

# **Low-Dose/Dose-Rate Low-LET Radiation Protects Us from Cancer**

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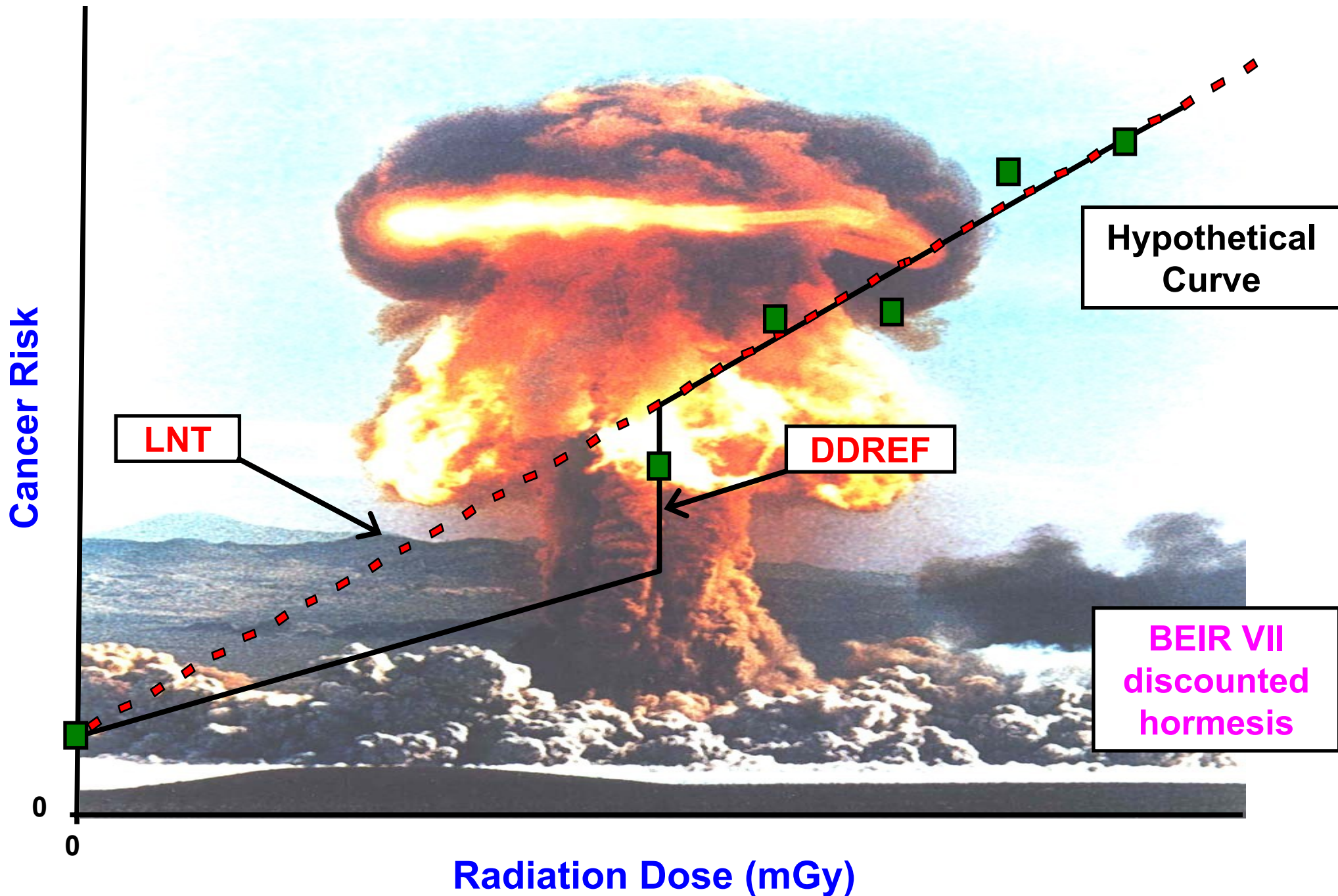
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**<http://www.radiation-scott.org>**

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



# Low Doses and Dose-Rates of Low-LET Radiation Protect Us From Harm: Adapted Protection

- Protect against cell killing by alpha particles (**Satin Sawant's work**)
- Protect against chromosomal damage (**Ed Azzam's group**)
- Protect against mutation induction (**Pam Sykes' group**), even when the low dose follows a large dose (**Tanya Day's work**).
- Protect against neoplastic transformation (**Les Redpath's group**).
- Protect against cancer occurrence (**epidemiological and animal data**).
- Suppress metastasis of existing cancer (**Kiyohiko Sakamoto's group**).
- Extend tumor latent period (**Ron Mitchel's group**).
- Protect against diseases other than cancer (**Kazuo Sakai's group**).

*The indicated results implicate hormetic dose-response curves that relate to induced adapted protection (i.e., adaptive response).*

# Why It's Important to Understand Mechanisms of Low-LET Radiation-Induced Adapted Protection

- Novel low-dose disease prevention strategies (including prevention of cancer) in high risk populations.
- Novel low-dose cures of existing cancer.
- Novel way to suppress metastasis of existing cancer.
- Facilitates minimizing radiation-phobia-associated casualties (LNT promoted) after a radiological terrorism act.

*Point of reference: More than 100,000 radiation phobia driven abortions occurred in Western Europe shortly after the Chernobyl Accident.*

# Approach to Integrating Molecular, Cellular, and Organismic Level Radiobiological Effects

- Our molecular and cellular effects dose-response characterizations are based on our published biological-based NEOTRANS<sub>3</sub> model.
- The NEOTRANS<sub>3</sub> model accounts for two components of adapted protection: (1) DNA repair/apoptosis (normal) and (2) the PAM process.
- Cancer *RR* is modeled as being proportional to the neoplastic transformation *RR*.

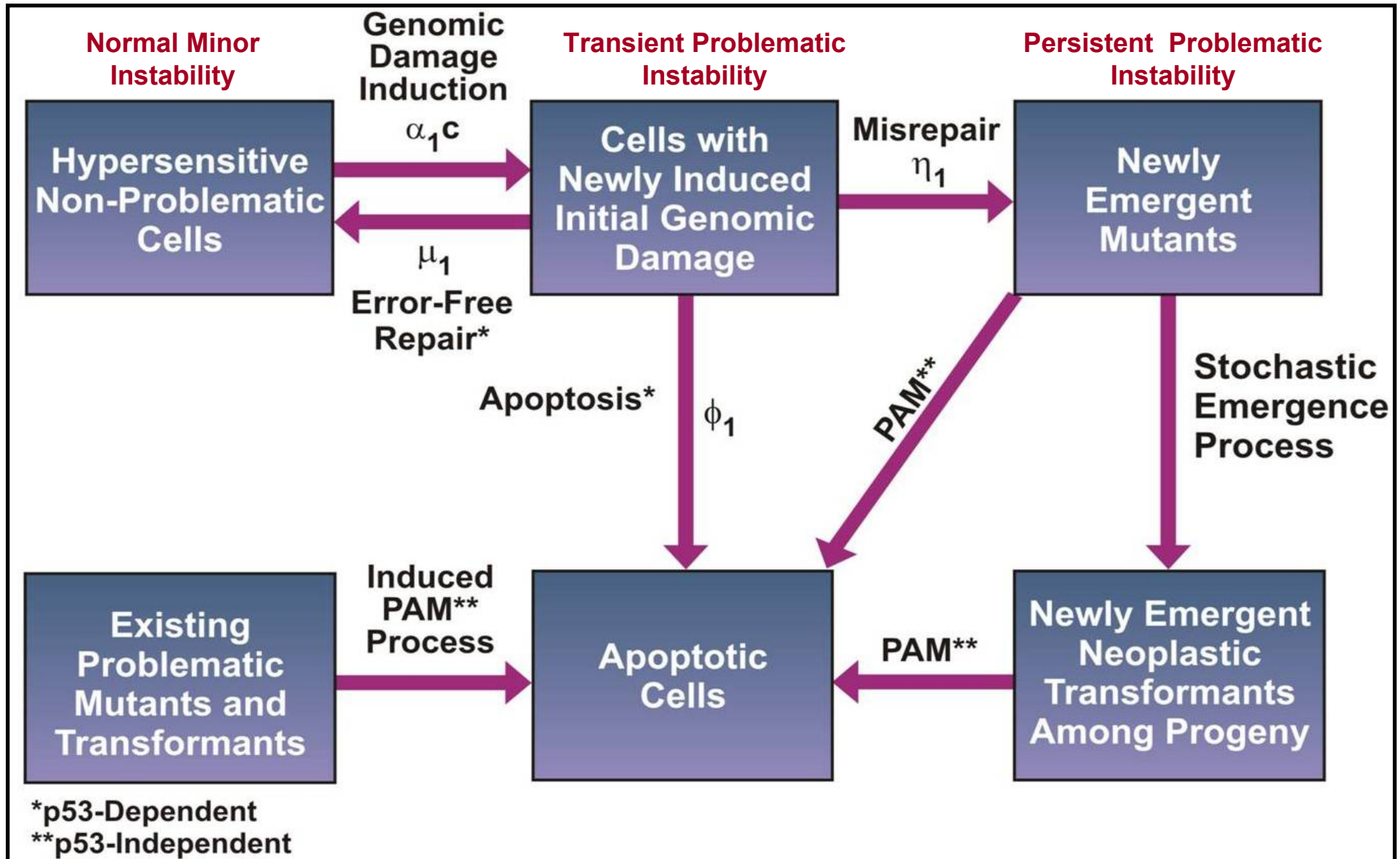
*Scott Mut. Res. 568:129-143 2004*

*Scott BELLE Newsletter 13(2), Part 2:22-27 2005a*

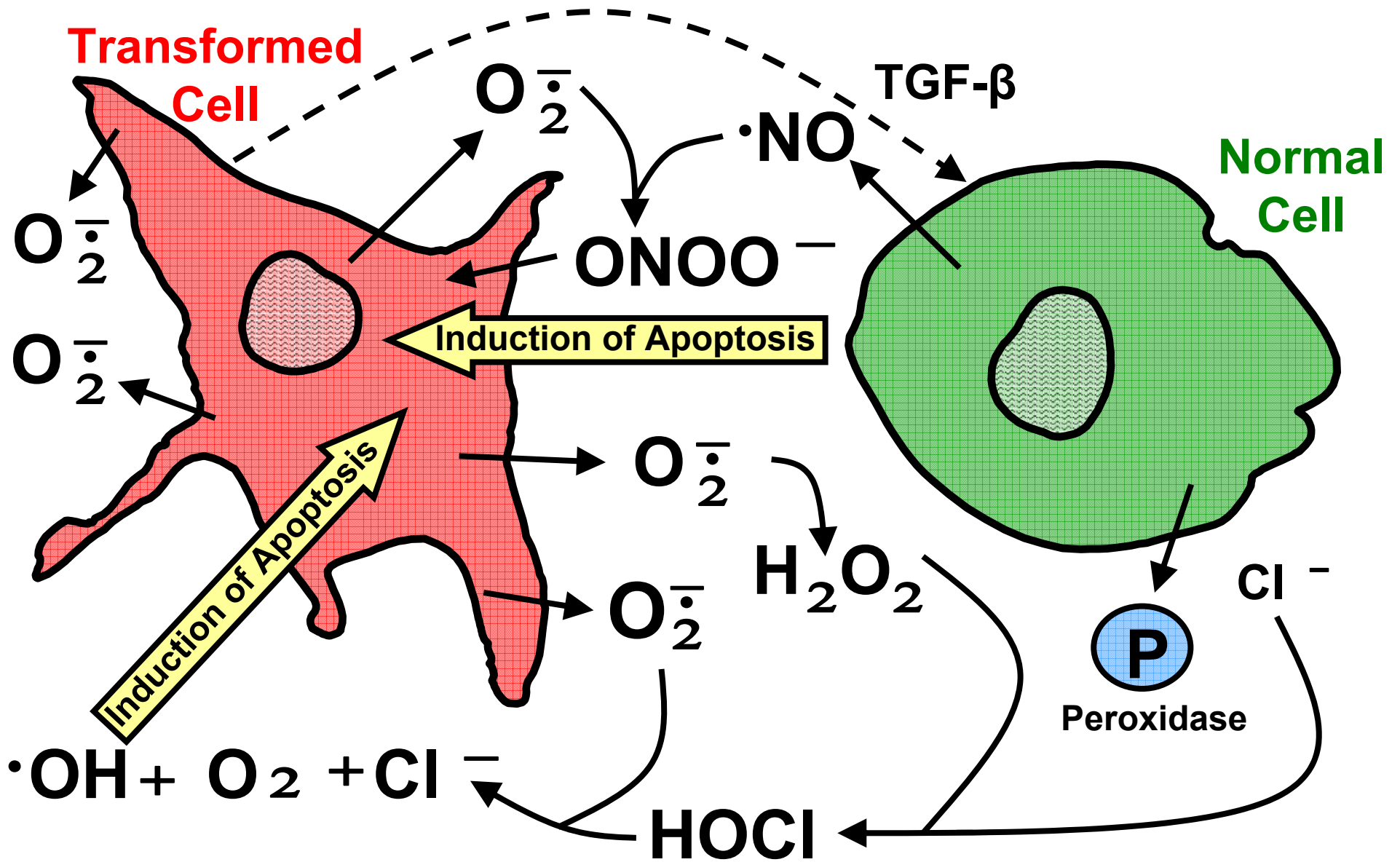
*Scott Dose-Response (in press) 2006a,b*

*Scott Int. J. Low Radiat. (in press) et al., 2006*

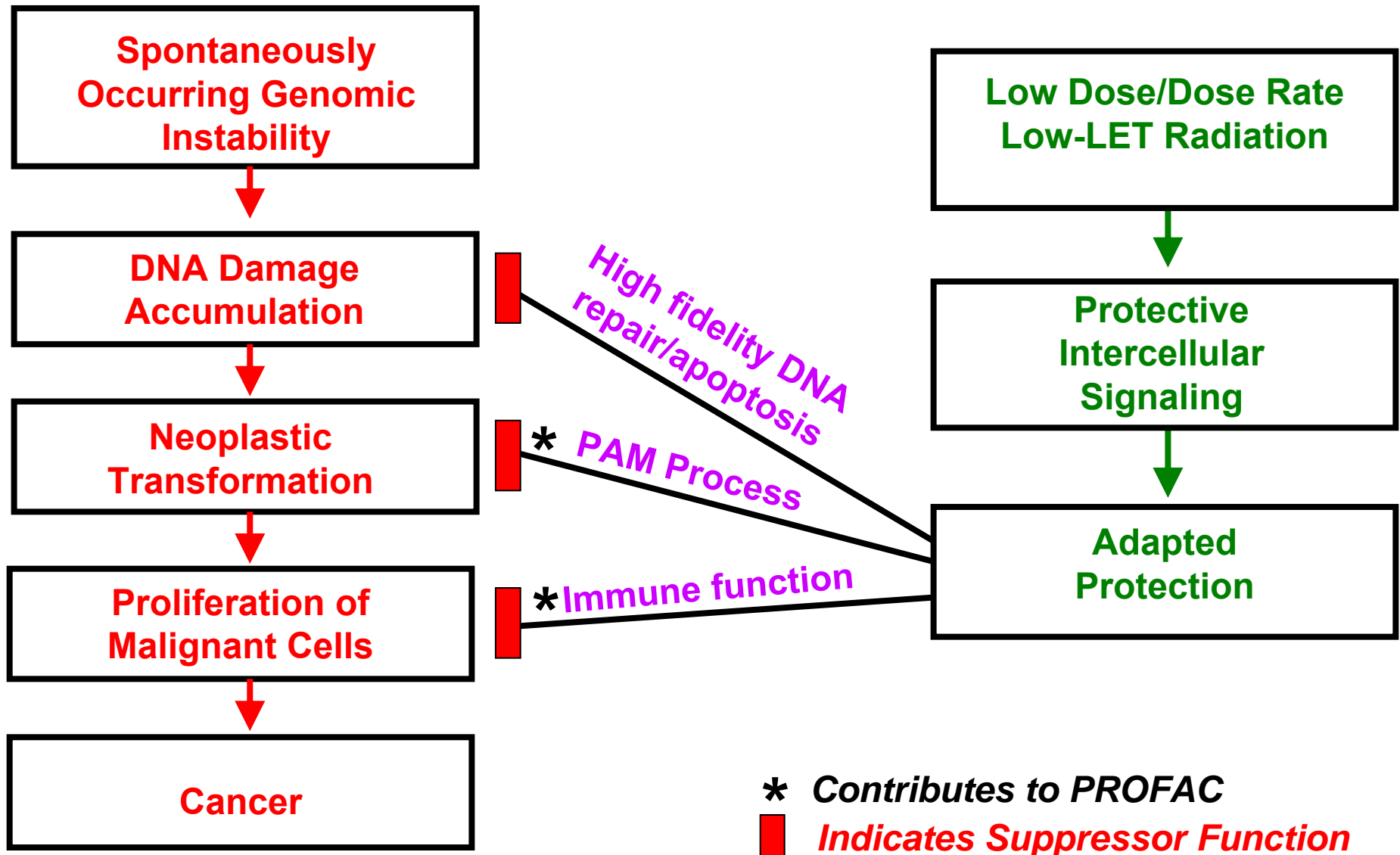
# Biological-Based NEOTRANS<sub>3</sub> Model for Low Dose Induced Stochastic Effects



# PAM Process In Fibroblast: Protective Intercellular Signaling



# Biological Basis for Low-LET Radiation-Induced Adapted Protection



# **Key Assumptions Related to Cancer Relative Risk Modeling**

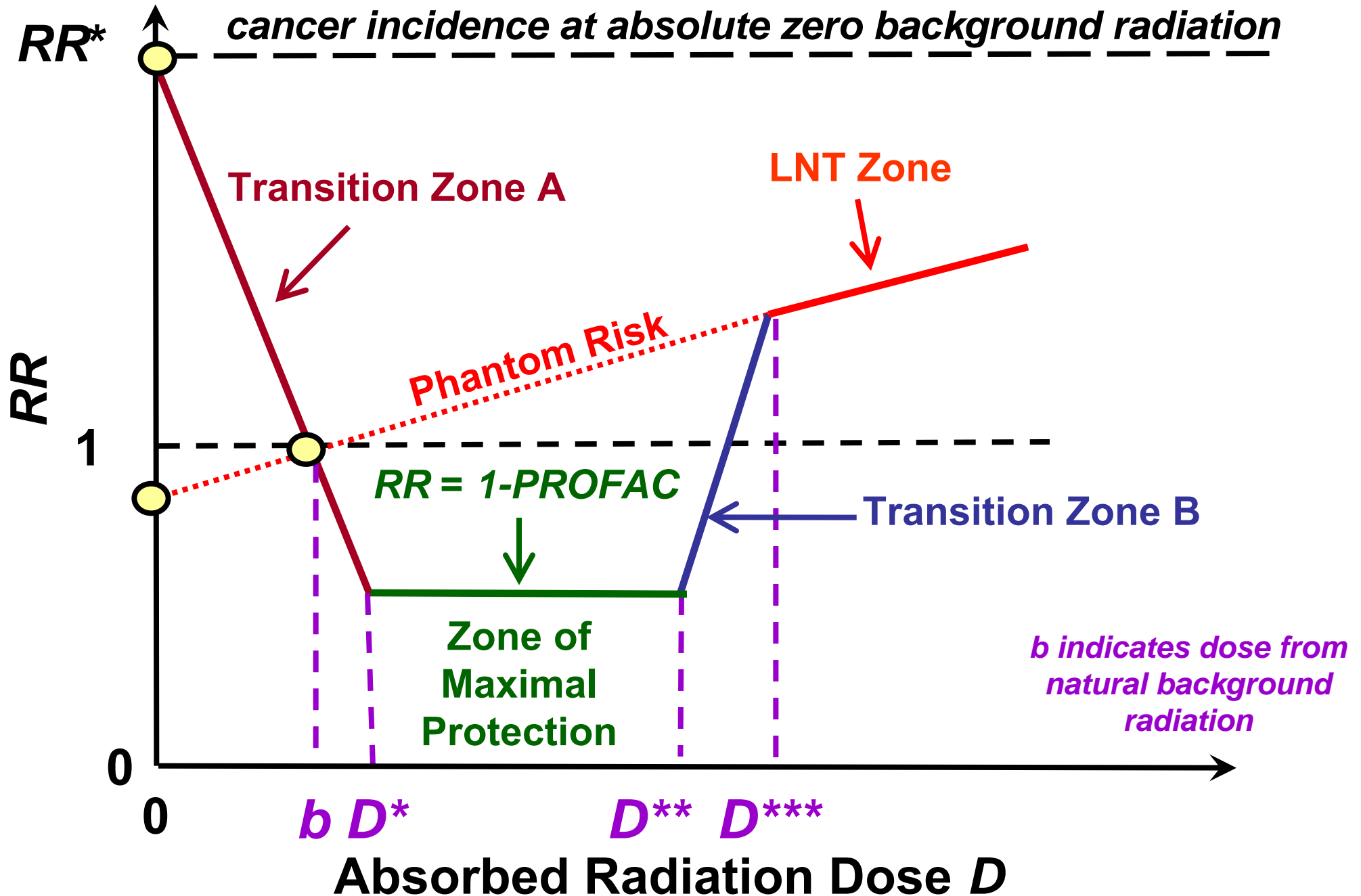
- **Cancer arises from cells with persistent instability through a series of stochastic changes, independent of how instability originates, but dependent on the number of cells with this instability in an organ.**
- **A system of induced protective processes suppress cancer occurrence (adapted protection): high-fidelity DNA repair/apoptosis; and auxiliary apoptosis process; induced immunity.**

## Implications of Key Assumptions

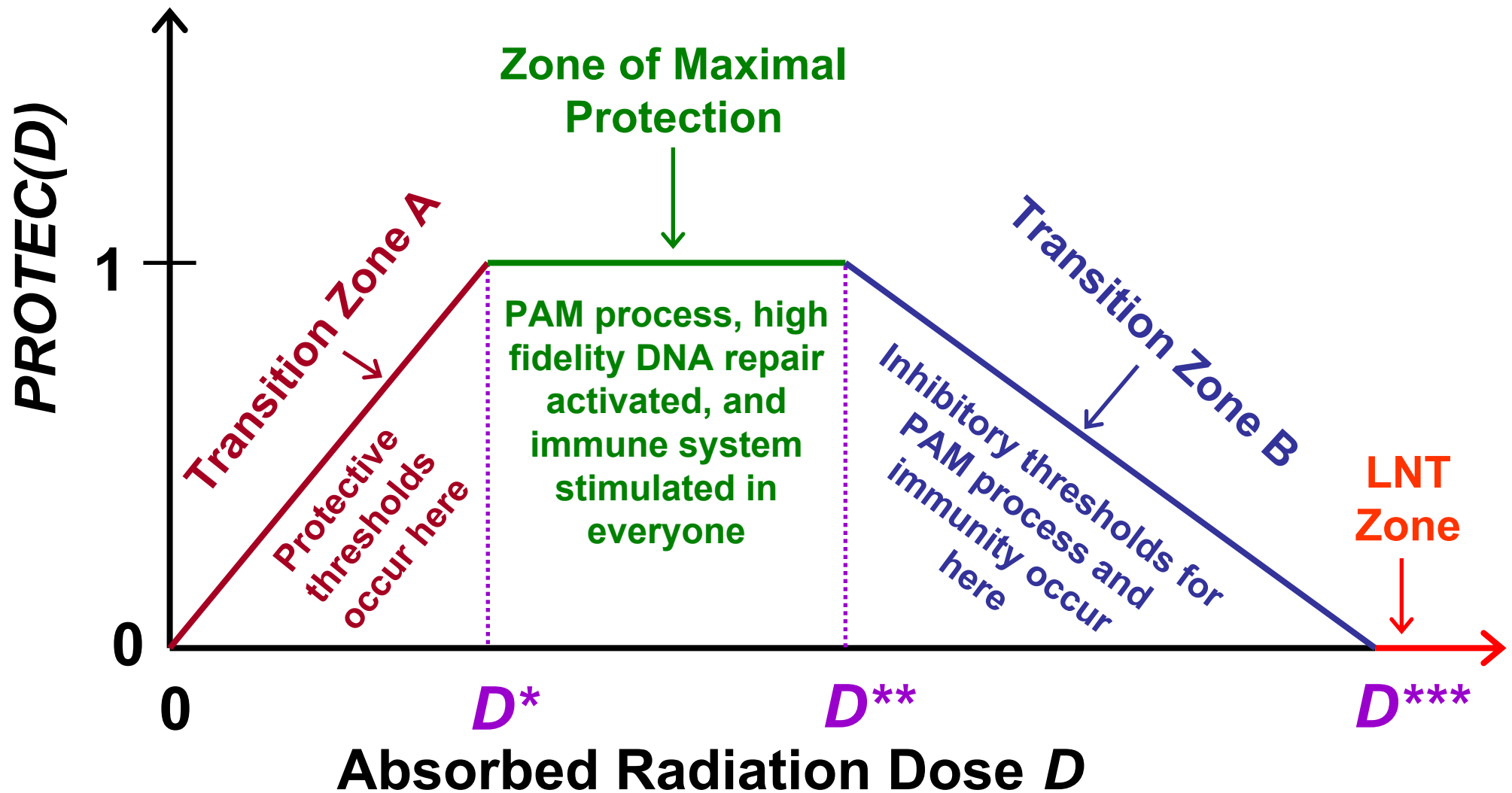
- Cancer relative risk ( $RR$ ) is proportional to the neoplastic transformation  $RR$  as has been demonstrated by Dr. Redpath's group.
- The  $PROFAC$  parameter can account for protection associated both with the **PAM process** and with **induced immunity**.

$$1 - PROFAC = (1 - PROFAC_{PAM})(1 - PROFAC_{Imm})$$

# Hormetic Relative Risk (HRR) Model



# Protection Probability Function $PROTEC(D)$ , A Consequence of Stochastic Modeling<sup>a</sup>



<sup>a</sup>Scott BR. Chapter, Nova Science Publishers, Inc. Book on Genomic Instability (accepted, 2006)

# Hormetic Relative Risk Function $RR_{HRR}$ for $D \geq b$

$$RR_{HRR} = PROTEC(D)RR_{HR} + [1 - PROTEC(D)]RR_{LNT}$$

$$RR_{HR} = (1 - PROFAC)RR_{LNT}$$

$$RR_{LNT} = 1 + [(1 - B)/B]K(D - b)$$

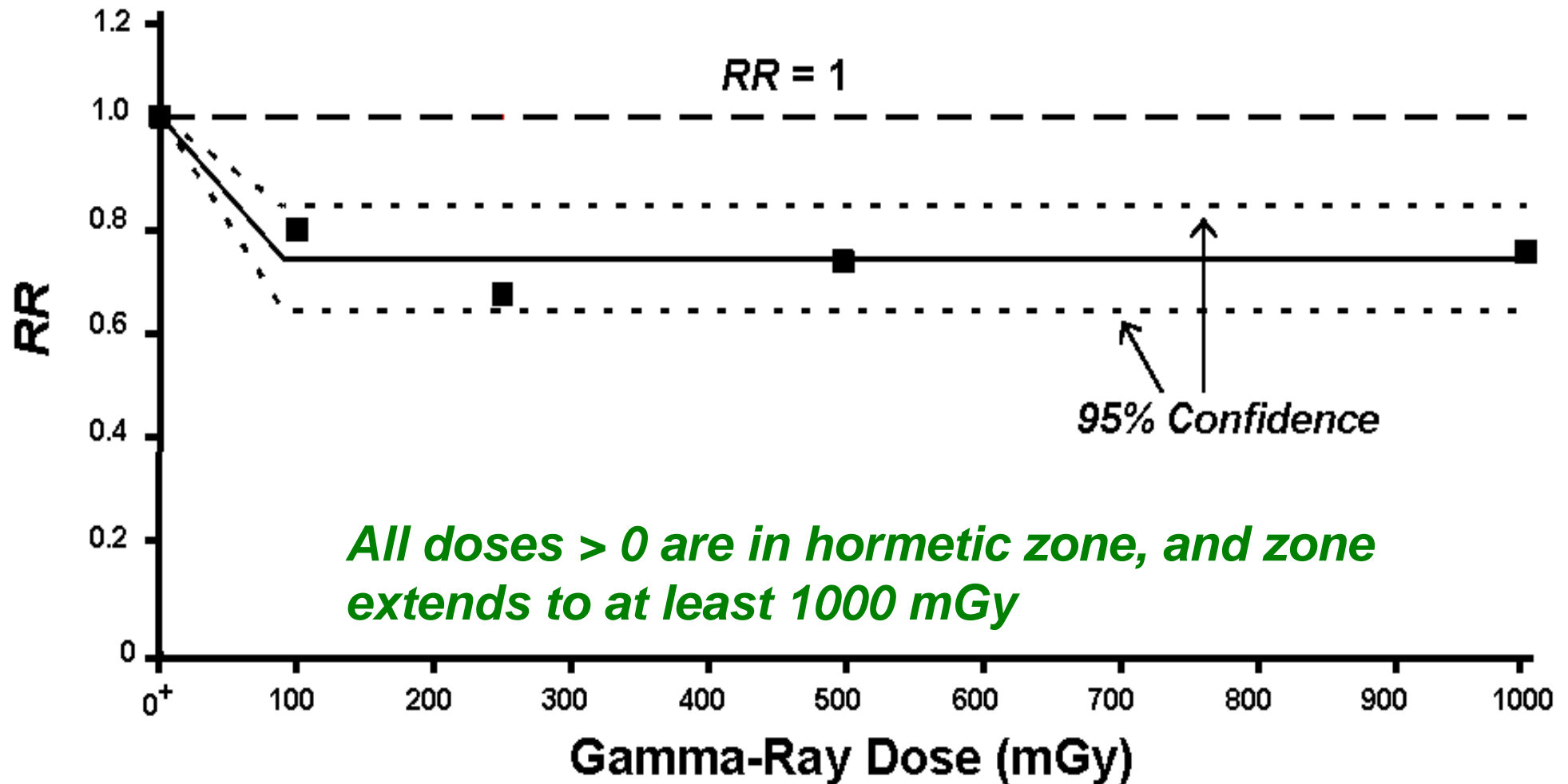
$$RR_{HRR} = RR^* - (RR^* - 1)S \text{ for } S < 1$$

$S = D/b$  is normalized dose relative to  $b$ .

# **Expectations for Low-LET Radiation-Induced Adapted Protection**

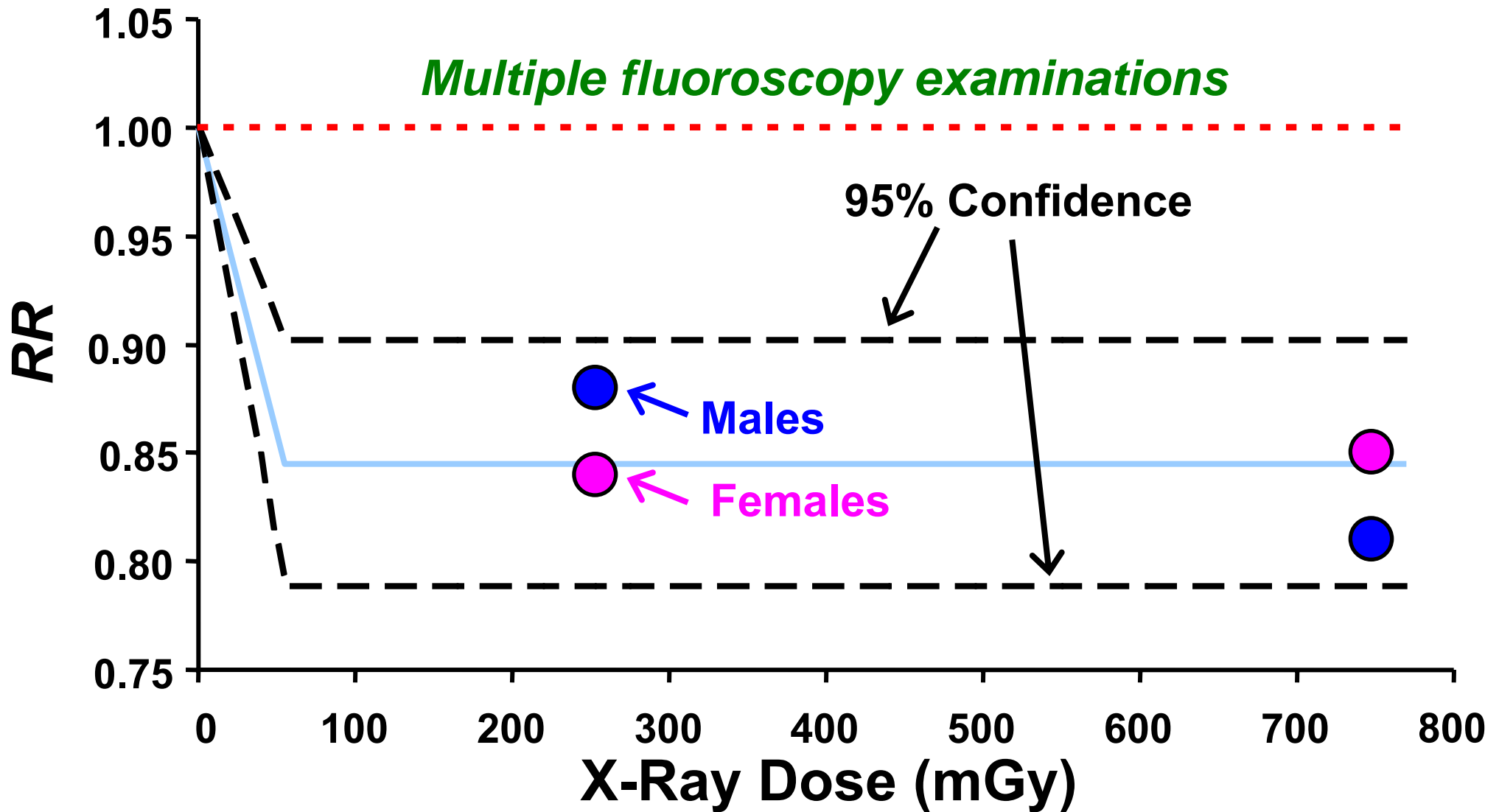
- **Increases with multiple small doses.**
- **Increases with duration of exposure when at very low rates.**
- **Increases with increasing photon radiation energy.**
- **Increases with age.**
- **May not occur for pure alpha radiation.**

# Lung Cancer in Mice: Within Zone of Maximal Protection



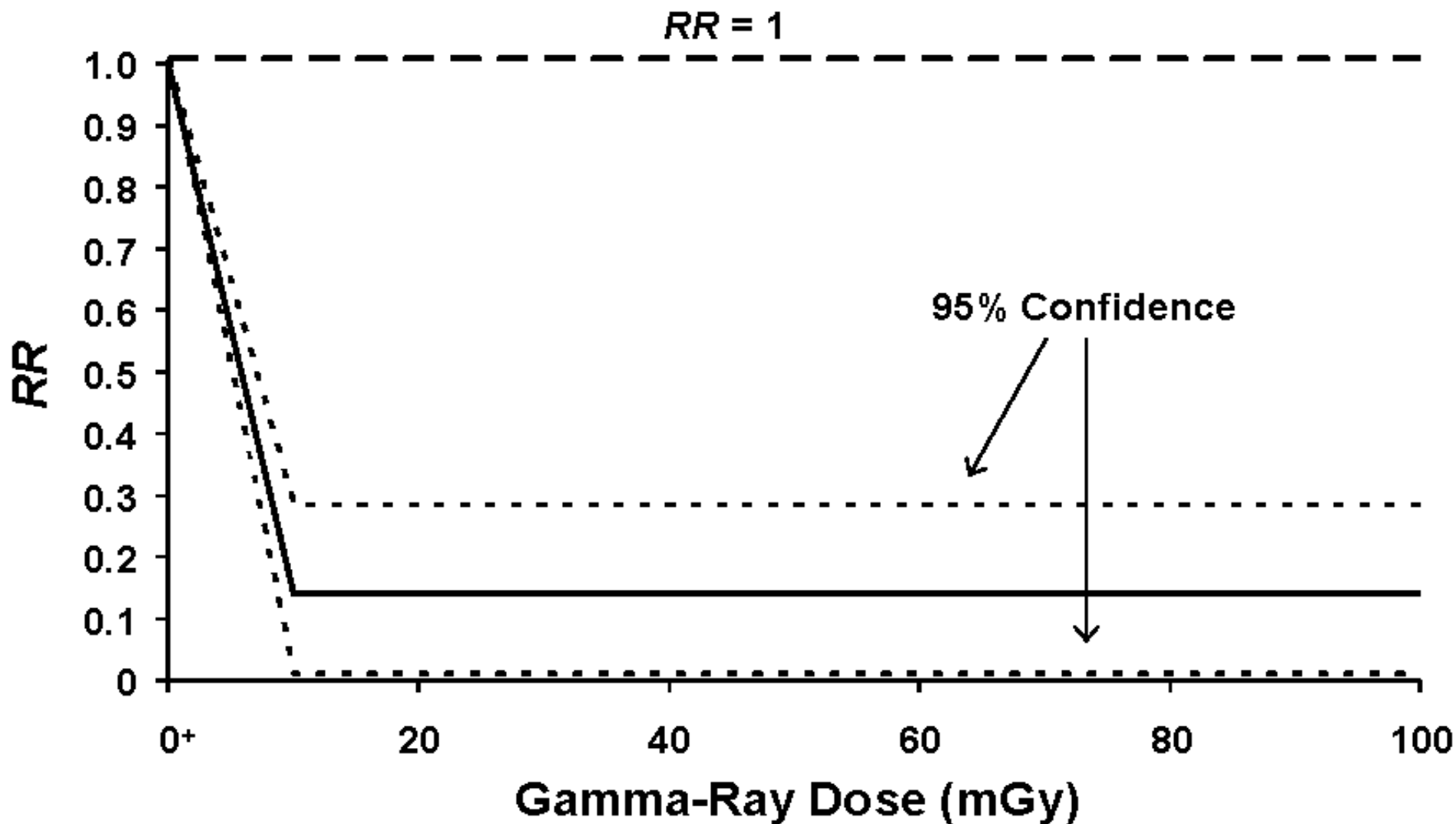
*Study involved more than 15,000 mice (Ulrich et al., 1976).  
Note that risk does not change with dose!*

# Lung Cancer in Humans: Within Zone of Maximal Protection



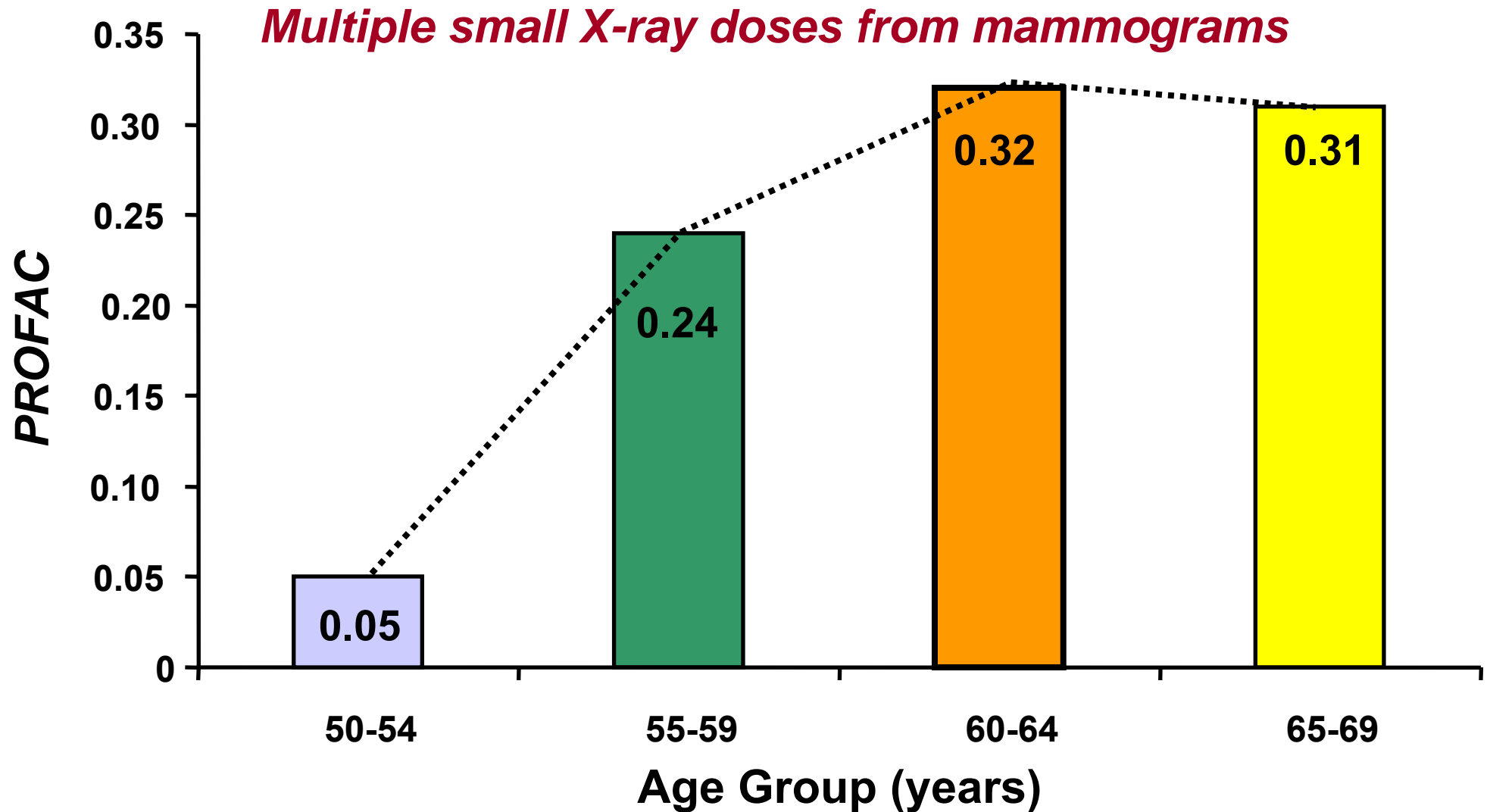
*Data from Howe GR. Radiat. Res. 142:295-304,1995. Similar findings have been reported for breast cancer (Miller. N. Engl. J. Med. 321:1285-1289, 1989)*

# Suppression of Spontaneous Lung Cancer in Mayak Plutonium Facility Workers



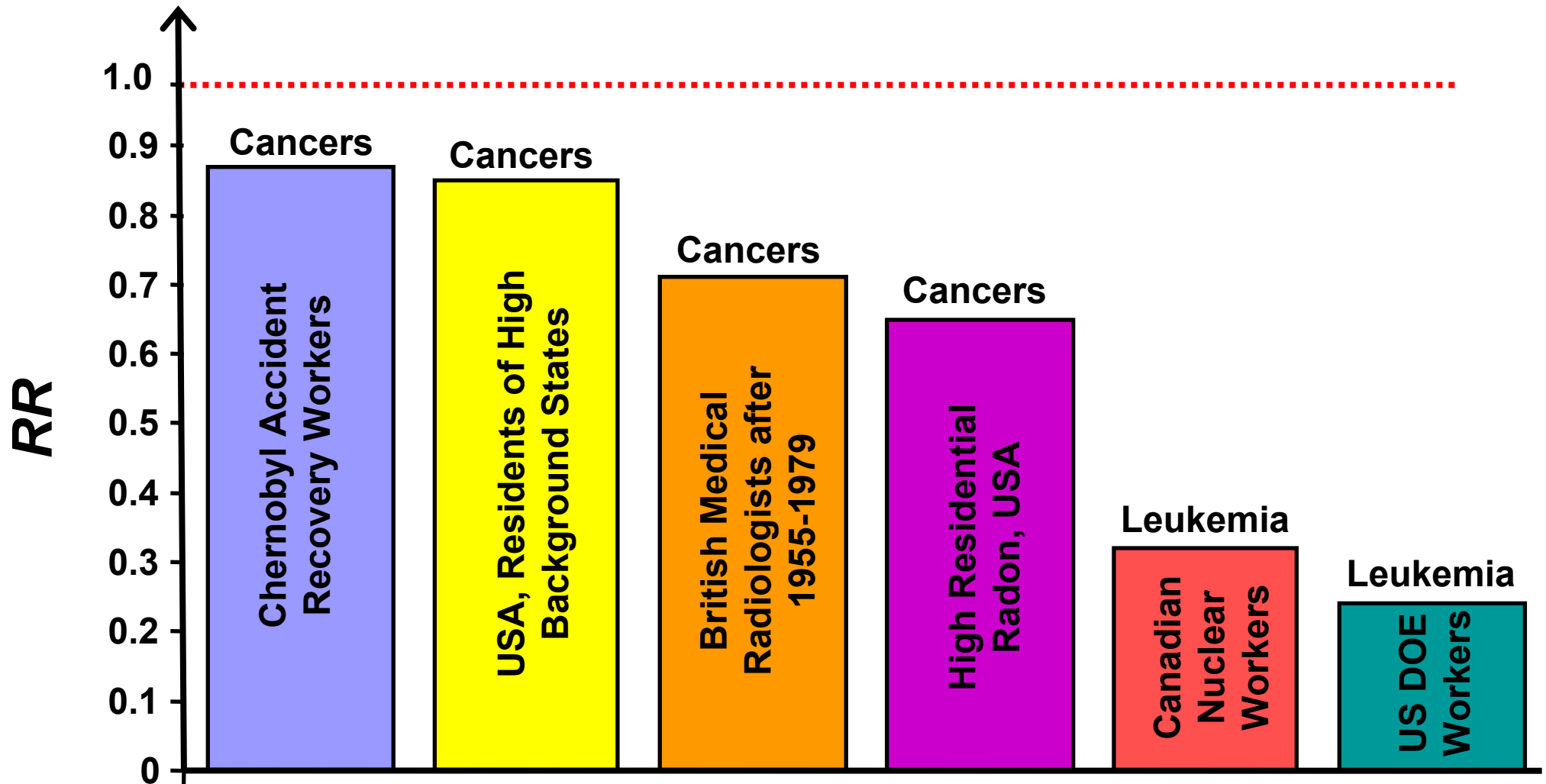
*Data corrected for influence of alpha radiation (Scott, 2006a).*

# Age-Dependency of Adapted Protection: Suppression of Breast Cancer in Humans



*Based on data from Nyström et al. The Lancet 2002; 359(9310):909-919.*

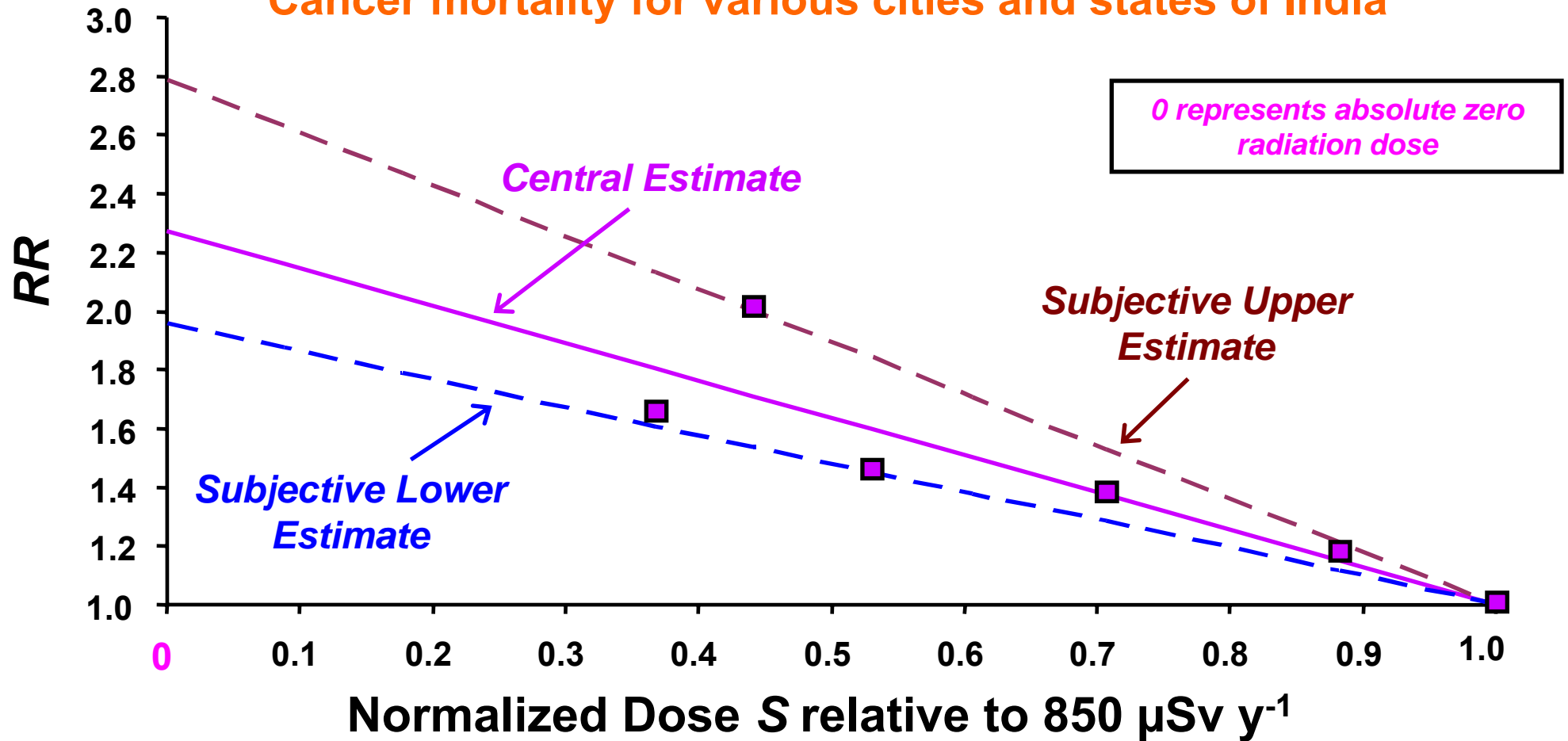
# Low-Rate Low-Dose Exposures Protected Young Adults and Populations of All Ages:



*RR < 0.85 cannot be due to healthy worker effect  
(Sponsler and Cameron, 2005; Scott and Di Palma, 2006)*

# Natural Background Radiation Falls in Transition Zone A

## Cancer mortality for various cities and states of India

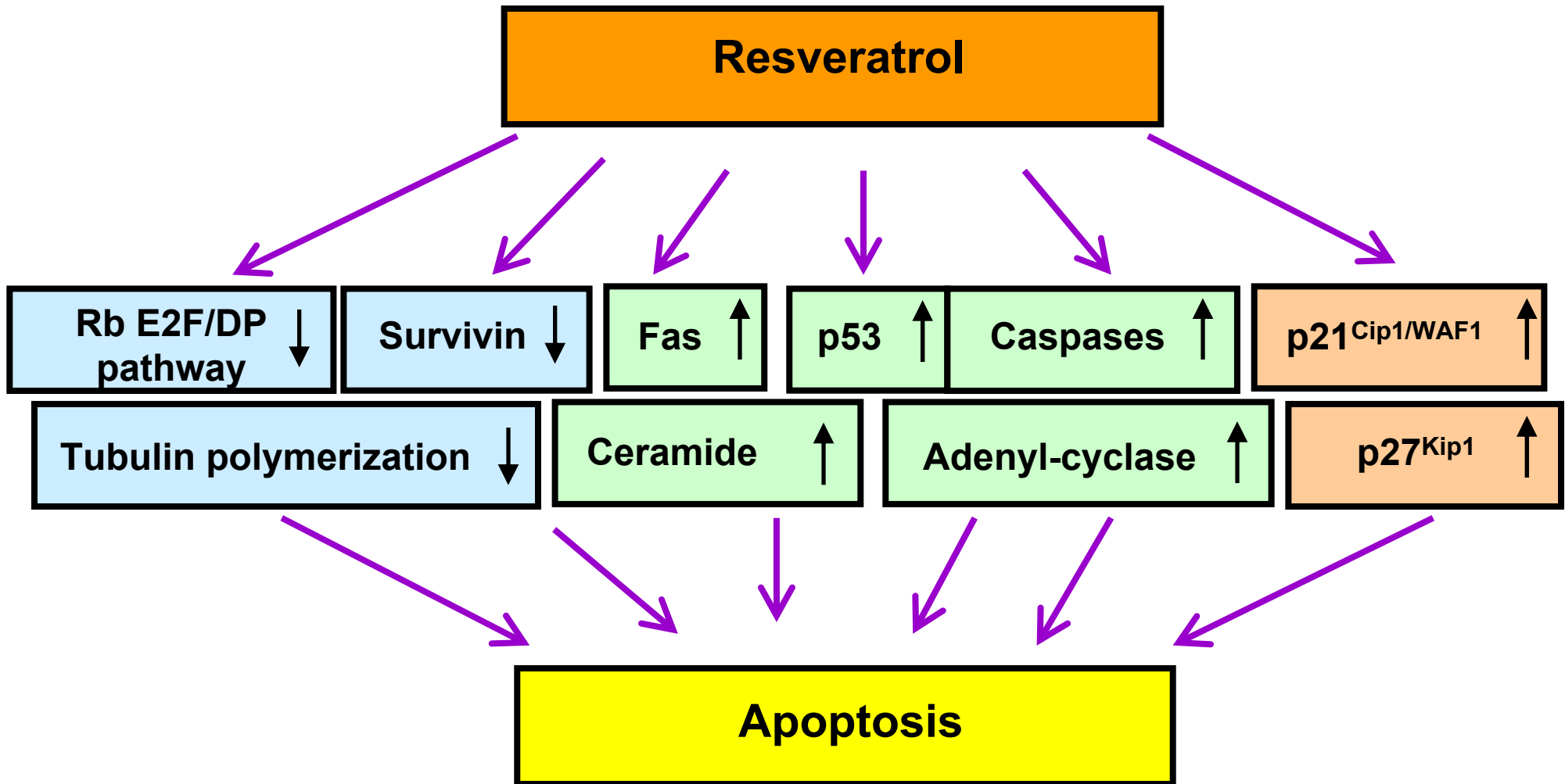


Only gamma-ray exposures were evaluated.  $RR = 1$  at  $0+ = 850 \mu\text{Sv y}^{-1}$ .

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

# Novel Low-Dose Cancer Therapy

- Use small (e.g., 1 mGy) multiple doses (or chronic low rates).
- Also use small multiple doses of an apoptosis-sensitizing agent (e.g., **resveratrol**) along with an antiangiogenic drug.



Multiple pathways to apoptosis (Aggarwal *et al.* Anticancer Research 24:3-60, 2004)

# How Adapted Protection is Inappropriately Discounted by Ecological/Epidemiological Studies

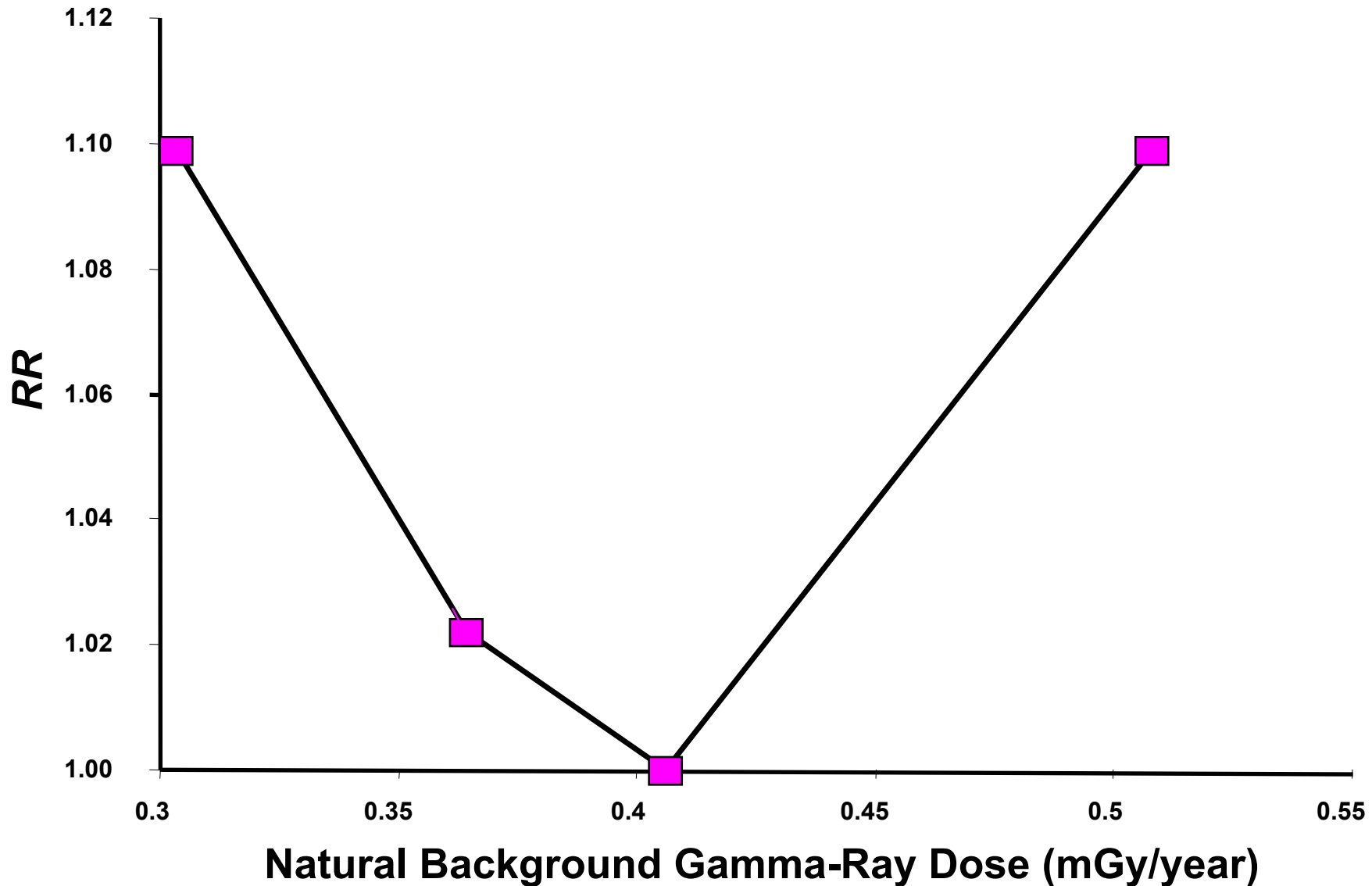
- **All radiation assumed harmful** including doses from diagnostic low-LET radiation (e.g., routine chest X-rays, CT scans, nuclear medicine diagnostic procedures).
- **Persons receiving low doses included with controls** when evaluating the shape of the dose-response curve.
- **Low-dose data are excluded**, ignored, or assigned low statistical weight.
- **Evidence for nonlinearity is ignored.**
- Ecological data showing hormesis are discounted based on poor dosimetry.
- **DNA repair, protective apoptosis, and induced immunity are ignored.**
- **Lifespan prolongation is not considered.**
- **Hormetic effects missed** due to assuming a healthy worker effect.
- **Years of radiation dose accumulation are simply thrown away (called dose lagging)** changing threshold-like dose responses into what appears to not have a threshold.

# Conclusions

- **The LNT hypothesis is not supported by cancer frequency data for low-dose, low dose-rate low-LET irradiation. The data are more consistent with the HRR model.**
- **Low doses and dose-rates of low-LET radiation (including natural background radiation) protect from cancer and other diseases.**
- **The level of protection against cancer increases with age and appears to be quite small for children if at all.**
- **Repeated exposures (or chronic low rate exposure) over a prolonged period to small doses of low-LET radiation in combination with antiangiogenic therapy and tumor sensitization therapy (e.g., application of resveratrol) might greatly increase the frequency of cancer cures while limiting harm to patients from their treatment.**

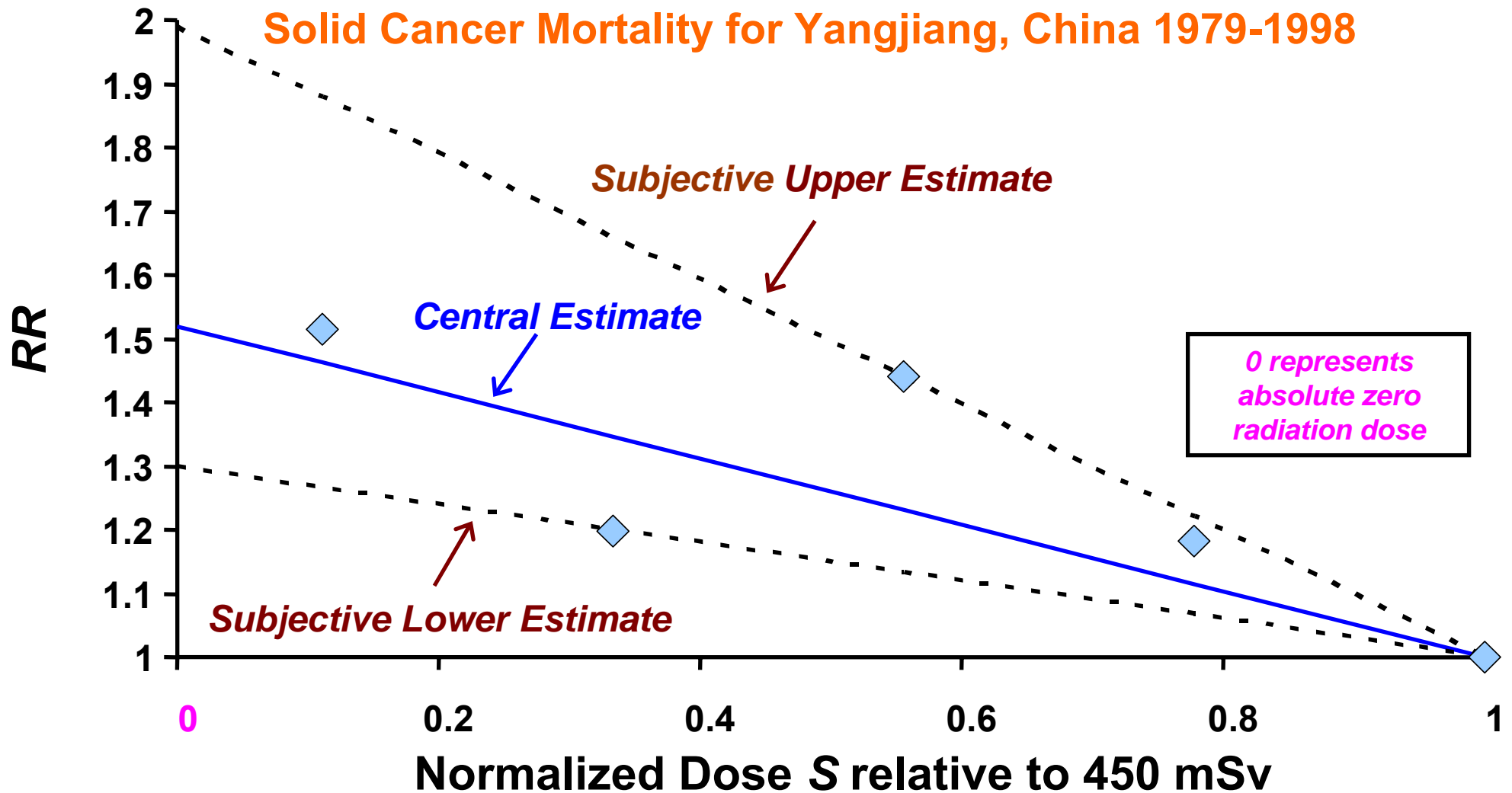
**Backup**

# Childhood Acute Myeloid Leukemia Relative Risk



*Data points based on data from A-S Evrard et al., Health Phys. 90(6):569-579, 2006.*

# Expected Effects of Reducing Natural Background Radiation on Cancer Mortality



Data from Wei and Sugahara. *Int. Congress Series 1236:91-99 (2002)*

