

Radiation Risk Estimates: Underlying Uncertainties



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- Estimates of cancer risk and other measures of the health detriment associated with radiation exposure are often presented as single numbers
 - *e.g. the ICRP Publication 60 estimate of 5 fatal cancers per 100 persons per Sv at low doses/low dose rates in a general population*
- However, there are various uncertainties associated with such risk estimates

- To highlight some key sources of uncertainty in radiation risk estimates
- In so doing, to distinguish between:
 - *uncertainties arising within an epidemiological study, and*
 - *uncertainties associated with extrapolation to other settings*
- To illustrate the impact of such uncertainties, through reference to recent analyses

Problems that can arise within epidemiological studies



- Bias
 - *systematic errors*
- Confounding
 - *variable(s) that may explain part or all of an association between exposure and disease*
- Low statistical power
 - *inability to detect small differences in risk*

Addressing potential problems within epidemiological studies



- Need well-designed studies
 - *cohort or case-control studies that collect data on exposures and health outcome for specific individuals are usually the most reliable*
- Care in data collection
 - *try to avoid variations in data quality between sub-sets of the study population, etc.*
- Assess statistical power in advance
 - *may consider subsequently combining data from similar studies (e.g. radon, nuclear workers)*

- Need to ensure that the estimation of exposures:
 - *is performed as accurately & precisely as possible, subject to the availability of resources*
 - *does not differ systematically between those with and those without the disease under study (differential errors)*
- In general, the impact of differential errors on epidemiological analyses cannot be quantified
- Also need to pay attention to *non-differential* errors

Sources of exposure data: contemporary records



*E.g. readings from dosimeters for radiation workers,
medical treatment records for irradiated patients*

- Objective approach
- Data usually not collected for epidemiological purposes
 - *review of dosimetry practices conducted as part of a recent international study of nuclear workers*
- Data not always specific to study subjects
 - *e.g. information from standard treatment protocols*

Sources of exposure data: interviews with study subjects



E.g. mailed questionnaire, in-person interview

- Specific to study subjects
 - *although surrogates sometimes used, e.g. if the disease is rapidly fatal*
- Possibility of recall bias in retrospective, but not prospective studies
 - *the ability to recall past events may be influenced by whether the person developed the disease under study*

Sources of exposure data: measurements for study subjects



E.g. blood sample, urine measurement, piece of tooth

- Objective approach
- Ethics - *require informed consent*
- Timing - *how long after exposure can reliable measurements be made?*
 - *impact of disease treatment on measurements made post-diagnosis?*
- Logistical/feasibility issues
 - *costs of making large numbers of measurements?*
 - *can people be traced many years after exposure?*

Sources of exposure data: environmental measurements



E.g. neutron activation measurements in Hiroshima, caesium measurements around Chernobyl, radon concentrations in homes

- Representative for members of the study population?
- Timing
 - *how long after exposure can reliable measurements be made?*
 - *impact of events between exposure and measurement (e.g. changes to dwellings in the case of radon)?*

Impact of “shared” errors in exposure assessment



- Suppose that the true exposure is randomly distributed about the value used in epidemiological analyses
 - *e.g. missing data on radon in homes are replaced by the mean value for homes in the same area*
- Such “shared” or “Berkson” errors do not tend to lead to notable bias in estimates of trends in risk with level of exposure
 - *but these errors do lead to wider confidence intervals*

Impact of “unshared” errors in exposure assessment



- Suppose that the exposure value used in epidemiological analyses is randomly distributed about the true exposure
 - *e.g. repeat measurements of radon in the same home can show notable variation*
- Such “unshared” or “classical measurement” errors bias the estimate of any trend in risk with exposure towards zero
 - *if the exposure estimates were complete ‘noise’, then no trend in risk would be expected*
 - *these errors also lead to wider confidence intervals*

Example of the impact of “unshared” errors in exposure assessment

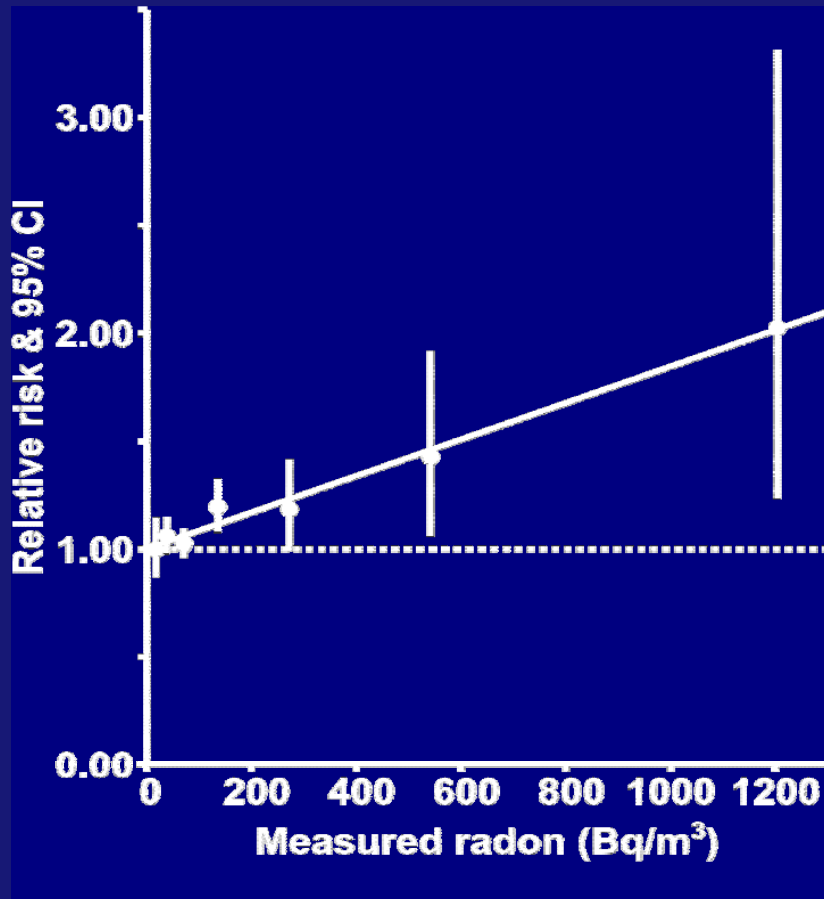


- Combined analysis of data from 13 studies of indoor radon and lung cancer in Europe (Darby *et al*, *Br Med J*, **330**, 223-6, 2005)
- Measurements of radon conducted in the same home in different years indicate coefficients of variation between 17% and 51%, depending on country
- Adjustments can be made in epidemiological analyses by replacing the measured radon value by an estimate of the “usual” (long-term) value

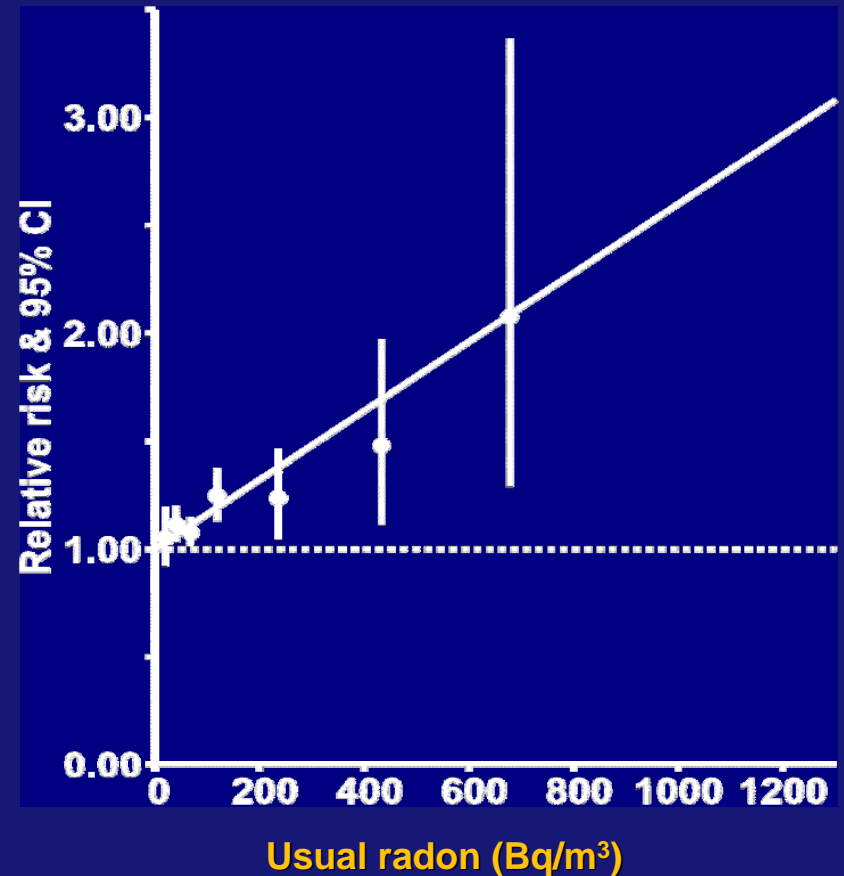
Average measured and usual radon concentrations by categories of measured radon concentration

Measured radon (Bq m ⁻³)	No of individuals	Mean (Bq/m ³)	
		Measured values	Estimated usual values
<25	2040	17	21
25-49	5904	39	42
50-99	7651	71	69
100-199	3543	136	119
200-399	1370	273	236
400-799	667	542	433
800+	181	1204	678

Relative risk of lung cancer according to measured and usual radon concentration



Increase in risk per 100
Bq/m³ = 8% (95% CI 3,16)



Increase in risk per 100
Bq/m³ = 16% (95% CI 5,31)

Extrapolation of findings from epidemiological studies

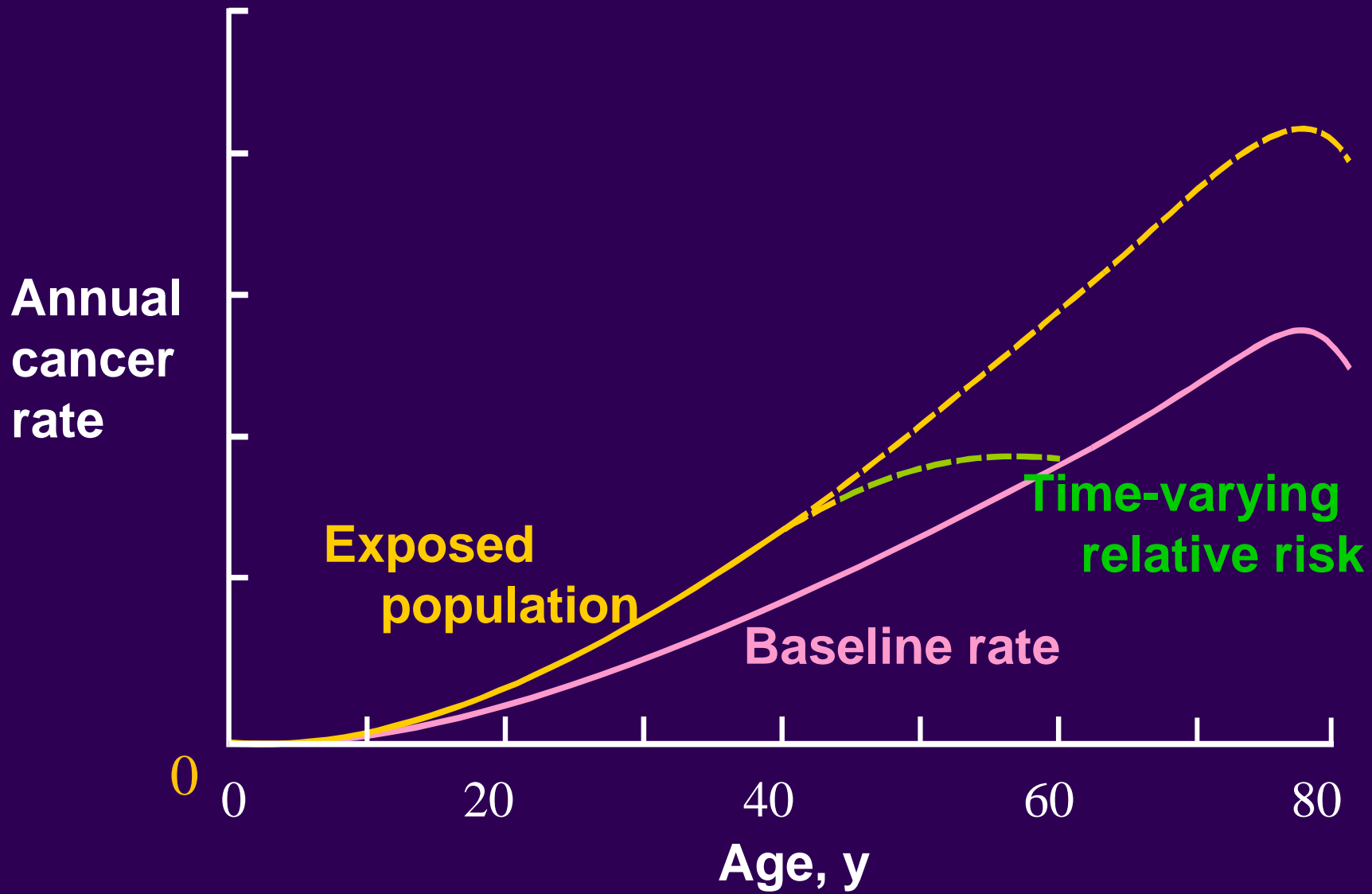


- Studies in radiation epidemiology often provide little or no information on cancer risks:
 - *many years after exposure*
 - *in populations in other countries*
 - *at low doses and/or for protracted exposures*
- Need models to:
 - *project risks over a lifetime*
 - *transfer risks to other populations*
 - *extrapolate to low doses and/or protracted*

ex

posures

UNSCEAR (1994) risk projection models



Estimated fatal lifetime cancer risk for an acute dose of 1 Sv to a Japanese population



Projection

model:

Solid cancers

Leukaemia

Relative risk

Male

Female

Male

Female

varies by:

Age-at-exposure

9.5%

12.9%

Attained-age

6.2%

8.5%

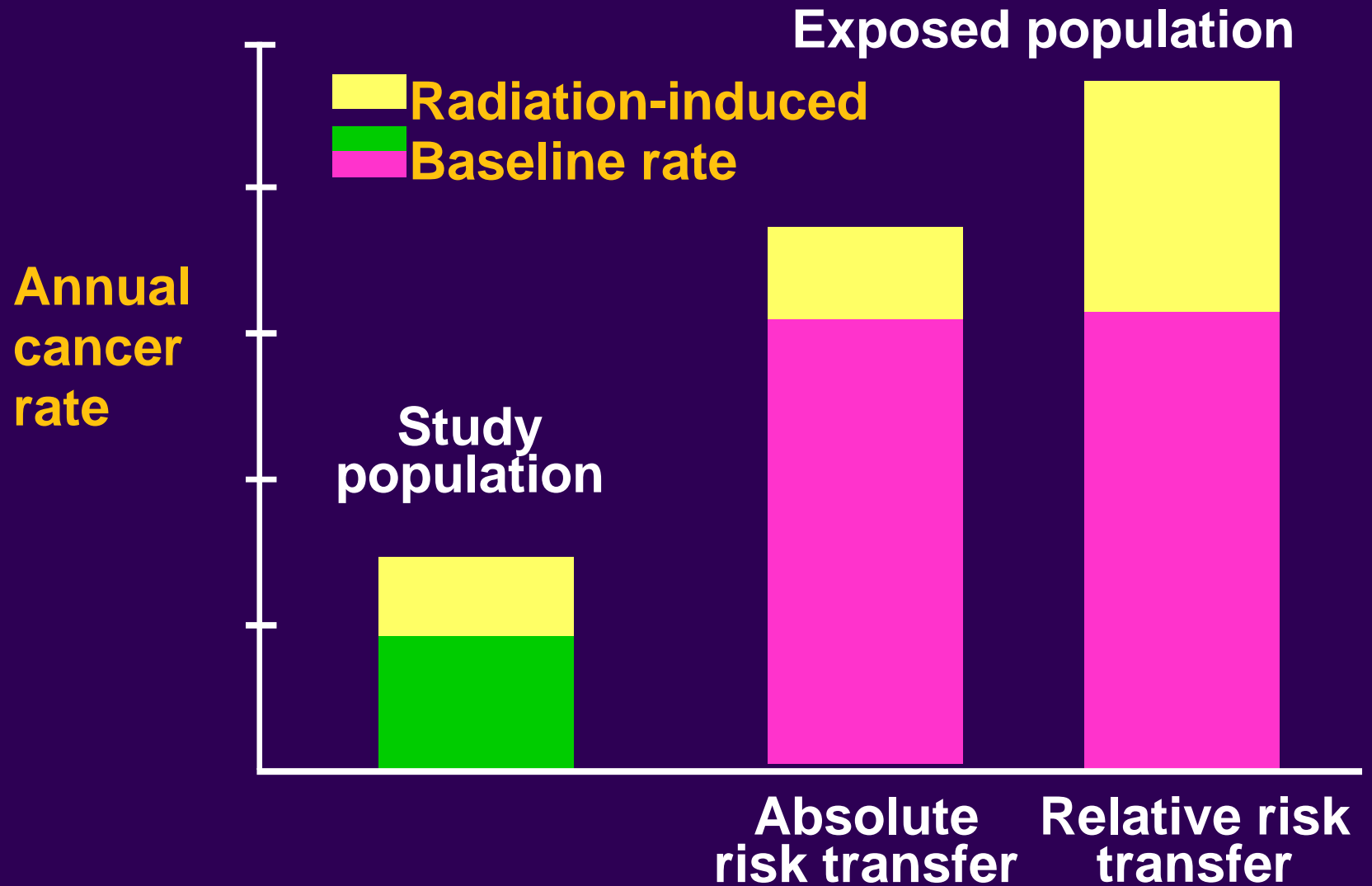
Age & time

1.0%

0.8%

(UNSCEAR, 2000)

Transferring cancer risks between populations



Effect of baseline rates on fatal lifetime cancer risk estimates using a relative risk transfer



<i>(UNSCEAR, 2000)</i>	<i>Males</i>	<i>Males</i>	<i>Females</i>	<i>Both</i>
	Stomach	Lung	Breast	All sites
China	0.7 %	0.5 %	0.6 %	7 %
Japan	1.0 %	1.8 %	1.3 %	9 %
Puerto Rico	0.5 %	0.2 %	2.2 %	7.5%
UK	0.3 %	3.6 %	5.8 %	12 %
USA	0.1 %	3.1 %	5.2 %	12 %

(Based on an acute dose of 1 Sv received at age 30 y, and using the UNSCEAR attained-age risk projection model)

- Much less variation between countries using an

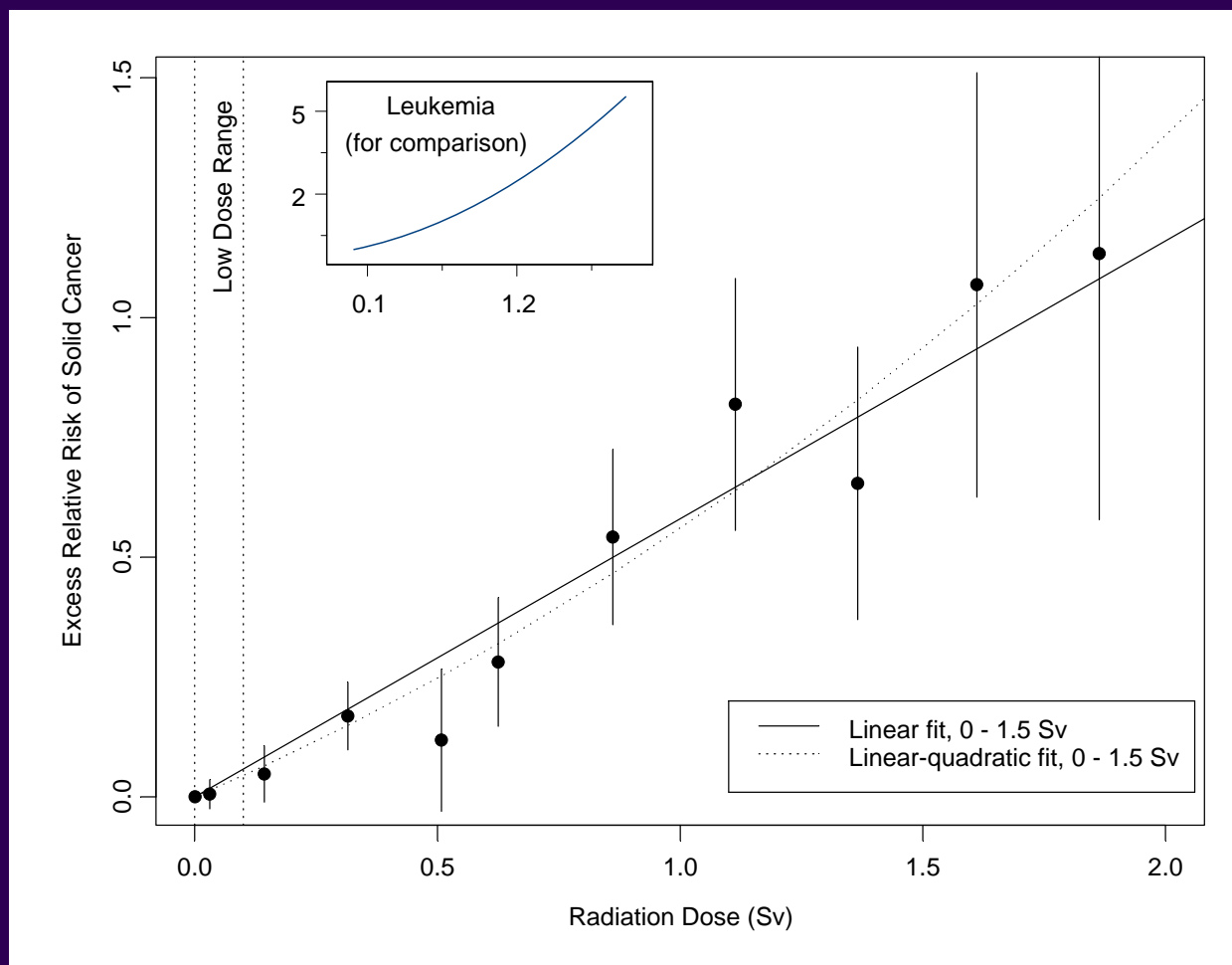
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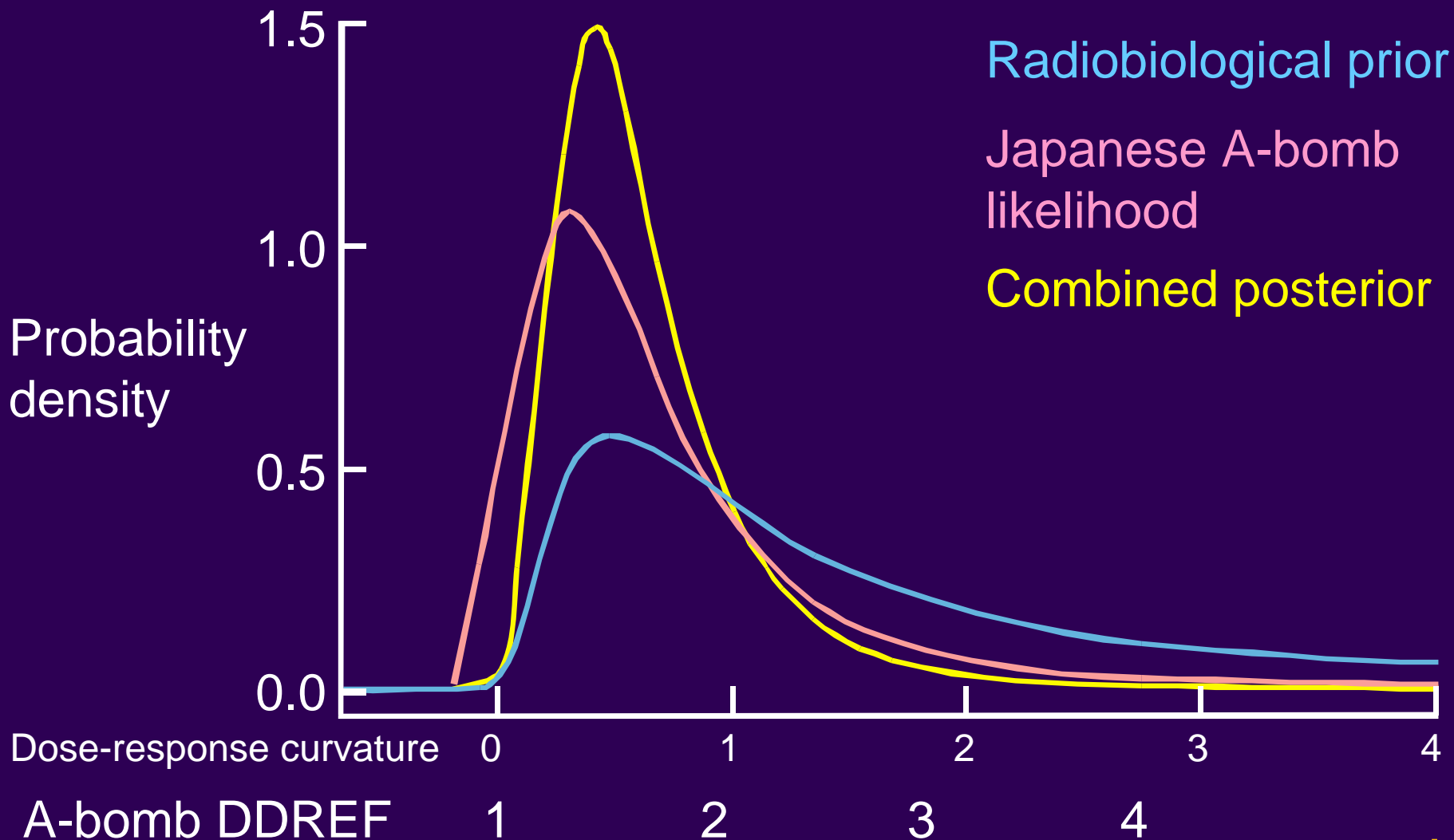
absolute risk transfer

- Use of Dose and Dose Rate Effectiveness Factor (DDREF)
 - *extrapolation of findings from high doses to low doses by fitting a dose-response model*
 - *extrapolation of findings from acute exposure to protracted exposures by applying a factor derived from radiobiological considerations*
- Study populations with such exposures directly
 - *e.g. radiation workers*

Excess relative risk of solid cancers for the Japanese A-bomb survivors



BEIR VII Bayesian analysis of DDREF for solid cancers



BEIR VII lifetime attributable risk per 100,000 persons per 0.1 Gy in USA (95% subjective confidence intervals)*



	Solid Cancers		Leukaemia	
	Male	Female	Male	Female
Excess cases incl. non fatal cases	800 (400-1600)	1300 (690-2500)	100 (30-300)	70 (20-250)
Background cases	45,000	36,900	830	590
Excess deaths	410 (200-830)	610 (300-1200)	70 (20-220)	50 (10-190)
Background deaths	22,100	17,500	710	530

* *Confidence intervals reflect statistical variation in Japanese A-bomb data, uncertainty in DDREF and uncertainty in transport of risks from Japan to USA*

Some means of reducing uncertainties in radiation risk estimates



- Projection over time
 - *continued follow-up of informative groups*
- Effects of dose and dose rate
 - *dose-response analyses using updated data for Japanese A-bomb survivors, etc*
 - *studies of groups with low and/or protracted exposures*
- Transfer between populations
 - *combined analyses of informative studies, e.g. A-bomb survivors and medically-exposed groups*