Ionizing Radiation and Cancer Risk

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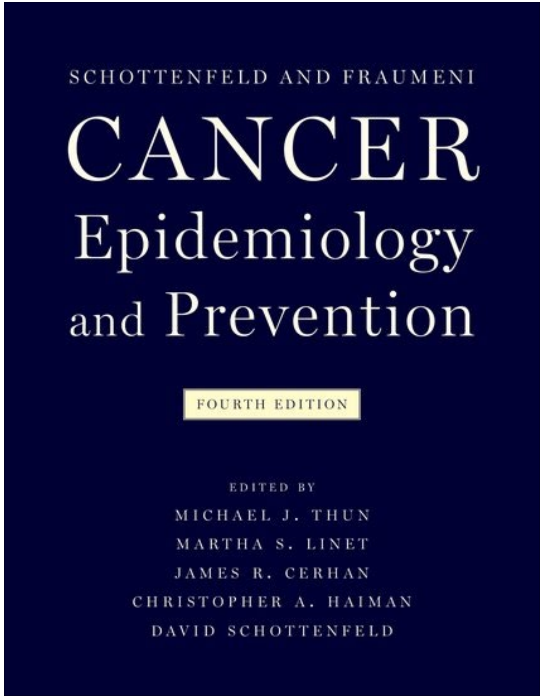
DCEG Radiation Epidemiology and Dosimetry Course 2019

Objectives

- Provide a broad overview of the current understanding of ionizing radiation and cancer risk from epidemiological studies
  - Features of high-quality studies for providing evidence

Key Reference



Chapter 13: Ionizing Radiation

Amy Berrington de González
André Bouville
Preetha Rajaraman
Mary Schubauer-Berigan

Introduction and Key Concepts

Ionizing radiation

Universal carcinogen

- Can cause cancer in *most* organs
- Can cause cancer at any age (including *in utero*)

Variation in the magnitude of risk

Large risks from childhood exposure

- Leukemia, breast, thyroid, CNS tumors

UNSCEAR 2006, BEIR VII 2006

Established carcinogen… fundamental questions

- Magnitude of risk at very low doses
- Risk from different types of radiation
- Modifiers of risk
  Joint effects
- Impact of rate (timing) of exposure
- Mechanisms of radiation-induced carcinogenesis
- Risk from emerging medical technologies

… and more!

Key concepts related to the exposure

Types of radiation

Modes and patterns of exposure

Sources of exposure

Types of Ionizing Radiation

- All types can cause cancer in humans
  - ➢ *sufficient evidence - IARC Group 1*
- Varying energies and ability to penetrate
  - ➢ potential variation in cancer risk

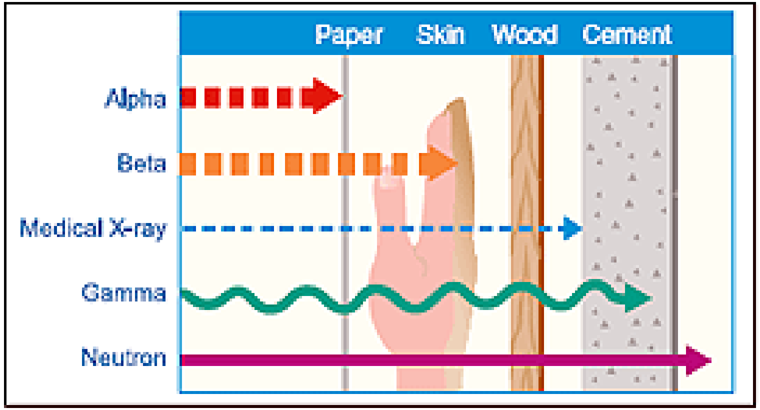


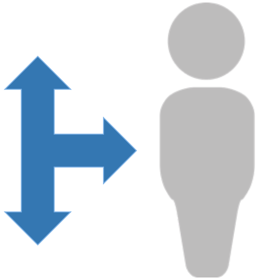
Image source: http://www.nrc.gov/about-nrc/radiation/health-effects/radiation-basics.html

IARC Monograph 100D 2012

Internal vs external exposure

- Internal – Source within the body
  - ➢ Ingestion, inhalation, injection of radioactive particles

- External – Source outside the body
  - ➢ Proximity to photon-emitting source

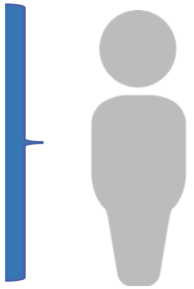


Rate of exposure

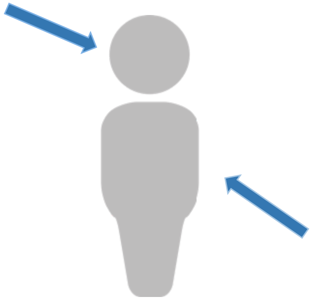
Type	Timing
Acute	Delivered within seconds
Fractionated	Multiple acute or short-term exposures delivered at intervals
Protracted	• Continuous, over relatively long time • Fairly constant rate

Full- or partial-body

- Full-body – (relatively) uniform exposure over the body



- Partial-body – only part of the body exposed



Patterns of exposure: Examples

Exposure/Study	Description
Atomic bomb survivors	• External • Acute • Whole-body
Diagnostic x-rays	• External • Fractionated • Partial-body
I^{131} from fallout	• Internal • Protracted • Largest exposure to thyroid, smaller exposures elsewhere

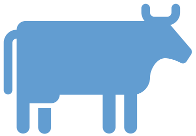
Units of exposure

Absorbed dose
- radiation energy absorbed per unit mass of organ or tissue
- Unit: Gray (Gy)
- Primary unit for epidemiologic studies

Equivalent dose
- mean absorbed dose to organ/tissue weighted by type and energy of radiation
- Unit: Sievert (Sv)

Effective dose
- sum of absorbed dose to organs multiplied by radiation and tissue weighting factors
- Unit: Sievert (Sv)
- Primary unit for regulatory purposes

Sources of exposure



Environmental

Medical

Occupational

Main sources of exposure – general population

- Medical (diagnostic)
- Low-level environmental

- Historic
  - Atomic bombs in Japan
  - Chernobyl accident
  - Therapeutic radiation for benign conditions

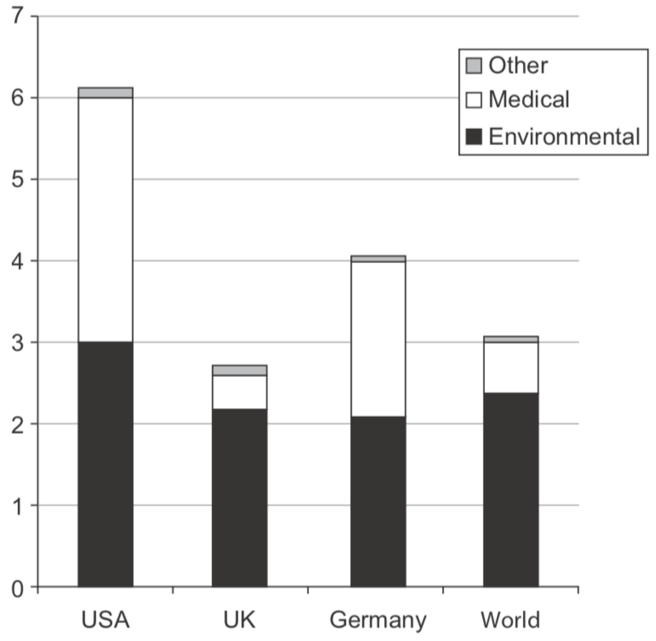


Figure 13–1. Comparison of current estimated annual per capita radiation exposure (mSv) for countries with a similar health-care level.

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Environmental Exposures

Natural background radiation	Man-made environmental exposures	Other
• Radon • Cosmic radiation • Radionuclides in food and earth	• Atomic bombs, nuclear weapons testing • Nuclear accidents	• Industrial activities, security inspection systems, medical facilities, educational/research institutions

Medical Exposures

- Primarily fractionated, partial-body

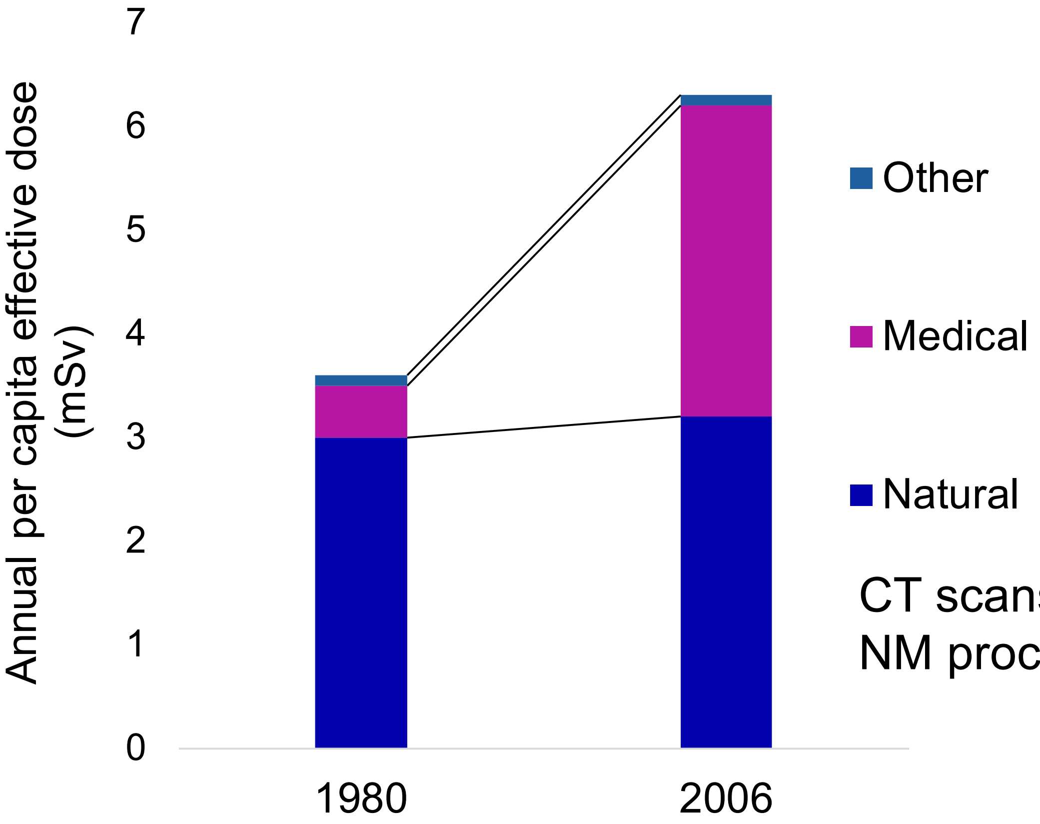
Diagnostic
X-rays, CT scans
Nuclear Medicine

Interventional Radiology

Radiotherapy

Images: https://lab.research.sickkids.ca/qbict/what-is-a-ct-scan/
https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam

Increasing medical radiation exposure in the U.S.



CT scans: 3 to 80 million
NM procedures: 6 to 18 million

NCRP Report 160 2009

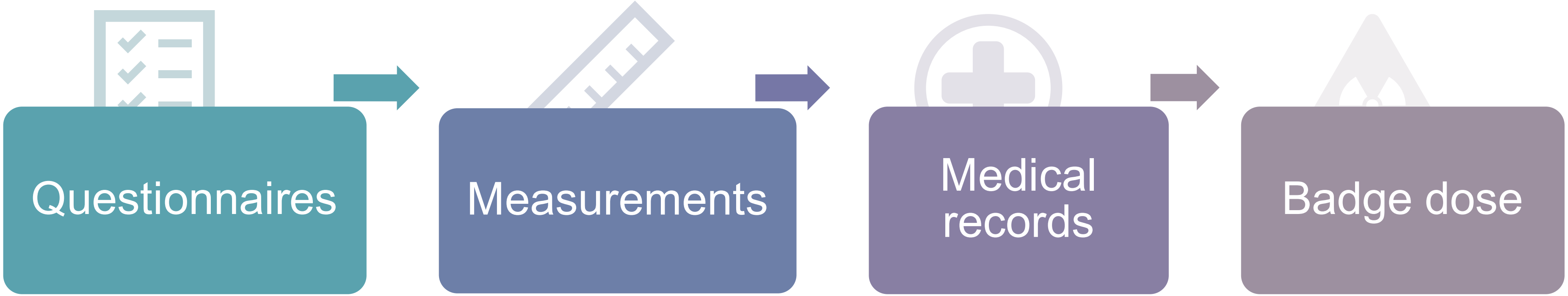
Occupational Exposures

Nuclear workers | Miners | Medical workers

- Trend towards decreasing exposures
- Exceptions - Interventional radiology physicians & nuclear medicine radiologic technologists

Exposure assessment and study design

Exposure assessment: Common sources



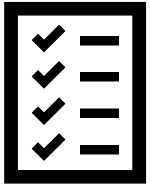
Exposure assessment: Considerations

Strength - Dose can be measured

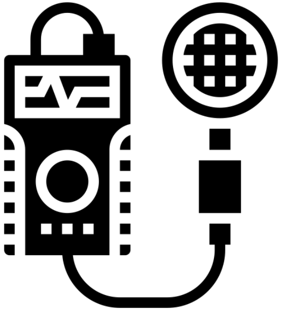
Challenges – quality, detail varies across studies

- From “exposed” vs. “unexposed” to individual organ dose estimates
- (Often) rely on historical information to reconstruct dose long after exposure
- (Often) need multiple sources of information

Sources and considerations: Environmental studies

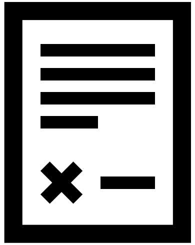


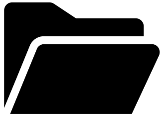
- Questionnaires:
  - level of detail
  - timing relative to exposure
- Measurements:
  - number of measurements
  - timing relative to exposure
  - coverage
- Challenge: Uncontrolled, unexpected exposure

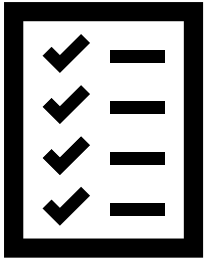


Created by Eucalyp
from Noun Project

Sources and considerations: Medical studies

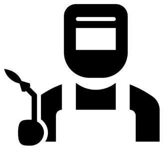


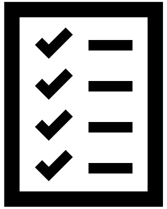




- Treatment records:
  - detail about patient and treatment
  - accuracy of treatment parameters
  - availability of treatment-planning images
- Medical records from diagnostic procedures:
  - detail about patient
  - types of machines
  - settings - individual vs typical protocols
- Questionnaires: Complement records (or be only source)

Sources and considerations: Occupational studies





- Badge dose measurements
  - Usage
  - Location, limit of detection
  - Not used < 1960s
- Bioassay measurements (internal exposures)
  - Coverage
- Questionnaires on work history
  - Level of detail

Quality of individual doses for epidemiologic studies

Lack human-based measurements

Sparse data

Based on retrospective interviews

Human-based measurements

- Reliable
- Available for all participants
- Representative of organ of interest

Lowest → Highest

Features of high-quality studies

Individual level data	Availability of covariate data	Exposure and outcome independent, reliable
Organ doses - estimate dose-response relation	Incident vs mortality data	Long-term follow-up
Completeness of follow-up	Appropriate comparison groups	Adequate statistical power

UNSCEAR 2000; BEIR VII 2006

Exposure collected independently of outcome ★

Follow-up ……………………………………………………

Prospective cohort

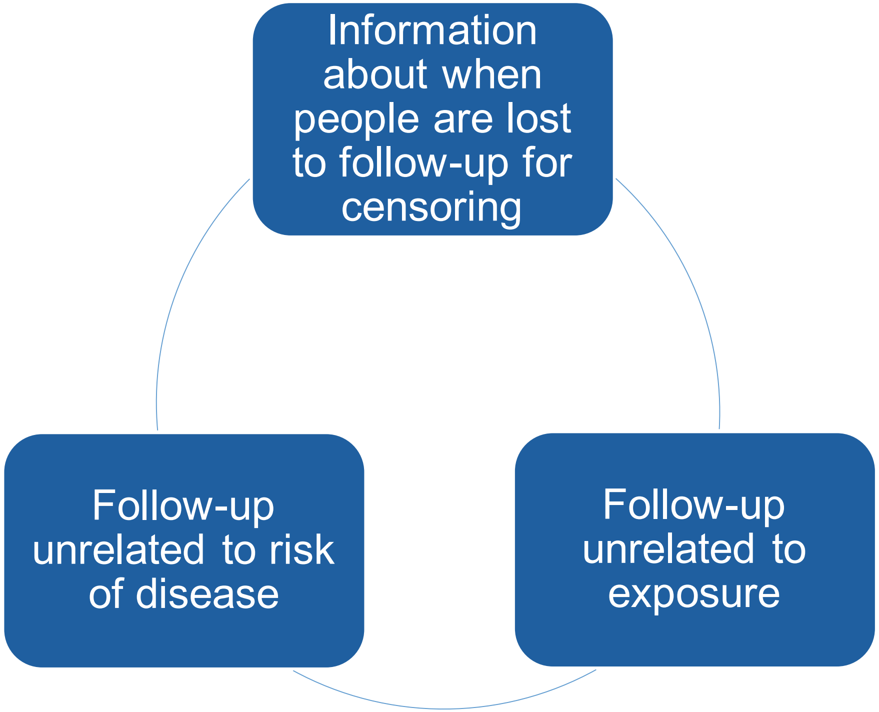
- Select participants
- Data collection designed specifically for study
- Requires long follow-up
    - Challenging given long latency radiation and solid cancers

Retrospective cohort

- Select participants
- Use existing records, measurements, etc… to determine exposure and outcome status

★ Possible from both prospective and retrospective cohort designs

Completeness of follow-up



- Improper censoring - immortal person-time
- Completeness of follow-up related to exposure or risk of disease *but not both*
  - underestimate rates, cumulative incidence but internal comparison can still be valid
- Completeness of follow-up related to both exposure and outcome
  - Bias risk estimates

Appropriate comparison groups

Internal comparison

- Dose-response analyses
- Improve comparability of groups although not immune to bias

Compare exposed versus unexposed

- Challenging due to underlying differences in these groups
- “Healthy worker effect”, confounding by indication

Incidence vs mortality

Mortality

- Often have national data
- Under-reporting of cancer on death certificates
- Less informative for non-fatal outcomes
- Reflects factors related to survival as well as risk

Incidence

- Ideal: population-based registries
- Often rely on self-report with subsequent validation
- Informative for non-fatal outcomes
- More informative for evaluating latency period

Life Span Study (LSS) of Japanese Atomic Bomb Survivors

“Gold Standard” of radiation epidemiology

- Large, unselected population
- Males and females
- Wide range of age at exposure
- Long-term, comprehensive follow-up
- Well-characterized doses across range

Acute, whole body exposures

Foundation of radiation protection standards

7 nested case-control studies of second GI cancers

- Nested within registry-based cohorts
  - Denmark, Finland, Iowa, Netherlands, Norway, Ontario, Sweden
- Detailed treatment data from medical records
- Dose reconstruction from RT records
- Dose-response relationship
- Joint effects – radiation and chemotherapy

First cancer	Second Cancer: Esophagus	Second Cancer: Stomach	Second Cancer: Pancreas
Breast cancer	X		
Hodgkin lymphoma	X	X	X
Testicular cancer		X	X
Cervical cancer		X	

VOLUME 31 · NUMBER 27 · SEPTEMBER 20 2013
JOURNAL OF CLINICAL ONCOLOGY — ORIGINAL REPORT

Stomach Cancer Risk After Treatment for Hodgkin Lymphoma

Lindsay M. Morton, Graça M. Dores, Rochelle E. Curtis, Charles F. Lynch, Marilyn Stovall, Per Hall, Ethel S. Gilbert, David C. Hodgson, Hans H. Storm, Tom Børge Johannesen, Susan A. Smith, Rita E. Weathers, Michael Andersson, Sophie D. Fossa, Michael Hauptmann, Eric J. Holowaty, Heikki Joensuu, Magnus Kaijser, Ruth A. Kleinerman, Frøydis Langmark, Eero Pukkala, Leila Vaalavirta, Alexandra W. van den Belt-Dusebout, Joseph F. Fraumeni Jr, Lois B. Travis, Berthe M. Aleman, and Flora E. van Leeuwen

BJC
British Journal of Cancer (2016) 115, 901–908 | doi: 10.1038/bjc.2016.27
Keywords: pancreatic cancer; radiotherapy; testicular cancer; chemotherapy; logistic regression

Increased pancreatic cancer risk following radiotherapy for testicular cancer

Michael Hauptmann[*,1], Tom Børge Johannesen [2], Ethel S Gilbert[3], Marilyn Stovall[4], Flora E van Leeuwen[1], Preetha Rajaraman[3], Susan A Smith[4], Rita E Weathers[4], Berthe MP Aleman[5], Michael Andersson[6], Rochelle E Curtis[3], Graça M Dores[3], Joseph F Fraumeni Jr[3], Per Hall[7,8], Eric J Holowaty[9], Heikki Joensuu[10], Magnus Kaijser[7], Ruth A Kleinerman[3], Frøydis Langmark[2], Charles F Lynch[11], Eero Pukkala[12,13], Hans H Storm[14], Leila Vaalavirta[10], Alexandra W van den Belt-Dusebout[1], Lindsay M Morton[3], Sophie D Fossa[15] and Lois B Travis[16]

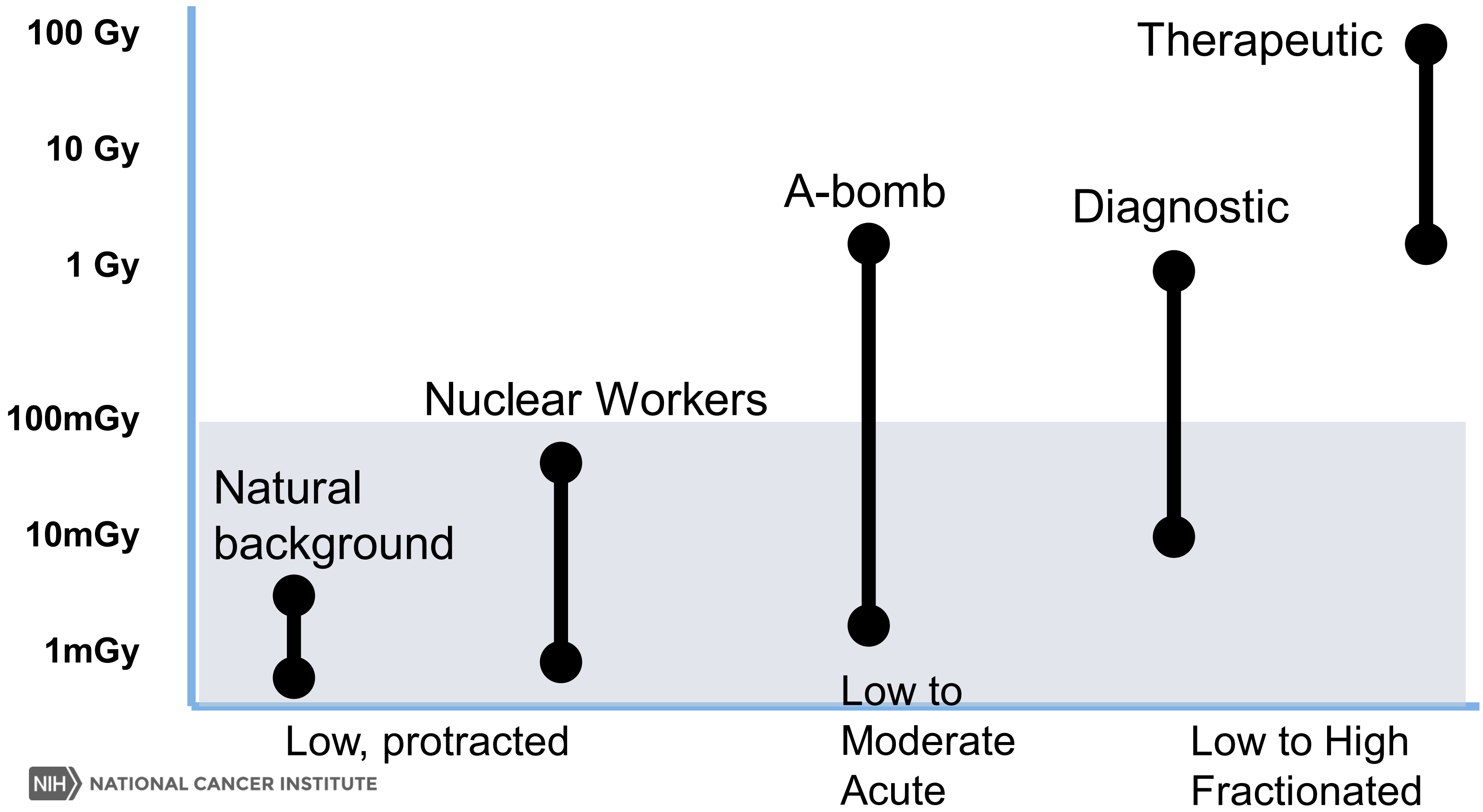
Thyroid Cancer in Children in Ukraine

- Key source of information about long-term risk of thyroid cancer from I-131
  - One of several studies in exposed areas
- Cohort of 12,514 children screened regularly for thyroid cancer
- Resident in 3 contaminated areas
- Dose estimates:
  - individual radioactivity measures
  - dietary/lifestyle patterns reported on questionnaires
  - environmental measurements

Brenner et al. *Environ Health Perspect* 2011

Cancer risks

Cancer risks observed



Classification of radiation-related cancers

"Yes"

Significant dose-response relationship from robust epi studies

"Possibly"

Some evidence for dose-response relationship

Questions about biases, potential confounding

"Unclear"

Lack of adequately powered, high-quality studies

Inconsistent findings across studies

Berrington de González et al. Cancer Epidemiology and Prevention

Cancers caused by radiation

Yes	Bladder, Breast, Lung, Leukemia (non-CLL), Brain/CNS, Ovary, Thyroid, Colon, Esophagus, Oral (salivary gland), Stomach, Liver, NMSC, Bone, Soft tissue, Pancreas, Rectum
Possibly	Endometrial, Multiple Myeloma, CLL
Unclear	Non-Hodgkin Lymphoma, Prostate, Renal cell, Cervix, Gallbladder, Melanoma

Berrington de González et al. Cancer Epidemiology and Prevention

“Possibly related”

Uterine corpus (endometrial)

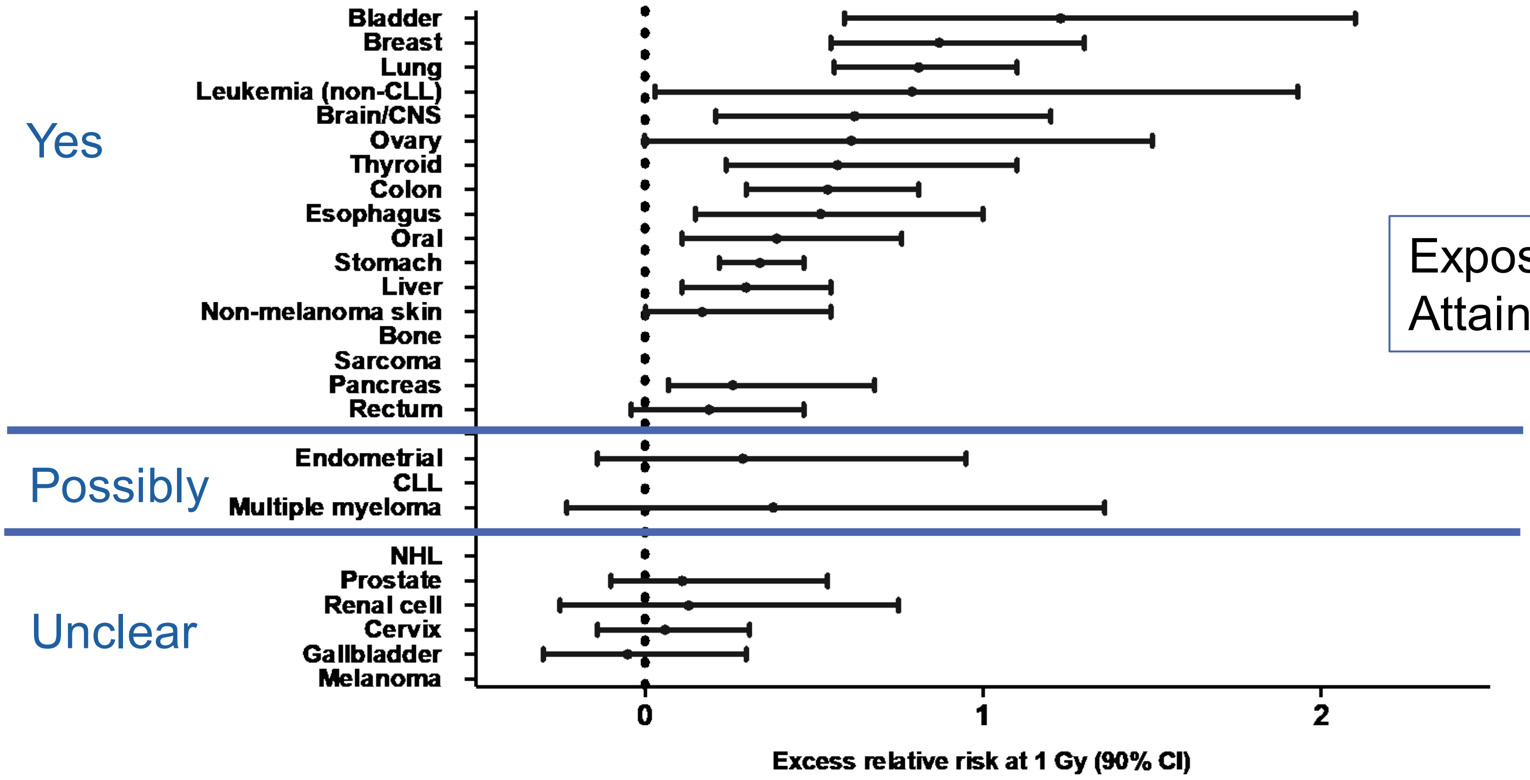
- Increased risk for certain ages at exposure?
- ERR greater when account for probability of hysterectomy

CLL

- Long thought to be unrelated to radiation
- Excess risk observed among Chernobyl clean-up workers

Utada et al. *JNCI Cancer Spec* 2018
Zablotska et al. *Environ Health Perspect*. 2013

Excess relative risks appear to vary by site



Exposure: age 30
Attained age: 70

Berrington de González et al. Cancer Epidemiology and Prevention
Preston et al., *Rad Res* 2007

NIH NATIONAL CANCER INSTITUTE

Questions

Why might magnitude of risk vary?

What can this variation teach us in terms of mechanisms?

What can we learn from sites with no apparent association?

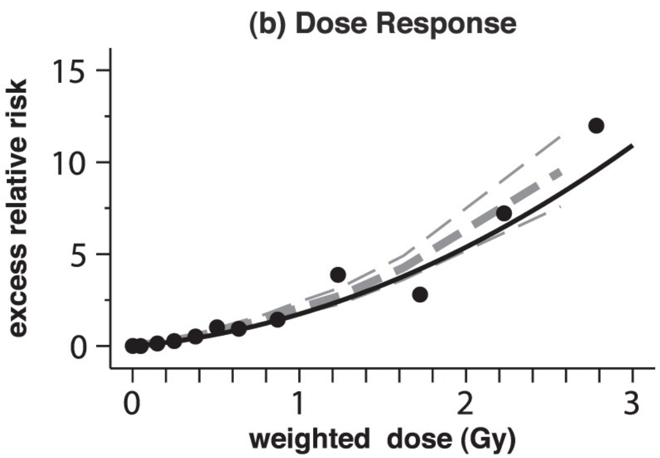
Linear model

- Most parsimonious
- Good representation for most sites
  - Acute low to moderate doses – LSS
  - Fractionated, high-dose (> 5 Gy) RT
- Power often limited to detect departure from linearity – even at high-doses

BEIR VII 2006; Preston et al. *Rad Res* 2007
Berrington de Gonzalez et al *Red Journal* 2013

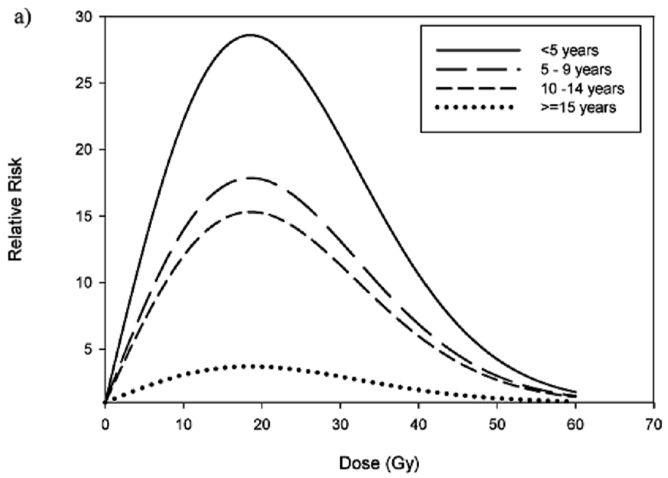
Non-linear relationships

- Leukemia (non CLL)



Hsu et al. *Rad Res* 2013

- Thyroid



Bhatti et al. *Rad Res* 2010

Why is shape important?

Radiation protection standards primarily based on extrapolation from LSS (low-to-moderate dose, high dose-rate)

Most exposures to workers and the general population at low(<100 mGy) dose, low dose-rate

What about risks from high-dose fractionated exposure (cancer survivors)?

How does variation in dose and dose-rate impact the risk?

Dose and dose-rate effectiveness factor (DDREF)

- Factor by which radiation effect changes at low doses, dose-rates compared with high dose, dose-rate
- BEIR VII: 1.5
    - Based on animal and epidemiological studies
    - Risk per unit dose reduced by 1/3 for protracted dose or total dose <100 mGy
- Use: risk projection, estimation of lifetime risks

BEIV VII 2006

Recent low dose, dose-rate studies

- Report risk estimates comparable to the LSS
  - ➢ Suggests similar risk from protracted or fractionated low-dose exposures
- Challenge to compare across study populations that differ beyond dose and dose-rate characteristics

Low dose, dose-rate studies: Two examples

Leukemia (non-CLL) ERR/Gy (95% CI) **Pearce et al. *Lancet* 2012**	
UK Childhood CT - Fractionated	LSS Age exposure <15
36 (5-120)	45 (16-188)

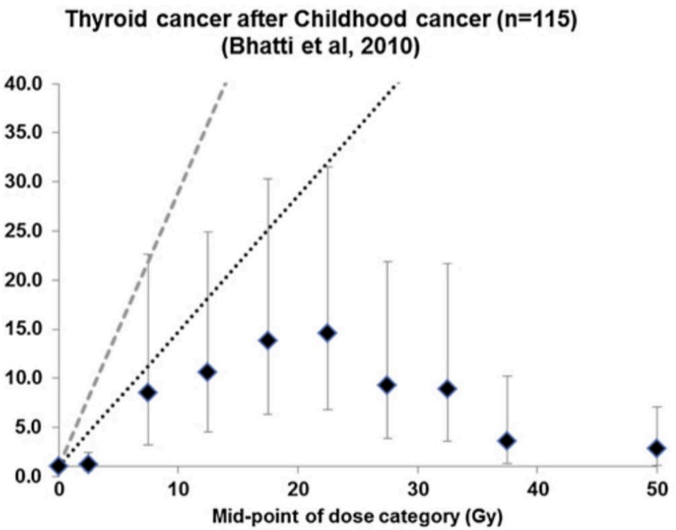
Solid cancer mortality ERR/Gy (95% CI) **Richardson et al. *BMJ* 2015**	
INWORKS - Protracted	LSS Age at exposure 20-60
0.47 (0.18-0.79)	0.32 (0.01-0.50)

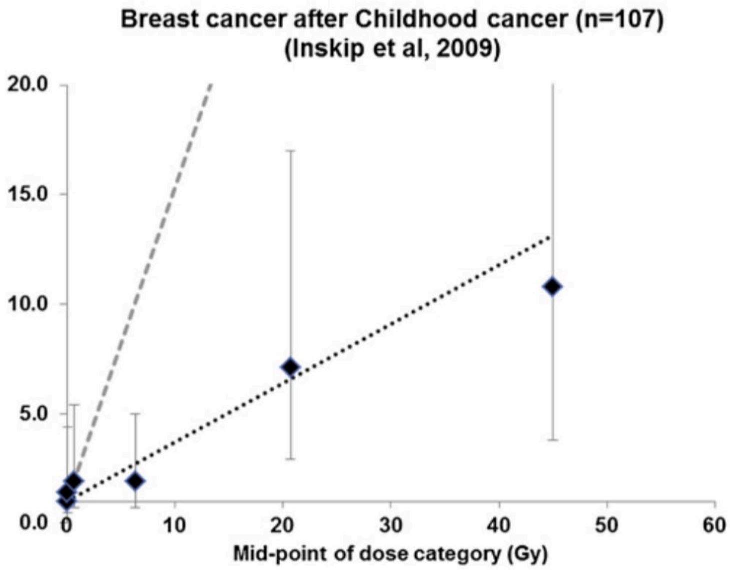
High-dose fractionated studies

- Therapeutic (high-dose) fractionated exposures
  - Risk estimates < LSS (5- to 10-fold)
  - Dose-response linear (exception thyroid) – unexpected
- Importance: Second cancer risks, inform risk/benefit assessment

Berrington de Gonzalez et al. *Red Journal* 2013

High-dose fractionated studies: Two examples





……. Fitted dose-response

- - - - For similar age (exposure, attained), BEIR VII model

Berrington de Gonzalez et al. *Red Journal* 2013

How does risk per unit of dose vary by type?

Estimates of relative biological effectiveness (RBE) largely from animal and laboratory studies

Lack of data from epidemiologic studies

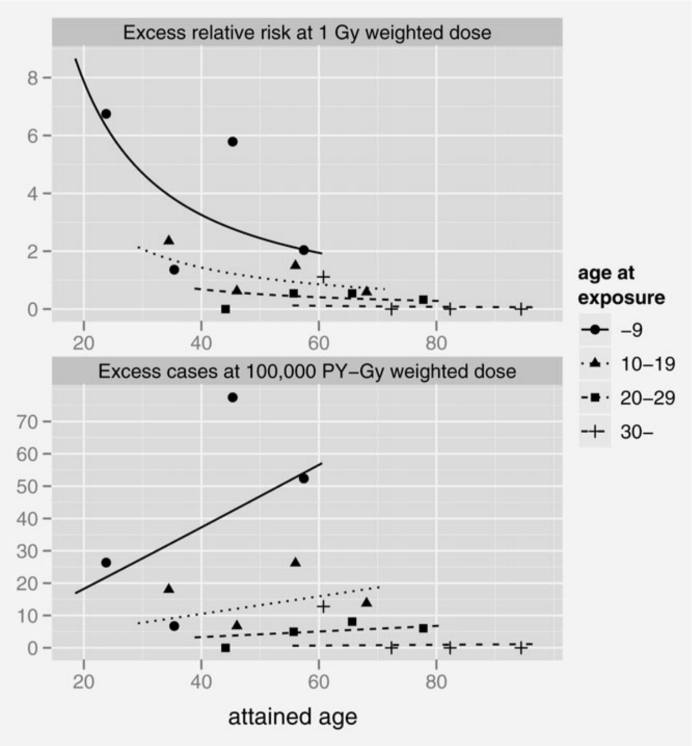
Implications for newer types of radiotherapies?

- Neutron scatter from proton - Neutrons 20 x > X-rays ?

Radiation-related risks by age - illustrated for thyroid cancer (1)

• Relative and absolute risks tend to be higher at earlier age at exposure

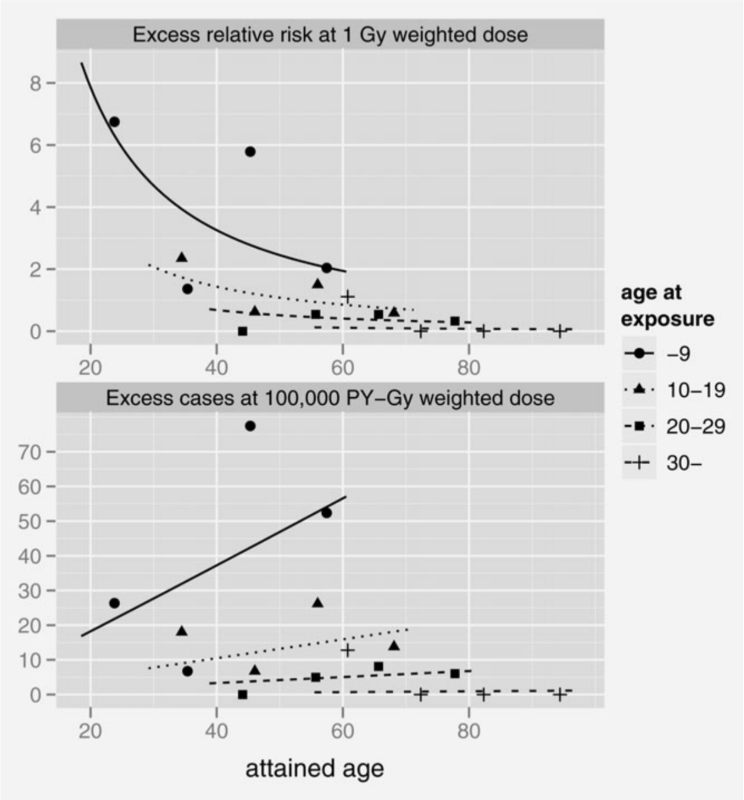
- ➢ Especially breast, leukemia, thyroid, brain
- ➢ Exceptions: Lung?
- ➢ Thyroid, brain – no apparent increase for exposure >20 y



Furukawa et al. *IJC* 2013

Radiation-related risks by age - illustrated for thyroid cancer (2)

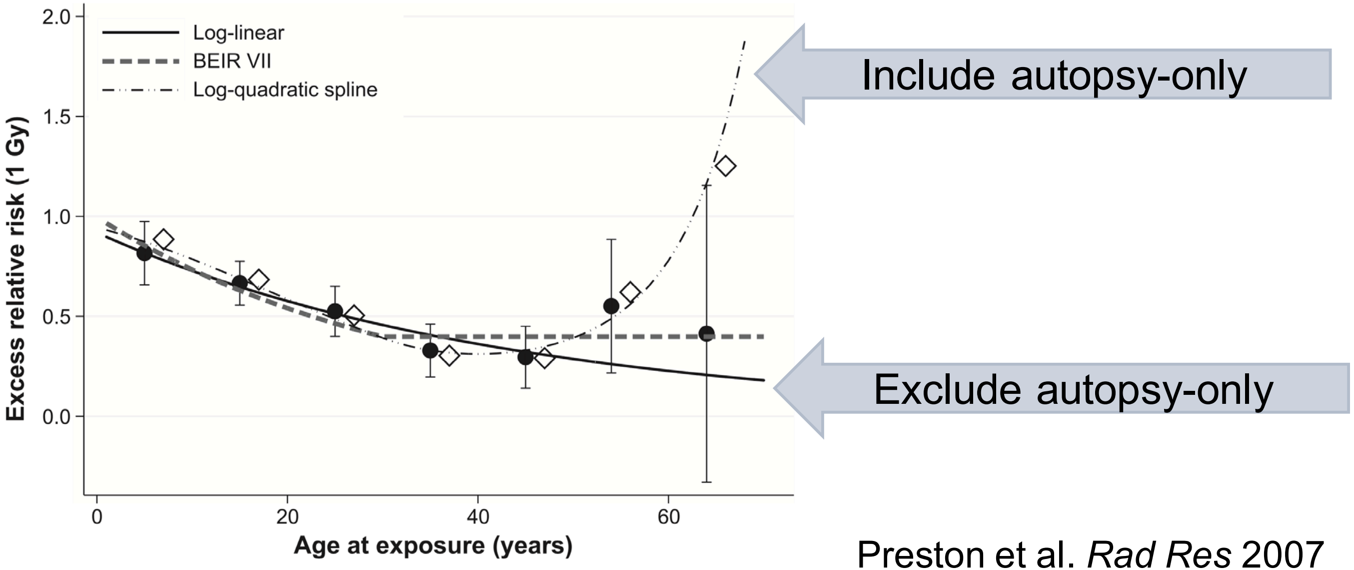
- ERR – decreases with attained age
- EAR – increases with attained age



Furukawa et al. *IJC* 2013

Age at exposure and solid cancer incidence in LSS

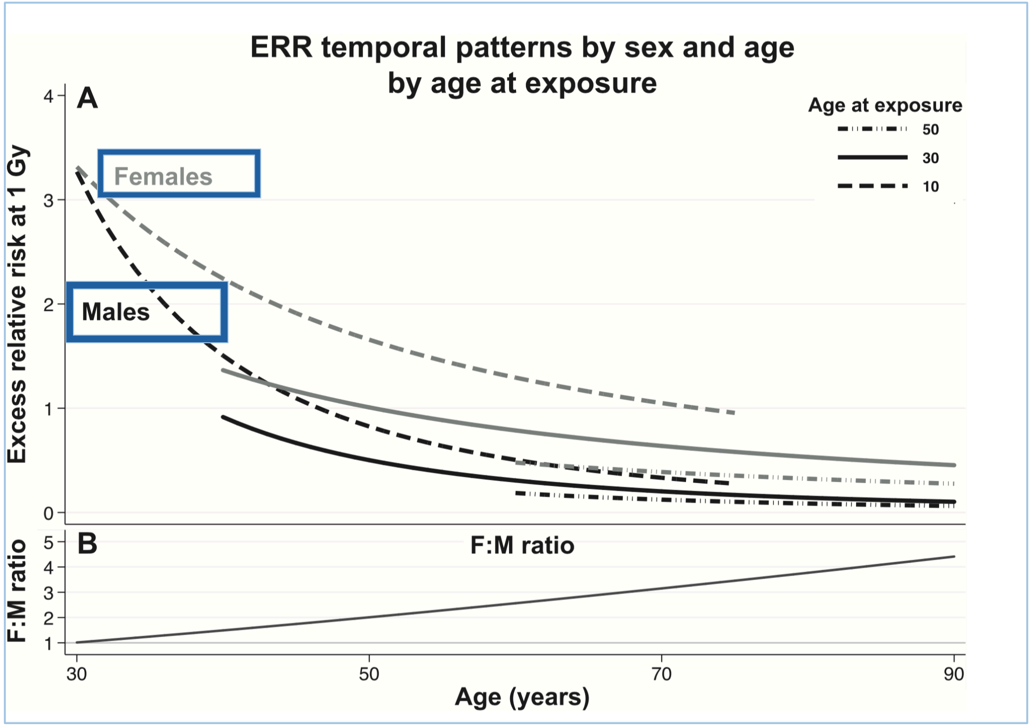
- Suggestion of upturn in ERR at older ages observed earlier
- Most recent study shows this was driven by inclusion of autopsy-only cases



Preston et al. *Rad Res* 2007
Grant et al. *Rad Res* 2017

Higher risk among females vs males?

- Observed in number of studies
- Differences in radiosensitivity?
- Modification by other factors?
- Differences in background rates?



Grant et al. *Rad Res* 2017

Time since exposure

- Minimum latency
  - ~ 2 years for leukemia
  - ~ 5 years for solid cancers
    - ➢ Need for long-term follow-up and value of retrospective design
- Risks persist long-term
  - Do not return to baseline
  - Important for estimating cumulative risk, screening of high-risk populations

BEIR VII 2006

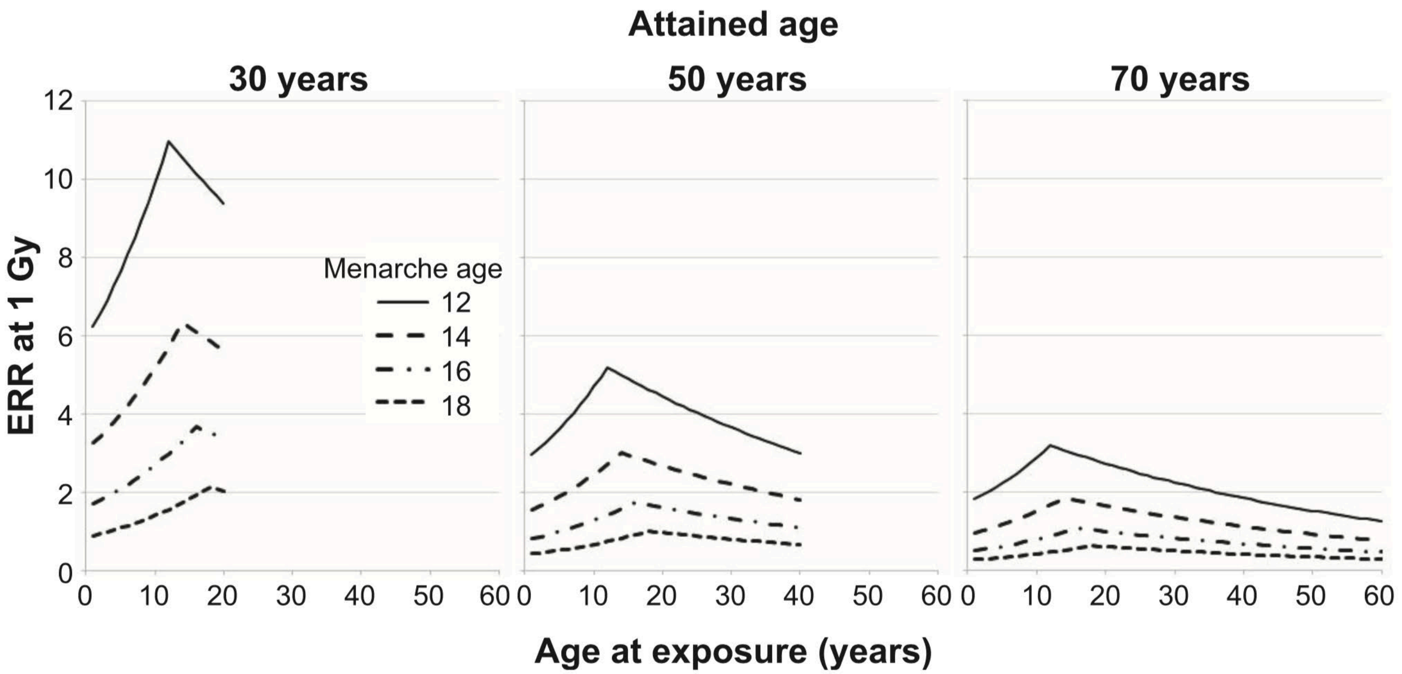
Joint effect of radiation and smoking

- Modification of radiation dose-response relationship by smoking observed across number of studies
- Nature of the interaction unclear

LSS Lung
$ERR_{non\text{-}smokers}$ > $ERR_{light\text{-}moderate\ smokers}$ > $ERR_{heavy\text{-}smokers}$ (Cahoon et al. *Rad Res* 2017)

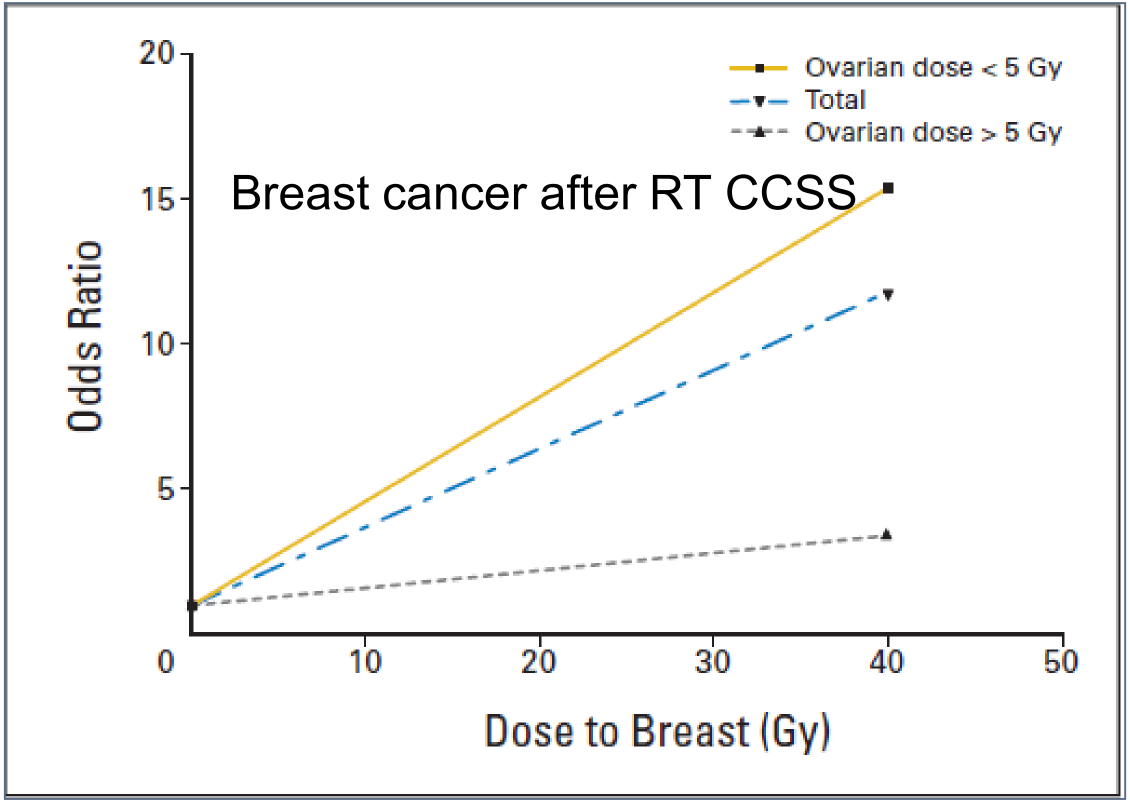
Radiotherapy Lung after HL
$ERR_{smokers}$ > $ERR_{nonsmokers}$ (Gilbert et al. *Rad Res* 2003)

Variation in breast dose-response by age at menarche?



Brenner et al. *Rad Res* 2018

RT - dose-response attenuated by ovary dose



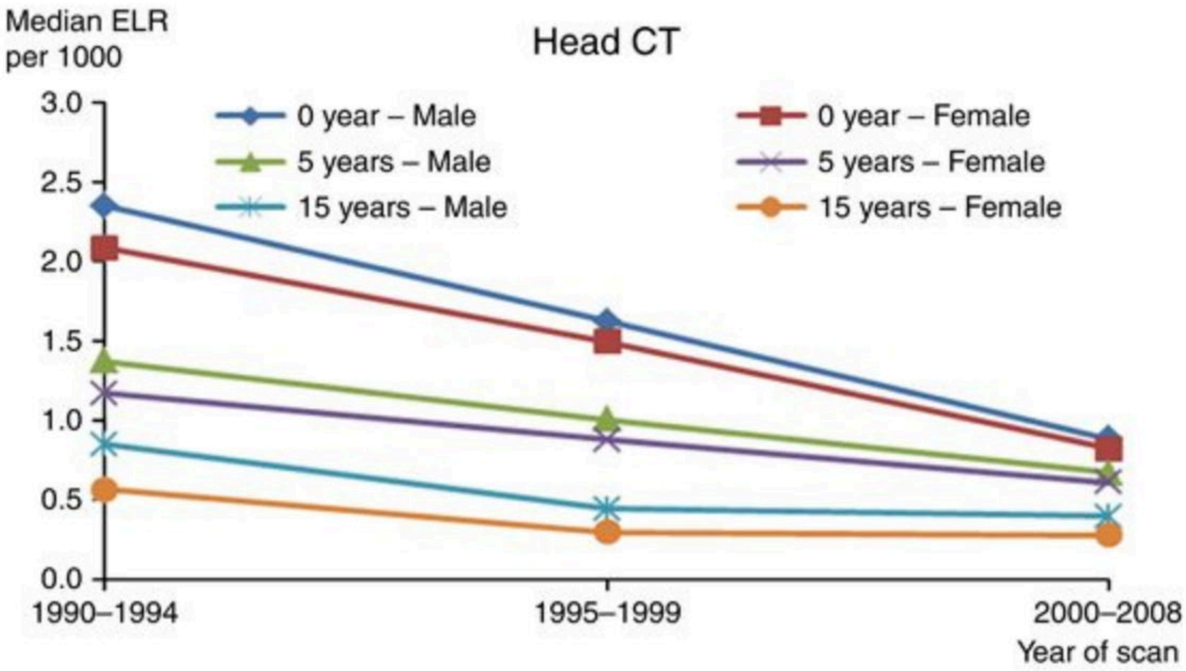
Inskip et al. *JCO* 2009

Genetic susceptibility

- Most knowledge to date based on rare mutations
  - Cancer-prone families
  - Highly-sensitive population
- Advances in technology
  - New opportunities to broaden the research

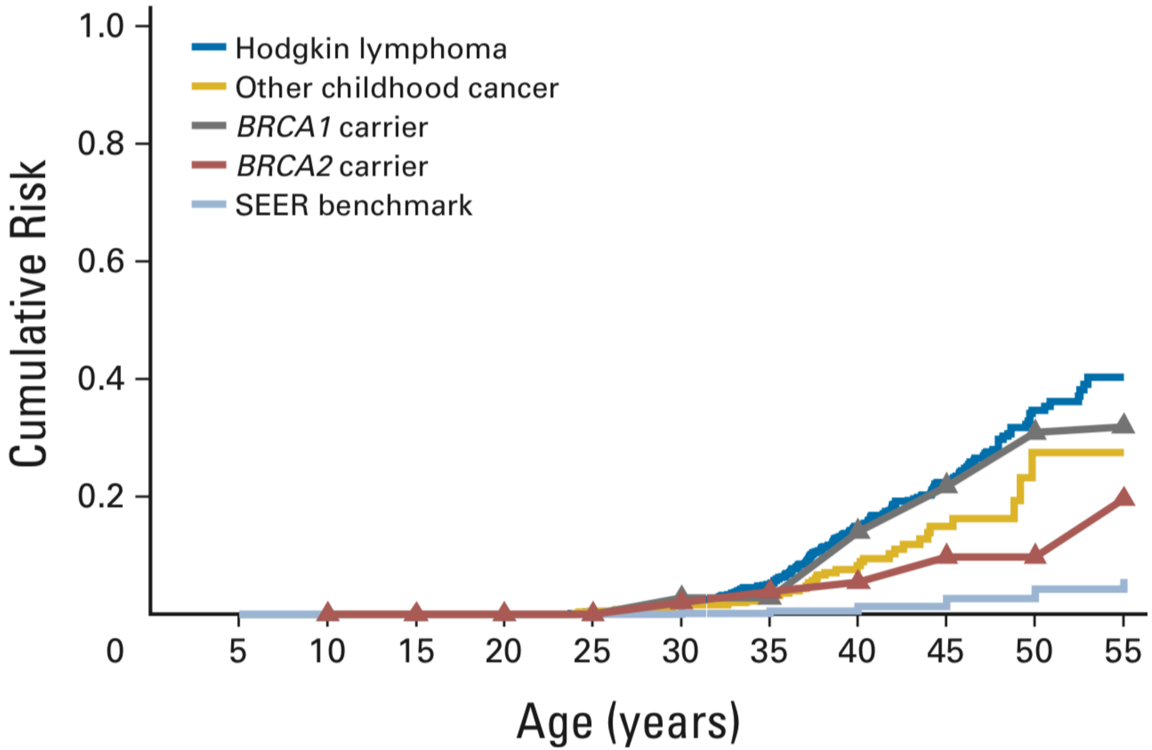
Absolute Risk & Attributable Fraction

Excess lifetime risk from pediatric CT: UK



Journy et al. *BJC* 2017

Cumulative breast cancer risk after chest RT



Moskowitz et al. *JCO* 2014

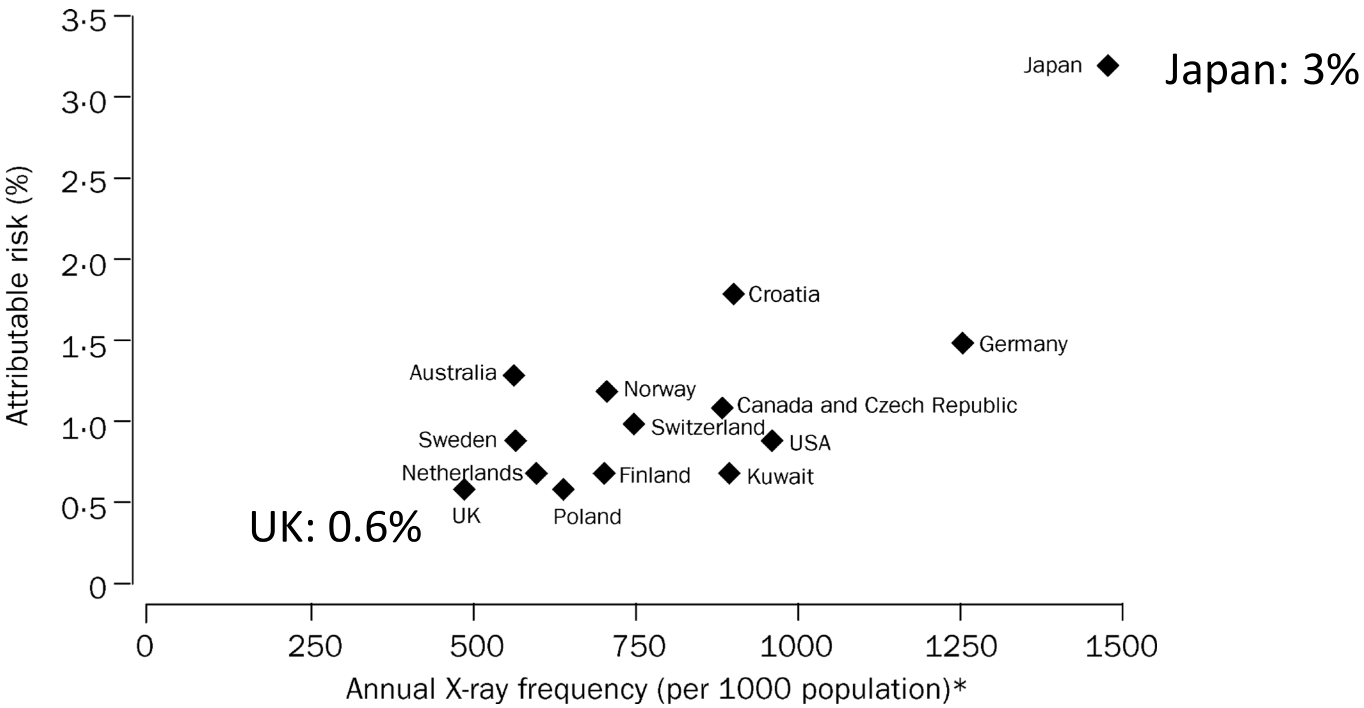
Estimated Attributable Fraction (AF)

- What proportion of cancers are caused by radiation?
- Contributing factors
  - exposure characteristics - dose and age at exposure distributions
  - population characteristics (age, sex, etc…)
  - distribution of cancers types

AF: Environmental Radiation Exposure

Source	Population	Outcome	Estimated AF	Reference
Background radiation	England – all ages (<15)	Leukemia	5% (15%)	Kendall et al. *Leuk Res* 2011
Residential radon	UK	Lung cancers	3%	Parkin and Darby *BJC* 2011
Chernobyl accident	Cleanup workers, residents, evacuees at highest exposure levels	Cancer deaths	3%-4%	WHO 2006
Japanese atomic bomb	Survivors	Solid cancers	10%	Grant et al. *Rad Res* 2017

AF: (up to age 75) from diagnostic medical radiation

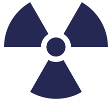


Berrington and Darby *Lancet* 2004

AF: Radiotherapy

Population	Outcome	Estimated AF	Reference
US adults treated for 15 cancers typically with RT	Solid cancers	8%	Berrington de Gonzalez et al. *Lancet* 2011
UK all ages treated for 13 cancers typically treated with RT	All cancers excluding NMSC	Males: 6% Females: 8%	Parkin and Darby *BJC* 2011
Female Hodgkin lymphoma survivors	All cancers excluding NMSC	19%	Parkin and Darby *BJC* 2011
Male Hodgkin lymphoma survivors	All cancers excluding NMSC	16%	Parkin and Darby *BJC* 2011

Opportunities for reducing exposures and risks



Radon remediation

Diagnostic

Careful clinical justification

Using lowest reasonable dose

Increase awareness

Technologies to monitor and control dose

Radiotherapy

Treatment-planning systems to optimize tumor treatment, minimize dose to surrounding tissue

Occupation

Monitoring

Improving protective gear to encourage use

Berrington de González et al. Cancer Epidemiology and Prevention

A few “classic studies”

Radiologists: First evidence that radiation can cause leukemia

Leukemia in Radiologists[1]

HERMAN C. MARCH, M.D.

Philadelphia, Penna.

TABLE II: DEATHS FROM LEUKEMIA IN RADIOLOGISTS, 1929–1943

Date of Death	Type of Leukemia Recorded	Age
Oct. 17, 1943	Lymphatic	54
July 15, 1943	Acute	43
April 23, 1943	Acute myelogenous	42
Feb. 22, 1942	Acute myelogenous	63
July 10, 1940	Leukemia	48
Jan. 23, 1939	Chronic lymphatic	65
June 24, 1938	Leukemia	52
Feb. 23, 1933	Lymphatic	69

Source: death notices in *JAMA*, 1929-1943

Comparison: radiologists and non-radiological physicians

Radium dial and clock painters

Early sources of data on cancer risk from high-let radiation

Excess risk of sarcoma and head carcinomas among female radium dial painters

Decades of research investigating:

Dose-response analyses	latency	age at exposure

RADIATION RESEARCH 76, 368–383 (1978)

Dose–Response Relationships for Female Radium Dial Workers [1,2]

R. E. ROWLAND, A. F. STEHNEY, AND H. F. LUCAS, JR.

Center for Human Radiobiology, Argonne National Laboratory, Argonne, Illinois 60439

THE AMERICAN JOURNAL OF CANCER

A Continuation of The Journal of Cancer Research

VOLUME XV — OCTOBER, 1931 — No. 4

THE OCCURRENCE OF MALIGNANCY IN RADIO-ACTIVE PERSONS

A GENERAL REVIEW OF DATA GATHERED IN THE STUDY OF THE RADIUM DIAL PAINTERS, WITH SPECIAL REFERENCE TO THE OCCURRENCE OF OSTEOGENIC SARCOMA AND THE INTER-RELATIONSHIP OF CERTAIN BLOOD DISEASES

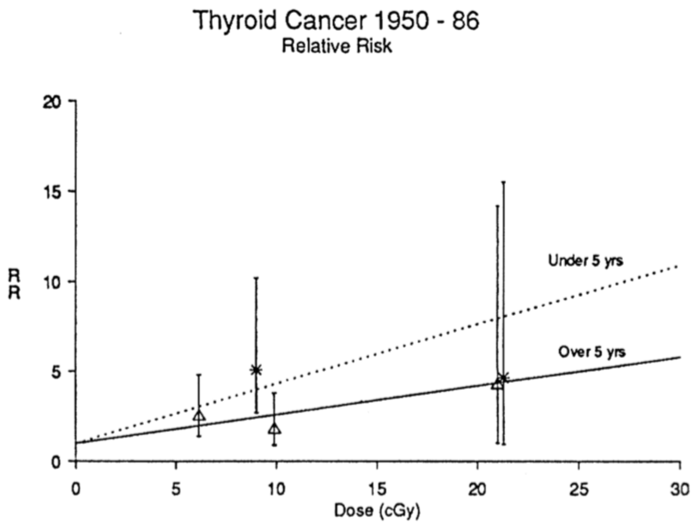
HARRISON S. MARTLAND, M.D.

RADIATION RESEARCH **150** (Suppl.), S21–S29 (1998)
0033-7587/98 $5.00

Studies of U.S. Radium Dial Workers: An Epidemiological Classic

Shirley A. Fry[1]

Israeli study of radiotherapy for tinea capitis



Ron et al. 1989

- Large cohort of patients who underwent radiotherapy for tinea capitis, matched unexposed groups
- Linkage with pathology and cancer registry data
- Radiotherapy treatment records
- Excess risks of thyroid, brain/CNS and skin cancer
- Refining of dosimetry over time
- Low- dose external exposure to thyroid

Sources: UNSCEAR 2000; Ron et al. *Rad Res* 1989

Bone sarcoma after treatment for childhood cancer

Table 2. Matched Relative Risk of Bone Cancer According to Type of First Cancer and Radiation Dose at the Site of Bone Cancer, Adjusted for Alkylating-Agent Treatment.

	Radiation Dose (rad)					
	0	*<1000*	*1000–2999*	*3000–3999*	*4000–5999*	*≥6000*
All types of cancers						
No. of cases	10	9	6	11	15	13
No. of controls*	51	70	30	18	23	12
Relative risk†	1.0‡	0.6	6.0	16.9	21.2	38.3

	0	*<1000*	*1000–3999*	*≥4000*
Retinoblastoma				
No. of cases	4	4	7	7
No. of controls	25	15	14	11
Relative risk†	1.0‡	1.3	12.7	19.4
All other types				
No. of cases	6	5	10	21
No. of controls	26	55	34	24
Relative risk†	1.0‡	0.2	12.0	28.8

*Five controls for whom the radiation dose to the site could not be estimated have been excluded from the analysis in this table.

†Risks for radiation dose above 1000 rad are statistically significant ($P<0.05$).

‡Referent category.

- Cohort study with nested case-control component
- One of the first studies to quantify risk using estimated dose to bone tumor site
- Quantified joint effects radiation and chemotherapy
- Evaluated risks by type of radiotherapy

Tucker et al., *NEJM* 1987

Moving forward

Challenges

Cancer risks from low doses

- Large sample size
- Long-term follow-up
- Minimize measurement error
- Availability of potential confounders?

Opportunities

- Electronic medical record linkages
- Pooled studies
- Biological samples – leveraging advances in genomics

Summary of ionizing radiation and cancer

- Universal carcinogen
- Not “weak”

Magnitude of risk appears to vary by site

Increasing evidence for risks at low dose, low dose-rate

Age - modifier of radiation-related risk

More research needed to understand the many other potential modifiers

Long history of radiation epidemiology

American Journal of Epidemiology
Vol. 154, No. 12, Supplement
Printed in U.S.A.

Radiation Exposure and Cancer: Case Study

Genevieve M. Matanoski,[1] John D. Boice, Jr.,[2] Stephen L. Brown,[3] Ethel S. Gilbert,[4] Jerome S. Puskin,[5] and Tara O'Toole[6]

Int. J. Radiat. Biol., Vol. 85, No. 6, June 2009, pp. 467–482

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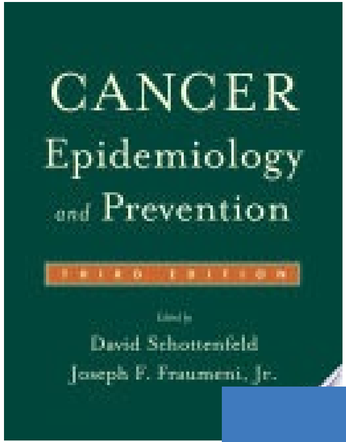
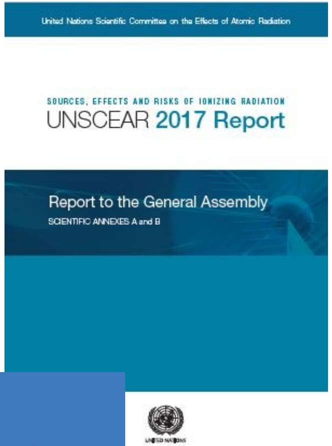
healthcare

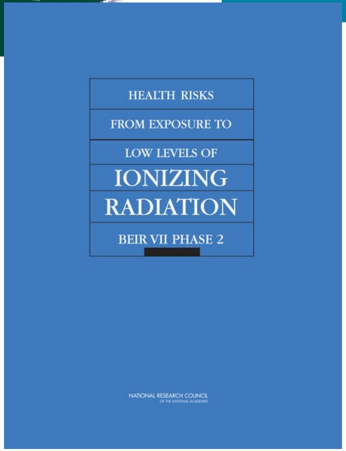
Ionising radiation and cancer risks: What have we learned from epidemiology?

ETHEL S. GILBERT

Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland, USA







Question #1: Which of the following is not clearly associated with radiation?

a. Breast cancer
b. Leukemia
c. Thyroid cancer
d. Prostate cancer

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Question #2: Studies of radiotherapy teach us about cancer risk from fractionated, high-dose exposures?

- a. True
- b. False

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- a. True
- b. False

Question #3: Which of the following are correct?

- a. Radiation-related relative risks tend to decrease with increasing age at exposure.
- b. Radiation-related absolute risks tend to increase with increasing attained age.
- c. Radiation-related risks do not tend to vary by age at exposure or attained age.
- d. Age effects have not been studied.

Question #3: Which of the following are correct?

- a. Radiation-related relative risks tend to decrease with increasing age at exposure.
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- c. Radiation-related risks do not tend to vary by age at exposure or attained age.
- d. Age effects have not been studied.

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1-800-4-CANCER

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