

Some New Low-Dose Studies Should Relate to Mechanistic Basis for Radiation Hormesis

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

Low-Dose, Low-LET Radiation Protects Us (Radiation Hormesis)

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

Induced Protective Processes Presumed Associated with Radiation Hormesis

- **High-fidelity DNA repair/apoptosis competition (p53-dependent).**
- **Special form of apoptosis (p53-independent) that selectively removes aberrant bystander cells.**
- **Immune system stimulation.**

High doses appear to inhibit p53-independent apoptosis and suppress immune system leading to increased cancer risk.

New Hormetic Relative Risk (HRR) Model Accounts for Indicated Induced Protection:

- **Scott BR. Nonlinearity (2 papers in press): Mutation induction, neoplastic transformation, and cancer induction.**
- **Scott BR, Haque M. and Di Palma J. International J. Low Radiation (accepted): Introduces weighted Bayesian analysis.**
- **Scott BR. J. Amer. Phys. Surg. (submitted): Cancer prevention/therapy implications.**
- **Scott BR. Health Phys. (being edited and formatted): Radiation protection implications.**

Hormetic Relative Risk (HRR) Model for Cancer Induction

Low-dose, low-dose-rate irradiation:

$$RR_{HRR} = 1, \text{ Dose} = 0$$

$$RR_{HRR} = (1 - PROFAC)RR_{LNT}, \text{ otherwise}$$

$RR_{HRR} \cong (1 - PROFAC)$, at low doses and
dose rates (*dose independent zone*)

RR_{LNT} is relative risk based on LNT.

***Stochastic thresholds associated with
activation of protective processes.***

PROFAC

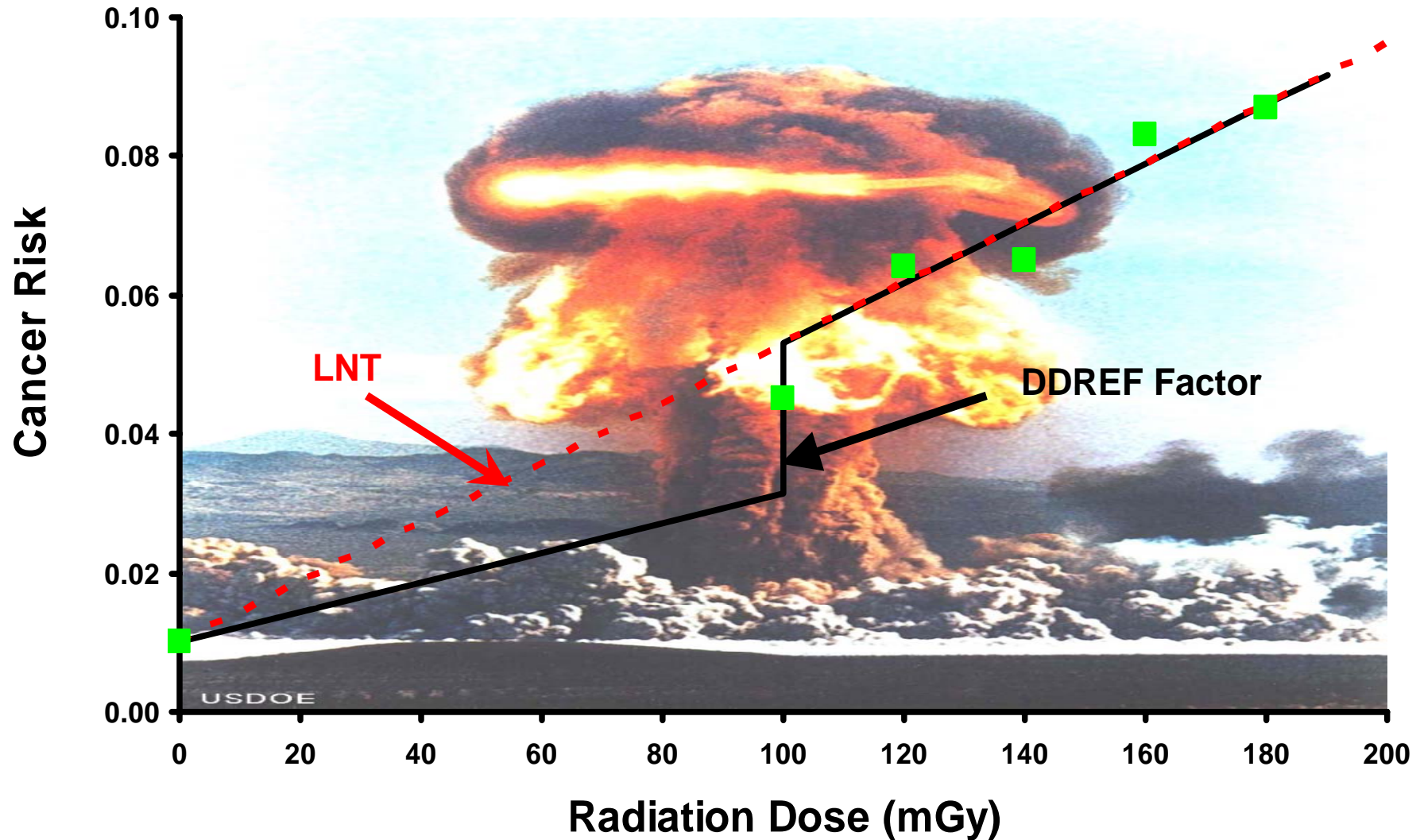
- For cancer induction, the ***PROFAC*** gives the proportion of cancers prevented due to radiation hormesis (associated with activated protective processes and low-LET dose component).
- ***PROFAC*** takes on values from 0 to 1 and is associated with the low-LET component of the dose.

Scott BR, Nonlinearity (in press), 2006a,b.

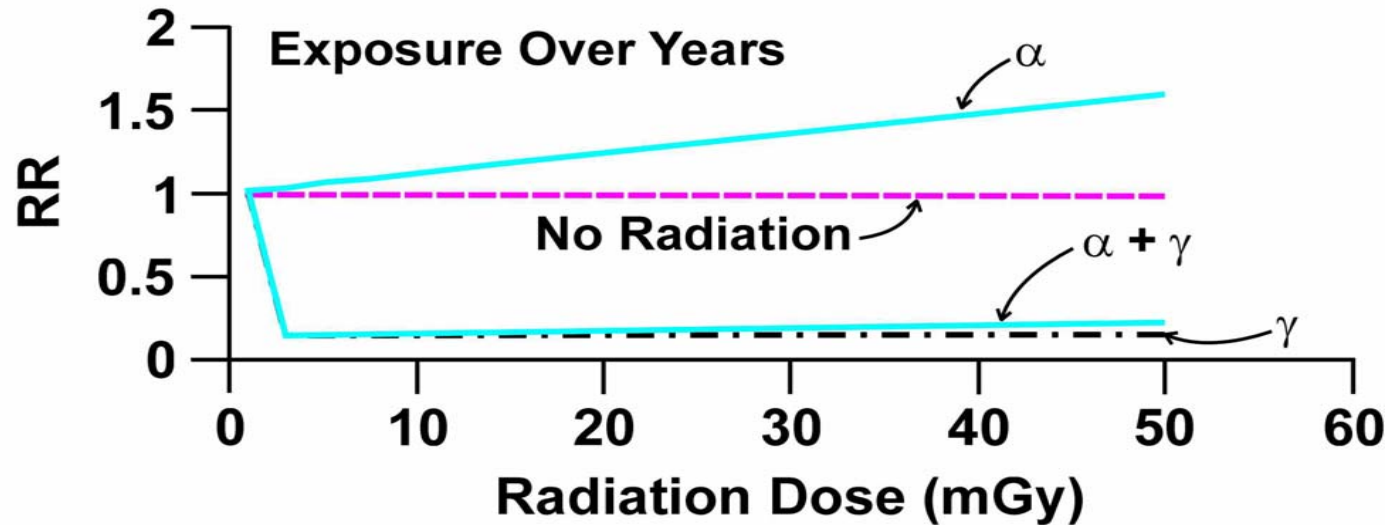
How Radiation Hormesis Usually Missed or Eliminated

- **Inappropriate application of LNT hypothesis, e.g. extrapolating more than 10 orders of magnitude from high to low dose rates.**
- **Inappropriately including irradiated individuals in the control group eliminating a hormetic zone.**
- **Assigning more weight to high-dose data (conventional un-weighted regression).**
- **Ignoring nonlinear data after prolonged protracted exposure (e.g. over years) in favor of data for high-dose-rate brief exposure.**
- **Throwing away dose (called dose lagging) while assuming any dose increment is harmful (LNT hypothesis).**

Inappropriate Extrapolation from High Dose Rate to Background Radiation



LUNG CANCER RELATIVE RISK: MAYAK WORKERS



5354-8

PROFAC=0.86 [Scott BR. Nonlinearity, 2006a
(in press)]

Similar results now found for liver cancer.

Protection Factors Against Cancer Associated with Chronically Irradiated Human Populations¹

Region or Group	Effect	PROFAC
Canada, nuclear industry workers	leukemia	0.68
US DOE labs workers	leukemia	0.78
Mayak Plutonium facility workers	lung cancer	0.86 ²
Taiwan, Cobalt-60 contaminated apartments	cancers	> 0.95 ²

¹*Jaworowski Z. Symposium “Entwicklungen im Strahleschutz”, Munich, 29 November 2001.*

²*Scott BR. Nonlinearity (in press), 2006a .*

Radon-Associated Protection Against Cancer

Cancer Site or Type	PROFAC	
	Females	Males
Leukemia	0.47	0.56
Stomach	0.55	0.60
Breast	0.74	-
Lung	0.81	0.53
Colon/rectum	0.86	0.70

***High-level-radon spa area in Japan (Misasa)
relative to Japanese population (1952-1992)
(Mifune et al. Jpn. J. Cancer Res. 83:1-5, 1992.***

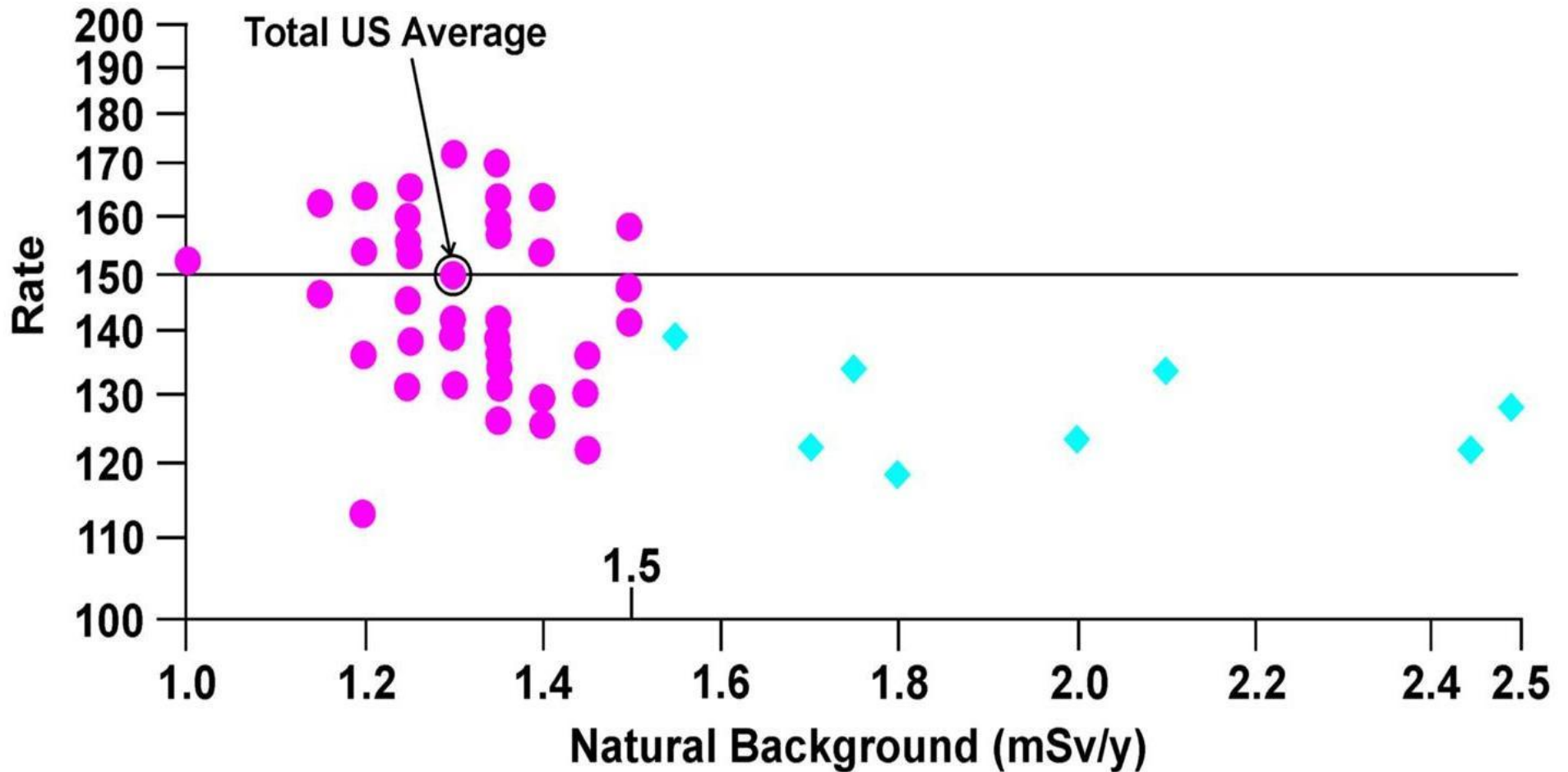
Chernobyl Accident and Hormesis

- Ivanov et al. (2001) found a **hormetic dose-response curve for cancer mortality** among Chernobyl emergency workers. *PROFAC* implicated to be 0.13 (95% CI:0.05, 0.2).
- Ivanov et al. (2004) found a **hormetic dose-response curve for the solid cancer incidence among nuclear workers** who participated in recovery operations after the Chernobyl accident. *PROFAC* implicated to be 0.17 (95% CI: 0. 0.31).

Ivanov VK et al. Health Phys. 81(5):514, 2001.

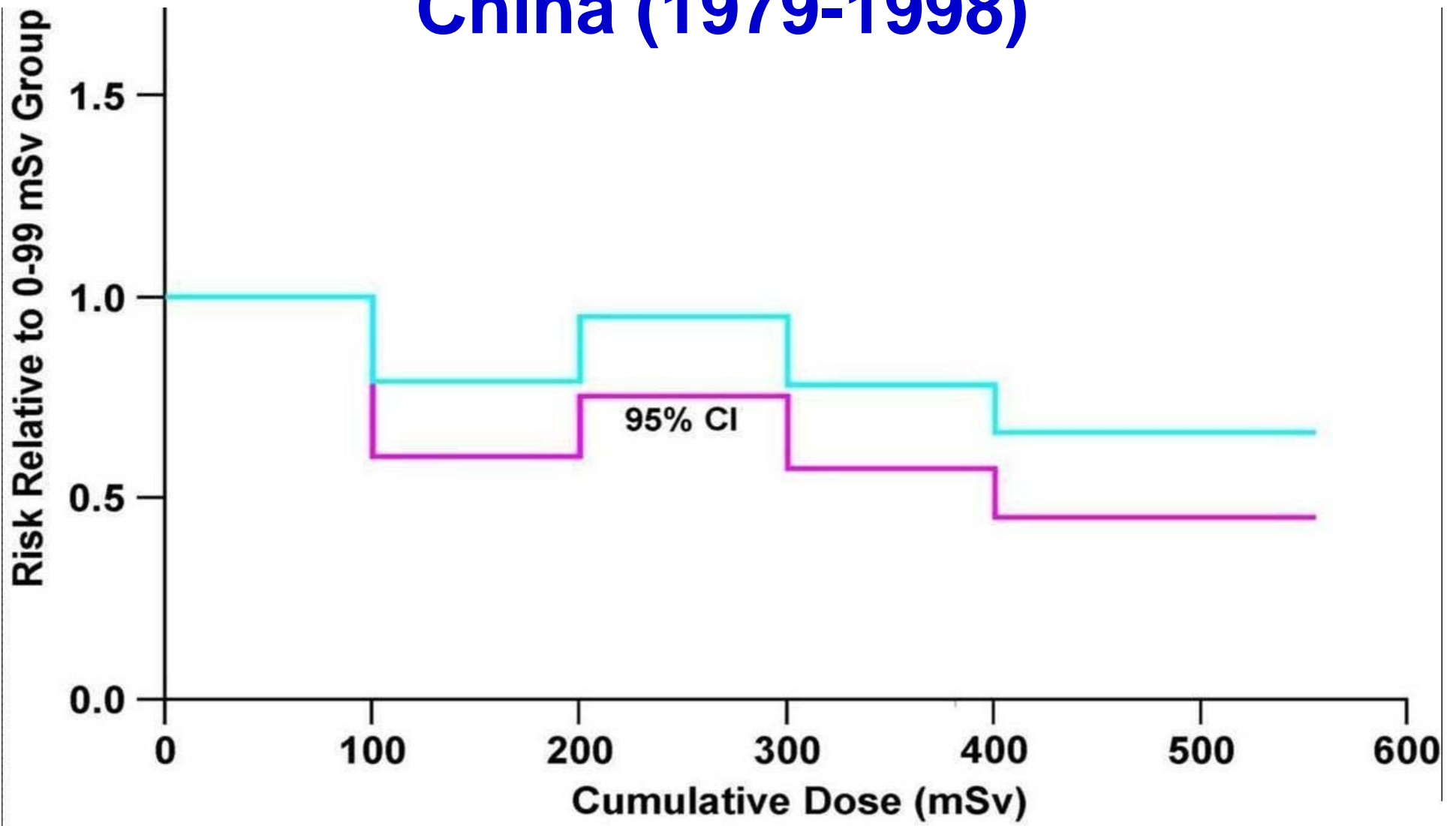
Ivanov VK et al. J. Radiat. Res. 45(1):41-44, 2004.

Annual Cancer Mortality/100,000 For US States (1950-1967)



Frigerio and Stowe, IAEA Publication, 1976.

Solid Cancer Mortality for Yangjiang, China (1979-1998)



Wei and Sugahara. Int. Congress Series 1236:91-99, 2002.

New Radiation Hormesis Research is Needed

- **To facilitate improving low-dose risk assessment.**
- **To facilitate improving homeland security practices regarding managing radiological terrorism events.**
- **To foster novel approaches to cancer prevention and cancer therapy.**

Research Should Include Hormetic Effects on:

- Genomic instability induction.
- DNA damage repair/apoptosis competition (p53-related).
- p53-independent apoptosis.
- Mutations induction *in vivo* and *in vitro*.
- Neoplastic transformation *in vitro*.
- Cancer induction in animals and in humans.

Modeling of the data obtain with a focus on public health and risk assessment implications should also be carried out.

Examples of Testable Hypotheses

- Below natural background radiation environments lead to an increase in persistent genomic instability.
- Below natural background radiation environments suppress high-fidelity DNA repair/apoptosis.
- Below natural background radiation environments lead to an increase in the rate of occurrence and persistence of mutant cells.
- Below natural background radiation environments lead to an increase in rate of occurrence and persistence of neoplastically transformed cells.
- Below natural background radiation environments lead to reduced life expectancy.
- Below natural background radiation environments lead to increase cancers and other diseases.