gamma-ray-induced adapted protection.**

Conclusions (continued)

- **LNT and HRR models have very different implications for managing radiological terrorist events.**
- **LNT promotes radiation phobia associated panic and was responsible for > 100,000 abortions of wanted pregnancies after Chernobyl in persons in Western Europe unlikely to have been harmed by their very low radiation doses.**
- **Many more casualties associated with LNT driven radiation phobia may be expected following a dirty bomb incident in the U.S. than from actual harm from irradiation.**

Conclusions (ended)

- **For persons receiving large radiation doses from a radiological terrorist act, low dose diagnostic X-rays plus low doses of radiological protectants (e.g., amifostine, resveratrol) should suppress cancer occurrence if applied at appropriate time intervals and frequencies.**
- **For persons receiving low doses of low- or low-plus high-LET radiation from a terrorist act, little to no harm may occur so that radiation protector usage may be unnecessary. Radioprotector usage may harm the very young and provide no benefit.**

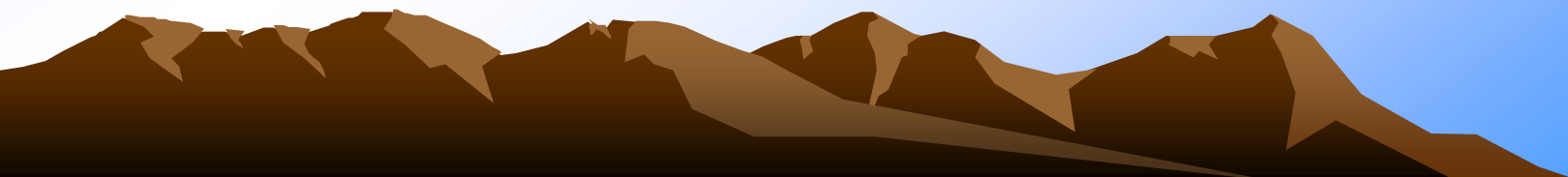
Acknowledgement

This work was supported by the Offices of Science (BER) and Environmental Management, U.S. Department of Energy, Grant Numbers DE-FG02-03ER63671 and DE-FG02-03ER63657.

Residual Risks For Lethality After Application Of Medical Countermeasures Against Damage From Inhaled Gamma-emitting Radionuclides Released From A Radiological Weapon

Bobby R. Scott, Ph.D.

Seminar presented at the AFRRI on April 28, 2005
Available online at:
http://www.radiation-scott.org/Residual_Risk_1B.pdf



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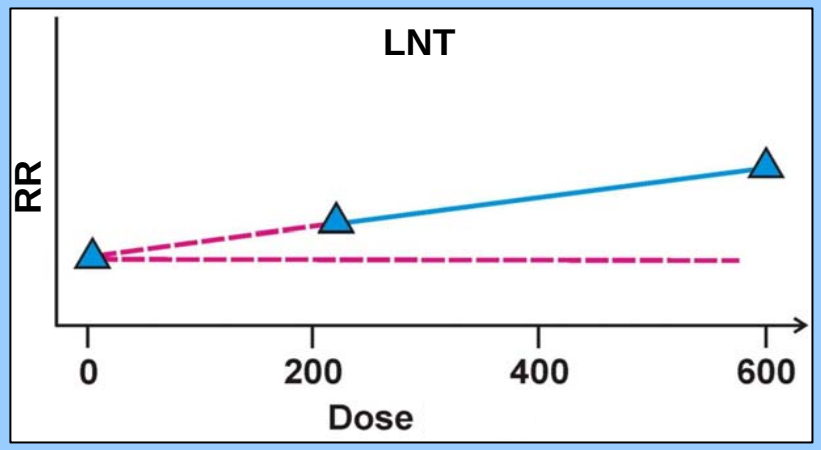

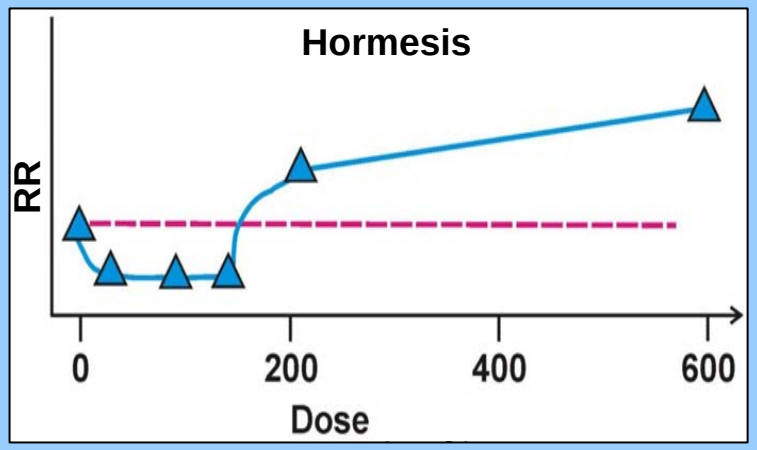

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Seminar Presented at the NIH/NIAID, Bethesda, MD on February 14, 2006

Available online at:
http://www.radiation-scott.org/NIAID_BScott.pdf