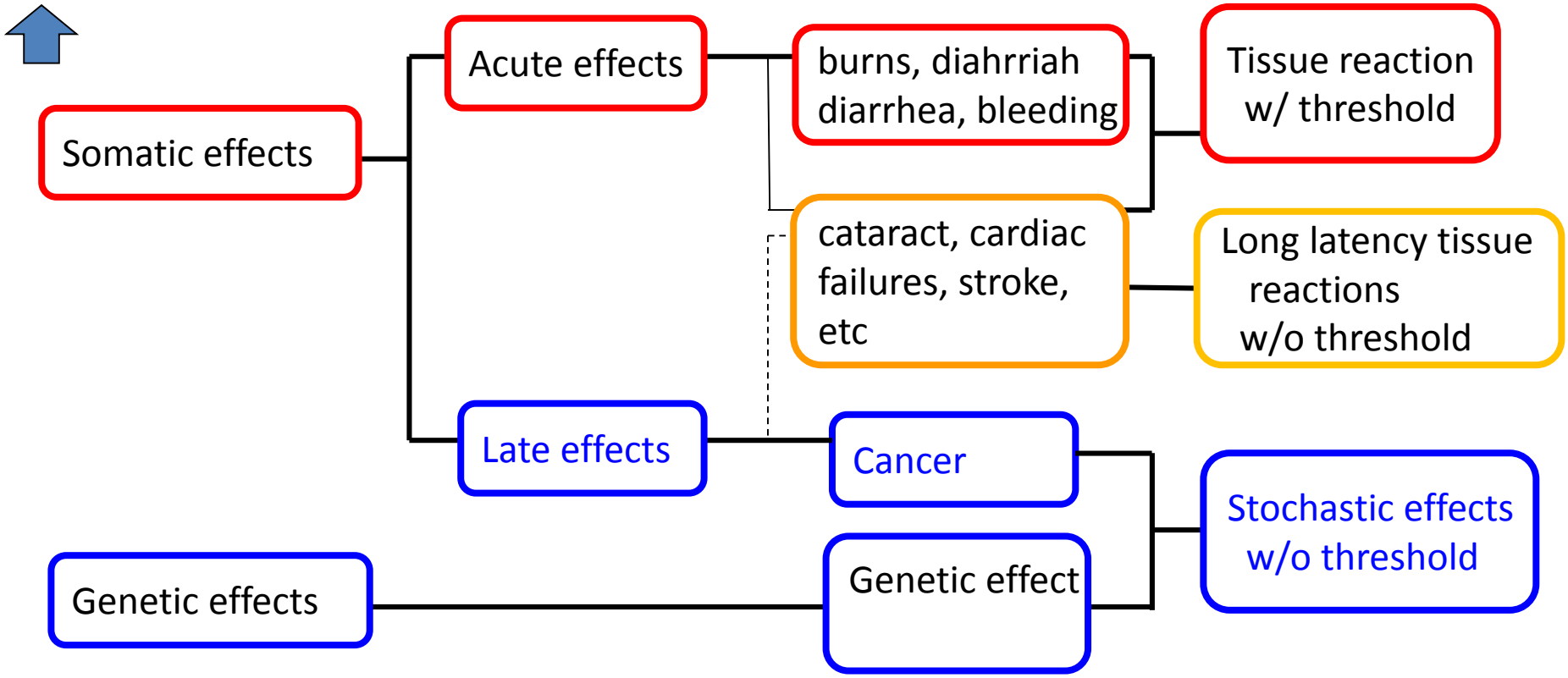
Science and the implication of the LNT model

Ohtsura Niwa, on 151106 in Kyoto

1. Various dose response relationships
2. Judgment on the use of the LNT model for radiation protection
3. LNT as a measuring stick for the size radiation risk
4. Ethical bases for the use of the LNT model for radiation protection
5. How much of the LNT model be understood mechanistically?

Health effects of radiation

Tissue reactions: doses higher than 500 mSv

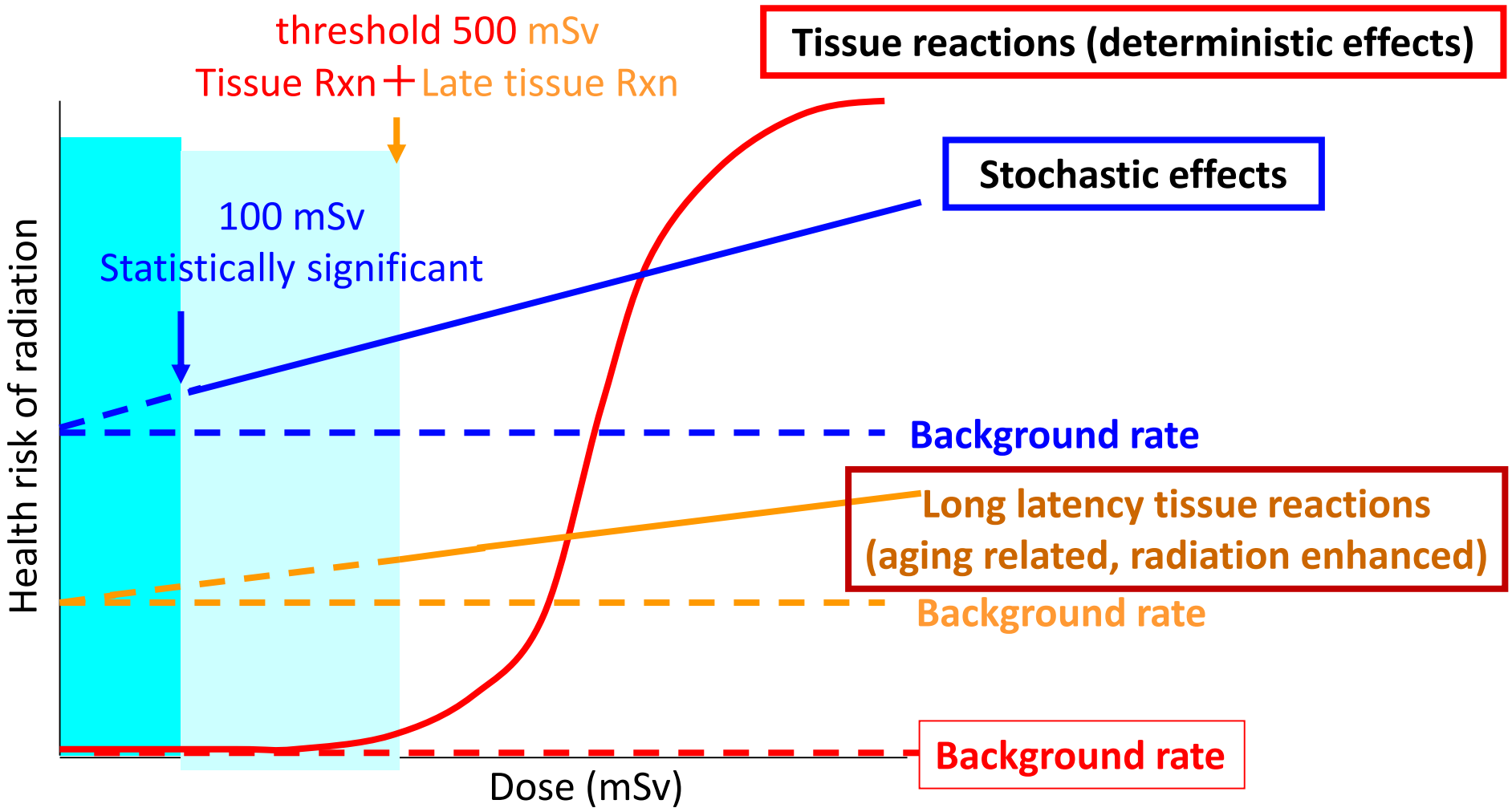


Stochastic effects: dose dependent increases

Long latency tissue reactions:

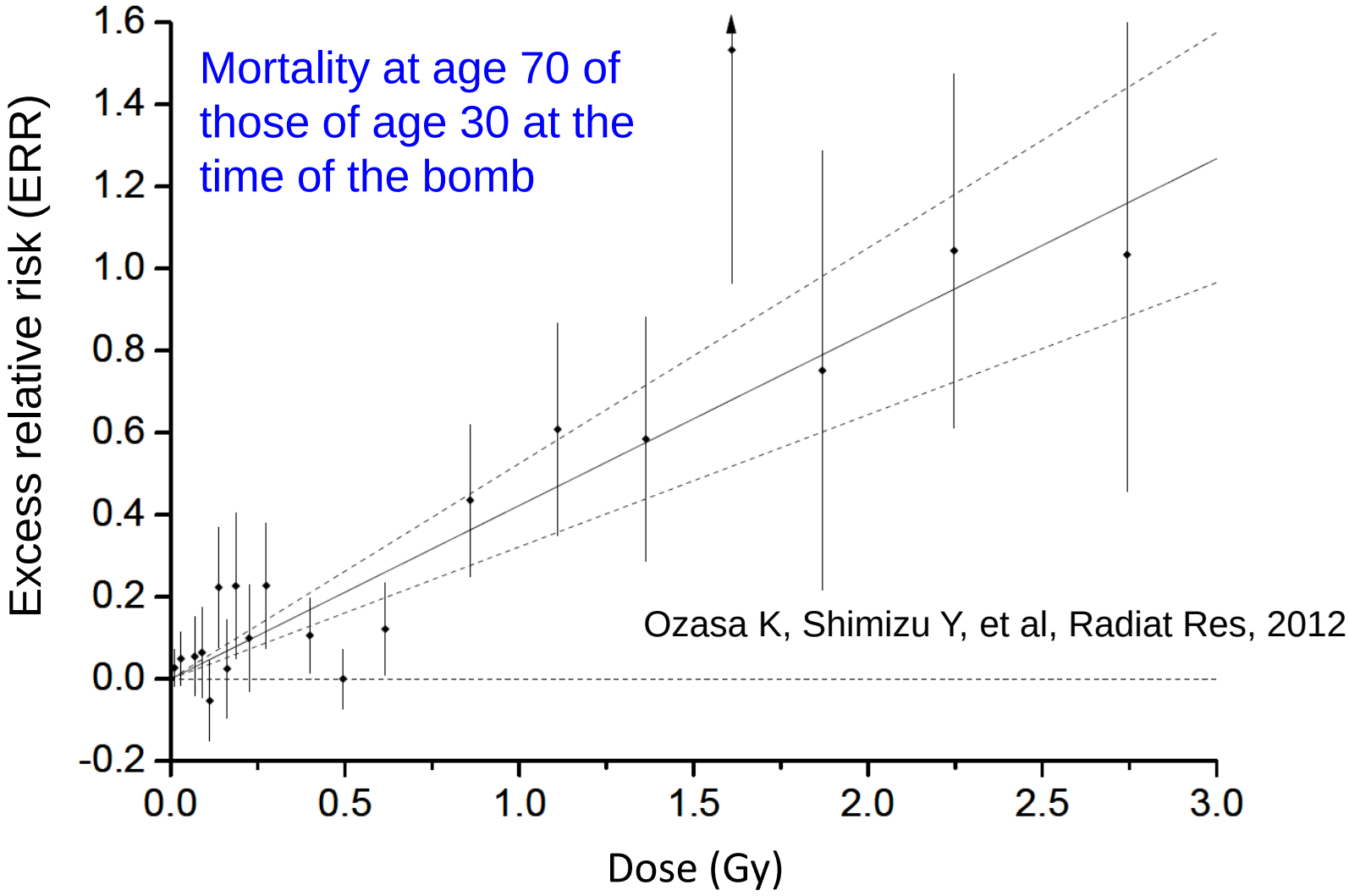
dose dependent increase above500 mSv

1. Various dose response relationships



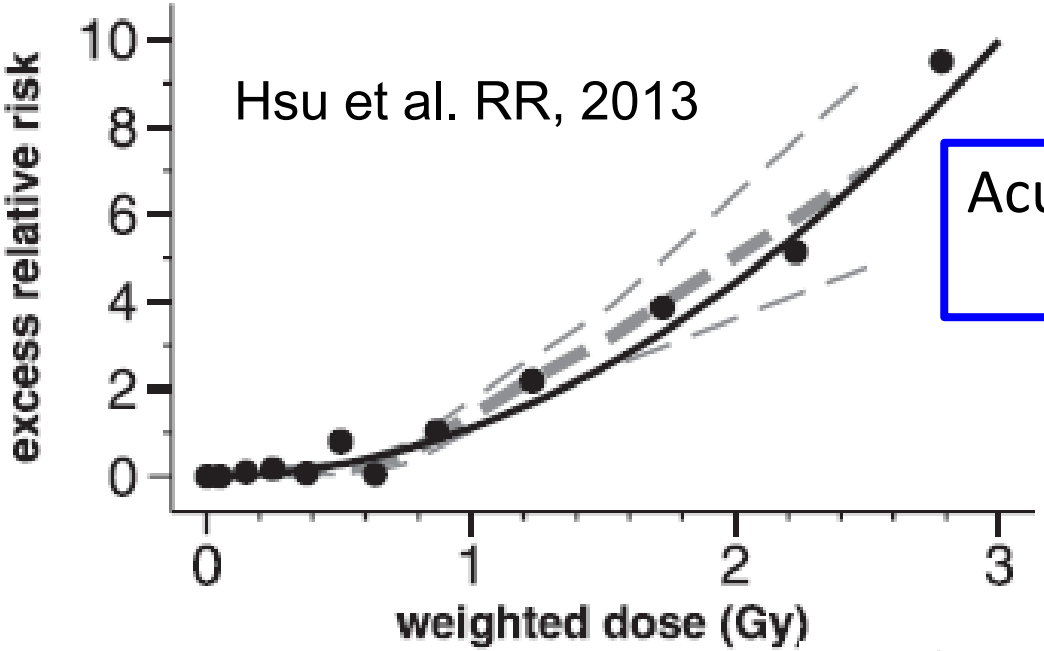
Stochastic effects are the risk of concern at low doses/low dose rates

Excess relative risk (ERR) for all solid cancer in relation to radiation exposure



ERR increases linearly by dose

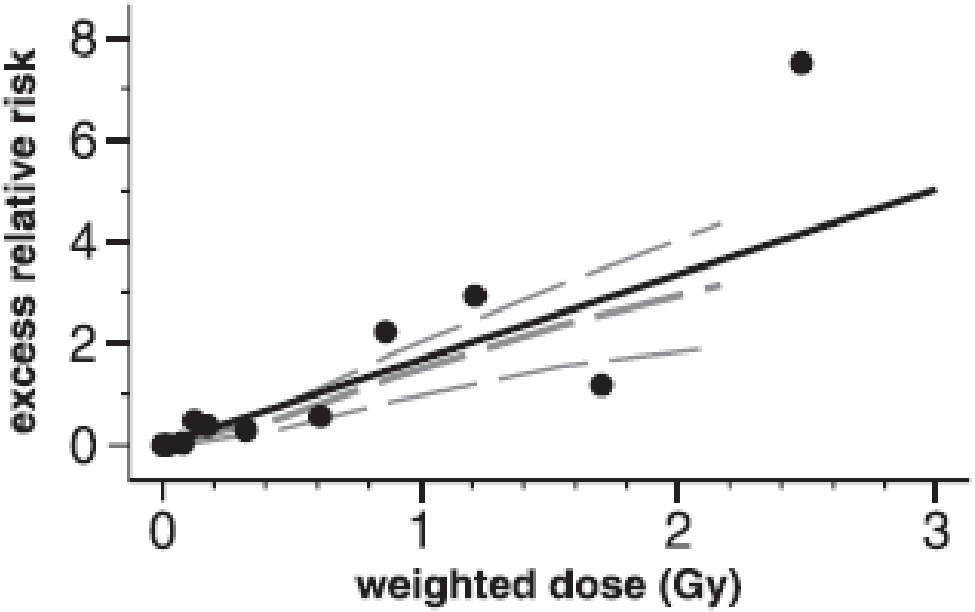
Dose response of leukemia (incidence)

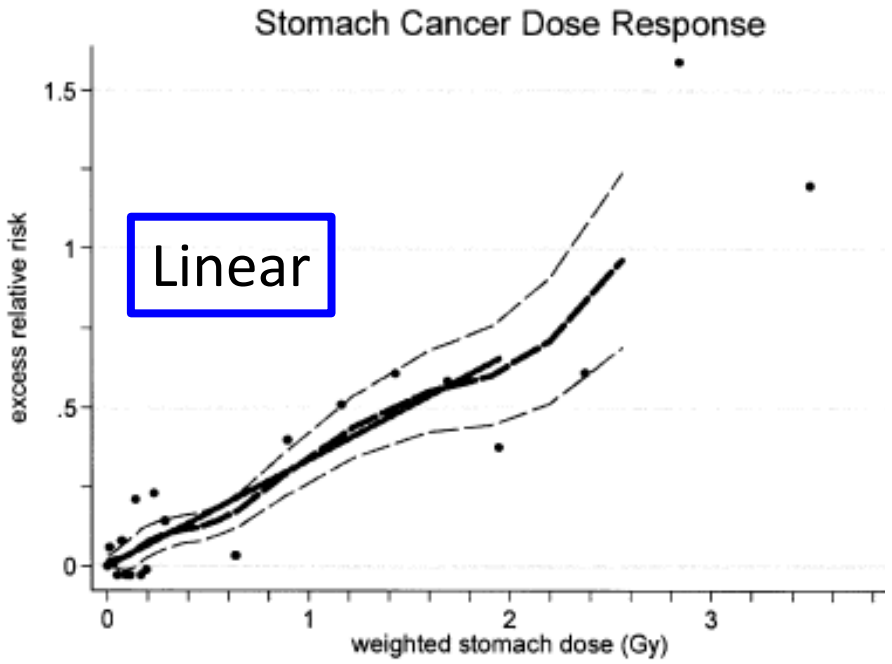


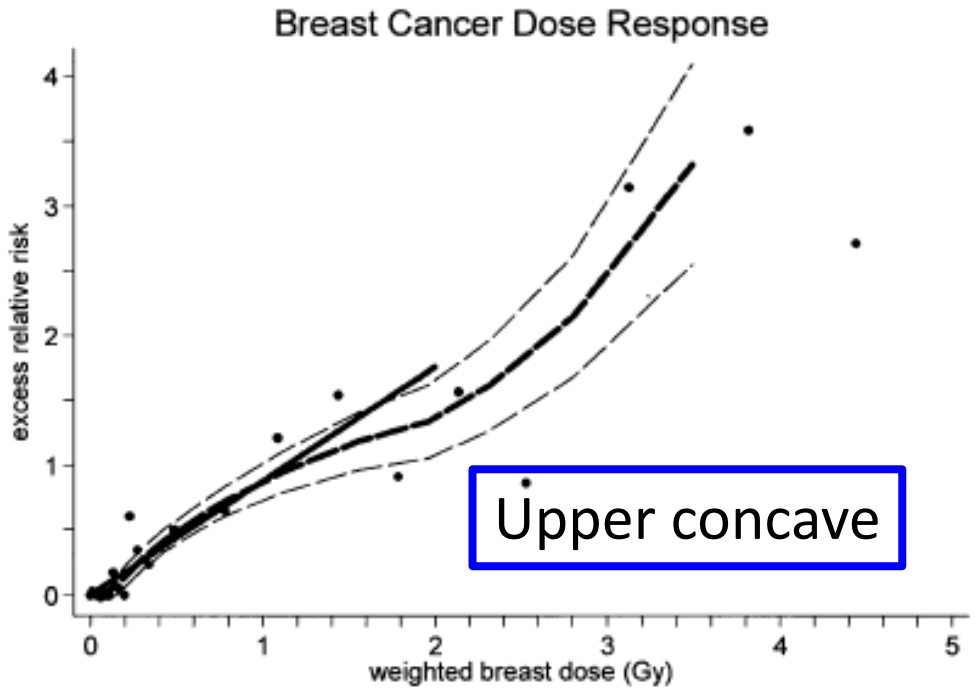
Acute myelocytic leukemia
ERR: LQ

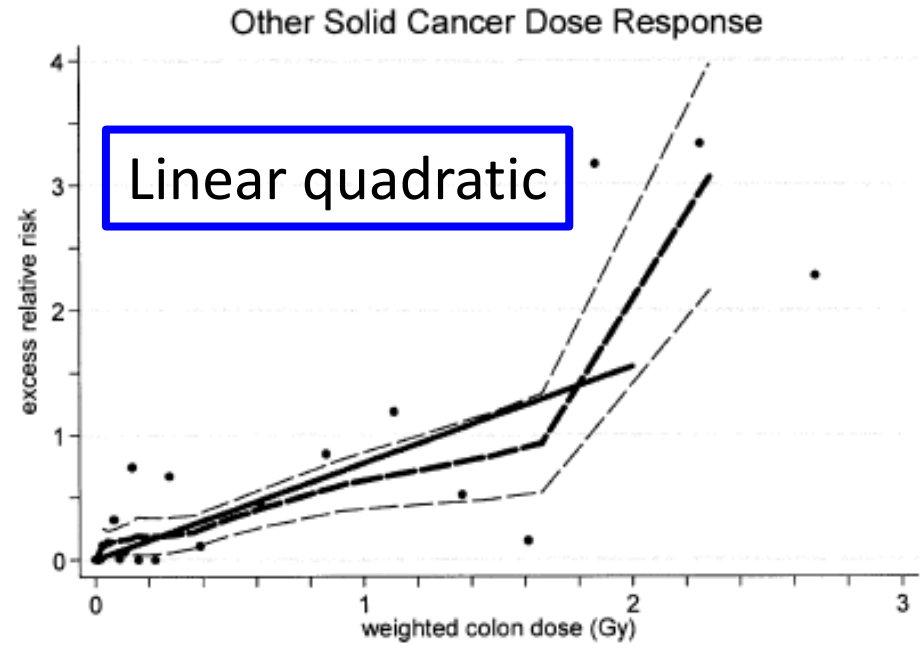
Acute lymphocytic leukemia
ERR: L

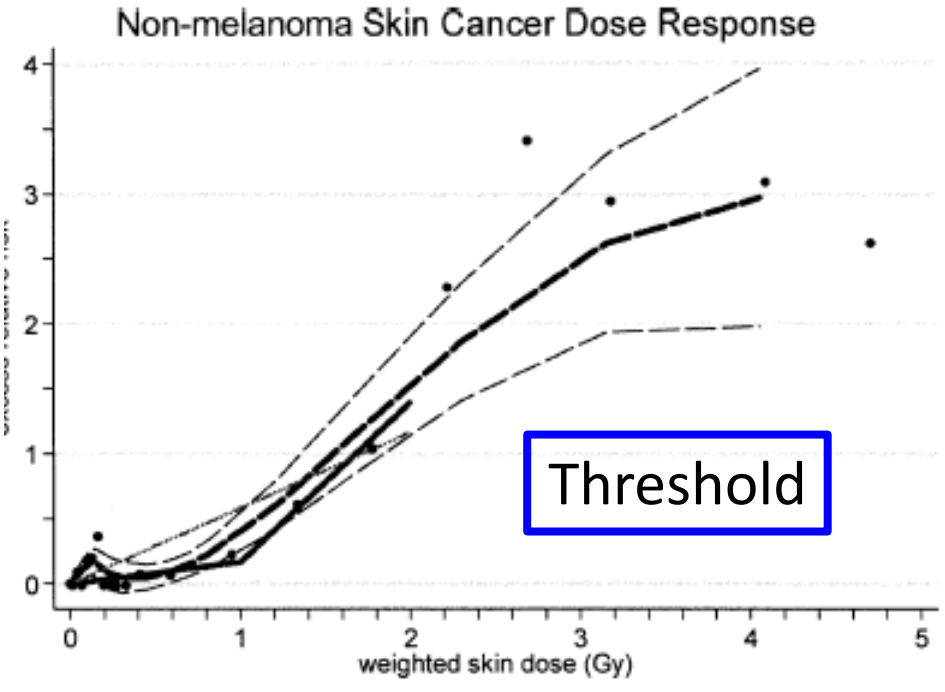
Short latency: 5-10 yrs



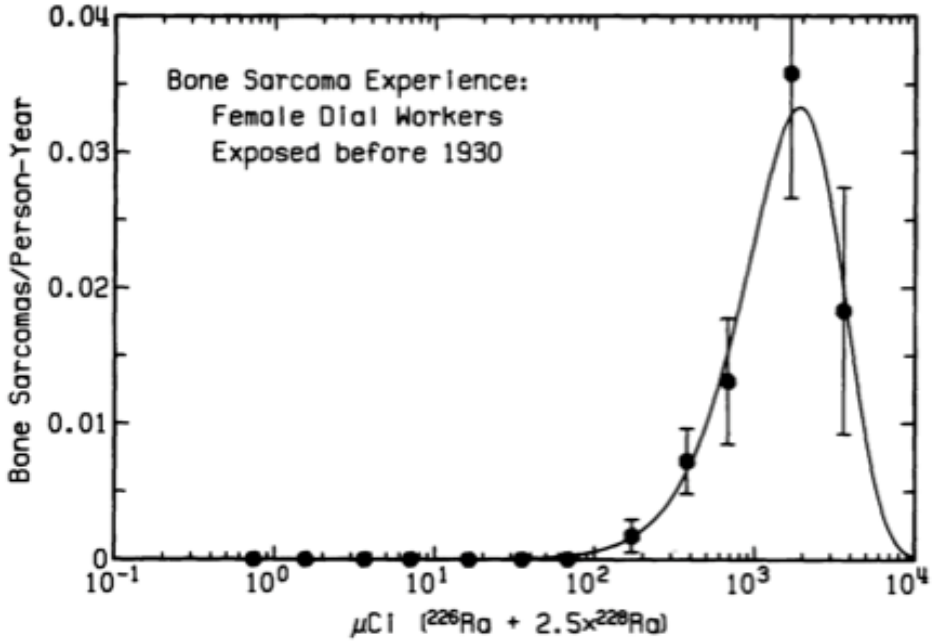

Stomach Cancer Dose Response
Linear
excess relative risk
0
.5
1
1.5
0
1
2
3
weighted stomach dose (Gy)


Breast Cancer Dose Response
Upper concave
excess relative risk
0
1
2
3
4
0
1
2
3
4
5
weighted breast dose (Gy)

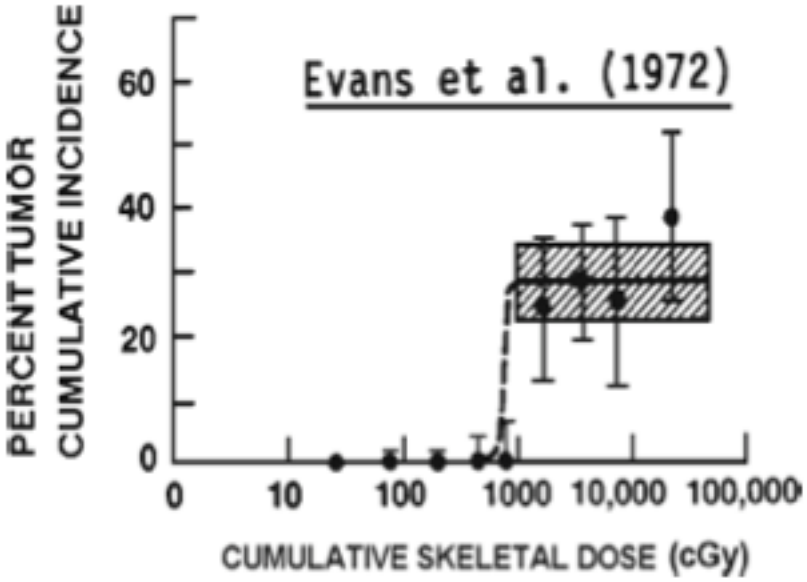

Other Solid Cancer Dose Response
Linear quadratic
excess relative risk
0
1
2
3
4
0
1
2
3
weighted colon dose (Gy)


Non-melanoma Skin Cancer Dose Response
Threshold
0
1
2
3
4
0
1
2
3
4
5
weighted skin dose (Gy)

An impressive threshold observed for bone tumor among radium dial painters



(Rowland,1978)



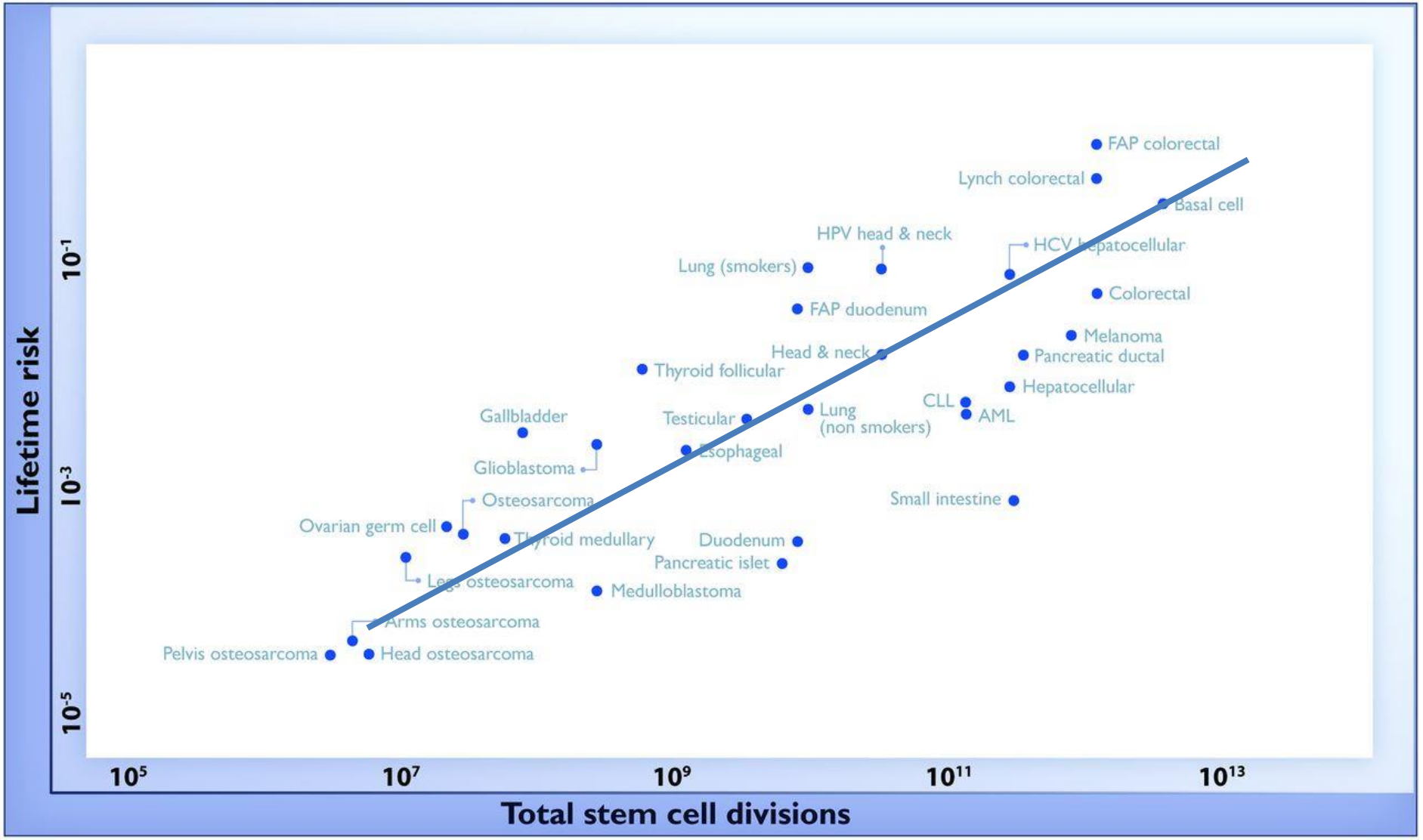
Threshold for the bone tumor by intake of radium was 1 Gy
A similar threshold was observed for thorotrast liver cancer

http://en.wikipedia.org/wiki/File:USRadiumGirls-Argonne1,ca1922-23-150dpi.jpg

The meaning of various dose responses

- The dose response of total cancer by low LET radiations follows a linear dose response
- However, the dose response relationship varies by cancer types
- The shape of the dose response is determined by the mechanism which varies by cancer types
- Nevertheless, a hypothesis of the linear dose response for the initial event of radiation induced mutation is a reasonable starting point on which the effects of various mechanisms are taken into account to explain a particular dose response curve for a specific cancer type
- Remember, the LNT model is just a coincidental outcome of the summation of the dose responses of various cancer types which involves a range of mechanisms operating at molecular, cellular and tissue levels

Tomasetti & Vogelstein, Science 2015



FAP = Familial Adenomatous Polyposis ◇ HCV = Hepatitis C virus ◇ HPV = Human papillomavirus ◇ CLL = Chronic lymphocytic leukemia ◇ AML = Acute myeloid leukemia

Tissue varies substantially for cancer rates

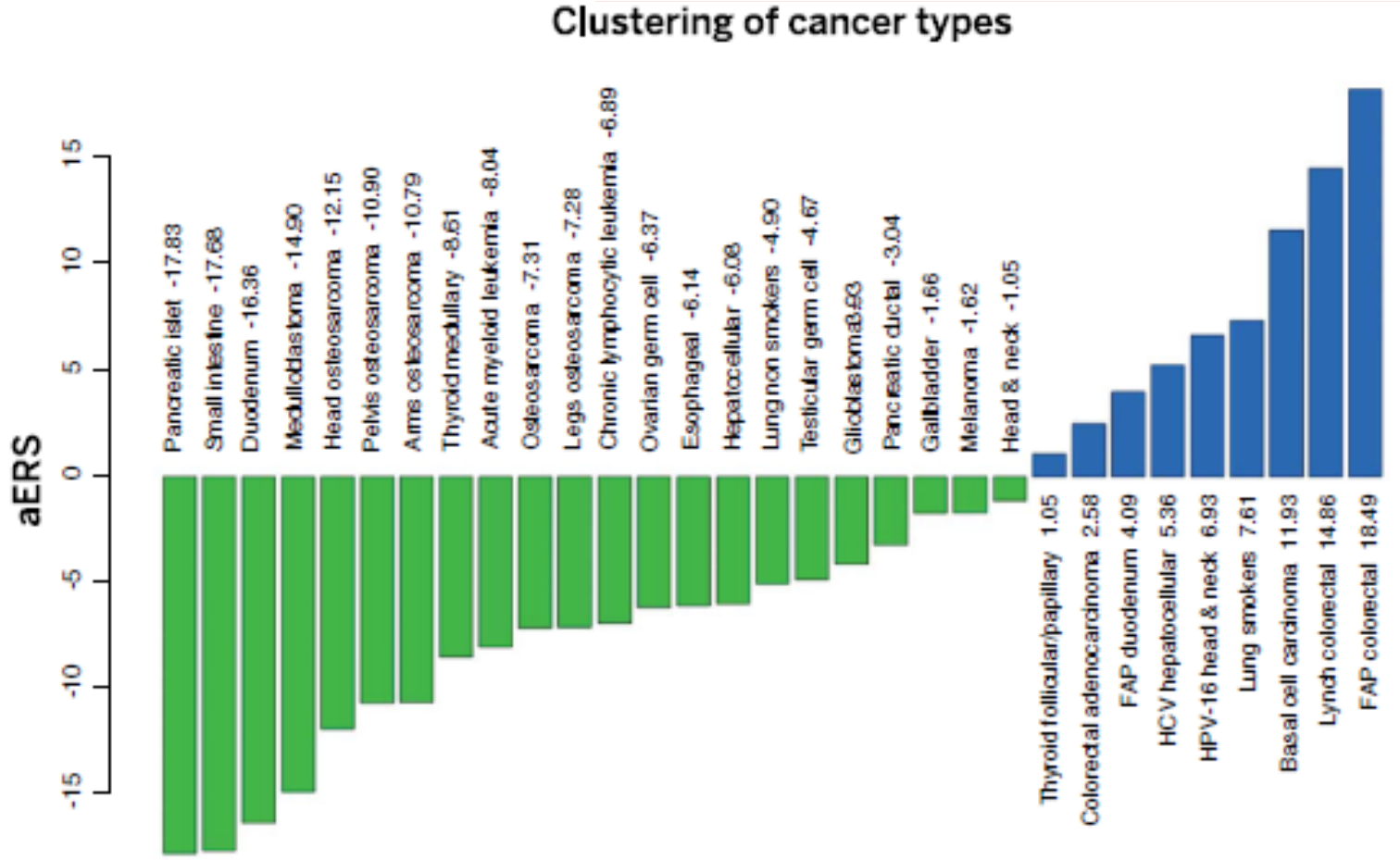


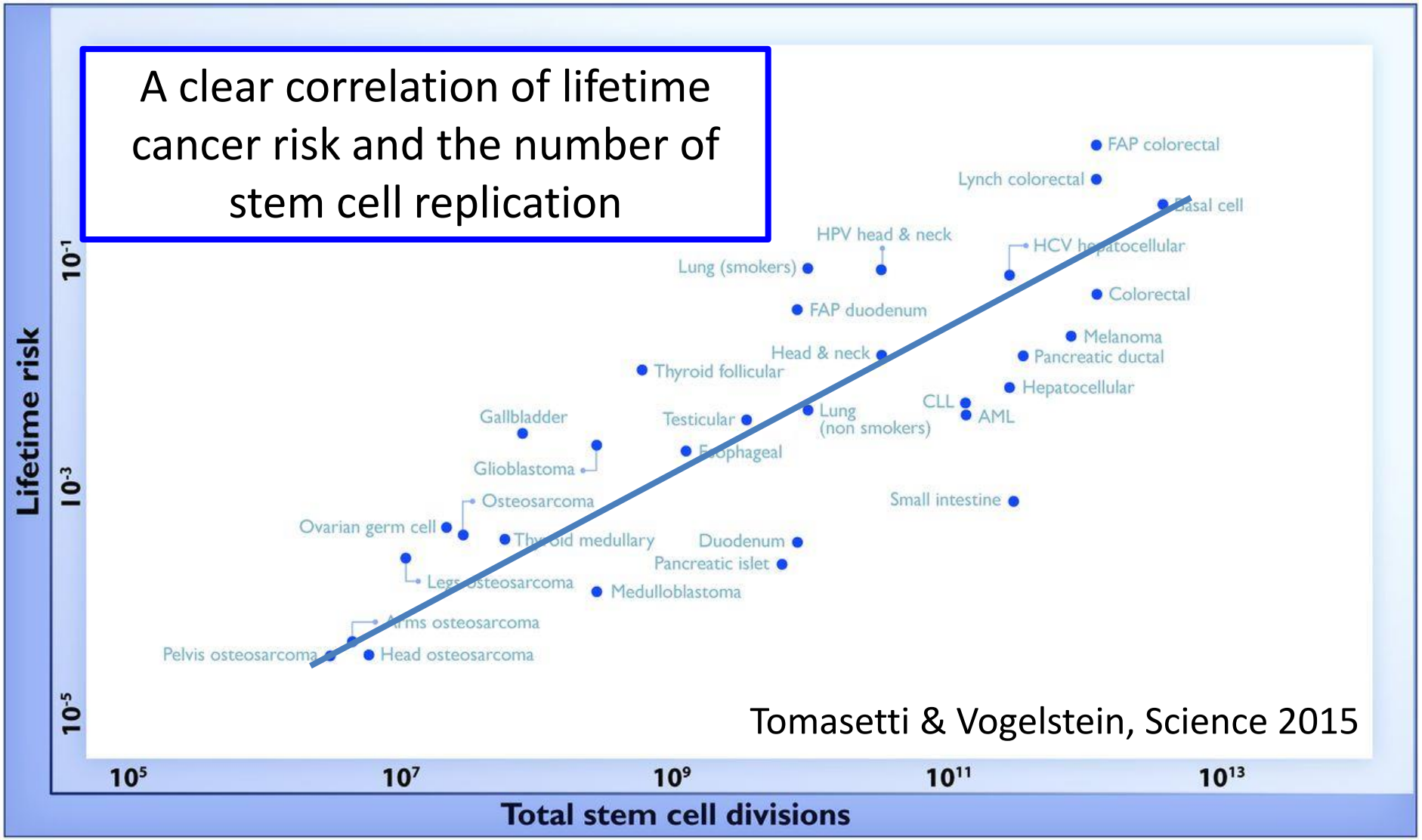
Fig. 2. Stochastic (replicative) factors versus environmental and inherited factors: R-tumor versus D-tumor classification. The adjusted ERS (aERS) is indicated next to the name of each cancer type. R-tumors (green) have negative aERS and appear to be mainly due to stochastic effects associated with DNA replication of the tissues' stem cells, whereas D-tumors (blue) have positive aERS. Importantly, although the aERS was calculated without any knowledge of the influence of environmental or inherited factors, tumors with high aERS proved to be precisely those known to be associated with these factors. For details of the derivation of aERS, see the supplementary materials.

2. Judgment on the use of the LNT model in RP

ICRP Pub 99 Executive Summary

(e) Current understanding of mechanisms and quantitative data on dose and time–dose relationships support a linear dose–response relationship at low doses (i.e. LNT).
(f) While existence of a low dose threshold does not seem unlikely for radiation-related cancers of certain tissues, and cannot be ruled out for all cancers as a group, the evidence as a whole does not favor the existence of a universal threshold, and there seems to be no particular reason to factor the possibility of a threshold into risk calculations for purposes of radiation protection. The LNT theory, combined with an uncertain DDREF for extrapolation of risk from high doses, remains a prudent basis for radiation protection at low doses and low dose rates.

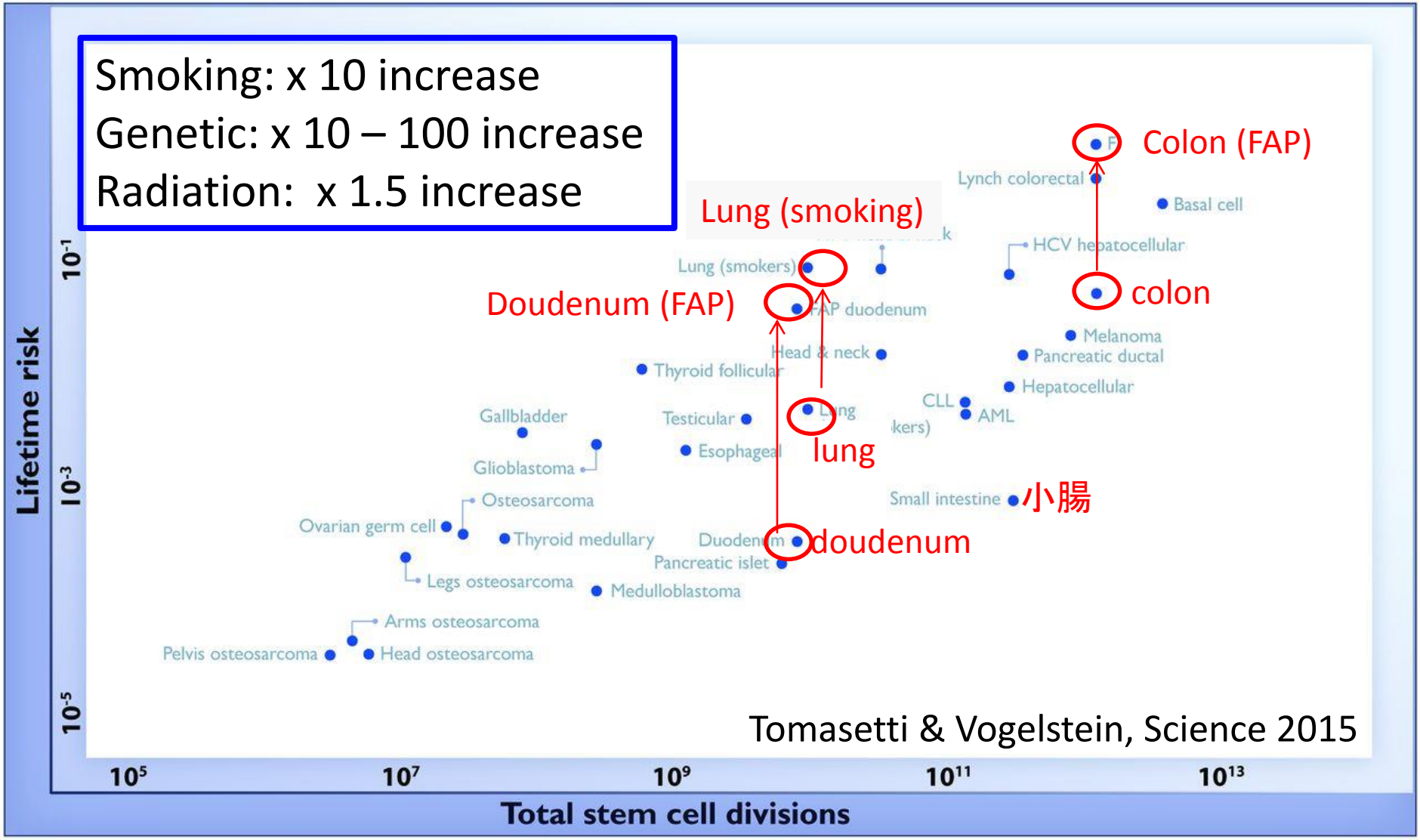
3. LNT as a measuring stick for the extent of the risk
How much is radiation risk compared with other factors?



Tomasetti & Vogelstein, Science 2015

FAP = Familial Adenomatous Polyposis ◇ HCV = Hepatitis C virus ◇ HPV = Human papillomavirus ◇ CLL = Chronic lymphocytic leukemia ◇ AML = Acute myeloid leukemia

Smoking: x 10 increase
Genetic: x 10 – 100 increase
Radiation: x 1.5 increase



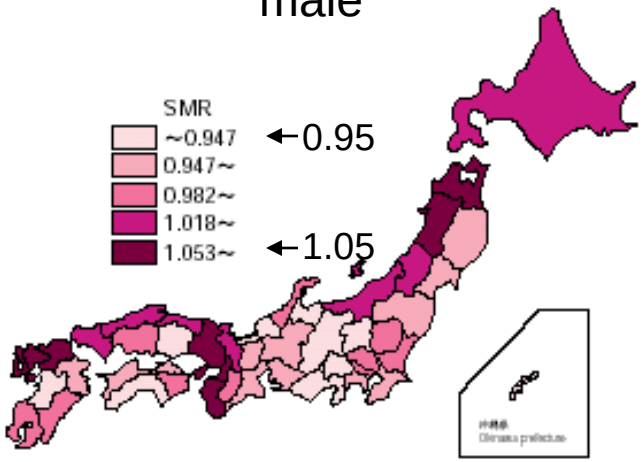
Tomasetti & Vogelstein, Science 2015

Life time cancer risk varies by 5 log and stem cell divisions by 8 log
Modification of the risk by genetics is in an order of 2 log, by smoking 1 log, by life style 1 log, and by radiation by < 1 log

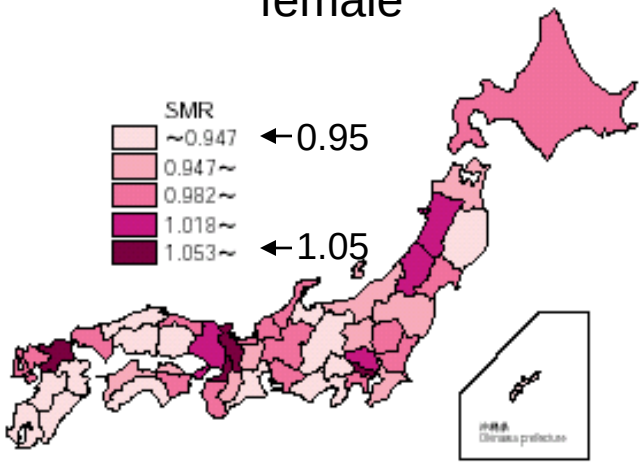
Prefectural variations of cancer mortality in Japan

total canc

male

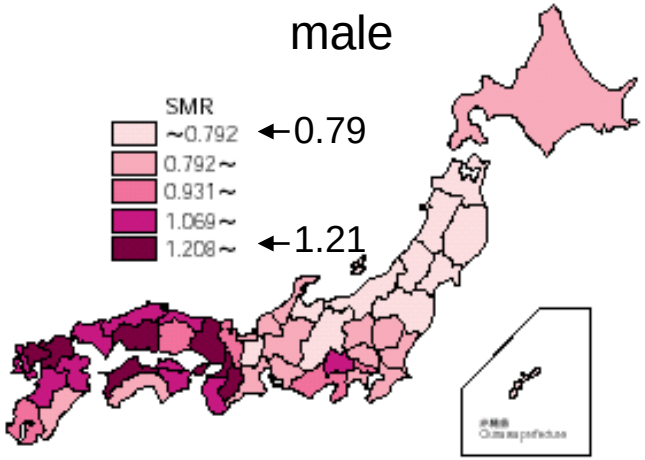


female

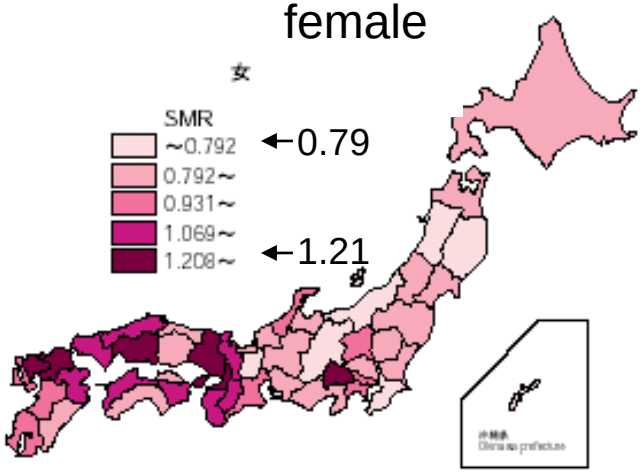


liver cancer

male



female

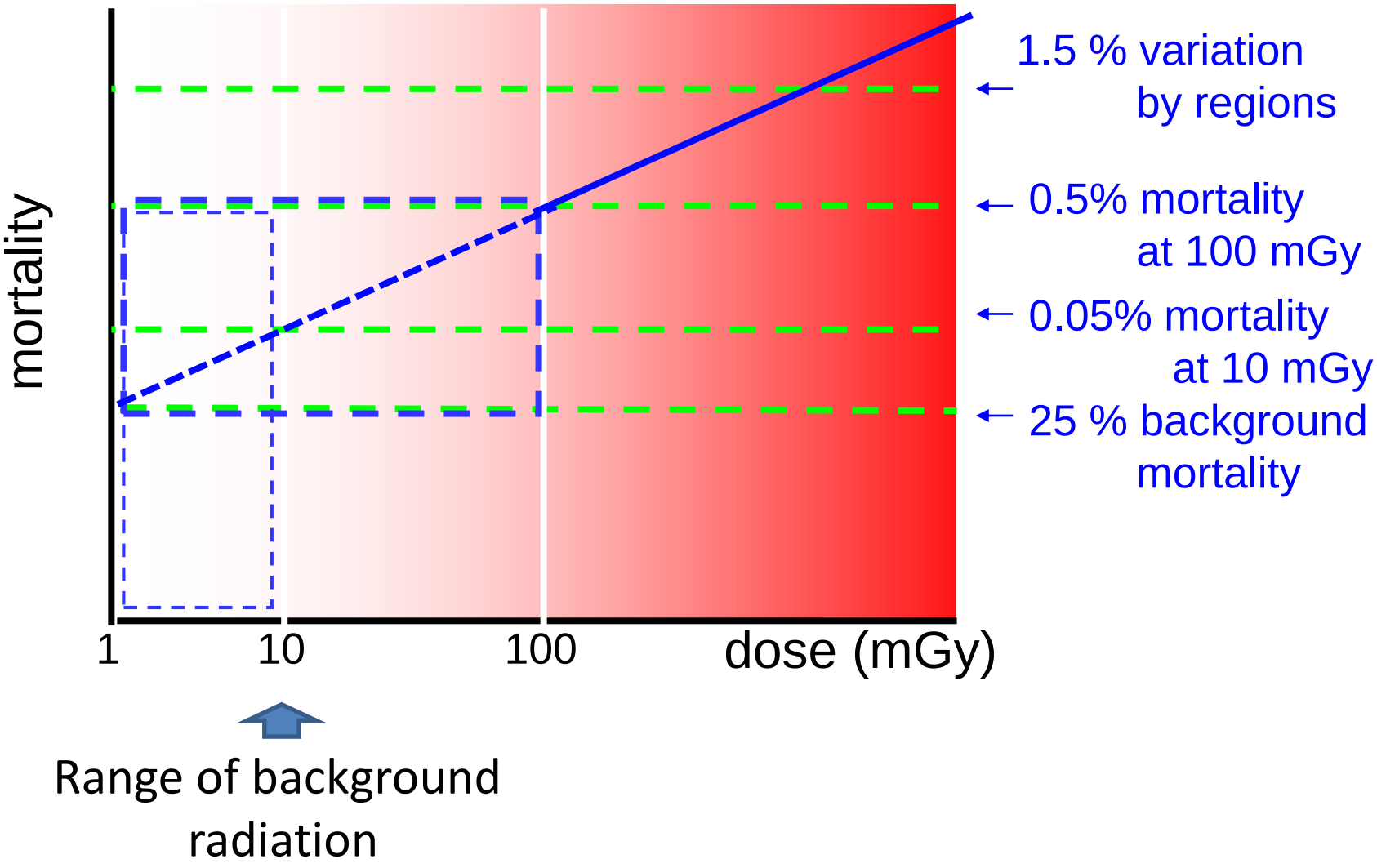


Regional variation is above 10%

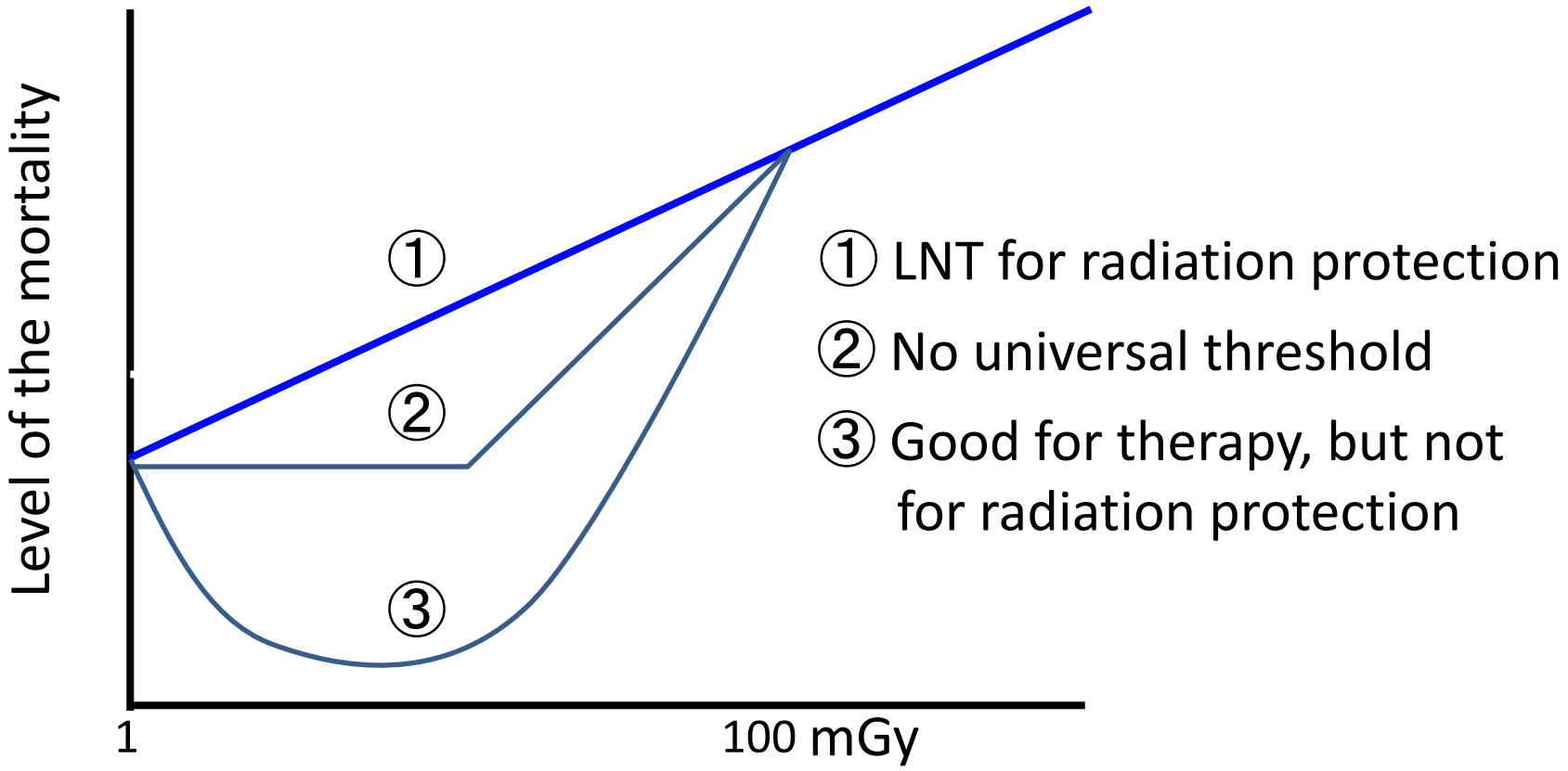
⇧

This comes from life style, prevalence of viral infection, environmental variation, and medicare

Summary of the radiation risk based on the LNT mode our surroundings

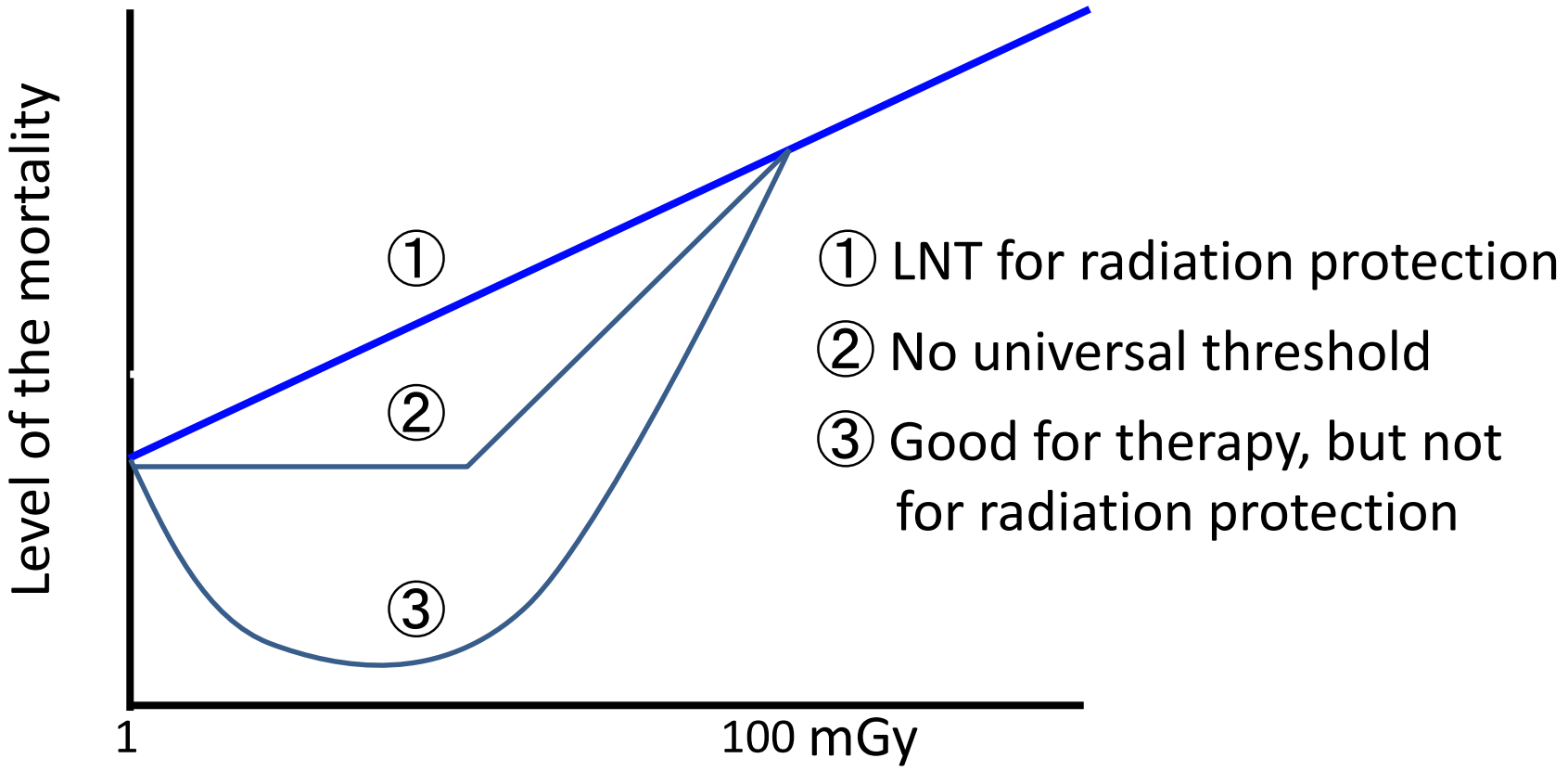


Practical reasons for the LNT model in RP



The use of the LNT model is a prudent judgment for RP
The threshold model is OK for a limited number of cancer
The hormetic model is OK for the therapy of sick people, but no good to be applied on the healthy population

Ethical bases of the LNT model in RP



The LNT model allows no line within the dose region for RP
The threshold model defines the region of safe and unsafe
Once a line is drawn, there starts discrimination of people by dose
ICRP hates to have discrimination of people by dose

5. How much of the LNT model be understood mechanistically?

A long story and please visit the upcoming ICRP Report